Industria y Comercio

SUPERINTENDENCIA

Delegatura de propiedad Industrial

División de Nuevas Creaciones

PCT

SOLICITUD

PATENTE DE INVENCIÓN

- PCT ENTRADA EN FASE NACIONAL -
(SEGUNDA PARTE)

05-110118

SUPERINDUSTRIA / COMERCIO
Radicacion : 05110118 00000000 Folios: 1167
Fecha (AMD): 2005-10-28 14:10:01
Tramite : 411 PCT-PATENT .CP9 FASE NACI 411 PRESENTAC
Dependencia: 2080 DIVISION DE NUEVAS CREACIONES

21. **EXPEDIENTE No.** 05-110118

54. **TÍTULO** "COMPUESTO PENTACICLICO HETEROAROMATICO Y USO MEDICINAL DEL MISMO"

51. **CLASIFICACIÓN INTERNACIONAL** A61K 31/421

71. **SOLICITANTE** JAPAN TOBACCO INC.

DOMICILIO 2-1, Toranomon, 2-chome, Minato-ku, Tokyo 105-8422, JAPON

74. **APODERADO** DRA. MARGARITA CASTELLANOS ABONDANO

22. **BOGOTÁ, D. C.,** 28 OCT. 2005

(FORMA P-10)

PETITORIO

Industria y Comercio
SUPERINTENDENCIA

SUPERINDUSTRIA Y COMERCIO
Radicacion : 05110118 00000000 Folios: 1167 In
Fecha (AMD): 2005-10-26 14:10:01
Tramite : 011 PCT-PATENT 379 FASE NACI 411 PRESENTAC
Dependencia: 2000 DIVISION DE NUEVAS CREACIONES

FORMULARIO UNICO DE SOLICITUD DE PATENTE
PCT
ENTRADA EN FASE NACIONAL

SOLICITUD DE:

①

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

[ ] Capítulo I [X] Capítulo II

② **SOLICITANTE (71)**

Nombre: JAPAN TOBACCO INC.
Dirección: 2-1, Toranomon 2-chome, Minato-ku, Tokyo 105-8422 - JAPON
Nacionalidad o Domicilio: Tokyo - JAPON
Lugar de Constitución: JAPON
Teléfono: Fax:
E-mail:

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

③ **REPRESENTANTE O APODERADO (74)**

Nombre: MARGARITA CASTELLANOS A.
Dirección: CALLE 94A No. 7A-09
Teléfono: 610 7420 Fax: 610 0706
E-mail: mail@alvarocastellanos.com

IDENTIFICACIÓN
C.C. [X] NIT [ ]
C.E. [ ] Otro [ ]
Cual
Número 39'779.654 TPA 70,819

④ **INVENTOR (ES) (72)**

Nombre: (VER ANEXO #1)
Dirección: (VER ANEXO # 1)
Nacionalidad o Domicilio (VER ANEXO # 1)

⑤ **PCT (86)**

Solicitud Internacional No. PCT/JP2004/005119 Fecha 09/04/2004
Publicación Internacional No. WO2004/089918 Fecha 21/10/2004

⑥ **Título (54)** COMPUESTO PENTACICLICO HETEROAROMATICO Y USO MEDICINAL DEL MISMO

⑦ **Clasificación Internacional (51)** C07D 263/32, 417/14, 333/20, 413/12, 417/06, 409/12, 333/38, 333/16, 333/18, 277/22, 277/28, 417/12, A61K 31/421, 31/4439, 31/4725, 31/538, 31/497, 31/4184, 31/427, 31/428, 31/381, 31/405, 31/4155, 31/423, 48/00, A61P 43/00, 3/10, 3/06, 3/04

⑧ **Prioridad** SI [X] NO [ ]

(33) País de Origen	(32) Fecha	(31) Número de Solicitud
JP	09/04/2003	2003-105267
JP	03/06/2003	2003-157590

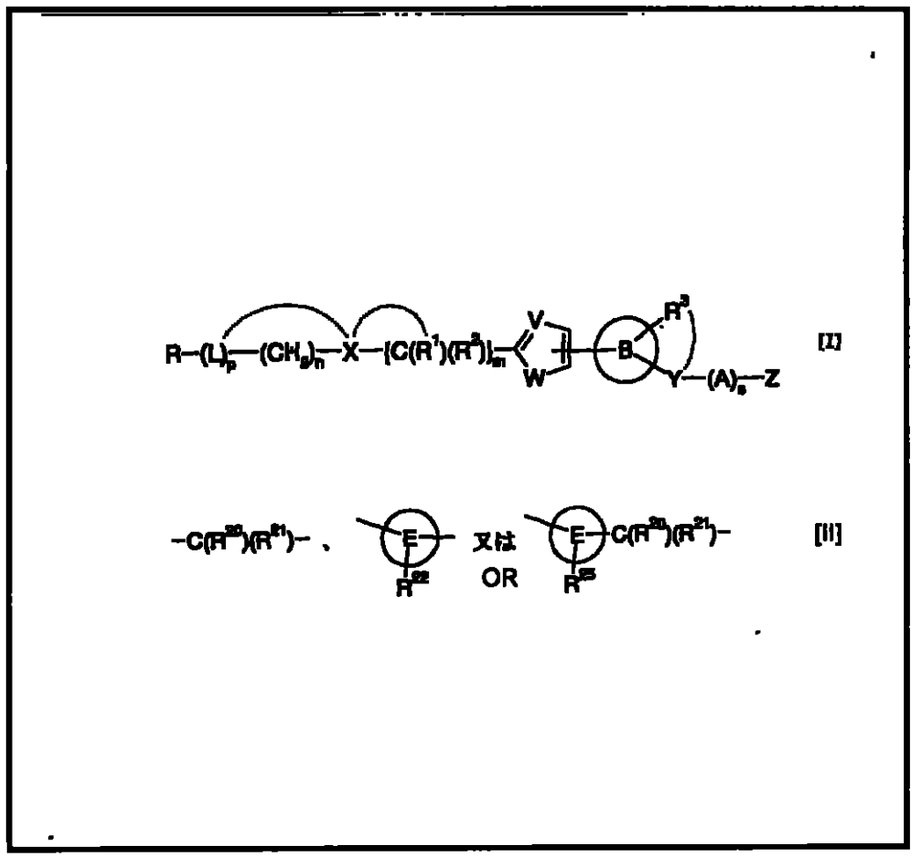
⑨ **Comprobante de pago No.** 05-75.353 **Fecha** Septiembre 29, 2005

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

(10) Anexos

- [X] Comprobante de pago de la tasa de presentación de la solicitud.
- [X] Documento que acredita la existencia y representación legal cuando el solicitante sea persona jurídica.
- [X] Poderes, si fuere el caso, junto con la sustitución del mismo a mi favor
- [X] Documento de cesión del inventor al solicitante o a su causante.
- [ ] Declaraciones.
- [X] Copia de la solicitud internacional (Resumen, descripción, reivindicaciones, dibujos).
- [X] Traducción de la solicitud internacional al castellano (Resumen, descripción, reivindicaciones, dibujos).
- [ ] Copia del examen preliminar internacional efectuado por la Autoridad Internacional de Examen Preliminar (IPEA).
- [ ] Traducción del examen preliminar internacional efectuado por la IPEA.
- [ ] De ser el caso, copia del contrato de acceso.
- [ ] De ser el caso, documento que acredite la licencia o autorización de uso de conocimientos tradicionales de las comunidades indígenas.
- [ ] De ser el caso, certificado de depósito del material biológico.
- [X] Arte final 12x12
- [ ] De ser el caso, información sobre otras solicitudes de patente o títulos obtenidos en el extranjero por el mismo titular o su causante, relacionadas parcial o totalmente con la invención de esta solicitud.
- [ ] De ser el caso, modificaciones efectuadas a la solicitud internacional.
- [X] Otros Tarjeta Propietario, Tarjeta Temática y Extracto para la Publicación - Disquet con el Extracto para la publicación.- Modificación de las reivindicaciones 1 y 2, de conformidad con el Artículo 19 del PCT

(11) FIGURA CARACTERISTICA:



(12) Solicito la concesión de la patente,

NOMBRE: MARGARITA CASTELLANOS ABONDANO

FIRMA:

C.C. No. 39'779.654 Usaquén - TPA 70.819 C.S.J.

Instrucciones para el diligenciamiento del presente formulario, ver reverso de esta página. - MCA/gcb - 6016-FNPCT

ALVARO CASTELLANOS M. & CIA.
ABOGADOS
Calle 94 A No. 7 A-09
Apartado 6349
Bogotá, D.C. – COLOMBIA

ANEXO # 1

INVENTOR(ES) (72)

	NOMBRE	DIRECCION	NACI NALIDAD O DOMICILIO
1	TOMOYUKI IKEMOTO	c/o Central Pharmaceutical Research Institute of Japan Tobacco Inc., 1-1, Murasaki-cho, Takatsuki-shi, Osaka 5691125 - JAPON	JAPONES
2	MASAHIRO TANAKA	c/o Central Pharmaceutical Research Institute of Japan Tobacco Inc., 1-1, Murasaki-cho, Takatsuki-shi, Osaka 5691125 - JAPON	JAPONES
3	TAKEO YUNO	c/o Central Pharmaceutical Research Institute of Japan Tobacco Inc., 1-1, Murasaki-cho, Takatsuki-shi, Osaka 5691125 - JAPON	JAPONES
4	JOHEI SAKAMOTO	c/o Central Pharmaceutical Research Institute of Japan Tobacco Inc., 1-1, Murasaki-cho, Takatsuki-shi, Osaka 5691125 - JAPON	JAPONES
5	HIROYUKI NAKANISHI	c/o Central Pharmaceutical Research Institute of Japan Tobacco Inc., 1-1, Murasaki-cho, Takatsuki-shi, Osaka 5691125 - JAPON	JAPONES
6	YUICHI NAKAGAWA	c/o Central Pharmaceutical Research Institute of Japan Tobacco Inc., 1-1, Murasaki-cho, Takatsuki-shi, Osaka 5691125 - JAPON	JAPONES
7	TAKESHI OHTA	c/o Central Pharmaceutical Research Institute of Japan Tobacco Inc., 1-1, Murasaki-cho, Takatsuki-shi, Osaka 5691125 - JAPON	JAPONES
8	SHOHEI SAKATA	c/o Central Pharmaceutical Research Institute of Japan Tobacco Inc., 1-1, Murasaki-cho, Takatsuki-shi, Osaka 5691125 - JAPON	JAPONES
9	HISAYO MORINAGA	c/o Central Pharmaceutical Research Institute of Japan Tobacco Inc., 1-1, Murasaki-cho, Takatsuki-shi, Osaka 5691125 - JAPON	JAPONES

4

SUPERINDUSTRIA Y COMERCIO
Radicacion : 05110118 00000000 Folios: 1167
Fecha (AMD): 2005-10-28 14:10:01
Tramite : 011 PCT-PATENT 379 PARE NACI 411 PRESENTAR
Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

RECIBO OFICIAL DE CAJA : 05 - 75,353
FECHA : SEPTIEMBRE 29 DE 2005

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

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
ALVARO CASTELLANOS	CONSIGNACION	BANCO POPULAR	050-00110-6	43460103	29/09/2005	5,536,000.00

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

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

SON: CUATROCIENTOS CUARENTA Y TRES MIL PESOS

RESPONSABLE : _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No._____

ALVARO CASTELLANOS M. & CIA.
ABOGADOS
Calle 94 A No. 7 A-09
Apartado 6349
Bogotá, D.C. – COLOMBIA

Señor

Jefe de la División de Nuevas Creaciones

Superintendencia de Industria y Comercio

Ministerio de Comercio, Desarrollo, Industria y Turismo

E. S. D.

Ref.: **PODER** conferido por la sociedad **JAPAN TOBACCO INC.**

Yo, **XIMENA CASTELLANOS ABONDANO,** mayor de edad, identificada y domiciliada como aparece al pié de mi firma, atentamente manifiesto a Uds. que sustituyo en la Dra. **MARGARITA CASTELLANOS ABONDANO,** el poder que me confirió la sociedad **JAPAN TOBACCO INC.,** con domicilio en **2-1, Toranomon 2-chome, Minato-ku, Tokyo 105-8422, JAPÓN** debidamente legalizado por Apostilla, bajo los Nos. **02041 y 02042** el día **14 de Junio de 2004,** con las mismas facultades que me fueron conferidas, para tramitar la solicitud de Patente PCT Entrada en Fase Nacional en Colombia, para: **"COMPUEST PENTACICLICO HETEROAROMATICO Y USO MEDICINAL DEL MISMO"**

Del Señor Jefe,

Ximena Castellanos Abondano
C.C. No. **39.773.330** de Usaquén
T.P.A. No. **58.236** del C.S.J.
Calle 94A No. 7A-09 – Bogotá, D.C.
Teléfonos: 6107420 – 6107480

Acepto

Margarita Castellanos Abondano
C.C. No. **39.779.654** de Usaquén
T.P.A. No. **70.819** del C.S.J.
Calle 94A No. 7A-09 – Bogotá, D.C.
Teléfonos: 6107420 – 6107480

Bogotá, D.C.
XCA/MCA/6016-FNPCT
G/USER/DEPTO PAT/PATENTES/60/6016-FNPCT/MEMORIAL SUSTITUCION PODER

AUTENTICACION DE FIRMA
MEDIANTE COMPARECENCIA PERSONAL
(Art. 84 C.R.C. mod. Decr. 2282 de 1989, art. 1 mod. 35)
Ante el Notario Cuarenta y Uno (41) del circulo
de esta ciudad compareció personalmente:
Identificado con C.C.
expedida en y tarjeta profesio-
nal de abogado(a) No. del Consejo
Superior de la Judicatura, con documento di-
rigido a
y declaro que la firma puesta en este escrito es
suya.

Firma del declarante

En Bogotá D.C. a 20 OCT 2005

AUTORIZÓ ESTA DILIGENCIA EL SUSCRITO

REPUBLICA DE COLOMBIA
Círculo de Santafé
de Bogotá, D.C.
NOTARIA 41
Carrera 12 Nº 93-28
AGUSTIN MORALES RIVERA
ORC-AU

AUTENTICACION DE FIRMA
MEDIANTE COMPARECENCIA PERSONAL
(Art. 84 C.R.C. mod. Decr. 2282 de 1989, art. 1 mod. 35)
Ante el Notario Cuarenta y Uno (41) del circulo
de esta ciudad compareció personalmente:
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AUTORIZÓ ESTA DILIGENCIA EL SUSCRITO

REPUBLICA DE COLOMBIA
Círculo de Santafé
de Bogotá, D.C.
NOTARIA 41
Carrera 12 Nº 93-28
AGUSTIN MORALES RIVERA
ORC-AU

4926-FNPCT, 4929-FNP1

6

PODER

El (los) suscrito (s): JAPAN TOBACCO INC.

domiciliado (s) en 2-1, Toranomon 2-chome, Minato-ku, Tokyo 105-8422 - JAPON

nombra(n) por el presente a XIMENA CASTELLANOS A. y/o MARGARITA CASTELLANOS A. abogadas con oficinas en la Carrera 9 No. 93-09, Bogotá - Colombia para

y para obtener la protección de mi (nuestra) propiedad industrial y con este fin autorizamos a dichos apoderados para que nos representen ante cualesquiera autoridades o personas de los órdenes administrativo, contencioso-administrativo y judicial en todo lo relacionado con los siguientes actos y gestiones:

a) Obtención de patentes de invención, modelos y dibujos industriales; registro de marcas de fábrica, de servicio, colectivas o defensivas y de denominaciones de origen; depósito de nombres y enseñas comerciales; su renovación prórroga, inscripción de traspaso y cambio de nombre o domicilio, cancelación voluntaria y el registro de licencias de uso de esos derechos; b) Para la obtención de Registros Sanitarios; c) Acciones de oposición, observación, cancelación, nulidad, medidas cautelares y en general los juicios civiles, penales, administrativos o contencioso-administrativos que promovamos o se nos promuevan, pudiendo en todos los actos y gestiones arriba determinados sustituir este mandato, transigir, desistir, recibir, cancelar, renunciar, aceptar notificaciones y nombrar apoderados judiciales y extrajudiciales.

Dado y firmado hoy 7 de Junio de 2004

en Tokyo, JAPON

Por Teruo DAITO

(Notary should execute on other side)
(Consular legalization necessary)

POWER OF ATTORNEY

I (we) the undersigned Japan Tobacco Inc.

of 2-1, Toranomon 2-chome, Minato-ku, Tokyo 105-8422 Japan

hereby grant(s) Power of Attorney to XIMENA CASTELLANOS A. and/or MARGARITA CASTELLANOS A. attorneys residing at Carrera 9 No. 93-09 Bogotá - COLOMBIA to

and to obtain the protection of my (our) industrial property, for which purpose we authorize the said attorneys to represent us before any authorities or persons, specially those, administrative contentious and judicial, in all matters concerning the following:

a) Obtention of patents, models and designs; registration of trademarks, service, collective and defensive marks, and of designations of origin; the deposit of commercial names and ensigns; its renewal, extension, recordal of assignments, change of name or domicile, voluntary cancellation; and the registration of licenses of use of the above rights; b) For de obtention of Sanitary Registrations; c) Actions of opposition, cancellation, nullity, infringement, granting of licenses; and in general the civil, criminal and administrative suits related to those rights; actions and suits instituted by us or against us; and that in all the above matters they may substitute this Power of Attorney, compromise, desist, cancel, receive, renounce, accept notifications and appoint attorneys in fact, in or out of Court.

Given and signed this June 7, 2004

in Tokyo - JAPAN

By Japan Tobacco Inc.

Teruo DAITO, Patent Attorney
General Manager,
Patent Information Dept.

(Notary should execute on other side)
(Consular legalization necessary)

ALVARO CASTELLANOS M. & CIA.
ABOGADOS COLOMBIA
Carrera 9 No. 93-09 - P.O. Box 4349 - Bogotá, Colombia.
Tels.: (571) 610 7420 /60 / 80 - Fax. (571) 610 0706 - e-mail acastel@impsat.net.co

Esta copia coincide con el original que tuve a la vista.
Bogotá, D.C.
18 OCT 2005
AGUSTIN MORALES RIVEIRA
NOTARIO CUARENTA Y UNO

APOSTILLE

(Convention de La Haye du 5 octobre 1961)

1. Country: **JAPAN**

   This public document

2. has been signed by — Katsuyuki YAMAGUCHI
3. acting in the capacity of — Notary Public of the Osaka Legal Affairs Bureau
4. bears the seal/stamp of — Katsuyuki YAMAGUCHI, Notary Public

Certified

5. at Osaka
6. JUN. 14. 2004
7. by the Ministry of Foreign Affairs
8. No. 02041
9. Seal/stamp:
10. Signature:

Tsutomu HIGUCHI
For the Minister for Foreign Affairs

La copia coincide con el original que tuve a la vista.
Bogotá, D.C.
18 OCT 2004
AGUSTIN MORALES RIVEIRA
NOTARIO CUARENTA Y UNO

認証登簿平成１６年第100号

嘱託人大東輝雄は、本公証人の面前で、別紙編綴の書面に署名した。

よって、これを認証する。

平成１６年３月３１日、本職の役場において。

大阪府高槻市芥川町１丁目１５番１８号(ミドリ芥川ビル内)

大阪法務局所属

公証人　山口勝之

Registerd No100(2004)

NOTARIAL CERTIFICATE

This is to certify that Teruo DAITO signed the attached document in my very presence on this 31st day of March 2004.

Katsuyuki Yamaguchi

Katsuyuki Yamaguchi
Notary, attached to
Osaka Legal affairs Bureau
15-18,1-chome,Akutagawa-cho,
Takatsuki-shi,Osaka,Japan.

OSAKA LEGAL AFFAIRS BUREAU
NOTARY
15-18,(Midori Akutagawa Bldg.)1-chome
Akutagawa-cho,Takatsuki-shi,Osaka,Japan

大阪法務局所属　公証人役場

Esta copia coincide con el original que tuve a la vista.
Bogotá, D.C.
18 OCT 2005
AGUSTIN MORALES
NOTARIO CUARENTA

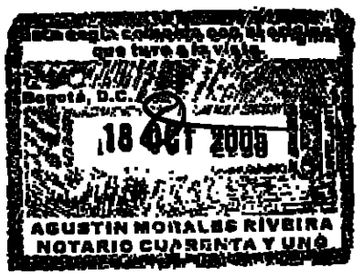
証明書

東京都港区虎ノ門二丁目２番１号を本店所在地とする日本国法人日本たばこ産業株式会社の代表取締役社長である私 本田勝彦 は、該法人を代表して知的財産権に係わる書類を署名作成する権限を有するものであることをここに宣言し、これをもって、２００４年３月３１日当時、該法人の医薬総合研究所特許情報室長職にあった大東輝雄　氏が、代理人に指名され、該法人名義にて外国に提出する特許、実用新案登録の出願等手続に要する願書、委任状、譲渡書、授権書、申請書、請求書、その他を含む関係書類について該法人を代表して署名、押印、作成する権限を有していたものであることを証明する。

２００４年６月７日

日本たばこ産業株式会社

代表取締役社長　本田　勝彦



CERTIFICATE

I, KATSUHIKO HONDA, President and Chief Executive Officer of JAPAN TOBACCO INC., a Japanese corporation located at 2-1, TORANOMON 2-CHOME, MINATO-KU, TOKYO 105-8422, JAPAN, hereby declare that I am authorized to sign and execute documents relating to intellectual property rights on behalf of the said corporation, and hereby certify that, as of March 31, 2004, Mr. TERUO DAITO was Director of Patent Information Dept. of Central Pharmaceutical Research Institute of the said corporation, was my proxy, and was authorized to sign and execute documents relating to intellectual property rights on behalf of the said corporation. Said documents include, but are not limited to, applications, powers of attorney, assignments, authorizations of agents, petitions and the like in connection with patent and utility model filed in foreign countries with the name of the said corporation.

Dated this 7 day of June, 2004,
JAPAN TOBACCO INC.

KATSUHIKO HONDA
President and Chief Executive Officer

Esta copia coincide con el original que tuve a la vista.
Bogotá, D.C.
18 OCT 2005
AGUSTIN MORALES RIVEIRA
NOTARIO CUARENTA Y UNO

APOSTILLE

(Convention de La Haye du 5 octobre 1961)

1. Country: **JAPAN**

   This public document

2. has been signed by — Katsuyuki YAMAGUCHI
3. acting in the capacity of — Notary Public of the Osaka Legal Affairs Bureau
4. bears the seal/stamp of — Katsuyuki YAMAGUCHI, Notary Public

Certified

5. at Osaka
6. JUN. 14. 2004
7. by the Ministry of Foreign Affairs
8. No. 02042
9. Seal/stamp:

MINISTRY OF FOREIGN AFFAIRS 外務省 JAPAN

10. Signature:

Tsutomu HIGUCHI
For the Minister for Foreign Affairs

Esta copia coincide con el original que tuve a la vista.
Bogotá, D.C.
18 OCT 2005
AGUSTIN MORALES NIVEIRA
NOTARIO CUARENTA Y UNO

登簿番号平成16年第１６８号

日本国法律に従い設立され、日本国東京都港区虎ノ門二丁目２番１号に所在する日本たばこ産業株式会社において、２００４年３月３１日当時、医薬総合研究所特許情報室長職にあった大東輝雄氏が、該法人名義で知的財産関係書類について該法人を代表して署名押印、作成する権限を有していたこと及び同氏が２００４年３月３１日、本職の面前で別紙書類に署名したことを証明する。

よって、ここにこれを認証する。

平成１６年６月８日、本職の役場において。

大阪府高槻市芥川町１丁目１５番１８号（ミドリ芥川ビル）

大阪法務局所属（高槻公証役場）

公証人　山口勝之

大阪法務局所属　公証人役場

Esta copia coincide con el original que tuve a la vista.
Bogotá, D.C.
18 OCT 2005
AGUSTIN MORALES RIVEIRA
NOTARIO CUARENTA Y UNO

Registration Book No.168 (2004)

NOTARIAL CERTIFICATE

This is to certify that :

1) Teruo Daito was Director of Patent Information Dept. of Central Pharmaceutical Reseearch Institute of JAPAN TOBACCO INC. ,a Japanese corporation of being legally constituted and in existance in accordance with the laws of Japan ,located at 2-1, Toranomon2-chome, Minato-ku, Tokyo 105-8422 Japan ,as of March 31,2004 and was authorized to sign and execute documents relating to intellectual property rights on behalf of the said corporation.

2) said Teruo Daito signed the attaced document in my presence on 31st day of March,2004.

IN TESTIMONY WHEREOF,I have hereto subscribed my name and affixed my seal of office.

On the 8th day of June,2004
at the Office of Notary Katsuyuki Yamaguchi

Katsuyuki Yamaguchi

Katsuyuki Yamaguchi
Notary,attached to
Osaka Legal affairs Bureau,
15-18,1-chome,Akutagawacho,
Takatsuki-shi, Osaka,Japan.

OSAKA LEGAL AFFAIRS BUREAU
NOTARY
15-18,(Midori Akutagawa Bldg.) 1-chome
Akutagawa-cho, Takatsuki-shi, Osaka, Japan

copia coincide con el origi
que tuve a la vista.
Bogotá, D.C.
18 OCT 2005
AGUSTIN
NOTARIO

総第 1558 号

証　　明

大阪法務局所属公証人　山口勝之

平成 16 年 3 月 31 日付

平成16年登第第100号

この認証の付与は，在職中の公証人がその権限に基づいてしたものであり，かつ，その押印は，真実のものであることを証明する。

平成16年6月14日
平成　　年　　月　　日

大阪法務局長　梅津和宏

CERTIFICATE

This is to certify that the annexed Notarial Certificate has been executed by Notary,duly authorized and practising in Osaka, Japan, and that the Official seal appearing on the same is genuine.

Date 04. 6.14

Director of the Osake Legal Affairs Bureau

Esta copia coincide con el original que tuve a la vista.
Bogotá, D.C.
18 OCT 2005
AGUSTIN MORALES RIVERA
NOTARIO CUARENTA Y UNO

15

総第 1559 号

証　　明

大阪法務局所属公証人　山口勝之

平成 16年 6 月 8 日付

平成16年 登簿 第 168 号

この認証の付与は，在職中の公証人がその権限に基づいてしたものであり，かつ，その押印は，真実のものであることを証明する。

平成16年6月14日
平成　　年　　月　　日

大阪法務局長　梅津和宏

CERTIFICATE

This is to certify that the annexed Notarial Certificate has been executed by Notary,duly authorized and practising in Osaka, Japan, and that the Official seal appearing on the same is genuine.

Date 04. 6.14

Director of the Osake Legal Affairs Bureau

Esta copia coincide con el original que tuve a la vista.
Bogotá, D.C.
18 OCT 2005
AGUSTIN MORALES RIVEIRA
NOTARIO CUARENTA Y UNO

----------TRADUCCION OFICIAL No. 04-0616----------

de un documento escrito en INGLES, el cual para su identificación lleva el sello de la Traductora e Intérprete Oficial, Res. 2755/68 y 01144/97 de Minjusticia, al igual que la presente.----------

(Anexo a un documento de poder otorgado por Japan Tobacco Inc.)

Registro No. 100 (2004)

CERTIFICADO NOTARIAL

La presente es para certificar que Teruo DAITO firmó el documento adjunto en mi propia presencia hoy día 31 de marzo de 2004.

(fdo) ilegible

Katsuyuki Yamaguchi

Notario adjunto a la Oficina de Asuntos Legales de Osaka – 15-18, 1-chome, Akutagawa-cho, Takatsuki-shi, Osaka, Japón

(Sello) Oficina de Asuntos Legales de Osaka

NOTARIO – 15-18 (Midori Akutagawa Bldg) 1-chome Akutagawa-cho, Takatsuki-shi, Osaka, Japón

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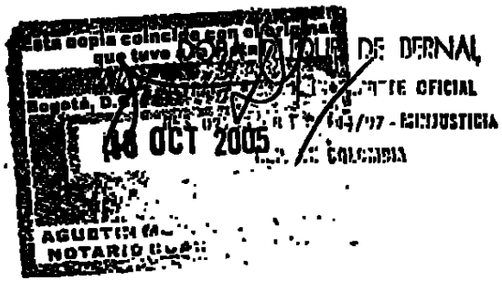
APOSTILLA

(Convención e La Haya del 5 de Octubre de 1961)

1. País: JAPON

Este documento público

2. ha sido firmado por Katsuyuki YAMAGUCHI
3. actuando en su carácter de Director de la Oficina de Asuntos legales de Osaka



4. lleva el sello de Katsuyuki YAMAGUCHI, Notario Público

Certificado

5. en Osaka 6. el 14 de Junio 2004

7. por el Ministerio de Relaciones Exteriores

8. No. 02041

9. Sello: 10: Firma

(fdo) ilegible

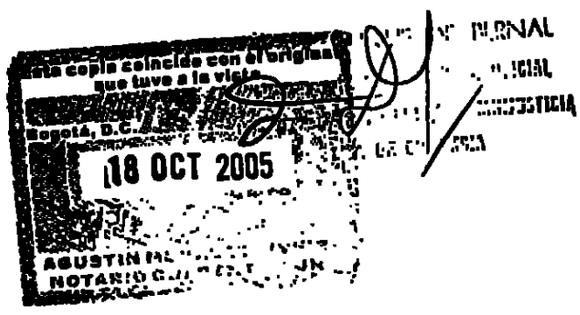
Tsutomu HIGUCHI

Por el Ministro de Relaciones Exteriores.

(Sello del Ministerio de Relaciones Exteriores de Japón)

CERTIFICADO

Yo, KATSUHIKO HONDA, Presidente y Funcionario jefe Ejecutivo de JAPAN TOBACCO INC., una sociedad japonesa situada en 2-1, TORANOMON 2-CHOME, MINATO-KU, TOKYO 105-8422, JAPON, declaro por medio del presente que estoy autorizado para firmar y otorgar documentos relacionados con derechos de propiedad intelectual en nombre de dicha sociedad, y por medio del presente certifico que, a Marzo 31 de 2004, el señor TERUO DAITO era el Director del Departamento de Información de Patentes del Instituto Central de Investigaciones Farmacéuticas de dicha sociedad, era mi apoderado y estaba autorizad para firmar y otorgar documentos relacionados con derechos de propiedad intelectual en nombre de dicha sociedad. Dichos documentos incluyen, pero no se limitan a, solicitudes, poderes, cesiones, autorizaciones de agentes, peticiones y similar en relación con



patentes y modelos de utilidad presentados en países extranjeros con el nombre de dicha sociedad.

Dado hoy día 7 de Junio de 2004

JAPAN TOBACCO INC.

KATSUHIKO HONDA

Presidente y Funcionario Jefe Ejecutivo

Libro de Registro No. 168 (2004)

CERTIFICADO NOTARIAL

La presente es para certificar que:

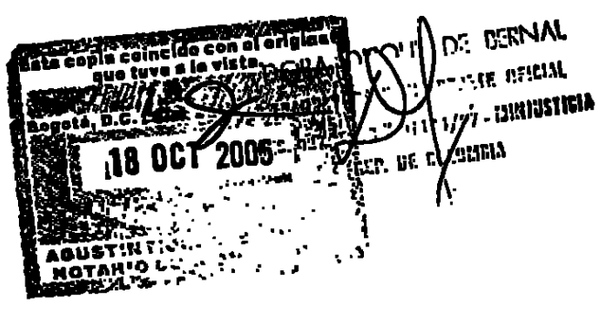
1) Teruo Daito era el Director del departamento de Información de Patentes del Instituto Central de Investigaciones Farmacéuticas de JAPAN TOBACCO INC., una sociedad japonesa que están legalmente constituida y existe de acuerdo con las leyes del Japón, situada en 2-1, Toranomon 2-chome, Minato-ku, Tokio 105-8422 Japón, a Marzo 31 de 2004, y estaba autorizado para firmar y otorgar documentos relacionados con derechos de propiedad intelectual en nombre de dicha sociedad.
2) Dicho Tereuo Daito firmó el documento adjunto en mi propia presencia el día 31 de Marzo de 2004.

EN TESTIMONIO DE LO CUAL, he suscrito aquí mi nombre y he fijado mi sello de oficio.

El día 8 de Junio de 2004

En la Oficina del Notario Katsuyuki Yamaguchi

(fdo) ilegible



Katsuyuki Yamaguchi

Notario adjunto a la Oficina de Asuntos Legales

De Osaka, 15-18, 1-chome, Akutagawacho

Takatsuki-shi, Osaka, Japón

(Sello) Oficina de Asuntos Legales de Osaka

NOTARIO – 15-18 (Midori Akutagawa Bldg) 1-chome

Akutagawa-cho, Takatsuki-shi, Osaka, Japón

CERTIFICADO 1558

La presente es para certificar que la firma que aparece anteriormente ha sido impuesta por Notario, debidamente autorizado y en ejercicio en Osaka, Japón y que el sello oficial que aparece en el mismo es auténtico.

Fecha: 04.6.14

Director de la Oficina de Asuntos Legales de Osaka

CERTIFICADO 1559

La presente es para certificar que la firma que aparece anteriormente ha sido impuesta por Notario, debidamente autorizado y en ejercicio en Osaka, Japón y que el sello oficial que aparece en el mismo es auténtico.

Fecha: 04.6.14

Director de la Oficina de Asuntos Legales de Osaka

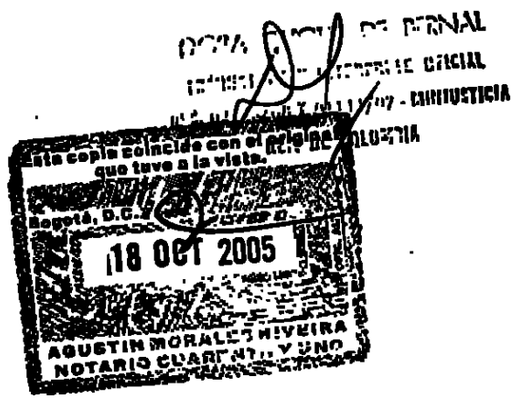
APOSTILLA

(Convención e La Haya del 5 de Octubre de 1961)

5. País: JAPON

Este documento público

6. ha sido firmado por Katsuyuki YAMAGUCHI



7. actuando en su carácter de Director de la Oficina de Asuntos legales de Osaka

8. lleva el sello de Katsuyuki YAMAGUCHI, Notario Público

Certificado

5. en Osaka 6. el 14 de Junio 2004

7. por el Ministerio de Relaciones Exteriores

8. No. 02042

9. Sello: 10: Firma

(fdo) ilegible

Tsutomu HIGUCHI

Por el Ministro de Relaciones Exteriores.

(Sello del Ministerio de Relaciones Exteriores de Japón)

Es traducción fiel y completa, a la cual me remito,

Bogotá, Junio 22, 2004.

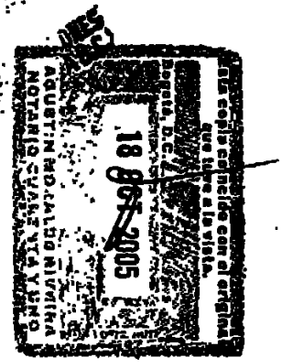
DORA DUQUE DE BERNAL,
TRADUCTORA E INTERPRETE OFICIAL
RES. 02755/68 Y 01144/97 - MINJUSTICIA
REP. DE COLOMBIA

Esta copia coincide con el original que tuve a la vista.
Bogotá, D.C.
18 OCT 2005
AGUSTIN MEJIA ALZATE RIVEIRA
NOTARIO 50

NO SE ASUME RESPONSABILIDAD

JUN 24 A 11:23

JEFE DE LEGALIZACIONES
SANTAFE DE BOGOTA D.C.



EXTERIORES

041035

CUYA FIRMA APARECE EN EL
DOCUMENTO DESEMPEÑA
LAS FUNCIONES INDICADAS

2004 JUN 24 A 11:23

JEFE DE LEGALIZACIONES
SANTAFE DE BOGOTA D.C.

6016-FNPCT

4/4
21.

P A T E N T S

CESION

El (los) suscrito (s)
TOMOYUKI IKEMOTO, MASAHIRO TANAKA, TAKEO YUNO, JOHEI SAKAMOTO, HIROYUKI NAKANISHI, YUICHI NAKAGAWA, TAKESHI OHTA, SHOKHI SAKATA, y HISAYO MORINAGA

en consideración al pago de la suma de
(.....US$ 1.oo.....), que he(mos) recibido, por el presente documento cedo (cedemos) a
JAPAN TOBACCO INC.

una compañía constituida de conformidad con las leyes de JAPON

con oficinas en
2-1, Toranomon 2-chome, Minato-ku,
Tokyo 105-8422 - JAPON
todos los derechos y titulos sobre la invención denominada "COMPUESTO PENTACICLICO HETERO AROMATICO Y USO MEDICINAL DEL MISMO"

EL CESIONARIO firma también el presente y declara que acepta dicha cesión

Dado y firmado hoy 28 de Septiembre de 2005

en Osaka, JAPON

ASSIGNMENT

The undersigned
Tomoyuki IKEMOTO, Masahiro TANAKA,
Takeo YUNO, Johei SAKAMOTO,
Hiroyuki NAKANISHI, Yuichi NAKAGAWA,
Takeshi OHTA, Shohei SAKATA
and Hisayo MORINAGA
in consideration of the sum of
(.....US$ 1.oo.....), the receipt of which is hereby acknowledged, by these presents do sell, assign and transfer unto

Japan Tobacco Inc.

a corporation organized under the laws of

Japan

having a place of business at
2-1, Toranomon 2-chome,
Minato-ku, Tokyo 105-8422 Japan
all rights and title to the invention related to
HETEROAROMATIC PENTACYCLIC COMPOUND AND MEDICINAL USE THEREOF

THE ASSIGNEE signs these presents and declares that accepts the aforesaid assignment

Given an signed this September 28, 2005

in Osaka, JAPAN

Inventors

Tomoyuki Ikemoto
Tomoyuki IKEMOTO

Masahiro Tanaka
Masahiro TANAKA

Takeo Yuno
Takeo YUNO

Johei Sakamoto
Johei SAKAMOTO

Hiroyuki Nakanishi
Hiroyuki NAKANISHI

Yuichi Nakagawa
Yuichi NAKAGAWA

Takeshi Ohta
Takeshi OHTA

Shohei Sakata
Shohei SAKATA

Hisayo Morinaga
Hisayo MORINAGA

Assignee
Japan Tobacco Inc.

Y. Inubushi
Yoshinori INUBUSHI
Vice President, Intellectual Prope

ALVARO CASTELLANOS M. & CIA.
ABOGADOS COLOMBIA.
Carrera 9 No. 73-49- P.O.Box 6347 - Bogotá, Colombia
Tels: (571) 610 74 20 / 60 / 80 - Fax (571) 610 07 06 - e-mail

Esta copia coincide con el original que tuve a la vista.
Bogotá, D.C.
19 OCT 2005
AGUSTIN MORALES RIVEIRA
NOTARIO CUARENTA Y UNO

22

APOSTILLE

(Convention de La Haye du 5 octobre 1961)

1. Country: **JAPAN**

   This public document

2. has been signed by — Katsuyuki YAMAGUCHI
3. acting in the capacity of — Notary Public of the Osaka Legal Affairs Bureau
4. bears the seal/stamp of — Katsuyuki YAMAGUCHI, Notary Public

Certified

5. at Osaka
6. OCT. -5. 2005
7. by the Ministry of Foreign Affairs
8. No. 03558
9. Seal/stamp: MINISTRY OF FOREIGN AFFAIRS JAPAN
10. Signature:

Tsutomu HIGUCHI

For the Minister for Foreign Affairs

Esta copia coincide con el original que tuve a la vista.
Bogotá, D.C.
19 OCT 2005
AGUSTIN MORALES RIVEIRA
NOTARIO CUARENTA Y UNO

認証登簿平成１７年第３０４号

嘱託人犬伏吉則、同池本知之、同田中正浩、同油納健夫、同坂本丞平、同中西博行、同中川祐一、同太田毅、同坂田昌平及び同森長寿代は、本公証人の面前で、別紙編綴の書面に署名した。

よって、これを認証する。

平成１７年９月２８日、本職の役場において。

大阪府高槻市芥川町１丁目１５番１８号（ミドリ芥川ビル内）

大阪法務局所属

公証人　山口勝之

Registerd No.304 (2005)

NOTARIAL CERTIFICATE

This is to certify that Yoshinori Inubushi, Tomoyuki Ikemoto, Masahiro Tanaka, Takeo Yuno, Johei Sakamoto, Hiroyuki Nakanishi, Yuichi Nakagawa, Takeshi Ohta, Shohei Sakata and Hisayo Morinaga signed to the attached document in my very presence.

Dated this 28th day of September, 2005.

Katsuyuki Yamaguchi

Katsuyuki Yamaguchi
Notary, attached to
Osaka Legal affairs Bureau
15-18,1-chome,Akutagawa-cho,
Takatsuki-shi,Osaka,Japan.

OSAKA LEGAL AFFAIRS BUREAU
NOTARY
15-18,(Midori Akutagawa Bldg.)1-chome
Akutagawa-cho,Takatsuki-shi,Osaka,Japan

19 OCT 2005
AGUSTIN MORALES RIVEIRA
NOTARIO CUARENTA Y UNO

第 2917 号

証　　明

大阪法務局所属公証人　山口勝之

平成 17 年 9 月 28 日付

平成17年 登簿 第 304 号

この認証の付与は，在職中の公証人がその権限に基づいてしたものであり，かつ，その押印は，真実のものであることを証明する。

平成17年10月5日
平成　　年　　月　　日

大阪法務局長　梅津和宏

CERTIFICATE

This is to certify that the annexed Notarial Certificate has been executed by Notary,duly authorized and practising in Osaka, Japan, and that the Official seal appearing on the same is genuine.

Date 05. 10. 5

Director of the Osaka Legal Affairs Bureau

Esta copia coincide con el original que tuve a la vista.
Bogotá, D.C.
19 OCT 2005
AGUSTIN MORALES RIVERA
NOTARIO CUARENTA Y UNO

TRADUCCIÓN OFICIAL No. 208-05. DE UN DOCUMENTO ESCRITO EN INGLES, SELLADO CON EL SELLO DEL SUSCRITO TRADUCTOR OFICIAL HOY OCTUBRE 18 DEL 2005, EN LA CIUDAD DE BOGOTA D.C., REPUBLICA DE COLOMBIA.

CESIÓN (/.../)

Registro No. 304 (2005)

CERTIFICADO NOTARIAL

Por medio del presente se certifica que Yoshinori Inubushi, Tomoyuki Ikemoto, Masahiro Tanaka, Takeo Yuno, Johei Sakamoto, Hiroyuki Nakanishi, Yuichi Nakagawa, Takeshi Ohta, Shohei Sakata, e Hisayo Morinaga firmaron el documento adjunto ante mi.
Firmado este día 28 de Septiembre del 2005.

Firmado
Katsuyuki Yamaguchi
Notario, adjunto al
Departamento de Asuntos Legales de Osaka
15-18, 1-chome, Akutagawa-Cho,
Takatsuki-shi, Osaka, Japón.

Sello de
DEPARTAMENTO DE ASUNTOS LEGALES DE OSAKA
NOTARIO
15-18, (Midori Akutagawa Boldg), 1-chome
akutagawa-cho, Takatsuki-shi, Osaka, Japón.

(ADJUNTO AL DOCUMENTO SE ENCUENTRA LO SIGUIENTE:

2917

CERTIFICADO

Por medio del presente se certifica el Certificado Notarial adjunto fue firmado por el Notario, debidamente autorizado y con ejercicio en Osaka, Japón y que el Sello oficial que aparece en el mismo es genuino.
Fecha: 05.10.6

Director del Departamento de Asuntos Legales de Osaka

Sergio Eleuterio Latorre Mendoza
Traductor e Intérprete Oficial
Resol. No. 2839 Minjusticia 1991

Esta copia coincide con el original que tuve a la vista.
Bogotá, D.C.
18 OCT 2005
AGUSTIN MORALES RIVERA
NOTARIO CUARENTA Y UNO

ADJUNTO AL DOCUMENTO SE ENCUENTRA LO SIGUIENTE:

APOSTILLE
(CONVENCION DE LA HAYE DE 5 OCTOBRE 1961)

1. PAIS: JAPON
   ESTE DOCUMENTO PUBLICO
2. HA SIDO FIRMADO POR: Katsuyuki YAMAGUCHI
3. ACTUANDO EN CAPACIDAD DE: NOTARIO PUBLICO DEL DEPARTAMENTO DE ASUNTOS LEGALES DE OSAKA
4. LLEVA EL SELLO/ESTAMPILLA DE: Katsuyuki YAMAGUCHI. NOTARIO PUBLICO

CERTIFICADO

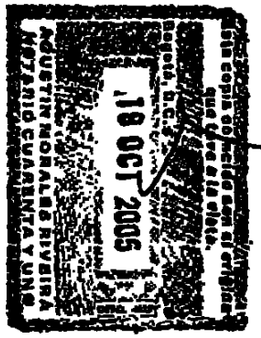
5. EN: OSAKA
6. OCT. 6. 2005
7. POR: EL MINISTRO DE RELACIONES EXTERIORES
8. No. 03558
9. SELLO/ESTAMPILLA
10. FIRMA

FIRMADO POR: TSUTOMU HIGUCHI
Para el Ministerio de Relaciones Exteriores
Sello
Ministerio Relaciones Exteriores
Japón

SELLO REDONDO EN TINTA AZUL DEL MINISTERIO DE RELACIONES EXTERIORES, JAPÓN.

Sergio Eleuterio Valorre Mendoza
Traductor e Intérprete Oficial
Resol. No. 2839 Minjusticia 1991

Esta copia coincide con el original que tuve a la vista.
Bogotá, D.C.
19 OCT 2005
AGUSTIN MO... LEGUIZAMON
NOTARIO CU... SENTA Y UNO



EXTERIORES

4778175

Sergio Latone

CUYA FIRMA APARECE EN EL DOCUMENTO DESEMPEÑA LAS FUNCIONES INDICADAS

NO SE ASUME RESPONSABILIDAD DEL TEXTO

2005 OCT 18 A 11:45

JEFE DE LEGALIZACIONES
SANTAFE DE BOGOTA D.C.

6016.27

(12) 許協力条約に基づいて公開された国際出願

(19) 世界知的所有権機関
国際事務局

(43) 国際公開日
2004年10月21日 (21.10.2004)

PCT

(10) 国際公開番号
WO 2004/089918 A1

(51) 国際特許分類7: C07D 263/32, 417/14, 333/20, 413/12, 417/06, 409/12, 333/38, 333/16, 333/18, 277/22, 277/28, 417/12, A61K 31/421, 31/4439, 31/4725, 31/538, 31/497, 31/4184, 31/427, 31/428, 31/381, 31/405, 31/4155, 31/423, 45/00, A61P 43/00, 3/10, 3/06, 3/04

(21) 国際出願番号: PCT/JP2004/005119

(22) 国際出願日: 2004年4月9日 (09.04.2004)

(25) 国際出願の言語: 日本語

(26) 国際公開の言語: 日本語

(30) 優先権データ:
特願2003-105267 2003年4月9日 (09.04.2003) JP
特願2003-157590 2003年6月3日 (03.06.2003) JP

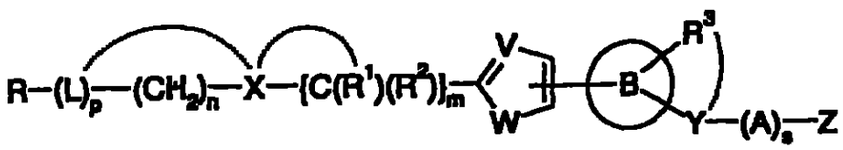
(71) 出願人 (米国を除く全ての指定国について): 日本たばこ産業株式会社 (JAPAN TOBACCO INC.) [JP/JP]; 〒1058422 東京都港区虎ノ門二丁目2番1号 Tokyo (JP).

(72) 発明者; および
(75) 発明者/出願人 (米国についてのみ): 池本 知之 (IKEMOTO, Tomoyuki) [JP/JP]; 〒5691125 大阪府高槻市紫町1番1号 日本たばこ産業株式会社 医薬総 研究所内 Osaka (JP). 田中 正浩 (TANAKA, Masahiro) [JP/JP]; 〒5691125 大阪府高槻市紫町1番1号 日本たばこ産業株式会社 医薬総合研究所内 Osaka (JP). 油納 健夫 (YUNO, Takeo) [JP/JP]; 〒5691125 大阪府高槻市紫町1番1号 日本たばこ産業株式会社 医薬総 研究所内 Osaka (JP). 坂本 浩平 (SAKAMOTO, Johei) [JP/JP]; 〒5691125 大阪府高槻市紫町1番1号 日本たばこ産業株式会社 医薬総合研究所内 Osaka (JP). 中西 博行 (NAKANISHI, Hiroyuki) [JP/JP]; 〒5691125 大阪府高槻市紫町1番1号 日本たばこ産業株式会社 医薬総合研究所内 Osaka (JP). 中川 祐一 (NAKAGAWA, Yuichi) [JP/JP]; 〒5691125 大阪府高槻市紫町1番1号 日本たばこ産業株式会社 医薬総合研究所内 Osaka (JP). 太田 毅 (OHTA, Takeshi) [JP/JP]; 〒5691125 大阪府高槻市紫町1番1号 日本たばこ産業株式会社 医薬総合研究所内 Osaka (JP). 坂田 真平 (SAKATA, Shinhei) [JP/JP]; 〒5691125 大阪府高槻市紫町1番1号 日本たばこ産業株式会社 医薬総合研究所内 Osaka (JP). 森長 尋代 (MORINAGA, Hiroyo) [JP/JP]; 〒5691125 大阪府高槻市紫町1番1号 日本たばこ産業株式会社 医薬総合研究所内 Osaka (JP).

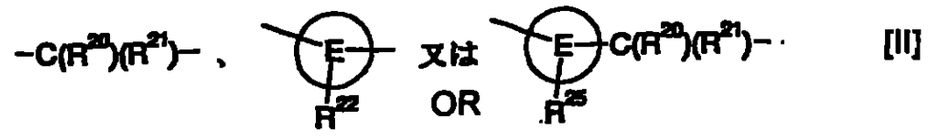
/続葉 /

(54) Title: HETEROAROMATIC PENTACYCLIC COMPOUND AND MEDICINAL USE THEREOF

(54) 発明の名称: 複素芳香5員環化合物及びその医薬用途



[I]



[II]

(57) Abstract: A heteroaromatic pentacyclic compound of the general formula: [I] [wherein V is CH or N; W is S or O; each of R^1 and R^2 is H, etc.; X is -N(R^4)-, -O-, -S-, -SO_2-N(R^5)-, -CO-N(R^7)-, etc.; L is formula [II]; (each of R^{20}, R^{21}, R^{22} and R^{25} is H, etc.; and E is an aryl or an aromatic heterocycle); R is -COOH, etc.; B is an aryl, etc.; R^3 is H, etc.; Y is -C(R^{13})(R^{14})-N(R^{12})-, -C(R^{13})(R^{14})-O-, -N(R^{11})-, -O-, etc.; A is an alkylene; Z is an aryl, etc.; etc.]. This compound or its prodrug or a pharmaceutically acceptable salt thereof has a protein tyrosine phosphatase 1B inhibiting activity and is useful as a curative medicine for diabetes mellitus, diabetes mellitus complications, hyperlipemia or obesity.

/続葉有/

WO 2004/089918 A1

SPECIFICATION

HETEROAROMATIC PENTACYCLIC COMPOUND AND MEDICINAL USE THERE F

TECHNICAL FIELD OF THE INVENTION

The present invention relates to a novel 5-membered heteroaromatic ring compound. More particularly, the present invention relates to a 5-membered heteroaromatic ring compound having a protein tyrosine phosphatase 1B (PTP1B) inhibitory activity, a pharmaceutically acceptable salt thereof, and a pharmaceutical composition containing the same.

BACKGROUND OF THE INVENTION

Diabetes causes various dysbolisms mainly characterized by a chronic state of high blood glucose level. It shows a broad range of symptoms based on high blood glucose level, such as mouth dryness, polydipsia, diuresis, loss of body weight and the like. When such a state of high blood glucose level lasts for a long time, it is known to cause all kinds of complications such as retinopathy, nephropathy, neuropathy, cardiac infarction and cerebral infarction based on arteriosclerosis, and the like.

Diabetes is generally classified into four types: type I diabetes (IDDM; insulin dependent diabetes mellitus) accompanying absolute insulin deficiency due to damage or destruction of pancreatic β cell; type II diabetes (NIDDM; non-insulin dependent diabetes mellitus) accompanying relative insulin deficiency due to insulin resistance and decreased insulin secretion; special diabetes secondarily developed by abnormality in gene, other diseases and the like; and gestational diabetes. In some cases, patients diagnosed with type II diabetes shortly after the onset may come to show decreased insulin secretion with the progression of the disease and ultimately lead to type I diabetes.

To treat diabetes, it is essential to improve the above-

mentioned states of high blood glucose level and prevent the onset and progression of complications. For this end, there have been tried diet therapy, exercise therapy and the like, as well as treatments using a variety of pharmaceutical agents with the aim of controlling the blood glucose level to be within the normal range. As the representative existing pharmaceutical agents, there are mentioned insulin preparations, insulin secretagogues (sulfonylurea agent, sulfonamide agent, phenylalanine derivative etc.) that promote insulin secretion from pancreatic β cell, α-glucosidase inhibitors that delay sugar absorption, biguanide agents considered to have a liver glyconeogensis inhibitory action, wherein the detail of the mechanism is unknown, insulin sensitivity enhancers (thiazolidinedione derivative etc.) that promote differentiation from fibroblast to adipose cell via a peroxisome proliferator-activated receptor (PPAR) agonist action to increase the number of insulin sensitive cells and the like. However, all these are problematic in terms of effectiveness and safety (e.g., secondary failure due to fatigue of pancreatic β cell, risk of hypoglycemia and promotion of obesity associated with insulin secretagogue, edema and adverse influence on the heart based thereon, anemia, overeating, promotion of obesity, presence of non-responder associated with insulin sensitivity enhancer and the like) and they fail to achieve sufficient control of blood glucose.

Referring to glucose metabolism in living organism, materials to be the energy source and constituent components of living organism have been intermittently taken into the body, and in contrast, for example, brain continuously consumes glucose. In this situation, the blood glucose level is maintained at a constant level, and blood glucose control is enabled by interaction among hormone involved in the blood glucose control, metabolism in organ, and exchange of

saccharide and the like between organs. Of these, the action of insulin, which is a hormone particularly responsible for the blood glucose control, is significant, and disorders thereof, in other words insulin resistance and decreased insulin secretion, are considered to be deeply involved in diabetes.

Insulin is secreted from pancreatic β cell and binds with insulin receptor, which is a receptor type tyrosine kinase present on the membrane surface of its target cell or skeletal muscle cell and adipose cell, after which the tyrosine residue in the intracellular domain is auto-phosphorylated. Thereafter, the tyrosine residue of IRS (insulin receptor substrate), APS (adapter protein containing PH and SH2 domain) and the like, which is a substrate of an insulin receptor, is phosphorylated and PI_3 kinase-Akt pathway is activated, which in turn transfers a glucose transporter onto the cell membrane, causing glucose uptake and decreased blood glucose concentration. On the other hand, tyrosine phosphatase is also present, which performs tyrosine dephosphorylation to negatively control intracellular signaling by insulin, thereby suppressing the activation. As mentioned above, tyrosine phosphorylation plays a major role in the action of insulin. In consideration of the fact that tyrosine phosphorylation is determined by the balance of the activity of tyrosine kinase (phosphorylation enzyme) and that of tyrosine phosphatase (dephosphorylation enzyme), tyrosine phosphatase is considered to directly play a significant role in controlling insulin signaling together with tyrosine kinase.

At present, tyrosine phosphatase forms a large gene family, and more than seven dozen kinds of isozymes have been reported. Of these, protein tyrosine phosphatase 1B (PTP1B) is considered to be a major phosphatase involved in insulin signaling. Particularly, because gene expression of PTP1B increases in high glucose culture and changes in intracellular

localization thereof decreases tyrosine phosphorylation of insulin receptor and IRS-1 and induces insulin resistance (J. Biol. Chem., 1995, Vol. 270, pp. 7724-7730; J. Biochem. (Tokyo), 1998, Vol. 123, pp. 813-820), introduction of wild type PTP1B inhibits translocation of glucose transporter GLUT4, such effect was not found in phosphatase activity defective mutants, and insulin sensitivity was enhanced in PTP1B knockout mice and the mice became obesity resistant to a high fat diet (Science, 1999, Vol. 283, pp. 1544-1548), there is a possibility that this enzyme may become one target to enhance the action of from activation of insulin receptor to glucose uptake that insulin is responsible for. In fact, vanadic acid conventionally known as a tyrosine phosphatase inhibitor shows an insulin-like action in animal tests and the like.

Accordingly, a drug that suppresses and/or inhibits activation of such tyrosine phosphatase, particularly PTP1B, enhances the action up to glucose uptake by inhibiting an insulin receptor activated signal from being negatively controlled through dephosphorylation, and can be a new type of therapeutic agent for diabetes, which decreases blood glucose based on direct enhancement of insulin action. In addition, application to various therapeutic agents for diseases such as obesity, neurodegenerative disease and the like is expected.

There are various reports in recent years on compounds aiming at treatment of diseases, such as diabetes and the like, by inhibiting such protein tyrosine phosphatase.

For example, WO00/17211 discloses a phosphonic acid derivative having a PTP1B inhibitory activity. However, this publication does not disclose a compound having a structure of the compound of the present invention, not to mention any description suggestive thereof.

JP-T-11-508919 (U.S. Patent No. 5,770,620) discloses an arylacrylic acid derivative useful as a protein tyrosine

phosphatase inhibitor. However, this publication does not disclose a compound having a structure of the compound of the present invention, not to mention any description suggestive thereof.

WO98/27092 (U.S. Patent No. 6,080,772) discloses a thiazole compound having a protein tyrosine phosphatase inhibitory action. However, this publication does not disclose a compound having a structure of the compound of the present invention, not to mention any description suggestive thereof.

WO99/58522 discloses naphtho[2,3-B]heteroar-4-yl derivative, WO99/58511 discloses an oxa/thiazole-aryl-carboxylic acid derivative; WO99/58521 and U.S. Patent No. 6,110,962 disclose a 11-aryl-benzo[B]naphtho[2,3-D]furan and 11-aryl-benzo[B]naphtho[2,3-D]thiophene derivatives; WO99/58518 discloses a biphenyl-oxo-acetic acid derivative; WO99/61419 discloses a 2,3,5-substituted biphenyl derivative; WO99/58520 discloses a biphenyl-sulfonyl-aryl-carboxylic acid derivative; WO99/61435 discloses benzothiophene, benzofuran and indole derivatives; U.S. Patent No. 6,103,708 discloses furan, benzofuran and thiophene derivatives; U.S. Patent No. 6,110,963 discloses an aryl-oxo-acetic acid derivative; U.S. Patent No. 6,001,867 discloses a 1-aryl-dibenzothiophene derivative; U.S. Patent No. 6,057,316 discloses a 4-aryl-1-oxa-9-thia-cyclopenta[B]fluorene derivative; U.S. Patent No. 6,063,815 discloses a benzophenone derivative, each of which having a protein tyrosine phosphatase inhibitory action. However, these publications do not disclose a compound having a structure of the compound of the present invention, not to mention any description suggestive thereof.

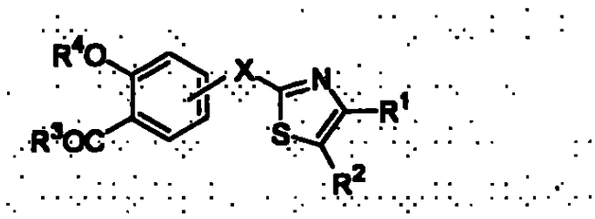
As a compound having a thiazole, thiophene or oxazole structure, the following have been reported.

WO00/45635 discloses a 2-substituted thiazole derivative. However, this compound has a carbamoyl group at the terminal of

the 2-position substituent of a thiazole ring, and this publication does not disclose a compound having a structure of the compound of the present invention, not to mention any description suggestive thereof. The compound of this publication is useful as an antibacterial agent or an analgesic agent, and this publication does not disclose usefulness as a PTP1B inhibitor, not to mention any description suggestive thereof.

JP-T-2000-504039 discloses a 2-anilino-4-phenylthiazole derivative. However, the compound of this publication has an anilino group substituted by a hydroxyl group or a carboxyl group at the 2-position of thiazole ring, and phenyl group at the 4-position, wherein the phenyl group at the 4-position has a substituent at the 2-position. This publication does not disclose a compound having a structure of the compound of the present invention, not to mention any description suggestive thereof. In addition, the compound of this publication is useful as a CRF (corticotropin releasing factor) antagonist. This publication does not disclose usefulness as a PTP1B inhibitor, not to mention any description suggestive thereof.

JP-A-4-154773 discloses a thiazole derivative of the formula

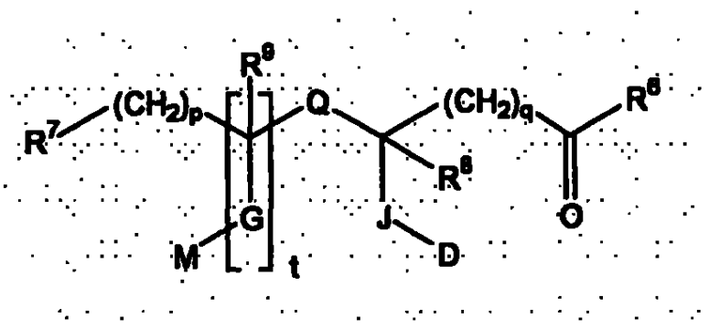


wherein R^1 and R^2 are the same or different and each is a hydrogen atom, a halogen atom, a lower alkyl group, a phenyl group, a substituted phenyl group, a pyridyl group or a substituted pyridyl group, R^3 is a hydroxyl group, a lower alkoxy group or a group represented by $-N(R^5)(R^6)$ wherein R^5 and

R^6 are the same or different and each is a hydrogen atom or a lower alkyl group, R^4 is a hydrogen atom or a lower alkyl group, and X is an amino group, an amide group, a carbonyl group, an alkylene group, an oxygen atom or a sulfur atom. However, this publication does not disclose a compound having a structure of the compound of the present invention, not to mention any description suggestive thereof. In addition, the compound of this publication is useful as an anti-inflammatory agent. This publication does not disclose usefulness as a PTP1B inhibitor, not to mention any description suggestive thereof.

WO94/08982 discloses a 4-phenylthiazole derivative. However, the compound of this publication has a phenyl group at the 4-position of thiazole ring, and phenyl group at the 4-position, wherein the phenyl group at the 4-position has a substituent at the 2-position. This publication does not disclose a compound having a structure of the compound of the present invention, not to mention any description suggestive thereof. In addition, the compound of this publication is useful as a noxious organism eliminator. This publication does not disclose usefulness as a PTP1B inhibitor, not to mention any description suggestive thereof.

WO02/39997 discloses a compound represented by the formula

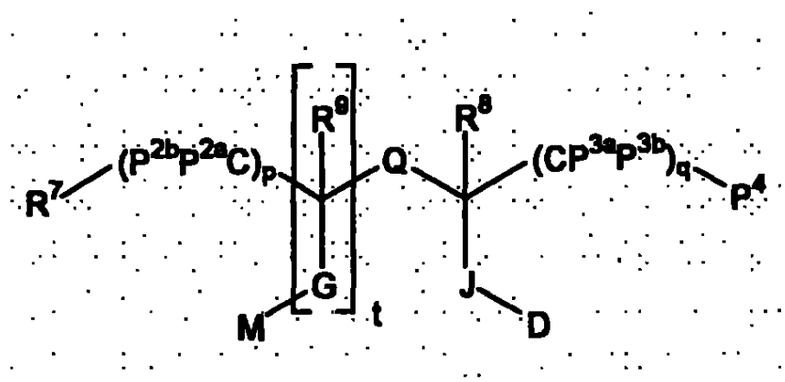


wherein R^6 is a hydroxyl group or a protective prodrug moiety, R^7 is a hydrogen atom, a carboxy group, an arylaminocarbonyl

group, an aroyl group, an aryl group, an alkylaminocarbonyl group, an aminocarbonyl group, an alkenylaminocarboxy group, a hydroxyl group, an alkoxy group, ether, thiol, an amino group-containing hetero ring group or a protective prodrug moiety, R^8 is a hydrogen atom or alkyl group that may bond with D to form a ring, R^9 is a lower alkyl group or a hydrogen atom, Q is a bond, an oxygen atom, a sulfur atom, CR^3OH, CR^3SH, $CR^3NR^{3a}R^{3b}$, NR^3, $(CR^3R^{3a})_n$, $O(CR^3R^{3b})_n$ or $(CR^3R^{3a})_nO(CR^{3b}R^{3c})_n$ wherein n is 0 or an integer of 1 to 3, R^3, R^{3a}, R^{3b} and R^{3c} are each independently a hydrogen atom, an optionally substituted straight chain, a cyclic or branched chain C_{1-6} alkyl group, a C_{2-6} alkenyl group, an acyl group, an arylalkyl group, aryloxycarbonyl group, an arylaminocarbonyl group, an arylalkylsulfonyl group or an aryl group), G is a linking moiety, M is an anchor moiety, J is a bond, an alkylene group, an alkenylene group or an alkynylene group, D is a hydrogen atom, an alkoxy group, amine, an alkyl group, an alkenyl group, an alkynyl group, an aryl group or a heteroaryl group that is bonded with G, M or Q to form a ring, t is 0 or 1, p is 0 or an integer of 1 to 5, and q is 0 or an integer of 1 to 3],

and

a compound represented by the formula

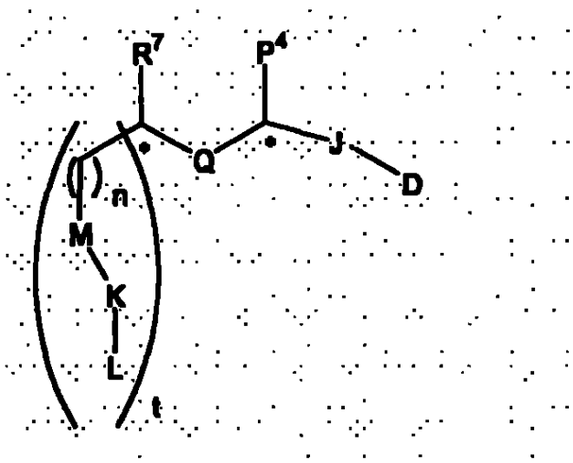


wherein P^4 is a carboxy group, a cleavable prodrug moiety, $COOP^{4'}$, $(CH_2)_{1-4}SP^{4'}$ or $C(O)NP^{4'}P^{4''}$, R^7 is a hydrogen atom, a

carboxy group, an optionally substituted lower alkyl ester, a lower alkenyl ester, an ester added with a secondary amine substituted by lower alkyl, an arylaminocarbonyl group, an aroyl group, an aryl group, an alkylaminocarbonyl group, an aminocarbonyl group, $COOR^{7'}$, $CONR^{7'}R^{7''}$, a hydroxyl group, ether, thiol, an amino group, $(CH_2)_{1-4}SR^{7'}$, a hetero ring group or a cleavable prodrug moiety, $P^{4'}$, $P^{4''}$, $R^{7'}$ and $R^{7''}$ are each independently a hydrogen atom, a C_{1-6} alkyl group, a C_{2-6} alkenyl group, a C_{2-6} alkynyl group or an optionally substituted aryl group, R^8 is a hydrogen atom, an alkyl group or a covalent bond with D, R^9 is a lower alkyl group or a hydrogen atom, Q is a bond, an oxygen atom, a sulfur atom, CR^3OH, CR^3SH, $CR^3NR^{3a}R^{3b}$, NR^3, $(CR^3R^{3a})_n$, $O(CR^3R^{3b})_n$ or $(CR^3R^{3a})_nO(CR^{3b}R^{3c})_n$ wherein n is 0 or an integer of 1 to 3, R^3, R^{3a}, R^{3b} and R^{3c} are each independently a hydrogen atom, an optionally substituted C_{1-6} straight chain or branched chain alkyl group, a C_{2-6} straight chain or branched chain alkenyl group, an aryloxycarbonyl group, an arylaminocarbonyl group, an arylalkylsulfonyl group, an arylalkyl group, an optionally substituted acyl group, an aryl group or a C_{3-8} ring optionally substituted by 4 heteroatoms at maximum, P^{2a}, P^{2b}, P^{3a} and P^{3b} are each independently a hydrogen atom or an optionally substituted straight chain, branched chain or cyclic C_{1-5} alkyl group, G is a linking moiety, M is an anchor moiety, J is a bond, an alkylene group, an alkenylene group or an alkynylene group, D is a hydrogen atom, an alkyl group, an alkenyl group, an alkynyl group or an aryl group or it may be bonded with G, M or Q to form a ring, t is 0 or 1, p is 0 or an integer of 1 to 5, and q is 0 or an integer of 1 to 3 and as examples of the anchor moiety in each formula, a thiazole group and an oxazole group having, as a substituent, an aryl group or a heteroaryl group substituted by $-NR'R''$, $-CONR'R''$, $-S(O)_2NR'R''$, $-S(O)_{0-2}R'$, $-NR'R''$, $-O(CR'R'')_{0-2}CF_3$, $-COR'$, $-CO_2R'$ and $-OR'$ wherein R' and R'' are each independently a

hydrogen atom, a C_{1-6} alkyl group, a C_{2-6} alkenyl group, a C_{2-6} alkynyl group or an optionally substituted aryl group, and as examples of the linking moiety, a covalent bond and a C_{1-6} alkyl group are described.

Furthermore, a compound represented by the formula



wherein M is a carbon ring group, a hetero ring group or $CONR'R''$ wherein R' and R'' are each independently a hydrogen atom, a C_{1-6} alkyl group, a C_{2-6} alkenyl group, a C_{2-6} alkynyl group or an optionally substituted aryl group, Q is a bond, an oxygen atom, a sulfur atom, CR^3OH, CR^3SH, $CR^3NR^{3a}R^{3b}$, NR^3, $(CR^3R^{3a})_n$, $O(CR^3R^{3b})_n$ or $(CR^3R^{3a})_nO(CR^{3b}R^{3c})_n$ wherein n is 0 or an integer of 1 to 3, R^3, R^{3a}, R^{3b} and R^{3c} are each independently a hydrogen atom, an optionally substituted branched chain, a cyclic or a straight chain C_{1-6} alkyl group, a C_{2-6} alkenyl group, an acyl group, an arylalkyl group, an aryloxycarbonyl group, an arylaminocarbonyl group, an arylalkylsulfonyl group or an aryl group, K is an independently selected secondary linking moiety, L is an independently selected secondary anchor moiety, P^4 is a hydrogen atom, a carboxy group, $(CH_2)_{1-4}SP^{4'}$, a cleavable prodrug moiety, $COOP^{4'}$ or $CONP^{4'}P^{4''}$, R^7 is a hydrogen atom, a carboxy group, an aroyl group, an aryl group, $COOR^{7'}$, $C(O)NR^{7'}R^{7''}$, a hydroxyl group, ether, thiol, $(CH_2)_{1-4}SR^{7'}$, a hetero ring group or a cleavable prodrug moiety, $P^{4'}$, $P^{4''}$, $R^{7'}$ and $R^{7''}$ are each

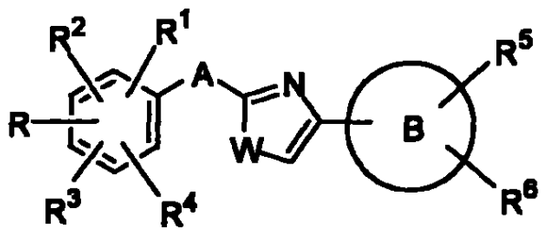
independently a hydrogen atom, a C_{1-6} alkyl group, a C_{2-6} alkenyl group, a C_{2-6} alkynyl group or an optionally substituted aryl group, n is 0 or an integer of 1 to 4, D is a hydrogen atom, an alkyl group, an alkoxy group, an alkenyl group, amine, a hydroxyl group, an alkynyl group, an aryl group or a heteroaryl group, and t is 0 or 1, is described and that it is described that the secondary linking moiety has a covalent bond, and the secondary anchor moiety has an optionally substituted aryl group.

However, this publication does not disclose a compound having a structure of the compound of the present invention, not to mention any description suggestive thereof.

In addition, the compound of this publication is useful as an angiotensin converting enzyme (ACE)-2 regulating agent. This publication does not disclose usefulness as a PTP1B inhibitor, not to mention any description suggestive thereof.

As reports on a compound having a thiazole or oxazole structure, which aims at treating not only diabetes but also hyperlipidemia by inhibiting PTP1B, the following can be mentioned.

JP-A-2003-231679 discloses an azole compound represented by the formula



[I]

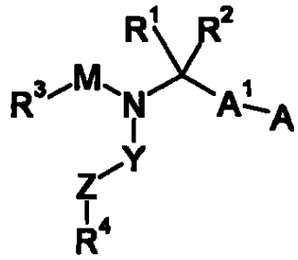
having a PTP1B inhibitory activity, and teaches that this compound is useful as a therapeutic agent for hyperlipidemia. However, the compound of this publication is essentially characterized in that nitrogen atom or carbonyl group at the

substituent A should be adjacent to carbon atom at the 2-position of thiazole or oxazole, or A is an alkylene; a bond between A and benzene ring is essential; and nitrogen atom, oxygen atom, sulfur atom or carbonyl group at the substituent R^6 should be adjacent to ring B, or R^6 is linked to a ring structure via an alkylene or a single bond is essential, and this publication does not disclose a compound having a structure of the compound of the present invention. In addition, this publication does not describe that the PTP1B inhibitory activity of this compound is higher than the activity of other protein tyrosine phosphatases.

As reports on a method using plural therapeutic drugs for diabetes or other diseases in combination, the following can be mentioned.

JP-A-9-67271 discloses a combination of an insulin sensitivity enhancer with an insulin preparation, an insulin secretagogue, an α-glucosidase inhibitor, a biguanide agent and the like. However, this publication does not disclose a PTP1B inhibitor or an inhibitor of receptor tyrosine kinase negative regulator such as the compound of the present invention, not to mention any description suggestive thereof.

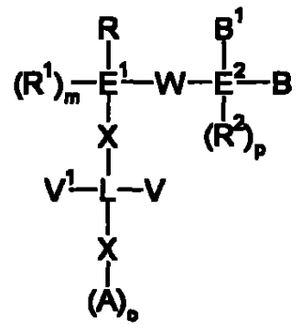
WO02/100846 discloses a thiophene derivative compound having the formula



wherein M is selected from $-SO_2-$, -C=O-, -C=S-, etc.; A^1 is selected from a bond, a C_{1-6} alkyl, a C_{2-6} alkenyl, etc.; A is selected from $COOR^5$, $CO-COOR^5$, $PO_3R^5R^5$, etc., wherein each R^5 is independently selected from a hydrogen atom and C_{1-6} alkyl; R^1

and R^2 are independently selected from a hydrogen atom, a C_{1-6} alkyl, a C_{6-12} aryl, etc.; R^3 is selected from a C_{6-12} aryl, a C_{3-10} heterocycle, a C_{6-12} aralkyl, etc.; Y is selected from a bond, $-CH_2-$, -CO-, etc.; Z is selected from a C_{1-6} alkyl, a C_{2-6} alkenyl, a C_{2-6} alkynyl, etc.; R^4 is selected from a hydrogen atom, halogen, CN, NO_2, etc.; or a salt thereof.

WO 02/34711 discloses a thiophene derivative compound having the formula

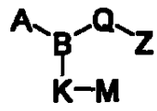


wherein

E^1 and L are each independently selected from a 5- to 7-membered saturated or unsaturated carbon ring, a 5- to 7-membered saturated or unsaturated hetero ring, a bicyclic saturated or unsaturated carbon ring, etc.; R is selected from $-CH=CH-R^2$, $-C\equiv C-R^2$, $-C(R^2)=CH$, etc.; R^1 is selected from a hydrogen atom, -R, $-NO_2$, etc.; m is 1 or higher; R^2 is selected from a hydrogen atom, a halogen, an alkyl, etc.; W is selected from a direct bond, $-CHR^2-$, $-CH=CR^2-$, etc.; E^2 is selected from a 5- to 7- membered saturated or unsaturated carbon ring, a 5- to 7- membered saturated or unsaturated hetero ring, a bicyclic ring system, etc.; each X is independently selected from a direct bond, a substituted or unsubstituted C_{1-4} methylene chain, O, etc., wherein said X at different places may be the same or different; B is selected from a hydrogen atom, -halo, -CN, etc.; B^1 is selected from B, wherein said B^1 and B may be the same or different; p is 1 or higher depending upon the size of the ring; A is selected from R^1 when o is 1, except that when L

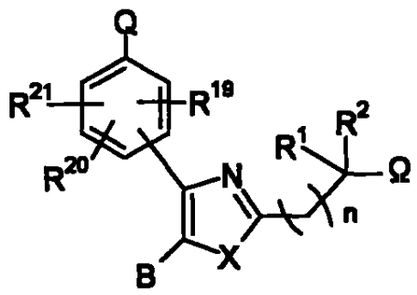
is a cyclic ring of more than 5 atoms, o is 1 or higher depending upon the size of the ring; V and V^1 are each independently selected from R^1 and N-alkyl substituted carboxamidyl (CONHR) wherein the alkyl group may be straight, branched, cyclic, or bicyclic, etc.; and n is 0 to 4.

WO 98/28264 discloses a thiophene derivative compound having the following formula



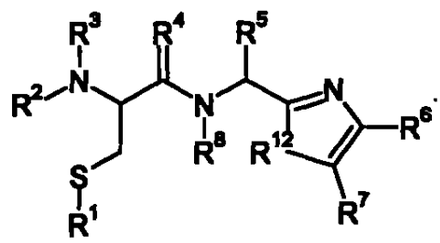
wherein B is N; A is selected from a C_{1-6} alkylsulfonyl, a C_{3-7} cycloalkylsulfonyl, a C_{3-7} cycloalkyl-C_{1-6} alkylsulfonyl, each of which is optionally mono-, di- or tri- substituted with a hydroxy group, a C_{1-4} alkyl or a halogen atom; Q is a $-C_{2-8}$ alkylene-W-C_{1-3} alkylene- or a $-C_{3-8}$ alkylene-, said $-C_{3-8}$ alkylene- is optionally substituted with up to four substituents independently selected from a fluorine atom, a C_{1-4} alkyl, -X-C_{1-5} alkylene-, etc., wherein X is a 5- or 6- membered aromatic ring optionally having one or two heteroatoms selected independently from an oxygen atom, a nitrogen atom and a sulfur atom; Z is carboxyl, a C_{1-6} alkoxycarbonyl, tetrazolyl, etc.; K is a bond, a C_{1-8} alkylene, a thio(C_{1-4})alkylene, etc., wherein said C_{1-8} alkylene is optionally mono-unsaturated and said K is optionally mono-, di- or tri-substituted with a fluorine atom, methyl or chlorine atom; and M is -Ar, $-Ar^1$-V-AP, $-Ar^1$-S-AP, etc., wherein Ar, Ar^1 and AP are each independently selected from a partially saturated, fully saturated or fully unsaturated 5- to 8- membered ring optionally having one to four heteroatoms selected from an oxygen atom, a sulfur atom and a nitrogen atom, etc.; or a pharmaceutically acceptable salt thereof or a prodrug thereof.

Furthermore, WO 01/26656 (JP-A-2003-511416) discloses a compound having the following formula



wherein Ω is $-NR^{46}R^{47}$ or $-OR^{48}$, wherein R^{46} and R^{47} are each independently selected from a hydrogen atom, an alkyl, a cycloalkyl, etc., and R^{48} is selected from a hydrogen atom, an alkyl, an alkynyl, etc.; B is a hydrogen atom or an alkyl; Q is selected from a hydrogen atom, $-OR^{22}$, $-SR^{22}$, etc., wherein R^{22} is selected from a hydrogen atom, an alkyl, an aryl optionally substituted with an alkyl, a hydroxyl group, a halogen atom, etc., etc.; R^{19}, R^{20} and R^{21} are each independently selected from a hydrogen atom, a halogen atom, a hydroxy group, etc.; X is NH or S; N is 0 to 6; R^1 and R^2 are each selected from a hydrogen atom, an alkyl and a cycloalkyl.

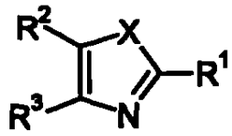
WO 97/30053 discloses a compound having the following formula



wherein R^1 is a hydrogen atom, a lower alkyl, a cycloalkylthio or a lower alkylthio, and R^2 and R^3 are each independently a hydrogen atom or a lower alkyl; or R^1 and R^2 may form $-CH_2-$, -CO- or $-C(CH_3)_2-$; R^4 is H2 or O; R^5 is selected from a hydrogen atom, a substituted or unsubstituted lower alkyl, a lower alkenyl, etc.; R^6 and R^7 are each independently selected from a hydrogen atom, $-C(O)NHCHR^{13}CO_2R^{14}$, a substituted or unsubstituted lower alkyl, etc., wherein R^{13} is selected from a substituted or unsubstituted lower alkyl, etc., and R^{14} is a hydrogen atom or lower alkyl, or R^6 and R^7 may form an aryl or

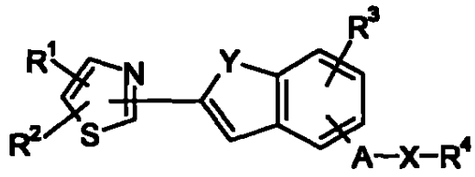
a heterocyclyl; R^8 and R^9 are each independently selected from a hydrogen atom, a substituted or unsubstituted lower alkyl, a cycloalkyl, etc.; and R^{12} is NR^9, S or O; or a pharmaceutically acceptable salt thereof.

WO 99/21555 and JP-A-2000-302680 disclose a compound having the following formula



wherein R^1 is selected from a hydrogen atom, a hydrocarbon group which may be substituted, a heterocyclic group which may be substituted, etc.; at least one of R^2 and R^3 is a hydrogen atom, a pyridyl which may be substituted or an aromatic hydrocarbon group which may be substituted, and the other is a pyridyl which may be substituted; and X is a sulfur atom which may be oxidized, an oxygen atom or a group represented by the formula NR^4, wherein R^4 is a hydrogen atom, a hydrocarbon group which may be substituted or an acyl; or a salt thereof, which may be N-oxidized.

JP-A-5-202040 discloses a compound having the following formula



wherein R^1 is an alkyl which may be substituted, or a cycloalkyl, tricycloalkyl or arylheterocyclic group which may be substituted; and R^2 is a hydrogen atom or a halogen atom, or R^1 and R^2, together with the adjacent atom, form a cycloalkene ring or an N-containing heterocyclic ring; R^3 is selected from a hydrogen atom, a halogen atom, OH, etc.; R^4 is selected from a hydrogen atom, an acyl group, CN, etc.; A is an alkylene, an alkenylene or a single bond; X is a single bond, O or S; and

Y is O or S, or a salt thereof.

However, these publications do not disclose a compound having a structure of the compound of the present invention, not to mention any description suggestive thereof.

SUMMARY OF THE INVENTION

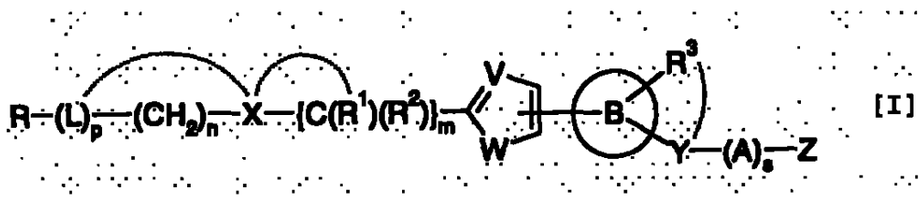
The present invention aims at providing a compound having a superior selective PTP1B inhibitory activity and an inhibitory activity of receptor tyrosine kinase negative regulator based thereon, which is useful as a therapeutic agent for diabetes, a therapeutic agent for hyperlipidemia, obesity or diabetic complication, and a therapeutic agent for a disease such as neurodegenerative disease and the like.

It is an object of the present invention to provide a PTP1B inhibitor, a therapeutic agent for diabetes, a therapeutic agent for hyperlipidemia, a therapeutic agent for obesity or a therapeutic agent for diabetic complication.

The present inventors have conducted intensive studies with the aim of achieving the above-mentioned object and found that a 5-membered heteroaromatic ring compound represented by the following formula [I] has a high PTP1B inhibitory activity but a lower inhibitory activity against other protein tyrosine phosphatases, namely, a superior selective PTP1B inhibitory activity absent in conventional compounds, and useful as a PTP1B inhibitor, a therapeutic agent for diabetes, a therapeutic agent for hyperlipidemia, a therapeutic agent for obesity or a therapeutic agent for diabetic complication, which resulted in the completion of the present invention.

The present invention relates to compounds and pharmaceutical use thereof represented by the following [1] to [113].

[1] A 5-membered heteroaromatic ring compound represented by the formula [I]



[I]

wherein

V is =N- or =CH-;

W is -S- or -O-;

m is 0, 1 or 2;

R^1 and R^2 are each independently a hydrogen atom or a C_{1-4} alkyl group;

X is $-N(R^4)-$, $-N(R^5)-CO-O-$, $-SO_2-N(R^5)-$, $-N(R^5)-SO_2-$, $-N(R^6)-SO_2-N(R^5)-$, $-CO-N(R^7)-$, $-N(R^8)-CO-$, $-N(R^9)-CO-N(R^5)-$, $-N(R^{10})-(CH_2)_k-N(R^5)-$, $-N(R^{10})-(CH_2)_k-N(R^5)-CO-$, $-C(R^{10})=N-N(R^7)-$, $-N(R^{10})-(CH_2)_k-CH(R^6)-$, $-O-$, $-S-$ or $-SO_2-$

wherein

k is 0 or an integer of 1 to 4,

R^4, R^5, R^6, R^7, R^8, R^9 and R^{10} are each independently

(1) a hydrogen atom,

(2) a C_{1-6} alkyl group

wherein said C_{1-6} alkyl group is optionally substituted by

(a) an optionally substituted aryl group,

(b) an optionally substituted heteroaromatic ring group,

(c) a carboxy group,

(d) a C_{1-4} alkoxycarbonyl group,

(e) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom, an optionally substituted aryl group, an optionally substituted heteroaromatic ring group, a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by substituent(s) selected from the group consisting of an optionally substituted aryl group, an optionally substituted heteroaromatic ring group, a C_{1-4} alkoxy group optionally substituted by an aryl group and an optionally substituted aryloxy group, or, together with the

nitrogen atom bonded thereto, may form an indoline ring or may form a 5- to 7-membered hetero ring optionally further containing at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom,

(f) $-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are as defined above,

(g) $-O-R^{17}$

wherein R^{17} is a hydrogen atom, an optionally substituted aryl group, an optionally substituted heteroaromatic ring group or a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by substituent(s) selected from the group consisting of an optionally substituted aryl group, an optionally substituted heteroaromatic ring group, a C_{1-4} alkoxy group optionally substituted by an aryl group and an optionally substituted aryloxy group,

(h) $-CO-R^{17}$

wherein R^{17} is as defined above,

(i) $-SO_2-R^{17}$

wherein R^{17} is as defined above or

(j) a C_{3-7} cycloalkyl group,

(3) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are as defined above,

(4) $-SO_2-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are as defined above,

(5) $-CO-R^{17}$

wherein R^{17} is as defined above,

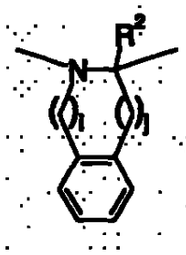
(6) $-SO_2-R^{17}$

wherein R^{17} is as defined above,

(7) an optionally substituted aryl group,

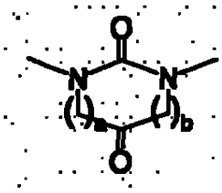
(8) an optionally substituted heteroaromatic ring group, or

(9) R^4 and R^1 are optionally linked to form



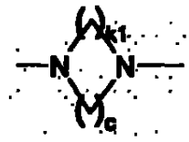
wherein i and j are each independently 0, 1 or 2 and R^2 is as defined above,

(10) R^5 and R^9 are optionally linked to form



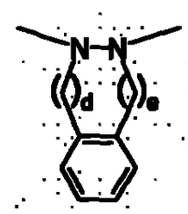
wherein a and b are each independently 0, 1 or 2,

(11) R^5 and R^{10} are optionally linked to form



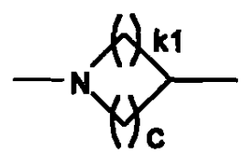
wherein k1 and c are each independently 0 or an integer of 1 to 4,

(12) R^5 and R^{10} are optionally linked to form



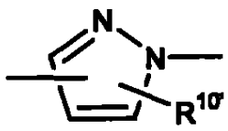
wherein d and e are each independently 0, 1 or 2,

(13) R^5 and R^{10} are optionally linked to form



wherein k1 and c are as defined above, or

(14) R^7 and R^{10} are optionally linked to form



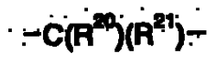
wherein $R^{10'}$ is a hydrogen atom or a C_{1-6} alkyl group;

n is 0 or an integer of 1 to 4;

p is 0 or 1;

L is

(1)



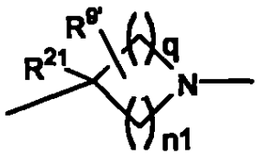
wherein

R^{20} is

(a) a hydrogen atom,

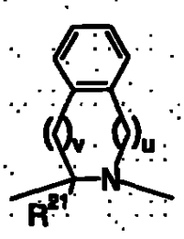
(b) a C_{1-6} alkyl group, or

(c) optionally linked with R^4 or R^8 to form



wherein n1 and q are each independently 0 or an integer of 1 to 4, $R^{9'}$ is a hydrogen atom, a hydroxyl group, a C_{1-6} alkyl group, a carboxy group or a C_{1-6} alkoxy group, or

(d) optionally linked with R^4 to form

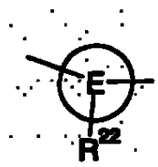


wherein u and v are each independently 0, 1 or 2,

R^{21} is a hydrogen atom, a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by an optionally

substituted aryl group or an optionally substituted heteroaromatic ring group, an optionally substituted aryl group or an optionally substituted heteroaromatic ring group,

(2)



wherein

E is an aryl group or a heteroaromatic ring group,

R^{22} is

(a) a hydrogen atom,

(b) a halogen atom,

(c) a C_{1-4} alkyl group,

(d) a C_{1-4} alkoxy group optionally substituted by a carboxy group,

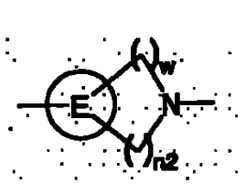
(e) a C_{1-6} alkylthio group,

(f) a nitro group,

(g) $-N(R^{23})(R^{24})$

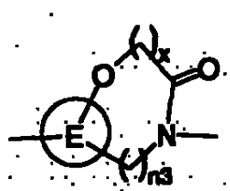
wherein R^{23} and R^{24} are each independently a hydrogen atom, a C_{1-6} alkyl group, a C_{1-4} alkylcarbonyl group wherein said C_{1-4} alkylcarbonyl group is optionally substituted by an amino group, a C_{1-4} alkylamino group or a di(C_{1-4} alkyl)amino group, or a C_{1-4} alkylsulfonyl group, or

(h) optionally linked with R^4 to form



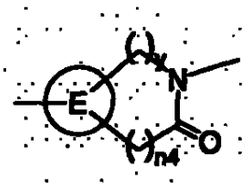
wherein n2 and w are each independently 0 or an integer of 1 to 3 and E is as defined above,

(i) optionally linked with R^4 to form



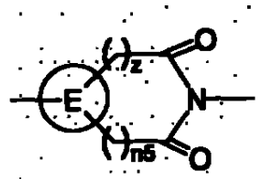
wherein n3 and x are each independently 0 or 1 and E is as defined above,

(j) optionally linked with R^7 to form



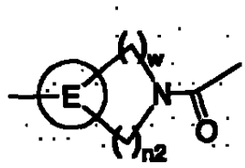
wherein n4 and y are each independently 0, 1 or 2 and E is as defined above,

(k) optionally linked with R^7 to form



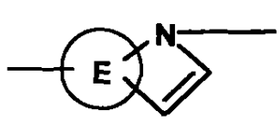
wherein n5 and z are each independently 0 or 1 and E is as defined above,

(l) optionally linked with R^8 to form



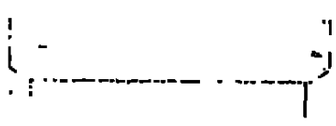
wherein n2 and w are each independently 0 or an integer of 1 to 3 and E is as defined above, or

(m) optionally linked with R^4 to form



wherein E is as defined above

or



(3)



wherein

R^{20}, R^{21} and E are as defined above,

R^{25} is

(a) a hydrogen atom,

(b) a halogen atom,

(c) a C_{1-4} alkyl group,

(d) a C_{1-4} alkoxy group optionally substituted by a carboxy group,

(e) a C_{1-6} alkylthio group,

(f) a nitro group or

(g) $-N(R^{23})(R^{24})$

wherein R^{23} and R^{24} are as defined above;

R is $-COO(R^{19})$, $-A^1-COO(R^{19})$ or $-O-A^1-COO(R^{19})$

wherein A^1 is a C_{1-4} alkylene group and R^{19} is a hydrogen atom or a C_{1-4} alkyl group;

B is an aryl group or a heteroaromatic ring group;

R^3 is

(1) a hydrogen atom,

(2) a halogen atom,

(3) a C_{1-6} alkyl group,

(4) a C_{1-6} alkoxy group,

(5) a C_{1-6} alkylamino group,

(6) a di(C_{1-6} alkyl)amino group,

(7) a cyano group,

(8) a nitro group,

(9) a C_{1-4} haloalkyl group,

(10) $-S-R^{18}$ wherein R^{18} is a C_{1-6} alkyl group or an aryl group,

(11) $-SO-R^{18}$ wherein R^{18} is a C_{1-6} alkyl group or an aryl group,

(12) $-SO_2-R^{18}$ wherein R^{18} is a C_{1-6} alkyl group or an aryl group,

(13) an aryl group or

(14) a heterocyclic group;

Y is -O-, -S-, -SO-, $-SO_2-$, $-N(R^{11})-$, $-N(R^{12})-CO-$, $-N(R^{12})-SO_2-$, $-SO_2-N(R^{12})-$, $-C(R^{13})(R^{14})-$, -CO-, $-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$

wherein

R^{11} is

(1) a hydrogen atom,

(2) a C_{1-8} alkyl group

wherein said C_{1-8} alkyl group is optionally substituted by substituent(s) selected from the group consisting of

(a) a C_{3-7} cycloalkyl group,

(b) an optionally substituted aryl group,

(c) an optionally substituted heterocyclic group,

(d) a hydroxyl group,

(e) a C_{1-4} alkylamino group and

(f) a di(C_{1-4} alkyl)amino group,

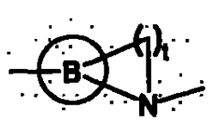
(3) a C_{2-4} alkenyl group,

(4) a C_{1-4} alkylsulfonyl group,

(5) a C_{1-4} alkylcarbonyl group

wherein said C_{1-4} alkylcarbonyl group is optionally substituted by a hydroxyl group or a C_{1-4} alkoxy group, or

(6) optionally linked with R^3 to form



wherein t is an integer of 1 to 4 and B is as defined above,

R^{12} is

(1) a hydrogen atom,

(2) a C_{1-8} alkyl group

wherein said C_{1-8} alkyl group is optionally substituted by substituent(s) selected from the group consisting of

(a) a C_{3-7} cycloalkyl group,

(b) an optionally substituted aryl group,

(c) an optionally substituted heterocyclic group,

(d) a hydroxyl group,

(e) a C_{1-4} alkylamino group and

(f) a di(C_{1-4} alkyl)amino group,

(3) a C_{2-4} alkenyl group,

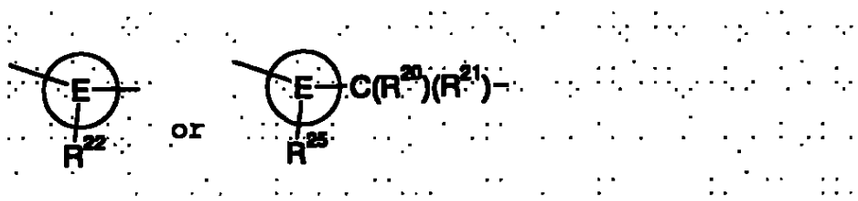
(4) a C_{1-4} alkylsulfonyl group or

(5) a C_{1-4} alkylcarbonyl group

wherein said C_{1-4} alkylcarbonyl group is optionally substituted by a hydroxyl group or a C_{1-4} alkoxy group,

R^{13} and R^{14} are each independently a hydrogen atom, a C_{1-4} alkyl group, or optionally form a C_{3-7} cycloalkane together with the carbon atom bonded thereto, or optionally form, together with the carbon atom bonded thereto, a 5- to 7-membered hetero ring optionally having at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom, provided that,

when m is 0, p is 1 and L is



wherein R^{20} and R^{21} are each a hydrogen atom, E is a phenyl group, R^{22} is a hydrogen atom, a halogen atom, a C_{1-4} alkyl group, a C_{1-4} alkoxy group or a nitro group, and R^{25} is a hydrogen atom, a halogen atom, a C_{1-4} alkyl group, a C_{1-4} alkoxy group or a nitro group,

Y should be

$-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$ wherein R^{12}, R^{13} and R^{14} are as defined above;

s is 0 or 1;

A is a C_{1-4} alkylene group optionally substituted by a C_{3-7}

cycloalkyl group;

Z is

(1) a C_{3-7} cycloalkyl group

wherein said C_{3-7} cycloalkyl group is optionally substituted by an aryl group wherein said aryl group is optionally substituted by a halogen atom or a C_{1-6} alkyl group, or a heteroaromatic ring group wherein said heteroaromatic ring group is optionally substituted by a halogen atom or a C_{1-6} alkyl group,

(2) an aryl group

wherein said aryl group is optionally substituted by substituent(s) selected from the group consisting of

(a) a heterocyclic group optionally substituted by a C_{1-4} alkyl group or a C_{1-4} alkylcarbonyl group,

(b) a C_{3-7} cycloalkyl group optionally substituted by a hydroxyl group, an oxo group, a halogen atom or a C_{1-6} alkyl group,

(c) a carboxy group,

(d) a halogen atom,

(e) a C_{1-6} alkyl group,

(f) a C_{1-4} haloalkyl group,

(g) a C_{1-4} alkylamino group,

(h) a di(C_{1-4} alkyl)amino group,

(i) a C_{1-6} alkylthio group,

(j) a C_{1-4} alkoxy group,

(k) a C_{1-4} alkylcarbonyl group and

(l) a nitro group,

(3) a heteroaromatic ring group

wherein said heteroaromatic ring group is optionally substituted by substituent(s) selected from the group consisting of

(a) a heterocyclic group optionally substituted by a C_{1-4} alkyl group or a C_{1-4} alkylcarbonyl group,

(b) a C_{3-7} cycloalkyl group optionally substituted by a

hydroxyl group, an oxo group, a halogen atom or a C_{1-6} alkyl group,

(c) a carboxy group,

(d) a halogen atom,

(e) a C_{1-8} alkyl group,

(f) a C_{1-4} haloalkyl group,

(g) a C_{1-4} alkylamino group,

(h) a di(C_{1-4} alkyl)amino group,

(i) a C_{1-6} alkylthio group,

(j) a C_{1-4} alkoxy group,

(k) a C_{1-4} alkylcarbonyl group and

(l) an aryl group optionally substituted by a halogen atom or a C_{1-4} haloalkyl group,

(4) an indanyl group or

(5) a piperazinyl group

wherein said piperazinyl group is optionally substituted by substituent(s) selected from the group consisting of

(a) a phenyl group,

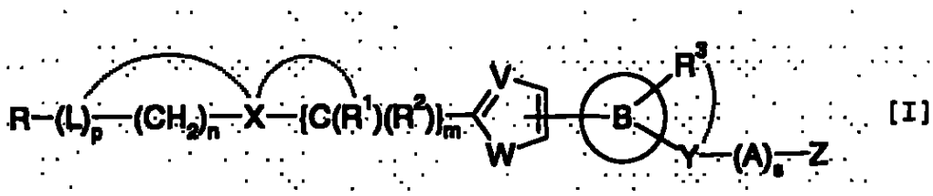
(b) a phenyl C_{1-4} alkyl group,

(c) a benzoyl group optionally substituted by a halogen atom and

(d) a phenyl C_{1-4} alkoxycarbonyl group

or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[2] The 5-membered heteroaromatic ring compound of [1], which is represented by the formula [I]



[I]

wherein

V is =N- or =CH-;

W is -S- or -O-;

m is 0, 1 or 2;

R^1 and R^2 are each independently a hydrogen atom or a C_{1-4} alkyl group;

X is $-N(R^4)-$, $-N(R^5)-CO-O-$, $-SO_2-N(R^5)-$, $-N(R^5)-SO_2-$, $-N(R^6)-SO_2-N(R^5)-$, $-CO-N(R^7)-$, $-N(R^8)-CO-$, $-N(R^9)-CO-N(R^5)-$, $-N(R^{10})-(CH_2)_k-N(R^5)-$, $-O-$, $-S-$ or $-SO_2-$

wherein

k is 0 or an integer of 1 to 4,

R^4, R^5, R^6, R^7, R^8, R^9 and R^{10} are each independently

(1) a hydrogen atom,

(2) a C_{1-6} alkyl group

wherein said C_{1-6} alkyl group is optionally substituted by

(a) an optionally substituted aryl group,

(b) an optionally substituted heteroaromatic ring group,

(c) a carboxy group,

(d) a C_{1-4} alkoxycarbonyl group,

(e) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom, an optionally substituted aryl group, an optionally substituted heteroaromatic ring group, a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by substituent(s) selected from the group consisting of an optionally substituted aryl group, an optionally substituted heteroaromatic ring group, a C_{1-4} alkoxy group optionally substituted by an aryl group and an optionally substituted aryloxy group, or, together with the nitrogen atom bonded thereto, may form an indoline ring or may form a 5- to 7-membered hetero ring optionally further containing at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom,

(f) $-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are as defined above,

(g) $-O-R^{17}$

wherein R^{17} is a hydrogen atom, an optionally substituted aryl

group, an optionally substituted heteroaromatic ring group or a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by substituent(s) selected from the group consisting of an optionally substituted aryl group, an optionally substituted heteroaromatic ring group, a C_{1-4} alkoxy group optionally substituted by an aryl group and an optionally substituted aryloxy group,

(h) $-CO-R^{17}$

wherein R^{17} is as defined above,

(i) $-SO_2-R^{17}$

wherein R^{17} is as defined above or

(j) a C_{3-7} cycloalkyl group,

(3) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are as defined above,

(4) $-SO_2-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are as defined above,

(5) $-CO-R^{17}$

wherein R^{17} is as defined above,

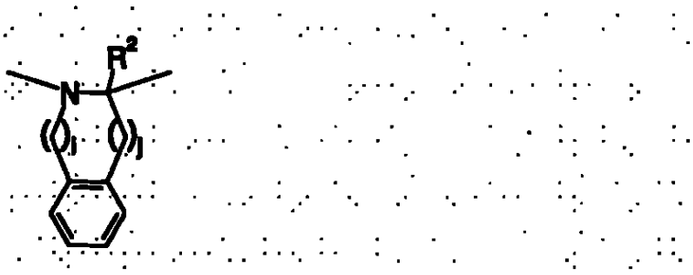
(6) $-SO_2-R^{17}$

wherein R^{17} is as defined above,

(7) an optionally substituted aryl group,

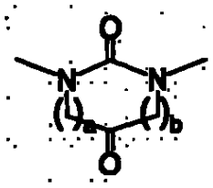
(8) an optionally substituted heteroaromatic ring group, or

(9) R^4 and R^1 are optionally linked to form



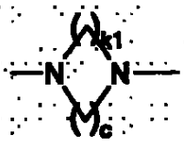
wherein i and j are each independently 0, 1 or 2 and R^2 is as defined above,

(10) R^5 and R^9 are optionally linked to form



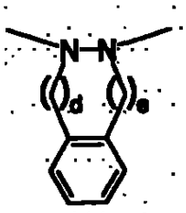
wherein a and b are each independently 0, 1 or 2,

(11) R^5 and R^{10} are optionally linked to form



wherein k1 and c are each independently 0 or an integer of 1 to 4, or

(12) R^5 and R^{10} are optionally linked to form



wherein d and e are each independently 0, 1 or 2;

n is 0 or an integer of 1 to 4;

p is 0 or 1;

L is

(1)



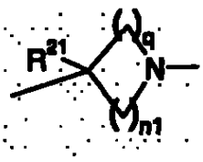
wherein

R^{20} is

(a) a hydrogen atom,

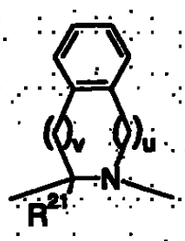
(b) a C_{1-6} alkyl group, or

(c) optionally linked with R^4 to form



wherein n1 and q are each independently 0 or an integer of 1 to 4, or

(d) optionally linked with R^4 to form



wherein u and v are each independently 0, 1 or 2,

R^{21} is a hydrogen atom, a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by an optionally substituted aryl group or an optionally substituted heteroaromatic ring group, an optionally substituted aryl group or an optionally substituted heteroaromatic ring group,

(2)



wherein

E is an aryl group or a heteroaromatic ring group,

R^{22} is

(a) a hydrogen atom,

(b) a halogen atom,

(c) a C_{1-4} alkyl group,

(d) a C_{1-4} alkoxy group optionally substituted by a carboxy group,

(e) a C_{1-6} alkylthio group,

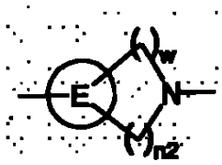
(f) a nitro group,



(g) $-N(R^{23})(R^{24})$

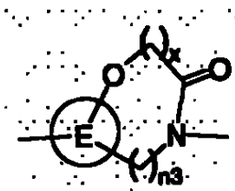
wherein R^{23} and R^{24} are each independently a hydrogen atom, a C_{1-6} alkyl group, a C_{1-4} alkylcarbonyl group wherein said C_{1-4} alkylcarbonyl group is optionally substituted by an amino group, a C_{1-4} alkylamino group or a di(C_{1-4} alkyl)amino group, or a C_{1-4} alkylsulfonyl group, or

(h) optionally linked with R^4 to form



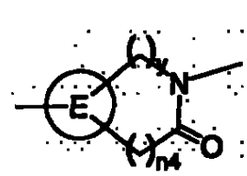
wherein n2 and w are each independently 0 or an integer of 1 to 3 and E is as defined above,

(i) optionally linked with R^4 to form



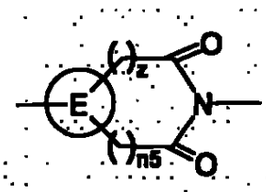
wherein n3 and x are each independently 0 or 1 and E is as defined above,

(j) optionally linked with R^7 to form



wherein n4 and y are each independently 0, 1 or 2 and E is as defined above,

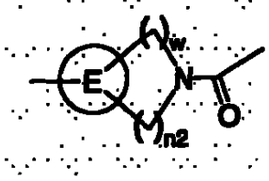
(k) optionally linked with R^7 to form



wherein n5 and z are each independently 0 or 1 and E is as

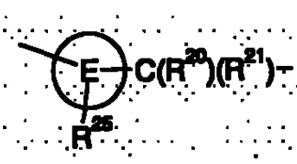
defined above, or

(1) optionally linked with R^8 to form



wherein n2 and w are each independently 0 or an integer of 1 to 3 and E is as defined above, or

(3)



wherein

R^{20}, R^{21} and E are as defined above,

R^{25} is

(a) a hydrogen atom,

(b) a halogen atom,

(c) a C_{1-4} alkyl group,

(d) a C_{1-4} alkoxy group optionally substituted by a carboxy group,

(e) a C_{1-6} alkylthio group,

(f) a nitro group or

(g) $-N(R^{23})(R^{24})$

wherein R^{23} and R^{24} are as defined above;

R is $-COO(R^{19})$, $-A^1-COO(R^{19})$ or $-O-A^1-COO(R^{19})$

wherein A^1 is a C_{1-4} alkylene group and R^{19} is a hydrogen atom or a C_{1-4} alkyl group;

B is an aryl group or a heteroaromatic ring group;

R^3 is

(1) a hydrogen atom,

(2) a halogen atom,

(3) a C_{1-8} alkyl group,

(4) a C_{1-6} alkoxy group,

(5) a C_{1-6} alkylamino group,

(6) a di(C_{1-6} alkyl)amino group,

(7) a cyano group,

(8) a nitro group,

(9) a C_{1-4} haloalkyl group,

(10) $-S-R^{18}$ wherein R^{18} is a C_{1-6} alkyl group or an aryl group,

(11) $-SO-R^{18}$ wherein R^{18} is a C_{1-6} alkyl group or an aryl group, or

(12) $-SO_2-R^{18}$ wherein R^{18} is a C_{1-6} alkyl group or an aryl group;

Y is $-O-$, $-S-$, $-SO-$, $-SO_2-$, $-N(R^{11})-$, $-N(R^{12})-CO-$, $-N(R^{12})-SO_2-$, $-SO_2-N(R^{12})-$, $-C(R^{13})(R^{14})-$, $-CO-$, $-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$

wherein

R^{11} is

(1) a hydrogen atom,

(2) a C_{1-8} alkyl group

wherein said C_{1-8} alkyl group is optionally substituted by substituent(s) selected from the group consisting of

(a) a C_{3-7} cycloalkyl group,

(b) an optionally substituted aryl group,

(c) an optionally substituted heterocyclic group,

(d) a hydroxyl group,

(e) a C_{1-4} alkylamino group and

(f) a di(C_{1-4} alkyl)amino group,

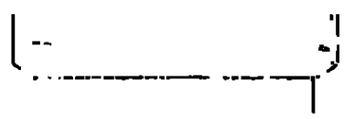
(3) a C_{2-4} alkenyl group,

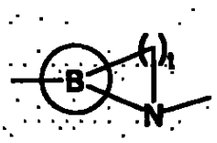
(4) a C_{1-4} alkylsulfonyl group,

(5) a C_{1-4} alkylcarbonyl group

wherein said C_{1-4} alkylcarbonyl group is optionally substituted by a hydroxyl group or a C_{1-4} alkoxy group, or

(6) optionally linked with R^3 to form





wherein t is an integer of 1 to 4 and B is as defined above,

R^{12} is

(1) a hydrogen atom,

(2) a C_{1-8} alkyl group

wherein said C_{1-8} alkyl group is optionally substituted by substituent(s) selected from the group consisting of

(a) a C_{3-7} cycloalkyl group,

(b) an optionally substituted aryl group,

(c) an optionally substituted heterocyclic group,

(d) a hydroxyl group,

(e) a C_{1-4} alkylamino group and

(f) a di(C_{1-4} alkyl)amino group,

(3) a C_{2-4} alkenyl group,

(4) a C_{1-4} alkylsulfonyl group or

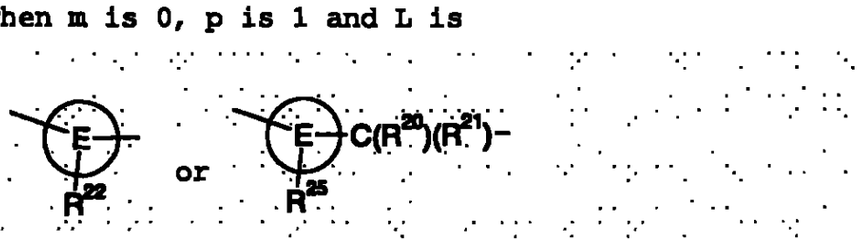
(5) a C_{1-4} alkylcarbonyl group

wherein said C_{1-4} alkylcarbonyl group is optionally substituted by a hydroxyl group or a C_{1-4} alkoxy group,

R^{13} and R^{14} are each independently a hydrogen atom, a C_{1-4} alkyl group, or optionally form a C_{3-7} cycloalkane together with the carbon atom bonded thereto, or optionally form, together with the carbon atom bonded thereto, a 5- to 7-membered hetero ring optionally having at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom,

provided that,

when m is 0, p is 1 and L is



wherein R^{20} and R^{21} are each a hydrogen atom, E is a phenyl

group, R^{22} is a hydrogen atom, a halogen atom, a C_{1-4} alkyl group, a C_{1-4} alkoxy group or a nitro group, and R^{25} is a hydrogen atom, a halogen atom, a C_{1-4} alkyl group, a C_{1-4} alkoxy group or a nitro group,

Y should be

$-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$ wherein R^{12}, R^{13} and R^{14} are as defined above;

s is 0 or 1;

A is a C_{1-4} alkylene group optionally substituted by a C_{3-7} cycloalkyl group;

Z is

(1) a C_{3-7} cycloalkyl group

wherein said C_{3-7} cycloalkyl group is optionally substituted by an aryl group wherein said aryl group is optionally substituted by a halogen atom or a C_{1-6} alkyl group, or a heteroaromatic ring group wherein said heteroaromatic ring group is optionally substituted by a halogen atom or a C_{1-6} alkyl group,

(2) an aryl group

wherein said aryl group is optionally substituted by substituent(s) selected from the group consisting of

(a) a heterocyclic group optionally substituted by a C_{1-4} alkyl group or a C_{1-4} alkylcarbonyl group,

(b) a C_{3-7} cycloalkyl group optionally substituted by a hydroxyl group, an oxo group, a halogen atom or a C_{1-6} alkyl group,

(c) a carboxy group,

(d) a halogen atom,

(e) a C_{1-8} alkyl group,

(f) a C_{1-4} haloalkyl group,

(g) a C_{1-4} alkylamino group,

(h) a di(C_{1-4} alkyl)amino group,

(i) a C_{1-6} alkylthio group,

(j) a C_{1-4} alkoxy group, and

(k) a C_{1-4} alkylcarbonyl group,

(3) a heteroaromatic ring group

wherein said heteroaromatic ring group is optionally substituted by substituent(s) selected from the group consisting of

(a) a heterocyclic group optionally substituted by a C_{1-4} alkyl group or a C_{1-4} alkylcarbonyl group,

(b) a C_{3-7} cycloalkyl group optionally substituted by a hydroxyl group, an oxo group, a halogen atom or a C_{1-6} alkyl group,

(c) a carboxy group,

(d) a halogen atom,

(e) a C_{1-8} alkyl group,

(f) a C_{1-4} haloalkyl group,

(g) a C_{1-4} alkylamino group,

(h) a di(C_{1-4} alkyl)amino group,

(i) a C_{1-6} alkylthio group,

(j) a C_{1-4} alkoxy group,

(k) a C_{1-4} alkylcarbonyl group and

(l) an aryl group optionally substituted by a halogen atom or a C_{1-4} haloalkyl group,

(4) an indanyl group or

(5) a piperazinyl group

wherein said piperazinyl group is optionally substituted by substituent(s) selected from the group consisting of

(a) a phenyl group,

(b) a phenyl C_{1-4} alkyl group,

(c) a benzoyl group optionally substituted by a halogen atom and

(d) a phenyl C_{1-4} alkoxycarbonyl group

or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[3] The 5-membered heteroaromatic ring compound of [1],

wherein, in the formula [I],

R^3 is

(1) a hydrogen atom,

(2) a halogen atom,

(3) a C_{1-6} alkyl group or

(4) a C_{1-4} alkoxy group;

Y is $-O-$, $-N(R^{11})-$, $-N(R^{12})-CO-$, $-C(R^{13})(R^{14})-$, $-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$

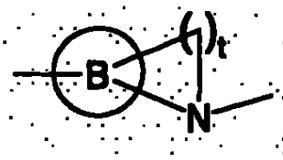
wherein

R^{11} is

(1) a hydrogen atom,

(2) a C_{1-8} alkyl group, or

(3) optionally linked with R^3 to form



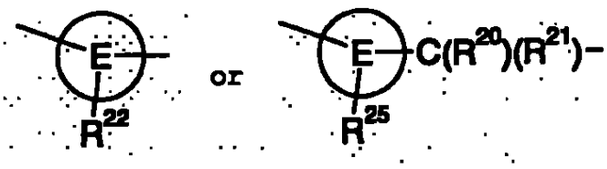
wherein t is 3 and B is as defined in [2] above,

R^{12} is a hydrogen atom or a C_{1-8} alkyl group,

R^{13} and R^{14} are each a hydrogen atom

provided that

when m is 0, p is 1, and L is



wherein R^{20} and R^{21} are each a hydrogen atom, E is a phenyl group, R^{22} is a hydrogen atom, a C_{1-4} alkoxy group or a nitro group, and R^{25} is a hydrogen atom, a C_{1-4} alkoxy group or a nitro group,

Y should be

$-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$ wherein R^{12},

R^{13} and R^{14} are as defined above;

s is 0 or 1;

A is a C_{1-4} alkylene group;

Z is an aryl group substituted by substituent(s) selected from the group consisting of

(a) a C_{3-7} cycloalkyl group optionally substituted by 1 to 3 substituent(s) selected from the group consisting of a halogen atom and a C_{1-6} alkyl group,

(b) a halogen atom,

(c) C_{1-8} alkyl group,

(d) a C_{1-4} haloalkyl group,

(e) a di(C_{1-4} alkyl)amino group,

(f) a C_{1-6} alkylthio group and

(g) a C_{1-4} alkylcarbonyl group,

or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[4] The 5-membered heteroaromatic ring compound of [3], wherein V is =N- and W is -S- or -O-, or V is =CH- and W is -S-, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[5] The 5-membered heteroaromatic ring compound of [4], wherein Z is a phenyl group substituted by a C_{1-8} alkyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[6] The 5-membered heteroaromatic ring compound of [5], wherein Y is $-C(R^{13})(R^{14})-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$ wherein R^{12}, R^{13} and R^{14} are as defined in [3] and s is 0, or Y is -O- or $-N(R^{11})-$ wherein R^{11} is as defined in [3], s is 1, and A is a methylene group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[7] The 5-membered heteroaromatic ring compound of [6], wherein V is =CH-, W is -S-, and the position of substitution of B on the thiophene ring formed by V together with W is the 4-position or 5-position, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[8] The 5-membered heteroaromatic ring compound of [7], wherein B is a phenyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[9] The 5-membered heteroaromatic ring compound of [8], wherein

m is 1;

R^1 and R^2 are each a hydrogen atom;

X is $-N(R^4)-$ or $-O-$

wherein R^4 is a C_{1-6} alkyl group optionally substituted by

(a) an aryl group,

(b) an heteroaromatic ring group optionally substituted by 1 to 3 C_{1-6} alkyl groups or

(c) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom or an aryl group wherein said aryl group is optionally substituted by 1 to 3 C_{1-6} alkyl groups;

n is 0 or 1;

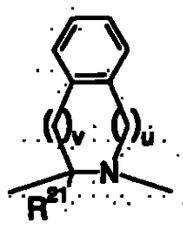
p is 0 or 1;

L is

(1)

$-C(R^{20})(R^{21})-$

wherein R^{20} is linked with R^4 to form



wherein u is 1, v is 1 and R^2 is as defined above,

R^{21} is a hydrogen atom, or

(2)



wherein E is an heteroaromatic ring group and R^{22} is a hydrogen atom;

R is $-COO(R^{19})$

wherein R^{19} is a hydrogen atom, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[10] The 5-membered heteroaromatic ring compound of [9], wherein X is $-N(R^4)$ wherein R^4 is as defined in [9], n is 1 and p is 0, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[11] The 5-membered heteroaromatic ring compound of [10], wherein R^4 is a methyl group substituted by a heteroaromatic ring group optionally substituted by one C_{1-6} alkyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[12] The 5-membered heteroaromatic ring compound of [11], wherein the heteroaromatic ring defined in [11] is a thiazolyl group, an oxazolyl group or a benzimidazolyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[13] The 5-membered heteroaromatic ring compound of [10], wherein R^4 is a methyl group substituted by $-CO-N(R^{15})(R^{16})$ wherein R^{15} is a hydrogen atom and R^{16} is an aryl group optionally substituted by one C_{1-6} alkyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[14] The 5-membered heteroaromatic ring compound of [6], wherein V is =N-, W is -S-, and the position of substitution of B on the thiazole ring formed by V together with W is the 4-position, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[15] The 5-membered heteroaromatic ring compound of [14], wherein B is a phenyl group, or a prodrug thereof, or a

pharmaceutically acceptable salt thereof.

[16] The 5-membered heteroaromatic ring compound of [15], wherein

m is 0 or 1;

R^1 and R^2 are each independently a hydrogen atom or a C_{1-4} alkyl group;

X is $-N(R^4)-$, $-N(R^5)-CO-O-$, $-SO_2-N(R^5)-$, $-CO-N(R^7)-$, $-N(R^9)-CO-N(R^5)-$, $-N(R^{10})-(CH_2)_k-N(R^5)-$, $-O-$, $-S-$ or $-SO_2-$

wherein

R^4 is

(1) a hydrogen atom,

(2) a C_{1-6} alkyl group

wherein said C_{1-6} alkyl group is optionally substituted by

(a) an aryl group optionally substituted by 1 to 3 substituent(s) selected from the group consisting of a halogen atom, a C_{1-8} alkyl group and a C_{1-4} haloalkyl group,

(b) a heteroaromatic ring group optionally substituted by 1 to 3 C_{1-8} alkyl group,

(c) a carboxy group,

(d) a C_{1-4} alkoxycarbonyl group,

(e) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom, an aryl group wherein said aryl group is optionally substituted by 1 to 3 substituent(s) selected from the group consisting of a C_{1-8} alkyl group, a C_{1-4} alkoxy group, a carboxy group and a di(C_{1-4} alkyl)amino group, a heteroaromatic ring group, a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by an aryl group, or, together with the nitrogen atom bonded thereto, may form a 5- to 7-membered hetero ring optionally further containing at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom,

(f) $-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom or an aryl group,

(g) $-O-R^{17}$

wherein R^{17} is an aryl group, or

(h) a C_{3-7} cycloalkyl group,

(3) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom, an aryl group wherein said aryl group is optionally substituted by 1 to 3 C_{1-8} alkyl groups, a C_{1-6} alkyl group, or, together with the nitrogen atom bonded thereto, may form an indoline ring or may form a 5- to 7-membered hetero ring optionally further containing at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom,

(4) $-SO_2-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently an aryl group or a C_{1-6} alkyl group,

(5) $-CO-R^{17}$

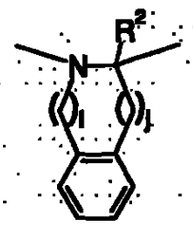
wherein R^{17} is an aryl group wherein said aryl group is optionally substituted by 1 to 3 substituent(s) selected from the group consisting of a C_{1-8} alkyl group and a C_{1-4} alkoxy group, a heteroaromatic ring group or a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by an aryl group optionally substituted by 1 to 3 substituent(s) selected from the group consisting of a halogen atom and a C_{1-8} alkyl group, a heteroaromatic ring group, a C_{1-4} alkoxy group optionally substituted by an aryl group or an aryloxy group optionally substituted by 1 to 3 C_{1-8} alkyl groups,

(6) $-SO_2-R^{17}$

wherein R^{17} is an aryl group,

(7) an aryl group, or

(8) optionally linked with R^1 to form



wherein i and j are each 1 and R^2 is as defined above,

R^5 is a hydrogen atom or a C_{1-6} alkyl group optionally substituted by an aryl group or a C_{3-7} cycloalkyl group,

R^7 is a hydrogen atom or a C_{1-6} alkyl group,

R^9 is a hydrogen atom or a C_{1-6} alkyl group,

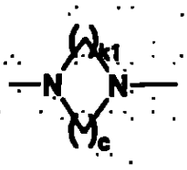
k is 2,

R^{10} is

(1) a hydrogen atom,

(2) a C_{1-6} alkyl group, or

(3) optionally linked with R^5 to form



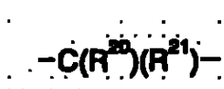
wherein k1 and c are each 2;

n is 0 or an integer of 1 to 3;

p is 0 or 1;

L is

(1)



wherein

R^{20} is

(a) a hydrogen atom,

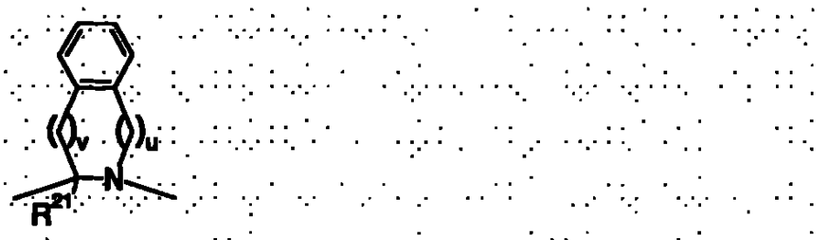
(b) a C_{1-6} alkyl group, or

(c) optionally linked with R^4 to form



wherein n1 and q are each independently an integer of 1 to 3, or

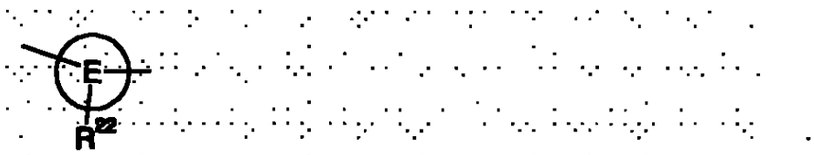
(d) optionally linked with R^4 to form



wherein u is 1 and v is 1,

R^{21} is a hydrogen atom, a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by an aryl group optionally substituted by 1 to 3 halogen atoms, or an aryl group or

(2)



wherein

E is an aryl group or a heteroaromatic ring group,

R^{22} is

(a) a hydrogen atom,

(b) a C_{1-4} alkoxy group optionally substituted by a carboxy group,

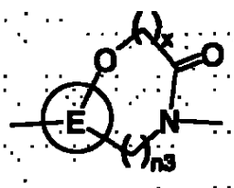
(c) a nitro group,

(d) $-N(R^{23})(R^{24})$

wherein R^{23} and R^{24} are each independently a hydrogen atom, a C_{1-4} alkylcarbonyl group wherein said C_{1-4} alkylcarbonyl group is optionally substituted by a C_{1-4} alkylamino group or a di(C_{1-4}

alkyl)amino group or a C_{1-4} alkylsulfonyl group, or

(e) optionally linked with R^4 to form



wherein n3 is 0, x is 1 and E is as defined above;

R is $-COO(R^{19})$

wherein R^{19} is a hydrogen atom or a C_{1-4} alkyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[17] The 5-membered heteroaromatic ring compound of [16], wherein m is 1 and R^1 and R^2 are each a hydrogen atom, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[18] The 5-membered heteroaromatic ring compound of [17], wherein X is $-N(R^4)$ wherein R^4 is as defined in [16], n is 1 and p is 0, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[19] The 5-membered heteroaromatic ring compound of [18], wherein

R^4 is a C_{1-6} alkyl group optionally substituted by

(a) an aryl group optionally substituted by 1 to 3 substituent(s) selected from the group consisting of a halogen atom, a C_{1-8} alkyl group and a C_{1-4} haloalkyl group,

(b) a heteroaromatic ring group optionally substituted by 1 to 3 C_{1-8} alkyl groups,

(c) a carboxy group,

(d) a C_{1-4} alkoxycarbonyl group,

(e) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom, an aryl group wherein said aryl group is optionally substituted by 1 to 3 substituent(s) selected from the group consisting of a C_{1-8} alkyl group, a C_{1-4} alkoxy group, a carboxy group and a

di(C_{1-4} alkyl)amino group, a heteroaromatic ring group, a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by an aryl group, or, together with the nitrogen atom bonded thereto, may form a 5- to 7-membered hetero ring optionally further containing at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom,

(f) $-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom or an aryl group,

(g) $-O-R^{17}$

wherein R^{17} is an aryl group, or

(h) a C_{3-7} cycloalkyl group,

or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[20] The 5-membered heteroaromatic ring compound of [19], wherein R^4 is a methyl group substituted by a heteroaromatic ring group optionally substituted by one C_{1-8} alkyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[21] The 5-membered heteroaromatic ring compound of [20], wherein the heteroaromatic ring defined in [20] is a thiazolyl group, an oxazolyl group, a benzimidazolyl group, a pyridyl group or a quinolyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[22] The 5-membered heteroaromatic ring compound of [19], wherein R^4 is a methyl group substituted by $-CO-N(R^{15})(R^{16})$ wherein R^{15} is a hydrogen atom and R^{16} is an aryl group optionally substituted by one C_{1-8} alkyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

[23] The 5-membered heteroaromatic ring compound of any of [1] to [22], which is selected from the group consisting of the following compounds, or a prodrug thereof, or a pharmaceutically acceptable salt thereof:

(1) 5-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}nicotinic acid;

(2) 4-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}benzoic acid;

(3) 6-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}nicotinic acid;

(4) 5-{4-[4-({methyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}nicotinic acid;

(5) 4-{4-[4-({methyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}benzoic acid;

(6) 6-[4-(4-{[(4-isopropylphenyl)(1-propylbutyl)amino]methyl}phenyl)thiazol-2-ylmethoxy]nicotinic acid;

(7) 5-[4-(4-{[(4-isopropylphenyl)(1-propylbutyl)amino]methyl}phenyl)thiazol-2-ylmethoxy]nicotinic acid;

(8) 5-[4-(4-{[isobutyl(4-isopropylphenyl)amino]methyl}phenyl)thiazol-2-ylmethoxy]nicotinic acid;

(9) 4-[4-(4-{[(4-isopropylphenyl)(1-propylbutyl)amino]methyl}phenyl)thiazol-2-ylmethoxy]benzoic acid;

(10) 3-[4-(4-{[(4-isopropylphenyl)(1-propylbutyl)amino]methyl}phenyl)thiazol-2-ylmethoxy]benzoic acid;

(11) 6-[4-(4-{[(1-ethylpropyl)(4-isopropylphenyl)amino]methyl}phenyl)thiazol-2-ylmethoxy]nicotinic acid;

(12) 5-[4-(4-{[(1-ethylpropyl)(4-isopropylphenyl)amino]methyl}phenyl)thiazol-2-ylmethoxy]nicotinic acid;

(13) 4-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethylthio}benzoic acid;

(14) 4-{4-[4-({methyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethylthio}benzoic acid;

(15) 4-(methyl-{4-[4-({methyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}sulfamoyl)benzoic acid;

(16) sodium 4-(methyl{4-[4-({methyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}sulfamoyl)butyrate;

(17) 4-{[(4-{4-[(4-cyclohexylphenylamino)methyl]phenyl}thiazol-2-yl)methylamino]methyl}benzoic acid;

(18) 4-({[4-(4-{[(4-cyclohexylphenyl)methylamino]methyl}phenyl)thiazol-2-yl]methylamino}methyl)benzoic acid;

(19) 4-[(methyl-{4-[4-({methyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-yl}amino)methyl]benzoic acid;

(20) 4-[({4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-yl}methylamino)methyl]benzoic acid;

(21) (S)-({4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}methylamino)phenylacetic acid;

(22) (S)-2-({4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}methylamino)-3-phenylpropionic acid;

(23) {benzyl[4-(4-{[(4-tert-

butylphenyl)isobutylamino]methyl}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(24) {benzyl[4-(4-{[(4-chloro-phenyl)isobutylamino]methyl}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(25) (benzyl{4-[4-({methyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(26) (benzyl{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(27) {1-[4-(4-{[(4-tert-butyl-phenyl)isobutylamino]methyl}phenyl)thiazol-2-ylmethyl]-3-phenylureido}acetic acid;

(28) {benzoyl-[4-(4-{[(4-tert-butylphenyl)isobutylamino]methyl}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(29) [[4-(4-{[(4-tert-butyl-phenyl)isobutylamino]methyl}phenyl)thiazol-2-ylmethyl]-(pyridin-2-ylcarbonyl)amino]acetic acid;

(30) [[4-(4-{[(4-tert-butyl-phenyl)isobutylamino]methyl}phenyl)thiazol-2-ylmethyl]-(pyridin-3-ylcarbonyl)amino]acetic acid;

(31) {benzenesulfonyl-[4-(4-{[(4-tert-butylphenyl)isobutylamino]methyl}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(32) 2-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(33) (S)-2-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(34) (S)-2-{4-[4-({methyl[4-(1-

propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(35) (S)-2-[4-(4-{[(1-ethylpropyl)-(4-isopropylphenyl)amino]methyl}phenyl)thiazol-2-ylmethyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(36) 4-({4-[4-(4-cyclohexylphenoxymethyl)phenyl]thiazol-2-yl}methylamino)benzoic acid;

(37) 4-[({4-[4-(4-cyclohexylphenoxymethyl)phenyl]thiazol-2-yl}methylamino)methyl]benzoic acid;

(38) 4-{[(4-{4-[4-(1,1-dimethylpropyl)phenoxymethyl]phenyl}thiazol-2-yl)methylamino]methyl}benzoic acid;

(39) 4-{(methyl-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-yl)amino]methyl}benzoic acid;

(40) sodium 4-{[methyl(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-yl)amino]methyl}-benzoate;

(41) (S)-[methyl-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]phenylacetic acid;

(42) (S)-2-[methyl-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]-3-phenylpropionic acid;

(43) (benzyl{4-[4-(2-tert-butyl-4-methyl-phenoxymethyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(44) [benzyl(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(45) 2-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(46) (S)-2-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-1,2,3,4-

tetrahydroisoquinoline-3-carboxylic acid;

(47) (R)-2-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(48) 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethoxy)nicotinic acid;

(49) 4-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethoxy)benzoic acid;

(50) 4-[methyl-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)sulfamoyl]benzoic acid;

(51) 4-[methyl-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)sulfamoyl]butyric acid;

(52) 4-({4-[4-(4-cyclohexylphenylcarbamoyl)phenyl]thiazol-2-yl}methylamino)benzoic acid;

(53) 4-[({4-[4-(4-cyclohexylphenylcarbamoyl)phenyl]thiazol-2-yl}methylamino)methyl]benzoic acid;

(54) [benzyl(4-{4-[4-(1-propylbutyl)phenylcarbamoyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(55) [benzyl(4-{4-[4-(1-propylbutyl)benzylcarbamoyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(56) {benzyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]-carbamoyl}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(57) {benzyl[4-(4-{ethyl-[4-(1-propylbutyl)benzyl]-carbamoyl}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(58) 5-{4-[4-({(2-hydroxy-2-methylpropyl)-[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}nicotinic acid;

(59) [[4-(4-{[(4-tert-butyl-phenyl)isobutylamino]methyl}phenyl)thiazol-2-ylmethyl]-

(morpholine-4-carbonyl)amino]acetic acid;

(60) sodium 5-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}-nicotinate;

(61) sodium (S)-2-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylate;

(62) sodium 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethoxy)nicotinate;

(63) 3-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}-5-methoxy-benzoic acid;

(64) (1-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-3-phenylureido)acetic acid;

(65) (1-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-3-p-tolylureido)acetic acid;

(66) [1-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-3-(4-isopropylphenyl)ureido]acetic acid;

(67) (1-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-3-methyl-3-phenylureido)acetic acid;

(68) 5-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}nicotinic acid;

(69) [3-phenyl-1-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)ureido]acetic acid;

(70) (3-(2,6-dimethylphenyl)-1-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-

ylmethyl}ureido)acetic acid;

(71) ({4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}phenylcarbamoylmethylamino)acetic acid;

(72) (1-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-3-isopropyl-ureido)acetic acid;

(73) 3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}-isoxazole-5-carboxylic acid;

(74) 5-[4-(4-{[(2-ethylbutyl)-(4-isopropylphenyl)amino]methyl}phenyl)thiazol-2-ylmethoxy]nicotinic acid;

(75) [{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-(piperidine-1-carbonyl)amino]acetic acid;

(76) 2-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethoxy)nicotinic acid;

(77) [{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-(p-tolylcarbamoylmethyl)amino]acetic acid;

(78) {{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-[(4-isopropylphenylcarbamoyl)methyl]amino}acetic acid;

(79) (1-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-3-methyl-3-phenylureido)acetic acid;

(80) (1-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-3-p-tolylureido)acetic acid;

(81) ((2,3-dihydro-indole-1-carbonyl)-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-

ylmethyl}amino)acetic acid;

(82) 3-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethoxy)pyridine-2-carboxylic acid;

(83) {[4-(4-{[(2-ethylbutyl)-(4-isopropylphenyl)amino]methyl}phenyl)thiazol-2-ylmethyl]phenylcarbamoylmethylamino}acetic acid;

(84) {[4-(4-{[(2-ethylbutyl)-(4-isopropylphenyl)amino]methyl}phenyl)thiazol-2-ylmethyl]-[(4-isopropylphenylcarbamoyl)methyl]amino}acetic acid;

(85) 4-(2-{carboxymethyl[4-(4-{[(2-ethylbutyl)-(4-isopropylphenyl)amino]methyl}phenyl)thiazol-2-ylmethyl]amino}-acetylamino)benzoic acid;

(86) 6-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethoxy)pyridine-2-carboxylic acid;

(87) 5-{4-[4-({isobutyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}nicotinic acid;

(88) (1-{4-[4-({isobutyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-3-phenylureido)acetic acid;

(89) 5-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}nicotinic acid methyl ester;

(90) 4-amino-3-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}benzoic acid;

(91) 3-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}benzoic acid;

(92) 3-({4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}amino)benzoic acid;

(93) 3-{4-[4-({[4-(1-

ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}-4-nitro-benzoic acid;

(94) ((1H-benzimidazol-2-ylmethyl)-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(95) [phenylcarbamoylmethyl(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(96) [(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-(pyridin-3-ylcarbamoylmethyl)amino]acetic acid;

(97) [[(4-dimethylaminophenylcarbamoyl)methyl]-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(98) [[(4-methoxyphenylcarbamoyl)methyl]-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(99) [[(isopropylphenylcarbamoyl)methyl]-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(100) [(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-(pyridin-2-ylcarbamoylmethyl)amino]acetic acid;

(101) [(2-oxo-2-pyrrolidin-1-yl-ethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(102) [(4-methylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(103) 4-(3-cyclohexylmethyl-3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}ureido)benzoic acid;

(104) 4-(3-isobutyl-3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}ureido)benzoic acid;

(105) (1-{4-[4-({isobutyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-3-methyl-3-phenylureido)acetic acid;

(106) ({4-[4-({isobutyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}phenylcarbamoylmethylamino)acetic acid;

(107) ({4-[4-({isobutyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-[(4-isopropylphenylcarbamoyl)methyl]amino}acetic acid;

(108) 4-acetylamino-3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}benzoic acid;

(109) 4-(2-dimethylaminoacetylamino)-3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}benzoic acid;

(110) ((1H-benzimidazol-2-ylmethyl)-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(111) [(1H-benzimidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(112) 3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}-4-methanesulfonylaminobenzoic acid;

(113) 4-isobutyrylamino-3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}benzoic acid;

(114) 4-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazine-6-carboxylic acid;

(115) 4-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-

ylmethyl}-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazine-8-carboxylic acid;

(116) ({4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-{methylphenylaminosulfonyl}amino)acetic acid;

(117) ([(4-isopropylphenylcarbamoyl)methyl]-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(118) ([(3,5-dimethylphenylcarbamoyl)methyl]-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(119) ([(4-dimethylaminophenylcarbamoyl)methyl]-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(120) ((benzylcarbamoylmethyl)-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(121) [{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-[2-(morpholin-4-yl)-2-oxo-ethyl]amino]acetic acid;

(122) [{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-(2-phenoxyethyl)amino]acetic acid;

(123) [{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-(2-phenylamino-ethyl)amino]acetic acid;

(124) 2-carboxymethoxy-5-({4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}methylamino)benzoic acid;

(125) 2-carboxymethoxy-5-[methyl(4-{4-[4-(1-

propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]benzoic acid;

(126) 3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}-4-(2-methylamino-acetylamino)benzoic acid;

(127) [(4-tert-butylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(128) [phenyl(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(129) [(2-phenoxyacetyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(130) [(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-(2-p-tolyloxy-acetyl)amino]acetic acid;

(131) (ethoxycarbonylmethyl{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid dihydrochloride;

(132) ((4-tert-butylthiazol-2-ylmethyl)-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(133) 6-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}-pyridine-2-carboxylic acid;

(134) [(2-benzyloxy-acetyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(135) [[2-(4-isopropylphenoxy)acetyl]-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(136) [(4,5-dimethylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-

ylmethyl)amino]acetic acid;

(137) 5-(4-{5-[4-(1-propylbutyl)phenoxymethyl]thiophen-2-yl}thiazol-2-ylmethoxy)nicotinic acid;

(138) ((4-tert-butylthiazol-2-ylmethyl)-{4-[6-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)benzoxazol-2-yl]thiazol-2-ylmethyl}amino)acetic acid;

(139) ((1H-benzimidazol-2-ylmethyl)-{4-[6-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)benzoxazol-2-yl]thiazol-2-ylmethyl}amino)acetic acid;

(140) 5-{4-[6-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)benzoxazol-2-yl]thiazol-2-ylmethoxy}nicotinic acid;

(141) [(5-tert-butylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(142) [{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-(2-oxo-2-piperidin-1-yl-ethyl)amino]acetic acid;

(143) 6-[methyl-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]pyridine-2-carboxylic acid;

(144) ({4-[6-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)benzoxazol-2-yl]thiazol-2-ylmethyl}amino)acetic acid;

(145) (S)-(carboxymethyl{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)phenylacetic acid;

(146) ((4,5-dimethylthiazol-2-ylmethyl)-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(147) [(5-tert-butyloxazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(148) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(149) (isobutoxycarbonylmethyl{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid dihydrochloride;

(150) ({4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-propoxycarbonylmethylamino)acetic acid dihydrochloride;

(151) 1-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)piperidine-4-carboxylic acid hydrochloride;

(152) 1-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}piperidine-4-carboxylic acid;

(153) 4-[4-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)piperazin-1-yl]benzoic acid;

(154) 4-(4-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-piperazin-1-yl)benzoic acid;

(155) 2-[4-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)piperazin-1-yl]benzoic acid;

(156) 3-[4-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)piperazin-1-yl]benzoic acid;

(157) 4-(4-{1-[4-(1-propylbutyl)benzyl]-1H-indol-3-yl}thiazol-2-ylmethoxy)benzoic acid;

(158) 4-{4-[1-(4-isopropylbenzyl)-5-(1-propylbutyl)-1H-benzimidazol-2-yl]thiazol-2-ylmethoxy}benzoic acid;

(159) 4-{4-[1-(6-methylpyridin-2-ylmethyl)-5-(1-propylbutyl)-1H-benzimidazol-2-yl]thiazol-2-ylmethoxy}benzoic acid;

(160) 2-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid;

(161) 4-[1-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-

ylmethyl)piperidin-4-yl]benzoic acid;

(162) 3-[1-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)piperidin-4-yl]benzoic acid;

(163) 6-[(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)carbamoyl]nicotinic acid;

(164) 2-[1-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)piperidin-4-yl]benzoic acid;

(165) 1-(4-{1-[4-(1-propylbutyl)benzyl]-1H-indol-3-yl}thiazol-2-ylmethyl)piperidine-4-carboxylic acid;

(166) 2-(4-{1-[4-(1-propylbutyl)benzyl]-1H-indol-3-yl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid;

(167) 3-[(4-{1-[4-(1-propylbutyl)benzyl]-1H-indol-3-yl}thiazol-2-ylmethyl)amino]benzoic acid;

(168) 6-[(2-aminoethyl)(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)carbamoyl]nicotinic acid hydrochloride;

(169) 2-(4-{1-[4-(1-propylbutyl)benzyl]-1H-benzimidazol-2-yl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid;

(170) 3-[4-(4-{1-[4-(1-propylbutyl)benzyl]-1H-benzimidazol-2-yl}thiazol-2-ylmethyl)piperazin-1-yl]benzoic acid;

(171) 4-[1-(4-{1-[4-(1-propylbutyl)benzyl]-1H-benzimidazol-2-yl}thiazol-2-ylmethyl)piperidin-4-yl]benzoic acid;

(172) 3-[4-(4-{1-[4-(1-propylbutyl)benzyl]-1H-indol-3-yl}thiazol-2-ylmethyl)piperazin-1-yl]benzoic acid;

(173) 3-(1-{4-[4-(3,4-dichloro-benzyloxy)phenyl]thiazol-2-ylmethyl}piperidin-4-yl)benzoic acid;

(174) 3-(1-{4-[4-(3,5-bis-trifluoromethylbenzyloxy)phenyl]thiazol-2-ylmethyl}piperidin-4-yl)benzoic acid;

(175) 3-(1-{4-[4-(4-butoxy-benzyloxy)phenyl]thiazol-2-ylmethyl}piperidin-4-yl)benzoic acid;

(176) 5-methyl-2-(4-{4-[4-(1-

propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-2H-pyrazole-3-carboxylic acid;

(177) 5-methyl-1-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-1H-pyrazole-3-carboxylic acid;

(178) 5-tert-butyl-1-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-1H-pyrazole-3-carboxylic acid;

(179) 5-tert-butyl-2-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-2H-pyrazole-3-carboxylic acid;

(180) (2S,4R)-4-hydroxy-1-(4-{1-[4-(1-propylbutyl)benzyl]-1H-indol-3-yl}thiazol-2-ylmethyl)pyrrolidine-2-carboxylic acid;

(181) 4-[4-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)piperidin-1-yl]benzoic acid;

(182) 1-(4-{1-[4-(1-propylbutyl)benzyl]-1H-indol-3-yl}thiazol-2-ylmethyl)-1H-indole-3-carboxylic acid;

(183) 1-(4-{2-phenyl-1-[4-(1-propylbutyl)benzyl]-1H-indol-3-yl}thiazol-2-ylmethyl)piperidine-4-carboxylic acid;

(184) 3-(1-{4-[4-(4-methyl-3-nitrobenzyloxy)phenyl]thiazol-2-ylmethyl}piperidin-4-yl)benzoic acid;

(185) 2-{4-[1-(4-isopropylbenzyl)-6-(morpholin-4-yl)-1H-benzimidazol-2-yl]thiazol-2-ylmethyl}-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid;

(186) 3-(4-{4-[1-(4-isopropylbenzyl)-6-(morpholin-4-yl)-1H-benzimidazol-2-yl]thiazol-2-ylmethyl}-piperazin-1-yl)benzoic acid;

(187) {benzyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)oxazol-2-ylmethyl]amino}acetic acid;

(188) 5-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethoxy)nicotinic acid;

(189) 4-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethoxy)benzoic acid;

(190) 4-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethylthio)benzoic acid;

(191) 4-{4-[4-(4-cyclohexylbenzyloxy)phenyl]thiazol-2-ylmethylthio}benzoic acid;

(192) 4-{4-[4-(4-cyclohexylbenzyloxy)phenyl]thiazol-2-ylmethanesulfonyl}benzoic acid;

(193) 4-[methyl-(4-{5-methyl-2-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)sulfamoyl]benzoic acid;

(194) 4-[methyl-(4-{5-methyl-2-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]benzoic acid;

(195) (benzyl{4-[5-methyl-2-(4-trifluoromethylbenzyloxy)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(196) [benzyl(4-{5-methyl-2-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(197) [benzyl(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(198) [benzyl(4-{4-[4-(1-ethylpropyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(199) (benzyl{4-[5-tert-butyl-2-(4-isobutylbenzyloxy)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(200) [benzyl(4-{5-chloro-2-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(201) [(4-{4-[4-(1-ethylpropyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-(4-fluoro-benzyl)amino]acetic acid;

(202) [(4-{4-[4-(1-ethylpropyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-(4-isopropylbenzyl)amino]acetic acid;

(203) [(4-{4-[4-(1-ethylpropyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-(4-trifluoromethylbenzyl)amino]acetic acid;

(204) [(4-chlorobenzyl)-(4-{4-[4-(1-ethylpropyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(205) [(3,5-dimethylbenzyl)-(4-{4-[4-(1-ethylpropyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(206) [(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-pyridin-2-ylmethylamino]acetic acid;

(207) [(4-{4-[4-(1-ethylpropyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-pyridin-2-ylmethylamino]acetic acid;

(208) [(4-{5-methyl-2-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-pyridin-2-ylmethylamino]acetic acid;

(209) [benzoyl-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(210) [(4-{4-[4-(1-ethylpropyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-(4-methylbenzoyl)amino]acetic acid;

(211) [(4-methoxybenzoyl)-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(212) 2-(4-{5-methyl-2-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(213) (S)-2-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(214) {benzyl[4-(4-{[4-(2,2-dimethylpropyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(215) {benzyl[4-(4-{[trans-4-(4-tert-butylphenyl)-cyclohexylmethyl]methylamino}phenyl)thiazol-2-

ylmethyl]amino}acetic acid;

(216) [benzyl(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(217) 3-[benzyl(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]propionic acid;

(218) (benzyl{4-[4-({2-[4-(2,2-dimethylpropyl)phenyl]-ethyl}methylamino)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(219) {benzyl[4-(4-{methyl[4-(trans-4-methylcyclohexyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(220) {benzyl[4-(4-{[4-(cis-4-fluorocyclohexyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(221) {benzyl[4-(4-{[trans-4-(4-chlorophenyl)-cyclohexylmethyl]methylamino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(222) {benzyl[4-(4-{[4-(4,4-dimethylcyclohexyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(223) {benzyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(224) (benzyl{4-[4-(biphenyl-4-ylmethylmethylamino)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(225) sodium [benzyl(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]-acetate;

(226) [benzyl(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(227) sodium {benzyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}-acetate;

(228) {benzyl[4-(4-{[4-(2,2-dimethylpropylthio)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(229) {benzyl[4-(4-{methyl[4-(3-methylbutylthio)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(230) [benzyl(4-{4-[(4-dipropylamino-benzoyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(231) [(4-{4-[ethyl(4-isopropylbenzyl)amino]phenyl}thiazol-2-ylmethyl)-(4-isopropylbenzyl)amino]acetic acid;

(232) [(4-isopropylbenzyl)-(4-{4-[isopropyl-(4-isopropylbenzyl)amino]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(233) [(4-tert-butylbenzyl)-(4-{4-[isopropyl-(4-isopropylbenzyl)amino]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(234) [(4-chlorobenzyl)-(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(235) {{4-[4-(benzylmethylamino)phenyl]thiazol-2-ylmethyl}-[4-(1-propylbutyl)benzyl]amino}acetic acid;

(236) [{4-[4-(benzylmethylamino)phenyl]thiazol-2-ylmethyl}-(4-chloro-benzyl)amino]acetic acid;

(237) [{4-[4-(benzylmethylamino)phenyl]thiazol-2-ylmethyl}-(2-chloro-benzyl)amino]acetic acid;

(238) [{4-[4-(benzylmethylamino)phenyl]thiazol-2-ylmethyl}-(3,4-dichloro-benzyl)amino]acetic acid;

(239) {[4-(4-{methyl[4-(trans-4-methyl-cyclohexyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]pyridin-2-

ylmethylamino}acetic acid;

(240) {[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]pyridin-2-ylmethylamino}acetic acid;

(241) ({4-[4-(benzylmethylamino)phenyl]thiazol-2-ylmethyl}-naphthalen-1-ylmethylamino)acetic acid;

(242) ({4-[4-(benzylmethylamino)phenyl]thiazol-2-ylmethyl}-quinolin-2-ylmethylamino)acetic acid;

(243) ((2-benzo[b]thiophen-3-yl-acetyl)-{4-[4-(benzylmethylamino)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(244) [[2-(4-chlorophenyl)acetyl]-(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(245) {(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-[2-(4-isopropylphenyl)acetyl]amino}acetic acid;

(246) [(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-(3-methyl-butyryl)amino]acetic acid;

(247) {1-[4-(4-{[4-(2,2-dimethylpropyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]-3-phenylureido}acetic acid;

(248) [benzoyl-(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(249) {(4-methylbenzoyl)-[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(250) sodium {(4-isopropylbenzoyl)-[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}-acetate;

(251) sodium (S)-{3-[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-yl]-3,4-dihydro-1H-isoquinolin-2-yl}-acetate;

(252) 1-(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-

2-ylmethyl)piperidine-4-carboxylic acid;

(253) 1-(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)piperidine-3-carboxylic acid;

(254) 1-(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-4-phenylpiperidine-4-carboxylic acid;

(255) 1-(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-4-(3-methylbutyl)piperidine-4-carboxylic acid;

(256) 1-[4-(4-{methyl[4-(trans-4-methyl-cyclohexyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]-4-phenylpiperidine-4-carboxylic acid;

(257) 1-[4-(4-{[trans-4-(4-chloro-phenyl)-cyclohexylmethyl]methylamino}phenyl)thiazol-2-ylmethyl]-4-phenylpiperidine-4-carboxylic acid;

(258) 2-[4-(4-{methyl[4-(trans-4-methyl-cyclohexyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(259) 2-(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(260) 2-[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(261) 2-[4-(4-{[4-(2,2-dimethylpropyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(262) 5-{[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-yl)methylamino]methyl}furan-2-carboxylic acid;

(263) 2-[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]-3-phenylpropionic acid;

(264) [(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]phenylacetic acid;

(265) 2-[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]propionic acid;

(266) 3-(4-chlorophenyl)-2-[(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]propionic acid;

(267) [(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylamino]acetic acid;

(268) 3-[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylamino]propionic acid;

(269) 4-{[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylamino]methyl}benzoic acid;

(270) 4-[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylamino]benzoic acid;

(271) 6-[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylamino]nicotinic acid;

(272) 2-[(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylamino]-3-phenylpropionic acid;

(273) (S)-2-{methyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}-3-phenylpropionic acid;

(274) (S)-{methyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}phenylacetic acid;

(275) {[4-(4-{[4-(2,2-dimethylpropyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]methylamino}phenylacetic acid;

(276) 2-{[4-(4-{[4-(2,2-dimethylpropyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]methylamino}-3-phenylpropionic acid;

(277) {carboxymethyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(278) [(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-(3-methylbutyl)amino]acetic acid;

(279) {(3-methylbutyl)-[4-(4-{methyl[4-(trans-4-methyl-cyclohexyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(280) [(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-(3-methylbutyl)amino]acetic acid;

(281) 5-[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethoxy]nicotinic acid;

(282) 4-[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethoxy]benzoic acid;

(283) 4-[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethylthio]benzoic acid;

(284) 4-[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)sulfamoyl]benzoic acid;

(285) 4-{[4-(4-{[4-(4,4-dimethyl-cyclohexyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]methylsulfamoyl}benzoic acid;

(286) {[4-(4-{[4-(4,4-dimethyl-cyclohexyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]methylsulfamoyl}acetic acid;

(287) 4-[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylsulfamoyl]benzoic acid;

(288) 3-[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylsulfamoyl]benzoic acid;

(289) [(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylsulfamoyl]acetic acid;

(290) 4-{[4-(4-{[4-(4,4-dimethyl-cyclohexyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]methylsulfamoyl}butyric acid;

(291) [(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)isobutyl-sulfamoyl]acetic acid;

(292) N-(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)oxamic acid;

(293) {benzyl[4-(4-{[4-(1-propylbutyl)benzyl]methylamino-carbonyl}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(294) N-(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-N-methylterephthalamic acid;

(295) {benzyl[4-(4-{methyl[4-(trans-4-methyl-cyclohexyl)benzyl]amino}phenyl)thiazol-2-ylmethoxycarbonyl]amino}acetic acid;

(296) [3-(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-3-methyl-ureido]acetic acid;

(297) (cyclohexylmethyl{4-[6-(3,4-dichlorobenzyloxy)benzoxazol-2-yl]thiazol-2-yl}amino)acetic acid;

(298) [4-(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)piperazin-1-yl]acetic acid;

(299) sodium (S)-2-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylate;

(300) sodium 5-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethoxy)nicotinate;

(301) 5-(4-{2-methyl-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethoxy)nicotinic acid;

(302) 5-(4-{3-methoxy-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethoxy)nicotinic acid;

(303) [(4-{2-methyl-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)phenylcarbamoylmethylamino]acetic acid;

(304) [[(4-isopropylphenylcarbamoyl)methyl]-(4-{2-methyl-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(305) 2-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-

ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(306) [(4-{3-methoxy-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)phenylcarbamoylmethylamino]acetic acid;

(307) [[(4-isopropylphenylcarbamoyl)methyl]-(4-{3-methoxy-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(308) [(4-{2-methyl-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)thiazol-4-ylmethylamino]acetic acid;

(309) [(4-{2-methyl-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-(2-methylthiazol-4-ylmethyl)amino]acetic acid hydrochloride;

(310) [(benzylcarbamoylmethyl)-(4-{2-methyl-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid hydrochloride;

(311) [(1H-benzimidazol-2-ylmethyl)-(4-{2-methyl-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(312) [(4-tert-butylthiazol-2-ylmethyl)-(4-{1-[4-(1-propylbutyl)benzyl]-1,2,3,4-tetrahydroquinolin-6-yl}thiazol-2-ylmethyl)amino]acetic acid;

(313) 1-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)piperidine-4-carboxylic acid hydrochloride;

(314) 4-[4-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)piperazin-1-yl]benzoic acid;

(315) 4-{4-[5-(1-ethylpropyl)-1-(4-isopropylbenzyl)-1H-benzimidazol-2-yl]thiazol-2-ylmethoxy}benzoic acid ethyl ester;

(316) 4-{4-[5-(1-ethylpropyl)-1-(4-isopropylbenzyl)-1H-benzimidazol-2-yl]thiazol-2-ylmethoxy}benzoic acid;

(317) 4-{4-[1-(4-acetylbenzyl)-5-(1-ethylpropyl)-1H-benzimidazol-2-yl]thiazol-2-ylmethoxy}benzoic acid;

(318) 4-{4-[1-(4-acetylbenzyl)-6-(1-ethylpropyl)-1H-

benżimidazol-2-yl]thiazol-2-ylmethoxy}benzoic acid;

(319) 4-{4-[1-cyclohexylmethyl-5-(1-ethylpropyl)-1H-benzimidazol-2-yl]thiazol-2-ylmethoxy}benzoic acid;

(320) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(321) 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinic acid;

(322) 5-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiophen-2-ylmethoxy}nicotinic acid;

(323) 5-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethoxy}nicotinic acid;

(324) 5-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinic acid;

(325) [(1H-benzimidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(326) 6-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)pyridine-2-carboxylic acid;

(327) [(1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(328) [[(4-isopropylphenylcarbamoyl)methyl]-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(329) [phenylcarbamoylmethyl(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(330) ({4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}phenylcarbamoylmethylamino)acetic acid;

(331) ((4-tert-butylthiazol-2-ylmethyl)-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}amino)acetic acid;

(332) [(5-tert-butylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)-amino]acetic acid;

(333) ((1H-benzimidazol-2-ylmethyl)-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}amino)acetic acid;

(334) [(4-tert-butylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(335) [phenylcarbamoylmethyl(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(336) 5-{5-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethoxy}nicotinic acid;

(337) 5-{5-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiophen-2-ylmethoxy}nicotinic acid;

(338) ((4-tert-butylthiazol-2-ylmethyl)-{5-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}amino)acetic acid;

(339) ((4-tert-butylthiazol-2-ylmethyl)-{5-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiophen-2-ylmethyl}amino)acetic acid;

(340) ((1H-benzimidazol-2-ylmethyl)-{5-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}amino)acetic acid;

(341) ((1H-benzimidazol-2-ylmethyl)-{5-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiophen-2-ylmethyl}amino)acetic acid;

(342) [(4,5-dimethylthiazol-2-ylmethyl)- (4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(343) (S)-2-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(344) {{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}-[(4-isopropylphenylcarbamoyl)methyl]amino}acetic acid;

(345) (S)-2-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(346) [[(4-isopropylphenylcarbamoyl)methyl]-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(347) (S)-2-{5-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(348) [(5-tert-butyloxazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(349) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(350) 6-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)pyridine-2-carboxylic acid;

(351) 6-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethoxy}-pyridine-2-carboxylic acid;

(352) ((5-tert-butylthiazol-2-ylmethyl)-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}amino)acetic acid;

(353) [{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}-(1-methyl-1H-benzimidazol-2-ylmethyl)amino]acetic acid;

(354) [(4-tert-butylthiazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(355) [{5-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}-(1-methyl-1H-benzimidazol-2-ylmethyl)amino]acetic acid;

(356) [(5-tert-butylthiazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(357) sodium [(1-methyl-1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]-acetate;

(358) calcium bis{[(1-methyl-1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]-acetate};

(359) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid toluene-4-sulfonate;

(360) 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinic acid sulfate;

(361) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophene-2-carbonyl)amino]acetic acid;

(362) [(5-tert-butylthiazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophene-2-carbonyl)amino]acetic acid;

(363) [(4-isopropylbenzyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophene-2-

carbonyl)amino]acetic acid;

(364) [(4-dimethylaminobenzyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophene-2-carbonyl)amino]acetic acid;

(365) [(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophene-2-carbonyl)-pyridin-2-ylmethylamino]acetic acid;

(366) [(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophene-2-carbonyl)-pyridin-3-ylmethylamino]acetic acid;

(367) 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinic acid methanesulfonate;

(368) [methanesulfonyl-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(369) sodium 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinate;

(370) 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinic acid hydrochloride;

(371) 4-[4-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophene-2-carbonyl)piperazin-1-yl]benzoic acid;

(372) 4-[1-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophene-2-carbonyl)piperidin-4-yl]benzoic acid;

(373) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid hydrochloride;

(374) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid sulfate;

(375) 4-(2-dimethylaminoacetylamino)-3-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)benzoic acid;

(376) 4-isobutyrylamino-3-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)benzoic acid;

(377) 4-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)benzoic acid;

(378) 4-(methanesulfonylmethylamino)-3-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)benzoic acid;

(379) 4-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethylthio)benzoic acid;

(380) 4-amino-3-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)benzoic acid;

(381) 1-{5-[1-(4-cyclohexylbenzyl)-1H-indol-3-yl]thiophen-2-ylmethyl}-4-phenylpiperidine-4-carboxylic acid hydrochloride;

(382) (benzyl{5-[1-(4-cyclohexylbenzyl)-1H-indol-3-yl]thiophen-2-ylmethyl}amino)acetic acid hydrochloride;

(383) [(methylphenylsulfamoyl)(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

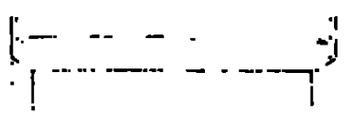
(384) [(5-tert-butylthiazol-2-ylmethyl)-(5-{4-[(4-cyclohexyl-phenyl)methylcarbamoyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(385) [(5-{4-[(4-cyclohexylbenzyl)ethylamino]phenyl}thiophen-2-ylmethyl)pyridin-2-ylmethylamino]acetic acid;

(386) [(5-{4-[(4-cyclohexylbenzyl)ethylamino]phenyl}thiophen-2-ylmethyl)-(2-phenoxyethyl)amino]acetic acid;

(387) 4-{1-[4-(4-{[trans-4-(4-tert-butylphenyl)-cyclohexylmethyl]ethylamino}phenyl)thiophen-2-ylmethyl]piperidin-4-yl}benzoic acid;

(388) [[2-(4-isopropylphenoxy)acetyl]-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;



(389) [(4-isopropylbenzoyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(390) [(3-methylbutyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(391) [3-methyl-3-phenyl-1-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)ureido]acetic acid;

(392) 2-(4-{3-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid;

(393) 4-[4-(5-{4-[4-(trans-4-methylcyclohexyl)benzyloxy]phenyl}thiophen-2-ylmethyl)piperazin-1-yl]benzoic acid;

(394) [(2-chloro-5-trifluoromethylbenzyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(395) 3-{[carboxymethyl(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]methyl}benzoic acid;

(396) [(4-methoxybenzyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(397) [(4-methylthiobenzyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(398) 4-[cyclohexylmethyl(5-{4-[4-(trans-4-methylcyclohexyl)benzyloxy]phenyl}thiophen-2-ylmethyl)sulfamoyl]benzoic acid;

(399) 4-[3-cyclohexylmethyl-3-(5-{4-[4-(trans-4-methylcyclohexyl)benzyloxy]phenyl}thiophen-2-ylmethyl)ureido]benzoic acid;

(400) [benzhydryl-(5-{4-[4-(1-

propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(401) [[2-oxo-2-(4-pyrrolidin-1-yl-phenyl)ethyl]-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid ethyl ester hydrochloride;

(402) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid ethyl ester;

(403) 3-(benzyl{5-[1-(4-cyclohexylbenzyl)-2,3-dihydro-1H-indol-5-yl]thiophen-2-ylmethyl}amino)propionic acid;

(404) [benzyl(4-{4-[2-(2,2-dimethylpropyl)benzimidazol-1-ylmethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(405) [(1-methyl-1H-indol-3-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(406) [(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)quinolin-2-ylmethylamino]acetic acid;

(407) [benzothiazol-2-ylmethyl(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(408) [(1-benzyl-1H-imidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(409) [(1H-indol-5-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(410) [(4-imidazol-1-ylbenzyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(411) [benzofuran-2-ylmethyl(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(412) [[2,2']bithiophenyl-5-ylmethyl(4-{4-[4-(1-

propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(413) [(2-phenyl-1H-imidazol-4-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(414) [(3-phenyl-1H-pyrazol-4-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(415) [benzoxazol-2-ylmethyl(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(416) [benzo[b]thiophen-2-ylmethyl(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(417) [(4-phenylthiophen-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(418) [benzothiazol-2-yl-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(419) [(5-chlorothiophene-2-sulfonyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(420) [(1-diethylcarbamoylmethyl-1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(421) (S)-({4-[2-(4-cyclohexylbenzyloxy)-5-methylphenyl]thiophen-2-ylmethyl}methylamino)-3-phenylpropionic acid;

(422) [benzyl(4-{4-[(4-butoxy-benzenesulfonyl)ethylamino]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(423) N-{4-[2-(4-cyclohexylbenzyloxy)-5-methylphenyl]thiophen-

2-ylmethyl}-N-(2-methylbenzothiazol-6-yl)oxamic acid;

(424) (benzyl{4-[4-(3,5-dichlorophenoxymethyl)phenyl]thiophen-2-ylmethyl}amino)acetic acid;

(425) [(1-allyl-1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid; and

(426) [[4-(4-chlorophenyl)thiazol-2-yl]-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid.

[24] The 5-membered heteroaromatic ring compound of any of [1] to [23], which is selected from the group consisting of the following compounds, or a prodrug thereof, or a pharmaceutically acceptable salt thereof:

(1) (S)-2-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(2) {{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-[(4-isopropylphenylcarbamoyl)methyl]amino}acetic acid;

(3) 4-(3-isobutyl-3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}ureido)benzoic acid;

(4) ({4-[4-({isobutyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}phenylcarbamoylmethylamino)acetic acid;

(5) ([(4-isopropylphenylcarbamoyl)methyl]-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(6) [(4-tert-butylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(7) [(4,5-dimethylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-

ylmethyl)amino]acetic acid;

(8) [(5-tert-butylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(9) [[2-(4-isopropylphenoxy)acetyl]-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(10) 4-[4-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)piperazin-1-yl]benzoic acid;

(11) {benzyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(12) [(1-methyl-1H-benzimidazol-2-ylmethyl)-5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(13) 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinic acid;

(14) [(1H-benzimidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(15) [(1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(16) [[(4-isopropylphenylcarbamoyl)methyl]-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(17) (S)-2-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(18) {{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}-[(4-isopropylphenylcarbamoyl)methyl]amino}acetic acid;

(19) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid; and

(20) [(4-tert-butylthiazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid.

[25] A pharmaceutical composition comprising the 5-membered heteroaromatic ring compound of any of [1] to [24], or a prodrug thereof, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

[26] A pharmaceutical composition for inhibition of a receptor tyrosine kinase negative regulator, which comprises a 5-membered heteroaromatic ring compound of any of [1] to [24], or a prodrug thereof, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

[27] A pharmaceutical composition for inhibition of protein tyrosine phosphatase 1B, which comprises a 5-membered heteroaromatic ring compound of any of [1] to [24], or a prodrug thereof, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

[28] A pharmaceutical composition for the prophylaxis or treatment of diabetes, which comprises a 5-membered heteroaromatic ring compound of any of [1] to [24], or a prodrug thereof, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

[29] A pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia, which comprises a 5-membered heteroaromatic ring compound of any of [1] to [24], or a prodrug thereof, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

[30] A pharmaceutical composition for the prophylaxis or treatment of obesity, which comprises a 5-membered heteroaromatic ring compound of any of [1] to [24], or a

prodrug thereof, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

[31] A pharmaceutical composition for the prophylaxis or treatment of diabetic complications, which comprises a 5-membered heteroaromatic ring compound of any of [1] to [24], or a prodrug thereof, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

[32] The pharmaceutical composition of [25], which is used in combination with a therapeutic agent for hyperlipidemia.

[33] The pharmaceutical composition of [32], wherein the therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of HMG-CoA reductase inhibitors (statins), fibrates, TNFSF6 expression inhibitors, HDL-cholesterol increasing agents, ApoA1 expression enhancers, SPP1 (osteopontin) expression inhibitors, drugs acting on peroxisome proliferator-activated receptors (PPAR), PPAR-alpha agonists, lipase clearing factor stimulants, cholesterol antagonists, platelet aggregation antagonists, antioxidants, cholesterol biosynthesis inhibitors, LDL-receptor up-regulators, bile acid sequestrants, cholesterol absorption inhibitors and nicotinic acids.

[34] The pharmaceutical composition of [33], wherein the therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of lovastatin, pravastatin (eptastatin) sodium, fluvastatin (fluindostainin) sodium, rosuvastatin calcium, atorvastatin calcium, simvastatin (synvinolin), pitavastatin (itavastatin, nisvastatin) calcium, ronifibrate (ronifibrato), binifibrate (binifibrato), clinofibrate, ciprofibrate, clofibrate, etofibrate, fenofibrate, bezafibrate, gemfibrozil, acipimox, eicosapentaenoic acid (icosapent, icopenate, icosapentate) ethyl ester, probucol, policosanol, colesevelam hydrochloride, colestyramine (cholestyramine resin), colestipol hydrochloride,

colestimide (colestilan), ezetimibe and niacin (nicotinic acid).

[35] The pharmaceutical composition of [25], which is used in combination with a therapeutic agent for diabetes.

[36] The pharmaceutical composition of [35], wherein the therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of insulin secretagogues, biguanides, α-glucosidase inhibitors, insulin preparations, insulin analogs, insulin sensitivity enhancers, IL-11, anti-CD25 (IL-2 Receptor) agents, angiotensin (AT1) antagonists, angiotensin-converting enzyme (ACE) inhibitors, aldose reductase inhibitors, antioxidants, carnitine acetyltransferase stimulant, antidepressants, glucocorticoids, retilin, radical formation agonists and transketolase activators.

[37] The pharmaceutical composition of [36], wherein the therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of nateglinide, glimepiride, glibenclamide, gliclazide, acetohexamide, tolbutamide, glyclopyramide, tolazamide, glybuzole, glipizide, glibornuride, gliquidone, repaglinide, metformin hydrochloride, buformin hydrochloride, voglibose, acarbose, epalrestat, miglitol, insulin, pioglitazone hydrochloride, rosiglitazone maleate, chromium picolinate/biotin, V-411, recombinant human interleukin-11, daclixiмab (daclizumab), losartan potassium, captopril, imidapril hydrochloride, alpha-lipoic acid, levacecarnine (acetyl-L-carnitine, levocarnitine acetyl) hydrochloride, captopril, retilin, verteporfin, benfotiamine and fluocinolone acetonide.

[38] The pharmaceutical composition of [25], which is used in combination with a therapeutic agent for obesity.

[39] The pharmaceutical composition of [38], wherein the therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, lipase

inhibitors, 5-HT/norepinephrine reuptake dual inhibitors, 5-HT reuptake inhibitors, supplements containing herbal ephedrine and caffeine, human chorionic gonadotropins, adrenoceptor agonists, methamphetamine, phentermine and amfepramone.

[40] The pharmaceutical composition of [39], wherein the therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, orlistat, sibutramine hydrochloride monohydrate, fluoxetine hydrochloride, chorionic gonadotropin (human), VNS therapy using NCP System, metaraminol, d-methamphetamine hydrochloride, phentermine, amfepramone hydrochloride (diethylpropion), benzfetamine hydrochloride and phendimetrazine tartrate.

[41] The pharmaceutical composition of [25], which is used in combination with a therapeutic agent for hypertension.

[42] The pharmaceutical composition of [41], wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of thiazides, aldosterone antagonists, adrenergic neuron blockers, calcium channel blockers; dopamine D2 antagonists, beta-adrenoceptor antagonists, alpha2-adrenoceptor agonists, guanylate cyclase activators, beta1-adrenoceptor antagonists, alpha1-adrenoceptor antagonists, antioxidants, angiotensin-I converting enzyme (ACE) inhibitors, Na+/H+ exchange inhibitors, alpha-adrenoceptor antagonists, nitric oxide donors, 5-HT2 antagonists, K(ATP) channel activators, potassium sparing diuretic prostaglandin synthase stimulants, imidazoline I1 receptor agonists, angiotensin AT1 antagonists, dopamine D1 agonists, guanylate cyclase stimulants, endothelin ETA receptor antagonists, endothelin ETB receptor antagonists, NOS3 expression enhancers, prostacyclin analogs, prostaglandins, angiotensin II antagonists, electrolyte absorption agonists, nicotinic antagonists, dopamine D2 agonists, prolactin inhibitors, platelet-activating factor (PAF) antagonists,

platelet aggregation antagonists, tumor necrosis factor antagonists, Rho kinase inhibitors, PPAR-alpha agonists, AMPA receptor modulators, GABA(A) receptor antagonists and phosphodiesterase V (PDE5A) inhibitors.

[43] The pharmaceutical composition of [42], wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of chlorothiazide, hydrochlorothiazide, hydroflumethiazide, methyclothiazide, polythiazide, xipamide, cyclopenthiazide, bendroflumethiazide (bendrofluazide), spironolactone, epoxymexrenone (eplerenone), guanethidine monosulfate, guanadrel sulfate, verapamil, propranolol hydrochloride, alprenolol hydrochloride, pindolol, oxprenolol hydrochloride, timolol maleate, sotalol hydrochloride, acebutolol hydrochloride, carteolol hydrochloride, mepindolol sulfate, arotinolol hydrochloride, indenolol hydrochloride, tertatolol hydrochloride, celiprolol hydrochloride, tilisolol hydrochloride, nebivolol, penbutolol sulfate, nadolol, cloranolol hydrochloride, bevantol (bevantolol) hydrochloride, clonidine, guanfacine hydrochloride, diltiazem hydrochloride, nicardipine hydrochloride, nitrendipine, felodipine, nilvadipine; nivadipine, nisoldipine, benidipine hydrochloride, amlodipine besylate, franidipine (manidipine) hydrochloride, lacidipine, isradipine, barnidipine (mepirodipine) hydrochloride, efonidipine hydrochloride ethanol, cinaldipine (cilnidipine), aranidipine, lercanidipine (masnidipine) hydrochloride, azelnidipine, amlodipine, manidipine (franidipine), sodium nitroprusside, atenolol, metoprolol tartrate, betaxolol hydrochloride, bopindolol, bisoprolol fumarate, esmolol hydrochloride, carvedilol, metoprolol succinate, talinolol, prazosin hydrochloride, urapidil, indoramin hydrochloride, bunazosin hydrochloride, terazosin hydrochloride, doxazosin mesylate, urapidil, nifedipine,

captopril, enalapril maleate, lisinopril, perindopril, alacepril, ramipril, quinapril hydrochloride, delapril hydrochloride, benazepril hydrochloride, cilazapril, fosinoprilat, fosinopril sodium, trandolapril, spirapril, temocapril hydrochloride, moexipril hydrochloride, imidapril hydrochloride, zofenopril calcium, enalaprilat, zofenoprilat, amiloride hydrochloride, labetalol hydrochloride, nipradilol (nipradolol), linsidomine, ketanserin, pinacidil, cicletanine (cycletanide), amosulalol hydrochloride, moxonidine hydrochloride hydrate, losartan potassium, valsartan, eprosartan mesylate, candesartan cilexetil (hexetil), irbesartan, telmisartan, olmesartan medoxomil, fenoldopam mesilate, cadralazine, rilmenidine dihydrogen phosphate, bosentan, beraprost sodium, limaprost alfadex (alpha-cyclodextrin), uniprost (treprostinil sodium), iloprost (ciloprost), mecamylamine hydrochloride, metergoline, guanabenz acetate, cloricromene, fasudil, doconexent (docosahexaenoic acid), cyclothiazide, sildenafil citrate, chlortalidone (chlorthalidone), quinethazone, indapamide, metolazone, phenoxybenzamine hydrochloride, metirosine (metyrosine), diazoxide, torasemide (torsemide), clopamide, hydralazine hydrochloride, reserpine and methyldopa.

[44] The pharmaceutical composition of [25], which is used in combination with a therapeutic agent for thrombosis.

[45] The pharmaceutical composition of [44], wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin preparations, low molecular weight heparins, heparin analogs, anticoagulants, thrombin inhibitors, anti-thrombin preparations, antiplatelet agents and thrombolytic agents.

[46] The pharmaceutical composition of [45], wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin calcium,

heparin sodium, dalteparin sodium, parnaparin sodium, reviparin sodium, danaparoid sodium, warfarin potassium, argatroban, gabexate mesylate, nafamostat mesylate, human anti-thrombin III, aspirin, dipyridamole, ticlopidine hydrochloride, cilostazol, limaprost alfadex, sodium ozagrel, sarpogrelate hydrochloride, ethyl icosapentate, beraprost sodium, urokinase, tisokinase, alteplase, nasaruplase, nateplase, monteplase, pamiteplase, batroxobin, sodium citrate and protein C.

[47] The pharmaceutical composition for the prophylaxis or treatment of diabetes according to [28], which is used in combination with a therapeutic agent for hyperlipidemia.

[48] The pharmaceutical composition for the prophylaxis or treatment of diabetes according to [47], wherein the therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of HMG-CoA reductase inhibitors (statins), fibrates, TNFSF6 expression inhibitors, HDL-cholesterol increasing agents, ApoA1 expression enhancers, SPP1 (osteopontin) expression inhibitors, drugs acting on peroxisome proliferator-activated receptors (PPAR), PPAR-alpha agonists, lipase clearing factor stimulants, cholesterol antagonists, platelet aggregation antagonists, antioxidants, cholesterol biosynthesis inhibitors, LDL-receptor up-regulators, bile acid sequestrants, cholesterol absorption inhibitors and nicotinic acids.

[49] The pharmaceutical composition for the prophylaxis or treatment of diabetes according to [48], wherein the therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of lovastatin, pravastatin (eptastatin) sodium, fluvastatin (fluindostainin) sodium, rosuvastatin calcium, atorvastatin calcium, simvastatin (synvinolin), pitavastatin (itavastatin, nisvastatin) calcium, ronifibrate (ronifibrato), binifibrate (binifibrato), clinofibrate, ciprofibrate, clofibrate,

etofibrate, fenofibrate, bezafibrate, gemfibrozil, acipimox, eicosapentaenoic acid (icosapent, icopenate, icosapentate) ethyl ester, probucol, policosanol, colesevelam hydrochloride, colestyramine (cholestyramine resin), colestipol hydrochloride, colestimide (colestilan), ezetimibe and niacin (nicotinic acid).

[50] The pharmaceutical composition for the prophylaxis or treatment of diabetes according to [28], which is used in combination with a different therapeutic agent for diabetes.

[51] The pharmaceutical composition for the prophylaxis or treatment of diabetes according to [50], wherein the different therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of insulin secretagogues, biguanides, α-glucosidase inhibitors, insulin preparations, insulin analogs, insulin sensitivity enhancers, IL-11, anti-CD25 (IL-2 Receptor) agents, angiotensin (AT1) antagonists, angiotensin-converting enzyme (ACE) inhibitors, aldose reductase inhibitors, antioxidants, carnitine acetyltransferase stimulant, antidepressants, glucocorticoids, retilin, radical formation agonists and transketolase activators.

[52] The pharmaceutical composition for the prophylaxis or treatment of diabetes according to [51], wherein the different therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of nateglinide, glimepiride, glibenclamide, gliclazide, acetohexamide, tolbutamide, glyclopyramide, tolazamide, glybuzole, glipizide, glibornuride, gliquidone, repaglinide, metformin hydrochloride, buformin hydrochloride, voglibose, acarbose, epalrestat, miglitol, insulin, pioglitazone hydrochloride, rosiglitazone maleate, chromium picolinate/biotin, V-411, recombinant human interleukin-11, dacliximab (daclizumab), losartan potassium, captopril, imidapril hydrochloride, alpha-lipoic acid, levacecarnine (acetyl-L-carnitine, levocarnitine acetyl)

hydrochloride, captopril, retilin, verteporfin, benfotiamine and fluocinolone acetonide.

[53] The pharmaceutical composition for the prophylaxis or treatment of diabetes according to [28], which is used in combination with a therapeutic agent for obesity.

[54] The pharmaceutical composition for the prophylaxis or treatment of diabetes according to [53], wherein the therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, lipase inhibitors, 5-HT/norepinephrine reuptake dual inhibitors, 5-HT reuptake inhibitors, supplements containing herbal ephedrine and caffeine, human chorionic gonadotropins, adrenoceptor agonists, methamphetamine, phentermine and amfepramone.

[55] The pharmaceutical composition for the prophylaxis or treatment of diabetes according to [54], wherein the therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, orlistat, sibutramine hydrochloride monohydrate, fluoxetine hydrochloride, chorionic gonadotropin (human), VNS therapy using NCP System, metaraminol, d-methamphetamine hydrochloride, phentermine, amfepramone hydrochloride (diethylpropion), benzfetamine hydrochloride and phendimetrazine tartrate.

[56] The pharmaceutical composition for the prophylaxis or treatment of diabetes according to [28], which is used in combination with a therapeutic agent for hypertension.

[57] The pharmaceutical composition for the prophylaxis or treatment of diabetes according to [56], wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of thiazides, aldosterone antagonists, adrenergic neuron blockers, calcium channel blockers; dopamine D2 antagonists, beta-adrenoceptor antagonists, alpha2-adrenoceptor agonists, guanylate cyclase activators, beta1-adrenoceptor antagonists,

alpha1-adrenoceptor antagonists, antioxidants, angiotensin-I converting enzyme (ACE) inhibitors, Na+/H+ exchange inhibitors, alpha-adrenoceptor antagonists, nitric oxide donors, 5-HT2 antagonists, K(ATP) channel activators, potassium sparing diuretic prostaglandin synthase stimulants, imidazoline I1 receptor agonists, angiotensin AT1 antagonists, dopamine D1 agonists, guanylate cyclase stimulants, endothelin ETA receptor antagonists, endothelin ETB receptor antagonists, NOS3 expression enhancers, prostacyclin analogs, prostaglandins, angiotensin II antagonists, electrolyte absorption agonists, nicotinic antagonists, dopamine D2 agonists, prolactin inhibitors, platelet-activating factor (PAF) antagonists, platelet aggregation antagonists, tumor necrosis factor antagonists, Rho kinase inhibitors, PPAR-alpha agonists, AMPA receptor modulators, GABA(A) receptor antagonists and phosphodiesterase V (PDE5A) inhibitors.

[58] The pharmaceutical composition for the prophylaxis or treatment of diabetes according to [57], wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of chlorothiazide, hydrochlorothiazide, hydroflumethiazide, methyclothiazide, polythiazide, xipamide, cyclopenthiazide, bendroflumethiazide (bendrofluazide), spironolactone, epoxymexrenone (eplerenone), guanethidine monosulfate, guanadrel sulfate, verapamil, propranolol hydrochloride, alprenolol hydrochloride, pindolol, oxprenolol hydrochloride, timolol maleate, sotalol hydrochloride, acebutolol hydrochloride, carteolol hydrochloride, mepindolol sulfate, arotinolol hydrochloride, indenolol hydrochloride, tertatolol hydrochloride, celiprolol hydrochloride, tilisolol hydrochloride, nebivolol, penbutolol sulfate, nadolol, cloranolol hydrochloride, bevantol (bevantolol) hydrochloride, clonidine, guanfacine hydrochloride, diltiazem hydrochloride,

nicardipine hydrochloride, nitrendipine, felodipine, nilvadipine; nivadipine, nisoldipine, benidipine hydrochloride, amlodipine besylate, franidipine (manidipine) hydrochloride, lacidipine, isradipine, barnidipine (mepirodipine) hydrochloride, efonidipine hydrochloride ethanol, cinaldipine (cilnidipine), aranidipine, lercanidipine (masnidipine) hydrochloride, azelnidipine, amlodipine, manidipine (franidipine), sodium nitroprusside, atenolol, metoprolol tartrate, betaxolol hydrochloride, bopindolol, bisoprolol fumarate, esmolol hydrochloride, carvedilol, metoprolol succinate, talinolol, prazosin hydrochloride, urapidil, indoramin hydrochloride, bunazosin hydrochloride, terazosin hydrochloride, doxazosin mesylate, urapidil, nifedipine, captopril, enalapril maleate, lisinopril, perindopril, alacepril, ramipril, quinapril hydrochloride, delapril hydrochloride, benazepril hydrochloride, cilazapril, fosinoprilat, fosinopril sodium, trandolapril, spirapril, temocapril hydrochloride, moexipril hydrochloride, imidapril hydrochloride, zofenopril calcium, enalaprilat, zofenoprilat, amiloride hydrochloride, labetalol hydrochloride, nipradilol (nipradolol), linsidomine, ketanserin, pinacidil, cicletanine (cycletanide), amosulalol hydrochloride, moxonidine hydrochloride hydrate, losartan potassium, valsartan, eprosartan mesylate, candesartan cilexetil (hexetil), irbesartan, telmisartan, olmesartan medoxomil, fenoldopam mesilate, cadralazine, rilmenidine dihydrogen phosphate, bosentan, beraprost sodium, limaprost alfadex (alpha-cyclodextrin), uniprost (treprostinil sodium), iloprost (ciloprost), mecamylamine hydrochloride, metergoline, guanabenz acetate, cloricromene, fasudil, doconexent (docosahexaenoic acid), cyclothiazide, sildenafil citrate, chlortalidone (chlorthalidone), quinethazone, indapamide, metolazone, phenoxybenzamine hydrochloride, metirosine (metyrosine),

diazoxide, torasemide (torsemide), clopamide, hydralazine hydrochloride, reserpine and methyldopa.

[59] The pharmaceutical composition for the prophylaxis or treatment of diabetes according to [28], which is used in combination with a therapeutic agent for thrombosis.

[60] The pharmaceutical composition for the prophylaxis or treatment of diabetes according to [59], wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin preparations, low molecular weight heparins, heparin analogs, anticoagulants, thrombin inhibitors, anti-thrombin preparations, antiplatelet agents and thrombolytic agents.

[61] The pharmaceutical composition for the prophylaxis or treatment of diabetes according to [60], wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin calcium, heparin sodium, dalteparin sodium, parnaparin sodium, reviparin sodium, danaparoid sodium, warfarin potassium, argatroban, gabexate mesylate, nafamostat mesylate, human anti-thrombin III, aspirin, dipyridamole, ticlopidine hydrochloride, cilostazol, limaprost alfadex, sodium ozagrel, sarpogrelate hydrochloride, ethyl icosapentate, beraprost sodium, urokinase, tisokinase, alteplase, nasaruplase, nateplase, monteplase, pamiteplase, batroxobin, sodium citrate and protein C.

[62] The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to [29], which is used in combination with a different therapeutic agent for hyperlipidemia.

[63] The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to [62], wherein the different therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of HMG-CoA reductase inhibitors (statins), fibrates, TNFSF6

expression inhibitors, HDL-cholesterol-increasing agents, ApoA1 expression enhancers, SPP1 (osteopontin) expression inhibitors, drugs acting on peroxisome proliferator-activated receptors (PPAR), PPAR-alpha agonists, lipase clearing factor stimulants, cholesterol antagonists, platelet aggregation antagonists, antioxidants, cholesterol biosynthesis inhibitors, LDL-receptor up-regulators, bile acid sequestrants, cholesterol absorption inhibitors and nicotinic acids.

[64] The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to [63], wherein the different therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of lovastatin, pravastatin (eptastatin) sodium, fluvastatin (fluindostainin) sodium, rosuvastatin calcium, atorvastatin calcium, simvastatin (synvinolin), pitavastatin (itavastatin, nisvastatin) calcium, ronifibrate (ronifibrato), binifibrate (binifibrato), clinofibrate, ciprofibrate, clofibrate, etofibrate, fenofibrate, bezafibrate, gemfibrozil, acipimox, eicosapentaenoic acid (icosapent, icopenate, icosapentate) ethyl ester, probucol, policosanol, colesevelam hydrochloride, colestyramine (cholestyramine resin), colestipol hydrochloride, colestimide (colestilan), ezetimibe and niacin (nicotinic acid).

[65] The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to [29], which is used in combination with a therapeutic agent for diabetes.

[66] The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to [65], wherein the therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of insulin secretagogues, biguanides, α-glucosidase inhibitors, insulin preparations, insulin analogs, insulin sensitivity enhancers, IL-11, anti-CD25 (IL-2 Receptor) agents, angiotensin (AT1) antagonists, angiotensin-converting enzyme (ACE) inhibitors,

aldose reductase inhibitors, antioxidants, carnitine acetyltransferase stimulant, antidepressants, glucocorticoids, retilin, radical formation agonists and transketolase activators.

[67] The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to [66], wherein the therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of nateglinide, glimepiride, glibenclamide, gliclazide, acetohexamide, tolbutamide, glyclopyramide, tolazamide, glybuzole, glipizide, glibornuride, gliquidone, repaglinide, metformin hydrochloride, buformin hydrochloride, voglibose, acarbose, epalrestat, miglitol, insulin, pioglitazone hydrochloride, rosiglitazone maleate, chromium picolinate/biotin, V-411, recombinant human interleukin-11, daclixiмab (daclizumab), losartan potassium, captopril, imidapril hydrochloride, alpha-lipoic acid, levacecarnine (acetyl-L-carnitine, levocarnitine acetyl) hydrochloride, captopril, retilin, verteporfin, benfotiamine and fluocinolone acetonide.

[68] The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to [29], which is used in combination with a therapeutic agent for obesity.

[69] The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to [68], wherein the therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, lipase inhibitors, 5-HT/norepinephrine reuptake dual inhibitors, 5-HT reuptake inhibitors, supplements containing herbal ephedrine and caffeine, human chorionic gonadotropins, adrenoceptor agonists, methamphetamine, phentermine and amfepramone.

[70] The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to [69], wherein the therapeutic agent for obesity is one or more pharmaceutical

agents selected from the group consisting of mazindol, orlistat, sibutramine hydrochloride monohydrate, fluoxetine hydrochloride, chorionic gonadotropin (human), VNS therapy using NCP System, metaraminol, d-methamphetamine hydrochloride, phentermine, amfepramone hydrochloride (diethylpropion), benzfetamine hydrochloride and phendimetrazine tartrate.

[71] The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to [29], which is used in combination with a therapeutic agent for hypertension.

[72] The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to [71], wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of thiazides, aldosterone antagonists, adrenergic neuron blockers, calcium channel blockers; dopamine D2 antagonists, beta-adrenoceptor antagonists, alpha2-adrenoceptor agonists, guanylate cyclase activators, beta1-adrenoceptor antagonists, alpha1-adrenoceptor antagonists, antioxidants, angiotensin-I converting enzyme (ACE) inhibitors, Na+/H+ exchange inhibitors, alpha-adrenoceptor antagonists, nitric oxide donors, 5-HT2 antagonists, K(ATP) channel activators, potassium sparing diuretic prostaglandin synthase stimulants, imidazoline I1 receptor agonists, angiotensin AT1 antagonists, dopamine D1 agonists, guanylate cyclase stimulants, endothelin ETA receptor antagonists, endothelin ETB receptor antagonists, NOS3 expression enhancers, prostacyclin analogs, prostaglandins, angiotensin II antagonists, electrolyte absorption agonists, nicotinic antagonists, dopamine D2 agonists, prolactin inhibitors, platelet-activating factor (PAF) antagonists, platelet aggregation antagonists, tumor necrosis factor antagonists, Rho kinase inhibitors, PPAR-alpha agonists, AMPA receptor modulators, GABA(A) receptor antagonists and phosphodiesterase V (PDE5A) inhibitors.

[73] The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to [72], wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of chlorothiazide, hydrochlorothiazide, hydroflumethiazide, methyclothiazide, polythiazide, xipamide, cyclopenthiazide, bendroflumethiazide (bendrofluazide), spironolactone, epoxymexrenone (eplerenone), guanethidine monosulfate, guanadrel sulfate, verapamil, propranolol hydrochloride, alprenolol hydrochloride, pindolol, oxprenolol hydrochloride, timolol maleate, sotalol hydrochloride, acebutolol hydrochloride, carteolol hydrochloride, mepindolol sulfate, arotinolol hydrochloride, indenolol hydrochloride, tertatolol hydrochloride, celiprolol hydrochloride, tilisolol hydrochloride, nebivolol, penbutolol sulfate, nadolol, cloranolol hydrochloride, bevantol (bevantolol) hydrochloride, clonidine, guanfacine hydrochloride, diltiazem hydrochloride, nicardipine hydrochloride, nitrendipine, felodipine, nilvadipine; nivadipine, nisoldipine, benidipine hydrochloride, amlodipine besylate, franidipine (manidipine) hydrochloride, lacidipine, isradipine, barnidipine (mepirodipine) hydrochloride, efonidipine hydrochloride ethanol, cinaldipine (cilnidipine), aranidipine, lercanidipine (masnidipine) hydrochloride, azelnidipine, amlodipine, manidipine (franidipine), sodium nitroprusside, atenolol, metoprolol tartrate, betaxolol hydrochloride, bopindolol, bisoprolol fumarate, esmolol hydrochloride, carvedilol, metoprolol succinate, talinolol, prazosin hydrochloride, urapidil, indoramin hydrochloride, bunazosin hydrochloride, terazosin hydrochloride, doxazosin mesylate, urapidil, nifedipine, captopril, enalapril maleate, lisinopril, perindopril, alacepril, ramipril, quinapril hydrochloride, delapril hydrochloride, benazepril hydrochloride, cilazapril,

fosinoprilat, fosinopril sodium, trandolapril, spirapril, temocapril hydrochloride, moexipril hydrochloride, imidapril hydrochloride, zofenopril calcium, enalaprilat, zofenoprilat, amiloride hydrochloride, labetalol hydrochloride, nipradilol (nipradolol), linsidomine, ketanserin, pinacidil, cicletanine (cycletanide), amosulalol hydrochloride, moxonidine hydrochloride hydrate, losartan potassium, valsartan, eprosartan mesylate, candesartan cilexetil (hexetil), irbesartan, telmisartan, olmesartan medoxomil, fenoldopam mesilate, cadralazine, rilmenidine dihydrogen phosphate, bosentan, beraprost sodium, limaprost alfadex (alpha-cyclodextrin), uniprost (treprostinil sodium), iloprost (ciloprost), mecamylamine hydrochloride, metergoline, guanabenz acetate, cloricromene, fasudil, doconexent (docosahexaenoic acid), cyclothiazide, sildenafil citrate, chlortalidone (chlorthalidone), quinethazone, indapamide, metolazone, phenoxybenzamine hydrochloride, metirosine (metyrosine), diazoxide, torasemide (torsemide), clopamide, hydralazine hydrochloride, reserpine and methyldopa.

[74] The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to [29], which is used in combination with a therapeutic agent for thrombosis.

[75] The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to [74], wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin preparations, low molecular weight heparins, heparin analogs, anticoagulants, thrombin inhibitors, anti-thrombin preparations, antiplatelet agents and thrombolytic agents.

[76] The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to [75], wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin calcium,

heparin sodium, dalteparin sodium, parnaparin sodium, reviparin sodium, danaparoid sodium, warfarin potassium, argatroban, gabexate mesylate, nafamostat mesylate, human anti-thrombin III, aspirin, dipyridamole, ticlopidine hydrochloride, cilostazol, limaprost alfadex, sodium ozagrel, sarpogrelate hydrochloride, ethyl icosapentate, beraprost sodium, urokinase, tisokinase, alteplase, nasaruplase, nateplase, monteplase, pamiteplase, batroxobin, sodium citrate and protein C.

[77] The pharmaceutical composition for the prophylaxis or treatment of obesity according to [30], which is used in combination with a therapeutic agent for hyperlipidemia.

[78] The pharmaceutical composition for the prophylaxis or treatment of obesity according to [77], wherein the therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of HMG-CoA reductase inhibitors (statins), fibrates, TNFSF6 expression inhibitors, HDL-cholesterol increasing agents, ApoA1 expression enhancers, SPP1 (osteopontin) expression inhibitors, drugs acting on peroxisome proliferator-activated receptors (PPAR), PPAR-alpha agonists, lipase clearing factor stimulants, cholesterol antagonists, platelet aggregation antagonists, antioxidants, cholesterol biosynthesis inhibitors, LDL-receptor up-regulators, bile acid sequestrants, cholesterol absorption inhibitors and nicotinic acids.

[79] The pharmaceutical composition for the prophylaxis or treatment of obesity according to [78], wherein the therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of lovastatin, pravastatin (eptastatin) sodium, fluvastatin (fluindostainin) sodium, rosuvastatin calcium, atorvastatin calcium, simvastatin (synvinolin), pitavastatin (itavastatin, nisvastatin) calcium, ronifibrate (ronifibrato), binifibrate (binifibrato), clinofibrate, ciprofibrate, clofibrate, etofibrate, fenofibrate,

bezafibrate, gemfibrozil, acipimox, eicosapentaenoic acid (icosapent, icopenate, icosapentate) ethyl ester, probucol, policosanol, colesevelam hydrochloride, colestyramine (cholestyramine resin), colestipol hydrochloride, colestimide (colestilan), ezetimibe and niacin (nicotinic acid).

[80] The pharmaceutical composition for the prophylaxis or treatment of obesity according to [30], which is used in combination with a therapeutic agent for diabetes.

[81] The pharmaceutical composition for the prophylaxis or treatment of obesity according to [80], wherein the therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of insulin secretagogues, biguanides, α-glucosidase inhibitors, insulin preparations, insulin analogs, insulin sensitivity enhancers, IL-11, anti-CD25 (IL-2 Receptor) agents, angiotensin (AT1) antagonists, angiotensin-converting enzyme (ACE) inhibitors, aldose reductase inhibitors, antioxidants, carnitine acetyltransferase stimulant, antidepressants, glucocorticoids, retilin, radical formation agonists and transketolase activators.

[82] The pharmaceutical composition for the prophylaxis or treatment of obesity according to [81], wherein the therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of nateglinide, glimepiride, glibenclamide, gliclazide, acetohexamide, tolbutamide, glyclopyramide, tolazamide, glybuzole, glipizide, glibornuride, gliquidone, repaglinide, metformin hydrochloride, buformin hydrochloride, voglibose, acarbose, epalrestat, miglitol, insulin, pioglitazone hydrochloride, rosiglitazone maleate, chromium picolinate/biotin, V-411, recombinant human interleukin-11, daclixiimab (daclizumab), losartan potassium, captopril, imidapril hydrochloride, alpha-lipoic acid, levacecarnine (acetyl-L-carnitine, levocarnitine acetyl) hydrochloride, captopril, retilin, verteporfin, benfotiamine

and fluocinolone acetonide.

[83] The pharmaceutical composition for the prophylaxis or treatment of obesity according to [30], which is used in combination with a different therapeutic agent for obesity.

[84] The pharmaceutical composition for the prophylaxis or treatment of obesity according to [83], wherein the different therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, lipase inhibitors, 5-HT/norepinephrine reuptake dual inhibitors, 5-HT reuptake inhibitors, supplements containing herbal ephedrine and caffeine, human chorionic gonadotropins, adrenoceptor agonists, methamphetamine, phentermine and amfepramone.

[85] The pharmaceutical composition for the prophylaxis or treatment of obesity according to [84], wherein the different therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, orlistat, sibutramine hydrochloride monohydrate, fluoxetine hydrochloride, chorionic gonadotropin (human), VNS therapy using NCP System, metaraminol, d-methamphetamine hydrochloride, phentermine, amfepramone hydrochloride (diethylpropion), benzfetamine hydrochloride and phendimetrazine tartrate.

[86] The pharmaceutical composition for the prophylaxis or treatment of obesity according to [30], which is used in combination with a therapeutic agent for hypertension.

[87] The pharmaceutical composition for the prophylaxis or treatment of obesity according to [86], wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of thiazides, aldosterone antagonists, adrenergic neuron blockers, calcium channel blockers; dopamine D2 antagonists, beta-adrenoceptor antagonists, alpha2-adrenoceptor agonists, guanylate cyclase activators, beta1-adrenoceptor antagonists, alpha1-adrenoceptor antagonists, antioxidants, angiotensin-I converting enzyme

(ACE) inhibitors, Na+/H+ exchange inhibitors, alpha-adrenoceptor antagonists, nitric oxide donors, 5-HT2 antagonists, K(ATP) channel activators, potassium sparing diuretic prostaglandin synthase stimulants, imidazoline I1 receptor agonists, angiotensin AT1 antagonists, dopamine D1 agonists, guanylate cyclase stimulants, endothelin ETA receptor antagonists, endothelin ETB receptor antagonists, NOS3 expression enhancers, prostacyclin analogs, prostaglandins, angiotensin II antagonists, electrolyte absorption agonists, nicotinic antagonists, dopamine D2 agonists, prolactin inhibitors, platelet-activating factor (PAF) antagonists, platelet aggregation antagonists, tumor necrosis factor antagonists, Rho kinase inhibitors, PPAR-alpha agonists, AMPA receptor modulators, GABA(A) receptor antagonists and phosphodiesterase V (PDE5A) inhibitors.

[88] The pharmaceutical composition for the prophylaxis or treatment of obesity according to [87], wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of chlorothiazide, hydrochlorothiazide, hydroflumethiazide, methyclothiazide, polythiazide, xipamide, cyclopenthiazide, bendroflumethiazide (bendrofluazide), spironolactone, epoxymexrenone (eplerenone), guanethidine monosulfate, guanadrel sulfate, verapamil, propranolol hydrochloride, alprenolol hydrochloride, pindolol, oxprenolol hydrochloride, timolol maleate, sotalol hydrochloride, acebutolol hydrochloride, carteolol hydrochloride, mepindolol sulfate, arotinolol hydrochloride, indenolol hydrochloride, tertatolol hydrochloride, celiprolol hydrochloride, tilisolol hydrochloride, nebivolol, penbutolol sulfate, nadolol, cloranolol hydrochloride, bevantol (bevantolol) hydrochloride, clonidine, guanfacine hydrochloride, diltiazem hydrochloride, nicardipine hydrochloride, nitrendipine, felodipine, nilvadipine; nivadipine, nisoldipine,

benidipine hydrochloride, amlodipine besylate, franidipine (manidipine) hydrochloride, lacidipine, isradipine, barnidipine (mepirodipine) hydrochloride, efonidipine hydrochloride ethanol, cinaldipine (cilnidipine), aranidipine, lercanidipine (masnidipine) hydrochloride, azelnidipine, amlodipine, manidipine (franidipine), sodium nitroprusside, atenolol, metoprolol tartrate, betaxolol hydrochloride, bopindolol, bisoprolol fumarate, esmolol hydrochloride, carvedilol, metoprolol succinate, talinolol, prazosin hydrochloride, urapidil, indoramin hydrochloride, bunazosin hydrochloride, terazosin hydrochloride, doxazosin mesylate, urapidil, nifedipine, captopril, enalapril maleate, lisinopril, perindopril, alacepril, ramipril, quinapril hydrochloride, delapril hydrochloride, benazepril hydrochloride, cilazapril, fosinoprilat, fosinopril sodium, trandolapril, spirapril, temocapril hydrochloride, moexipril hydrochloride, imidapril hydrochloride, zofenopril calcium, enalaprilat, zofenoprilat, amiloride hydrochloride, labetalol hydrochloride, nipradilol (nipradolol), linsidomine, ketanserin, pinacidil, cicletanine (cycletanide), amosulalol hydrochloride, moxonidine hydrochloride hydrate, losartan potassium, valsartan, eprosartan mesylate, candesartan cilexetil (hexetil), irbesartan, telmisartan, olmesartan medoxomil, fenoldopam mesilate, cadralazine, rilmenidine dihydrogen phosphate, bosentan, beraprost sodium, limaprost alfadex (alpha-cyclodextrin), uniprost (treprostinil sodium), iloprost (ciloprost), mecamylamine hydrochloride, metergoline, guanabenz acetate, cloricromene, fasudil, doconexent (docosahexaenoic acid), cyclothiazide, sildenafil citrate, chlortalidone (chlorthalidone), quinethazone, indapamide, metolazone, phenoxybenzamine hydrochloride, metirosine (metyrosine), diazoxide, torasemide (torsemide), clopamide, hydralazine hydrochloride, reserpine and methyldopa.

[89] The pharmaceutical composition for the prophylaxis or treatment of obesity according to [30], which is used in combination with a therapeutic agent for thrombosis.

[90] The pharmaceutical composition for the prophylaxis or treatment of obesity according to [89], wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin preparations, low molecular weight heparins, heparin analogs, anticoagulants, thrombin inhibitors, anti-thrombin preparations, antiplatelet agents and thrombolytic agents.

[91] The pharmaceutical composition for the prophylaxis or treatment of obesity according to [90], wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin calcium, heparin sodium, dalteparin sodium, parnaparin sodium, reviparin sodium, danaparoid sodium, warfarin potassium, argatroban, gabexate mesylate, nafamostat mesylate, human anti-thrombin III, aspirin, dipyridamole, ticlopidine hydrochloride, cilostazol, limaprost alfadex, sodium ozagrel, sarpogrelate hydrochloride, ethyl icosapentate, beraprost sodium, urokinase, tisokinase, alteplase, nasaruplase, nateplase, monteplase, pamiteplase, batroxobin, sodium citrate and protein C.

[92] The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to [31], which is used in combination with a therapeutic agent for hyperlipidemia.

[93] The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to [92], wherein the therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of HMG-CoA reductase inhibitors (statins), fibrates, TNFSF6 expression inhibitors, HDL-cholesterol increasing agents, ApoA1 expression enhancers, SPP1 (osteopontin) expression inhibitors, drugs acting on peroxisome proliferator-activated receptors

(PPAR), PPAR-alpha agonists, lipase clearing factor stimulants, cholesterol antagonists, platelet aggregation antagonists, antioxidants, cholesterol biosynthesis inhibitors, LDL-receptor up-regulators, bile acid sequestrants, cholesterol absorption inhibitors and nicotinic acids.

[94] The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to [93], wherein the therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of lovastatin, pravastatin (eptastatin) sodium, fluvastatin (fluindostainin) sodium, rosuvastatin calcium, atorvastatin calcium, simvastatin (synvinolin), pitavastatin (itavastatin, nisvastatin) calcium, ronifibrate (ronifibrato), binifibrate (binifibrato), clinofibrate, ciprofibrate, clofibrate, etofibrate, fenofibrate, bezafibrate, gemfibrozil, acipimox, eicosapentaenoic acid (icosapent, icopenate, icosapentate) ethyl ester, probucol, policosanol, colesevelam hydrochloride, colestyramine (cholestyramine resin), colestipol hydrochloride, colestimide (colestilan), ezetimibe and niacin (nicotinic acid).

[95] The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to [31], which is used in combination with a therapeutic agent for diabetes.

[96] The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to [95], wherein the therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of insulin secretagogues, biguanides, α-glucosidase inhibitors, insulin preparations, insulin analogs, insulin sensitivity enhancers, IL-11, anti-CD25 (IL-2 Receptor) agents, angiotensin (AT1) antagonists, angiotensin-converting enzyme (ACE) inhibitors, aldose reductase inhibitors, antioxidants, carnitine acetyltransferase stimulant, antidepressants, glucocorticoids, retilin, radical formation agonists and

transketolase activators.

[97] The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to [96], wherein the therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of nateglinide, glimepiride, glibenclamide, gliclazide, acetohexamide, tolbutamide, glyclopyramide, tolazamide, glybuzole, glipizide, glibornuride, gliquidone, repaglinide, metformin hydrochloride, buformin hydrochloride, voglibose, acarbose, epalrestat, miglitol, insulin, pioglitazone hydrochloride, rosiglitazone maleate, chromium picolinate/biotin, V-411, recombinant human interleukin-11, dacliximab (daclizumab), losartan potassium, captopril, imidapril hydrochloride, alpha-lipoic acid, levacecarnine (acetyl-L-carnitine, levocarnitine acetyl) hydrochloride, captopril, retilin, verteporfin, benfotiamine and fluocinolone acetonide.

[98] The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to [31], which is used in combination with a therapeutic agent for obesity.

[99] The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to [98], wherein the therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, lipase inhibitors, 5-HT/norepinephrine reuptake dual inhibitors, 5-HT reuptake inhibitors, supplements containing herbal ephedrine and caffeine, human chorionic gonadotropins, adrenoceptor agonists, methamphetamine, phentermine and amfepramone.

[100] The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to [99], wherein the therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, orlistat, sibutramine hydrochloride monohydrate, fluoxetine hydrochloride,

chorionic gonadotropin (human), VNS therapy using NCP System, metaraminol, d-methamphetamine hydrochloride, phentermine, amfepramone hydrochloride (diethylpropion), benzfetamine hydrochloride and phendimetrazine tartrate.

[101] The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to [31], which is used in combination with a therapeutic agent for hypertension.

[102] The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to [101], wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of thiazides, aldosterone antagonists, adrenergic neuron blockers, calcium channel blockers; dopamine D2 antagonists, beta-adrenoceptor antagonists, alpha2-adrenoceptor agonists, guanylate cyclase activators, beta1-adrenoceptor antagonists, alpha1-adrenoceptor antagonists, antioxidants, angiotensin-I converting enzyme (ACE) inhibitors, Na+/H+ exchange inhibitors, alpha-adrenoceptor antagonists, nitric oxide donors, 5-HT2 antagonists, K(ATP) channel activators, potassium sparing diuretic·prostaglandin synthase stimulants, imidazoline I1 receptor agonists, angiotensin AT1 antagonists, dopamine D1 agonists, guanylate cyclase stimulants, endothelin ETA receptor antagonists, endothelin ETB receptor antagonists, NOS3 expression enhancers, prostacyclin analogs, prostaglandins, angiotensin II antagonists, electrolyte absorption agonists, nicotinic antagonists, dopamine D2 agonists, prolactin inhibitors, platelet-activating factor (PAF) antagonists, platelet aggregation antagonists, tumor necrosis factor antagonists, Rho kinase inhibitors, PPAR-alpha agonists, AMPA receptor modulators, GABA(A) receptor antagonists and phosphodiesterase V (PDE5A) inhibitors.

[103] The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to [102], wherein

the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of chlorothiazide, hydrochlorothiazide, hydroflumethiazide, methyclothiazide, polythiazide, xipamide, cyclopenthiazide, bendroflumethiazide (bendrofluazide), spironolactone, epoxymexrenone (eplerenone), guanethidine monosulfate, guanadrel sulfate, verapamil, propranolol hydrochloride, alprenolol hydrochloride, pindolol, oxprenolol hydrochloride, timolol maleate, sotalol hydrochloride, acebutolol hydrochloride, carteolol hydrochloride, mepindolol sulfate, arotinolol hydrochloride, indenolol hydrochloride, tertatolol hydrochloride, celiprolol hydrochloride, tilisolol hydrochloride, nebivolol, penbutolol sulfate, nadolol, cloranolol hydrochloride, bevantol (bevantolol) hydrochloride, clonidine, guanfacine hydrochloride, diltiazem hydrochloride, nicardipine hydrochloride, nitrendipine, felodipine, nilvadipine; nivadipine, nisoldipine, benidipine hydrochloride, amlodipine besylate, franidipine (manidipine) hydrochloride, lacidipine, isradipine, barnidipine (mepirodipine) hydrochloride, efonidipine hydrochloride ethanol, cinaldipine (cilnidipine), aranidipine, lercanidipine (masnidipine) hydrochloride, azelnidipine, amlodipine, manidipine (franidipine), sodium nitroprusside, atenolol, metoprolol tartrate, betaxolol hydrochloride, bopindolol, bisoprolol fumarate, esmolol hydrochloride, carvedilol, metoprolol succinate, talinolol, prazosin hydrochloride, urapidil, indoramin hydrochloride, bunazosin hydrochloride, terazosin hydrochloride, doxazosin mesylate, urapidil, nifedipine, captopril, enalapril maleate, lisinopril, perindopril, alacepril, ramipril, quinapril hydrochloride, delapril hydrochloride, benazepril hydrochloride, cilazapril, fosinoprilat, fosinopril sodium, trandolapril, spirapril, temocapril hydrochloride, moexipril hydrochloride, imidapril

hydrochloride, zofenopril calcium, enalaprilat, zofenoprilat, amiloride hydrochloride, labetalol hydrochloride, nipradilol (nipradolol), linsidomine, ketanserin, pinacidil, cicletanine (cycletanide), amosulalol hydrochloride, moxonidine hydrochloride hydrate, losartan potassium, valsartan, eprosartan mesylate, candesartan cilexetil (hexetil), irbesartan, telmisartan, olmesartan medoxomil, fenoldopam mesilate, cadralazine, rilmenidine dihydrogen phosphate, bosentan, beraprost sodium, limaprost alfadex (alpha-cyclodextrin), uniprost (treprostinil sodium), iloprost (ciloprost), mecamylamine hydrochloride, metergoline, guanabenz acetate, cloricromene, fasudil, doconexent (docosahexaenoic acid), cyclothiazide, sildenafil citrate, chlortalidone (chlorthalidone), quinethazone, indapamide, metolazone, phenoxybenzamine hydrochloride, metirosine (metyrosine), diazoxide, torasemide (torsemide), clopamide, hydralazine hydrochloride, reserpine and methyldopa.

[104] The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to [31], which is used in combination with a therapeutic agent for thrombosis.

[105] The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to [104], wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin preparations, low molecular weight heparins, heparin analogs, anticoagulants, thrombin inhibitors, anti-thrombin preparations, antiplatelet agents and thrombolytic agents.

[106] The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to [105] wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin calcium, heparin sodium, dalteparin sodium, parnaparin sodium, reviparin sodium, danaparoid sodium, warfarin potassium,

argatroban, gabexate mesylate, nafamostat mesylate, human antithrombin III, aspirin, dipyridamole, ticlopidine hydrochloride, cilostazol, limaprost alfadex, sodium ozagrel, sarpogrelate hydrochloride, ethyl icosapentate, beraprost sodium, urokinase, tisokinase, alteplase, nasaruplase, nateplase, monteplase, pamiteplase, batroxobin, sodium citrate and protein C.

[107] A pharmaceutical composition for inhibition of a receptor tyrosine kinase negative regulator, which is used in combination with a therapeutic agent for hyperlipidemia.

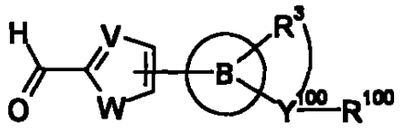
[108] A pharmaceutical composition for inhibition of a receptor tyrosine kinase negative regulator, which is used in combination with a therapeutic agent for diabetes.

[109] A pharmaceutical composition for inhibition of a receptor tyrosine kinase negative regulator, which is used in combination with a therapeutic agent for obesity.

[110] A pharmaceutical composition for inhibition of a receptor tyrosine kinase negative regulator, which is used in combination with a therapeutic agent for hypertension.

[111] A pharmaceutical composition for inhibition of a receptor tyrosine kinase negative regulator, which is used in combination with a therapeutic agent for thrombosis.

[112] A 5-membered heteroaromatic ring compound represented by the formula [II]



[II]

wherein

Y^{100} is $-C(R^{13})(R^{14})-$ (R^{13} and R^{14} are each as defined in [1]);

R^{100} is a hydroxyl group or a halogen atom, and

V, W and R^3 are each as defined in [1], or a pharmaceutically acceptable salt thereof.

[113] The 5-membered heteroaromatic ring compound of [112], wherein, in the formula [II], R^{13} and R^{14} are each a hydrogen

atom, V is =CH- and W is -S-, or a pharmaceutically acceptable salt thereof.

DETAILED DESCRIPTION OF THE INVENTION

The definition of each substituent and each moiety used in the present specification is as follows.

The "halogen atom" is a fluorine atom, a chlorine atom, a bromine atom or an iodine atom, preferably a fluorine atom or a chlorine atom.

The "C_{1-4} alkyl group" is a straight chain or branched chain alkyl group having 1 to 4 carbon atoms, which is specifically exemplified by methyl group, ethyl group, propyl group, isopropyl group, butyl group, isobutyl group, sec-butyl group and tert-butyl group.

It is preferably methyl group for R^1 or R^2, and methyl group or ethyl group for R^{13}, R^{14}, R^{19}, R^{22} or R^{25}.

The "C_{1-6} alkyl group" is a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, which is specifically exemplified by methyl group, ethyl group, propyl group, isopropyl group, butyl group, isobutyl group, sec-butyl group, tert-butyl group, pentyl group, isopentyl group, neopentyl group, tert-pentyl group, 1-ethylpropyl group, hexyl group and the like. Preferred are branched chain alkyl group, methyl group and ethyl group, each having 3 to 6 carbon atoms, such as isopropyl group, isobutyl group, tert-butyl group, isopentyl group, neopentyl group, tert-pentyl group, 1-ethylpropyl group and the like.

Preferably, it is methyl group, ethyl group or isopentyl group for R^4, methyl group or isobutyl group for R^5, R^6, R^7, R^8, R^9 or R^{10}, methyl group, ethyl group or isopropyl group for R^{15} or R^{16}, methyl group or isobutyl group for R^{17}, methyl group or isopentyl group for R^{20} or R^{21}, and methyl group, isobutyl group, tert-butyl group, isopentyl group, neopentyl group, tert-pentyl group or 1-ethylpropyl group for R^{18}, R^{23} or R^{24}.

The "C_{1-8} alkyl group" is a straight chain or branched chain alkyl group having 1 to 8 carbon atoms, which is specificaliy exemplified by methyl group, ethyl group, propyl group, isopropyl group, butyl group, isobutyl group, sec-butyl group, tert-butyl group, pentyl group, isopentyl group, neopentyl group, tert-pentyl group, 1-ethylpropyl group, hexyl group, 2-ethylbutyl group, 3,3-dimethylbutyl group, heptyl group, 1-propylbutyl group, 3-ethylpentyl group, octyl group and the like. Preferably, it is methyl group, ethyl group, propyl group, isopropyl group or a branched chain alkyl group having 4 to 8 carbon atoms such as isobutyl group, sec-butyl group, tert-butyl group, isopentyl group, neopentyl group, tert-pentyl group, 1-ethylpropyl group, 2-ethylbutyl group, 1-propylbutyl group and the like.

Preferably, it is methyl group, tert-butyl group or 1-ethylpropyl group for R^3, and methyl group, ethyl group, propyl group, isopropyl group, isobutyl group, sec-butyl group, tert-butyl group, isopentyl group, neopentyl group, tert-pentyl group, 1-ethylpropyl group, 2-ethylbutyl group or 1-propylbutyl group for R^{11} or R^{12}. It is particularly preferably isopropyl group for R^{11} or R^{12}.

The "C_{1-4} haloalkyl group" is a haloalkyl group wherein a straight chain or branched chain alkyl group having 1 to 4 carbon atoms is substituted by the above-defined "halogen atom", which is specifically exemplified by fluoromethyl group, difluoromethyl group, trifluoromethyl group, bromomethyl group, chloromethyl group, 1,2-dichloromethyl group, 2,2-dichloromethyl group, 2,2,2-trifluoroethyl group and the like, with preference given to trifluoromethyl group.

It is preferably trifluoromethyl group for R^3.

The "C_{1-4} alkylene group" is a straight chain or branched chain alkylene group having 1 to 4 carbon atoms, which is specifically exemplified by methylene group, ethylene group,

trimethylene group, propylene group, tetramethylene group and the like. Preferably, it is methylene group or ethylene group, more preferably methylene group.

Preferably, it is methylene group or ethylene group for A, and methylene group for A^1.

The "C_{1-4} alkoxy group" is a straight chain or branched chain alkoxy group having 1 to 4 carbon atoms, which is specifically exemplified by methoxy group, ethoxy group, propoxy group, isopropoxy group, butoxy group, isobutoxy group, tert-butoxy group and the like. Preferably, it is methoxy group.

Preferably, it is methoxy group for R^{22} or R^{25}.

The "C_{1-6} alkoxy group" is a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms, which is specifically exemplified by methoxy group, ethoxy group, propoxy group, isopropoxy group, butoxy group, isobutoxy group, tert-butoxy group, pentyloxy group, isopentyloxy group, neopentyloxy group, tert-pentyloxy group, 1-ethylpropoxy group, hexyloxy group and the like. It is preferably methoxy group, ethoxy group or branched chain alkoxy group having 3 to 6 carbon atoms (e.g., isopropoxy group, isobutoxy group, tert-butoxy group, isopentyloxy group, neopentyloxy group, tert-pentyloxy group, 1-ethylpropoxy group etc.).

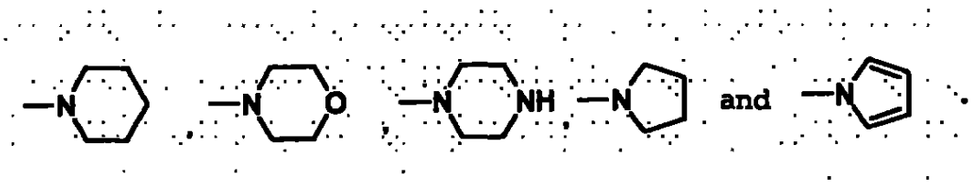
Preferably, it is methoxy group, ethoxy group, isopropoxy group, isobutoxy group, tert-butoxy group, isopentyloxy group, neopentyloxy group, tert-pentyloxy group or 1-ethylpropoxy group for R^3.

The "aryl group" is an aromatic hydrocarbon group having 6 to 14 carbon atoms, which is specifically exemplified by phenyl group, naphthyl group, biphenylyl group (e.g., 2-biphenylyl group, 3-biphenylyl group, 4-biphenylyl group etc.), anthryl group and the like. Preferably, it is phenyl group, naphthyl group or biphenylyl group, more preferably phenyl

group.

Preferably, it is phenyl group or biphenylyl group for Z, phenyl group for B or E, phenyl group or naphthyl group for R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{15}, R^{16}, R^{17}, R^{18} or R^{21}. It is particularly preferably phenyl group for Z.

The "heterocyclic group" is "a saturated or unsaturated 5- to 7-membered heterocyclic group containing 1 to 3 heteroatoms selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom", which is specifically exemplified by furyl group, thienyl group, pyrrolyl group, oxazolyl group, isoxazolyl group, thiazolyl group, isothiazolyl group, imidazolyl group, pyrazolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, tetrahydrofuryl group, tetrahydrothienyl group, pyrrolidinyl group, pyrazolidinyl group, imidazolidinyl group, oxazolidinyl group, thiazolidinyl group, tetrahydropyranyl group, dioxanyl group, piperidinyl group, piperazinyl group, morpholinyl group and the like, preferably a heterocyclic group selected from the group consisting of



The "heteroaromatic ring group" is "a 5- to 14-membered mono or fused heteroaromatic ring group containing 1 to 3 heteroatoms selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom, which is specifically exemplified by furyl group, thienyl group, pyrrolyl group, oxazolyl group, isoxazolyl group, thiazolyl group, isothiazolyl group, imidazolyl group, pyrazolyl group, 1,3,4-thiadiazolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, indolyl group, isoindolyl group, benzofuranyl group,

benzothienyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, indolizinyl group, quinolyl group, isoquinolyl group, quinazolinyl group, cinnolinyl group, quinoxalinyl group, phthalazinyl group, acridinyl group, phenazinyl group, naphthyridinyl group and the like. Preferably, "a 5- to 10-membered mono or fused heteroaromatic ring group containing 1 to 3 heteroatoms selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom", which is specifically exemplified by furyl group, thienyl group, pyrrolyl group, oxazolyl group, isoxazolyl group, thiazolyl group, isothiazolyl group, imidazolyl group, pyrazolyl group, 1,3,4-thiadiazolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, indolyl group, isoindolyl group, benzofuranyl group, benzothienyl group, benzimidazolyl group, benzothiazolyl group, benzoxazolyl group, indolizinyl group, quinolyl group, isoquinolyl group and the like.

Preferably, it is thienyl group, thiazolyl group, pyrazolyl group, 1,3,4-thiadiazolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, indolyl group, benzimidazolyl group, benzothiazolyl group or benzoxazolyl group for B, furyl group, isoxazolyl group or pyridyl group for E, thienyl group or pyridyl group for Z, and oxazolyl group, thiazolyl group, pyridyl group, benzothienyl group, benzimidazolyl group or quinolyl group for R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{15}, R^{16}, R^{17} or R^{21}.

The "C_{3-7} cycloalkyl group" is a cycloalkyl group having 3 to 7 carbon atoms, which is specifically exemplified by cyclopropyl group, cyclobutyl group, cyclopentyl group, cyclohexyl group and cycloheptyl group. Preferably, it is cycloalkyl group having 5 to 7 carbon atoms, particularly preferably cyclohexyl group.

Preferably, it is cyclohexyl group for Z.

The "C_{2-4} alkenyl group" is a straight chain or branched

chain alkenyl group having 2 to 4 carbon atoms, which is specifically exemplified by vinyl group, 1-propenyl group, allyl group, 1-methyl-2-propenyl group, 1-butenyl group, 2-butenyl group, 3-butenyl group and the like.

Preferably, it is allyl group for R^{11} or R^{12}.

The "C_{1-4} alkylsulfonyl group" is that wherein the "alkyl" moiety is alkylsulfonyl group having the above-defined "C_{1-4} alkyl group", which is specifically exemplified by methylsulfonyl group, ethylsulfonyl group, propylsulfonyl group, isopropylsulfonyl group, butylsulfonyl group, isobutylsulfonyl group, sec-butylsulfonyl group and tert-butylsulfonyl group.

Preferably, it is methylsulfonyl group (i.e., mesyl group) for R^{11}, R^{12}, R^{23} or R^{24}.

The "C_{1-4} alkylcarbonyl group" is that wherein the "alkyl" moiety is alkylcarbonyl group having the above-defined "C_{1-4} alkyl group", with preference given to acetyl group, propionyl group, butyryl group, isobutyryl group, valeryl group, isovaleryl group, pivaloyl group and the like.

Preferably, it is acetyl group for R^{11} or R^{12}, and acetyl group or isobutyryl group for R^{23} or R^{24}.

The "C_{1-4} alkoxycarbonyl group" is alkoxycarbonyl group wherein the "alkoxy" moiety is the above-defined "C_{1-4} alkoxy group", which is specifically exemplified by methoxycarbonyl group, ethoxycarbonyl group, propoxycarbonyl group, isopropoxycarbonyl group, butoxycarbonyl group, isobutoxycarbonyl group, tert-butoxycarbonyl group and the like.

The "aryloxy group" is aryloxy group wherein the "aryl" moiety is the above-defined "aryl group", which is specifically exemplified by phenoxy group, naphthyloxy group and the like.

The "aralkyl group" is a "C_{1-4} alkyl group" substituted by "aryl group", wherein the "aryl group" and "C_{1-4} alkyl group" are as defined above. The "aralkyl group" is specifically exemplified by benzyl group and the like.

The "C_{1-4} alkylamino group" is alkylamino group wherein the "alkyl" moiety is the above-defined "C_{1-4} alkyl group", which is specifically exemplified by methylamino group, ethylamino group, propylamino group, isopropylamino group, butylamino group, isobutylamino group, sec-butylamino group, tert-butylamino group and the like.

The "C_{1-6} alkylamino group" is alkylamino group wherein the "alkyl" moiety is the above-defined "C_{1-6} alkyl group", which is specifically exemplified by methylamino group, ethylamino group, propylamino group, isopropylamino group, butylamino group, isobutylamino group, sec-butylamino group, tert-butylamino group, pentylamino group, isopentylamino group, neopentylamino group, tert-pentylamino group, hexylamino group and the like.

Preferably, it is methylamino group, ethylamino group, isopropylamino group, isobutylamino group, sec-butylamino group, tert-butylamino group, isopentylamino group, neopentylamino group or tert-pentylamino group for R^{22} or R^{25}.

The "di(C_{1-4} alkyl)amino group" is di(alkyl)amino group wherein the "alkyl" moiety is the above-defined "C_{1-4} alkyl group", which is specifically exemplified by dimethylamino group, diethylamino group, dipropylamino group, diisopropylamino group, dibutylamino group, diisobutylamino group, di(sec-butyl)amino group, di(tert-butyl)amino group, N-ethyl-N-methylamino group, N-methyl-N-propylamino group, N-ethyl-N-propylamino group and the like.

The "di(C_{1-6} alkyl)amino group" is di(alkyl)amino group wherein the "alkyl" moiety is the above-defined "C_{1-4} alkyl group", which is specifically exemplified by dimethylamino group, diethylamino group, dipropylamino group, diisopropylamino group, dibutylamino group, diisobutylamino group, di(sec-butyl)amino group, di(tert-butyl)amino group, dipentylamino group, diisopentylamino group, di(tert-

pentyl)amino group, dihexylamino group, N-ethyl-N-methylamino group, N-methyl-N-propylamino group, N-ethyl-N-propylamino group and the like.

Preferably, it is dimethylamino group, diethylamino group, dipropylamino group, dibutylamino group, dipentylamino group, diisopentylamino group, dihexylamino group, N-ethyl-N-methylamino group, N-methyl-N-propylamino group or N-ethyl-N-propylamino group for R^{22} or R^{25}.

The "C_{1-6} alkylthio group" is alkylthio group wherein the "alkyl" moiety is the above-defined "C_{1-6} alkyl group", which is specifically exemplified by methylthio group, ethylthio group, propylthio group, isopropylthio group, butylthio group, isobutylthio group, sec-butylthio group, tert-butylthio group, pentylthio group, isopentylthio group, neopentylthio group, tert-pentylthio group, 1-ethylpropylthio group, hexylthio group and the like.

Preferably, it is methylthio group for R^{22} or R^{25}.

The "di(C_{1-6} alkyl)aminocarbonyl group" is di(alkyl)aminocarbonyl group wherein the "di(C_{1-6} alkyl)amino" moiety is the above-defined "di(C_{1-6} alkyl)amino group", which is specifically exemplified by dimethylaminocarbonyl group, diethylaminocarbonyl group, dipropylaminocarbonyl group, diisopropylaminocarbonyl group, dibutylaminocarbonyl group, diisobutylaminocarbonyl group, di(sec-butyl)aminocarbonyl group, di(tert-butyl)aminocarbonyl group, dipentylaminocarbonyl group, diisopentylaminocarbonyl group, di(tert-pentyl)aminocarbonyl group, dihexylaminocarbonyl group, N-ethyl-N-methylaminocarbonyl group, N-methyl-N-propylaminocarbonyl group, N-ethyl-N-propylaminocarbonyl group and the like.

When R^{19} of the -COO(R^{19}) moiety for R is hydrogen atom, this carboxy group may form a salt. As the salt, alkali metal salts (e.g., potassium salt, sodium salt etc.), alkaline earth metal salts (e.g., calcium salt, magnesium salt etc.) and the

like can be mentioned, with preference given to sodium salt and calcium salt.

The "C_{1-6} alkyl group" for R^4, R^5, R^6, R^7, R^8, R^9 or R^{10} is optionally substituted by optionally substituted aryl group, optionally substituted heteroaromatic ring group, carboxy group, C_{1-4} alkoxycarbonyl group, $-CO-N(R^{15})(R^{16})$, $-N(R^{15})(R^{16})$, $-O-R^{17}$, $-CO-R^{17}$, $-SO_2-R^{17}$ or C_{3-7} cycloalkyl group. Such "C_{1-6} alkyl group" may be C_{1-6} alkyl group substituted by plural substituents like, for example, benzhydryl group. Preferably, the number of substituent is 1. When the "C_{1-6} alkyl group" is substituted, the "C_{1-6} alkyl group" moiety is preferably methyl group.

The "aryl group" moiety of the "optionally substituted aryl group", which is a substituent on the "C_{1-6} alkyl group" for R^4, R^5, R^6, R^7, R^8, R^9 or R^{10} is the above-defined "aryl group", preferably, phenyl group or naphthyl group.

The "optionally substituted aryl group", which is a substituent on the "C_{1-6} alkyl group" for R^4, R^5, R^6, R^7, R^8, R^9 or R^{10} is optionally substituted by 1 to 3 substituents selected from the following. As such substituent, halogen atom, C_{1-8} alkyl group, C_{1-8} alkyl group substituted by di(C_{1-6} alkyl)aminocarbonyl group, C_{1-4} haloalkyl group, C_{1-4} alkoxy group, C_{2-4} alkenyl group, carboxy group, hydroxyl group, cyano group, nitro group, amino group, C_{1-4} alkylamino group, di(C_{1-4} alkyl)amino group, 1-pyrrolidinyl group, 1-piperidyl group, morpholino group, C_{1-4} alkoxycarbonyl group, C_{1-6} alkylthio group, heteroaromatic ring group optionally substituted by halogen atom, aralkyl group and the like can be mentioned. Preferable substituents include halogen atoms (e.g., fluorine atom, chlorine atom etc.), C_{1-8} alkyl groups (e.g., methyl group, isopropyl group, tert-butyl group, 1-propylbutyl group etc.), C_{1-4} haloalkyl groups (e.g., trifluoromethyl group etc.), C_{2-4} alkenyl groups (e.g., allyl group etc.), C_{1-6} alkylthio groups (e.g., methylthio group etc.), C_{1-8} alkyl group (e.g., methyl

group etc.) substituted by di(C_{1-6} alkyl)aminocarbonyl group (e.g., diethylaminocarbonyl group etc.), heteroaromatic ring group (e.g., thienyl group, imidazolyl group etc.) optionally substituted by halogen atom (e.g., chlorine atom etc.) and aralkyl groups (e.g., benzyl group etc.).

The "optionally substituted heteroaromatic ring group", which is a substituent on the "C_{1-6} alkyl group" for R^4, R^5, R^6, R^7, R^8, R^9 or R^{10} is the above-defined "heteroaromatic ring group", which is preferably oxazolyl group, thiazolyl group, pyridyl group, benzothienyl group, benzimidazolyl group or quinolyl group.

The "optionally substituted heteroaromatic ring group", which is a substituent on the "C_{1-6} alkyl group" for R^4, R^5, R^6, R^7, R^8, R^9 or R^{10} is optionally substituted by 1 to 3 substituents selected from the following. As such substituent, halogen atom, C_{1-8} alkyl group, C_{1-8} alkyl group substituted by di(C_{1-6} alkyl)aminocarbonyl group, C_{1-4} haloalkyl group, C_{1-4} alkoxy group, C_{2-4} alkenyl group, carboxy group, hydroxyl group, cyano group, nitro group, amino group, C_{1-4} alkylamino group, di(C_{1-4} alkyl)amino group, 1-pyrrolidinyl group, 1-piperidyl group, morpholino group, C_{1-4} alkoxycarbonyl group, C_{1-6} alkylthio group, aryl group optionally substituted by halogen atom, heteroaromatic ring group optionally substituted by halogen atom, aralkyl group and the like can be mentioned. Preferable substituents include halogen atoms (e.g., fluorine atom, chlorine atom etc.), C_{1-8} alkyl groups (e.g., methyl group, isopropyl group, tert-butyl group, 1-propylbutyl group etc.), C_{1-4} haloalkyl groups (e.g., trifluoromethyl group etc.), C_{2-4} alkenyl groups (e.g., allyl group etc.), C_{1-6} alkylthio groups (e.g., methylthio group etc.), C_{1-8} alkyl group (e.g., methyl group etc.) substituted by di(C_{1-6} alkyl)aminocarbonyl group (e.g., diethylaminocarbonyl group etc.), aryl group (e.g., phenyl group etc.) optionally substituted by halogen atom (e.g.,

chlorine atom etc.), heteroaromatic ring group (e.g., thienyl group, imidazolyl group etc.) optionally substituted by halogen atom (e.g., chlorine atom etc.) and aralkyl groups (e.g., benzyl group etc.).

The "C_{1-4} alkoxycarbonyl group", which is a substituent on the "C_{1-6} alkyl group" for R^4, R^5, R^6, R^7, R^8, R^9 or R^{10} is the above-defined "C_{1-4} alkoxycarbonyl group", which is preferably ethoxycarbonyl group, propoxycarbonyl group or isobutoxycarbonyl group.

The "C_{3-7} cycloalkyl group", which is a substituent on the "C_{1-6} alkyl group" for R^4, R^5, R^6, R^7, R^8, R^9 or R^{10} is the above-defined "C_{3-7} cycloalkyl group", which is preferably cyclohexyl group.

The "optionally substituted aryl group" for R^4, R^5, R^6, R^7, R^8, R^9 or R^{10} is optionally substituted by 1 to 3 substituents selected from the following. As such substituent, halogen atom, C_{1-8} alkyl group, C_{1-4} haloalkyl group, C_{1-4} alkoxy group, carboxy group, hydroxyl group, cyano group, nitro group, amino group, C_{1-4} alkylamino group, di(C_{1-4} alkyl)amino group, 1-pyrrolidinyl group, 1-piperidyl group, morpholino group, C_{1-4} alkoxycarbonyl group, heteroaromatic ring group optionally substituted by halogen atom, aralkyl group and the like can be mentioned. Preferable substituents include halogen atoms (e.g., fluorine atom, chlorine atom etc.), C_{1-8} alkyl groups (e.g., methyl group, isopropyl group, tert-butyl group, 1-propylbutyl group etc.), C_{1-4} haloalkyl groups (e.g., trifluoromethyl group etc.), heteroaromatic ring groups (e.g., thienyl group, imidazolyl group etc.) optionally substituted by halogen atom (e.g., chlorine atom etc.) and aralkyl groups (e.g., benzyl group etc.).

The "optionally substituted heteroaromatic ring group" for R^4, R^5, R^6, R^7, R^8, R^9 or R^{10} is optionally substituted by 1 to 3 substituents selected from the following. As such

substituent, halogen atom, C_{1-8} alkyl group, C_{1-4} haloalkyl group, C_{1-4} alkoxy group, carboxy group, hydroxyl group, cyano group, nitro group, amino group, C_{1-4} alkylamino group, di(C_{1-4} alkyl)amino group, 1-pyrrolidinyl group, 1-piperidyl group, morpholino group, C_{1-4} alkoxycarbonyl group, aryl group optionally substituted by halogen atom, heteroaromatic ring group optionally substituted by halogen atom, aralkyl group and the like can be mentioned. Preferable substituents include halogen atoms (e.g., fluorine atom, chlorine atom etc.), C_{1-8} alkyl groups (e.g., methyl group, isopropyl group, tert-butyl group, 1-propylbutyl group etc.), C_{1-4} haloalkyl groups (e.g., trifluoromethyl group etc.), aryl group (e.g., phenyl group etc.) optionally substituted by halogen atom (e.g., chlorine atom etc.), heteroaromatic ring group (e.g., thienyl group, imidazolyl group etc.) optionally substituted by halogen atom (e.g., chlorine atom etc.), and aralkyl group (e.g., benzyl group etc.).

The "optionally substituted aryl group" for R^{15}, R^{16} or R^{17}" is optionally substituted by 1 to 3 substituents selected from the following. As such substituents, halogen atom, C_{1-8} alkyl group, C_{1-4} haloalkyl group, C_{1-4} alkoxy group, carboxy group, hydroxyl group, cyano group, nitro group, amino group, C_{1-4} alkylamino group, di(C_{1-4} alkyl)amino group, 1-pyrrolidinyl group, 1-piperidyl group, morpholino group, C_{1-4} alkoxycarbonyl group and the like can be mentioned. Preferable substituents include halogen atoms (e.g., chlorine atom etc.), C_{1-8} alkyl groups (e.g., methyl group, isopropyl group etc.), C_{1-4} alkoxy groups (e.g., methoxy group etc.), carboxy groups and di(C_{1-4} alkyl)amino groups (e.g., dimethylamino group etc.).

The "optionally substituted heteroaromatic ring group" for R^{15}, R^{16} or R^{17} is optionally substituted by 1 to 3 substituents selected from the following. As such substituents, halogen atom, C_{1-8} alkyl group, C_{1-4} haloalkyl group, C_{1-4} alkoxy

group, carboxy group, hydroxyl group, cyano group, nitro group, amino group, C_{1-4} alkylamino group, di(C_{1-4} alkyl)amino group, 1-pyrrolidinyl group, 1-piperidyl group, morpholino group, C_{1-4} alkoxycarbonyl group and the like can be mentioned. Preferable substituents include halogen atoms (e.g., chlorine atom etc.), C_{1-8} alkyl groups (e.g., methyl group, isopropyl group etc.), C_{1-4} alkoxy groups (e.g., methoxy group etc.), carboxy group and di(C_{1-4} alkyl)amino groups (e.g., dimethylamino group etc.).

The "C_{1-6} alkyl group" for R^{15}, R^{16} or R^{17} is optionally substituted by optionally substituted aryl group, optionally substituted heteroaromatic ring group, C_{1-4} alkoxy group optionally substituted by aryl group or optionally substituted aryloxy group. As the "C_{1-6} alkyl group" moiety when the "C_{1-6} alkyl group" is substituted is preferably methyl group.

The "aryl group" of the "optionally substituted aryl group", which is a substituent on the "C_{1-6} alkyl group" for R^{15}, R^{16} or R^{17} is the above-defined "aryl group", preferably phenyl group or naphthyl group.

The "optionally substituted aryl group", which is a substituent on the "C_{1-6} alkyl group" for R^{15}, R^{16} or R^{17} is optionally substituted by 1 to 3 substituents selected from the following. As such substituents, halogen atom, C_{1-8} alkyl group, C_{1-4} haloalkyl group, C_{1-4} alkoxy group, carboxy group, hydroxyl group, cyano group, nitro group, amino group, C_{1-4} alkylamino group, di(C_{1-4} alkyl)amino group, 1-pyrrolidinyl group, 1-piperidyl group, morpholino group, C_{1-4} alkoxycarbonyl group and the like can be mentioned. Preferable substituents include halogen atoms (e.g., chlorine atom etc.), C_{1-8} alkyl groups (e.g., methyl group, isopropyl group etc.), C_{1-4} alkoxy groups (e.g., methoxy group etc.), carboxy group, di(C_{1-4} alkyl)amino groups (e.g., dimethylamino group etc.), 1-pyrrolidinyl group, 1-piperidyl group and morpholino group.

The "heteroaromatic ring group" moiety of the "optionally

substituted heteroaromatic ring group", which is a substituent on the "C_{1-6} alkyl group" for R^{15}, R^{16} or R^{17} is the above-defined "heteroaromatic ring group", preferably oxazolyl group, thiazolyl group, pyridyl group, benzothienyl group, benzimidazolyl group or quinolyl group.

The "optionally substituted heteroaromatic ring group", which is a substituent on the "C_{1-6} alkyl group" for R^{15}, R^{16} or R^{17} is optionally substituted by 1 to 3 substituents selected from the following. As such substituents, halogen atom, C_{1-8} alkyl group, C_{1-4} haloalkyl group, C_{1-4} alkoxy group, carboxy group, hydroxyl group, cyano group, nitro group, amino group, C_{1-4} alkylamino group, di(C_{1-4} alkyl)amino group, 1-pyrrolidinyl group, 1-piperidyl group, morpholino group, C_{1-4} alkoxycarbonyl group and the like can be mentioned. Preferable substituents include halogen atoms (e.g., chlorine atom etc.), C_{1-8} alkyl groups (e.g., methyl group, isopropyl group etc.), C_{1-4} alkoxy groups (e.g., methoxy group etc.), carboxy group, di(C_{1-4} alkyl)amino groups (e.g., dimethylamino group etc.), 1-pyrrolidinyl group, 1-piperidyl group and morpholino group.

The "C_{1-4} alkoxy group" moiety of the "C_{1-4} alkoxy group optionally substituted by aryl group", which is a substituent on the "C_{1-6} alkyl group" for R^{15}, R^{16} or R^{17} is the above-defined "C_{1-4} alkoxy group", preferably methoxy group.

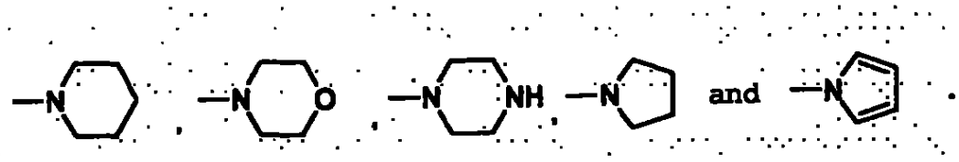
The "aryl group" moiety of the "C_{1-4} alkoxy group optionally substituted by aryl group", which is a substituent on the "C_{1-6} alkyl group" for R^{15}, R^{16} or R^{17} is the above-defined "aryl group", preferably phenyl group.

The "aryloxy group" moiety of the "optionally substituted aryloxy group", which is a substituent on the "C_{1-6} alkyl group" for R^{15}, R^{16} or R^{17} is the above-defined "aryloxy group", preferably phenoxy group.

The "optionally substituted aryloxy group", which is a substituent on the "C_{1-6} alkyl group" for R^{15}, R^{16} or R^{17} is

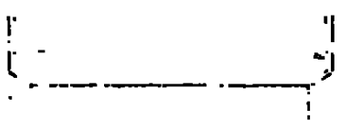
optionally substituted by 1 to 3 substituents selected from the following. As such substituents, halogen atom, C_{1-8} alkyl group, C_{1-4} haloalkyl group, C_{1-4} alkoxy group, carboxy group, hydroxyl group, cyano group, nitro group, amino group, C_{1-4} alkylamino group, di(C_{1-4} alkyl)amino group, 1-pyrrolidinyl group, 1-piperidyl group, morpholino group, C_{1-4} alkoxycarbonyl group and the like can be mentioned. Preferable substituents include halogen atom (e.g., chlorine atom etc.), C_{1-8} alkyl group (e.g., methyl group, isopropyl group etc.), C_{1-4} alkoxy group (e.g., methoxy group etc.), carboxy group, di(C_{1-4} alkyl)amino group (e.g., dimethylamino group etc.), 1-pyrrolidinyl group, 1-piperidyl group and morpholino group.

The "5- to 7-membered hetero ring optionally containing at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom", which is formed by R^{15} and R^{16} together with the nitrogen atom bonded thereto is preferably a "saturated or unsaturated 5- to 7-membered hetero ring containing 1 to 3 heteroatoms selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom", which is specifically exemplified by a hetero ring selected from the group consisting of



The "C_{1-6} alkyl group" for R^{21} is optionally substituted by optionally substituted aryl group or optionally substituted heteroaromatic ring group.

The "aryl group" moiety of the "optionally substituted aryl group", which is a substituent on the "C_{1-6} alkyl group" for R^{21} is the above-defined "aryl group", preferably phenyl



group.

The "optionally substituted aryl group", which is a substituent on the "C_{1-6} alkyl group" for R^{21} is optionally substituted by 1 to 3 substituents selected from the following. As such substituents, halogen atom, C_{1-8} alkyl group, C_{1-4} haloalkyl group, C_{1-4} alkoxy group, carboxy group, hydroxyl group, cyano group, nitro group, amino group, C_{1-4} alkylamino group, di(C_{1-4} alkyl)amino group, 1-pyrrolidinyl group, 1-piperidyl group, morpholino group, C_{1-4} alkoxycarbonyl group and the like can be mentioned. Preferable substituents include halogen atoms (e.g., chlorine atom, fluorine atom etc.), C_{1-8} alkyl groups (e.g., methyl group etc.) and C_{1-4} haloalkyl groups (e.g., trifluoromethyl group etc.).

The "heteroaromatic ring group" moiety of the "optionally substituted heteroaromatic ring group", which is a substituent on the "C_{1-6} alkyl group" for R^{21} is the above-defined "heteroaromatic ring group", preferably oxazolyl group, thiazolyl group, pyridyl group, benzothienyl group, benzimidazolyl group or quinolyl group.

The "optionally substituted heteroaromatic ring group", which is a substituent on the "C_{1-6} alkyl group" for R^{21} is optionally substituted by 1 to 3 substituents selected from the following. As such substituents, halogen atom, C_{1-8} alkyl group, C_{1-4} haloalkyl group, C_{1-4} alkoxy group, carboxy group, hydroxyl group, cyano group, nitro group, amino group, C_{1-4} alkylamino group, di(C_{1-4} alkyl)amino group, 1-pyrrolidinyl group, 1-piperidyl group, morpholino group, C_{1-4} alkoxycarbonyl group and the like can be mentioned. Preferable substituents include halogen atom (e.g., chlorine atom, fluorine atom etc.), C_{1-8} alkyl group (e.g., methyl group etc.) and C_{1-4} haloalkyl group (e.g., trifluoromethyl group etc.).

The "optionally substituted aryl group" for R^{21} is optionally substituted by 1 to 3 substituents selected from the

following. As such substituents, halogen atom, C_{1-8} alkyl group, C_{1-4} haloalkyl group, C_{1-4} alkoxy group, carboxy group, hydroxyl group, cyano group, nitro group, amino group, C_{1-4} alkylamino group, di(C_{1-4} alkyl)amino group, 1-pyrrolidinyl group, 1-piperidyl group, morpholino group, C_{1-4} alkoxycarbonyl group and the like can be mentioned. Preferable substituents include halogen atom (e.g., chlorine atom, fluorine atom etc.), C_{1-8} alkyl group (e.g., methyl group etc.) and C_{1-4} haloalkyl group (e.g., trifluoromethyl group etc.).

The "optionally substituted heteroaromatic ring group" for R^{21} is optionally substituted by 1 to 3 substituents selected from the following. As such substituents, halogen atom, C_{1-8} alkyl group, C_{1-4} haloalkyl group, C_{1-4} alkoxy group, carboxy group, hydroxyl group, cyano group, nitro group, amino group, C_{1-4} alkylamino group, di(C_{1-4} alkyl)amino group, 1-pyrrolidinyl group, 1-piperidyl group, morpholino group, C_{1-4} alkoxycarbonyl group and the like can be mentioned. Preferable substituents include halogen atom (e.g., chlorine atom, fluorine atom etc.), C_{1-8} alkyl group (e.g., methyl group etc.) and C_{1-4} haloalkyl group (e.g., trifluoromethyl group etc.).

The "C_{1-4} alkylcarbonyl group" for R^{23} or R^{24} is optionally substituted by amino group, C_{1-4} alkylamino group or di(C_{1-4} alkyl)amino group.

The "C_{1-4} alkylamino group", which is a substituent on the "C_{1-6} alkyl group" for R^{23} or R^{24} is the above-defined "C_{1-4} alkylamino group", preferably methylamino group.

The "di(C_{1-4} alkyl)amino group", which is a substituent on the "C_{1-6} alkyl group" for R^{23} or R^{24} is the above-defined "di(C_{1-4} alkyl)amino group", preferably dimethylamino group.

The "C_{1-8} alkyl group" for R^{11} or R^{12} is optionally substituted by a substituent selected from the group consisting of C_{3-7} cycloalkyl group, optionally substituted aryl group, optionally substituted hetero ring group, hydroxyl group, C_{1-4}

alkylamino group and di(C_{1-4} alkyl)amino group.

The "aryl group" moiety of the "optionally substituted aryl", which is a substituent on the "C_{1-8} alkyl group" for R^{11} or R^{12} is the above-defined "aryl group", preferably phenyl group.

The "optionally substituted aryl group", which is a substituent on the "C_{1-8} alkyl group" for R^{11} or R^{12} is optionally substituted by 1 to 3 substituents selected from the following. As such substituents, halogen atom, C_{1-4} alkyl group, C_{1-4} haloalkyl group, C_{1-4} alkoxy group, carboxy group, hydroxyl group, cyano group, nitro group, amino group, C_{1-4} alkoxycarbonyl group and the like can be mentioned. Preferable substituents include halogen atom and C_{1-4} haloalkyl group.

The "heterocyclic group" moiety of the "optionally substituted heterocyclic group", which is a substituent on the "C_{1-8} alkyl group" for R^{11} or R^{12} is "a saturated or unsaturated 5- to 7-membered heterocyclic group containing 1 to 3 heteroatoms selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom", which is specifically exemplified by furyl group, thienyl group, pyrrolyl group, oxazolyl group, isoxazolyl group, thiazolyl group, isothiazolyl group, imidazolyl group, pyrazolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, tetrahydrofuryl group, tetrahydrothienyl group, pyrrolidinyl group, pyrazolidinyl group, imidazolidinyl group, oxazolidinyl group, thiazolidinyl group, tetrahydropyranyl group, dioxanyl group, piperidinyl group, piperazinyl group, morpholinyl group and the like, preferably tetrahydropyranyl group.

The "optionally substituted heterocyclic group", which is a substituent on the "C_{1-8} alkyl group" for R^{11} or R^{12} is optionally substituted by 1 to 3 substituents selected from the following. As such substituents, halogen atom, C_{1-4} alkyl group, C_{1-4} haloalkyl group, C_{1-4} alkoxy group, carboxy group, hydroxyl

group, cyano group, nitro group, amino group, C_{1-4} alkoxycarbonyl group and the like can be mentioned.

The "C_{1-4} alkylamino group", which is a substituent on the "C_{1-8} alkyl group" for R^{11} or R^{12} is the above-defined "C_{1-4} alkylamino group", preferably methylamino group.

The "di(C_{1-4}alkyl)amino group", which is a substituent on the "C_{1-8} alkyl group" for R^{11} or R^{12} is the above-defined "di(C_{1-4} alkyl)amino group", preferably dimethylamino group.

The "C_{1-4}alkylcarbonyl group" for R^{11} or R^{12} is optionally substituted by hydroxyl group or C_{1-4} alkoxy group.

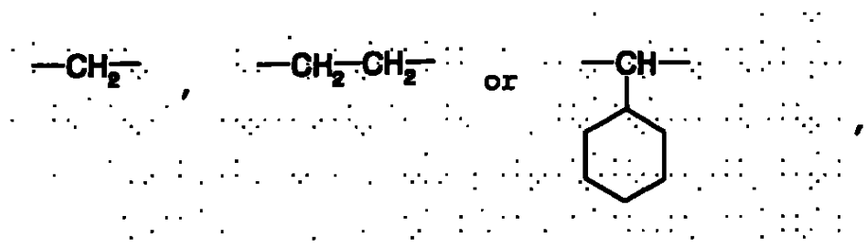
The "C_{1-4} alkoxy group", which is a substituent on the "C_{1-4} alkylcarbonyl group" for R^{11} or R^{12} is the above-defined "C_{1-4} alkoxy group".

The "C_{3-7} cycloalkane" formed by R^{13} and R^{14} together with the carbon atom bonded thereto is cycloalkane having 3 to 7 carbon atoms, which is specifically exemplified by cyclopropane, cyclobutane, cyclopentane, cyclohexane and cycloheptane. Preferred is cycloalkane having 5 to 7 carbon atoms, particularly preferably cyclopentane or cyclohexane.

The "5- to 7-membered hetero ring optionally having at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom", which is formed by R^{13} and R^{14} together with the carbon atom bonded thereto is preferably a "5- to 7-membered hetero ring optionally containing at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom", which is specifically exemplified by tetrahydropyrane, thiane and the like, particularly preferably tetrahydropyrane.

The C_{1-4} alkylene group for A is optionally substituted by C_{3-7} cycloalkyl group. As such C_{3-7} cycloalkyl group, the above-defined "C_{3-7} cycloalkyl group" can be mentioned.

The "C_{1-4} alkylene group optionally substituted by C_{3-7} cycloalkyl group" for A is preferably



more preferably $-CH_2-$.

The "C_{3-7} cycloalkyl group" for Z is preferably cyclopentyl group or cyclohexyl group, more preferably cyclohexyl group.

The "C_{3-7} cycloalkyl group" for Z is optionally substituted by aryl group (this aryl group is optionally substituted by 1 to 5 (preferably 1 to 3) halogen atoms or C_{1-6} alkyl group) or heteroaromatic ring group (this heteroaromatic ring group is optionally substituted by 1 to 5 (preferably 1 to 3) halogen atoms or C_{1-6} alkyl group). Such substituent of the "C_{3-7} cycloalkyl group" is preferably phenyl group optionally substituted by 1 to 3 halogen atoms or C_{1-6} alkyl group.

The "aryl group" for Z is preferably phenyl group or biphenylyl group (e.g., 2-biphenylyl group, 3-biphenylyl group, 4-biphenylyl group), more preferably phenyl group.

The "aryl group" for Z is optionally substituted by 1 to 5 (preferably 1 to 3) substituents selected from the following.

(a) heterocyclic group optionally substituted by C_{1-4} alkyl group or C_{1-4} alkylcarbonyl group,

(b) C_{3-7} cycloalkyl group optionally substituted by hydroxyl group, oxo group, halogen atom or C_{1-6} alkyl group,

(c) carboxy group,

(d) halogen atom,

(e) C_{1-6} alkyl group,

(f) C_{1-4} haloalkyl group,

(g) C_{1-4} alkylamino group,

(h) di(C_{1-4} alkyl)amino group,

(i) C_{1-6} alkylthio group,

(j) C_{1-4} alkoxy group,

(k) C_{1-4} alkylcarbonyl group and

(l) nitro group.

As such substituents, preferred are C_{1-6} alkyl group.

The "heterocyclic group" of the "heterocyclic group optionally substituted by C_{1-4} alkyl group or C_{1-4} alkylcarbonyl group", which is a substituent on the "aryl group" for Z is preferably a "saturated or unsaturated 5- to 7-membered heterocyclic group optionally containing 1 to 3 heteroatoms selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom", which is specifically exemplified by furyl group, thienyl group, pyrrolyl group, oxazolyl group, isoxazolyl group, thiazolyl group, isothiazolyl group, imidazolyl group, pyrazolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, tetrahydrofuryl group, tetrahydrothienyl group, pyrrolidinyl group, pyrazolidinyl group, imidazolidinyl group, oxazolidinyl group, thiazolidinyl group, tetrahydropyranyl group, dioxanyl group, piperidinyl group, piperazinyl group, morpholinyl group and the like. Preferred are piperidinyl group, morpholinyl group, piperazinyl group, pyrrolidinyl group, pyrrolyl group and tetrahydropyranyl group.

The substituent on the "heterocyclic group" is preferably C_{1-4} alkyl group or C_{1-4} alkylcarbonyl group.

The "C_{3-7} cycloalkyl" of the "C_{3-7} cycloalkyl group optionally substituted by hydroxyl group, oxo group, halogen atom or C_{1-6} alkyl group", which is a substituent on the "aryl group" for Z is preferably cyclopentyl group or cyclohexyl group, more preferably cyclohexyl group. The "C_{3-7} cycloalkyl group" is optionally substituted by 1 to 5 (preferably 1 to 3) substituents selected from the group consisting of hydroxyl group, oxo group, halogen atom and C_{1-6} alkyl group. As the

substituent on the "C_{3-7} cycloalkyl group" is preferably halogen atom or C_{1-4} alkyl group.

As the "halogen atom", which is a substituent on the "aryl group" for Z, the above-defined "halogen atom" can be mentioned, which is preferably a fluorine atom, a chlorine atom or a bromine atom, particularly preferably a chlorine atom.

As the "C_{1-8} alkyl group", which is the substituent on the "aryl group" for Z, the above-defined "C_{1-8} alkyl group" can be mentioned. Preferably, it is isopropyl group, isobutyl group, sec-butyl group, tert-butyl group, isopentyl group, neopentyl group, tert-pentyl group, 1-ethylpropyl group or 1-propylbutyl group, more preferably isopentyl group, neopentyl group, tert-pentyl group, 1-ethylpropyl group or 1-propylbutyl group, particularly preferably neopentyl group, 1-ethylpropyl group or 1-propylbutyl group.

As the "C_{1-4} haloalkyl group", which is the substituent on the "aryl group" for Z, the above-defined "C_{1-4} haloalkyl group" can be mentioned, with preference given to trifluoromethyl group.

As the "C_{1-4} alkylamino group", which is the substituent on the "aryl group" for Z, the above-defined "C_{1-4} alkylamino group" can be mentioned, with preference given to methylamino group, ethylamino group and isopropylamino group.

As the "di(C_{1-4} alkyl)amino group", which is the substituent on the "aryl group" for Z, the above-defined "di(C_{1-4} alkyl)amino group" can be mentioned, with preference given to dimethylamino group, diethylamino group and dipropylamino group.

As the "C_{1-6} alkylthio group", which is the substituent on the "aryl group" for Z, the above-defined "C_{1-6} alkylthio group" can be mentioned, with preference given to isopentylthio group.

As the "C_{1-4} alkoxy group", which is the substituent on the "aryl group" for Z, the above-defined "C_{1-4} alkoxy group"

can be mentioned.

As the "C_{1-4} alkylcarbonyl group", which is the substituent on the "aryl group" for Z, the above-defined "C_{1-4} alkylcarbonyl group" can be mentioned, with preference given to acetyl group.

The "heteroaromatic ring group" for Z is preferably a "5- to 10-membered mono or fused heteroaromatic ring group containing 1 to 3 heteroatoms selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom", which is specifically exemplified by furyl group, thienyl group, pyrrolyl group, oxazolyl group, isoxazolyl group, thiazolyl group, isothiazolyl group, imidazolyl group, pyrazolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, indolyl group, isoindolyl group, benzofuranyl group, benzothienyl group, benzoimidazolyl group, benzothiazolyl group, benzoxazolyl group and the like. Particularly preferred are thiazolyl group and pyridyl group.

The "heteroaromatic ring group" for Z is optionally substituted by 1 to 5 (preferably 1 to 3) substituents selected from the following.

(a) heterocyclic group optionally substituted by C_{1-4} alkyl group or C_{1-4} alkylcarbonyl group,

(b) C_{3-7} cycloalkyl group optionally substituted by hydroxyl group, oxo group, halogen atom or C_{1-6} alkyl group,

(c) carboxy group,

(d) halogen atom,

(e) C_{1-8} alkyl group,

(f) C_{1-4} haloalkyl group,

(g) C_{1-4} alkylamino group,

(h) di(C_{1-4} alkyl)amino group,

(i) C_{1-6} alkylthio group,

(j) C_{1-4} alkoxy group,

(k) C_{1-4} alkylcarbonyl group and

(1) aryl group optionally substituted by halogen atom or C_{1-4} haloalkyl group.

As such substituents, preferred are (a) heterocyclic group, (b) C_{1-8} alkyl group and (c) aryl group optionally substituted by halogen atom or C_{1-4} haloalkyl group.

The "heterocyclic group" of the "heterocyclic group optionally substituted by C_{1-4} alkyl group or C_{1-4} alkylcarbonyl group", which is a substituent on the "heteroaromatic ring group" for Z is preferably, a "saturated or unsaturated 5- to 7-membered heterocyclic group optionally containing 1 to 3 heteroatoms selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom", which is specifically exemplified by furyl group, thienyl group, pyrrolyl group, oxazolyl group, isoxazolyl group, thiazolyl group, isothiazolyl group, imidazolyl group, pyrazolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, pyrazinyl group, tetrahydrofuryl group, tetrahydrothienyl group, pyrrolidinyl group, pyrazolidinyl group, imidazolidinyl group, oxazolidinyl group, thiazolidinyl group, tetrahydropyranyl group, dioxanyl group, piperidinyl group, piperazinyl group, morpholinyl group and the like. Preferred are piperidinyl group, morpholinyl group, piperazinyl group, pyrrolidinyl group, pyrrolyl group and tetrahydropyranyl group.

The substituent on the "heterocyclic group" is preferably C_{1-4} alkyl group or C_{1-4} alkylcarbonyl group.

The "C_{3-7} cycloalkyl" of the "C_{3-7} cycloalkyl group optionally substituted by hydroxyl group, oxo group, halogen atom or C_{1-6} alkyl group", which is a substituent on the "heteroaromatic ring group" for Z is preferably cyclopentyl group or cyclohexyl group, more preferably cyclohexyl group. The "C_{3-7} cycloalkyl group" is optionally substituted by 1 to 5 (preferably 1 to 3) substituents selected from the group consisting of hydroxyl group, oxo group, halogen atom and C_{1-6}

alkyl group. The substituent on the "C_{3-7} cycloalkyl group" is preferably halogen atom or C_{1-4} alkyl group.

As the "halogen atom", which is the substituent on the "heteroaromatic ring group" for Z, the above-defined "halogen atom" can be mentioned, with preference given to fluorine atom, chlorine atom and bromine atom, particularly preferably chlorine atom.

As the "C_{1-8} alkyl group", which is the substituent on the "heteroaromatic ring group" for Z, the above-defined "C_{1-8} alkyl group" can be mentioned. Preferred are isopropyl group, isobutyl group, sec-butyl group, tert-butyl group, isopentyl group, neopentyl group, tert-pentyl group, 1-ethylpropyl group and 1-propylbutyl group, more preferred are isopentyl group, neopentyl group, tert-pentyl group, 1-ethylpropyl group and 1-propylbutyl group, particularly preferred are neopentyl group, 1-ethylpropyl group and 1-propylbutyl group.

As the "C_{1-4} haloalkyl group", which is the substituent on the "heteroaromatic ring group" for Z, the above-defined "C_{1-4} haloalkyl group" can be mentioned, with preference given to trifluoromethyl group.

As the "C_{1-4} alkylamino group", which is the substituent on the "heteroaromatic ring group" for Z, the above-defined "C_{1-4} alkylamino group" can be mentioned, with preference given to methylamino group, ethylamino group and isopropylamino group.

As the "di(C_{1-4} alkyl)amino group", which is the substituent on the "heteroaromatic ring group" for Z, the above-defined "di(C_{1-4} alkyl)amino group" can be mentioned, with preference given to dimethylamino group, diethylamino group and dipropylamino group.

As the "C_{1-6} alkylthio group", which is the substituent on the "heteroaromatic ring group" for Z, the above-defined "C_{1-6} alkylthio group" can be mentioned, with preference given to isopentylthio group.

As the "C_{1-4} alkoxy group", which is the substituent on the "heteroaromatic ring group" for Z, the above-defined "C_{1-4} alkoxy group" can be mentioned.

As the "C_{1-4} alkylcarbonyl group", which is the substituent on the "heteroaromatic ring group" for Z, the above-defined "C_{1-4} alkylcarbonyl group" can be mentioned, with preference given to acetyl group.

As the "aryl group optionally substituted by halogen atom or C_{1-4} haloalkyl group", which is the substituent on the "heteroaromatic ring group" for Z, "phenyl group optionally substituted by halogen atom or C_{1-4} haloalkyl group" can be preferably mentioned.

The "piperazinyl group" for Z is optionally substituted by 1 to 5 (preferably 1 to 3) substituents selected from the following.

(a) phenyl group,

(b) phenyl C_{1-4} alkyl group,

(c) benzoyl group optionally substituted by halogen atom and

(d) phenyl C_{1-4} alkoxycarbonyl group.

The "phenyl C_{1-4} alkyl group", which is a substituent on the "piperazinyl group" for Z is phenylalkyl group having the above-defined "C_{1-4} alkyl group" as the "alkyl moiety", which is specifically exemplified by benzyl group, phenethyl group, 1-phenylethyl group, 3-phenylpropyl group and the like. Preferably, it is benzyl group.

The "benzoyl group optionally substituted by halogen atom", which is a substituent on the "piperazinyl group" for Z, is preferably benzoyl group optionally substituted by 1 to 5 of the above-defined "halogen atom", which is specifically exemplified by chlorobenzoyl group, bromobenzoyl group and the like.

The "phenyl C_{1-4} alkoxycarbonyl group", which is a substituent on the "piperazinyl group" for Z is a

"phenylalkoxycarbonyl group having the above-defined C_{1-4} alkoxy group as the alkoxy moiety, which is specifically exemplified by benzyloxycarbonyl group and the like. Preferred is benzyloxycarbonyl group.

In the formula [I], preferable embodiments include the following.

V is preferably =N- or =CH-.

W is preferably -S-.

m is preferably 1 or 2.

R^1 and R^2 are preferably each a hydrogen atom.

X is preferably the following (1) to (4).

(1)

$-N(R^4)-$, $-SO_2-N(R^5)-$, $-CO-N(R^7)-$ or $-O-$

wherein R^4 is a hydrogen atom or a C_{1-6} alkyl group, R^5 is a hydrogen atom or a C_{1-6} alkyl group and R^7 is a hydrogen atom or a C_{1-6} alkyl group,

(2)

$-N(R^4)-$

wherein R^4 is a C_{1-6} alkyl group substituted by

(a) aryl group optionally substituted by 1 to 3 substituents selected from the group consisting of halogen atom, a C_{1-8} alkyl group and a C_{1-4} haloalkyl group,

(b) heteroaromatic ring group optionally substituted by 1 to 3 C_{1-8} alkyl groups,

(c) carboxy group,

(d) C_{1-4} alkoxycarbonyl group,

(e) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom, an aryl group (this aryl group is optionally substituted by 1 to 3 substituents selected from the group consisting of C_{1-8} alkyl group, C_{1-4} alkoxy group, carboxy group and di(C_{1-4} alkyl)amino group), a heteroaromatic ring group, a C_{1-6} alkyl group (this C_{1-6} alkyl group is optionally substituted by aryl group), or,

together with the nitrogen atom bonded thereto, may form a 5- to 7-membered hetero ring optionally further containing at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom,

(f) $-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom or an aryl group,

(g) $-O-R^{17}$

wherein R^{17} is an aryl group or

(h) C_{3-7} cycloalkyl group,

(3) $-N(R^4)-$

wherein R^4 is

(a) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom, an aryl group (this aryl group is optionally substituted by 1 to 3 C_{1-8} alkyl groups), a C_{1-6} alkyl group, or, together with the nitrogen atom bonded thereto, may form an indoline ring or may form a 5- to 7-membered hetero ring optionally further containing at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom,

(b) $-SO_2-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently an aryl group or a C_{1-6} alkyl group,

(c) $-CO-R^{17}$

wherein R^{17} is an aryl group (this aryl group is optionally substituted by 1 to 3 substituents selected from the group consisting of C_{1-8} alkyl group and C_{1-4} alkoxy group), a heteroaromatic ring group or a C_{1-6} alkyl group (this C_{1-6} alkyl group is optionally substituted by an aryl group optionally substituted by 1 to 3 substituents selected from the group consisting of a halogen atom and a C_{1-8} alkyl group, a heteroaromatic ring group, a C_{1-4} alkoxy group optionally substituted by aryl group or an aryloxy group optionally

substituted by 1 to 3 C_{1-8} alkyl groups),

(d) $-SO_2-R^{17}$

wherein R^{17} is an aryl group or

(e) aryl group

or

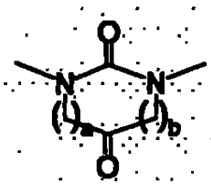
(4) $-N(R^8)-CO-$, $-N(R^9)-CO-N(R^5)-$ or $-N(R^{10})-(CH_2)_k-N(R^5)-$

wherein

R^5 is a C_{1-6} alkyl group optionally substituted by hydrogen atom or aryl group,

R^8 is a hydrogen atom or C_{1-6} alkyl group,

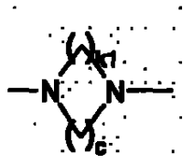
R^9 is linked with R^5 to form



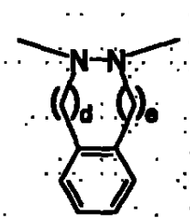
wherein a and b are each independently 0, 1 or 2,

k is 0 or an integer of 1 to 4,

R^{10} is linked with R^5 to form



wherein k1 and c are each independently 0 or an integer of 1 to 4 or



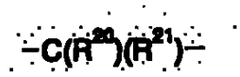
wherein d and e are each independently 0, 1 or 2.

n is preferably 0 or an integer of 1 to 3.

P is preferably 0 or 1.

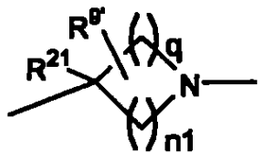
L is preferably the following (1) to (4).

(1)



wherein

R^{20} is linked with R^4 to form



wherein n1 and q are each independently 0 or an integer of 1 to 4 and $R^{9'}$ is a hydrogen atom, a hydroxyl group, a C_{1-6} alkyl group, a carboxy group or a C_{1-6} alkoxy group or



wherein u and v are each independently 0, 1 or 2,

R^{21} is a hydrogen atom,

(2)



wherein E is a phenyl group, a furyl group, an isoxazolyl group

or a pyridyl group and R^{22} is a hydrogen atom,

(3)



wherein

E is a phenyl group,

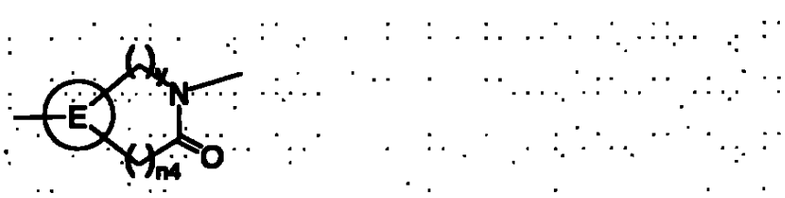
R^{22} is

(a) linked with R^4 to form



wherein n2 and w are each independently 0 or an integer of 1 to 3,

(b) linked with R^7 to form



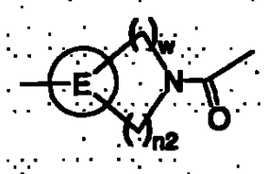
wherein n4 and y are each independently 0, 1 or 2,

(c) linked with R^7 to form



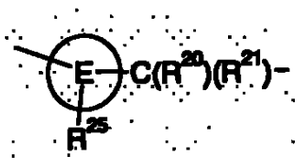
wherein n5 and z are each independently 0 or 1 or

(d) linked with R^8 to form



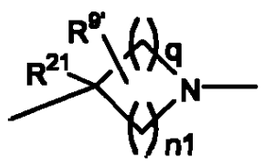
wherein n2 and w are each independently 0 or an integer of 1 to 3 or

(4)



wherein

R^{20} is linked with R^4 to form



wherein n1 and q are each independently 0 or an integer of 1 to 4 and $R^{9'}$ is a hydrogen atom, a hydroxyl group, a C_{1-6} alkyl group, a carboxy group or a C_{1-6} alkoxy group,

R^{21} is a hydrogen atom,

E is a phenyl group, a furyl group, an isoxazolyl group or a pyridyl group, and

R^{25} is a hydrogen atom.

R is preferably $-COO(R^{19})$, $-A^1-COO(R^{19})$ or $-O-A^1-COO(R^{19})$ wherein A^1 is a C_{1-4} alkylene group and R^{19} is a hydrogen atom or a C_{1-4} alkyl group.

B is preferably a phenyl group or a heteroaromatic ring group (this heteroaromatic ring group is preferably selected from the group consisting of thienyl group, thiazolyl group,

pyrazolyl group, 1,3,4-thiadiazolyl group, pyridyl group, pyridazinyl group, pyrimidinyl group, indolyl group, benzimidazolyl group, benzothiazolyl group and benzoxazolyl group).

When V is =CH-, the position of substitution of B on the thiophene or furan ring formed by V together with W is preferably the 4-position or 5-position, and when V is =N-, the position of substitution of B on the thiazole or oxazole ring formed by V together with W is preferably the 4-position.

R^3 is preferably a hydrogen atom.

Y is preferably $-C(R^{13})(R^{14})-N(R^{12})-$, $-C(R^{13})(R^{14})-O-$, $-N(R^{11})-$ or $-O-$

wherein R^{11} is a hydrogen atom or a C_{1-8} alkyl group, R^{12} is a hydrogen atom or a C_{1-8} alkyl group, and R^{13} and R^{14} are each a hydrogen atom.

s is preferably 0 or 1.

A is preferably a methylene group.

Y, s and A are preferably the following (1) or (2).

(1) Y is $-C(R^{13})(R^{14})-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$

wherein R^{12} is a hydrogen atom or a C_{1-8} alkyl group and R^{13} and R^{14} are each a hydrogen atom,

and

s is 0.

(2) Y is $-N(R^{11})-$ or $-O-$

wherein R^{11} is a hydrogen atom or a C_{1-8} alkyl group,

and

s is 1 and A is a methylene group.

Z is preferably an aryl group substituted by substituents selected from the group consisting of,

(a) C_{3-7} cycloalkyl group optionally substituted by 1 to 3 substituents selected from the group consisting of halogen atom and C_{1-6} alkyl group,

(b) halogen atom,

(c) C_{1-8} alkyl group,

(d) C_{1-4} haloalkyl group,

(e) di(C_{1-4} alkyl)amino group,

(f) C_{1-6} alkylthio group and

(g) C_{1-4} alkylcarbonyl group.

Z is more preferably a phenyl group substituted by a C_{1-8} alkyl group (this C_{1-8} alkyl group is selected from the group consisting of isopropyl group, isobutyl group, sec-butyl group, tert-butyl group, isopentyl group, neopentyl group, tert-pentyl group, 1-ethylpropyl group and 1-propylbutyl group).

Z is particularly preferably a phenyl group substituted by 1-ethylpropyl group or 1-propylbutyl group.

In the formula [I], particularly preferable embodiments include the following.

V is particularly preferably =N- or =CH-.

W is particularly preferably -S-.

m is particularly preferably 1.

R^1 and R^2 are each preferably a hydrogen atom.

X, n, p and L are particularly preferably the following (1) to (7).

(1)

X is $-N(R^4)-$

wherein R^4 is a C_{1-6} alkyl group substituted by heteroaromatic ring group optionally substituted by 1 to 3 C_{1-8} alkyl groups and

n is 1 and p is 0.

(2)

X is $-N(R^4)-$

wherein R^4 is a C_{1-6} alkyl group substituted by $-CO-N(R^{15})(R^{16})$ wherein R^{15} and R^{16} are each independently hydrogen atom, an aryl group (this aryl group is optionally substituted by 1 to 3 substituents selected from the group consisting of C_{1-8} alkyl group, C_{1-4} alkoxy group, carboxy group and di(C_{1-4} alkyl)amino

group), a heteroaromatic ring group, a C_{1-6} alkyl group (this C_{1-6} alkyl group is optionally substituted by aryl group), or, together with the nitrogen atom bonded thereto, may form a 5- to 7-membered hetero ring optionally further containing at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom

and

n is 1 and p is 0.

(3)

X is $-N(R^4)-$

wherein R^4 is $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom, an aryl group (this aryl group is optionally substituted by 1 to 3 C_{1-8} alkyl groups), or a C_{1-6} alkyl group, or, together with the nitrogen atom bonded thereto, may form an indoline ring or may form a 5 to 7-membered hetero ring optionally further containing at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom

and

n is 1 and p is 0.

(4)

X is $-N(R^4)-$, $-SO_2-N(R^5)-$, $-CO-N(R^7)-$ or $-O-$

wherein R^4 is a hydrogen atom or a C_{1-6} alkyl group, R^5 is a hydrogen atom or a C_{1-6} alkyl group, and R^7 is a hydrogen atom or a C_{1-6} alkyl group,

and

n is 0, p is 1 and L is



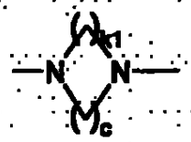
wherein E is a pyridyl group and R^{22} is a hydrogen atom.

(5)

X is $-N(R^{10})-(CH_2)_k-N(R^5)-$

wherein k is 0 or an integer of 1 to 4, and

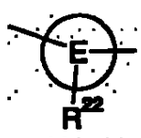
R^{10} is linked with R^5 to form



wherein k1 and c are each independently 0 or an integer of 1 to 4,

and

n is 0 or an integer of 1 to 4, p is 1 and L is



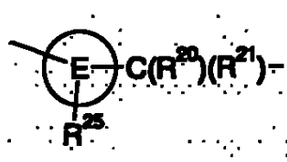
wherein E is a phenyl group, a furyl group, an isoxazolyl group or a pyridyl group and R^{22} is a hydrogen atom.

(6)

X is $-N(R^4)-$

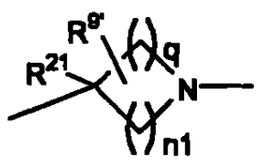
and

n is 0 or an integer of 1 to 4, p is 1 and L is



wherein

R^{20} is linked with R^4 to form



wherein n1 and q are each independently 0 or an integer of 1 to 4 and $R^{9'}$ is a hydrogen atom, a hydroxyl group, a C_{1-6} alkyl group, a carboxy group or a C_{1-6} alkoxy group,

R^{21} is a hydrogen atom,

E is a phenyl group, a furyl group, an isoxazolyl group or a pyridyl group, and

R^{25} is a hydrogen atom.

(7)

X is $-N(R^4)-$

and

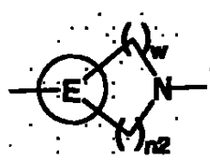
n is 0 or an integer of 1 to 3, p is 1 and L is



wherein

E is a phenyl group,

R^{22} is linked with R^4 to form



wherein n2 and w are each independently 0 or an integer of 1 to 3.

R is particularly preferably $-COO(R^{19})$

wherein R^{19} is a hydrogen atom or a C_{1-4} alkyl group.

B is particularly preferably a phenyl group.

When V is =CH-, the position of substitution of B on the

thiophene or furan ring formed by V together with W is preferably the 4-position or 5-position, and when V is =N-, the position of substitution of B on the thiazole or oxazole ring formed by V together with W is particularly preferably the 4-position.

R^3 is particularly preferably a hydrogen atom.

Y, s and A are each particularly preferably the following (1) or (2).

(1)

Y is $-C(R^{13})(R^{14})-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$

wherein R^{12} is a hydrogen atom or a C_{1-8} alkyl group and R^{13} and R^{14} are each a hydrogen atom,

and

s is 0.

(2)

Y is $-N(R^{11})-$ or $-O-$

wherein R^{11} is a hydrogen atom or a C_{1-8} alkyl group,

and

s is 1 and A is a methylene group.

Z is particularly preferably a phenyl group substituted by 1-ethylpropyl group or 1-propylbutyl group.

In the formula [II], preferable embodiments include the following.

V is preferably =CH-.

W is preferably -S-.

Y^{100} is preferably $-CH_2-$.

R^{100} is preferably a hydroxyl group or a chlorine atom.

B is preferably a phenyl group.

The position of substitution of B on the thiophene ring formed by V together with W is preferably the 4-position.

R^3 is preferably a hydrogen atom.

The "pharmaceutically acceptable salt" may be any salt as long as it forms a non-toxic salt with a compound of the above-

mentioned the formula [I], and can be obtained by reaction with inorganic acids such as hydrochloric acid, sulfuric acid, phosphoric acid, hydrobromic acid and the like; organic acids such as oxalic acid, malonic acid, citric acid, fumaric acid, lactic acid, malic acid, succinic acid, tartaric acid, acetic acid, trifluoroacetic acid, gluconic acid, ascorbic acid, methylsulfonic acid, benzylsulfonic acid and the like; inorganic bases such as sodium hydroxide, potassium hydroxide, calcium hydroxide, magnesium hydroxide, ammonium hydroxide and the like; organic bases such as methylamine, diethylamine, triethylamine, triethanolamine, ethylenediamine, tris(hydroxymethyl)methylamine, guanidine, choline, cinchonine, N-methyl-D-glucamine and the like; or amino acids such as lysin, histidine, arginine, alanine and the like. The present invention also encompasses water-containing products, hydrates and solvates of each compound.

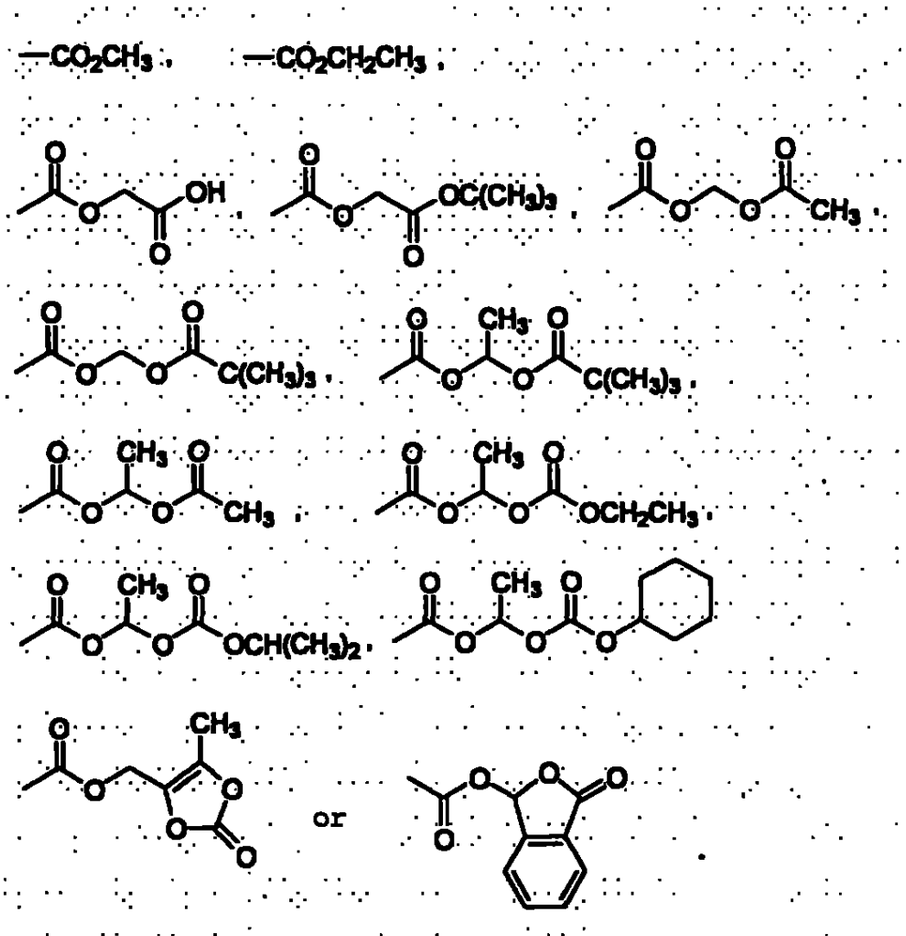
There exist various isomers of the compound represented by the above-mentioned formula [I]. For example, E-form and Z-form are present as geometric isomers, and when an asymmetric carbon atom exists, enantiomer and diastereomer are present as stereoisomers based thereon. In some cases, a tautomer can be present. Accordingly, the present invention encompasses all these isomers and mixtures thereof.

The present invention also encompasses prodrug and metabolite of the compound represented by the formula [I].

A "prodrug" is a derivative of the compound of the present invention, which has a group capable of chemical or metabolic decomposition, and shows inherent efficacy upon restoration to the original compound after administration to a living organism. It includes complexes and salts free of a covalent bond.

For example, an ester derivative known as a prodrug in the field of pharmaceutical agents can be used, which is

specifically an ester derivative wherein the -COOR^7 moiety for R is represented by the following formula.



When the compound of the present invention is used as a pharmaceutical preparation, it is generally admixed with pharmacologically acceptable carrier, excipient, diluent, extending agent, disintegrant, stabilizer, preservative, buffer, emulsifier, aromatic, coloring agent, sweetener, thickener, corrigent, dissolution aids, and other additive generally known *per se*, which are specifically water, vegetable oil, alcohol such as ethanol, benzyl alcohol etc., polyethylene glycol, glycerol triacetate, gelatin, lactose, carbohydrate such as starch and the like, magnesium stearate, talc, lanolin, vaseline and the like, and systemically or topically, orally or

parenterally administered in the form of tablet, pill, powder, granule, suppository, injection, eye drop, liquid, capsule, troche, aerosol, elixir, suspension, emulsion, syrup and the like by conventional methods.

While the dose of the compound of the present invention varies depending on age, body weight, symptoms, disease to be treated, administration method and the like, it is generally 1 mg to 1,000 mg for one dose to an adult, which is administered once a day to several times a day.

The compound [I] of the present invention can be administered as a PTP1B inhibitor or an inhibitor of receptor tyrosine kinase negative regulator, a drug for the prophylaxis or treatment of diabetes, a drug for the prophylaxis or treatment of diabetic complications (retinopathy, nephropathy, neuropathy, syndrome X or metabolic syndrome, ischemic heart diseases (cardiac infarction, angina pectoris etc.) and strokes (cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage etc.), a drug for the prophylaxis or treatment of hyperlipidemia, a drug for the prophylaxis or treatment of obesity, a drug for the prophylaxis or treatment of neurodegenerative diseases (macula edema, macular degeneration etc.), a drug for the prophylaxis or treatment of diseases mediated by PTP1B and the like to mammals (human, mouse, rat, rabbit, dog, cat, bovine, swine, simian etc.).

The compound [I] of the present invention has a superior selective PTP1B inhibitory activity. By the "superior selective PTP1B inhibitory activity" is meant that the PTP1B inhibitory activity is stronger as compared to other protein tyrosine phosphatases (e.g., T-cell protein tyrosine phosphatase (TCPTP) inhibitory activity), which specifically means, for example, IC_{50} for PTP1B is as low as 1/10 or below that for TCPTP, more preferably 1/60 or below, particularly preferably 1/300 or below. Thus, the compound [I] of the

present invention can be used as a PTP1B inhibitor, an inhibitor of receptor tyrosine kinase negative regulator, a drug for the prophylaxis or treatment of diabetes, a drug for the prophylaxis or treatment of diabetic complications, a drug for the prophylaxis or treatment of hyperlipidemia, a drug for the prophylaxis or treatment of obesity, neurodegenerative disease and the like or a drug for the prophylaxis or treatment of diseases mediated by PTP1B, which causes a fewer side effects.

The "inhibitor of receptor tyrosine kinase negative regulator" refers to a pharmaceutical agent that inhibits a factor that regulates intracellular signaling toward a negative direction, which signaling stems from activation of a receptor tyrosine kinase upon binding with a ligand, thereby enhancing the signal. In the case of an insulin receptor, for example, which is one of the receptor tyrosine kinases, wherein, as results of activation of the receptor as bound with insulin, intracellular region of the receptor itself, IRS (insulin receptor substrate) and the like are phosphorylated and intracellular signaling causing glucose uptake occurs, a pharmaceutical agent that inhibits a factor that regulates such signaling towards the negative direction is an inhibitor of receptor tyrosine kinase negative regulator, wherein a representative example is a PTP1B inhibitor. The inhibitor of receptor tyrosine kinase negative regulator is different from existing insulin sensitivity enhancers (PPAR agonists such as thiazolidindione derivative etc.). To be precise, because an inhibitor of receptor tyrosine kinase negative regulator, as represented by PTP1B inhibitor, directly acts on an intracellular signal induced by insulin, high efficacy is expected in mammals (non-obesity type diabetic patients etc.) that exhibit insufficient efficacy by the administration of existing insulin sensitivity enhancers, and side effects of

existing insulin sensitivity enhancers have can be avoided.

The compound [I] of the present invention can be used in combination with other therapeutic agents for diabetes for the purpose of prophylaxis or treatment of diabetes or diabetic complications (particularly, microangio complications, in other words, retinopathy, nephropathy, neuropathy etc.) and concurrently administered to mammals. In the present invention, the "therapeutic agents for diabetes" encompasses therapeutic agents for diabetic complications (particularly, microangio complications). In addition, the compound [I] of the present invention can be used in combination with other therapeutic agents for hyperlipidemia for the purpose of prophylaxis or treatment of hyperlipidemia and concurrently administered to mammals. Furthermore, the compound [I] of the present invention can be used in combination with other therapeutic agents for obesity for the purpose of prophylaxis or treatment of obesity and concurrently administered to mammals.

Further, the compound [I] of the present invention can be used in combination with therapeutic agents for diabetes, therapeutic agents for hyperlipidemia, therapeutic agents for obesity, therapeutic agents for hypertension and/or therapeutic agents for thrombosis for the purpose of prophylaxis or treatment of diabetic complications (particularly, large artery complications, in other words, syndrome X or metabolic syndrome, ischemic heart diseases (cardiac infarction, angina pectoris etc.), strokes (cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage etc.) etc.) and concurrently administered to mammals.

When the compound is used in combination with therapeutic agents for diabetes, therapeutic agent for hyperlipidemia, therapeutic agents for obesity, therapeutic agent for hypertension or therapeutic agent for thrombosis (hereinafter to be referred to as a concomitant pharmaceutical agent), the

compound of the present invention may be simultaneously administered along with a concomitant pharmaceutical agent, or may be administered with time intervals. When the compound is used in combination with a concomitant pharmaceutical agent, the compound of the present invention and a concomitant pharmaceutical agent can be administered as a pharmaceutical composition containing them. Alternatively, a pharmaceutical composition containing the compound of the present invention and a pharmaceutical composition containing a concomitant pharmaceutical agent may be administered separately. The administration route of each pharmaceutical composition may be the same or different.

When the compound is used in combination with a concomitant pharmaceutical agent and when the concomitant pharmaceutical agent has a different action mechanism from the compound of the present invention (e.g., insulin secretagogue, biguanide agent, α-glucosidase inhibitor, insulin preparation, insulin sensitivity enhancer, inhibitor of receptor tyrosine kinase negative regulator other than PTP1B inhibitor etc.), an additive prophylaxis or treatment effect based on respective actions of the compound of the present invention and the concomitant pharmaceutical agent, as well as an amplified prophylaxis or treatment effect combining the both actions are expected. Thus, in each case of the compound of the present invention and the concomitant pharmaceutical agent, it is expected to have high efficacy by administration of fewer dose compared to that administered alone and, as a result, to solve side effect that cannot be avoided in case administered alone. Therefore, the compound of the present invention can be administered at a single dose of 1 mg to 1,000 mg, or even a smaller dose, once a day to several times a day. The concomitant pharmaceutical agent can be administered at a dose generally employed for the prophylaxis or treatment of diabetes

or diabetic complications, hyperlipidemia or obesity, or even at a smaller dose.

As therapeutic agents for diabetes that are used as concomitant pharmaceutical agents, insulin secretagogues (ATP-dependent potassium (K(ATP)) channel blockers (sulfonylureas, sulfonamides, phenylalanine derivatives, etc)), biguanides, α-glucosidase inhibitors, insulin formulations, insulin analogs, insulin sensitivity enhancers (peroxisome proliferators-activated receptor (PPAR)-gamma agonists such as thiazolidinedione derivatives (glitazones)), IL-11, anti-CD25 (IL-2 Receptor) agents (such as monoclonal antibodies), angiotensin (AT1) antagonists, angiotensin-converting enzyme (ACE) inhibitors, aldose reductase inhibitors, antioxidants (protein kinase activators/reverse transcriptase inhibitors), carnitine acetyltransferase stimulant, antidepressants, glucocorticoids, retilin, radical formation agonists and transketolase activatorscan be mentioned. Also can be mentioned are beta3-adrenoceptor agonists, insulin sensitivity enhancers, nuclear receptor modulators, peroxisome proliferator-activated receptors, PPAR-alpha agonists, PPAR-gamma antagonists, PPAR-delta ligands (agonists or antagonists), fibrates, drugs acting on retinoid receptors (retinoids, etc.), protein tyrosine phosphatase (PTP) inhibitors (other than compounds of the invention), protein tyrosine phosphatase-1B (PTP1B) inhibitors (other than compounds of the invention), T-cell protein tyrosine phosphatase (TCPTP) inhibitors (other than compounds of the invention), leukocyte common antigen-related protein (LAR) inhibitors, SH2-containing inositol phosphatase 2 (SHIP2) inhibitors, c-Jun NH2-terminal kinase (JNK) inhibitors, insulin receptor agonists, insulin receptor kinase stimulants, insulin-like growth factor (IGF)-1 antagonists, dipeptidyl-peptidase IV inhibitors, glucagon-like peptide 1 (GLP1) agonists, GLP1, leptin, ATP-dependent

potassium channel activators; VPAC2 (receptor for vasoactive intestinal peptide (VIP)) agonists, P2Y agonists; beta amyloid protein antagonists, apoptosis inhibitors, TGR79 agonists, GPR40 agonists, sodium-glucose co-transporter inhibitors (SGLT-2 inhibitors, etc.), glycogen phosphorylase inhibitors, fructose-biphosphatase inhibitors, phosphoenolpyruvate carboxykinase (PEPCK) inhibitors, pyruvate dehydrogenase kinase inhibitors, glucose-6-phosphatase inhibitors, glycogen synthase kinase (GSK)-3 inhibitors, glucokinase activators, glucagon antagonists, signal transducer and activator of transcription (STAT)-3 modulators, forkhead transcription factor (FOXO-1) inhibitors, interleukin (IL) agonists such as IL-10 agonists and IL-4 agonists, IL-6 production inhibitors, tumor necrosis factor (TNF)-alpha production inhibitors, monocyte chemoattractant protein (MCP)-1 expression inhibitors, adipocytokine modulators, plasminogen activator inhibitor type 1 (PAI-1) production inhibitors, adiponectin production enhancers, adiponectin receptor agonists, adiponectin, resistine production inhibitors, resistine receptor antagonists, alpha 2 adrenoreceptor antagonists, beta2-adrenoceptor antagonists, 5-HT6 antagonists, serine carboxypeptidase inhibitor, ATP-binding cassette A1 (ABCA1) expression enhancers, retinoid X receptor (RXR) agonists, liver X receptor (LXR) ligands (agonists or antagonists), adypocite fatty acid binding protein (FABP) (aP2) inhibitors, cholesterol antagonists, adenosine A2B antagonists, alpha1-adrenoreceptor agonists, alpha2-adrenoreceptors, carnitine O-palmitoyltransferase inhibitors, AMP-activated protein kinase (AMPK) activators, glucose transporter (GLUT)-4 translocation activators, glucocorticoid receptor antagonists, glucocorticoid receptor modulators, 11beta-hydroxysteroid dehydrogenase inhibitors, growth hormone release inhibitors, somatostatin analogs, somatostatin sst5 agonists, somatostatin sst2 agonists, growth

hormone-releasing factors (GHRF), ghrelin production inhibitors, ghrelin receptor antagonists, kinase inhibitors, PTPN1 expression inhibitor oligonucleotides, antioxidants, nitric oxide scavengers, free radical scavengers, heme oxygenase (HO)-1 inducers, EGFR (erbB1) inhibitors, phosphodiesterase III inhibitors, phosphodiesterase IV inhibitors, acetyl-CoA carboxylase (ACC) inhibitors, carnitine palmitoyltransferase (CPT) 1 inhibitors, glucose sensor activators, microsomal triglyceride transfer protein (MTP) inhibitors, diacylglycerol acyltransferase (DGAT) inhibitors, statins, cholesteryl ester transfer protein (CETP) inhibitors, any other glucose lowering agents, anti-CD3 agents (such as monoclonal antibodies), glutamate decarboxylase stimulants, combination of gastrin and epidermal growth factor (EGF), calcineurin inhibitors, antioxidants (metalloporphyrins, etc.), NAD+ ADP-ribosyltransferase (poly(ADP-ribose)polymerase; PARP) inhibitors, immunostimulants, chemokine receptor agonist, chemokine receptor antagonist, vanadium complexes, p38 protein kinase inhibitors, advanced glycation end product (AGE) inhibitors (Maillard's reaction inhibitors), low molecular weight (LMW) heparins, inducible nitric oxide synthase inhibitors, anti-platelet-derived growth factor (PDGF) agents (such as monoclonal antibodies), angiogenesis inhibitors (apoptosis inducers, endothelin (ETA) antagonists, etc.), somatostatin sst2 antagonists, growth factor modulators, cell adhesion inhibitors, amadorase inhibitors, transforming growth factor (TGF)-beta receptor antagonists, TGF-beta receptor signal inhibitors, TGF-beta production inhibitors, anti-TGF-beta antibodies, anti-TGF-beta receptor antibodies, anti-lectin-like oxidized low-density lipoprotein receptor (LOX)-1 agents (such as monoclonal antibodies), Edge receptor antagonists, Edge receptor signal inhibitors, neurotrophic factor enhancers, neurotrophic agents, nerve growth factor

(NGF), NGF agonists, vascular endothelial growth factor (VEGF), neurotrophin (NT)-3, NT-3 inducers, protein kinase (PK) C beta inhibitors, drugs acting on gamma-aminobutyric acid (GABA)-mediated transmission, 5-HT reuptake inhibitors; 5-HT2A antagonists, norepinephrine reuptake inhibitors, drugs acting on vanilloid receptors, cannabinoid receptor agonists, IL-6, N-methyl-D-aspartate (NMDA) antagonists, prostaglandin E1, prostacyclin analogs, pyruvate dehydrogenase activators, nitric oxide synthase (NOS) 3 expression enhancers, heat shock protein general agonists, sodium channel blockers, NAALADase inhibitors, general pump inhibitors, sonic hedgehog-IgG, VEGF receptor antagonists, VEGF receptor signal inhibitors, pigment epithelial-derived factor (PEDF), anti-VEGF monoclonal antibodies, matrix metalloproteinase inhibitors, methionine aminopeptidase-2 inhibitors, somatostatin sst1 agonists, tyrosine kinase inhibitors, endothelial growth factor antagonists, vitronectin (alphavbeta3, alphavbeta5, etc.) antagonists, hypoxia-inducible factor (HIF) inhibitors, neuropilin-1 receptor antagonists, angiopoietin-2 receptor antagonists, angiopoietin-2 production inhibitors, angiopoietin-1 receptor agonists, angiopoietin-1 inducers, and the like. For example, nateglinide, glimepiride, glibenclamide, gliclazide, acetohexamide, tolbutamide, glyclopyramide, tolazamide, glybuzole, glipizide, glibornuride, gliquidone, repaglinide, metformin hydrochloride, buformin hydrochloride, voglibose, acarbose, epalrestat, miglitol, insulin, pioglitazone hydrochloride, rosiglitazone maleate, chromium picolinate/biotin, V-411, recombinant human interleukin-11, dacliximab (daclizumab), losartan potassium, captopril, imidapril hydrochloride, alpha-lipoic acid, levacecarnine (acetyl-L-carnitine, levocarnitine acetyl) hydrochloride, captopril, retilin, verteporfin, benfotiamine and fluocinolone acetonide are used in combination as concomitant pharmaceutical

agents for the compound of the present invention. Also used as concomitant pharmaceutical agents are balaglitazone, rivoglitazone, isaglitazone (netoglitazone), cryptolepine hydrochloride, triproamylin (pramlintide) acetate, mitiglinide calcium hydrate, muraglitazar, tesaglitazar, oxeglitazar, insulin glulisine, insulin detemir, hexyl-insulin monoconjugate 2, AeroDose insulin inhaler, AIR-insulin, Technosphere/insulin, rDNA insulin, any other inhaled, pulmonary or oral human insulin, exendin-4, sulphostin, liraglutide, recombinant glucagon-like peptide-1 (7-36) amide (AC-2592), dexlipotam, cyclipostin R, ramipril, dehydrotrametenolic acid, famoxin, methoxime-3,4-dephostatin, demethylasterriquinone B-1, adiponectin (human), salacinol, leporin B, TAK-654, MBX-102, ADD-9918, ADD-9922, NN-304, NN-344, BIM-51077, LABI (NN-1215), SNAC/Insulin, LAF-237, 823093, 825964, 815541, P93/01, SSR-162329, LY-510929 (LY-929), LBL-752 (DRF-MDX8, DRF-4158), GW-677954, LY-307161 SR, CJC-1131, SUN-E7001, ZP-10A (AVE-0010), MB-6322 (CS-917), BVT-2498, INGAP peptide, LY-818, TH-9507, ISIS-113715, SR-58611, YM-178, SB-418790 (AZ-40140, GW-427353), N-5984, NN-2501, RF-1051, HMR-1426, NOX-700, ATL-962, 869682, R-1439, R-765, GW-501516, GI-181771, ST-1326, VDO-52, A-348441, BLX-1002, TLK-19781, ZYH-2, BLX-2001, NC-1567, R-1440, (FMS)3-insulin, insulin chain B (9-23) peptide, Genapol-stabilized insulin, insulin transdermal, metreleptin (recombinant methionyl human leptin), islet neogenesis therapy, NBI-6024, NN-344, O-346, DiaPep227 (AVE-0277), TRX-4, rhGAD65, rhIGF-I (rhIGFBP-3), R-1524 (ISA-247, ISAtx-247), TRX-4-TolerMab, MnTE-2-Pyp5+ (AEOL-10113), CTCM-226, irbesartan, telmisartan, candesartan cilexetil (hexetil), pratosartan, pyridoxamine (pyridoxylamine), magnesium lithospermate B (Lithospermic acid B magnesium salt), sulodexide, aminoguanidine (pimagedine), pirfenidone, 1D11, CR-002, T-8, (+)-A-127722 (A-147627, ABT-627), ED-4914, fidarestat, nefazodone hydrochloride,

venlafaxine hydrochloride, pregabalin, ruboxistaurin mesilate hydrate, recombinant human nerve growth factor, capsavanil, dronabinol/cannabidiol, atexakin alfa (interleukin-6), memantine hydrochloride, dexlipotam, beraprost sodium, arimoclomol maleate, SX-3201 (AS-3201, SX-3030), TAK-428, QR-333, ruboxistaurin hydrochloride, octreotide acetate, aminoguanidine (pimagedine), pegaptanib octasodium, hyaluronidase, sescandelin, batimastat, recombinant angiopoietin-1, LY-338522, BIM-23190, AdPEDF.11 (Ad(GV)PEDF.11D), VEGF Trap (VEG Trap(R1R2), CVT-3634, and the like. Preferably, other therapeutic agents for diabetes include insulin preparation, insulin secretagogue, biguanide, α-glucosidase inhibitor and insulin sensitivity enhancer, such as insulin, glibenclamide, tolbutamide, nateglinide, metformin hydrochloride, voglibose and pioglitazone hydrochloride.

As therapeutic agents for hyperlipidemia that are used as concomitant pharmaceutical agents, HMG-CoA reductase inhibitors (statins), fibrates, TNFSF6 expression inhibitors, HDL-cholesterol increasing agents, ApoA1 expression enhancers, SPP1 (osteopontin) expression inhibitors, drugs acting on peroxisome proliferator-activated receptors (PPAR), PPAR-alpha agonists, lipase clearing factor stimulants, cholesterol antagonists, platelet aggregation antagonists, antioxidants, cholesterol biosynthesis inhibitors, LDL-receptor up-regulators, bile acid sequestrants, cholesterol absorption inhibitors and nicotinic acids, can be mentioned. Also can be mentioned are ACAT inhibitors, adenosine A1 agonists, ApoB expression inhibitors, ApoB secretion inhibitors, microsomal triglyceride transfer protein (MTP) inhibitors, HDL-cholesterol increasing agents, cholesteryl ester transfer protein (CETP) inhibitors, ileal bile acid transporter inhibitors, insulin sensitivity enhancers, PPAR-alpha agonists, PPAR-gamma agonists, PPAR-delta agonists, squalene synthase inhibitors, testosterone agonists, 11beta-

hydroxysteroid dehydrogenase inhibitors, 15-lipoxygenase inhibitors, 5-HT2 antagonists, ABCA1 expression enhancers, ACAT inhibitors, retinoid RXR agonists, liver X receptor (LXR) agonists, acetyl-CoA carboxylase inhibitors, acetyl-CoA thiolase inhibitors, adenosine A2A agonists, adenylate cyclase activators, adypocite FABP (aP2) inhibitors, keratinocyte FABP (k-FABP) inhibitors, aldose reductase inhibitors, angiogenesis inhibitors, anti-ICAM-1 agents, antioxidants, VCAM-1 antagonists, antiestrogens, estrogen agonists, lipid peroxidation inhibitors, ApoB secretion inhibitors, ApoB-100 lowering agents, apoptosis inducers, apoptosis inhibitors, ATP citrate lyase inhibitors, beta3-adrenoceptor agonists, calcium channel blockers, carnitine O-palmitoyltransferase inhibitors, cholesterol esterase inhibitors, drugs acting on farnesoid X receptors (FXR), farnesoid X receptor (FXR) agonists, drugs acting on thyroid hormone receptors, drugs acting on thyroid hormones, thyroid hormones, parathyroid hormones, farnesyl transferase inhibitors, glycogen phosphorylase a inhibitors, lanosterol 14alpha-demethylase inhibitors, lanosterol synthase inhibitors, histamine H1 antagonists, nitric oxide synthase inhibitors, thromboxane A2 antagonists, triacylglycerol lipase inhibitors, alpha-glucosidase inhibitors, LDL-receptor up-regulators, LYPLA1 expression inhibitors, non-steroidal antiinflammatory drugs, PDGFR inhibitors, phospholipase A2 inhibitors, platelet-activating factor (PAF) antagonists, potassium channel activators, prostaglandins, SCAP ligands, squalene epoxidase inhibitors, selective estrogen receptor modulators (SERM), sterol DELTA14-reductase inhibitors, vasopressin V1a antagonists, and the like. For example, lovastatin, pravastatin (eptastatin) sodium, fluvastatin (fluindostainin) sodium, rosuvastatin calcium, atorvastatin calcium, simvastatin (synvinolin), pitavastatin (itavastatin, nisvastatin) calcium, ronifibrate (ronifibrato), binifibrate

(binifibrato), clinofibrate, ciprofibrate, clofibrate, etofibrate, fenofibrate, bezafibrate, gemfibrozil, acipimox, eicosapentaenoic acid (icosapent, icopenate, icosapentate) ethyl ester, probucol, policosanol, colesevelam hydrochloride, colestyramine (cholestyramine resin), colestipol hydrochloride, colestimide (colestilan), ezetimibe and niacin (nicotinic acid) are used in combination as concomitant pharmaceutical agents for the compound of the present invention. Also used as concomitant pharmaceutical agents are pactimibe, eflucimibe, implitapide, large unilamellar vesicles, campestanol ascorbyl phosphate, sitostanol ascorbyl phosphate, amlodipine besylate, GW-493838, RPR-749, BAY-13-9952, CP-346086, BTG-511, JTT-705, LY-518674 (LY-674), ESP-31015 (ETC-1001), ETC-642 (ESP-24228, RLT), DRF-4832, S-8921, LY-510929 (LY-929), GW-501516 (GW-516), FM-VP4, JTT-130, GW-590735, 641597, KRP-101, TAK-475, HE-2200 (3beta,7beta,17beta-androstenetriol), D-003, PLT-732, NS-220, KS-01-019, AZD-7806, AZD-4619, AZD-6610, AZD-8294, ZYH-1, DRF-10945, SMP-797, and the like.

As therapeutic agent for obesity that are used as concomitant pharmaceutical agents, mazindol, lipase inhibitors, 5-HT/norepinephrine reuptake dual inhibitors, 5-HT reuptake inhibitors, supplements containing herbal ephedrine and caffeine, human chorionic gonadotropins, adrenoceptor agonists, methamphetamine, phentermine and amfepramone can be mentioned. Also can be mentioned are drugs acting on cannabinoid receptors, cannabinoid CB1 receptor antagonists, cannabinoid CB1 receptor inverse agonists, ciliary neurotrophic factor (CNTF), growth hormones, growth hormone secretagogues, triacylglycerol lipase inhibitors, ABCA1 expression enhancers, acetyl-CoA carboxylase inhibitors, adypocite FABP (aP2) Inhibitors, aldose reductase inhibitors, alpha-glucosidase inhibitors, alpha-mannosidase inhibitors, ATP citrate lyase inhibitors, adenosine A1 receptor agonists, serine carboxypeptidase inhibitors, 11beta-

hydroxysteroid dehydrogenase inhibitors, drugs acting on neuropeptide Y (NPY) receptors, neuropeptide Y2 (NPY Y2) receptor agonists, neuropeptide Y1 (NPY Y1) receptor antagonists, neuropeptide Y5 (NPY Y5) receptor antagonists, CCK antagonists, CCK1 (CCKA) agonists, CCK2 (CCKB/gastrin) antagonists, CRF1 antagonists, CRF2 agonists, drugs acting on melanin-concentrating hormone (MCH) receptors, MCH receptor antagonists, drugs acting on melanocortin receptors, melanocortin MC1 agonists, melanocortin MC3 agonists, melanocortin MC4 agonists, melanocortin MC5 agonists, orexin receptor antagonists, orexin OX-1 antagonists, orexin OX-2 antagonists, neurotensin agonists, tachykinin NK2 antagonists, drugs acting on thyroid hormones, thyroid hormone receptor beta agonists, galanin GAL1 antagonists, GHS (Ghrelin) receptor inverse agonists, glucocorticoid receptor modulators, beta2-adrenoceptor agonists, beta2-adrenoceptor antagonists, beta3-adrenoceptor agonists, alpha2-adrenoceptor antagonists, MAO inhibitors, dopamine D1 antagonists, dopamine D5 antagonists, dopamine reuptake inhibitors, dopamine-releasing drugs, norepinephrine reuptake inhibitors, drugs acting on 5-hydroxytryptamine receptors, 5-HT release stimulants, 5-HT1A antagonists, 5-HT1B agonists, drugs binding to 5-HT2 receptors, 5-HT2A antagonists, 5-HT2B agonists, 5-HT2C (5-HT1C) agonists, drugs binding to 5-HT6 receptors, 5-HT6 antagonists, drugs binding to histamine H3 receptors, histamine H3 antagonists, opioid antagonists, kappa-opioid antagonists, estrogen agonists, selective estrogen receptor modulators (SERM), apoB secretion inhibitors, microsomal triglyceride transfer protein (MTP) inhibitors, benzodiazepines, GABA(A) BZ site receptor agonists, CEBPA expression inhibitor oligonucleotides, SAPK1 (JNK) inhibitors, DAT inhibitors, NET inhibitors, SERT inhibitors, dipeptidyl-peptidase IV inhibitors, drugs acting on glucagon-like peptide 1 (GLP-1) receptors, tripeptidyl peptidase II

inhibitors, drugs acting on peroxisome proliferator-activated receptors (PPAR), PPAR-alpha agonists, PPAR-gamma agonists, PPAR-gamma antagonists, PPAR-gamma partial agonists, PPAR-delta agonists, retinoid RXR agonists, retinoid RXR antagonists, fatty acid synthase inhibitors, glycogen phosphorylase inhibitors, HMG-CoA reductase inhibitors, protein tyrosine phosphatase (PTP)-1B inhibitors (other than compounds of the invention), metalloporphyrins, nitric oxide synthase inhibitors, non-steroidal antiinflammatory drugs, phosphodiesterase III inhibitors, phosphodiesterase PDE3B inhibitors, SGLT-1 inhibitors, SGLT-2 inhibitors, sigma-receptor ligands, and the like. For example, mazindol, orlistat, sibutramine hydrochloride monohydrate, fluoxetine hydrochloride, chorionic gonadotropin (human), VNS therapy using NCP System, metaraminol, d-methamphetamine hydrochloride, phentermine, amfepramone hydrochloride (diethylpropion), benzfetamine hydrochloride and phendimetrazine tartrate are used in combination as concomitant pharmaceutical agents for the compound of the present invention. Also used as concomitant pharmaceutical agents are rimonabant hydrochloride, SR-147778, CNTF (Ax15) (RG-228, RPN-228), pegylated axokine, GI-181771, SR-146131, SR-125180, AOD-9604, ATL-962, PYY3-36 (AC-162352), N-5984, L-796568, garcinia acid ((-)-Hydroxycitric acid), HMR-1426, P-57, 1954, chromium picolinate/conjugated linoleic acid, S-2367, APD-356, BVT-5182, Ucn II, C-75, gAcrp30, KB-141, NLC-002, BLX-2002, P-64, T-71 and the like.

As therapeutic agents for hypertension that are used as concomitant pharmaceutical agents, thiazides, aldosterone antagonists, adrenergic neuron blockers, calcium channel blockers; dopamine D2 antagonists, beta-adrenoceptor antagonists, alpha2-adrenoceptor agonists, guanylate cyclase activators, beta1-adrenoceptor antagonists, alpha1-adrenoceptor antagonists, antioxidants, angiotensin-I converting enzyme

(ACE) inhibitors, Na+/H+ exchange inhibitors, alpha-adrenoceptor antagonists, nitric oxide donors, 5-HT2 antagonists, K(ATP) channel activators, potassium sparing diuretic prostaglandin synthase stimulants, imidazoline I1 receptor agonists, angiotensin AT1 antagonists, dopamine D1 agonists, guanylate cyclase stimulants, endothelin ETA receptor antagonists, endothelin ETB receptor antagonists, NOS3 expression enhancers, prostacyclin analogs, prostaglandins, angiotensin II antagonists, electrolyte absorption agonists, nicotinic antagonists, dopamine D2 agonists, prolactin inhibitors, platelet-activating factor (PAF) antagonists, platelet aggregation antagonists, tumor necrosis factor antagonists, Rho kinase inhibitors, PPAR-alpha agonists, AMPA receptor modulators; GABA(A) receptor antagonists and phosphodiesterase V (PDE5A) inhibitors can be mentioned. Also can be mentioned are 5-HT1A receptor agonists, 5-HT1B antagonists, {5-HT2 antagonists,} 5-HT2A antagonists, ACAT inhibitors, adenosine A1 agonists, adenosine A1 antagonists, adenosine A2A agonists, adenosine A2A antagonists, adenylate cyclase activators, adrenergic neuron blockers, AGE inhibitors (Maillard's reaction inhibitors), aldose reductase inhibitors, {aldosterone antagonists,} alkaloids, alpha-adrenoceptor ligands, {alpha-adrenoceptor antagonists, alpha1-adrenoceptor antagonists,} alpha1A-adrenoceptor antagonists, {alpha2-adrenoceptor agonists,} alpha2-adrenoceptor antagonists, beta2-adrenoceptor antagonists, {beta-adrenoceptor antagonists, beta1-adrenoceptor antagonists,} beta2-adrenoceptor agonists, alpha-atrial natriuretic peptides, {AMPA receptor modulators,} angiogenesis inhibitors, apoptosis inhibitors, {angiotensin-I converting enzyme (ACE) inhibitors, angiotensin AT1 antagonists}, angiotensin AT2 antagonists, angiotensin receptor antagonists, antiinflammatory drugs, free radical scavengers, {antioxidants,} calcium channel activators, {calcium channel

blockers,} L-type calcium channel blockers, {platelet-activating factor (PAF) antagonists,} cAMP phosphodiesterase inhibitors, cannabinoid CB2 agonists, cannabinoid receptor agonists, vanilloid VR1 receptor agonists, chymase inhibitors, cyclooxygenase-2 inhibitors, dopamine autoreceptor agonists, dopamine receptor agonists, dopamine D1 agonists, {dopamine D2 agonists,} dopamine D1 antagonists, {dopamine D2 antagonists,} dopamine-beta-monooxygenase inhibitors, endothelin receptor antagonists, {endothelin ETA receptor antagonists, endothelin ETB receptor antagonists,} endothelin receptor agonists, endothelin-converting enzyme inhibitors, enkephalinase inhibitors, {GABA(A) receptor antagonists,} glycogen phosphorylase a inhibitors, growth hormone release inhibitors, somatostatin analogs, {guanylate cyclase activators,} histamine H1 agonists, histamine H1 antagonists, hypoxia inducible factor 1-alpha (HIF-1alpha) inhibitors, drugs acting on imidazoline receptors, {imidazoline I1 receptor agonists,} insulin analogs (zinc complexes), insulin sensitivity enhancers, {PPAR-alpha agonists,} PPAR-gamma agonists, insulin lowering agents, {K(ATP) channel activators,} K(ATP) channel blockers, lipoxygenase inhibitors, large conductance BK(Ca) channel activators, {Na+/H+ exchange inhibitors,} Na+/K+-ATPase inhibitors, NADPH oxidase inhibitors, neprilysin inhibitors, neuropeptide Y1 (NPY Y1) antagonists, neuropeptide Y4 (NPY Y4) agonists, {nicotinic antagonists,} nitrates, {nitric oxide donors,} non-steroidal antiinflammatory drugs, protein kinase C (PKC) inhibitors, {NOS3 expression enhancers,} oligonucleotides, PDGFR inhibitors, phosphodiesterase inhibitors, phosphodiesterase I inhibitors, phosphodiesterase III inhibitors, phosphodiesterase IV inhibitors, {phosphodiesterase V (PDE5A) inhibitors,} potassium channel activators, {prostacyclin analogs, prostaglandins,} prostanoid IP agonists, prostanoid TP (thromboxane A2) antagonists, thromboxane

synthase inhibitors, protease inhibitors, proteasome inhibitors, protein kinase C (PKC) inhibitors, renin inhibitors, {Rho kinase inhibitors,} sigma-receptor antagonists, sodium channel blockers, thiazides, triglyceride lowering agents, vasopressin antagonists, vasopressin V1a antagonists, vasopressin V2 antagonists, and the like. For example, chlorothiazide, hydrochlorothiazide, hydroflumethiazide, methyclothiazide, polythiazide, xipamide, cyclopenthiazide, bendroflumethiazide (bendrofluazide), spironolactone, epoxymexrenone (eplerenone), guanethidine monosulfate, guanadrel sulfate, verapamil, propranolol hydrochloride, alprenolol hydrochloride, pindolol, oxprenolol hydrochloride, timolol maleate, sotalol hydrochloride, acebutolol hydrochloride, carteolol hydrochloride, mepindolol sulfate, arotinolol hydrochloride, indenolol hydrochloride, tertatolol hydrochloride, celiprolol hydrochloride, tilisolol hydrochloride, nebivolol, penbutolol sulfate, nadolol, cloranolol hydrochloride, bevantol (bevantolol) hydrochloride, clonidine, guanfacine hydrochloride, diltiazem hydrochloride, nicardipine hydrochloride, nitrendipine, felodipine, nilvadipine; nivadipine, nisoldipine, benidipine hydrochloride, amlodipine besylate, franidipine (manidipine) hydrochloride, lacidipine, isradipine, barnidipine (mepirodipine) hydrochloride, efonidipine hydrochloride ethanol, cinaldipine (cilnidipine), aranidipine, lercanidipine (masnidipine) hydrochloride, azelnidipine, amlodipine, manidipine (franidipine), sodium nitroprusside, atenolol, metoprolol tartrate, betaxolol hydrochloride, bopindolol, bisoprolol fumarate, esmolol hydrochloride, carvedilol, metoprolol succinate, talinolol, prazosin hydrochloride, urapidil, indoramin hydrochloride, bunazosin hydrochloride, terazosin hydrochloride, doxazosin mesylate, urapidil, nifedipine, captopril, enalapril maleate, lisinopril, perindopril, alacepril, ramipril, quinapril hydrochloride,

delapril hydrochloride, benazepril hydrochloride, cilazapril, fosinoprilat, fosinopril sodium, trandolapril, spirapril, temocapril hydrochloride, moexipril hydrochloride, imidapril hydrochloride, zofenopril calcium, enalaprilat, zofenoprilat, amiloride hydrochloride, labetalol hydrochloride, nipradilol (nipradolol), linsidomine, ketanserin, pinacidil, cicletanine (cycletanide), amosulalol hydrochloride, moxonidine hydrochloride hydrate, losartan potassium, valsartan, eprosartan mesylate, candesartan cilexetil (hexetil), irbesartan, telmisartan, olmesartan medoxomil, fenoldopam mesilate, cadralazine, rilmenidine dihydrogen phosphate, bosentan, beraprost sodium, limaprost alfadex (alpha-cyclodextrin), uniprost (treprostinil sodium), iloprost (ciloprost), mecamylamine hydrochloride, metergoline, guanabenz acetate, cloricromene, fasudil, doconexent (docosahexaenoic acid), cyclothiazide, sildenafil citrate, chlortalidone (chlorthalidone), quinethazone, indapamide, metolazone, phenoxybenzamine hydrochloride, metirosine (metyrosine), diazoxide, torasemide (torsemide), clopamide, hydralazine hydrochloride, reserpine and methyldopa are used in combination as concomitant pharmaceutical agents for the compound of the present invention. Also used as concomitant pharmaceutical agents are omapatrilat, aladotril (alatriopril, fasidotril), AVE-7688 (MDL-107688), 796406, lemildipine, pranidipine, clevidipine, levamlodipine ((S)-amlodipine), ambrisentan, sitaxsentan sodium, SPP-301 (R-639, RO-67-0565), TBC-3711, PMD-2850 (angiotensin vaccine), PMD-3117, Binodenoson, alagebrium chloride, SLV-306, aliskiren fumarate, NV-04, MC-4232, ENO, MDL-72832, BP-554, (+)-OSU-191 (OSU-191-(+), U-86192A), WAY-100339, QF-303B (QF-0303B), QF-307B (QF-0307B), QF-311B (QF-0311B), lidanserin (ZK-33839), AP-1067, AHR-16303B, QF-313B (QF-0313B), S-14280, S-35031, S-35120, PR-1173, RG-14718, CCPA, S-ENBA, Sch-59761, FR-166124, GU-285, MDL-101483, CVT-2995,

CVT-3032, CVT-3033, 2HE-NECA (HENECA), CGS-21680, CGS-22492, CGS-22989, SHA-40, APEC, KF-17837, OPB-9195, lithospermic acid B magnesium salt (magnesium lithospermate B), 6-iodoamiloride, 6-protoberberine (PTB-6), CR-2991, HSR-175, CDRI-93/478, DC-015 (DC-028, DL-028A), BAM-2202, GB-67, YM-11133, Abbott-65265, SK&F-104856, MG-1, L-765314, KMUP-880602, A-68828, YC-1, AB-47, C-112, utibaprilat, FPL-63674 (FPL-63674XX, FPL-63547-diacid), FPL-66564, MDL-100173, MDL-27467A, glycopril, ROO 911, SQ-31440, DU-1777, S-nitrosocaptopril (SNOCAP), Y-23785, enalapril nitrate, moexiprilat (RS-10029), temocaprilat (RS-5139), CV-5975, imidaprilat (6366 A), REV-6134, BW-B385C, CGS-26582, SA-6817, SA-7060, Sch-54470, S-allylmercaptocaptopril (CPSSA), RB-106, MDL-101628, mixanpril, fasidotrilat (alatrioprilat), BMS-182657, ER-32897, ER-32935, ER-40121, ER-40133 (E-4030), CGS-28106, CGS-30440, Sch-50690, A-81282 (Abbott-81282), A-81988, GA-0050, GA-0113, ZD-7155, RU-63455, RU-64276, RU-65868, embusartan (Bay-10-6734), BIBS-39, BMS-180560, BMS-181688, BMS-184698, EXP-063, EXP6155, EXP-7711 (IMI), EXP-9270, S-8308, XD-937, XH-148, UP-221-78, UP-275-22, FI-6828K, FR-130739, FR-143187, FR-149581, LR-B/087, RWJ-38970, RWJ-46458, WK-1492 (WK-1492.2K), KR-31080 (SK-1080), KT3-579, KT3-866, KW-3433, LY-285434, LY-301875, LY-302289, L-158338, L-158659, L-158978, L-159093, L-159689, L-161177, L-162154, L-162223, L-162234, L-162393, L-162474, L-163313, L-163579, EMD-69943, EMD-90423, tisartan (CGP-48369), abitesartan (CGP-49870), CP-161418, CP-191166, PD-123177 (EXP-655), PD-123319, PD-150304, SC-50560, SC-51316, SC-51757, SC-51895, SC-54628, SC-54629, U-97018, RWJ-47639, TH-142177, CV-11194, 606A, TA-606, LCY-018, CR-3210, UP-275-13, UR-7198, UR-7280, WK-1260, CL-190133 (CL-332877, CL-190733, CL-190734), WAY-126227, YM-31472, EXP-408, XR-510, L-161021, L-162389, L-162441, L-162537, L-163007, L-163017, L-163958, BMS-248360, DMP-811 (DuP-811, L-708404), SB-203220, LR-B/057, L-159913, L-161816, sesamin, ferulinolol, PF-9104, TZC-

1370, O-palmitoyl tilisolol, BG6, TZC-8159, Y-22516, olradipine hydrochloride (S-11568), PCA-50938, H-324/38, ZM-224832, HP-406, BMY-43011, SQ-32321, SQ-32547, SQ-33351, elnadipine, rhynchophylline, SUN-5647, VULM-999, DCDDP, sagandipine, GR-60139, Goe-5584-A, siratiazem hydrobromide LR-A/113), GS-386, sornidipine, MCF-1084, MCF-1113, dibudipine, deuterated nifedipine (ISA-1058), McN-6497 (RWJ-26902), CRL-41695, (4S)-(+)-AE0047, Y-24149, s-petasin, NIP-101, UK-52831, UK-55444, UK-56593, UK-51656, P-1268, BBR-2160, RS-88007, RS-5773, SL-85.1097, 83-0256, 83-0327, S-312 (83-0312), MR-14134, AHR-12742, AHR-16462B, AHR-5360C (AHR-5360), BMY-20014, BMY-20064, BMY-42803, veroxan, labedipinedilol B, labedipinedilol A, FR-172516, vanidipinedilol, xanthonolol, Z-6568, F-1850, Wy-27569, M-54033, HU-308, arvanil, BL-3875, BL-4027, TEI-E00548, rutaecarpine (rutecarpine), PD-139899, FPL-65447AA, Z-12571, Z-7760, (S)-Z-11410, FR-138104, MDL-43925, SK&F-102698, A-292438, A-306552, RPR-117820A, RPR-118031A, J-105510, J-105859, J-112287, BMS-182874, TBC-11040, TBC-11192, TBC-2576, TBC-3214, SB-247083, EMD-122946, EMD-94246, fandosentan potassium (CI-1034, PD-180988), PABSA, YM-62899, YM-91746, LU-302872 (BSF-420627, LU-420627), BMS-187308, IRL-3630, L-747844, RPR-111844, PD-163070, PD-166309, PD-142893, A-192621, CGS-31398, IRL-1620, BQ-485, FR-901366 (WS-009A), KET-011, RES-701-1 (KF-20704), L-744453, L-749329, L-749805, IRL-1737, PD-155080, PD-156252, T-0115 (TA-0115), S-17162, WS-79089B (WS-79089-3, FR-901533), SM-19712, CGS-26303, CGS-26393, CGS-30084, CGS-34043, CGS-34225, CGS-34226, CGS-34753, CGS-35066, KC-12792, SQ-28603, CP-91149, BAY-41-2272, BAY-41-8543, BAY-58-2667, KMUP-1, methylhistaprodifen, suprahistaprodifen, S-23515, S-23757, LNP-509, LNP-911, Zn(car)2Cl2, DRF-4158 (DRF-MDX8, LBL-752), DY-9804, MJ-355, BPDZ-79, BPDZ-83, YM-099, sarakalim (RS-91309), PNU-96293, NS-1608, CPU-23, PST-2107, apocynin, CGS-24128, CGS-24592, CGS-25155, H-394/84, BIBO-3304, 1229U91 (GR-231118, BW-1229U91, GW-

1229), RS-7897, C92-4609 (CAS-1609), CHF-2363 (SN011), PROLI/NO, FR-144420, GEA-3175, DS1, NOC-7, MAHMA MONOate, PF-9404, EDTA (edetic acid), AS-AT1R-ODN mRNA, NX-1975, 5E3623, Sch-51866, Sch-59498, LAS-31180, SK&F-94120, SK&F-95654, Win-63291, DMPPO, DF-100 (A80a), E-4010, zaprinast (M&B-22948), T-1032, iptakalim hydrochloride, ZM-260384, RP-66784, S-0121, BMS-182264, KC-399, KC-515, SG-209, DY-9708, ER-001533, RWJ-26629, U-94968, KI-4032, KRN-4884, KR-30818 (SKP-818), P-1060, LM-3339, MCC-134, AL-0671, AL-0670, Y-26763, PC-286, TAK-636, dioclein, UR-8081, UR-8218, UR-8225, UR-8267, CL-188294, LP-805, KMUP-880708, cromakalim, BW-68C, FR-181157, FR-181877, ER-017996, PSI, MDL-29152, A-62198, A-65317, A-68064, A-82110, A-70461, ICI-219623, MDL-73323, MDL-74147, S-2864, BW-175, BILA-2157, SQ-30774, SQ-31844, SQ-33800, JTP-2438, JTP-2724, JTP-3072, JTP-4129, JTV-505 (JTP-4761), KRI-1177, KRI-1314, CGP-44099A, CGP-54061, CGP-55128A, CGP-56346A, CGP-56962A, CGP-62198A, CP-108671, CP-71362, PD-132002, SC-46944, SC-56525, U-77436, Ro-44-9375, Ro-66-1132 (RO-0661132, RO-X1), RO-X2, SPP-600, CL-331049, WAY-121604, YM-21095, YM-26365, hydroxyfasudil, Y-30141, H-1152 (HMN-1152), CNS-1307, Ono-1505, JTV-605, YM-176770, JNJ-17079166, FR-161282, and the like.

As therapeutic agents for thrombosis that are used as concomitant pharmaceutical agents, heparin preparations, low molecular weight heparins, heparin analogs, anticoagulants, thrombin inhibitors, anti-thrombin preparations, antiplatelet agents thrombolytic agents and the like can be mentioned. For example, heparin calcium, heparin sodium, dalteparin sodium, parnaparin sodium, reviparin sodium, danaparoid sodium, warfarin potassium, argatroban, gabexate mesylate, nafamostat mesylate, human anti-thrombin III, aspirin, dipyridamole, ticlopidine hydrochloride, cilostazol, limaprost alfadex, sodium ozagrel, sarpogrelate hydrochloride, ethyl icosapentate, beraprost sodium, urokinase, tisokinase, alteplase, nasaruplase,

nateplase, monteplase, pamiteplase, batroxobin, sodium citrate, protein C, and the like are used in combination as concomitant pharmaceutical agents for the compound of the present invention.

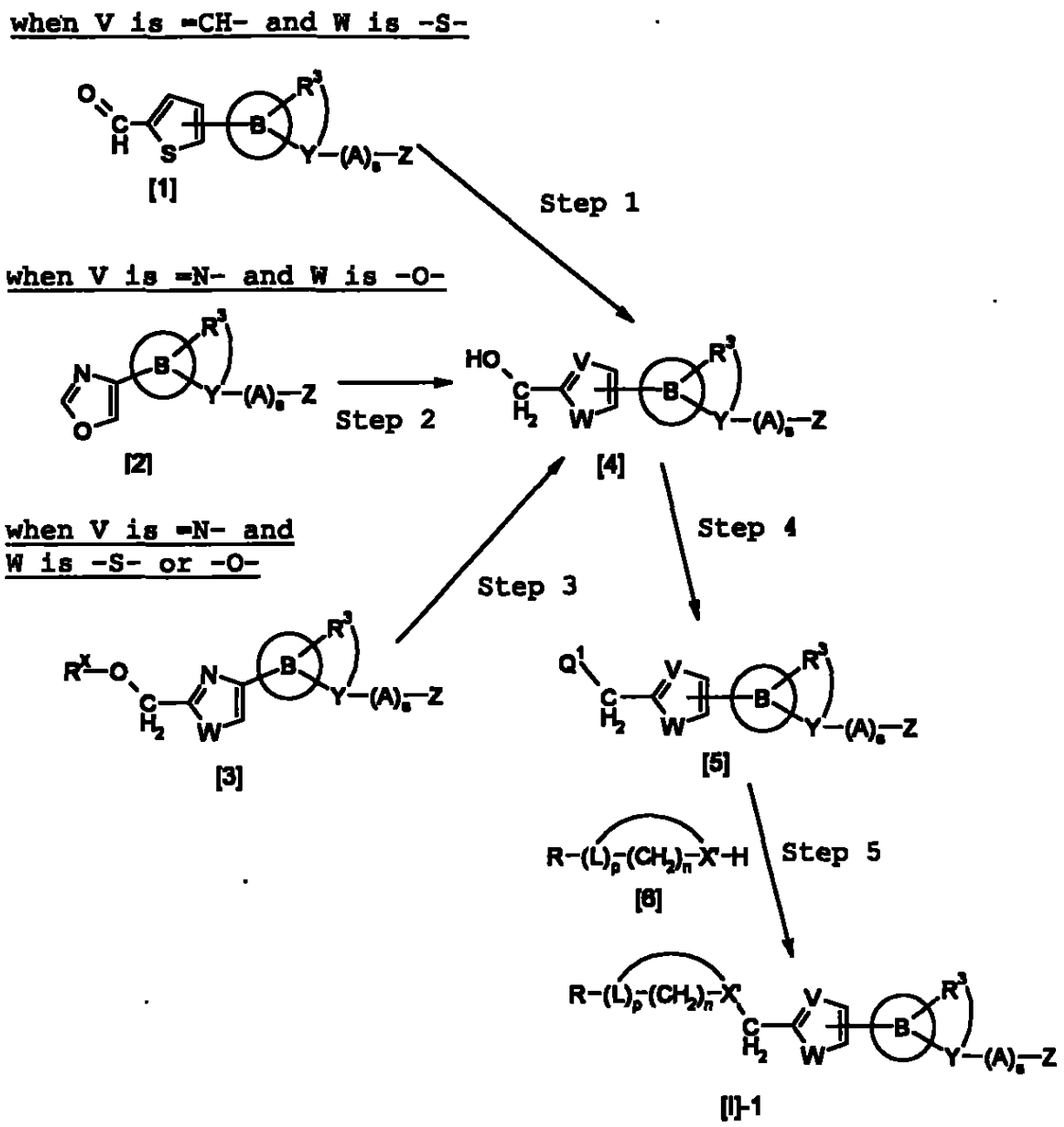
In the following, examples of production methods of the compound of the present invention used to practice the present invention are given. However, the production methods of the compound of the present invention are not limited to those exemplified below.

Even in the absence of specific description in the present production methods, efficiently production can be performed by incorporating modification where necessary, such as introducing a protecting group into a functional group, followed by deprotection in a later step, exchanging the order of production method and steps and the like.

The work-up in each step can be performed according to methods generally employed, such as extraction, washing, concentration, filtration, adjustment of pH and the like, wherein isolation and purification can be performed by employing suitable conventional methods such as crystallization, recrystallization, silica gel chromatography, preparative HPLC and the like, which may be a single method or two or more methods in combination.

Production Method 1

In this Production Method, compound [I] wherein m is 1, R^1 and R^2 are each a hydrogen atom and X is $-N(R^4)-$, $-N(R^5)-CO-O-$, $-O-$ or $-S-$ is produced.



wherein Q^1 is a general leaving group (e.g., halogen atom (bromine atom, iodine atom, chlorine atom etc.), a mesyloxy group, a tosyloxy group, a trifluoromethanesulfonyloxy group etc.), R^X is a general hydroxyl-protecting group (e.g., tert-butyldimethylsilyl group, benzoyl group etc.), X' is $-N(R^4)-$, $-N(R^5)-CO-O-$, -O- or -S- wherein each symbol is as defined above and other symbols are as defined above.

Step 1

Compound [4] can be obtained by reduction of compound [1] in a solvent using a conventional reducing agent. As the

solvent, alcohols (methanol, ethanol etc.), ether solvents (tetrahydrofuran, dioxane etc.), toluene and the like, and a mixed solvent thereof can be mentioned. As the reducing agent, sodium borohydride, lithium borohydride, diborane, lithium aluminum hydride and the like can be mentioned. The reaction can be carried out under cooling to heating.

Step 2

Compound [4] can be obtained by reacting compound [2] with paraformaldehyde in a solvent in the presence of a base for hydroxymethylation. As the solvent, toluene, ether solvents (tetrahydrofuran, diethyl ether etc.) and the like and a mixed solvent thereof can be mentioned. As the base, a base obtained using alkyllithium (n-butyllithium, sec-butyllithium, tert-butyllithium etc.) and 2,2,6,6-tetramethylpiperidine, lithium diisopropylamine and the like can be mentioned. The reaction can be carried out under cooling.

Step 3

Compound [4] can be obtained by deprotection of R^X of compound [3] according to conventional methods. When R^X is a benzoyl group, for example, the object product can be obtained by a reaction similar to the method exemplified in Step 30 of Production Method 19.

Step 4

Compound [5] can be obtained by substituting a hydroxyl group of compound [4] with a conventional leaving group in a similar manner as in Step 18 of Production Method 10.

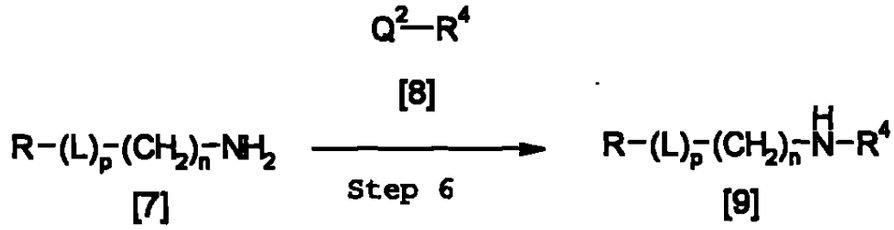
Step 5

Compound [I]-1 can be obtained by reacting compound [5] with compound [6] in a solvent in the presence of base and in the presence or absence of a catalyst. As the solvent, N,N-dimethylacetamide, N,N-dimethylformamide, acetonitrile, ethyl acetate, toluene, alcohol solvents (methanol, ethanol etc.), ether solvents (tetrahydrofuran, dioxane etc.), halogenated

solvents (chloroform, dichloromethane etc.) and the like and a mixed solvent thereof can be mentioned. As the base, inorganic bases such as potassium carbonate, sodium carbonate and the like and organic bases such as triethylamine, diisopropylethylamine and the like can be mentioned. As the catalyst, potassium iodide, quaternary ammonium salt (tetrabutylammonium iodide, tetrabutylammonium bromide etc.) and the like can be mentioned. The reaction can be carried out under cooling to heating.

Production Method 2

In this Production Method, of the compounds [6] used in Step 5 of Production Method 1, a compound wherein X' is $-N(R^4)-$ is produced.



wherein Q^2 is a general leaving group as described in Production Method 1 and other symbols are as defined above.

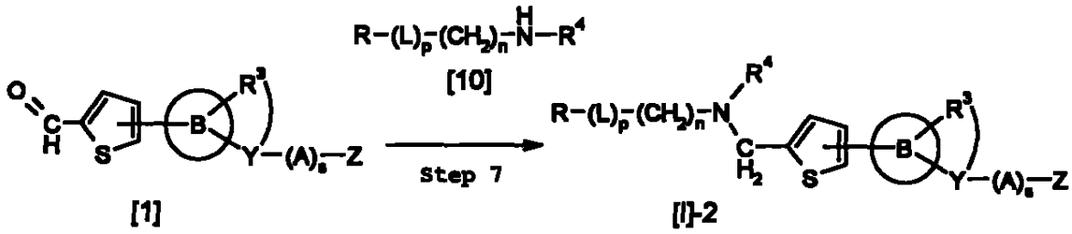
Step 6

Compound [9] can be obtained by reacting compound [7] with compound [8] in a solvent in the presence of a base and in the presence or absence of a catalyst. As the solvent, N,N-dimethylacetamide, N,N-dimethylformamide, acetonitrile, ethyl acetate, toluene, alcohol solvents (methanol, ethanol etc.), ether solvents (tetrahydrofuran, dioxane etc.), halogenated solvents (chloroform, dichloromethane etc.) and the like and a mixed solvent thereof can be mentioned. As the base, inorganic bases such as potassium carbonate, sodium carbonate and the like and organic bases such as triethylamine, diisopropylethylamine and the like can be mentioned. As the

catalyst, potassium iodide, quaternary ammonium salt (tetrabutylammonium iodide, tetrabutylammonium bromide etc.) and the like can be mentioned. The reaction can be carried out under cooling to heating.

Production Method 3

In this Production Method, compound [I] wherein V is =CH-, W is -S-, m is 1, R^1 and R^2 are each a hydrogen atom and X is -$N(R^4)$- is produced.



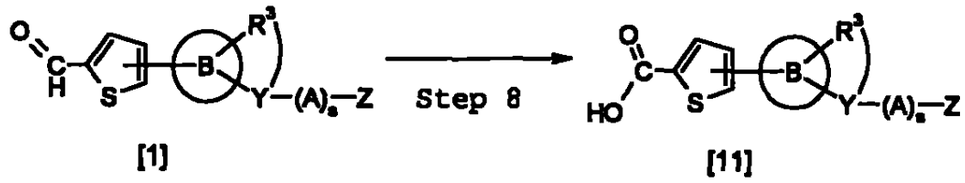
wherein each symbol is as defined above.

Step 7

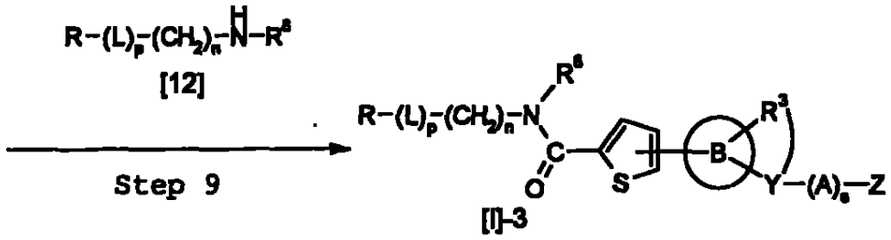
Compound [I]-2 can be obtained by reacting compound [1] with compound [10] in a solvent in the presence of a reducing agent and in the presence or absence of a base. As the solvent, N,N-dimethylacetamide, N,N-dimethylformamide, acetonitrile, ethyl acetate, toluene, ether solvents (tetrahydrofuran, dioxane etc.), halogenated solvents (chloroform, dichloromethane, 1,2-dichloroethane etc.), alcohol solvents (methanol, ethanol etc.), acetic acid and the like and a mixed solvent thereof can be mentioned. As the reducing agent, sodium borohydride, sodium triacetoxyborohydride, sodium cyanoborohydride and the like can be mentioned. As the base, organic bases such as pyridine and the like can be mentioned. The reaction temperature is preferably 0°C - 80°C.

Production Method 4

In this Production Method, compound [I] wherein V is =CH-, W is -S-, m is 0 and X is -$N(R^8)$-CO- is produced.



[1] Step 8 [11]



[12] Step 9 [I]-3

wherein each symbol is as defined above.

Step 8

Compound [11] can be obtained by oxidation of aldehyde of compound [1] using a conventional oxidizing agent in a solvent. As the solvent, alcohols (methanol, ethanol etc.), ether solvents (tetrahydrofuran, dioxane etc.), acetone, acetic acid, water and the like, and a mixed solvent thereof can be mentioned. As the oxidizing agent, sodium chlorite (where necessary, a chlorine scavenger (sulfamic acid etc.) is added), sodium hypochlorite, potassium permanganate, sodium chromate, silver nitrate, silver oxide, 2,2,6,6-tetramethylpiperidine-N-oxide and the like can be mentioned. The reaction can be carried out under cooling to heating.

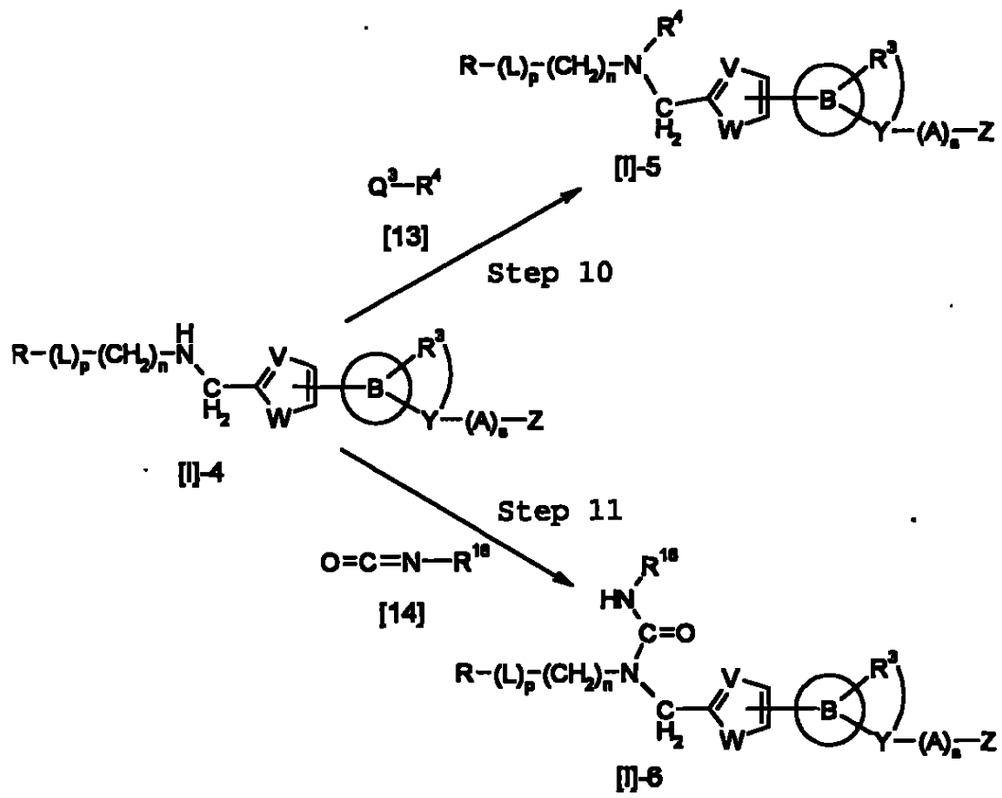
Step 9

Compound [I]-3 can be obtained by amide condensation of compound [11] with compound [12] obtained by a method similar to that to give compound [9] in Production Method 2. The amide condensation can be performed according to conventional methods. For example, a method comprising condensation in a solvent such as N,N-dimethylformamide, acetonitrile, tetrahydrofuran, chloroform, ethyl acetate, methylene chloride, toluene and the like, in the presence of a condensing agent such as

dicyclohexylcarbodiimide, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, diphenylphosphoryl azide and the like, and in the presence or absence of N-hydroxysuccinimide, 1-hydroxybenzotriazole and the like can be mentioned. The reaction temperature is preferably 0°C - 100°C.

Production Method 5

In this Production Method, compound [I] wherein m is 1, R^1 and R^2 are each a hydrogen atom and X is $-N(R^4)-$ is produced.



wherein Q^3 is a general leaving group as described in Production Method 1 and other symbols are as defined above.

Step 10

Compound [I]-5 can be obtained by reaction of compound [I]-4 obtained by a method similar to that to give compound [I]-1 in Production Method 1 with compound [13] in a solvent in the presence or absence of a base. As the solvent, N,N-

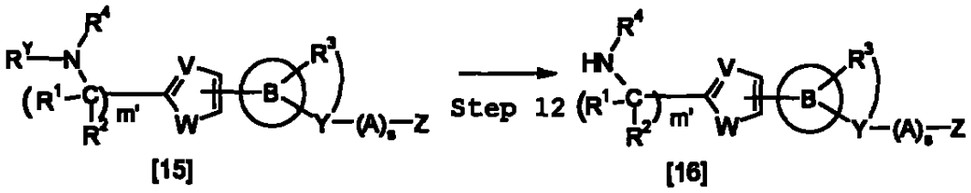
dimethylacetamide, N,N-dimethylformamide, acetonitrile, ethyl acetate, toluene, ether solvents (tetrahydrofuran, dioxane etc.), halogenated solvents (chloroform, dichloromethane etc.) and the like and a mixed solvent thereof can be mentioned. As the base, inorganic bases such as potassium carbonate, sodium carbonate and the like and organic bases such as triethylamine, diisopropylethylamine and the like can be mentioned. The reaction can be carried out under cooling to heating.

Step 11

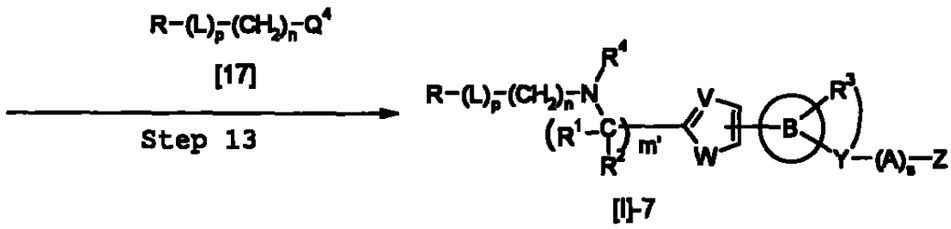
Compound [I]-6 can be obtained by reacting compound [I]-4 with compound [14] in a solvent in the presence or absence of a base. As the solvent, N,N-dimethylacetamide, N,N-dimethylformamide, acetonitrile, ethyl acetate, toluene, ether solvents (tetrahydrofuran, dioxane etc.), halogenated solvents (chloroform, dichloromethane etc.) and the like and a mixed solvent thereof can be mentioned. As the base, inorganic bases such as potassium carbonate, sodium carbonate and the like and organic bases such as triethylamine, diisopropylethylamine and the like can be mentioned. The reaction can be carried out under cooling to heating.

Production Method 6

In this Production Method, compound [I] wherein m is 1 or 2 and X is $-N(R^4)-$ is produced.



[15] [16]



[I]-7

wherein m' is 1 or 2, Q^4 is a general leaving group as described in Production Method 1, R^Y is an amine-protecting group such as tert-butoxycarbonyl group, benzyloxycarbonyl group and the like, and other symbols are as defined above.

Step 12

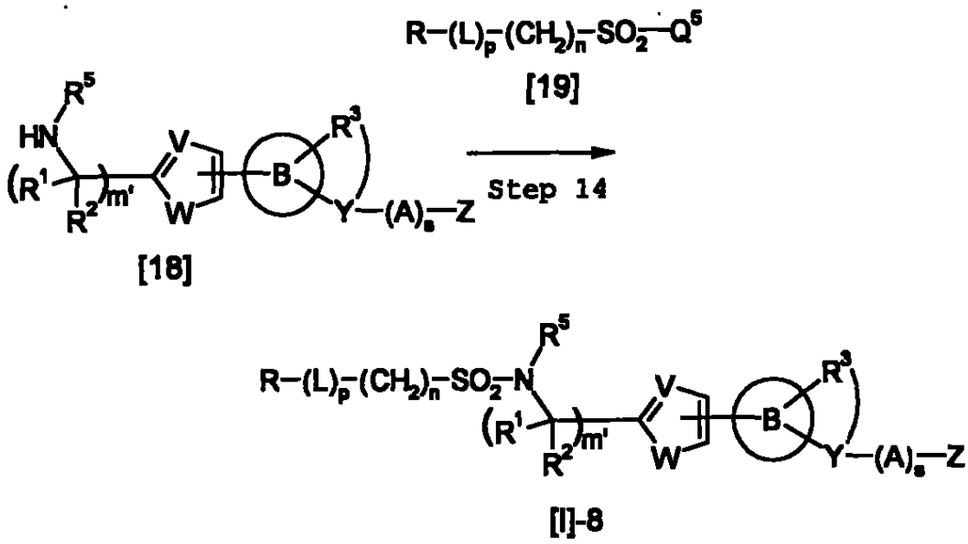
Compound [16] can be obtained by deprotection of R^Y of compound [15]. The deprotection can be conducted according to conventional methods. For example, when R^Y is a tert-butoxycarbonyl group, a method comprising reaction with hydrogen chloride in a solvent such as dioxane and the like can be mentioned. The reaction temperature is preferably 0°C - room temperature.

Step 13

Compound [I]-7 can be obtained by reacting compound [16] with compound [17] in a solvent in the presence of a base. As the solvent, N,N-dimethylacetamide, N,N-dimethylformamide, acetonitrile, ethyl acetate, toluene, ether solvents (tetrahydrofuran, dioxane etc.), halogenated solvents (chloroform, dichloromethane etc.) and the like and a mixed solvent thereof can be mentioned. As the base, inorganic bases such as potassium carbonate, sodium carbonate and the like and organic bases such as triethylamine, diisopropylethylamine and the like can be mentioned. The reaction can be carried out under cooling to heating.

Production Method 7

In this Production Method, compound [I] wherein m is 1 or 2 and X is $-SO_2-N(R^5)-$ is produced.



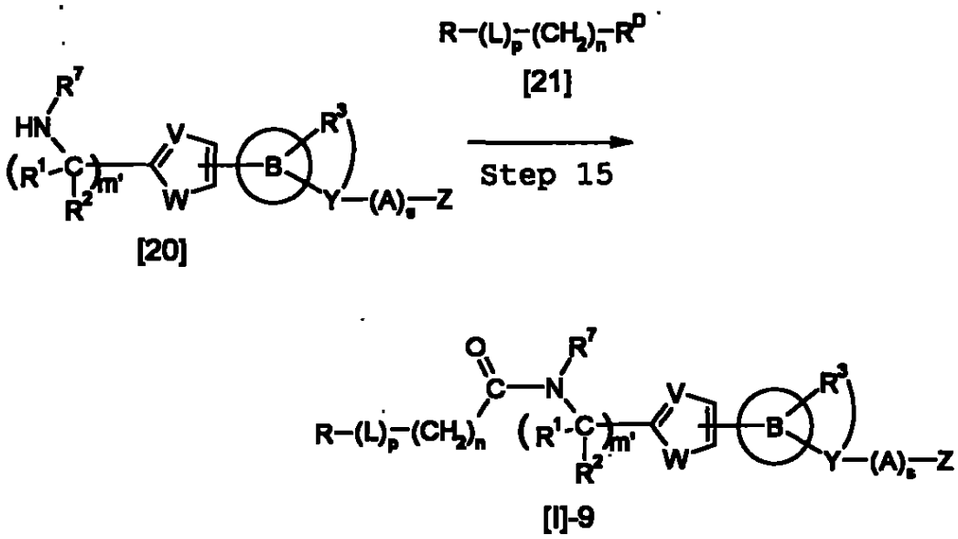
wherein Q^5 is a halogen atom (bromine atom, iodine atom, fluorine atom, chlorine atom etc.) and other symbols are as defined above.

Step 14

Compound [I]-8 can be obtained by reacting compound [18] obtained by a method similar to that to give compound [16] in Production Method 6 with compound [19] in a solvent in the presence of a base. As the solvent, N,N-dimethylacetamide, N,N-dimethylformamide, acetonitrile, ethyl acetate, toluene, ether solvents (tetrahydrofuran, dioxane etc.), halogenated solvents (chloroform, dichloromethane etc.) and the like, and a mixed solvent thereof can be mentioned. As the base, inorganic bases such as potassium carbonate, sodium carbonate and the like and organic bases such as triethylamine, diisopropylethylamine and the like can be mentioned. The reaction can be carried out at room temperature to under heating.

Production Method 8

In this Production Method, compound [I] wherein m is 1 or 2 and X is $-CO-N(R^7)-$ is produced.



wherein R^D is a carboxy group or a formyl group substituted by a halogen atom (bromine atom, iodine atom, fluorine atom, chlorine atom etc.), and other symbols are as defined above.

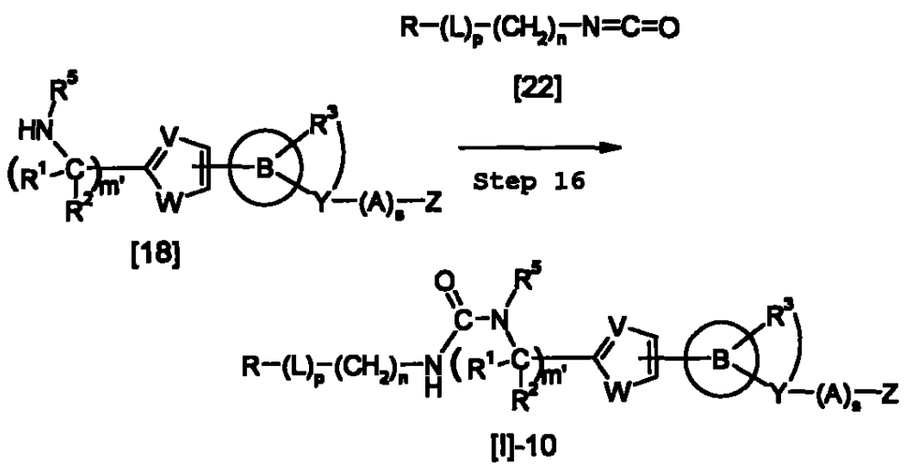
Step 15

Compound [I]-9 can be obtained by amide condensation of compound [20] obtained by a method similar to that to give compound [16] in Production Method 6 with compound [21]. The amide condensation can be performed according to conventional methods. For example, in a case of R^D being a carboxy group, a method comprising condensation in a solvent such as N,N-dimethylformamide, acetonitrile, tetrahydrofuran, chloroform, ethyl acetate, methylene chloride, toluene and the like, in the presence of a condensing agent such as dicyclohexylcarbodiimide, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, diphenylphosphoryl azide and the like, and in the presence or absence of N-hydroxysuccinimide, 1-hydroxybenzotriazole and the like can be mentioned. The reaction can be carried out under cooling to heating. In addition, in a case of R^D being a formyl group substituted by a halogen atom, a method comprising condensation in a solvent such as N,N-dimethylformamide, acetonitrile, tetrahydrofuran, chloroform, ethyl acetate, methylene chloride, toluene, water and the like and a mixed

solvent thereof, and in the presence of a base such as inorganic bases (sodium hydrogen carbonate, potassium carbonate, potassium hydrogen carbonate, sodium hydroxide, etc.) and organic bases (triethylamine, diisopropylethylamine, pyridine, etc.), can be mentioned as an example. The reaction can be carried out under cooling to heating.

Production Method 9

In this Production Method, compound [I] wherein m is 1 or 2 and X is -NH-CO-N(R^5)- is produced.



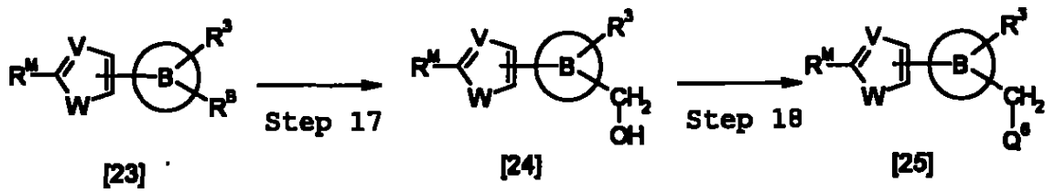
wherein each symbol is as defined above.

Step 16

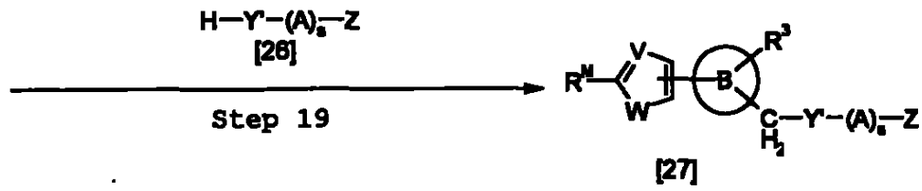
Compound [I]-10 can be obtained by reacting compound [18] with compound [22] in a solvent in the presence or absence of a base. As the solvent, N,N-dimethylacetamide, N,N-dimethylformamide, acetonitrile, ethyl acetate, toluene, ether solvents (tetrahydrofuran, dioxane etc.), halogenated solvents (chloroform, dichloromethane etc.) and the like and a mixed solvent thereof can be mentioned. As the base, inorganic bases such as potassium carbonate, sodium carbonate and the like and organic bases such as triethylamine, diisopropylethylamine and the like can be mentioned. The reaction can be carried out under cooling to heating.

Production Method 10

In this Production Method, of compounds [I], compounds [1] used in Production Methods 1, 3 and 4, compounds [2] used in Production Method 1, compounds [3] used in Production Method 1 and compounds [15] used in Production Method 6, a compound wherein Y is $-CH_2-N(R^{12})-$, $-CH_2-O-$ or $-CH_2-S-$ is produced.

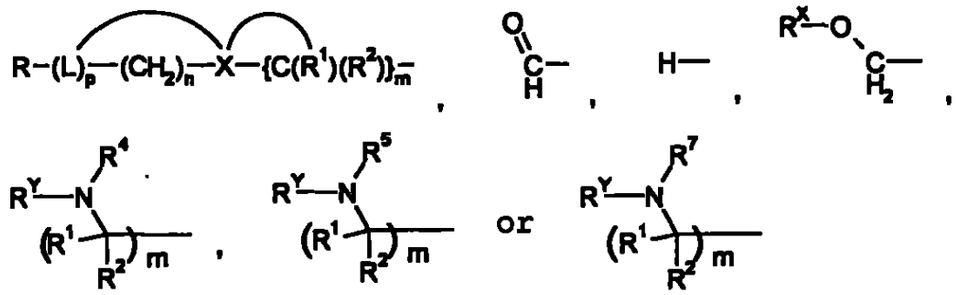


[23] [24] [25]



[27]

wherein R^M is



wherein each symbol is as defined above, R^B is a carboxy group, a carboxy group substituted by an alkyl group (methyl group, ethyl group etc.) or a formyl group, Q^6 is a conventional leaving group as described in Production Method 1, Y' is $-N(R^{12})-$, $-O-$ or $-S-$wherein each symbol is as defined above, and other symbols are as defined above.

Step 17

Compound [24] can be obtained by activation of compound [23] in a solvent using an activating agent where necessary, and reduction thereof using a conventional reducing agent. As the solvent, alcohols (methanol, ethanol etc.), ether solvents

(tetrahydrofuran, dioxane etc.), toluene and the like, and a mixed solvent thereof can be mentioned. As the reducing agent, sodium borohydride, lithium borohydride, diborane, lithium aluminum hydride and the like can be mentioned. As the activating agent, for example, when R^8 is a carboxy group, carbonyldiimidazole and the like can be mentioned. The reaction can be carried out under cooling to heating.

Step 18

Compound [25] can be obtained by substituting a hydroxyl group of compound [24] with a conventional leaving group according to conventional methods. For example, conversion to a mesyloxy group, a tosyloxy group and the like can be performed using such sulfonyl chloride in a solvent in the presence of an organic base. As the solvent, toluene, ethyl acetate, halogenated solvents (chloroform, dichloromethane etc.), ether solvents (tetrahydrofuran, dioxane etc.), acetonitrile, N,N-dimethylformamide and a mixed solvent thereof can be mentioned, and as the organic base, pyridine, triethylamine, diisopropylethylamine and the like can be mentioned. The reaction can be carried out under cooling to heating. In addition, conversion to a chlorine atom can be performed using thionyl chloride without solvent or in a solvent. As the solvent, toluene, ethyl acetate, halogenated solvents (chloroform, dichloromethane etc.), ether solvents (tetrahydrofuran, dioxane etc.) and a mixed solvent thereof can be mentioned. As a catalyst, N,N-dimethylformamide may be added. The reaction can be carried out under cooling to heating. In addition, conversion to a chlorine atom can be also performed by converting to a mesyloxy group, a tosyloxy group and the like, and further reacting with an alkali metal chloride (lithium chloride etc.) or quaternary ammonium chloride. As the solvent, acetonitrile, N,N-dimethylformamide and the like can be mentioned. The reaction can be carried out

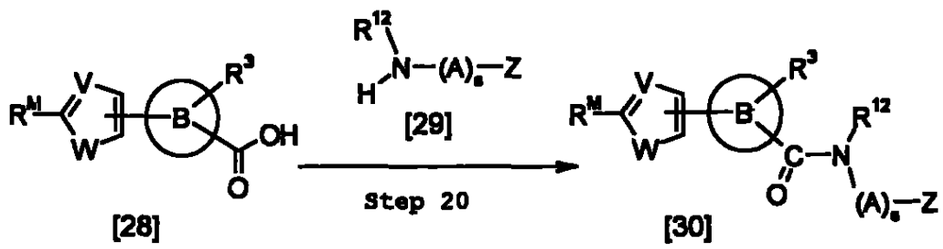
under cooling to heating.

Step 19

Compound [27] can be obtained by reacting compound [25] with compound [26] in a solvent in the presence of a base and in the presence or absence of a catalyst. As the solvent, N,N-dimethylacetamide, N,N-dimethylformamide, acetonitrile, ethyl acetate, toluene, alcohol solvents (methanol, ethanol etc.), ether solvents (tetrahydrofuran, dioxane etc.), halogenated solvents (chloroform, dichloromethane etc.) and the like and a mixed solvent thereof can be mentioned. As the base, inorganic bases such as potassium carbonate, sodium carbonate and the like and organic bases such as triethylamine, diisopropylethylamine, potassium tert-butoxide and the like can be mentioned. As the catalyst, potassium iodide, quaternary ammonium salts (tetrabutylammonium iodide, tetrabutylammonium bromide etc.) and the like can be mentioned. The reaction can be carried out at room temperature to under heating.

Production Method 11

In this Production Method, of compounds [I], compounds [1] used in Production Methods 1, 3 and 4, compounds [2] used in Production Method 1, compounds [3] used in Production Method 1 and compounds [15] used in Production Method 6, a compound wherein Y is $-CO-N(R^{12})-$ is produced.



wherein each symbol is as defined above.

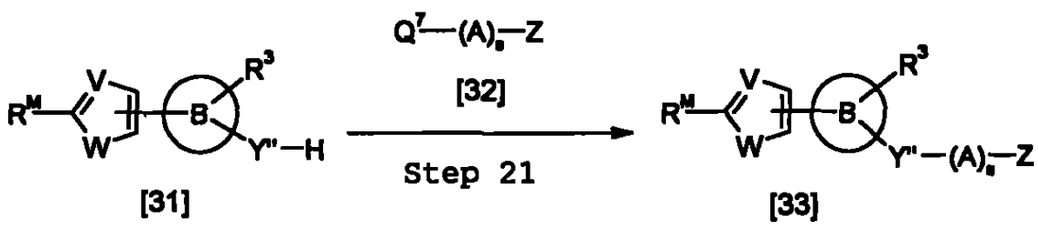
Step 20

Compound [30] can be obtained by amide condensation of compound [28] with compound [29]. Amide condensation can be

performed according to conventional methods. For example, a method comprising condensation in a solvent such as N,N-dimethylformamide, acetonitrile, tetrahydrofuran, chloroform, ethyl acetate, methylene chloride, toluene and the like, in the presence of a condensing agent such as dicyclohexylcarbodiimide, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, diphenylphosphoryl azide and the like, and in the presence or absence of N-hydroxysuccinimide, 1-hydroxybenzotriazole and the like can be mentioned. The reaction temperature is preferably 0°C - 100°C

Production Method 12

In this Production Method, of compounds [I], compounds [1] used in Production Methods 1, 3 and 4, compounds [2] used in Production Method 1, compounds [3] used in Production Method 1 and compounds [15] used in Production Method 6, a compound wherein Y is $-N(R^{11})-$, -O- or -S- is produced.



wherein Q^7 is a general leaving group as described in Production Method 1, Y″ is $-N(R^{11})-$, -O- or -S- and other symbols are as defined above.

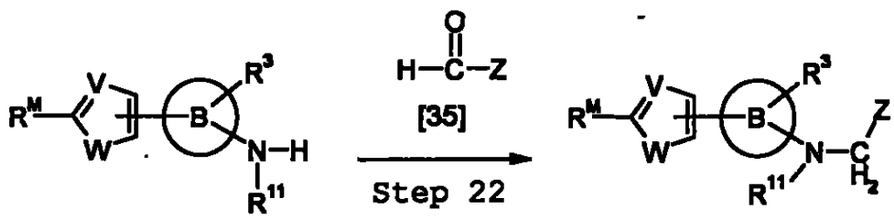
Step 21

Compound [33] can be obtained by reacting compound [31] with compound [32] in a solvent in the presence of a base and in the presence or absence of a catalyst. As the solvent, N,N-dimethylacetamide, N,N-dimethylformamide, acetonitrile, ethyl acetate, toluene, alcohol solvents (methanol, ethanol etc.), ether solvents (tetrahydrofuran, dioxane etc.), halogenated solvents (chloroform, dichloromethane etc.) and the like and a

mixed solvent thereof can be mentioned. As the base, inorganic bases such as potassium carbonate, sodium carbonate and the like and organic bases such as triethylamine, diisopropylethylamine and the like can be mentioned. As the catalyst, potassium iodide, quaternary ammonium salts (tetrabutylammonium iodide, tetrabutylammonium bromide etc.) and the like can be mentioned. The reaction can be carried out at room temperature to under heating.

Production Method 13

In this Production Method, of compounds [I], compounds [1] used in Production Methods 1, 3 and 4, compounds [2] used in Production Method 1, compounds [3] used in Production Method 1 and compounds [15] used in Production Method 6, a compound wherein Y is $-N(R^{11})-$, s is 1 and A is a methylene group is produced.



wherein each symbol is as defined above.

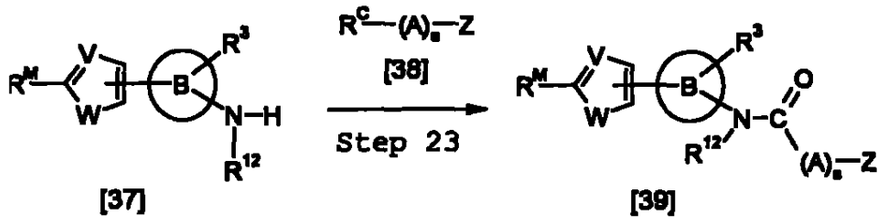
Step 22

Compound [36] can be obtained by reacting compound [34] with compound [35] in a solvent in the presence of a reducing agent. As the solvent, N,N-dimethylacetamide, N,N-dimethylformamide, acetonitrile, ethyl acetate, toluene, ether solvents (tetrahydrofuran, dioxane etc.), halogenated solvents (chloroform, dichloromethane etc.), acetic acid and the like and a mixed solvent thereof can be mentioned. As the reducing agent, sodium triacetoxyborohydride, sodium cyanoborohydride and the like can be mentioned. The reaction temperature is

preferably 0°C - 80°C.

Production Method 14

In this Production Method, of compounds [I], compounds [1] used in Production Methods 1, 3 and 4, compounds [2] used in Production Method 1, compounds [3] used in Production Method 1 and compounds [15] used in Production Method 6, a compound wherein Y is $-N(R^{12})-CO-$ is produced.



wherein R^C is a carboxy group or a formyl group substituted by a halogen atom (bromine atom, iodine atom, fluorine atom, chlorine atom etc.), and other symbols are as defined above.

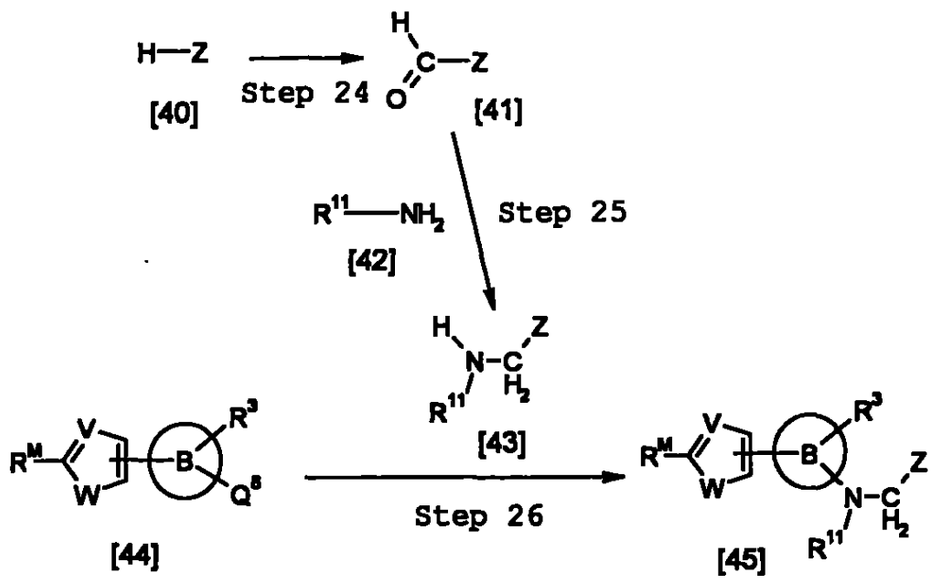
Step 23

Compound [39] can be obtained by amide condensation of compound [37] with compound [38]. The amide condensation can be performed according to conventional methods. For example, in a case of R^C being a carboxy group, a method comprising condensation in a solvent such as N,N-dimethylformamide, acetonitrile, tetrahydrofuran, chloroform, ethyl acetate, methylene chloride, toluene and the like, in the presence of a condensing agent such as dicyclohexylcarbodiimide, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, diphenylphosphoryl azide and the like, and in the presence or absence of N-hydroxysuccinimide, 1-hydroxybenzotriazole and the like can be mentioned. In addition, in a case of R^C being a formyl group substituted by a halogen atom, a method comprising condensation in a solvent such as N,N-dimethylformamide, acetonitrile, tetrahydrofuran, chloroform, ethyl acetate, methylene chloride, toluene, water and the like and a mixed

solvent thereof, and in the presence of a base such as inorganic bases (sodium hydrogen carbonate, potassium carbonate, potassium hydrogen carbonate, sodium hydroxide, etc.) and organic bases (triethylamine, diisopropylethylamine, pyridine, etc.), can be mentioned as an example. The reaction can be carried out under cooling to heating.

Production Method 15

In this Production Method, of compound [I], compound [1] used in Production Methods 1, 3 and 4, compound [2] used in Production Method 1, compound [3] used in Production Method 1 and compound [15] used in Production Method 6, a compound wherein Y is $-N(R^{11})-$, s is 1, and A is a methylene group is produced.



wherein Q^8 is a general leaving group as described in Production Method 1 and other symbols are as defined above.

Step 24

Compound [41] can be obtained by introducing a formyl group into compound [40] according to conventional methods. For example, when Z is an aryl group or a heteroaromatic ring group (said aryl group or heteroaromatic ring group is

optionally substituted as described above), compound [41] can be synthesized by reacting compound [40] with dichloromethyl methyl ether in a solvent in the presence of a Lewis acid and hydrolyzing the obtained methoxychloromethyl compound. As the solvent, halogenated solvents (chloroform, dichloromethane etc.) and the like can be mentioned. As the Lewis acid, aluminum chloride, titanium tetrachloride, tin tetrachloride and the like can be mentioned. The reaction can be carried out under cooling to room temperature.

Step 25

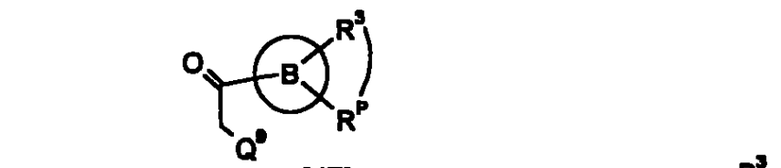
Compound [43] can be obtained by reacting compound [41] with compound [42] in a solvent in the presence of a reducing agent. As the solvent, N,N-dimethylacetamide, N,N-dimethylformamide, acetonitrile, ethyl acetate, toluene, ether solvents (tetrahydrofuran, dioxane etc.), halogenated solvents (chloroform, dichloromethane, 1,2-dichloroethane etc.), alcohol solvents (methanol, ethanol etc.), acetic acid and the like and a mixed solvent thereof can be mentioned. As the reducing agent, sodium borohydride, sodium triacetoxyborohydride, sodium cyanoborohydride and the like can be mentioned. The reaction temperature is preferably 0°C - 80°C.

Step 26

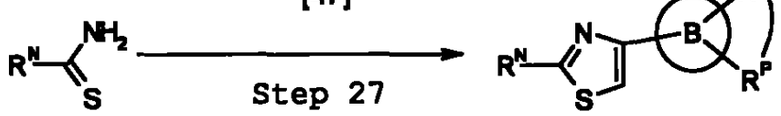
Compound [45] can be obtained by reacting compound [43] with compound [44] in a solvent in the presence of a base and in the presence of a catalyst. As the solvent, toluene, xylene, ether solvents (tetrahydrofuran, dioxane, 1,2-dimethoxyethane etc.) and the like and a mixed solvent thereof can be mentioned. As the base, cesium carbonate, sodium tert-butoxide, tripotassium phosphate and the like can be mentioned. As the catalyst, a palladium complex (e.g., a complex formed using palladium acetate and (R)-(+)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl) and the like can be mentioned. The reaction can be carried out at room temperature to under heating.

Production Method 16

In this Production Method, of compound [I], compound [3] used in Production Method 1, compound [15] used in Production Method 6, compound [23] used in Production Method 10, compound [28] used in Production Method 11, compound [31] used in Production Method 12, compound [34] used in Production Method 13, compound [37] used in Production Method 14, and compound [44] used in Production Method 15, a compound wherein V is =N-, W is -S- and the position of substitution of B on the thiazole ring formed by the above-mentioned V and W is the 4-position is produced.

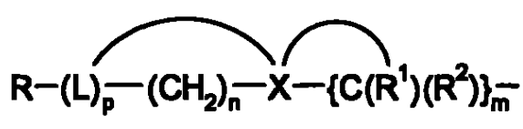


[47]

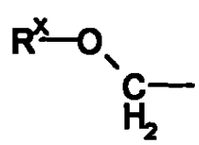


[46] [48]

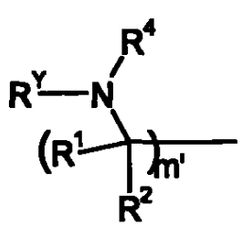
wherein R^N is



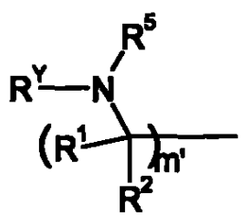
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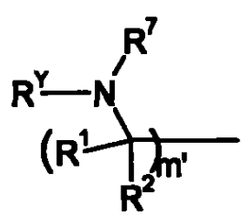
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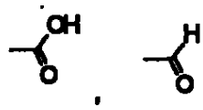
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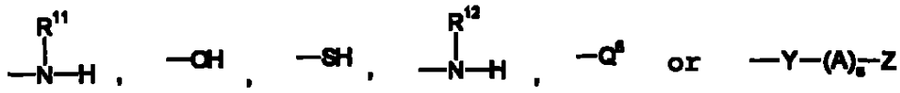


or



wherein each symbol is as defined above, R^P is

 substituted by a halogen atom (bromine atom, iodine atom, fluorine atom, chlorine atom etc.),



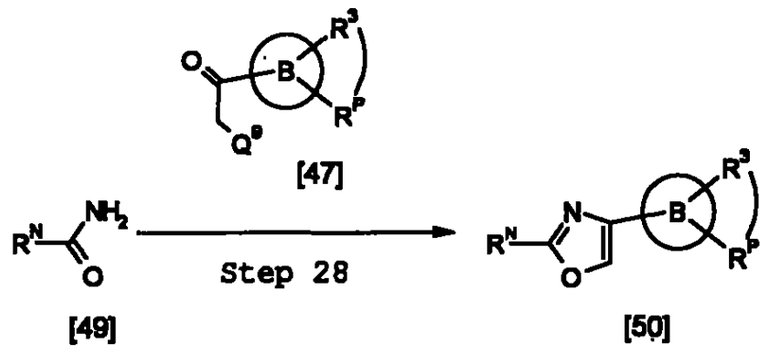
wherein each symbol is as defined above, Q^9 is a general leaving group as described in Production Method 1 and other symbols are as defined above.

Step 27

Compound [48] can be obtained by reacting compound [46] with compound [47] in a solvent in the presence or absence of a base. As the solvent, N,N-dimethylacetamide, N,N-dimethylformamide, acetonitrile, ethyl acetate, alcohol solvents (methanol, ethanol etc.), ether solvents (tetrahydrofuran, dioxane etc.), halogenated solvents (chloroform, dichloromethane etc.) and the like and a mixed solvent thereof can be mentioned. As the base, inorganic bases such as sodium hydrogen carbonate and the like and organic bases such as diisopropylethylamine and the like can be mentioned. The reaction can be carried out under cooling to heating.

Production Method 17

In this Production Method, of compounds [I], compounds [3] used in Production Method 1, compounds [15] used in Production Method 6, compounds [23] used in Production Method 10, compounds [28] used in Production Method 11, compounds [31] used in Production Method 12, compounds [34] used in Production Method 13, compounds [37] used in Production Method 14 and compounds [44] used in Production Method 15, a compound wherein V is =N-, W is -O- and the position of substitution of B on the oxazole ring formed by the above-mentioned V and W is the 4-position is produced.



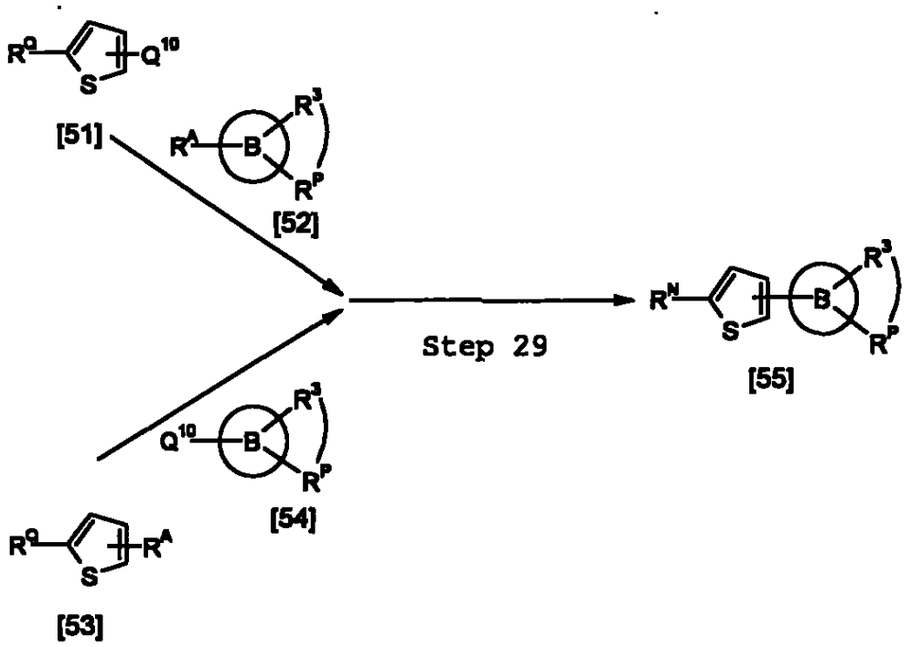
wherein each symbol is as defined above.

Step 28

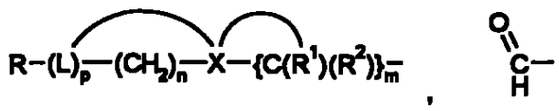
Compound [50] can be obtained by reacting compound [49] with compound [47] without solvent or in a solvent. As the solvent, acetonitrile, alcohols (methanol, ethanol, isopropyl alcohol etc.), xylene, toluene and the like and a mixed solvent thereof can be mentioned. The reaction can be carried out under heating.

Production Method 18

In this Production Method, of compounds [I], compounds [1] used in Production Method 1, 3 and 4, compounds [15] used in Production Method 6, compounds [23] used in Production Method 10, compounds [28] used in Production Method 11, compounds [31] used in Production Method 12, compounds [34] used in Production Method 13, compounds [37] used in Production Method 14 and compounds [44] used in Production Method 15, compound [I] wherein V is =CH- and W is -S- is produced.

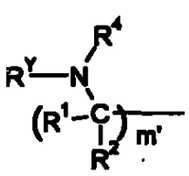


wherein R^Q is

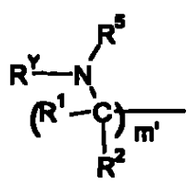


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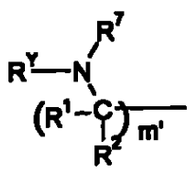
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,



or



wherein each symbol is as defined above, Q^{10} is a general leaving group as described in Production Method 1, R^A is a boronic acid group ($-B(OH)_2$), and other symbols are as defined above.

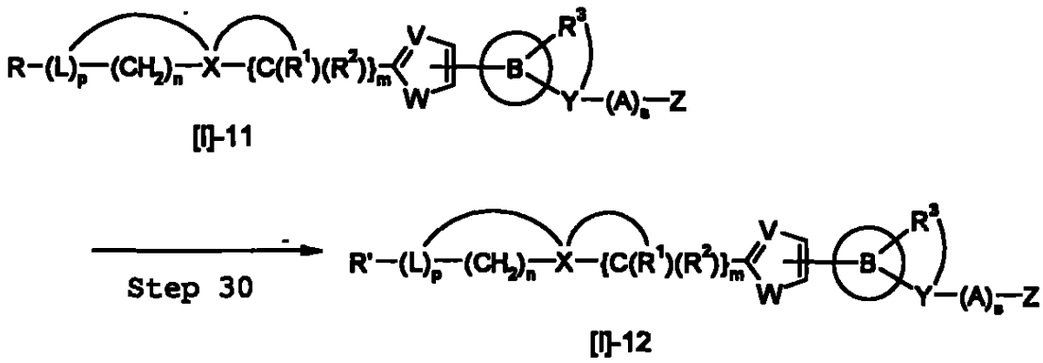
Step 29

Compound [55] can be obtained by reacting compound [51] with compound [52] or by reacting compound [53] with compound [54] in a solvent in the presence of a base and in the presence of a catalyst. As the solvent, N,N-dimethylformamide, acetonitrile, alcohol solvents (methanol, ethanol etc.), ether solvents (tetrahydrofuran, 1,2-dimethoxyethane etc.), toluene, water and the like and a mixed solvent thereof can be mentioned. As the base, inorganic bases such as potassium carbonate,

potassium hydrogen carbonate, sodium hydrogen carbonate, potassium phosphate and the like and organic bases such as triethylamine and the like can be mentioned. As the catalyst, palladium catalysts (tetrakis(triphenylphosphine)palladium, bis(triphenylphosphine)palladium(II) dichloride, palladium acetate-triphenylphosphine etc.) and the like can be mentioned. The reaction can be carried out at room temperature to under heating.

Production Method 19

In this Production Method, compound [I] wherein R is -COOH, $-A^1-COOH$ or $-O-A^1-COOH$ is produced.



[I]-11

Step 30

[I]-12

wherein R' is -COOH, $-A^1-COOH$ or $-O-A^1-COOH$ and other symbols are as defined above.

Step 30

When R^{19} for R in compound [I]-11 is a C_{1-4} alkyl group, compound [I]-12 can be obtained by deprotection according to conventional methods to give carboxylic acid. For example, a method comprising hydrolysis in a solvent in the presence of a base can be mentioned. As the solvent, alcohols (methanol, ethanol, isopropyl alcohol etc.), tetrahydrofuran, 1,2-dimethoxyethane, N,N-dimethylformamide, dimethyl sulfoxide, water and the like and a mixed solvent thereof can be mentioned. As the base, alkali metal hydroxides such as sodium hydroxide and the like, potassium carbonate, sodium carbonate and the like can be mentioned. The reaction can be carried out under

cooling to heating.

Moreover, by stirring compound [I] obtained in the above-mentioned Production Methods in a solvent upon addition of an acid or a base, a pharmaceutically acceptable salt of compound [I] can be obtained. As the solvent, 2-butanone, acetone, tetrahydrofuran, ethyl acetate, methanol, ethanol, water, hexane, and a mixed solvent thereof can be mentioned. As the acid, inorganic acids such as hydrochloric acid, sulfuric acid, phosphoric acid and the like and organic acids such as oxalic acid, malonic acid, trifluoroacetic acid, methanesulfonic acid, p-toluenesulfonic acid, benzenesulfonic acid and the like can be mentioned. As the base, inorganic bases such as sodium hydroxide, potassium hydroxide, calcium hydroxide and the like and organic bases such as triethylamine, ethylenediamine, tris(hydroxymethyl)aminomethane, N-methyl-D-glucamine and the like can be mentioned. The reaction can be carried out at room temperature.

Compound [I] obtained above or a pharmaceutically acceptable salt thereof is dissolved or suspended in a solvent at room temperature to under heating and stirred or stood at 0°C-150°C to allow precipitation of crystals, which are added with a poor solvent of the compound or a salt thereof where necessary under cooling to room temperature, and filtered to give crystals of compound [I] or a pharmaceutically acceptable salt thereof. As the solvent, 2-butanone, acetone, tetrahydrofuran, ethyl acetate, methanol, ethanol, water, hexane and a mixed solvent thereof can be mentioned.

The Production Methods described in the present specification are examples of the Production Methods of the compound of the present invention, and compounds other than those explained above can be also produced by combining conventional methods known in the field of organic synthetic chemistry.

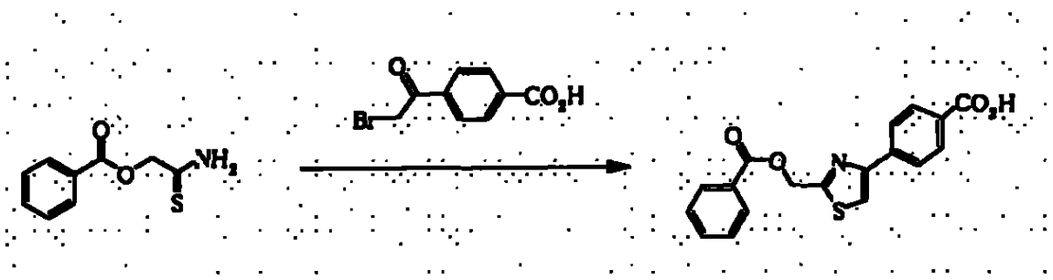
Examples

The compound represented by the formula [I] of the present invention and a production method thereof are explained in detail by referring to Examples, which are not to be construed as limitative.

Example 1-1

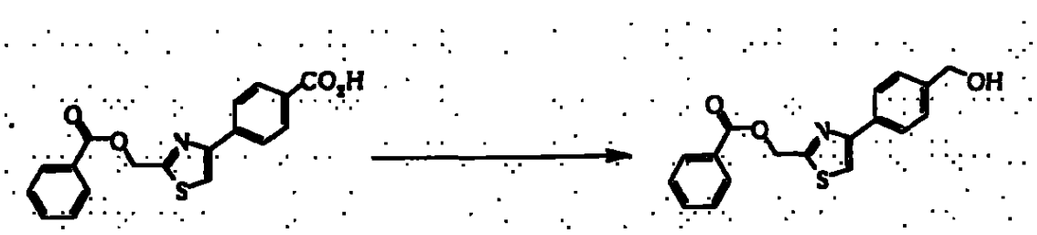
5-{4-[4-({[4-(1-Ethylpropyl)phenyl]isopropylamino}methyl)-phenyl]thiazol-2-ylmethoxy}nicotinic acid

(1) 4-(2-(Benzoyloxymethyl)thiazol-4-yl)benzoic acid



To a solution of 4-(bromoacetyl)benzoic acid (10 g, 41.14 mmol) in N,N-dimethylformamide (40 ml) was added 2-(benzoyloxy)ethanethioamide (8.03 g, 41.14 mmol) under ice-cooling, and the mixture was stirred at room temperature for 1.5 hr. After the completion of the reaction, sodium hydrogen carbonate (3.46 g, 41.14 mmol) and water were added under ice-cooling and the mixture was stirred at room temperature for 0.5 hr. The precipitates were collected by filtration. The obtained solid was dried under reduced pressure to give the title compound (13.089 g, 93.3%).

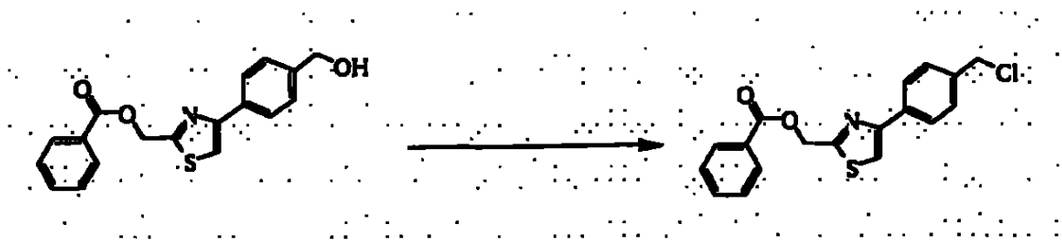
(2) (4-(4-Hydroxymethylphenyl)thiazol-2-yl)methyl benzoate



To a suspension of 4-(2-(benzoyloxymethyl)thiazol-4-

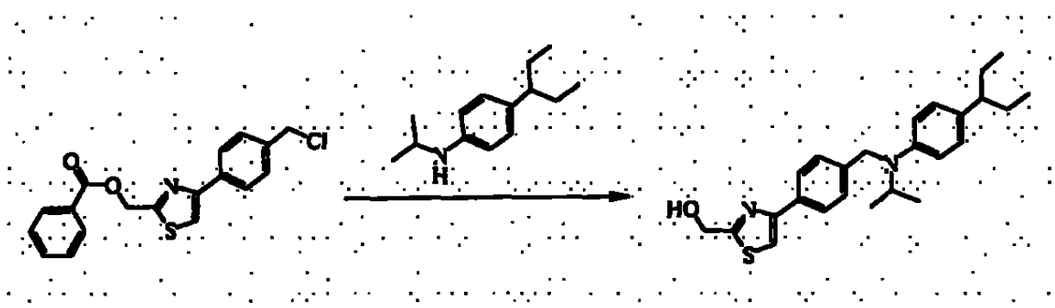
yl)benzoic acid (0.5 g, 1.47 mmol) obtained in Example 1-1(1) in tetrahydrofuran (5 ml) was added 1,1'-carbonyldiimidazole (0.358 g, 2.21 mmol) at room temperature and the mixture was stirred at 65°C for 2 hr. Then an aqueous solution of sodium borohydride (0.056 g, 1.47 mmol) was added dropwise at room temperature and the mixture was stirred at the same temperature for 20 min. After the completion of the reaction, ethyl acetate and an aqueous sodium hydrogen carbonate solution were added for extraction, and the organic layer was washed with water and saturated brine and dried over sodium sulfate. The solvent was evaporated and the residue was washed with a mixed solvent of hexane-ethyl acetate and collected by filtration. The obtained solid was dried under reduced pressure to give the title compound (370.7 mg, 77.5%).

(3) (4-(4-Chloromethylphenyl)thiazol-2-yl)methyl benzoate



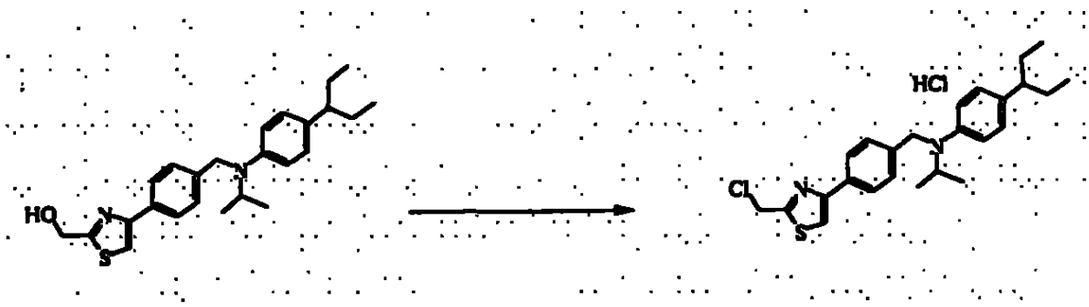
To a solution of (4-(4-hydroxymethylphenyl)thiazol-2-yl)methyl benzoate (5.55 g, 17.06 mmol) obtained in Example 1-1(2) in chloroform (100 ml) were added thionyl chloride (1.49 ml, 20.67 mmol) and N,N-dimethylformamide (catalytic amount) under ice-cooling. The mixture was stirred at room temperature for 1 hr. After the completion of the reaction, the solvent was evaporated and the residue was concentrated by adding chloroform. Hexane was added and the precipitates were collected by filtration. The obtained solid was dried under reduced pressure to give the title compound (5.804 g, 98.9%).

(4) (4-(4-(N-Isopropyl-4-(1-ethylpropyl)phenylamino)methylphenyl)thiazol-2-yl)methanol



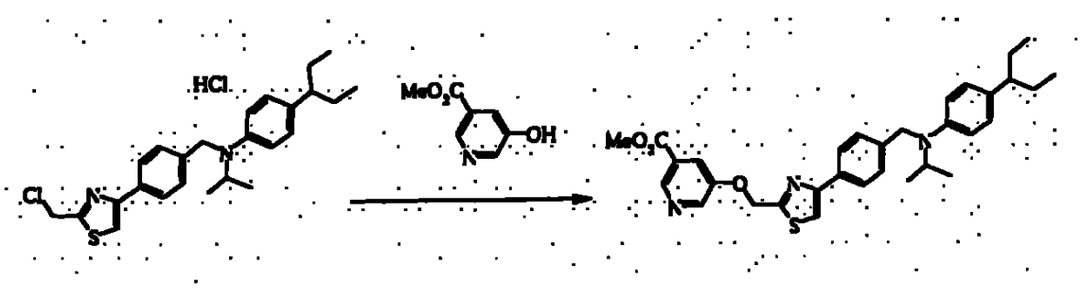
To a solution of N-isopropyl-4-(1-ethylpropyl)aniline (7.34 g, 35.78 mmol) in N,N-dimethylacetamide (35 ml) were successively added (4-(4-chloromethylphenyl)thiazol-2-yl)methyl benzoate (11.18 g, 32.52 mmol) obtained in Example 1-1(3), potassium carbonate (4.95 g, 35.78 mmol) and potassium iodide (0.54 g, 3.25 mmol) and the mixture was stirred at 80°C for 3 hr. Then potassium carbonate (0.449 g, 3.252 mmol) was added and the mixture was stirred at 70°C for 12 hr. After the completion of the reaction, a mixture of 50% ethyl acetate-hexane and water were added for extraction, and the organic layer was washed successively with water and saturated brine and dried over sodium sulfate. The solvent was evaporated and tetrahydrofuran (60 ml), methanol (60 ml) and a 1N-aqueous sodium hydroxide solution (48.8 ml) were successively added to the obtained residue at room temperature. The mixture was stirred at 75°C for 1.5 hr. After the completion of the reaction, the solvent was evaporated and ethyl acetate and water were added for extraction, and the organic layer was washed successively with water and saturated brine and dried over sodium sulfate and the solvent was evaporated. The obtained residue was purified by silica gel column chromatography (hexane:ethyl acetate=4:1→2:1) to give the title compound (10.664 g, 80.3%).

(5) (4-(4-(N-Isopropyl-4-(1-ethylpropyl)phenylamino)methylphenyl)thiazol-2-yl)methyl chloride hydrochloride



Thionyl chloride (2.7 ml, 37.1 mmol) and N,N-dimethylformamide (catalytic amount) were added to chloroform (30 ml) at room temperature and a solution of (4-(4-(N-isopropyl-4-(1-ethylpropyl)phenylamino)methylphenyl)thiazol-2-yl)methanol (10.1 g, 24.7 mmol) obtained in Example 1-1(4) in chloroform (30 ml) was added dropwise under ice-cooling. The mixture was stirred at room temperature for 1 hr. After the completion of the reaction, the solvent was evaporated and the residue was concentrated by adding chloroform. Ethyl acetate was added and the mixture was stirred for 0.5 hr. The precipitates were collected by filtration and the obtained solid was dried under reduced pressure to give the title compound (10.23 g, 89.4%).

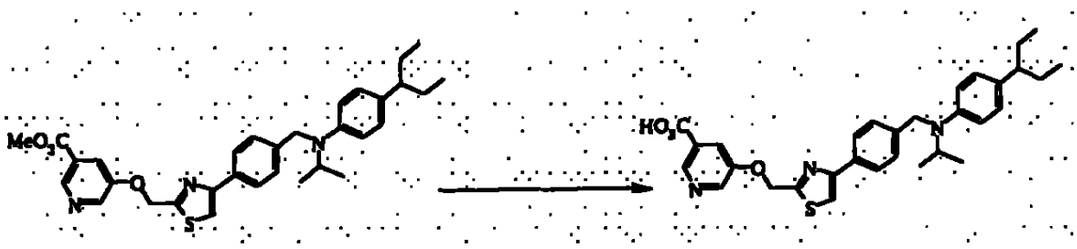
(6) 5-{4-[4-({[4-(1-Ethyl-propyl)phenyl]isopropyl-amino}-methyl)phenyl]thiazol-2-ylmethoxy}nicotinic acid methyl ester



To a solution of (4-(4-(N-isopropyl-4-(1-ethylpropyl)phenylamino)methylphenyl)thiazol-2-yl)methyl chloride hydrochloride (9.92 g, 21.4 mmol) obtained in Example 1-1(5) and methyl 5-hydroxynicotinate (3.61 g, 23.5 mmol) in

N,N-dimethylformamide were added potassium carbonate (6.8 g, 49.2 mmol) and potassium iodide (0.355 g, 2.14 mmol) under ice-cooling, and the mixture was stirred at 60°C for 12 hr. After the completion of the reaction, ethyl acetate and water were added for extraction and the organic layer was washed successively with water and saturated brine and dried over sodium sulfate and the solvent was evaporated. The obtained residue was purified by silica gel column chromatography (hexane:ethyl acetate=8:1) and then (chloroform:ethyl acetate=20:1) to give the title compound (5.32 g, 45.7%).

(7) 5-{4-[4-({[4-(1-Ethylpropyl)phenyl]isopropylamino}-methyl)phenyl]thiazol-2-ylmethoxy}nicotinic acid



To a solution of 5-{4-[4-({[4-(1-ethylpropyl)-phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}-nicotinic acid methyl ester (5.32 g, 9.78 mmol) obtained in Example 1-1(6) in 50% tetrahydrofuran-methanol (32 ml) was added a 2N-aqueous sodium hydroxide solution (9.78 ml) at room temperature and the mixture was stirred at 75°C for 2 hr. After the completion of the reaction, a 2N-hydrochloric acid (9.78 ml) was added under ice-cooling and the precipitates were collected by filtration. The obtained solid was dried under reduced pressure to give the title compound (5.00 g, 96.5%).

^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.69(t, J=7.3Hz, 6H), 1.16(d, J=6.5Hz, 6H), 1.48-1.31(m, 2H), 1.64-1.48(m, 2H), 2.19-2.06(m, 1H), 4.23(quint, J=6.6Hz, 1H), 5.67(s, 2H), 6.62(d, J=8.7Hz, 2H), 6.89(d, J=8.6Hz, 2H), 7.36(d, J=8.2Hz, 2H), 7.90(d, J=8.2Hz, 2H), 7.99(dd, J=3.0, 1.5Hz, 1H), 8.11(s, 1H), 8.64(d,

J=2.9Hz, 1H), 8.72(d, J=1.5Hz, 1H), 13.43(br s, 1H)
melting point: 201.5°C

Examples 1-2 to 1-186

In the same manner as in Example 1-1 and using other conventional methods where necessary, the compounds of Examples 1-2 to 1-186 were produced. The structural formulas and property values of the obtained compounds, as well as those of Example 1-1, are shown in the following Tables.

Table 1-1

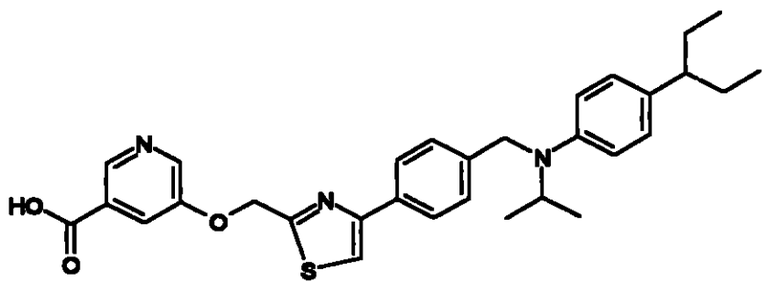
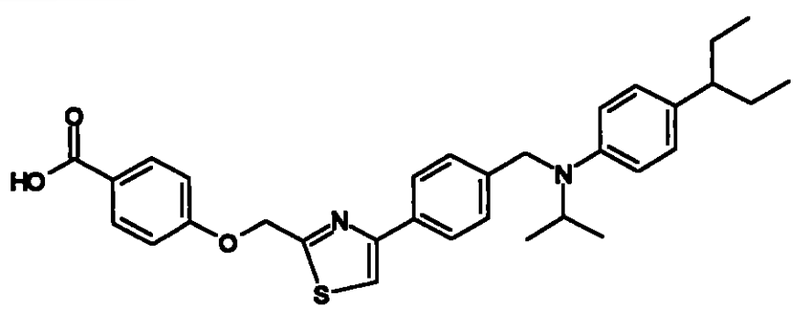
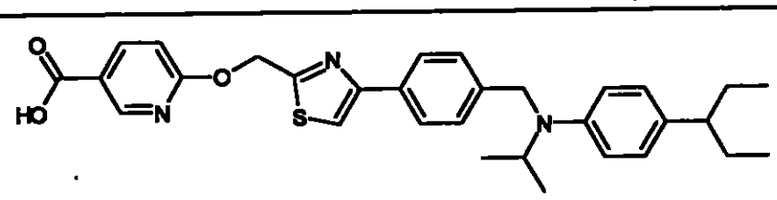
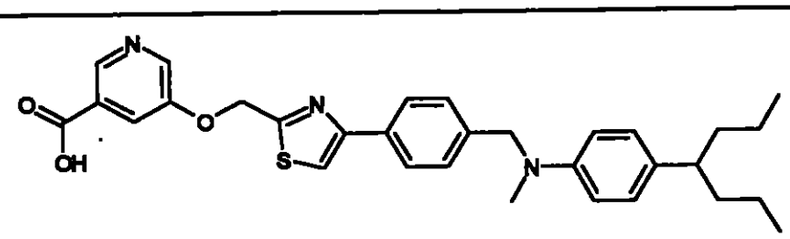
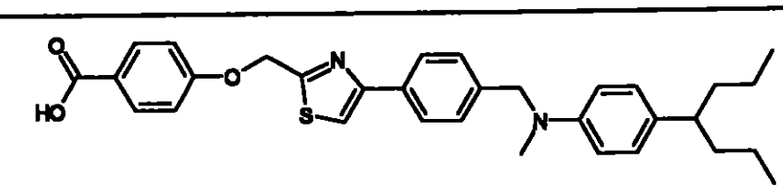
Example	Structural formula	m.p.(°C)
1-1		201.5
1-2		219
1-3		177 - 181
1-4		135 - 138
1-5		161 - 163

Table 1-2

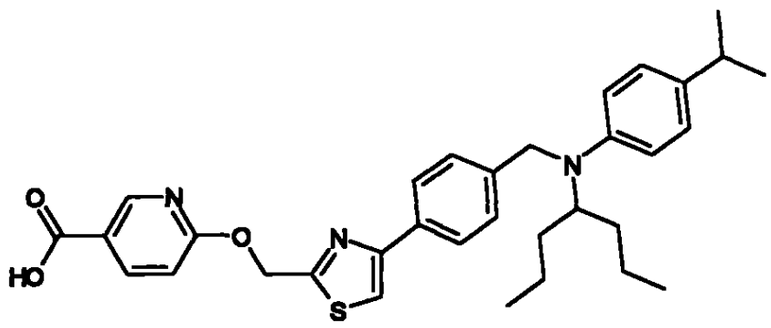
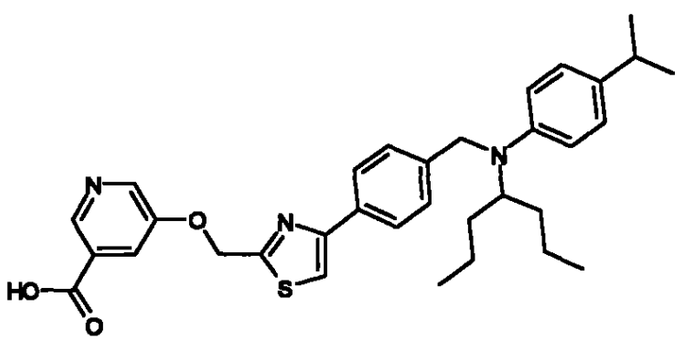
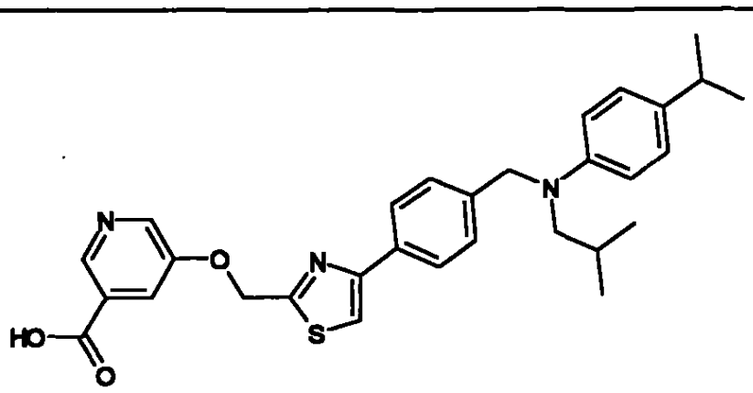
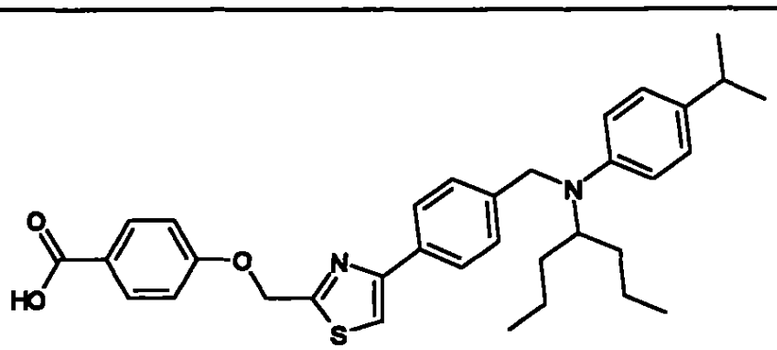
Example	Structural formula	m.p.(°C)
1-6		141 - 143
1-7		184 - 185
1-8		196 - 197
1-9		166 - 168

Table 1-3

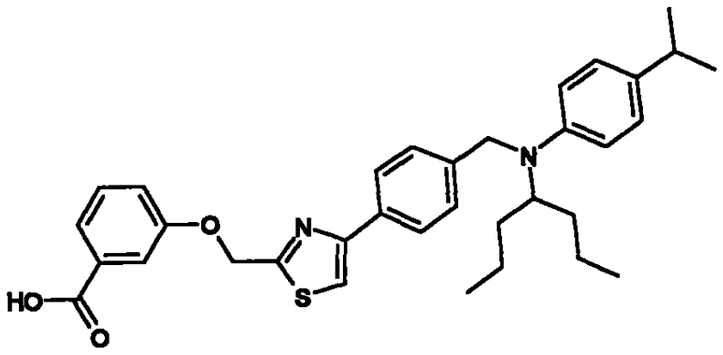
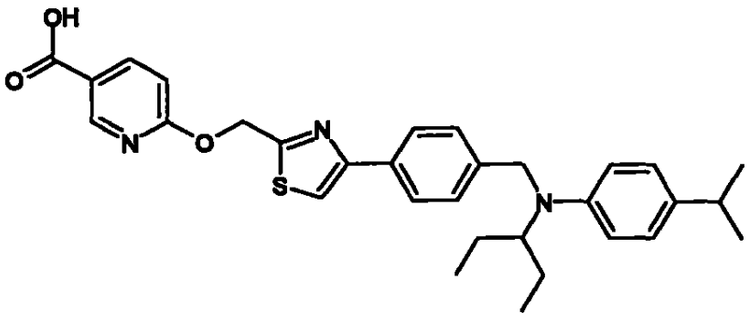
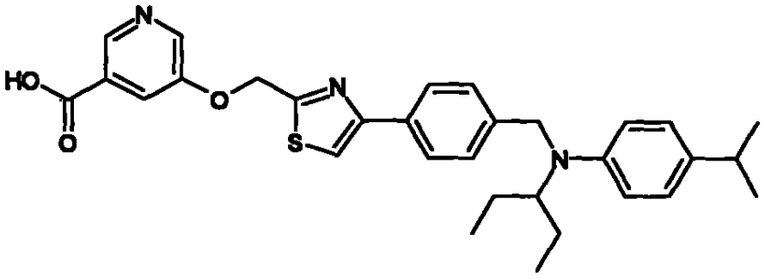
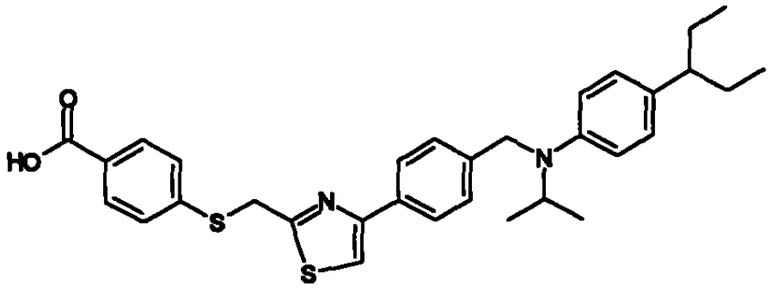
Example	Structural formula	m.p.(°C)
1-10		127 - 129
1-11		155 - 157
1-12		110 - 114
1-13		132.5

Table 1-4

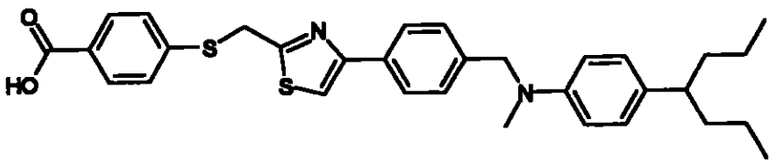
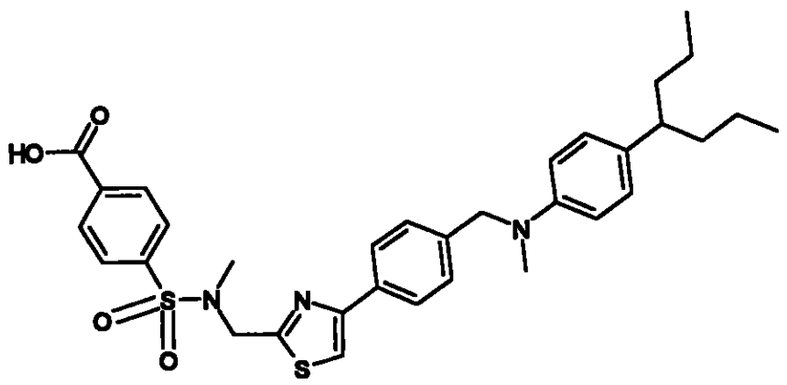
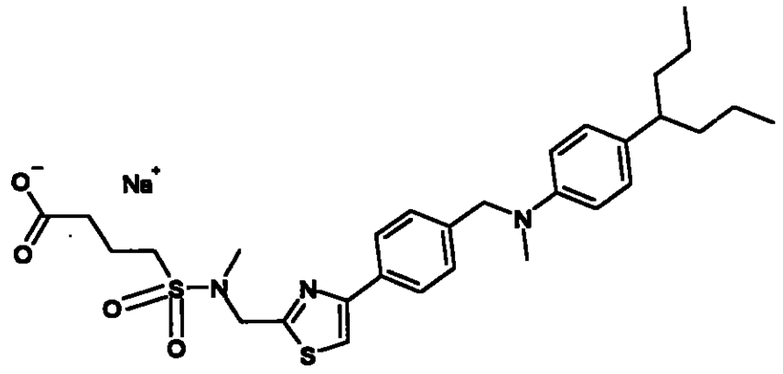
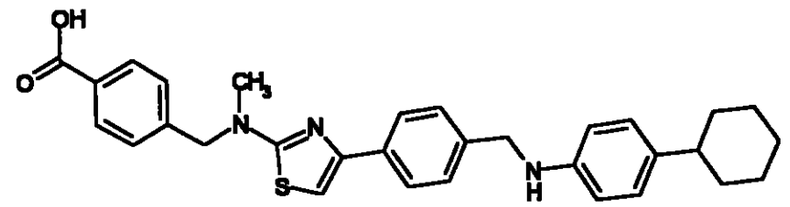
Example	Structural formula	m.p.(°C)
1-14		122 – 124
1-15		amorphous
1-16		217 – 220
1-17		206 – 210

Table 1-5

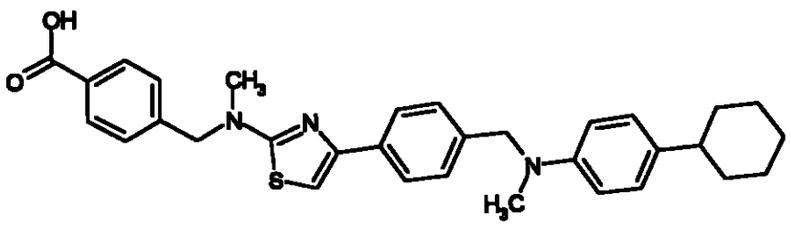
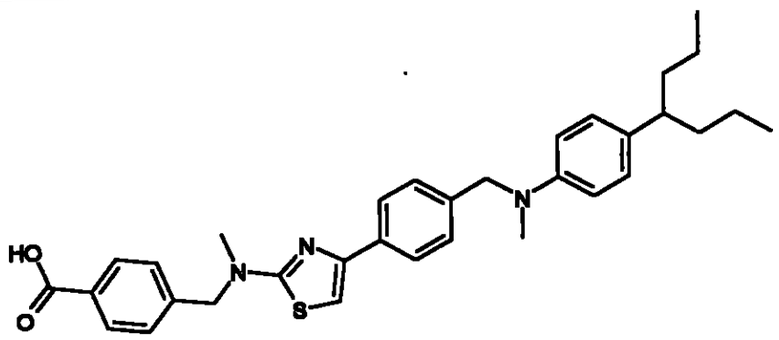
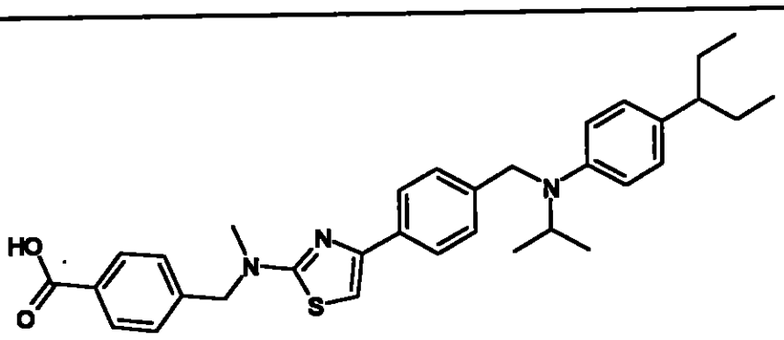
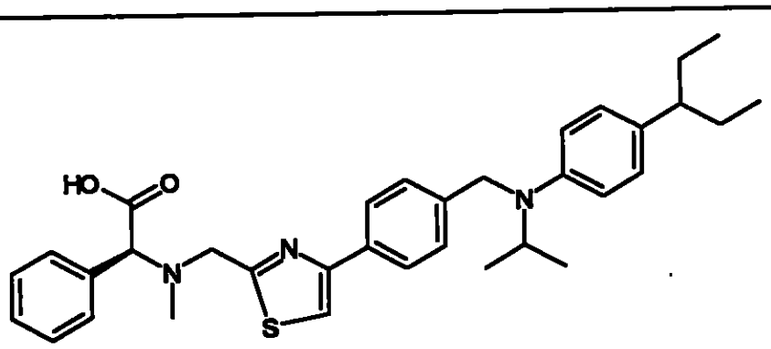
Example	Structural formula	m.p.(°C)
1-18		190 – 192
1-19		110 – 113
1-20		150 – 153
1-21		amorphous

Table 1-6

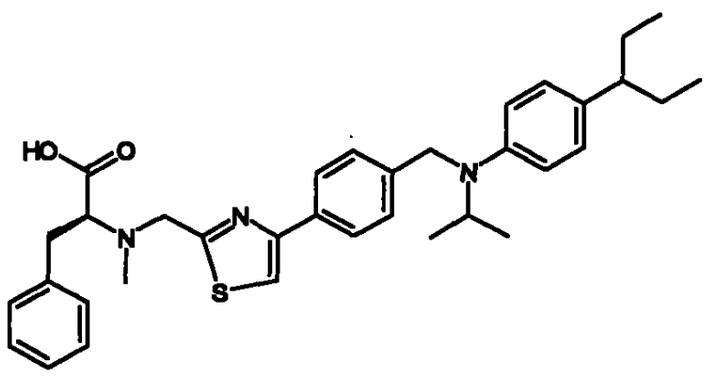
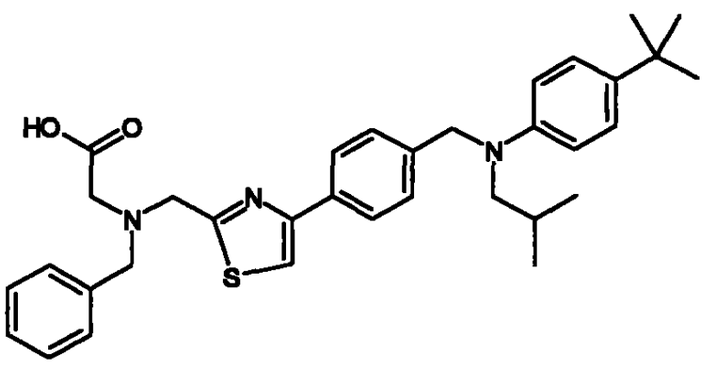
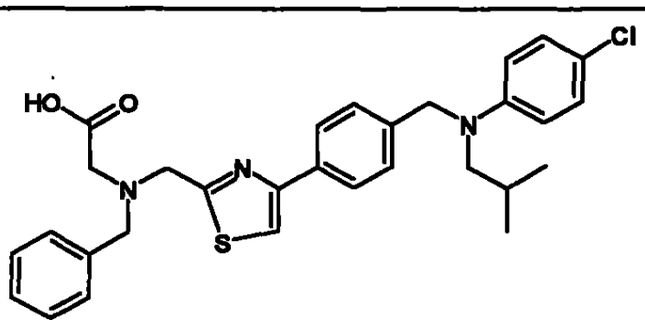
Example	Structural formula	m.p.(°C)
1-22		80
1-23		133
1-24		152

Table 1-7

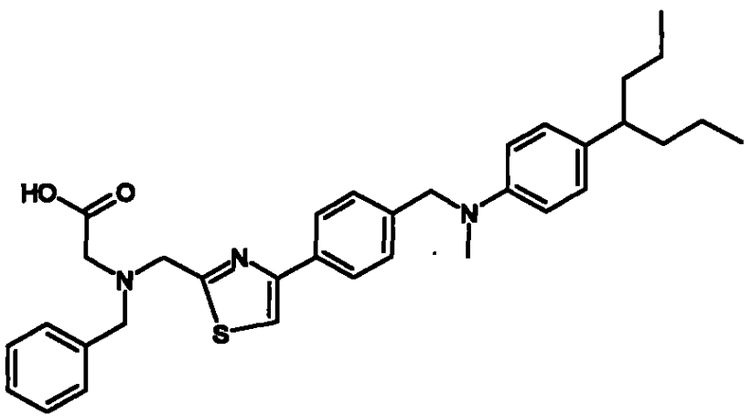
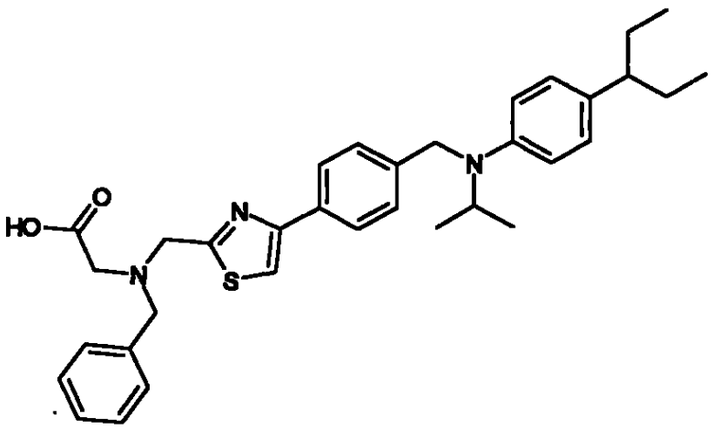
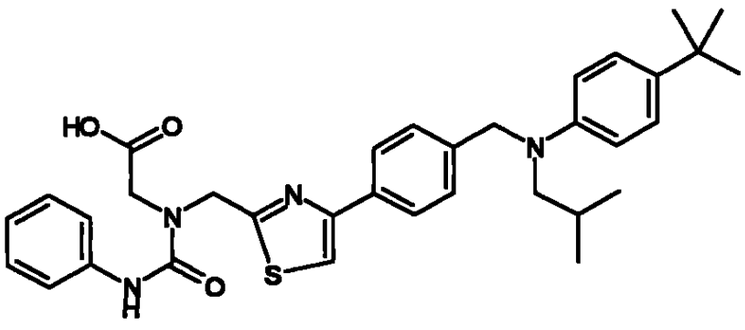
Example	Structural formula	m.p.(°C)
1-25		138
1-26		amorphous
1-27		119

Table 1-8

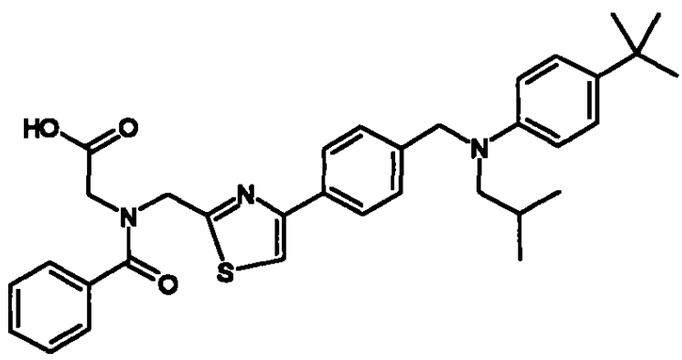
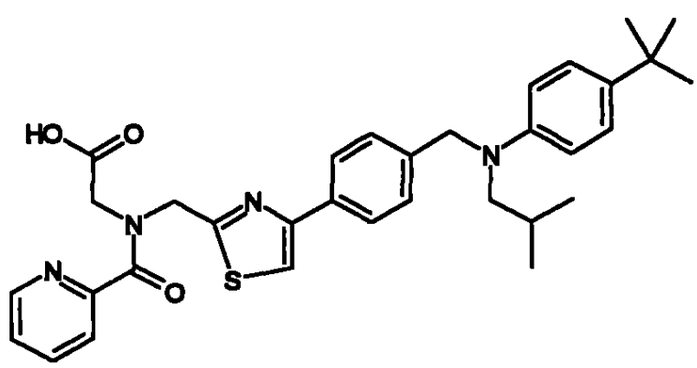
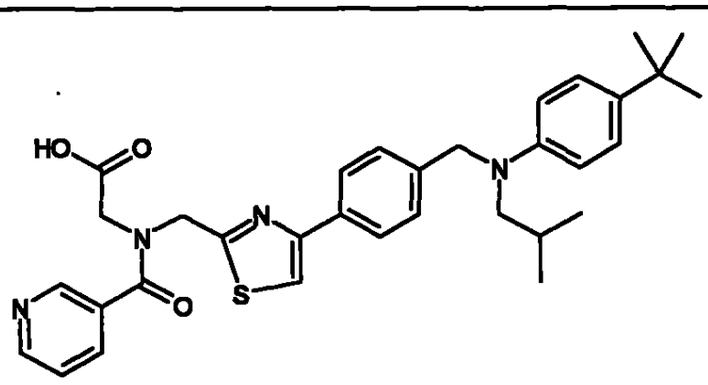
Example	Structural formula	m.p.(°C)
1-28		147
1-29		160
1-30		193

Table 1-9

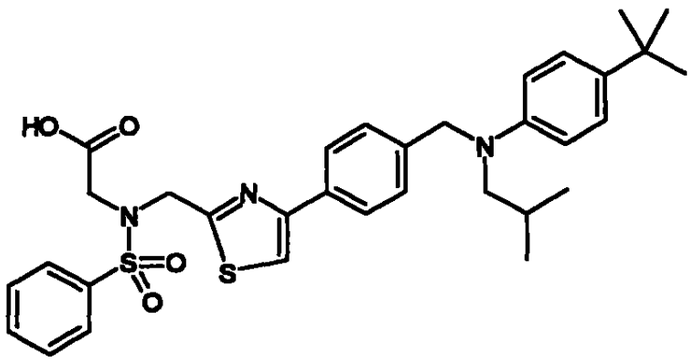
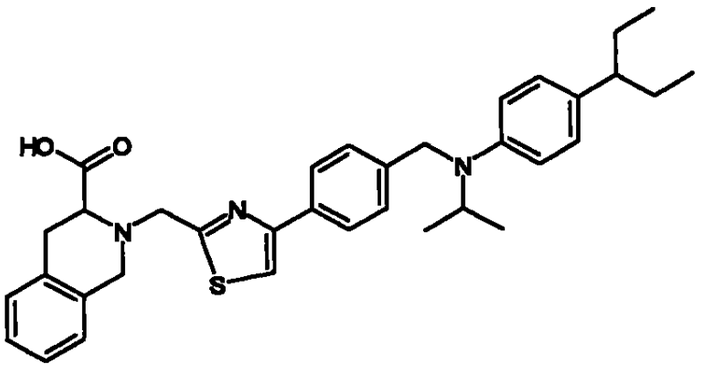
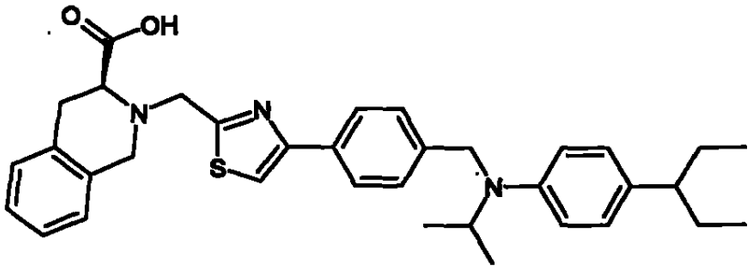
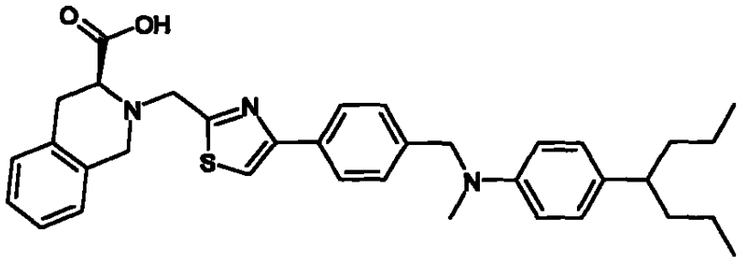
Example	Structural formula	m.p.(°C)
1-31		168.5
1-32		127.5
1-33		amorphous
1-34		amorphous

Table 1-10

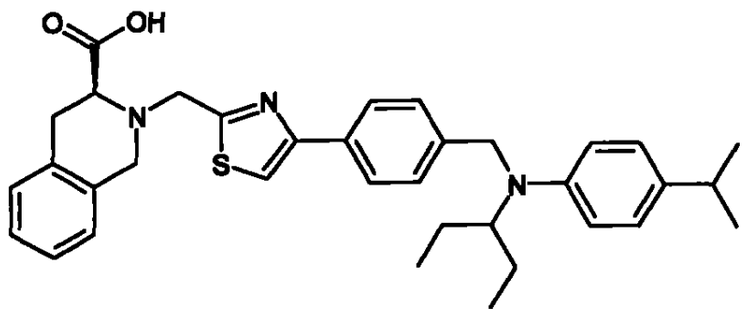
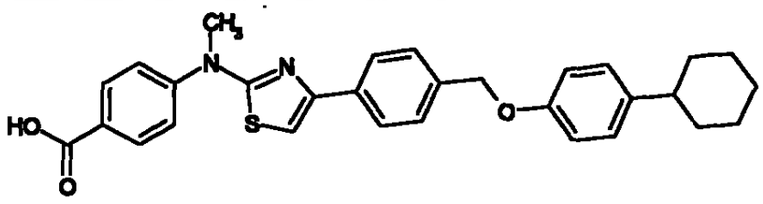
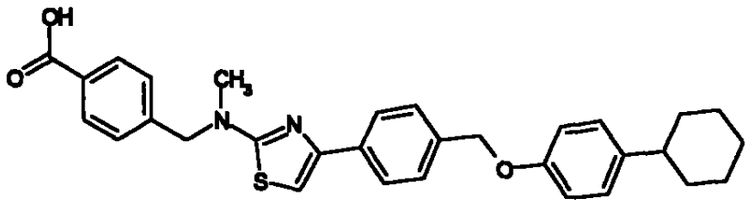
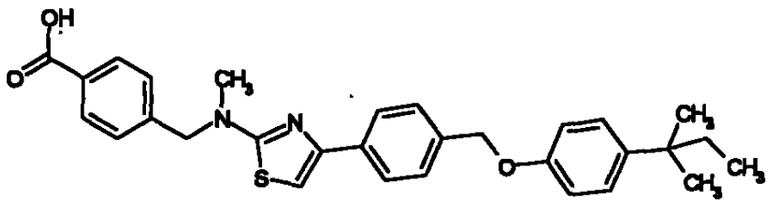
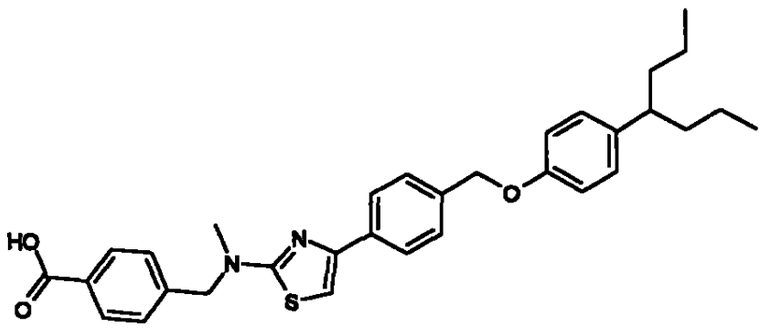
Example	Structural formula	m.p.(°C)
1-35		110 - 113
1-36		230 -
1-37		209 - 211
1-38		155 - 157
1-39		156 - 158

Table 1-11

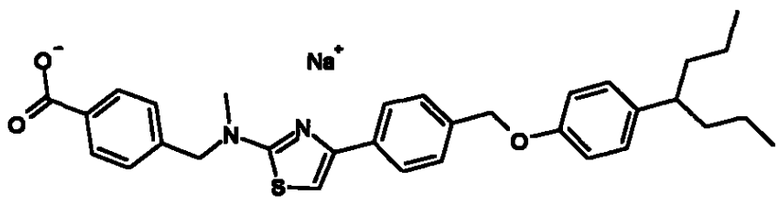
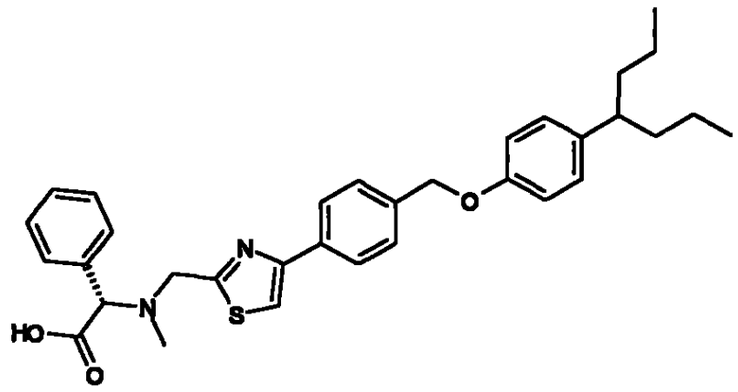
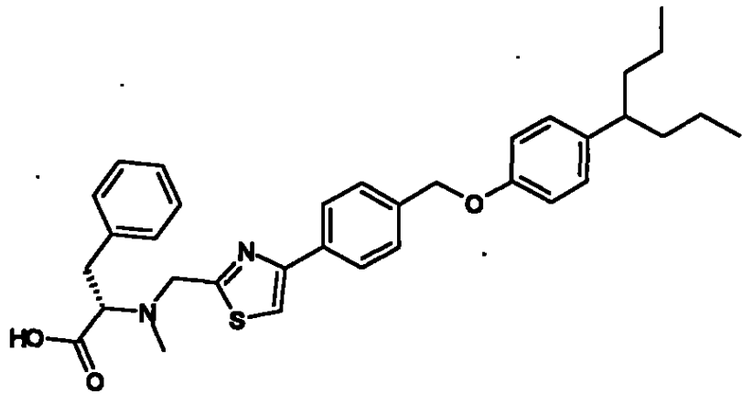
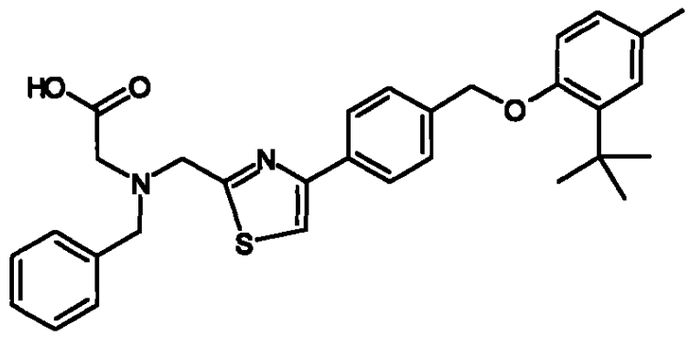
Example	Structural formula	m.p.(°C)
1-40		250 –
1-41		amorphous
1-42		114 – 118
1-43		146

Table 1-12

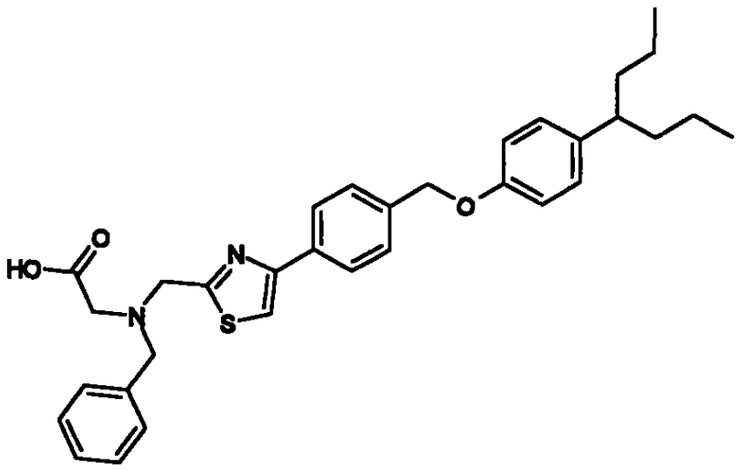
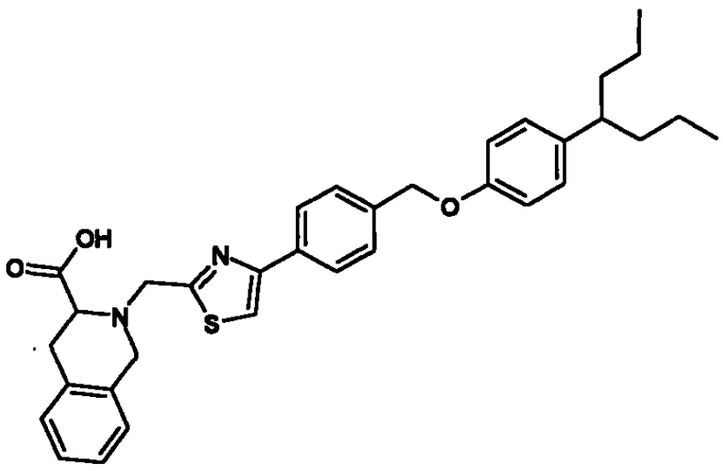
Example	Structural formula	m.p.(℃)
1-44		138 – 142
1-45		117 – 126

Table 1-13

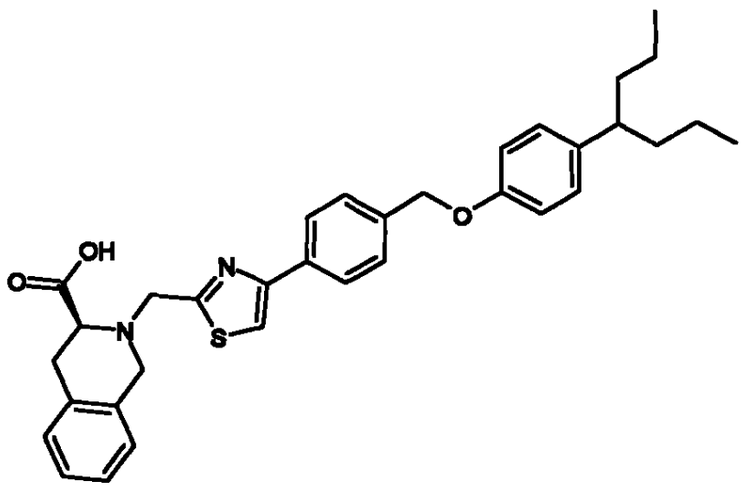
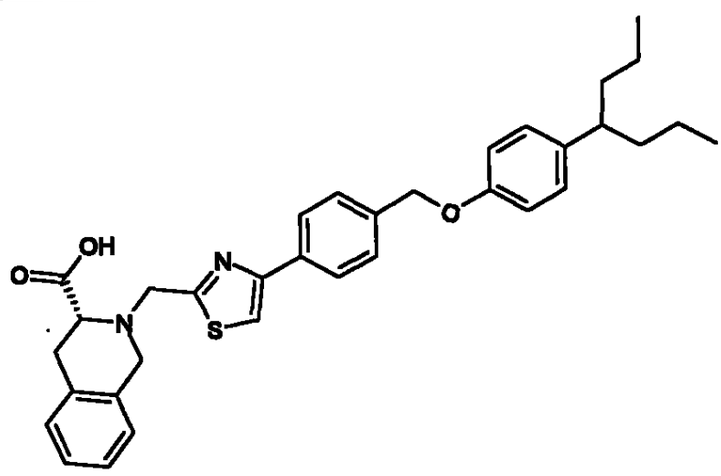
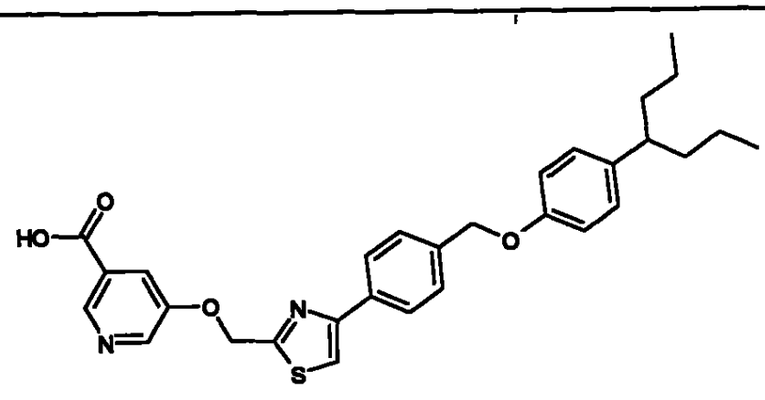
Example	Structural formula	m.p.(°C)
1-46		77 – 82
1-47		77 – 82
1-48		165 – 171

Table 1-14

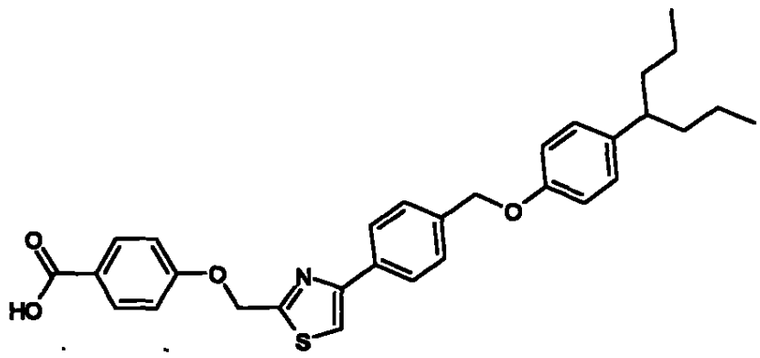
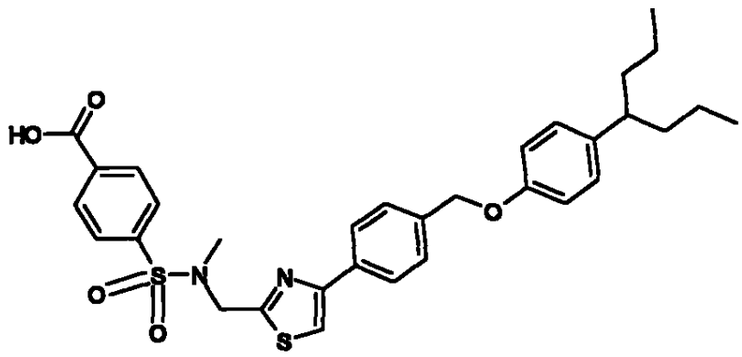
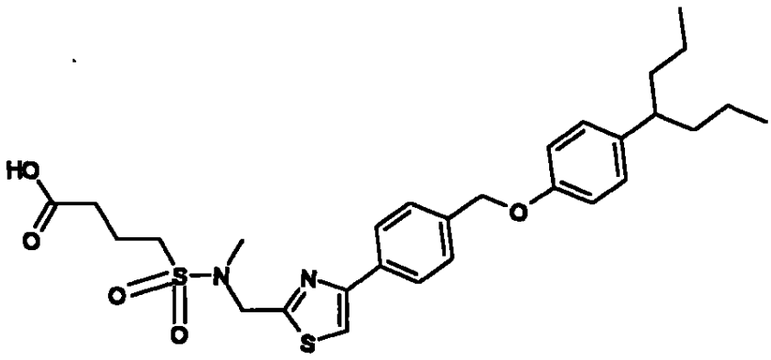
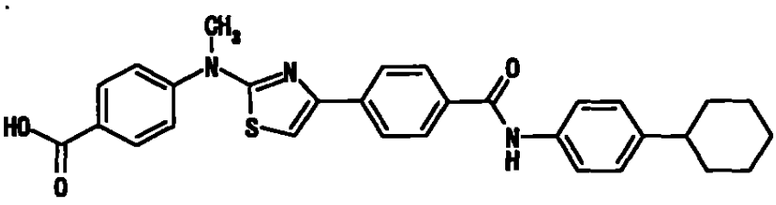
Example	Structural formula	m.p.(°C)
1-49		199 - 202
1-50		amorphous
1-51		103.3 - 106.3
1-52		250 decomp.

Table 1-15

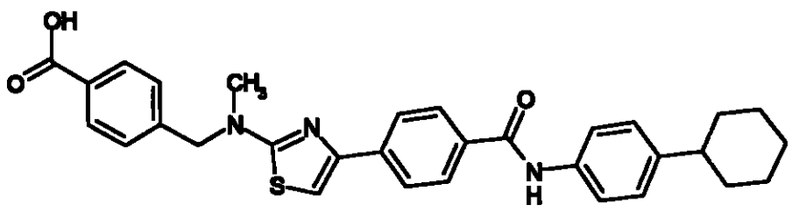
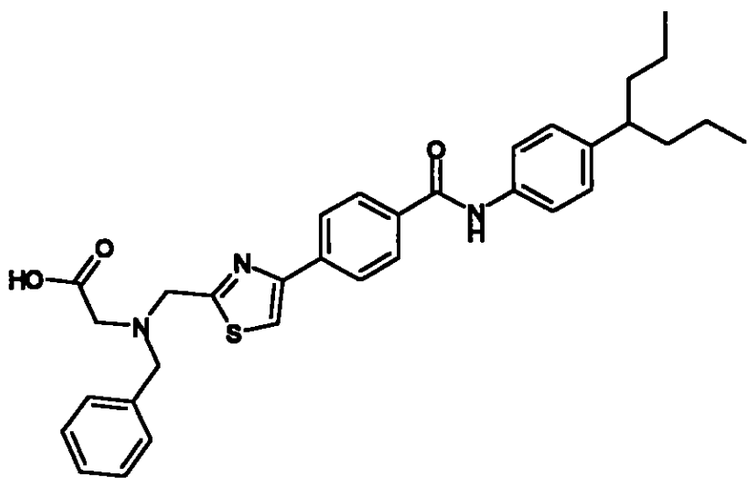
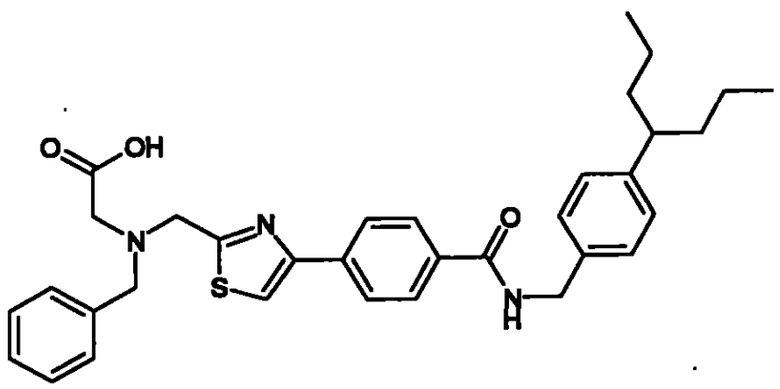
Example	Structural formula	m.p.(°C)
1-53		250 -
1-54		201 - 202
1-55		141 - 143

Table 1-16

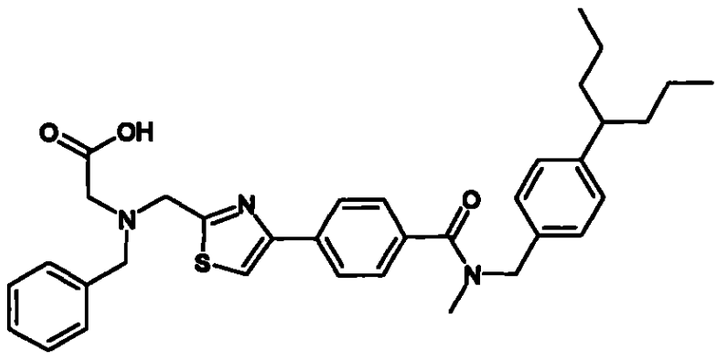
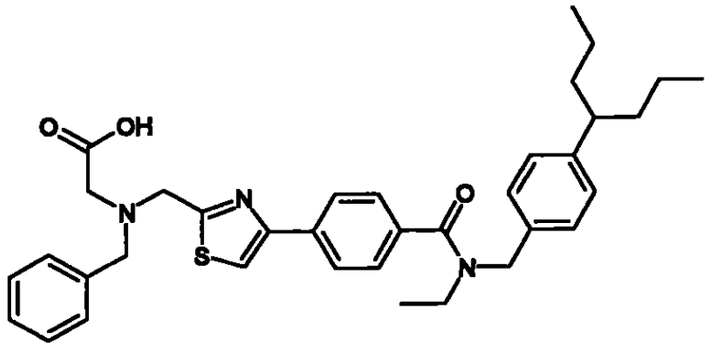
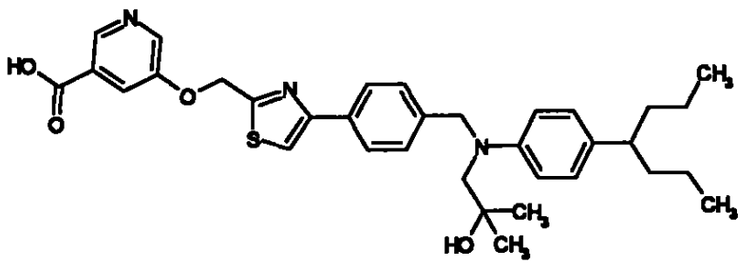
Example	Structural formula	m.p.(°C)
1-56		65 - 71
1-57		59 - 65
1-58		amorphous

Table 1-17

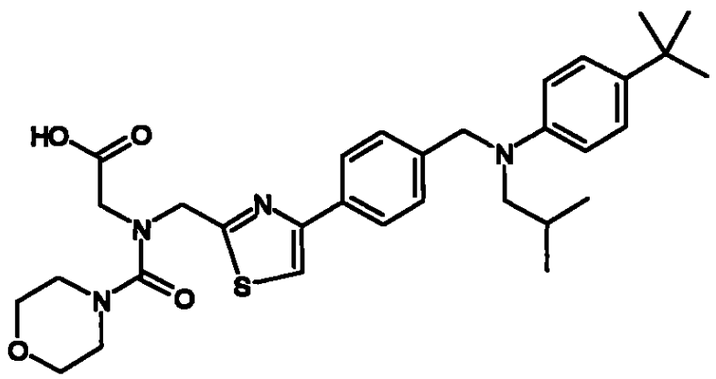
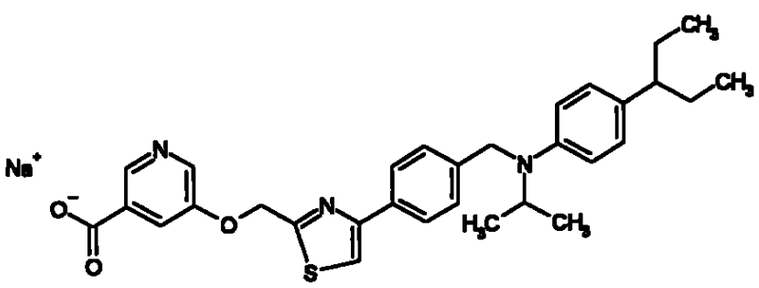
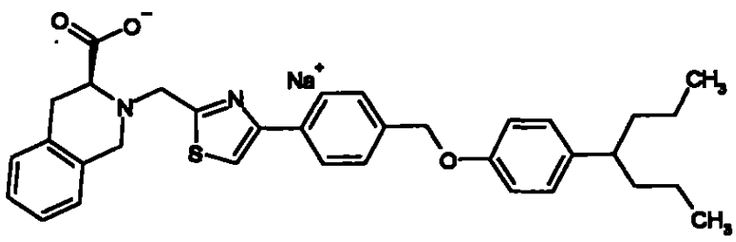
Example	Structural formula	m.p.(°C)
1-59		138
1-60		amorphous
1-61		250 -

Table 1-18

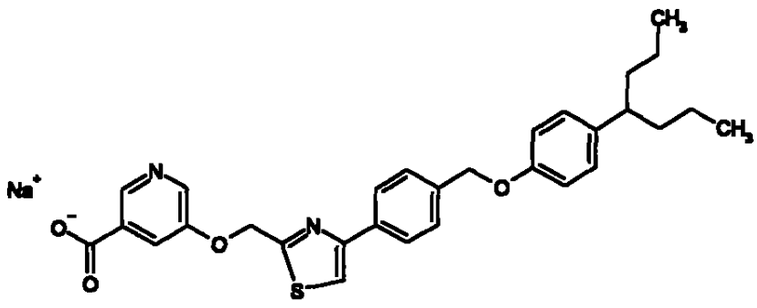
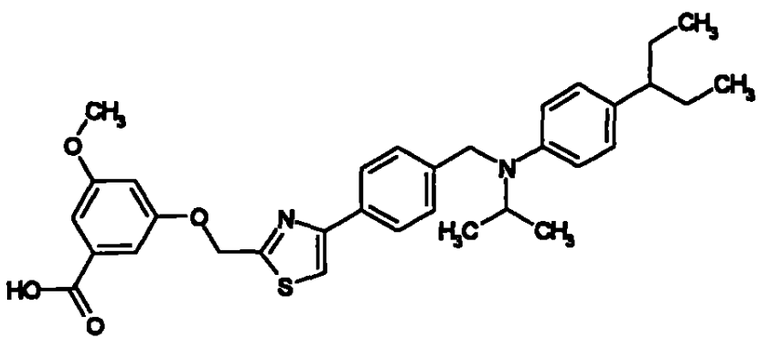
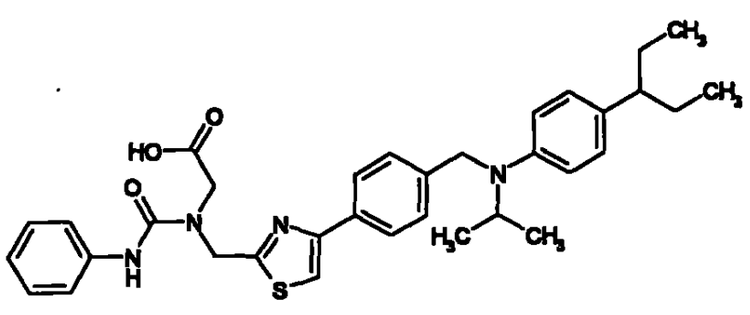
Example	Structural formula	m.p.(°C)
1-62		250 –
1-63		131
1-64		amorphous

Table 1-19

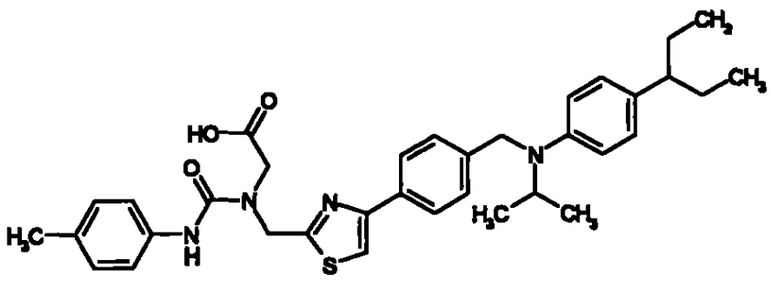
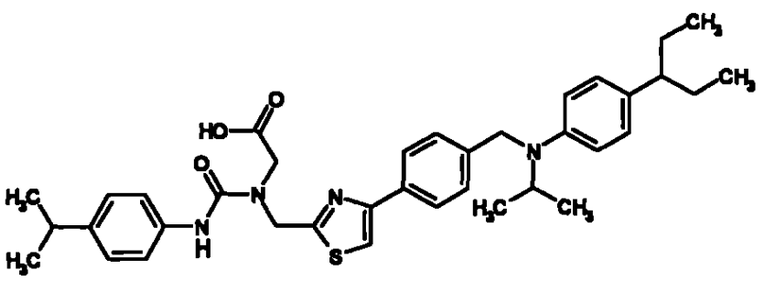
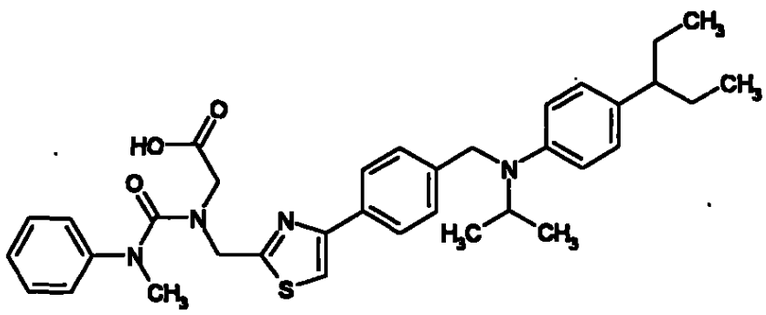
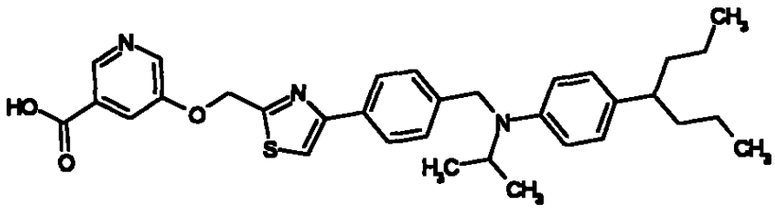
Example	Structural formula	m.p.(°C)
1-65		amorphous
1-66		amorphous
1-67		amorphous
1-68		185 decomp.

Table 1-20

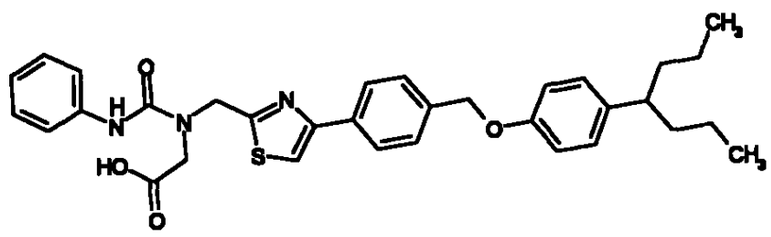
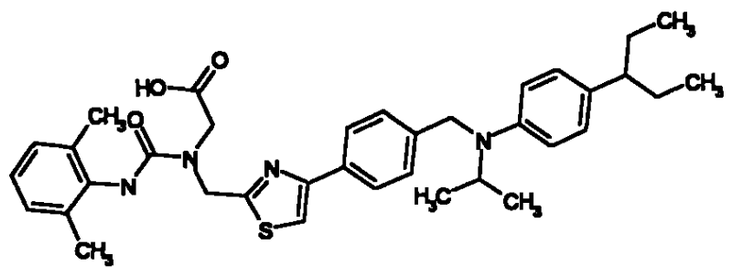
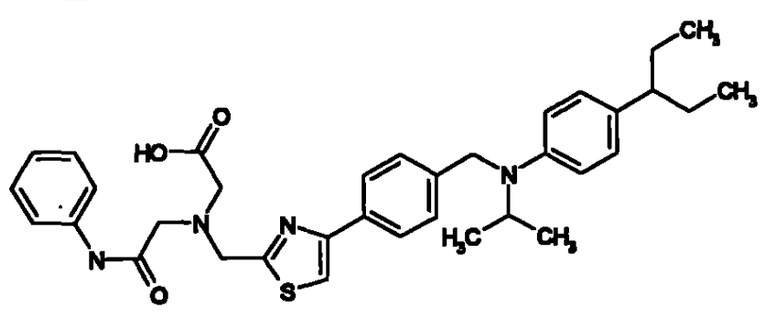
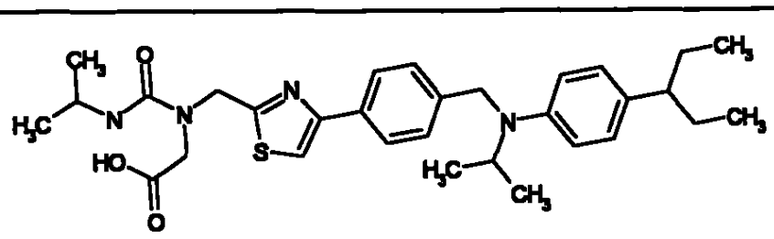
Example	Structural formula	m.p.(°C)
1-69		amorphous
1-70		amorphous
1-71		amorphous
1-72		amorphous

Table 1-21

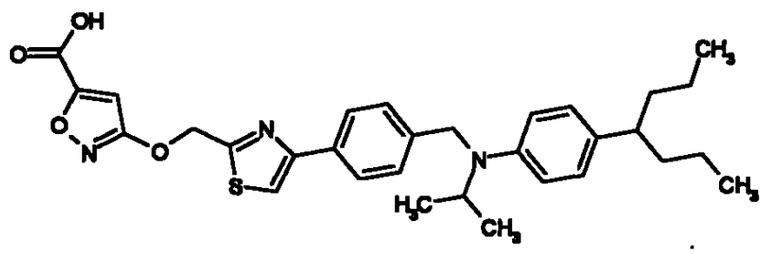
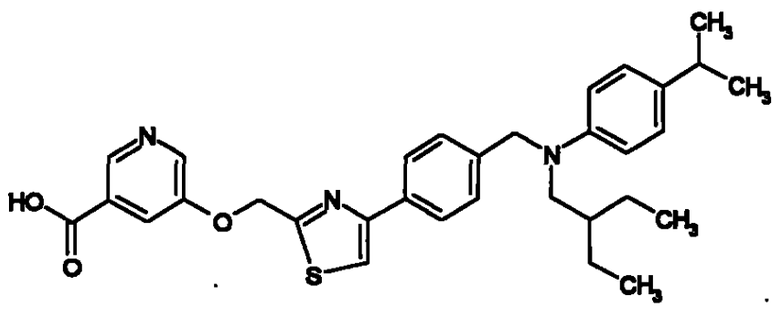
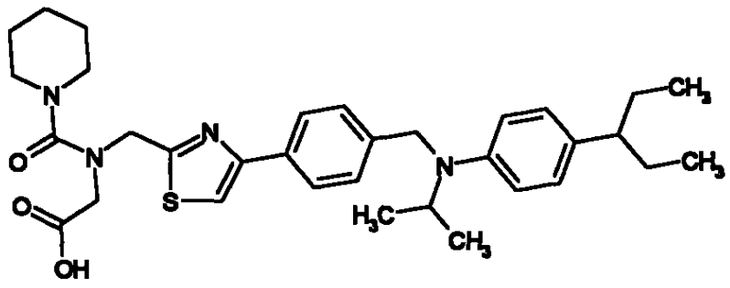
Example	Structural formula	m.p.(°C)
1-73		amorphous
1-74		181
1-75		amorphous

Table 1-22

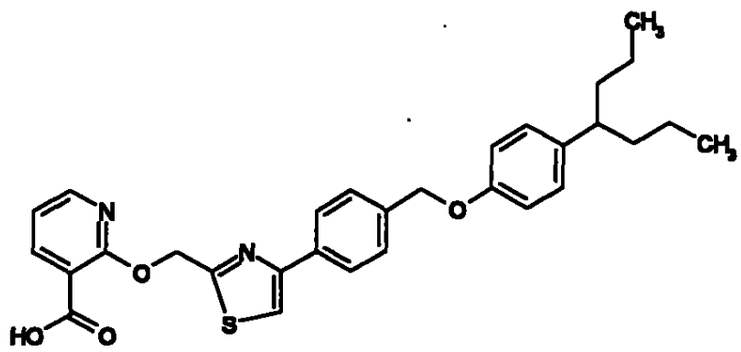
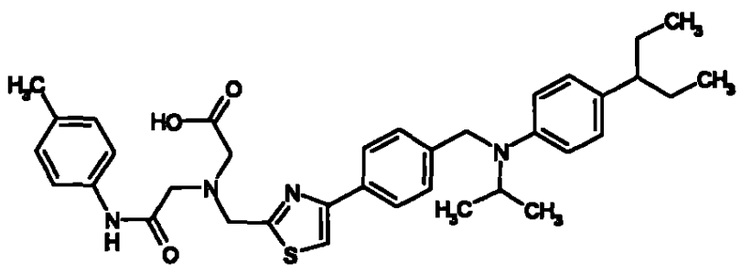
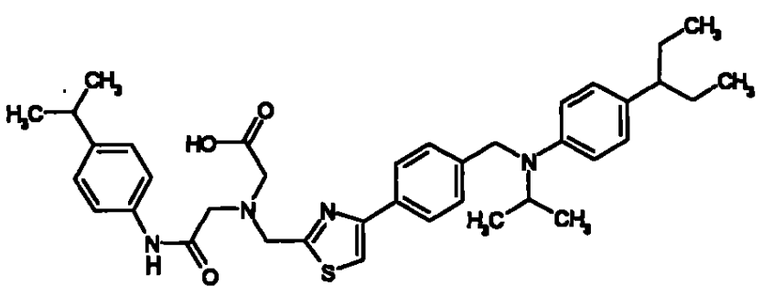
Example	Structural formula	m.p.(°C)
1-76		154.5
1-77		amorphous
1-78		amorphous

Table 1-23

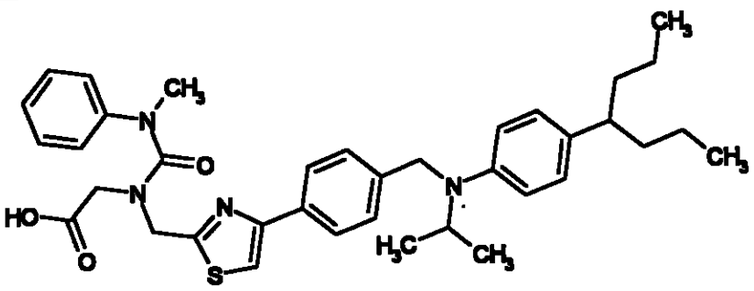
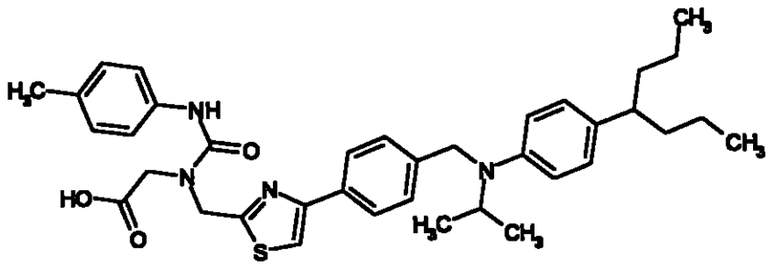
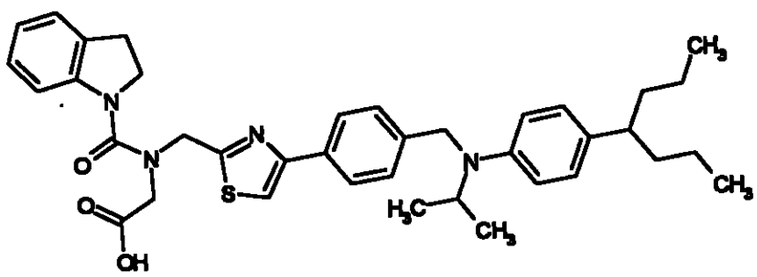
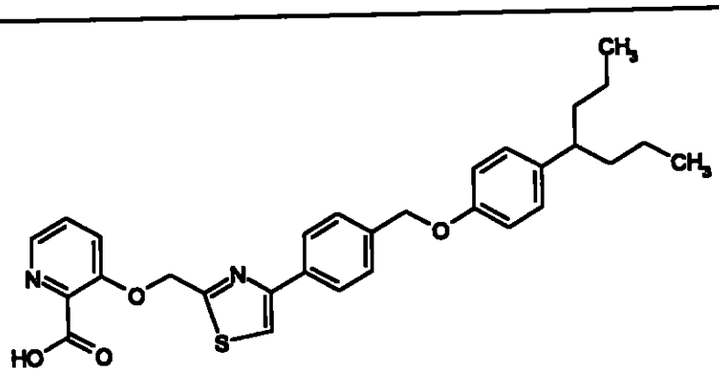
Example	Structural formula	m.p.(°C)
1-79		amorphous
1-80		amorphous
1-81		amorphous
1-82		138.5 decomp.

Table 1-24

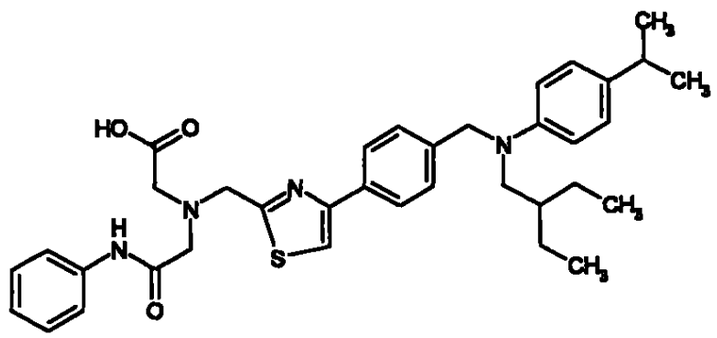
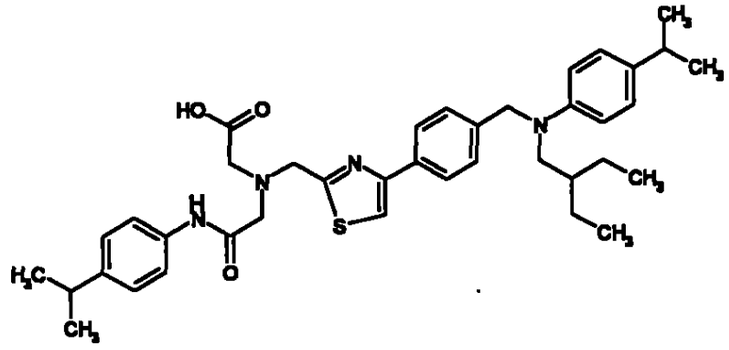
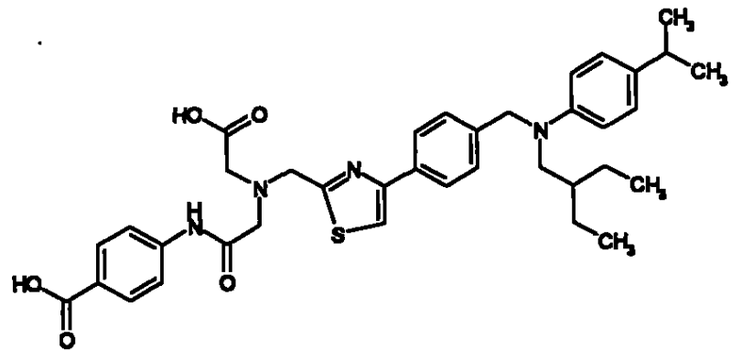
Example	Structural formula	m.p.(°C)
1-83		amorphous
1-84		amorphous
1-85		amorphous

Table 1-25

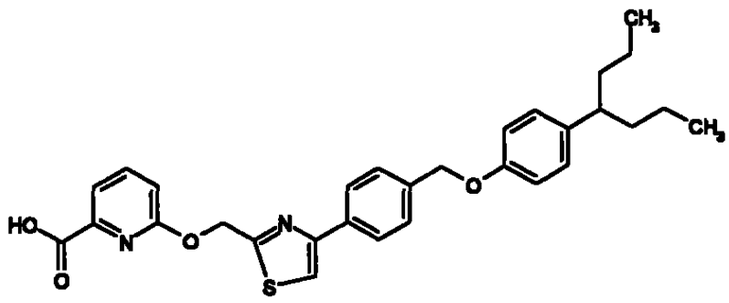
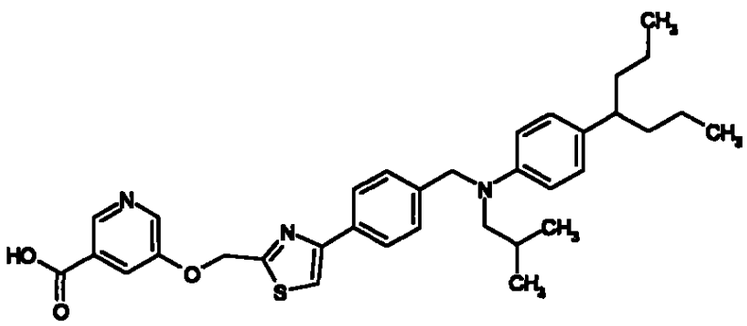
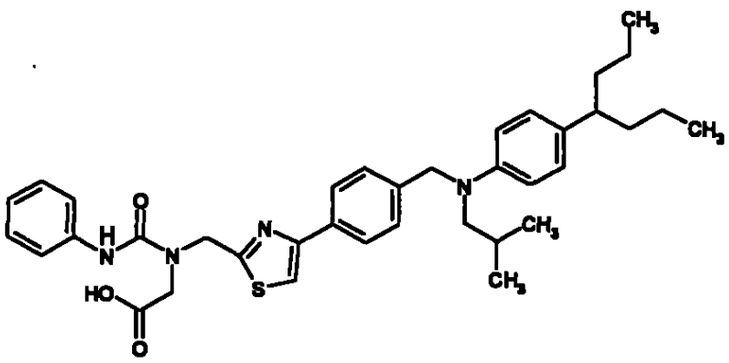
Example	Structural formula	m.p.(°C)
1-86		amorphous
1-87		amorphous
1-88		amorphous

Table 1-26

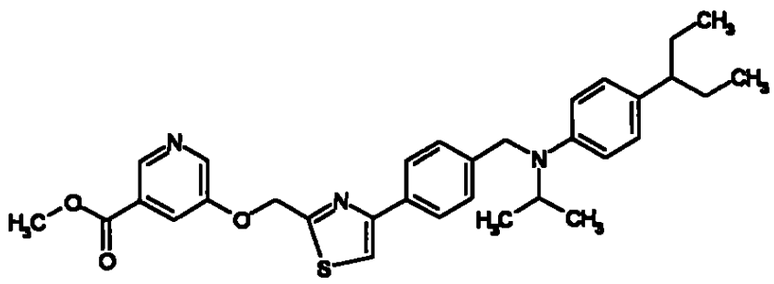
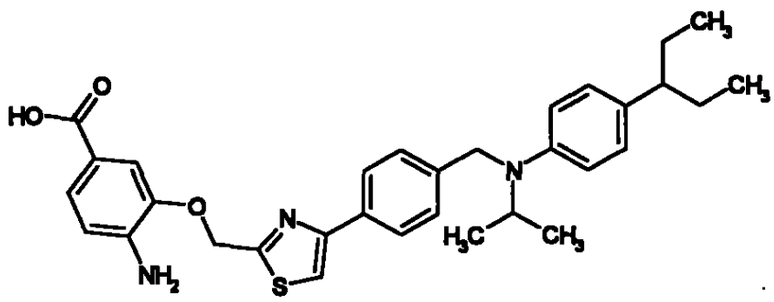
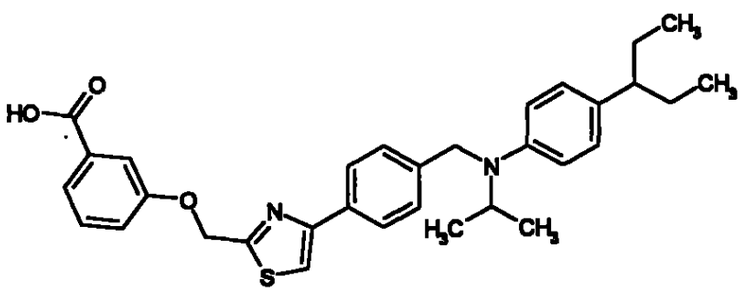
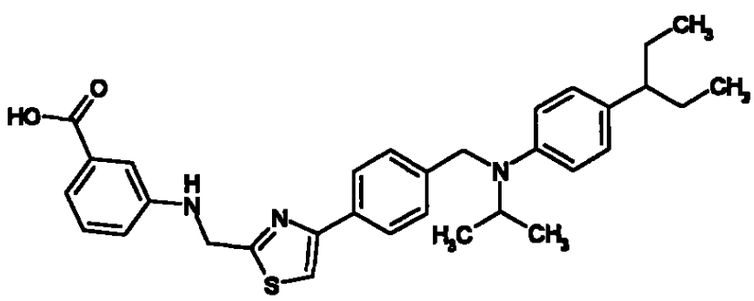
Example	Structural formula	m.p.(°C)
1-89		111 - 113
1-90		179 - 181
1-91		165 - 167
1-92		159 - 160

Table 1-27

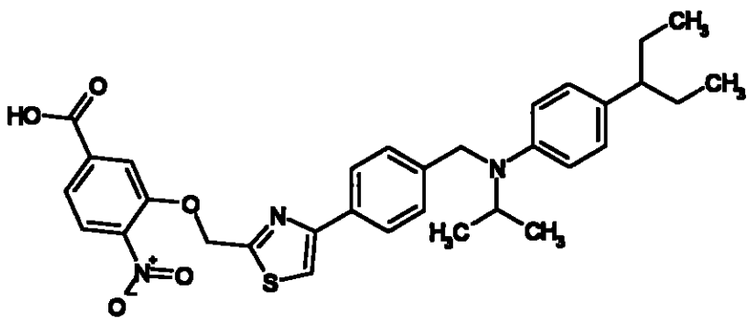
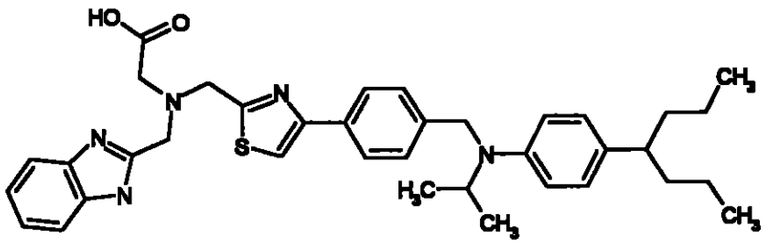
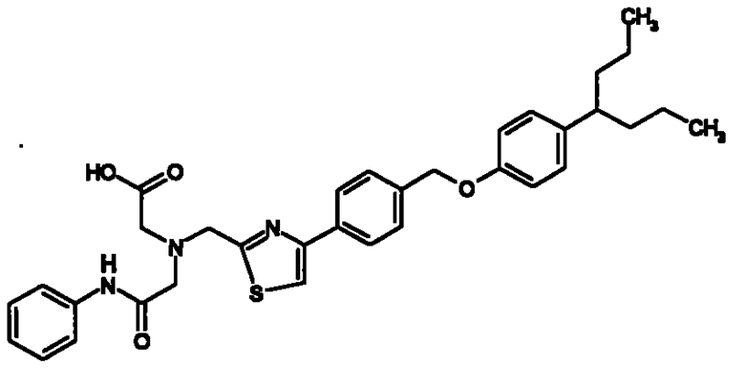
Example	Structural formula	m.p.(°C)
1-93		198 – 200
1-94		amorphous
1-95		149.5

Table 1-28

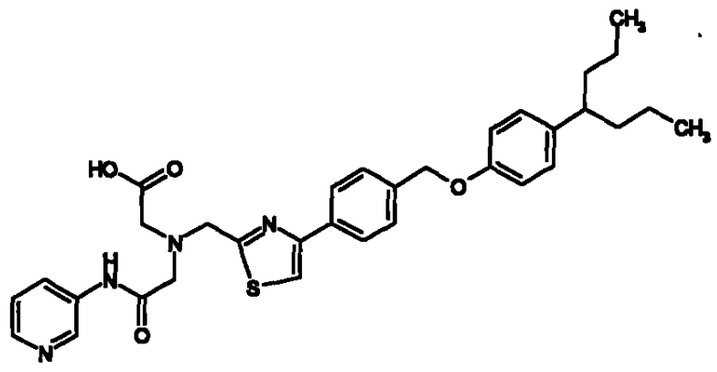
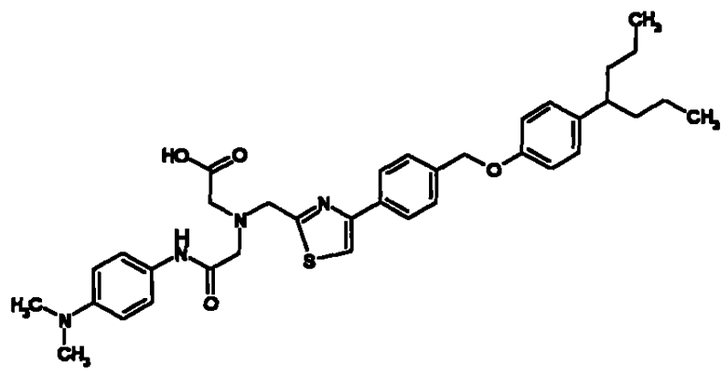
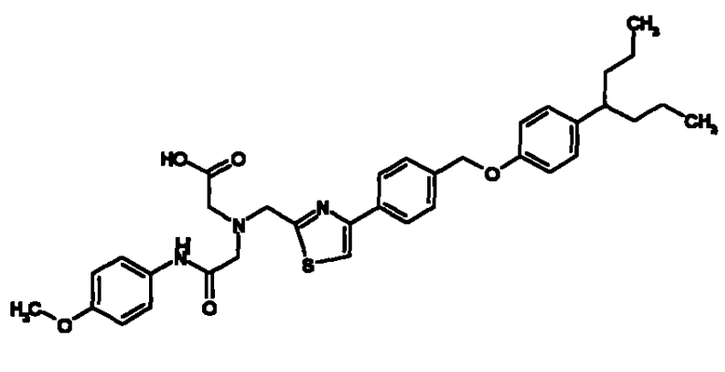
Example	Structural formula	m.p.(°C)
1-96		162.5
1-97		192.5
1-98		176.5

Table 1-29

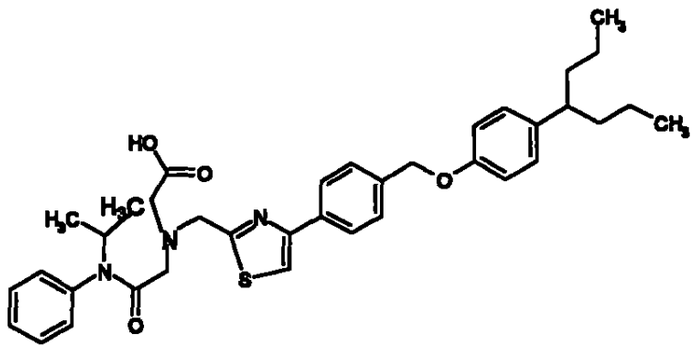
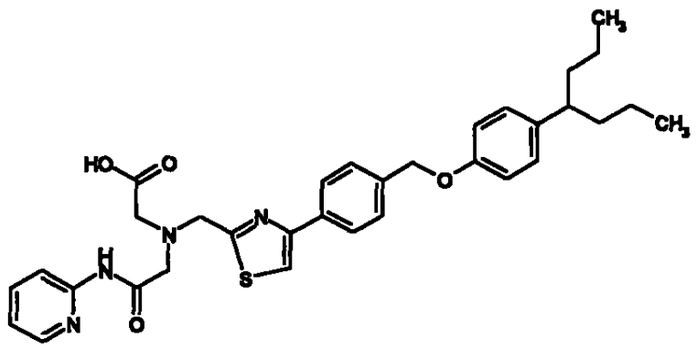
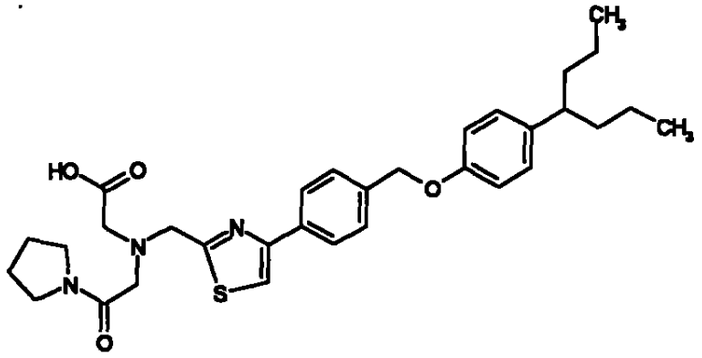
Example	Structural formula	m.p.(°C)
1-99		115.5
1-100		133.5
1-101		amorphous

Table 1-30

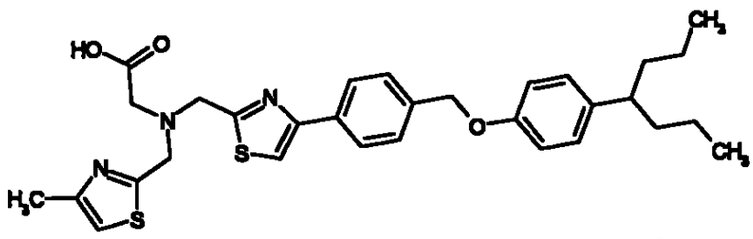
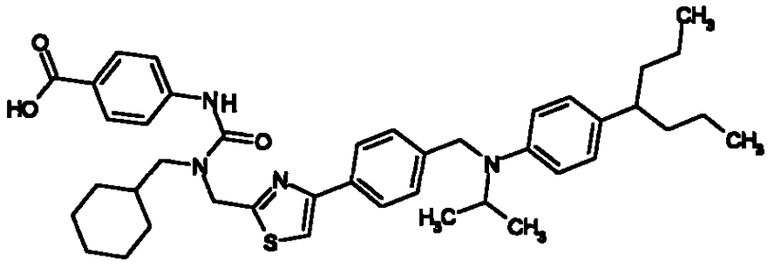
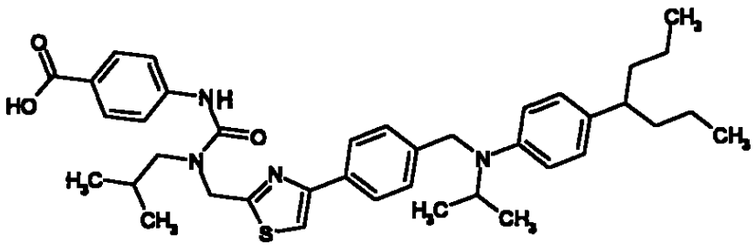
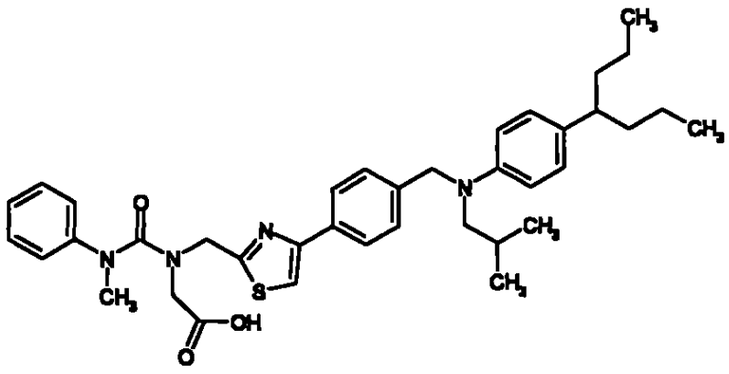
Example	Structural formula	m.p.(°C)
1-102		amorphous
1-103		amorphous
1-104		amorphous
1-105		amorphous

Table 1-31

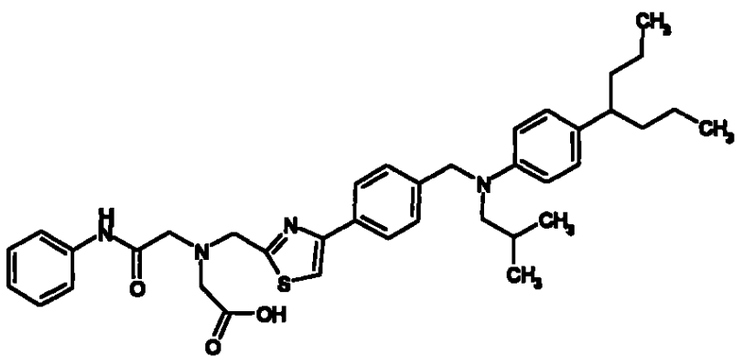
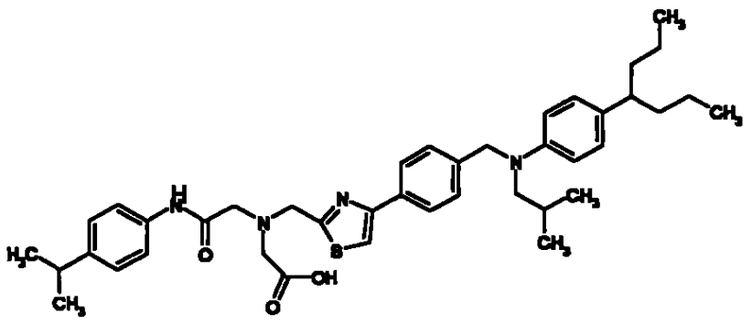
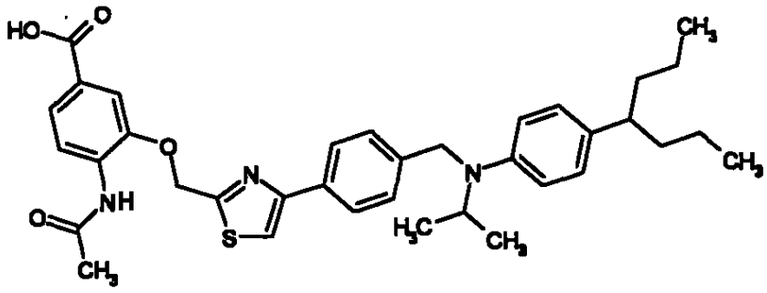
Example	Structural formula	m.p.(°C)
1-106		amorphous
1-107		amorphous
1-108		129 - 131

Table 1-32

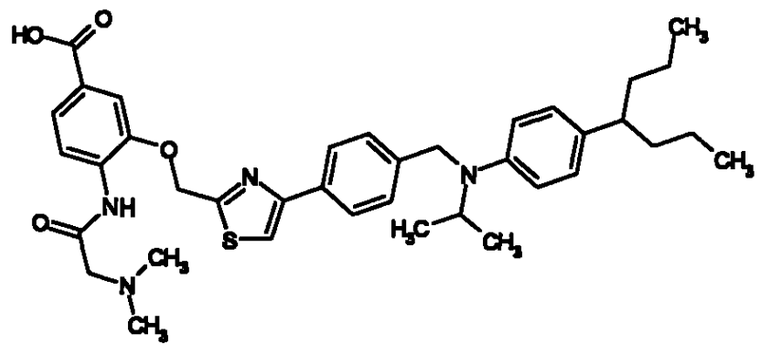
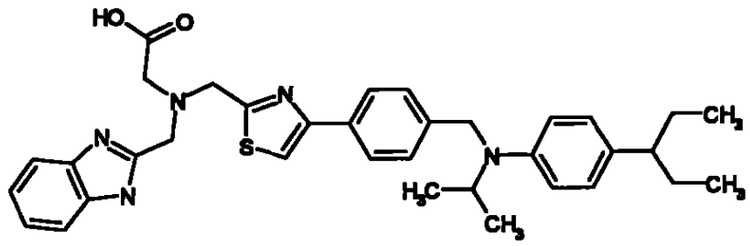
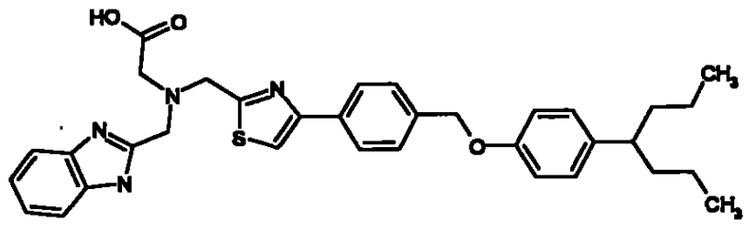
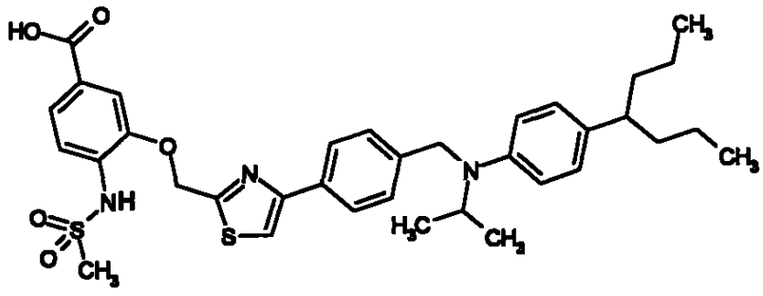
Example	Structural formula	m.p.(°C)
1-109		amorphous
1-110		amorphous
1-111		amorphous
1-112		amorphous

Table 1-33

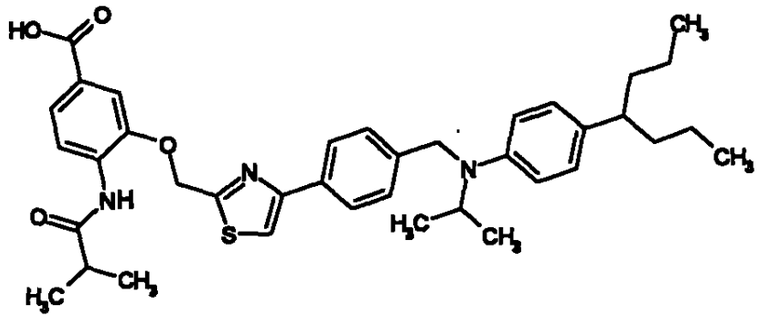
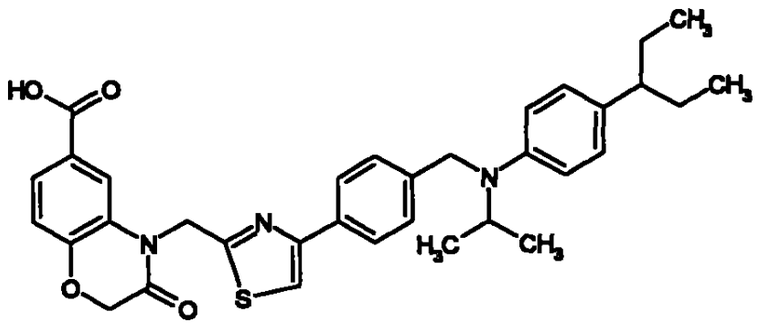
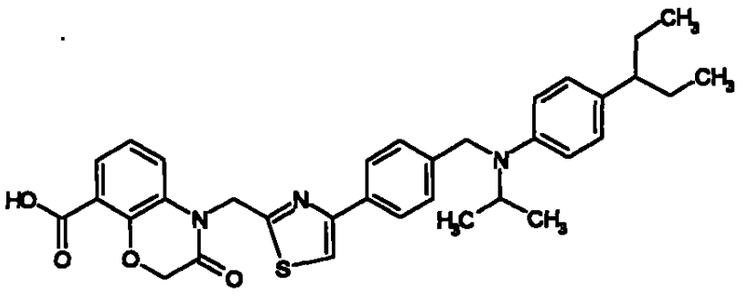
Example	Structural formula	m.p.(°C)
1-113		166 – 168
1-114		amorphous
1-115		amorphous

Table 1-34

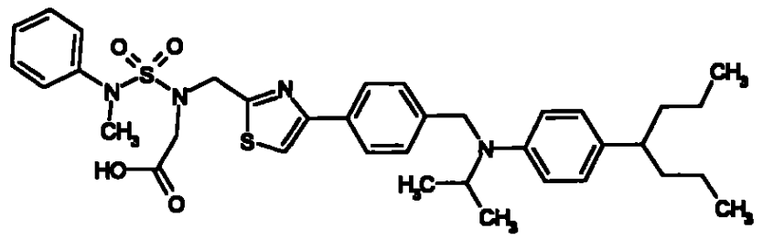
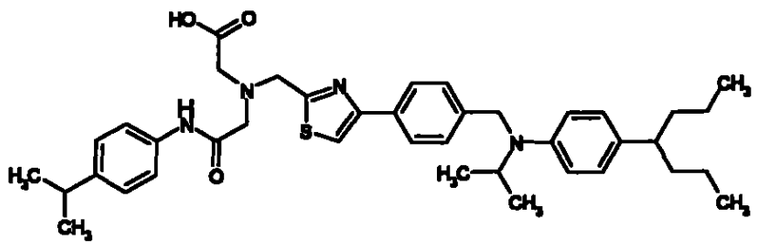
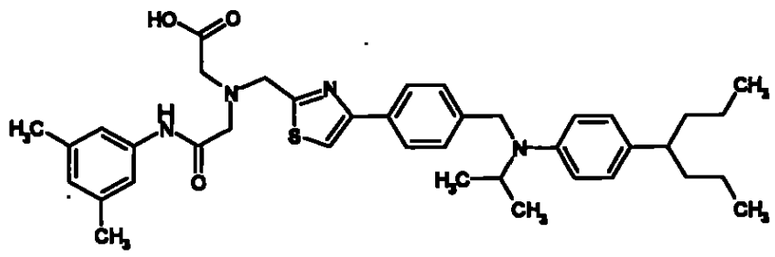
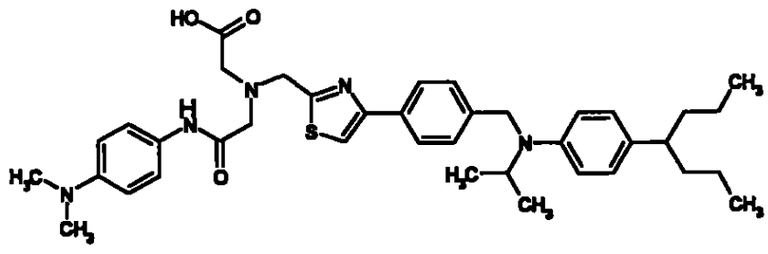
Example	Structural formula	m.p.(°C)
1-116		146 - 148
1-117		amorphous
1-118		amorphous
1-119		amorphous

Table 1-35

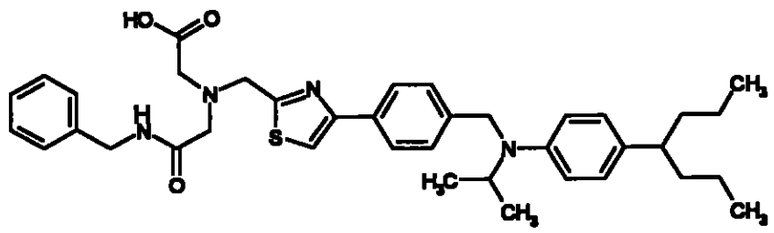
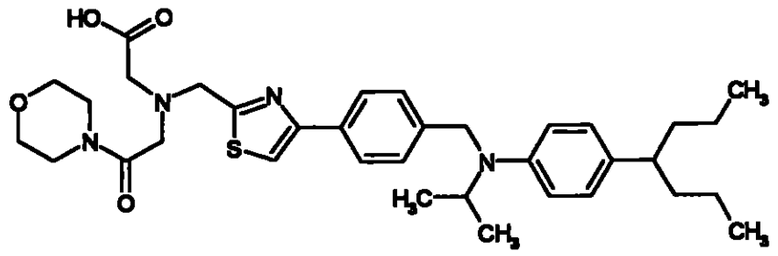
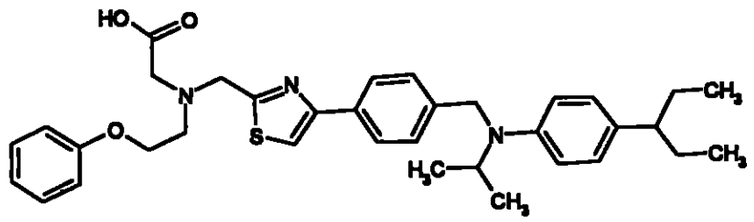
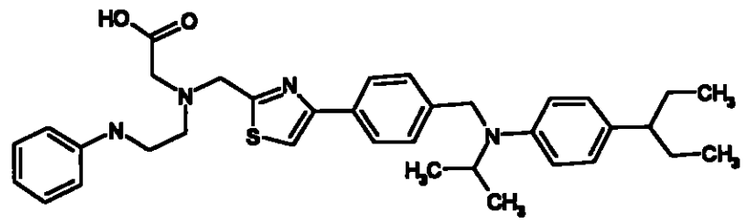
Example	Structural formula	m.p.(°C)
1-120		amorphous
1-121		amorphous
1-122		amorphous
1-123		amorphous

Table 1-36

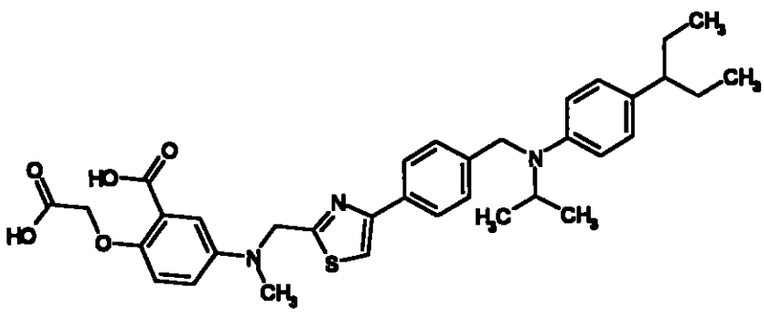
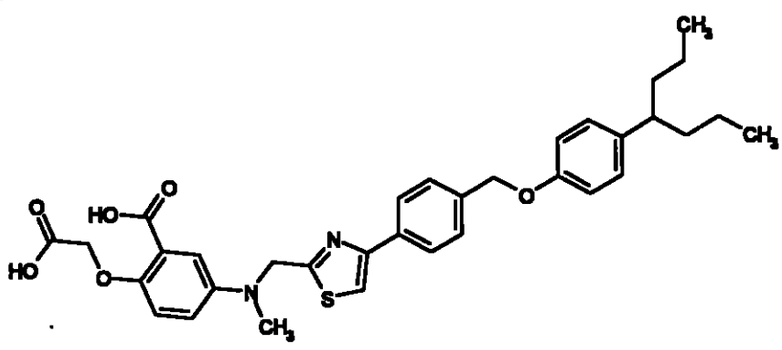
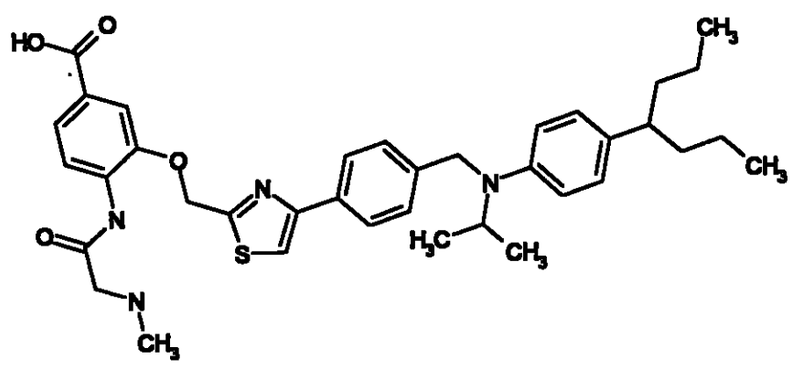
Example	Structural formula	m.p.(°C)
1-124		124
1-125		122
1-126		210 - 212

Table 1-37

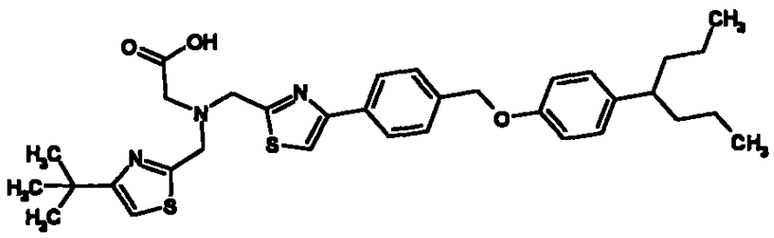
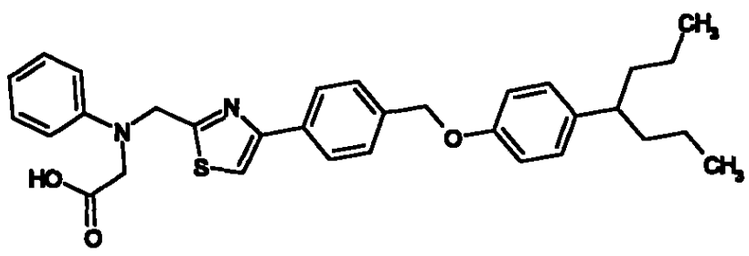
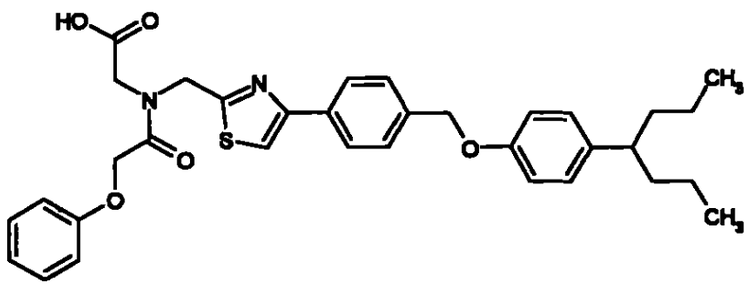
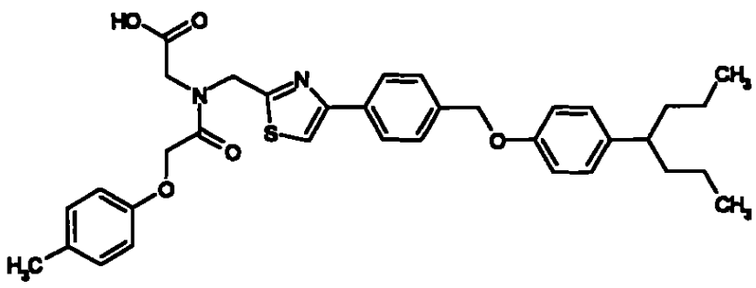
Example	Structural formula	m.p.(°C)
1-127		amorphous
1-128		amorphous
1-129		143 - 145
1-130		170 - 172

Table 1-38

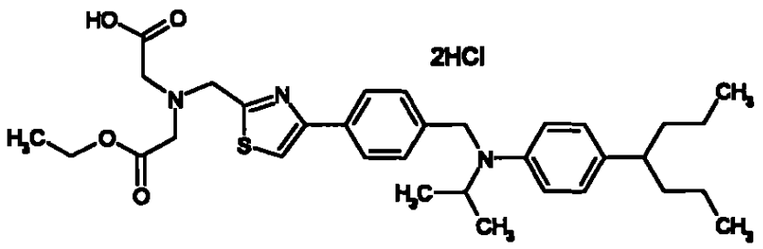
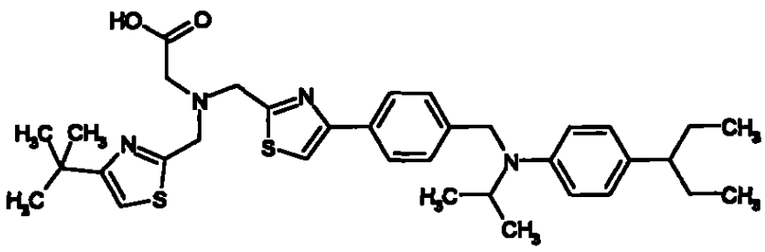
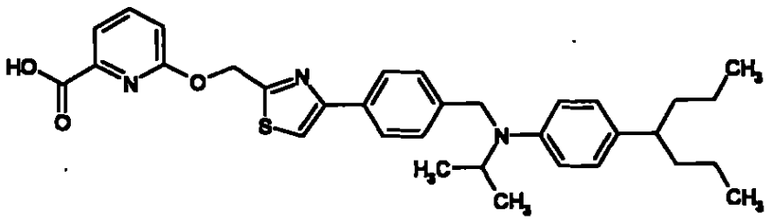
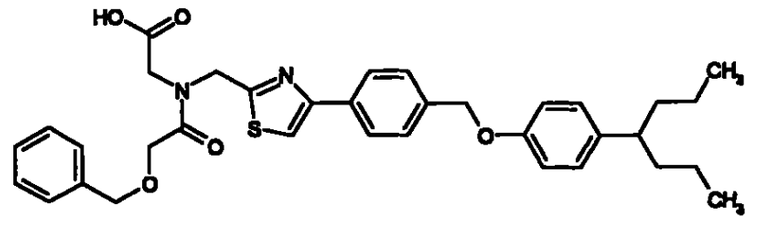
Example	Structural formula	m.p.(°C)
1-131		amorphous
1-132		amorphous
1-133		amorphous
1-134		158 - 160

Table 1-39

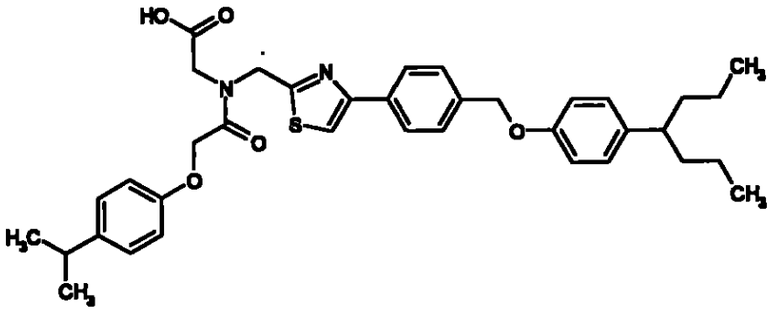
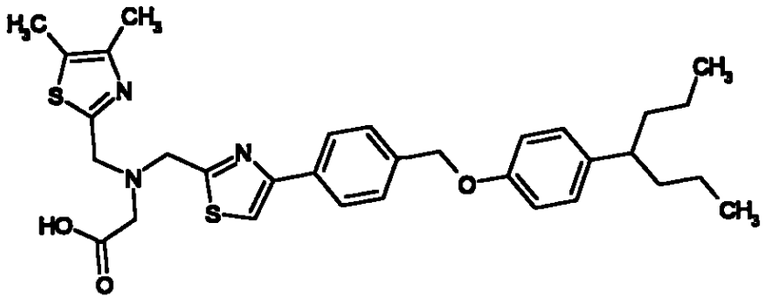
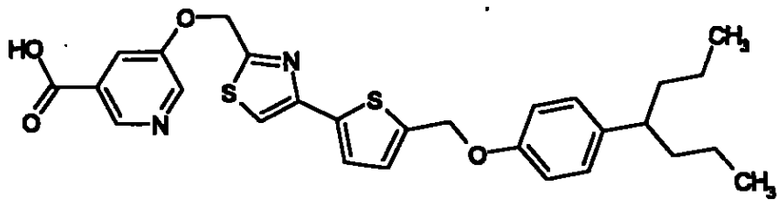
Example	Structural formula	m.p.(°C)
1-135		192 – 194
1-136		amorphous
1-137		amorphous

Table 1-40

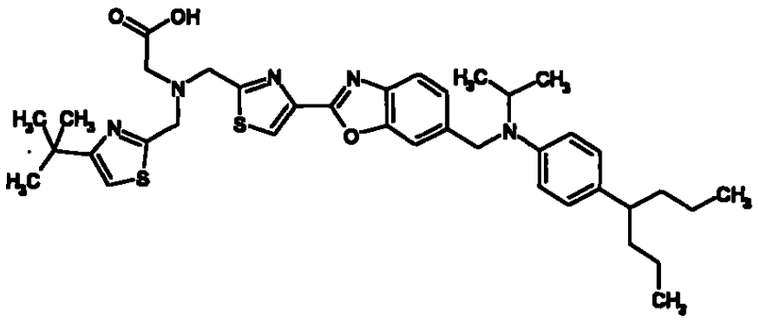
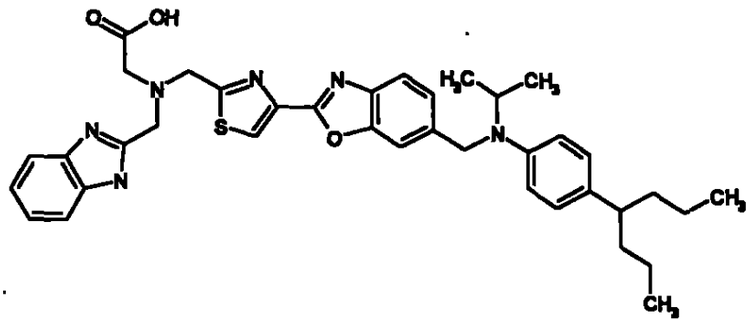
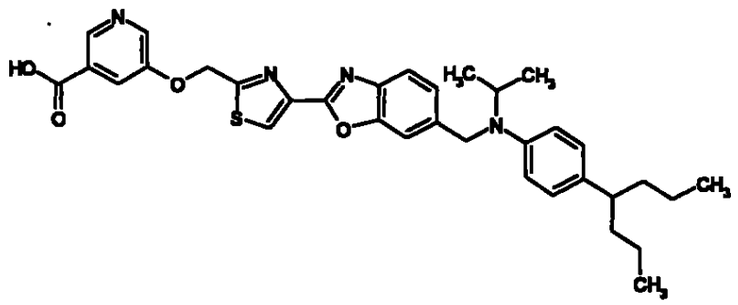
Example	Structural formula	m.p.(°C)
1-138		98 - 100
1-139		127 - 133
1-140		135 - 138

Table 1-41

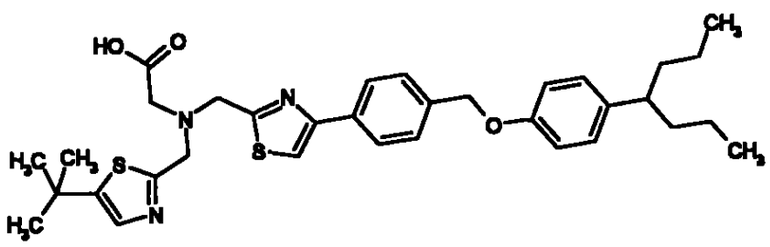
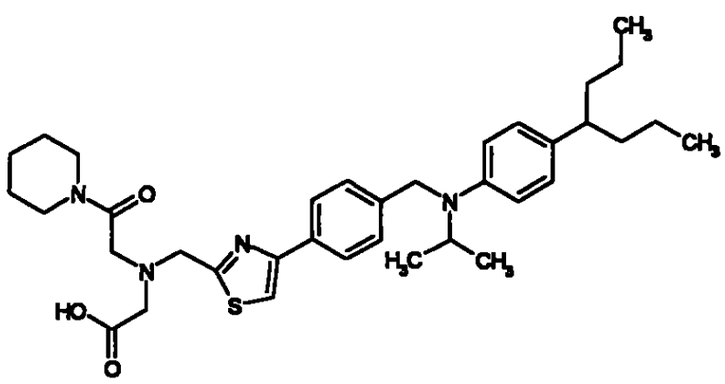
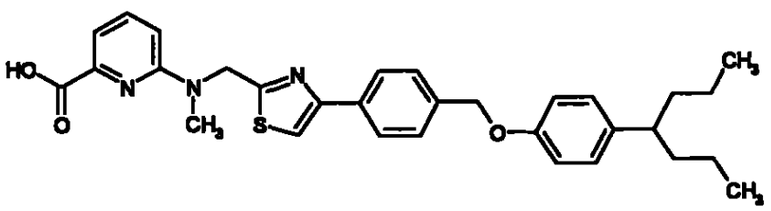
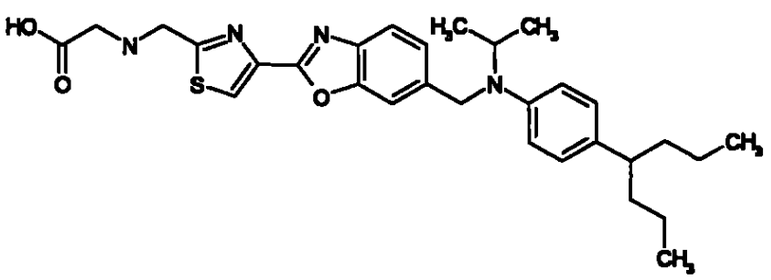
Example	Structural formula	m.p.(°C)
1-141		amorphous
1-142		amorphous
1-143		123 - 125
1-144		200 -

Table 1-42

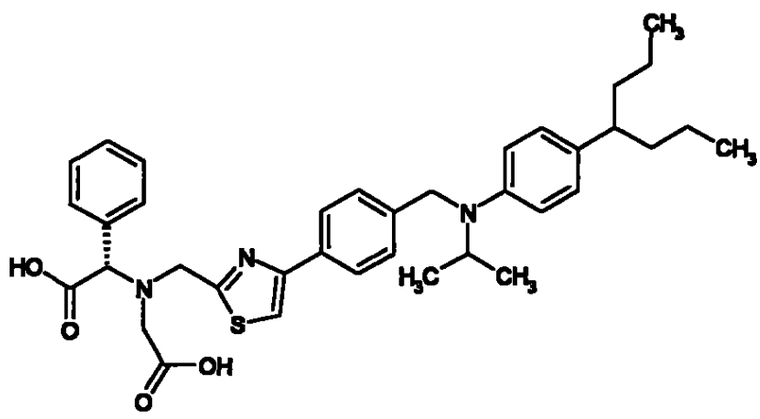
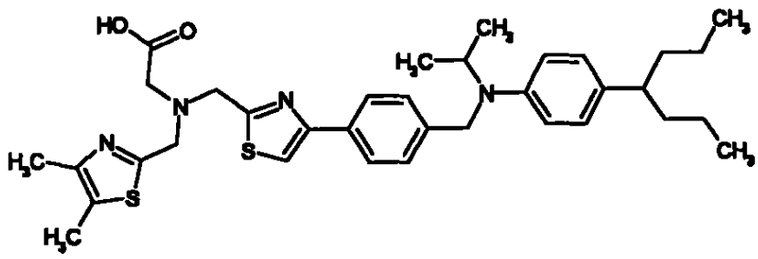
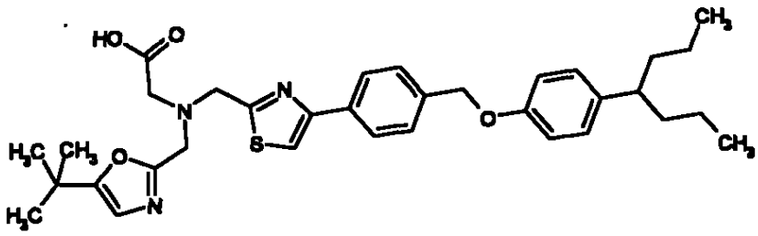
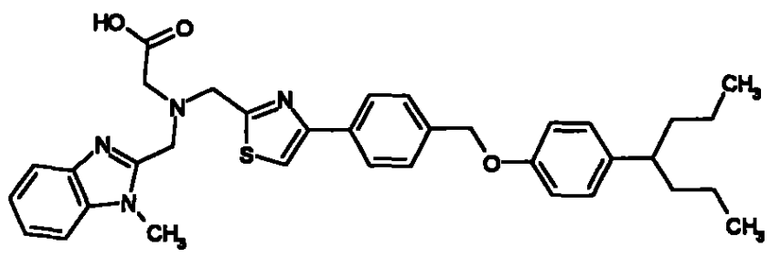
Example	Structural formula	m.p.(°C)
1-145		amorphous
1-146		156 - 157
1-147		amorphous
1-148		amorphous

Table 1-43

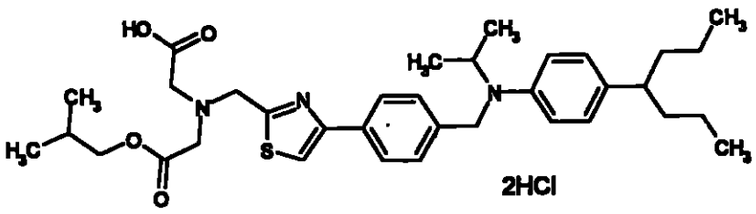
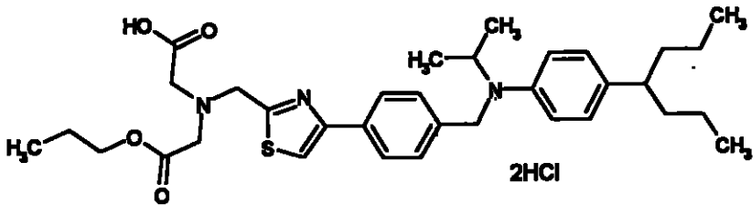
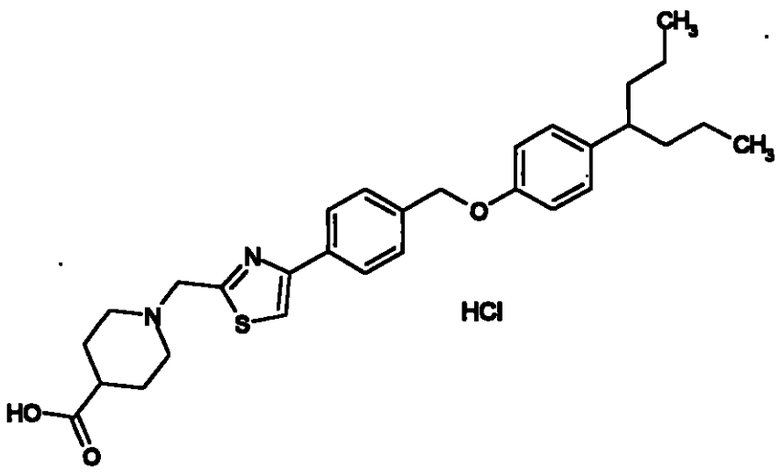
Example	Structural formula	m.p.(°C)
1-149	 2HCl	amorphous
1-150	 2HCl	amorphous
1-151	 HCl	amorphous

Table 1-44

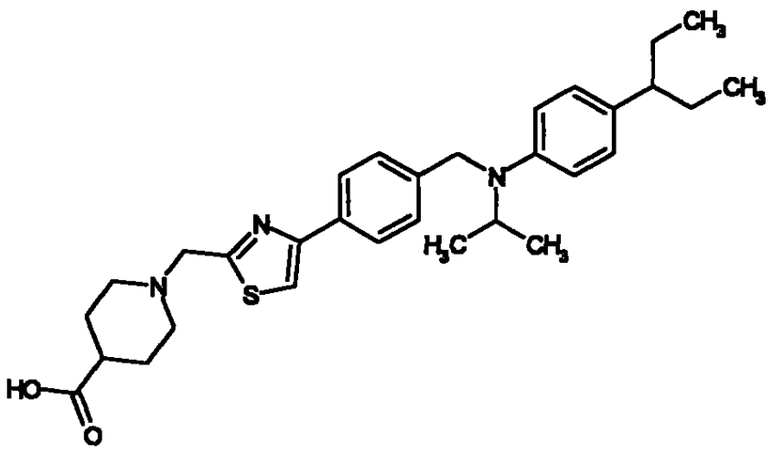
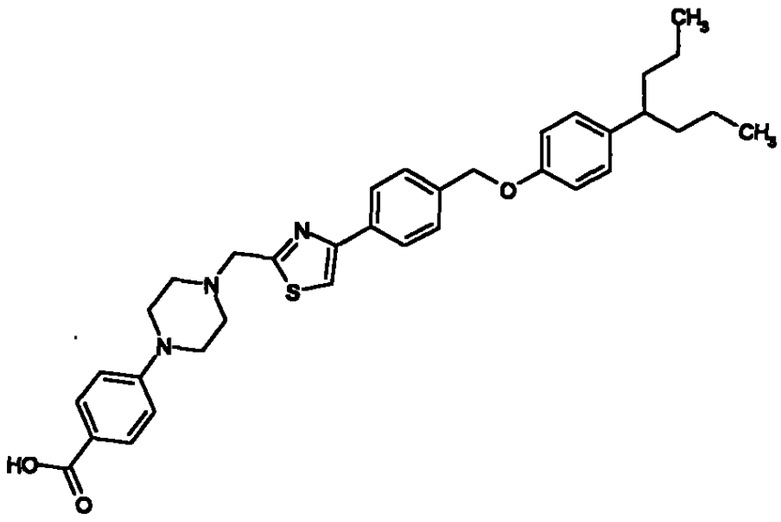
Example	Structural formula	m.p.(°C)
1-152		149 – 151
1-153		amorphous

Table 1-45

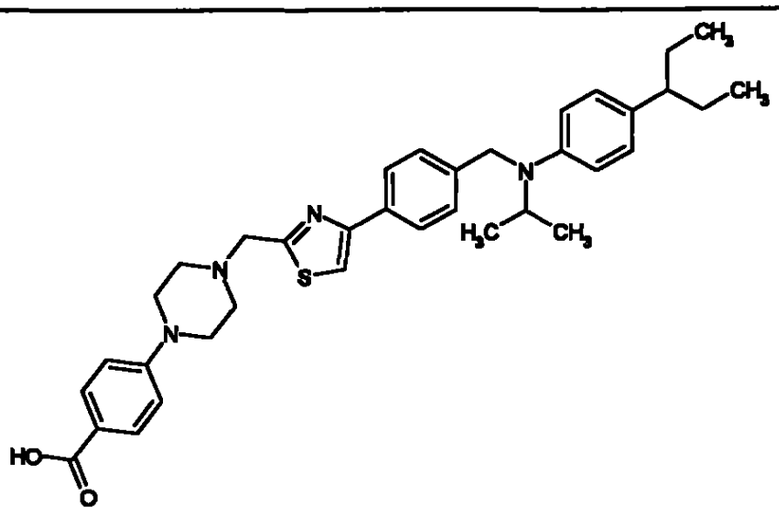
Example	Structural formula	m.p.(°C)
1-154		232 – 234

Table 1-46

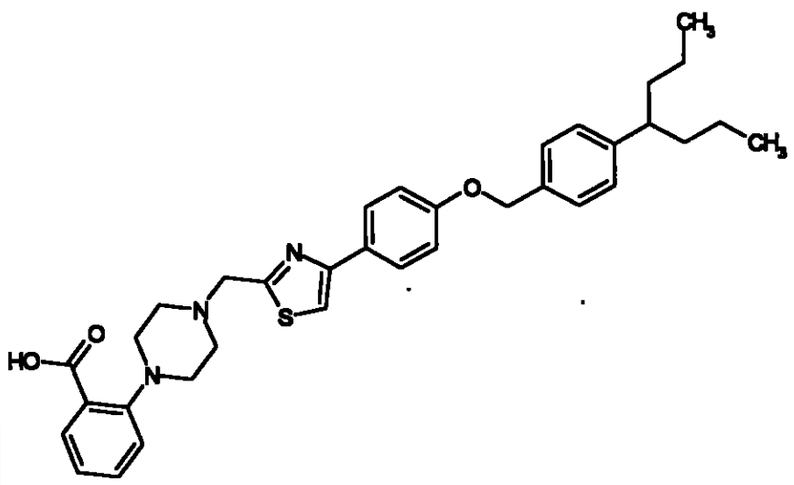
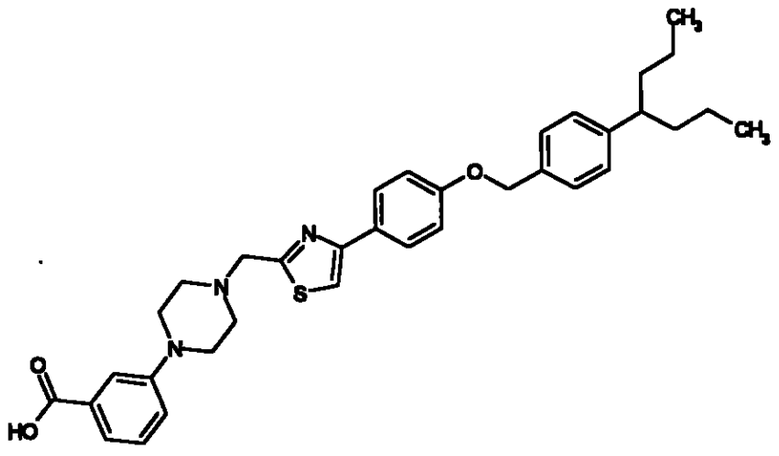
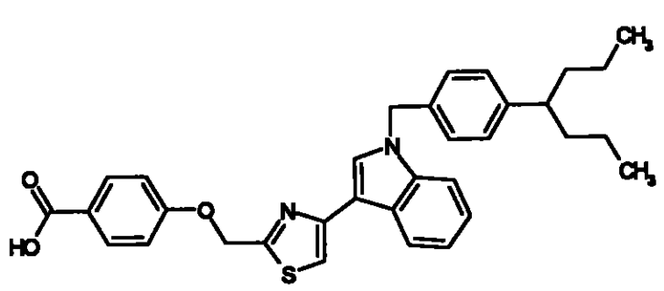
Example	Structural formula	m.p.(°C)
1-155		137 - 138
1-156		153 - 154
1-157		199 - 200

Table 1-47

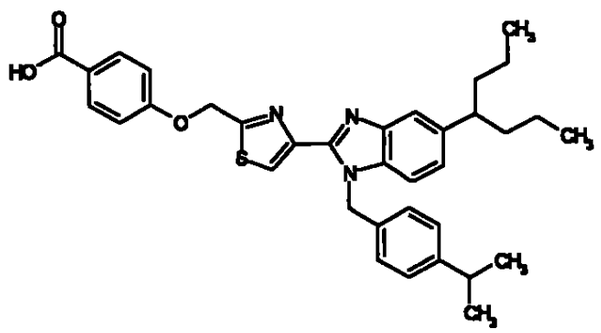
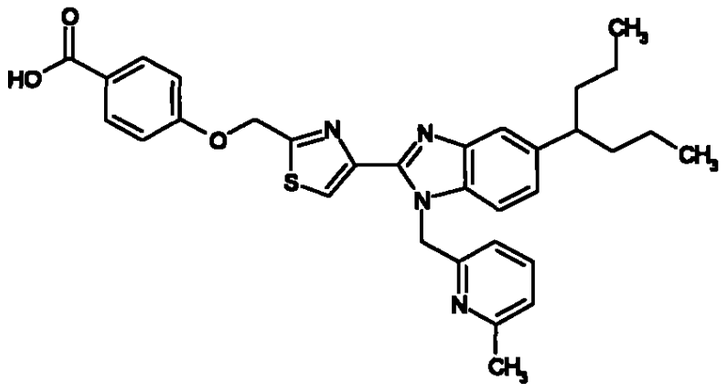
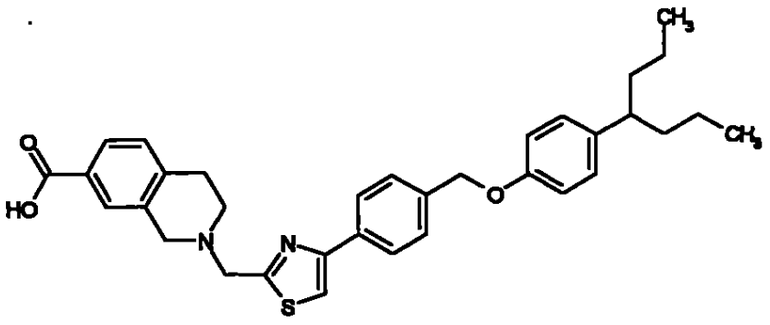
Example	Structural formula	m.p.(°C)
1-158		147 – 152
1-159		113 – 116
1-160		148.5 – 149.5

Table 1-48

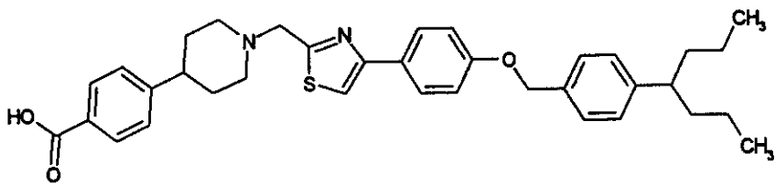
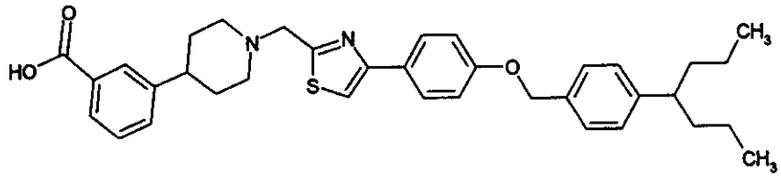
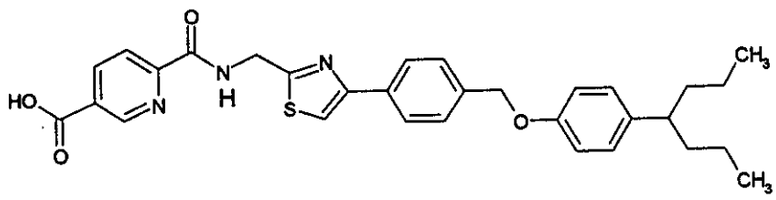
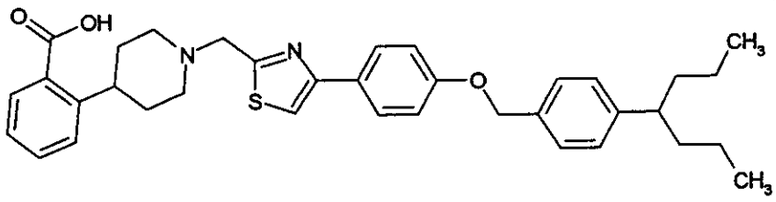
Example	Structural formula	m.p.(°C)
1-161		191 – 193
1-162		187 – 189
1-163		164 – 166
1-164		170 – 172

Table 1-49

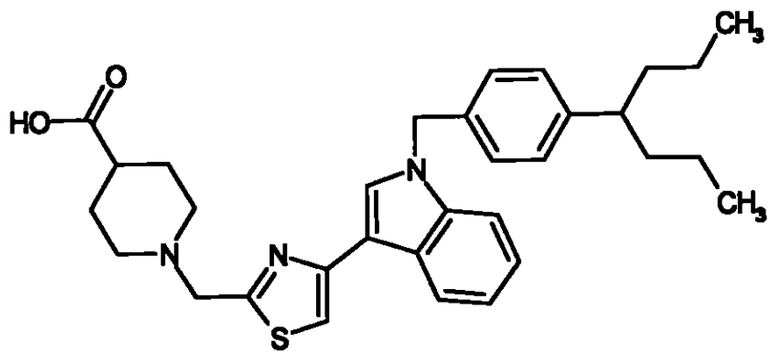
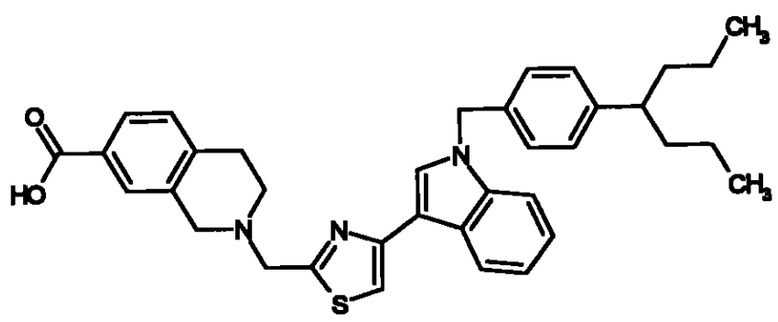
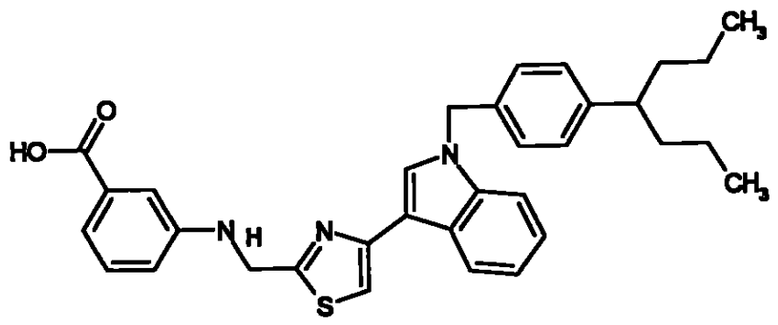
Example	Structural formula	m.p.(°C)
1-165		111 – 115
1-166		124 – 128
1-167		83 – 85

Table 1-50

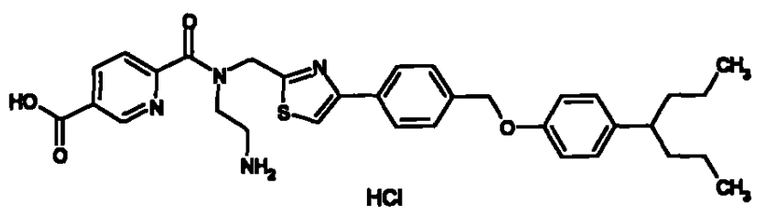
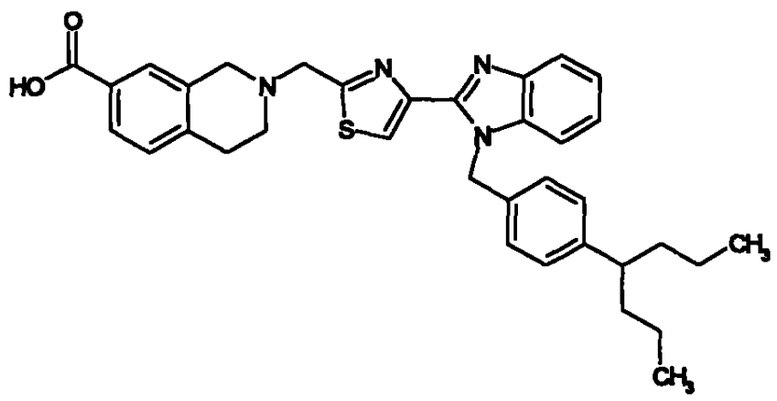
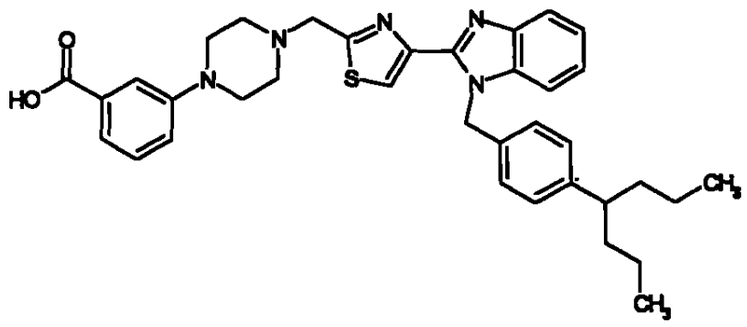
Example	Structural formula	m.p.(°C)
1-168	 HCl	227 – 229
1-169		189.2 – 190.3
1-170		179.8 – 181.2

Table 1-51

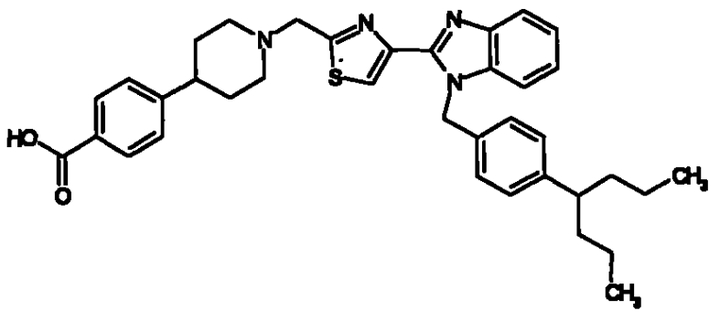
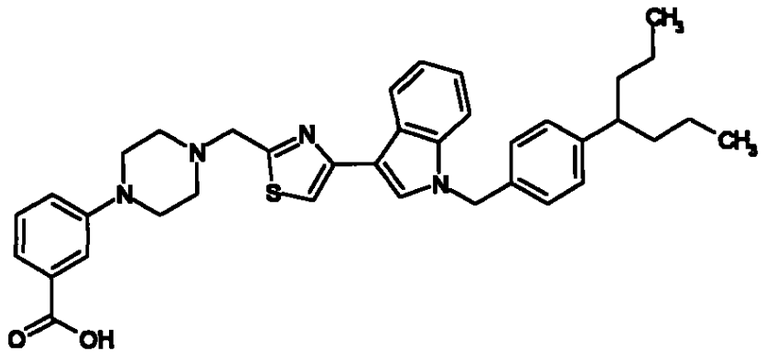
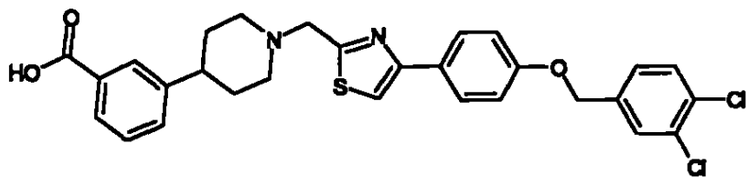
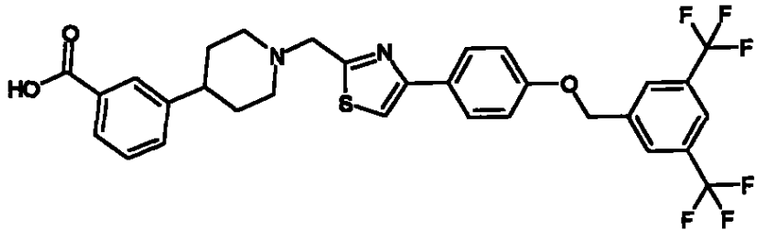
Example	Structural formula	m.p.(°C)
1-171		208.5 – 209.8
1-172		107 – 110
1-173		197 – 199
1-174		222 – 228

Table 1-52

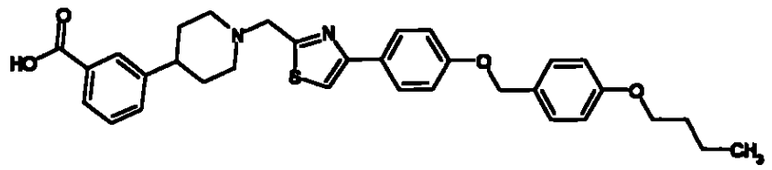
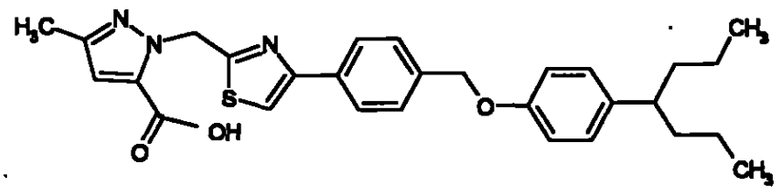
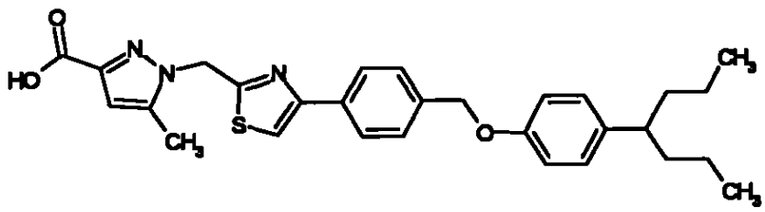
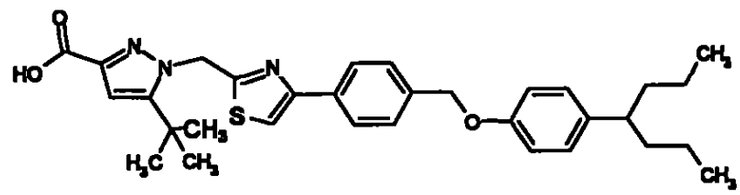
Example	Structural formula	m.p.(°C)
1-175		222 – 225
1-176		141 – 143
1-177		185 – 194
1-178		195 – 196.5

Table 1-53

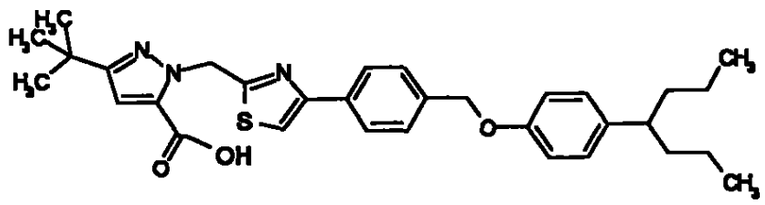
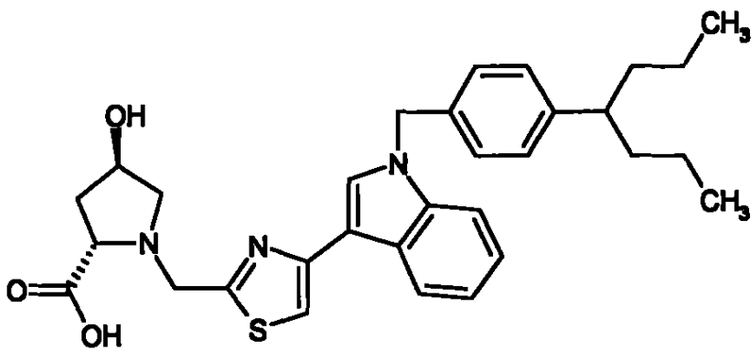
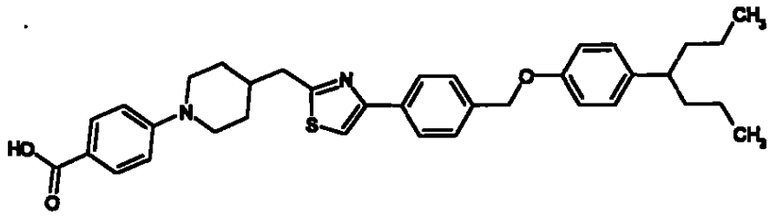
Example	Structural formula	m.p.(°C)
1-179		123 – 125
1-180		105 – 107
1-181		174 – 175

Table 1-54

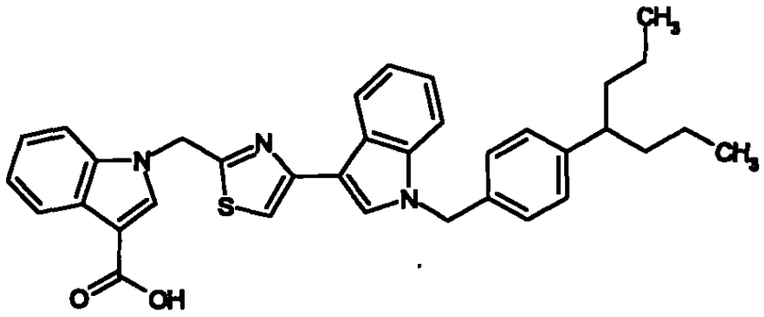
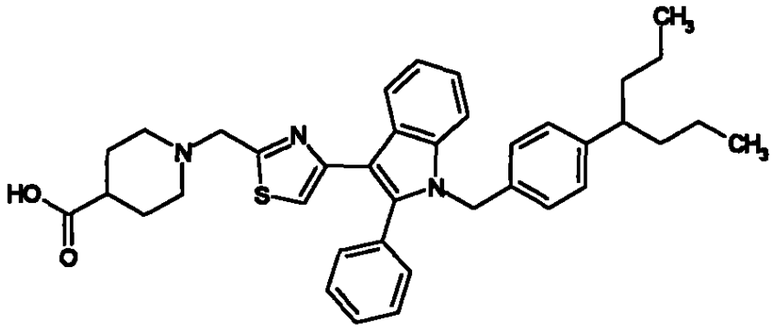
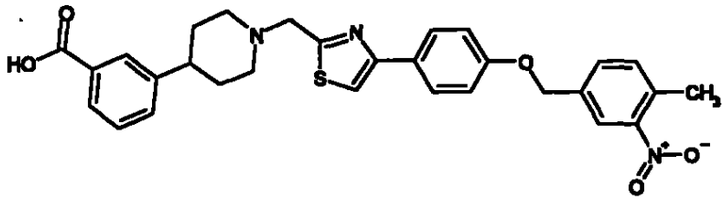
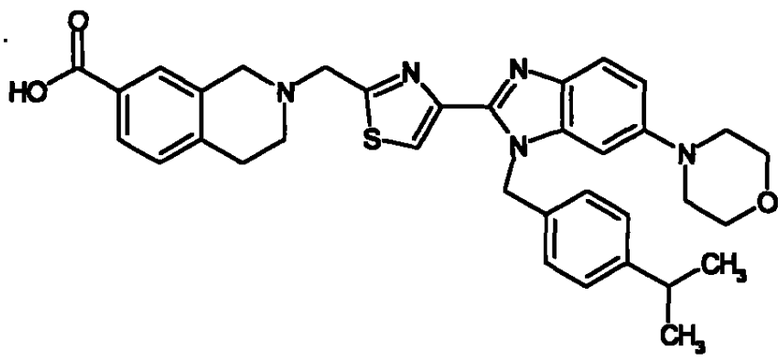
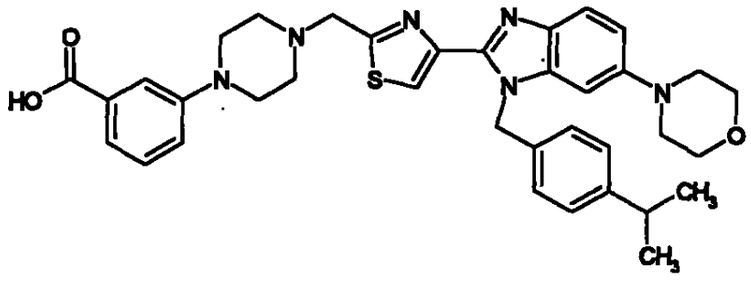
Example	Structural formula	m.p.(°C)
1-182		148 – 152
1-183		101 – 103
1-184		205 – 210

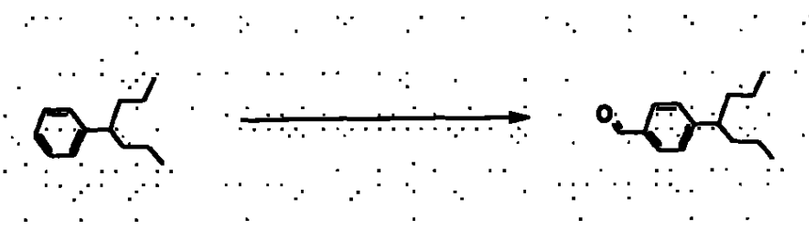
Table 1-55

Example	Structural formula	m.p.(°C)
1-185		141 - 143.2
1-186		128.5 - 131.5

Example 2-1

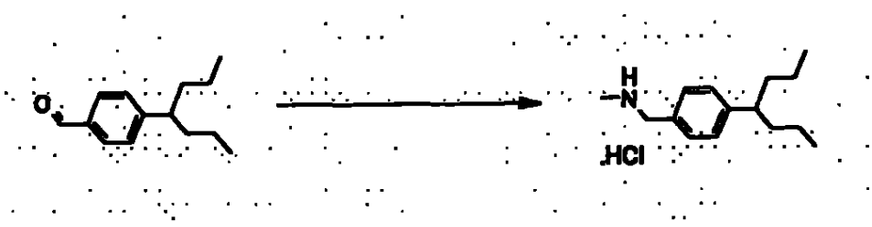
{Benzyl-[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}-phenyl)oxazol-2-ylmethyl]amino}acetic acid

(1) 4-(1-Propylbutyl)benzaldehyde



To a solution of titanium tetrachloride (18.7 ml, 170 mmol) in chloroform (50 ml) was added dropwise a solution of (1-propylbutyl)benzene (10.0 g, 56.7 mmol) and dichloromethyl methyl ether (7.70 ml, 85.1 mmol) in chloroform (40 ml) under ice-cooling, and the mixture was stirred at the same temperature for 1 hr. The reaction mixture was poured into ice (100 g) and the mixture was stirred at room temperature for 1 hr. The organic layer was washed successively with water, a 0.5N aqueous sodium hydroxide solution, water and saturated brine and dried over magnesium sulfate. After filtration, the solvent was removed and the residue was purified by silica gel column chromatography (eluent; ethyl acetate-hexane 1:50) to give the title compound (10.0 g, yield 87%).

(2) N-Methyl-4-(1-propylbutyl)benzylamine hydrochloride

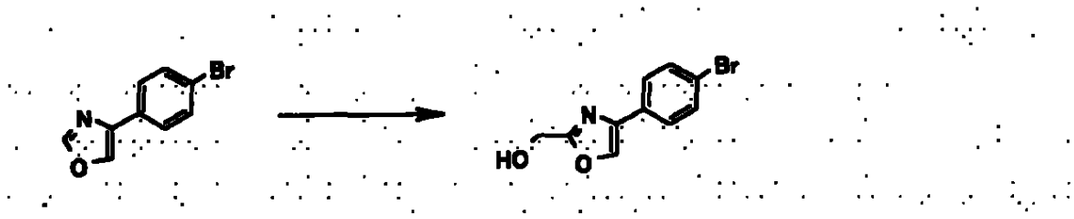


To a solution of 4-(1-propylbutyl)benzaldehyde (1.00 g, 4.89 mmol) obtained in Example 2-1(1) in ethanol was added a solution (2 mol/l, 2.94 ml) of methylamine in methanol under

ice-cooling, and the mixture was stirred at room temperature for 30 min. The solvent was removed and the residue was dissolved in tetrahydrofuran (10 ml). Sodium borohydride (285 mg, 7.53 mmol) was added under ice-cooling, and the mixture was stirred at room temperature for 1 hr. Ethanol was added and the mixture was stirred for 6 hr. The solvent was removed and chloroform (10 ml) was added to the residue. Water and 2N-hydrochloric acid were added under ice-cooling and the mixture was stirred at room temperature for 3 hr. To the organic layer, a saturated aqueous sodium hydrogen carbonate solution and di-tert-butyl dicarbonate (1.28 g, 5.87 mmol) were added. The mixture was stirred for 3 hr. After partitioning, the organic layer was washed with saturated brine and dried over sodium sulfate. The solvent was removed and the residue was purified by silica gel column chromatography (eluent; ethyl acetate-hexane 5:95) to give an oil.

The obtained oil was dissolved in ethyl acetate (2 ml) and a 4N-hydrogen chloride - ethyl acetate solution (10 ml) was added and the mixture was stirred for 3 hr. Hexane (10 ml) was added and the precipitates were collected by filtration and dried to give the title compound (650 mg, yield 52%).

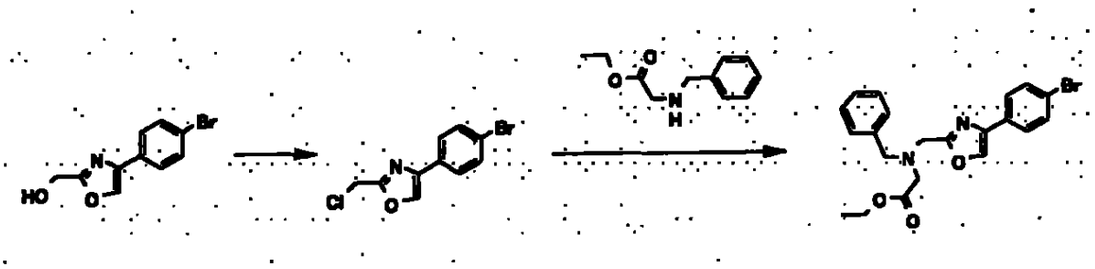
(3) (4-(4-Bromophenyl)oxazol-2-yl)methanol



Under an argon atmosphere, to a solution of 2,2,6,6-tetramethylpiperidine (227 mg, 1.61 mol) in tetrahydrofuran (3.0 ml, 13 v/w) was added n-butyllithium (1.56 M hexane solution, 0.944 ml, 1.47 mmol) at 0°C and the mixture was stirred for 30 min. After cooling to -78°C, 4-(4-

bromophenyl)oxazole (300 mg, 1.34 mmol) was added and the mixture was stirred for 45 min. A suspension of paraformaldehyde (100 mg, 3.35 mmol) in tetrahydrofuran (1.5 ml, 15 v/w) was added and the mixture was stirred for 20 min. After heating to room temperature, a saturated aqueous ammonium chloride solution (5.0 ml) was added. The solvent was removed and the mixture was extracted with ethyl acetate (15 ml), washed with saturated brine (10 ml) and dried over sodium sulfate (1.0 g). The solvent was removed and the residue was purified by silica gel column chromatography (developing solvent, chloroform-chloroform:ethyl acetate=8:2) to give the title compound (210 mg, yield 62%).

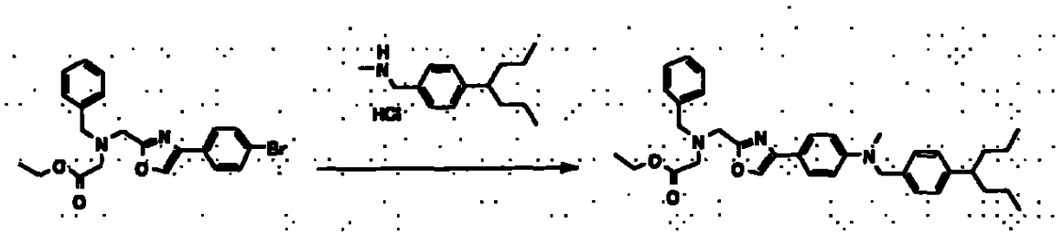
(4) N-Benzyl-N-((4-(4-bromophenyl)oxazol-2-yl)methyl)glycine ethyl ester



Under an argon atmosphere, to a suspension of (4-(4-bromophenyl)oxazol-2-yl)methanol (200 mg, 0.787 mmol) obtained in Example 2-1(3) in chloroform (4.0 ml, 20 v/w) was added thionyl chloride (103 mg, 0.866 mmol) at 0°C. The mixture was stirred at room temperature for 1 hr and at 60°C for 1 hr. Thionyl chloride (103 mg, 0.866 mmol) was added at room temperature and the mixture was stirred for 12 hr. After removal of the solvent, acetonitrile (2.0 ml), N-benzylglycine ethyl ester (0.221 ml, 1.18 mmol), potassium carbonate (326 mg, 2.36 mmol) and potassium iodide (13 mg, 0.0787 mmol) were successively added. The mixture was stirred at 60°C for 1 hr. Distilled water (5.0 ml) was added at room temperature, and the

mixture was extracted with a mixed solvent of hexane:ethyl acetate=1:1, washed with saturated brine (5.0 ml) and dried over sodium sulfate (1.0 g). The solvent was removed and the residue was purified by silica gel column chromatography (developing solvent; hexane:ethyl acetate=9:1) to give the title compound (220 mg, yield 65%).

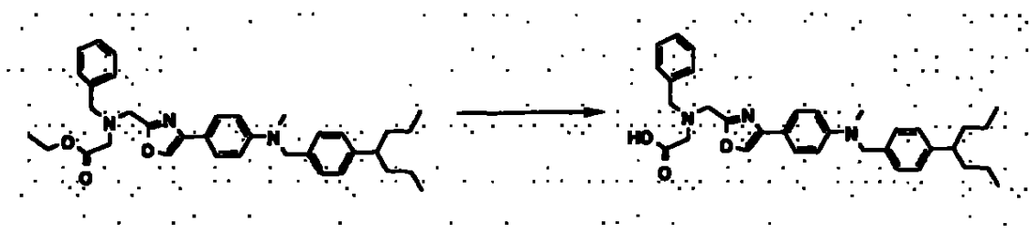
(5) {Benzyl-[4-(4-{methyl-[4-(1-propyl-butyl)benzyl]amino}phenyl)oxazol-2-ylmethyl]amino}acetic acid ethyl ester



Under an argon atmosphere, to a solution of N-benzyl-N-((4-(4-bromophenyl)oxazol-2-yl)methyl)glycine ethyl ester (200 mg, 0.466 mmol) obtained in Example 2-1(4) in dioxane (2.0 ml) were successively added N-methyl-4-(1-propylbutyl)benzylamine hydrochloride (131 mg, 0.512 mmol) obtained in Example 2-1(2), (R)-(+)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (29.0 mg, 0.0466 mmol), cesium carbonate (334 mg, 1.03 mmol) and palladium acetate (5.20 mg, 0.0233 mmol). The mixture was stirred at 90°C for 18 hr and (R)-(+)-2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (70.0 mg, 0.112 mmol) and palladium acetate (10.0 mg, 0.0445 mmol) were added. The mixture was stirred at 100°C for 3 hr and cesium carbonate (200 mg, 0.614 mmol) was added. The mixture was stirred for 12 hr. 4-Morpholinoaniline (83.0 mg, 0.466 mmol) was added and the mixture was stirred for 4 hr and passed through Celite at room temperature. The solvent was removed and the residue was purified by silica gel column chromatography (developing solvent; hexane:ethyl acetate=9:1) to give the title compound

(35.0 mg, yield 13%).

(6) {Benzyl-[4-(4-{methyl-[4-(1-propylbutyl)benzyl]amino}-phenyl)oxazol-2-ylmethyl]amino}acetic acid



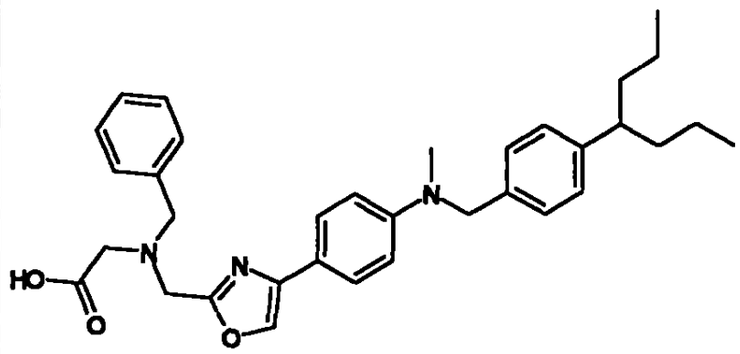
Under an argon atmosphere, to a solution of {benzyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)oxazol-2-ylmethyl]amino}acetic acid ethyl ester (30.0 mg, 0.0528 mmol) obtained in Example 2-1(5) in tetrahydrofuran (0.50 ml) were added methanol (0.50 ml) and a 2N aqueous sodium hydroxide solution (0.0528 ml, 0.106 mmol). The mixture was stirred at 70°C for 1.5 hr and 1N hydrochloric acid (0.106 ml, 0.106 mmol) and distilled water (2.0 ml) were successively added at room temperature. The solvent was removed, and hexane (0.2 ml) and distilled water (2.0 ml) were successively added. The precipitates were collected by filtration, and dried to give the title compound (16.0 mg, yield 56%).

^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.79(t, J=7.3Hz, 6H), 0.95-1.20(m, 4H), 1.40-1.65(m, 4H), 2.40-2.60(m, 1H), 3.02(s, 3H), 3.81(s, 2H), 3.93(s, 2H), 4.57(s, 2H), 6.78(d, J=8.8Hz, 2H), 7.00-7.40(m, 9H), 7.55(d, J=8.8Hz, 2H), 8.30(s, 1H), 12.30(br s, 1H).

melting point: 129°C-131°C

The structural formula and property value of Example 2-1 is shown in the following Table 2.

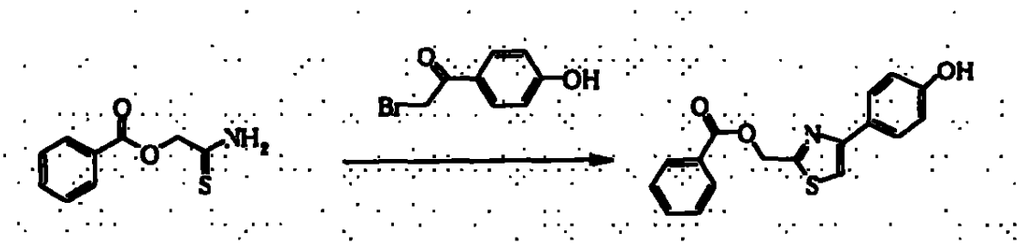
Table 2

Example	Structural formula	m.p. (°C)
2-1		129 - 131

Example 3-1

5-(4-{4-[4-(1-Propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethoxy)nicotinic acid

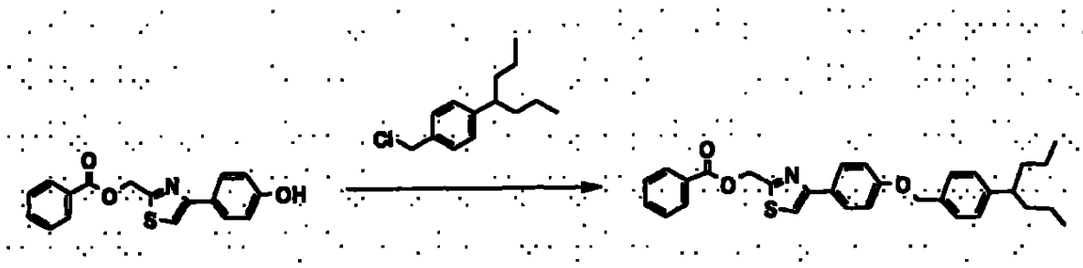
(1) (4-(4-Hydroxyphenyl)thiazol-2-yl)methyl benzoate



To a solution of 2-(benzoyloxy)ethanethioamide (4 g, 20.488 mmol) and sodium hydrogen carbonate (1.72 g, 20.488 mmol) in N,N-dimethylacetamide (4 ml) was added dropwise a solution of 2-bromo-4'-hydroxyacetophenone (5 g, purity 88%, 20.488 mmol) in N,N-dimethylacetamide (8 ml) at room temperature, and the mixture was stirred at the same temperature for 2 hr. After the completion of the reaction, ethanol and water were added and the precipitates were collected by filtration and washed with 50% ethanol. The obtained solid was dried under reduced pressure to give the title compound (5.336 g, 84.1%).

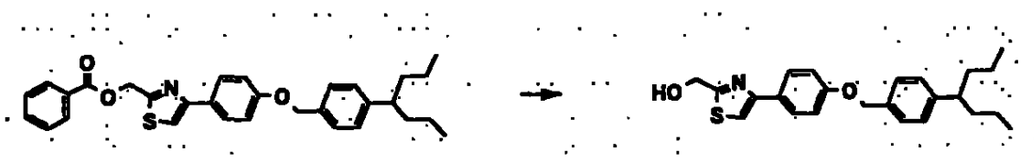
(2) (4-(4-(4-(1-Propylbutyl)benzyloxy)phenyl)thiazol-2-

yl)methyl benzoate



To a solution of (4-(4-hydroxyphenyl)thiazol-2-yl)methyl benzoate (14.0 g, 44.9 mmol) obtained in Example 3-1(1) in N,N-dimethylacetamide (70 ml) were added 4-(1-propylbutyl)benzyl chloride (10.1 g, 44.9 mmol), potassium carbonate (12.4 g, 89.9 mmol) and potassium iodide (75 mg, 0.45 mmol) and the mixture was stirred at 80°C for 3 hr. After allowing to cool, ethyl acetate was added and the mixture was washed successively with water and saturated brine and dried over magnesium sulfate. After filtration, the solvent was removed and ethanol (120 ml) was added. The mixture was heated to 50°C. After allowing to cool, the precipitated crystals were collected by filtration and dried to give the title compound (19.5 g, yield 87%).

(3) (4-(4-(4-(1-Propylbutyl)benzyloxy)phenyl)thiazol-2-yl)methanol



To (4-(4-(4-(1-propylbutyl)benzyloxy)phenyl)thiazol-2-yl)methyl benzoate (26.5 g, 53.1 mmol) obtained in Example 3-1(2) were added methanol (159 ml), tetrahydrofuran (27 ml) and a 2N-aqueous sodium hydroxide solution (39.8 ml, 79.6 mmol) and the mixture was stirred at 80°C for 1 hr. The solvent was removed and water (265 ml) was added. The mixture was stirred at room temperature for 1 hr. The crystals were collected by

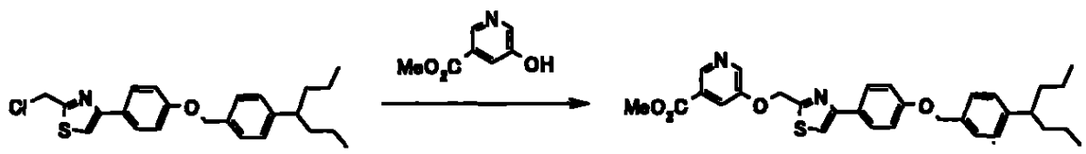
filtration, dissolved in toluene (100 ml) and ethyl acetate (10 ml). The mixture was washed with saturated brine and dried over magnesium sulfate and filtered and the solvent was removed to give the title compound (20.5 g, yield 98%).

(4) (4-(4-(4-(1-Propylbutyl)benzyloxy)phenyl)thiazol-2-yl)methyl chloride



To a solution of (4-(4-(4-(1-propylbutyl)benzyloxy)phenyl)thiazol-2-yl)methanol (20.5 g, 51.8 mmol) obtained in Example 3-1(3) in chloroform (103 ml) was added thionyl chloride (9.17 g, 77.7 mmol) and the mixture was stirred at room temperature for 1 hr. The solvent was removed to give the title compound (21.9 g, quant.).

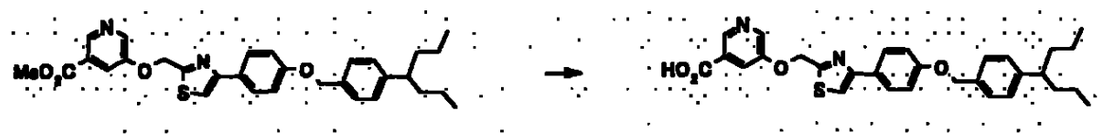
(5) 5-(4-{4-[4-(1-Propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethoxy)nicotinic acid methyl ester



N,N-Dimethylacetamide (104 ml), methyl 5-hydroxynicotinate (5.25 g, 40.8 mmol), potassium carbonate (13.0 g, 94.2 mmol) and potassium iodide (520 mg, 3.1 mmol) were added to (4-(4-(4-(1-propylbutyl)benzyloxy)phenyl)thiazol-2-yl)methyl chloride (13.0 g, 31.4 mmol) obtained in Example 3-1(4) and the mixture was stirred at 75°C for 2 hr. After allowing to cool, ethyl acetate was added and the mixture was washed successively with water, a saturated aqueous sodium

hydrogen carbonate solution, water and saturated brine, and dried over magnesium sulfate. After filtration, the solvent was removed and the residue was purified by silica gel column chromatography (eluent; toluene-ethyl acetate, 5:1). The obtained crude crystals were slurried for washing with ether to give the title compound (9.91 g, yield 59%).

(6) 5-(4-{4-[4-(1-Propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethoxy)nicotinic acid



To 5-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethoxy)nicotinic acid methyl ester (9.50 g, 17.9 mmol) obtained in Example 3-1(5) were added tetrahydrofuran (62.5 ml), ethanol (62.5 ml) and a 2N-aqueous sodium hydroxide solution (17.9 ml, 35.8 mmol), and the mixture was stirred at 70°C for 2.5 hr. 2N-Hydrochloric acid (17.9 ml, 35.8 mmol) was added under ice-cooling and the mixture was concentrated under reduced pressure. Ethanol (19 ml) and water (9.5 ml) were added, and after stirring, the crystals were collected by filtration and dried to give the title compound (9.15 g, yield 99%).

^{1}H NMR (DMSO-d_6, 400 MHz) δ 0.81(t, J=7.3Hz, 6H), 1.05-1.13(m, 4H), 1.48-1.57(m, 4H), 2.5-2.56(m, 1H), 5.09(s, 2H), 5.66(s, 2H), 7.09(d, J=9.04Hz, 2H), 7.19(d, J=8.32Hz, 2H), 7.38(d, J=8.12Hz, 2H), 7.91(d, J=9.04Hz, 2H), 7.98-7.99(m, 1H), 8.03(s, 1H), 8.64(d, J=3Hz, 1H), 8.72(d, J=1.4Hz, 1H), 13.52(s, 1H)

melting point: 172-174°C

Examples 3-2 to 3-132

In the same manner as in Example 3-1 and using other conventional methods where necessary, the compounds of Examples 3-2 to 3-132 were produced. The structural formulas and

property values of the obtained compounds, as well as those of Example 3-1, are shown in the following Tables.

Table 3-1

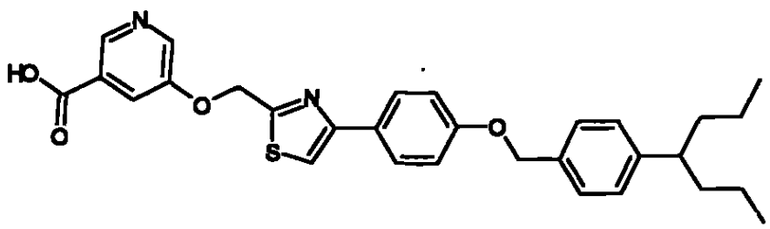
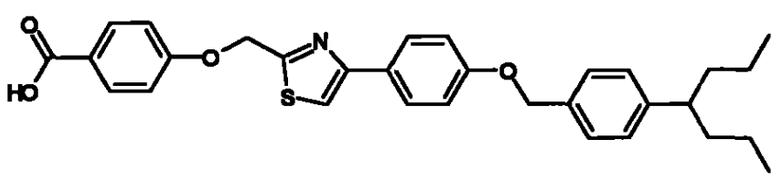
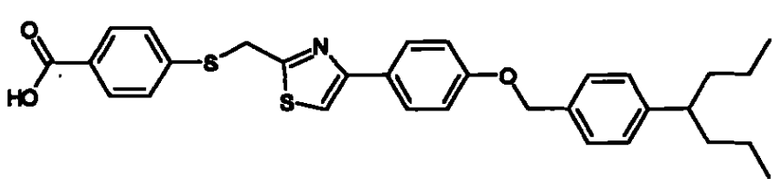
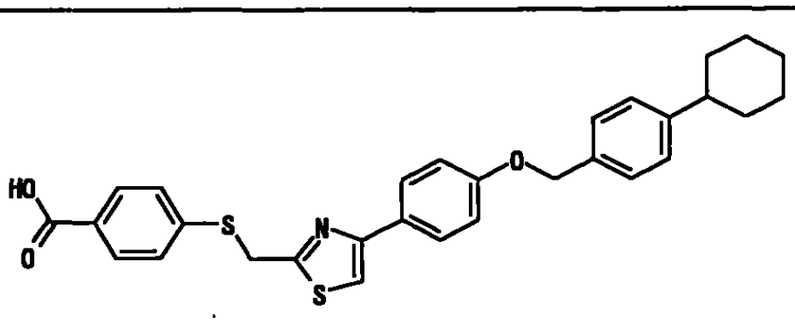
Example	Structural formula	m.p.(℃)
3-1		172 - 174
3-2		204 - 207
3-3		117 - 118
3-4		amorphous

Table 3-2

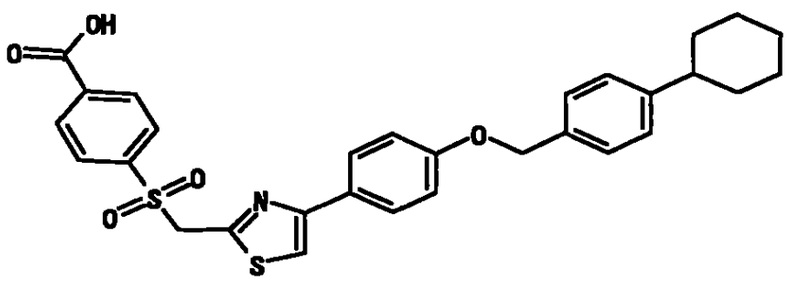
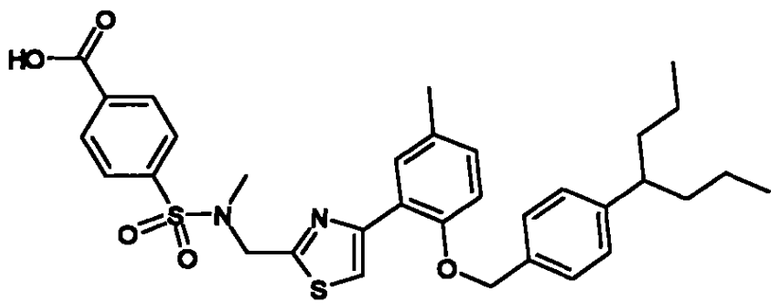
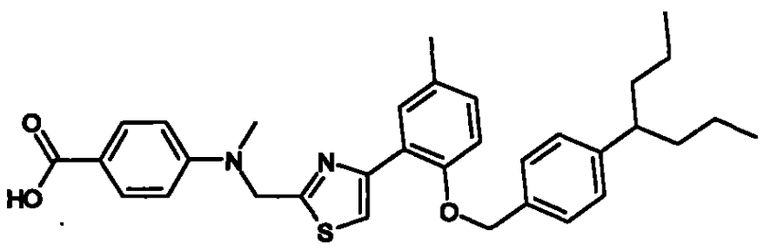
Example	Structural formula	m.p.(°C)
3-5		amorphous
3-6		130 – 132
3-7		184 – 187

Table 3-3

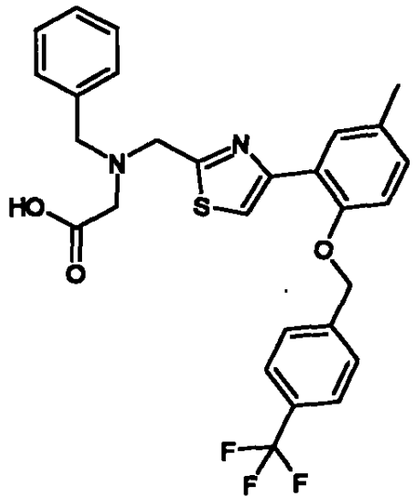
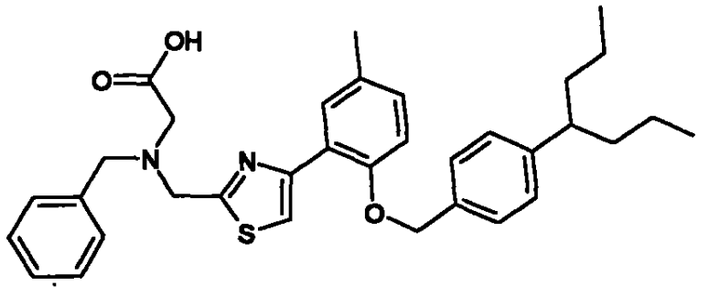
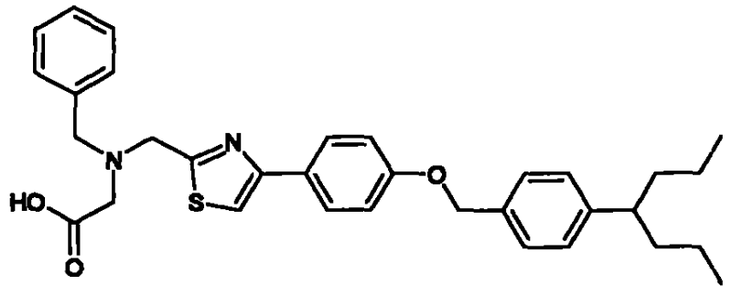
Example	Structural formula	m.p.(°C)
3-8		168 - 170
3-9		126 - 128
3-10		145 - 148

Table 3-4

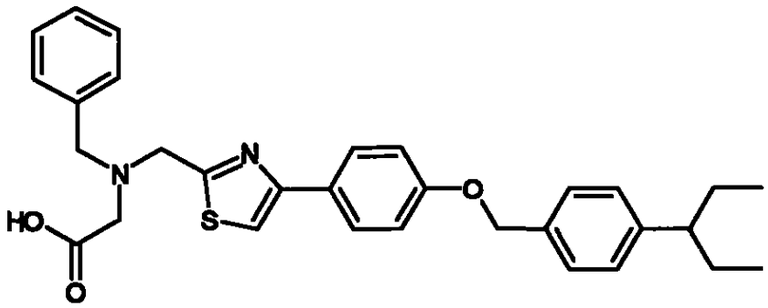
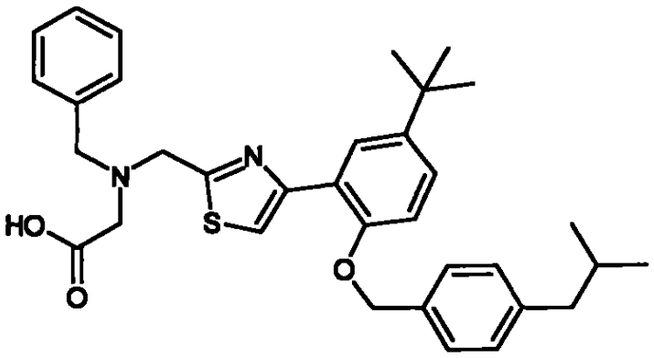
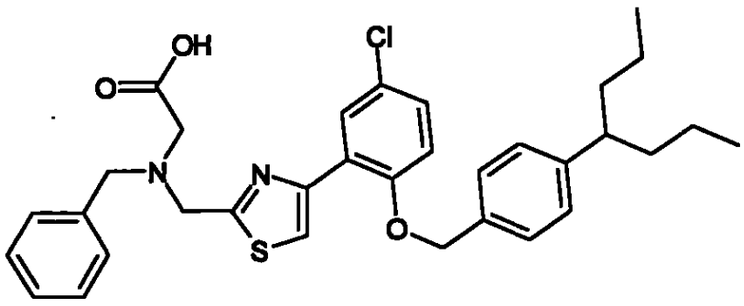
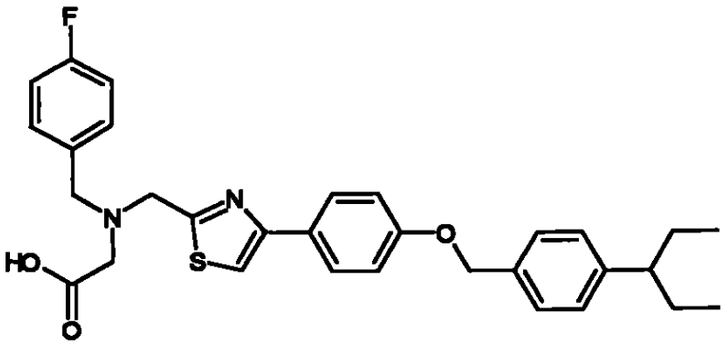
Example	Structural formula	m.p.(°C)
3-11		144 – 146
3-12		155 – 157
3-13		130 – 131
3-14		153 – 155

Table 3-5

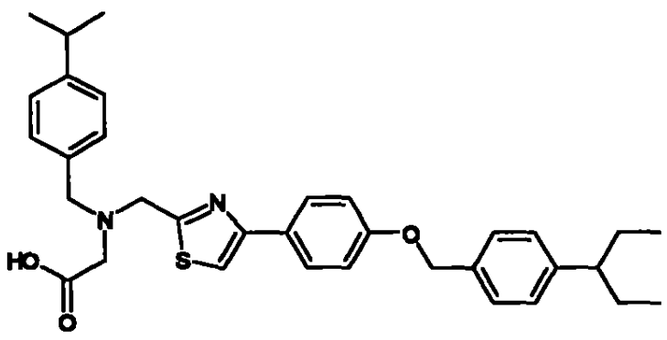
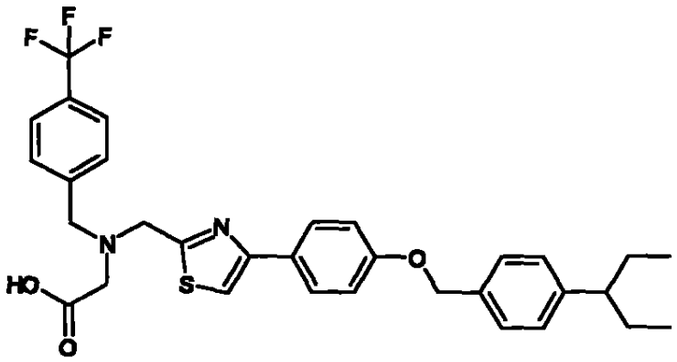
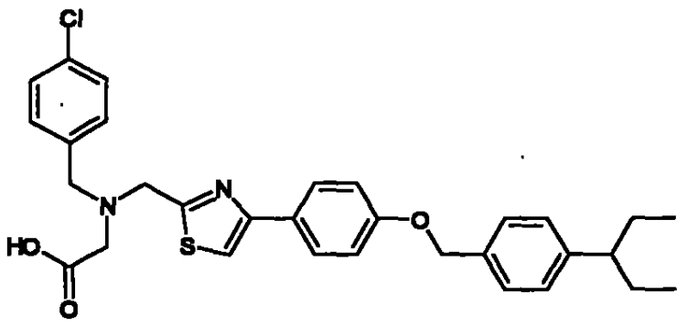
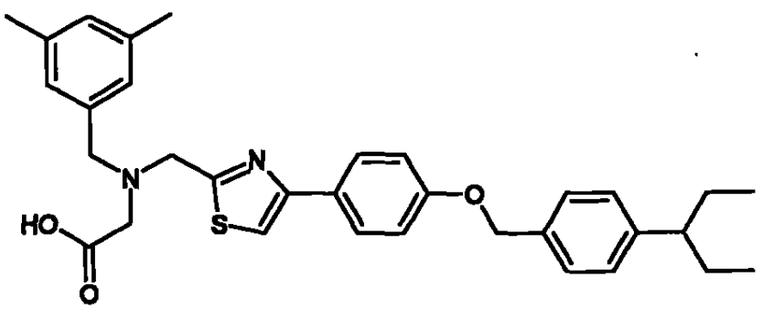
Example	Structural formula	m.p.(°C)
3-15		138 – 140
3-16		136 – 138
3-17		154 – 157
3-18		114 – 119

Table 3-6

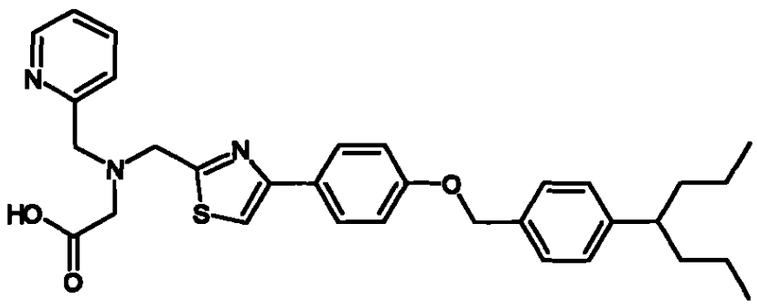
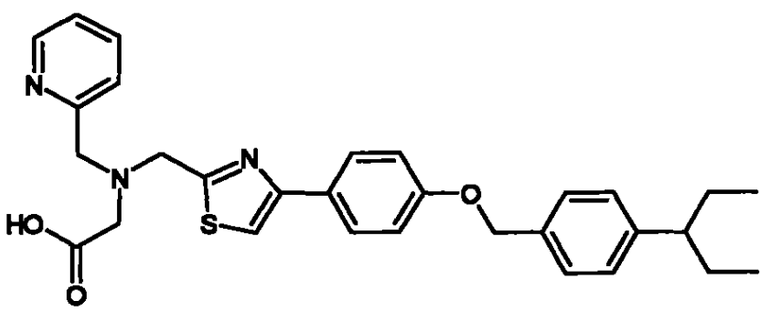
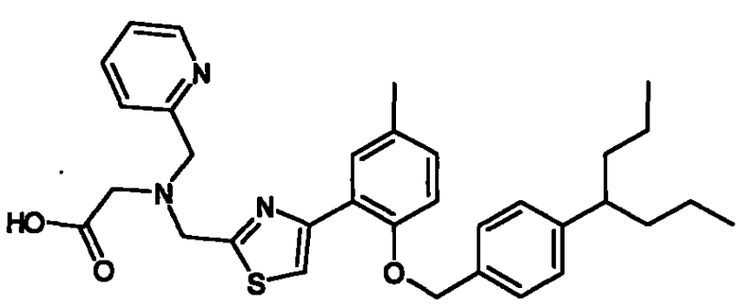
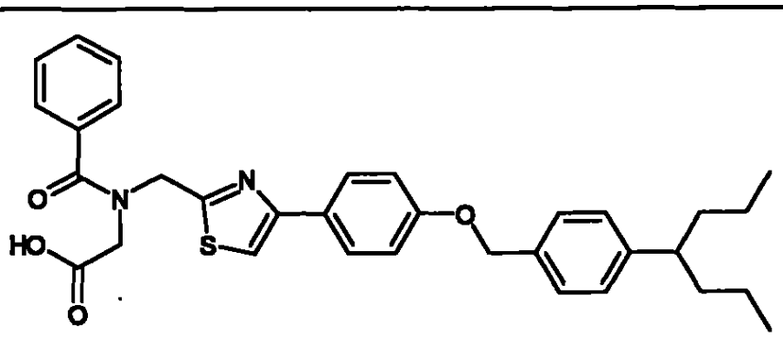
Example	Structural formula	m.p.(°C)
3-19		155 – 156
3-20		156 – 157
3-21		118 – 120
3-22		141 – 144

Table 3-7

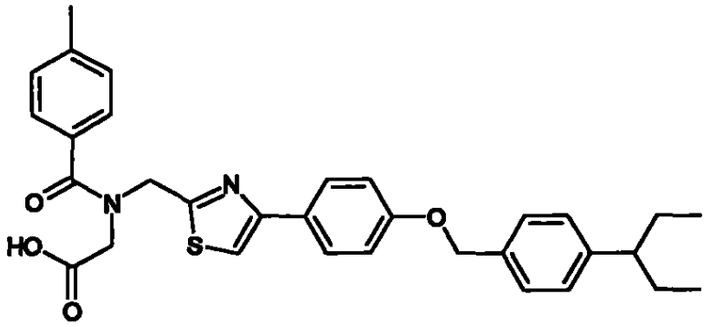
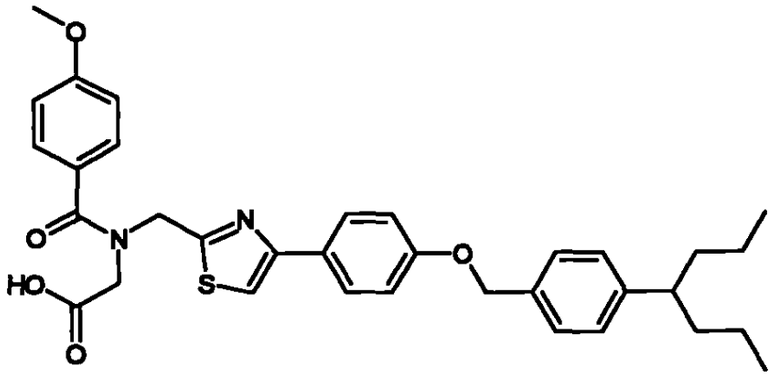
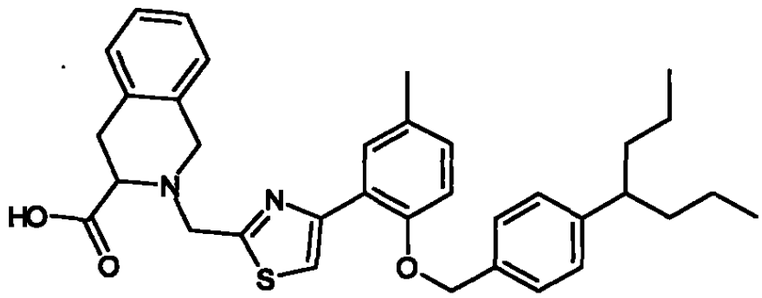
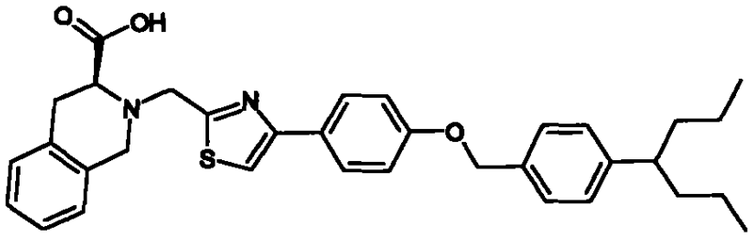
Example	Structural formula	m.p.(°C)
3-23		142 - 144
3-24		99 - 101
3-25		149 - 152
3-26		90 - 93

Table 3-8

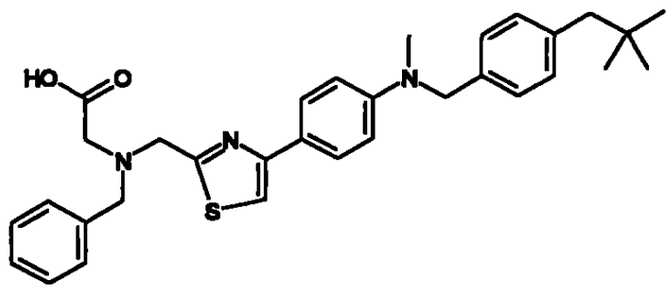
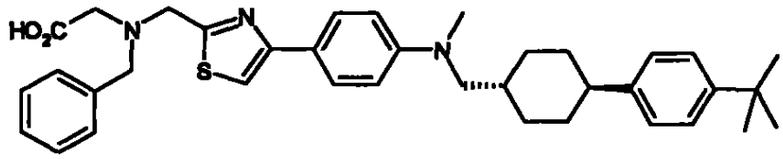
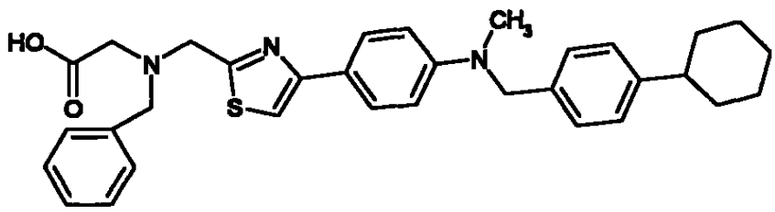
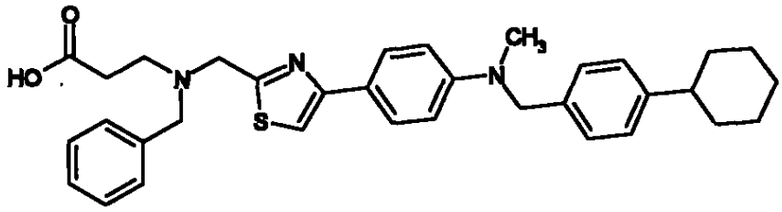
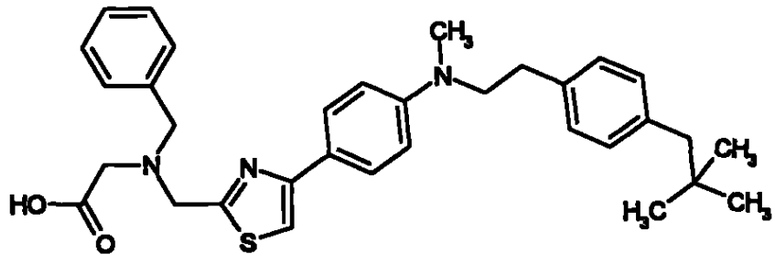
Example	Structural formula	m.p.(°C)
3-27		159 – 160
3-28		192 – 195
3-29		148 – 150
3-30		amorphous
3-31		133 – 134

Table 3-9

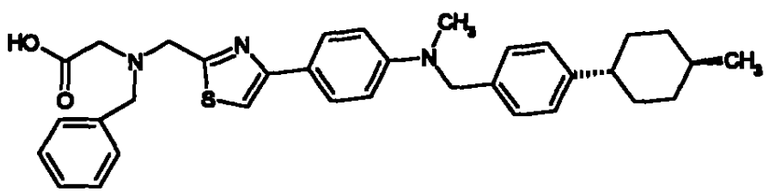
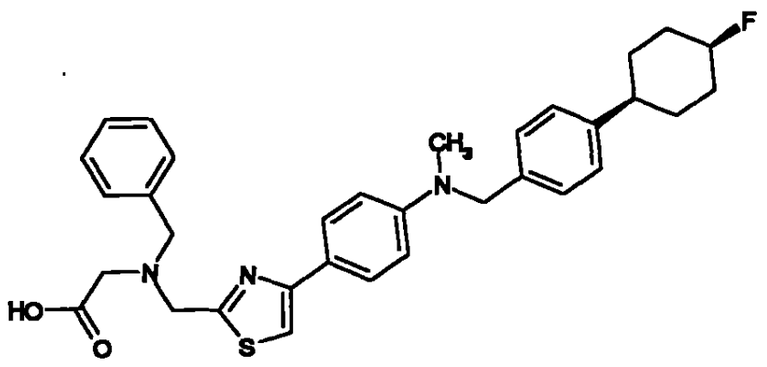
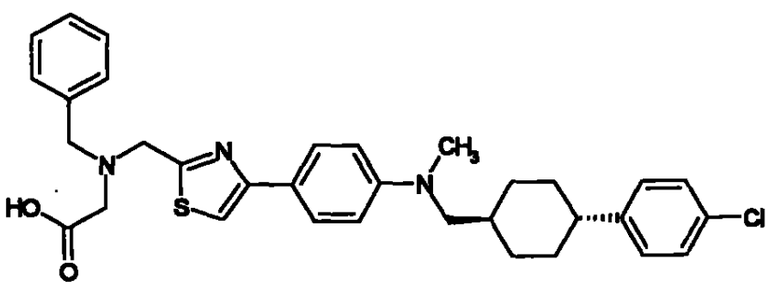
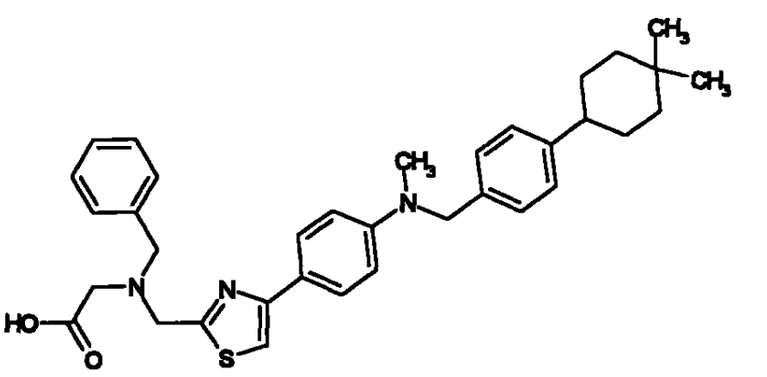
Example	Structural formula	m.p.(°C)
3-32		157 – 159
3-33		146 – 147
3-34		180 – 182
3-35		amorphous

Table 3-10

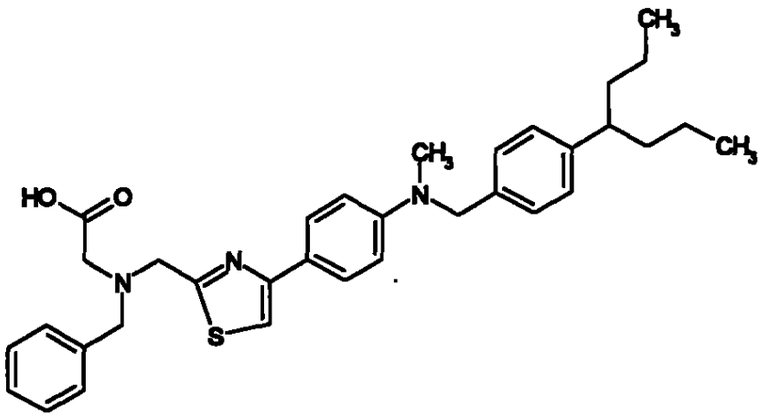
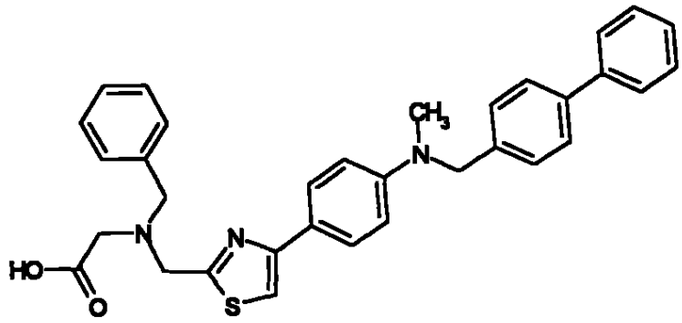
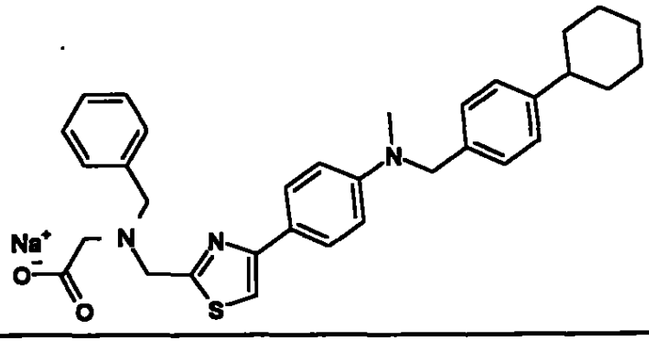
Example	Structural formula	m.p.(°C)
3-36		amorphous
3-37		167 – 170
3-38		250 –

Table 3-11

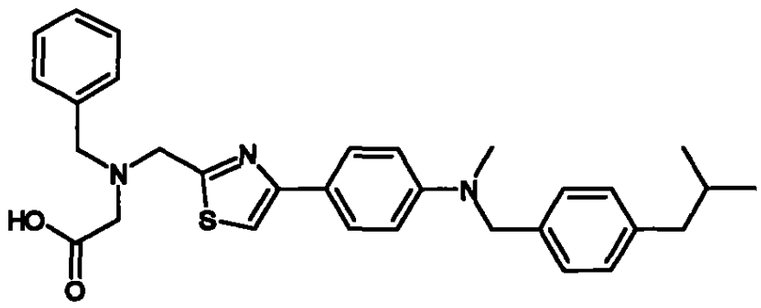
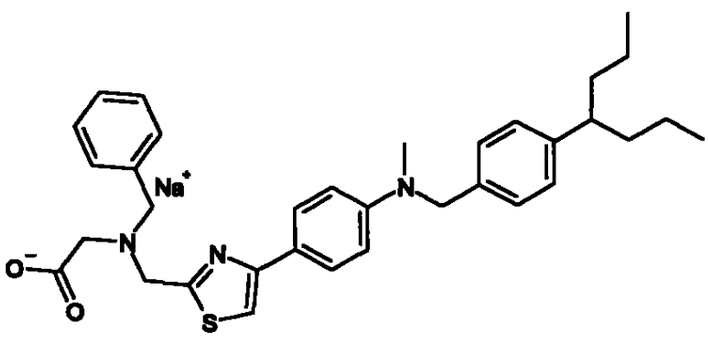
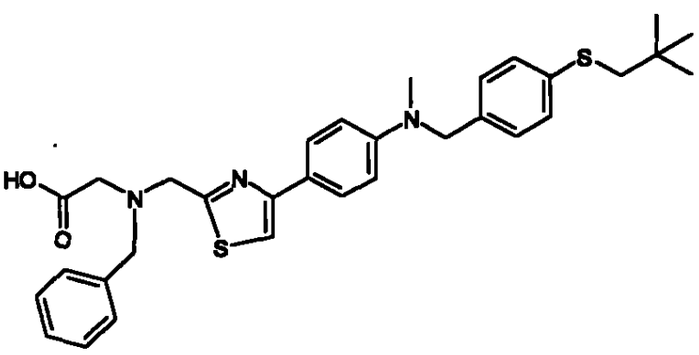
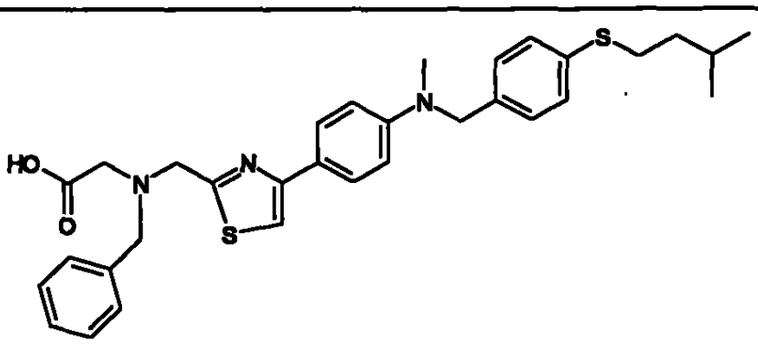
Example	Structural formula	m.p.(°C)
3-39		149 - 151
3-40		amorphous
3-41		143
3-42		122

Table 3-12

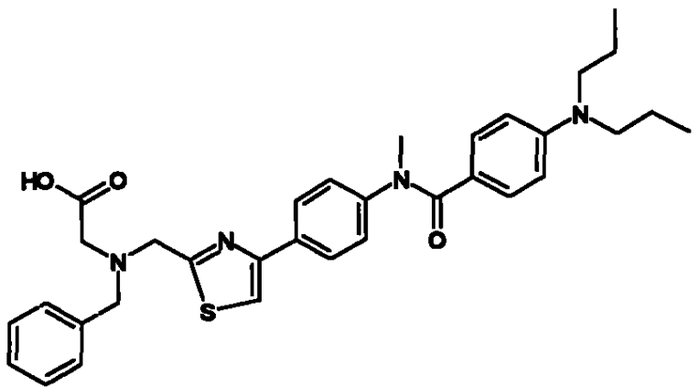
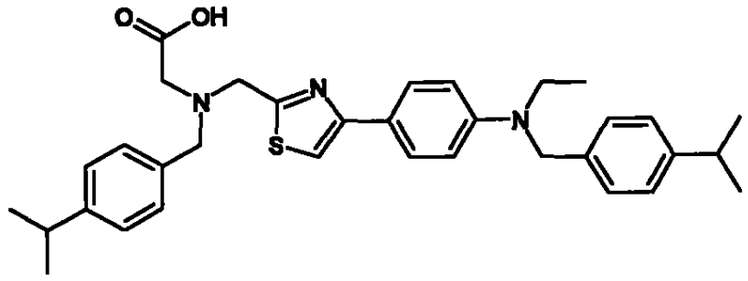
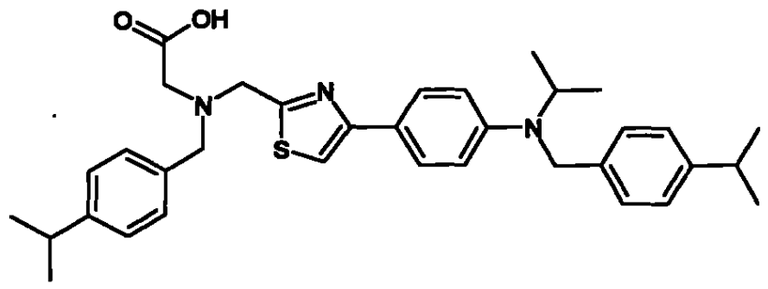
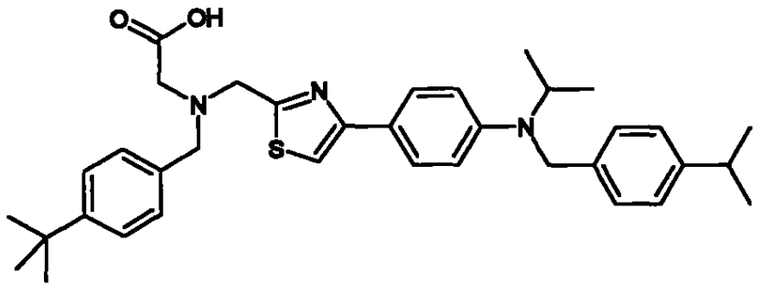
Example	Structural formula	m.p.(°C)
3-43		amorphous
3-44		74 – 78
3-45		77 – 82
3-46		82 – 87

Table 3-13

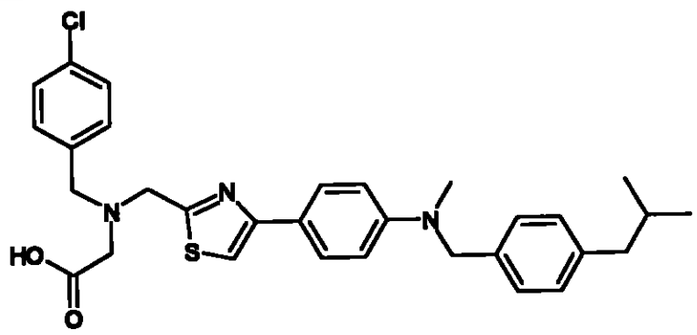
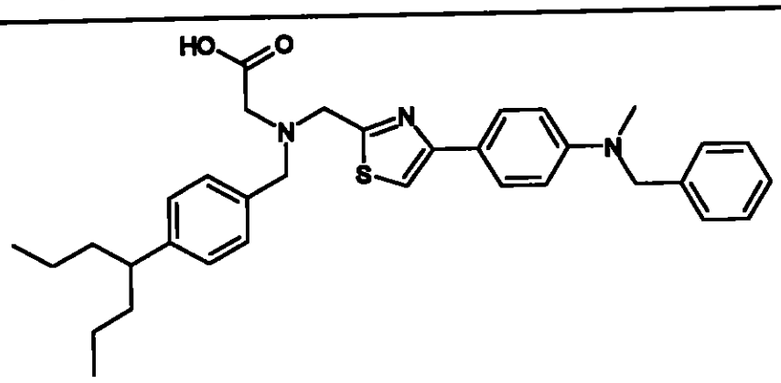
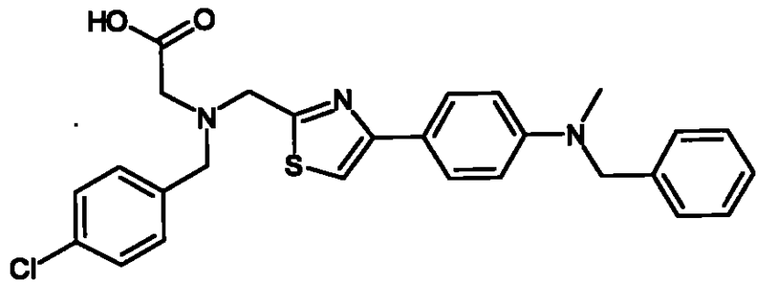
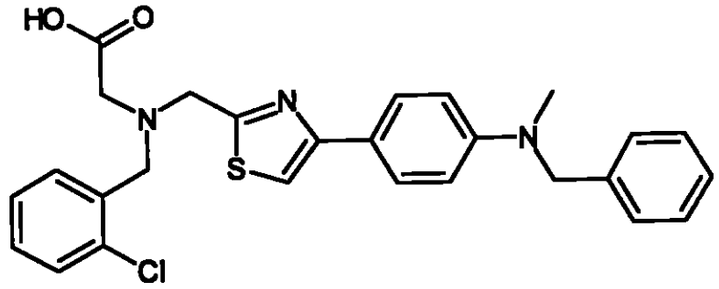
Example	Structural formula	m.p.(°C)
3-47		153 – 157
3-48		137 – 140
3-49		140 – 142
3-50		132 – 134

Table 3-14

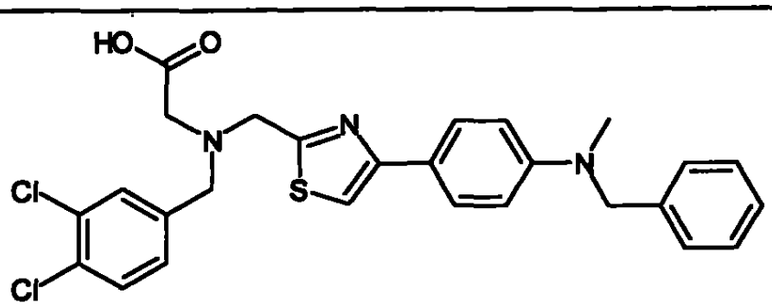
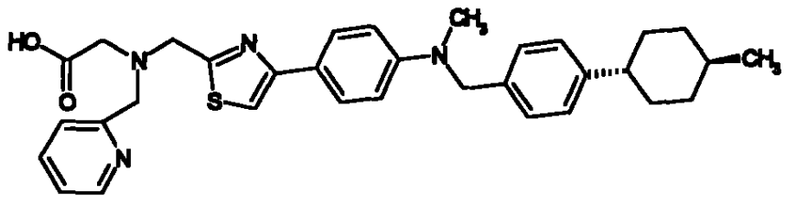
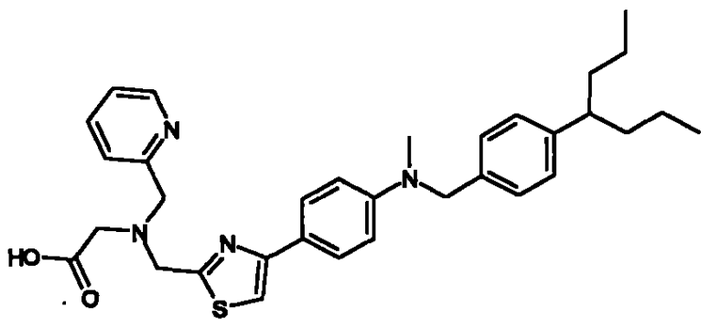
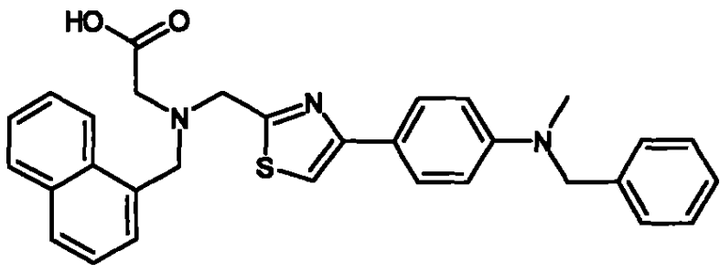
Example	Structural formula	m.p.(°C)
3-51		69 - 72
3-52		230 -
3-53		117 - 120
3-54		78 - 83

Table 3-15

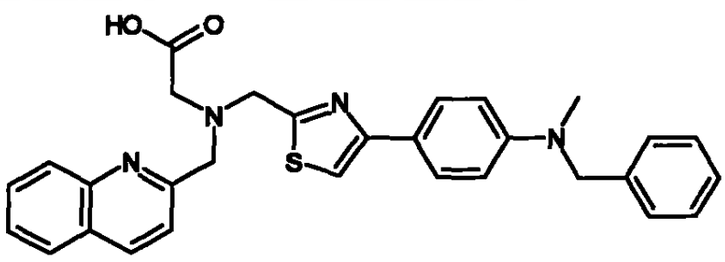
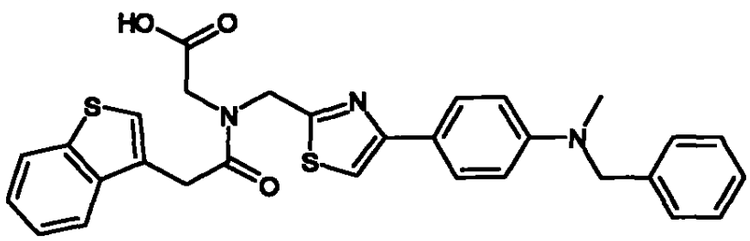
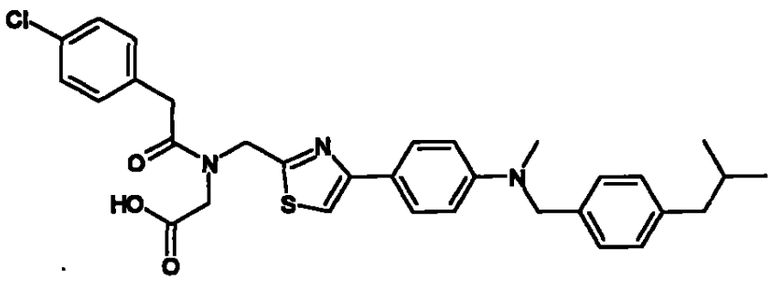
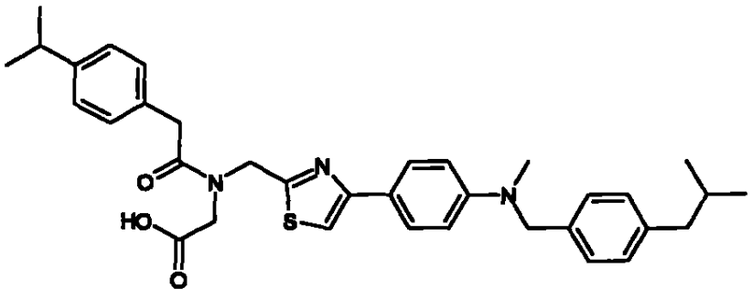
Example	Structural formula	m.p.(°C)
3-55		144 – 147
3-56		186 – 188
3-57		150 – 152
3-58		124 – 126

Table 3-16

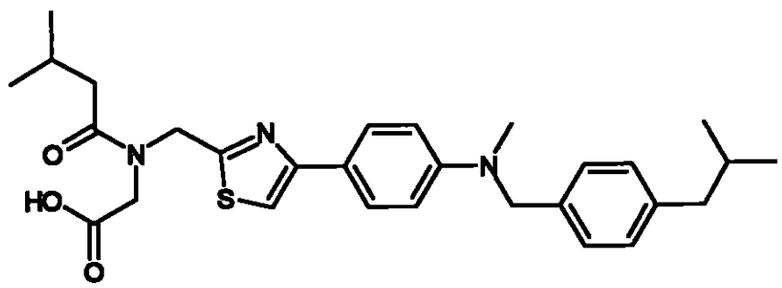
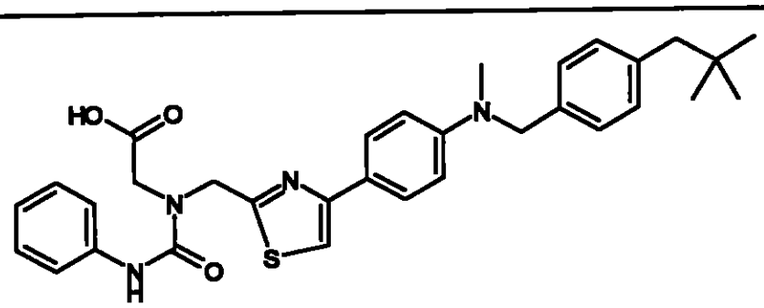
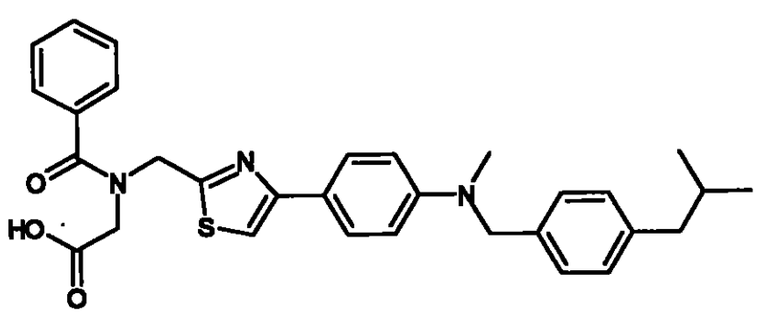
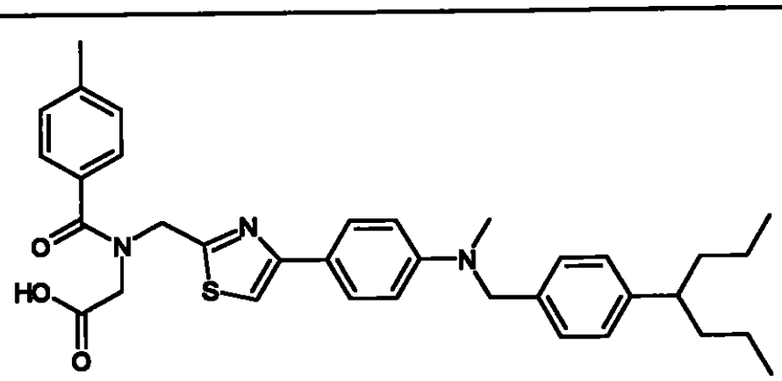
Example	Structural formula	m.p.(°C)
3-59		117 – 118
3-60		152 – 153
3-61		143 – 145
3-62		114 – 117

Table 3-17

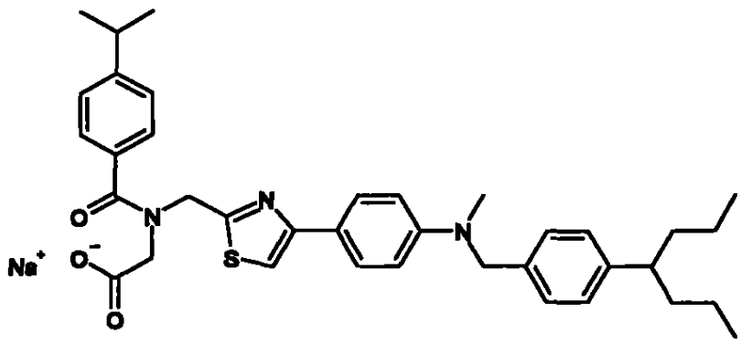
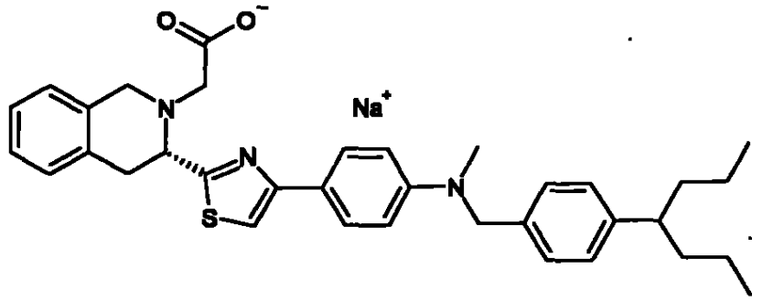
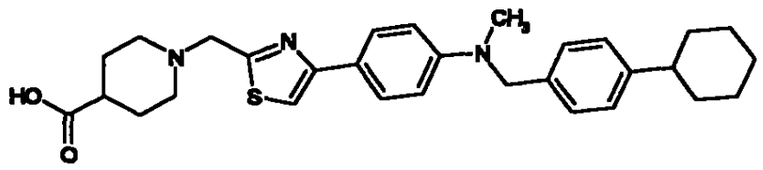
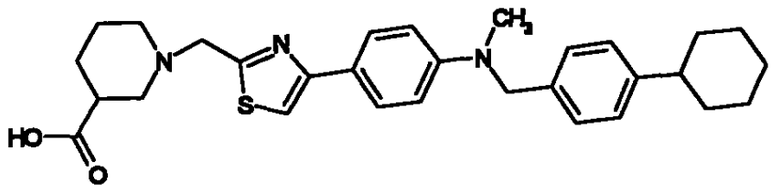
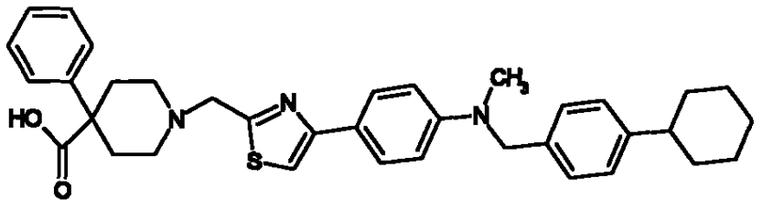
Example	Structural formula	m.p.(°C)
3-63		183 - 188
3-64		186 - 187
3-65		amorphous
3-66		176 - 180
3-67		220 - 222

Table 3-18

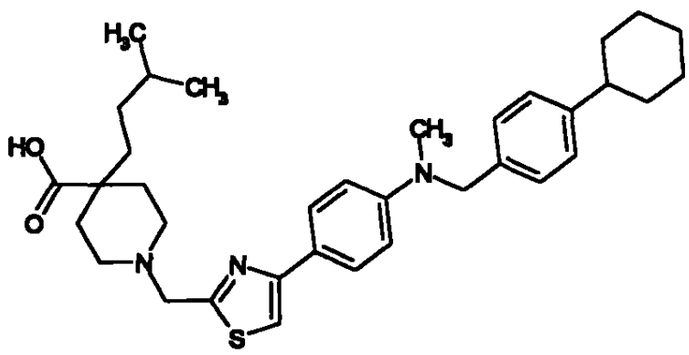
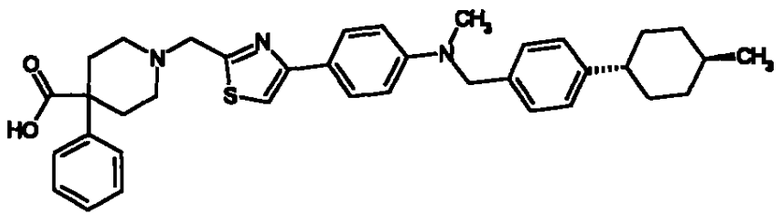
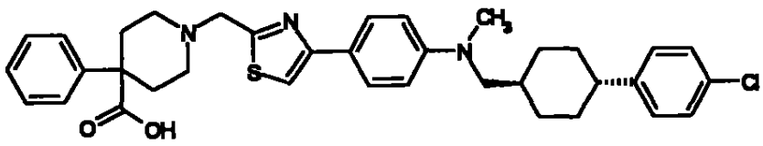
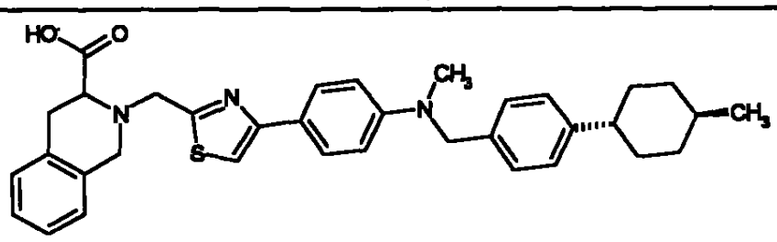
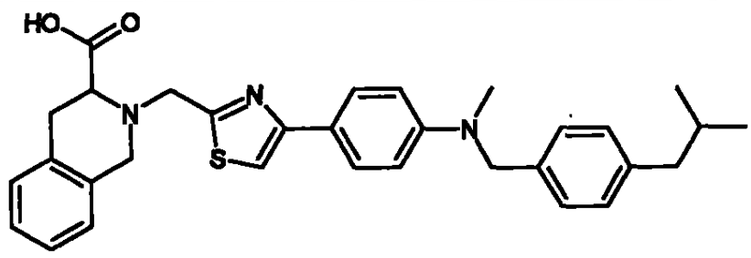
Example	Structural formula	m.p.(°C)
3-68		233 - 235
3-69		229 - 231
3-70		167 - 170 decomp.
3-71		202 - 205
3-72		168 - 170

Table 3-19

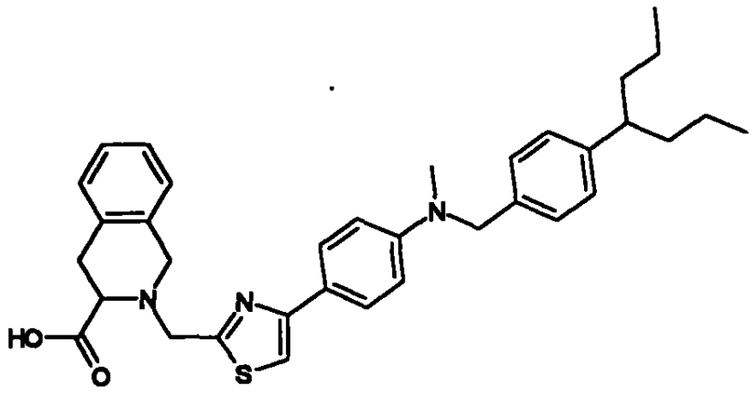
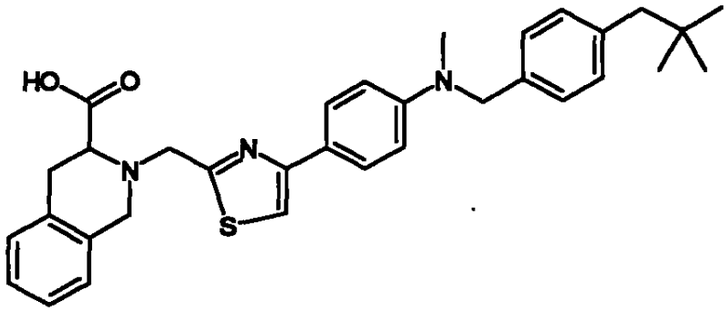
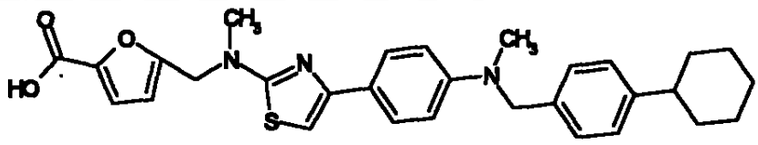
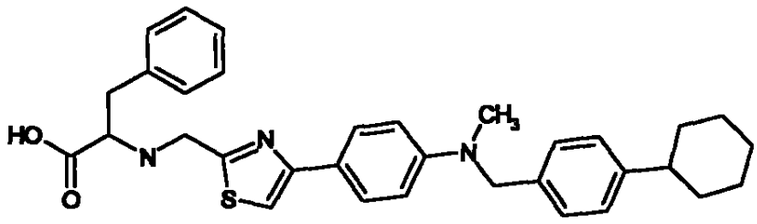
Example	Structural formula	m.p.(°C)
3-73		176 - 179
3-74		175 - 177
3-75		158 - 161
3-76		185 - 190

Table 3-20

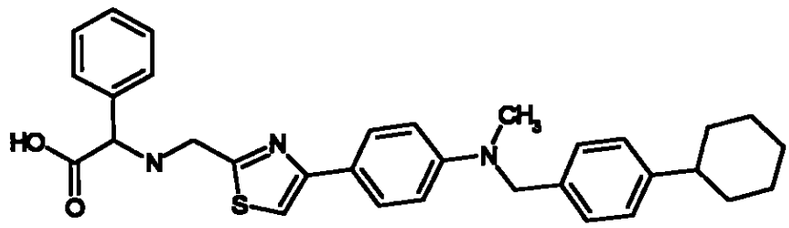
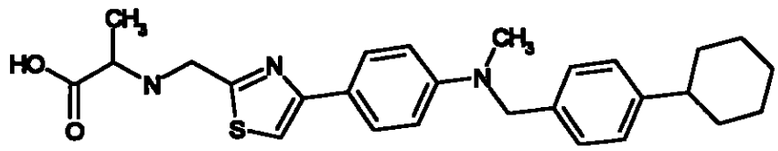
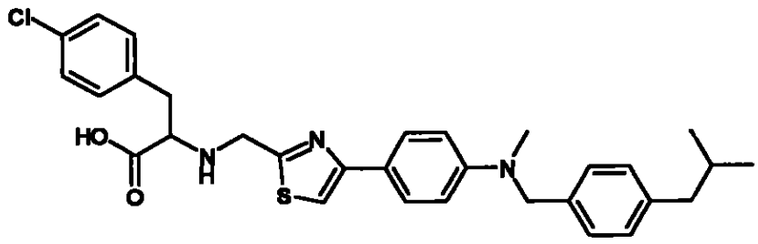
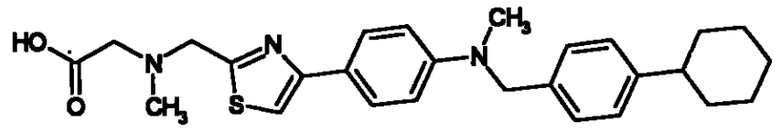
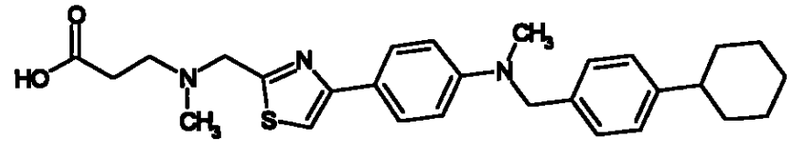
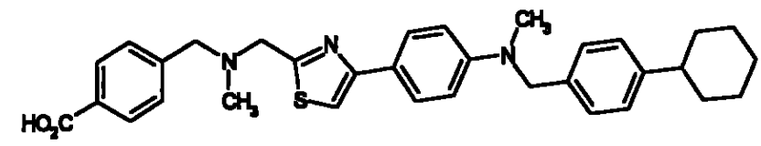
Example	Structural formula	m.p.(°C)
3-77		183 – 186
3-78		135 – 138
3-79		199 – 204
3-80		152 – 155
3-81		amorphous
3-82		amorphous

Table 3-21

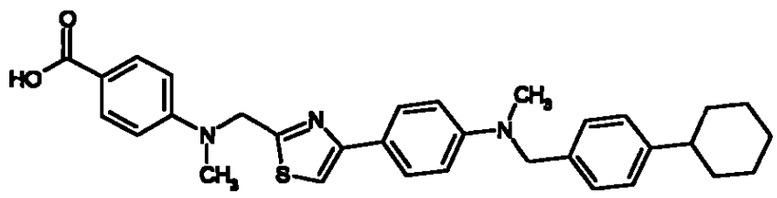
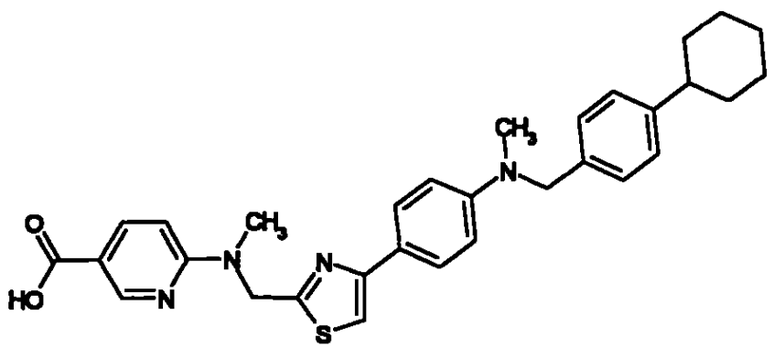
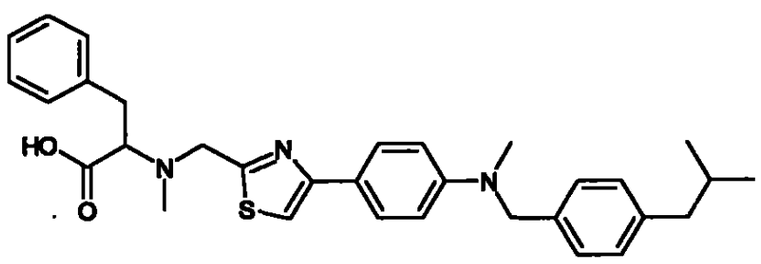
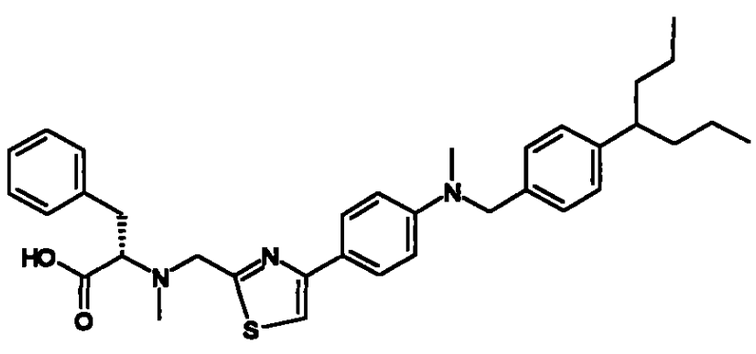
Example	Structural formula	m.p.(°C)
3-83		amorphous
3-84		226 – 228
3-85		138 – 139
3-86		143

Table 3-22

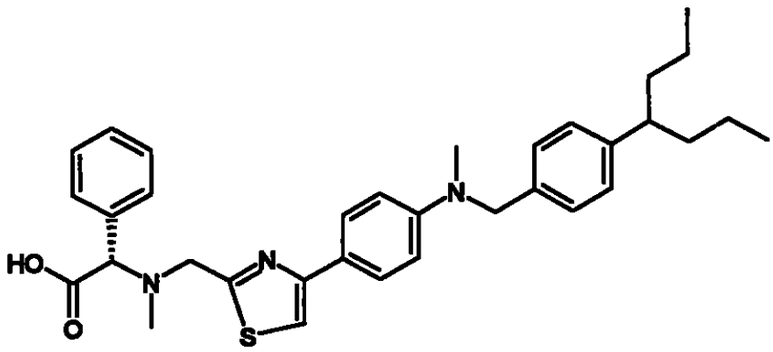
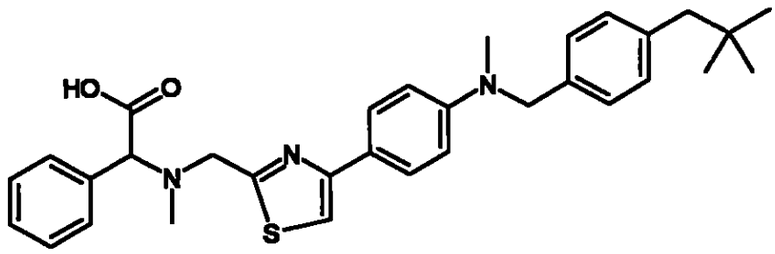
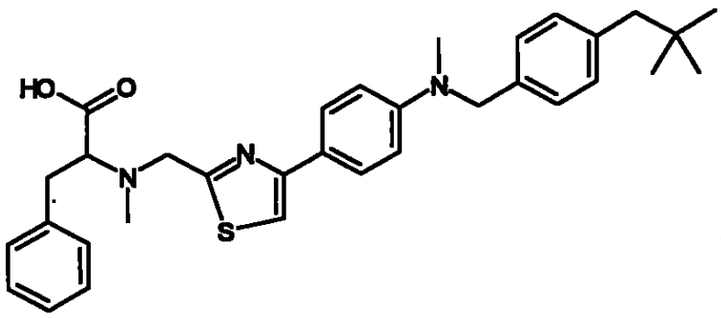
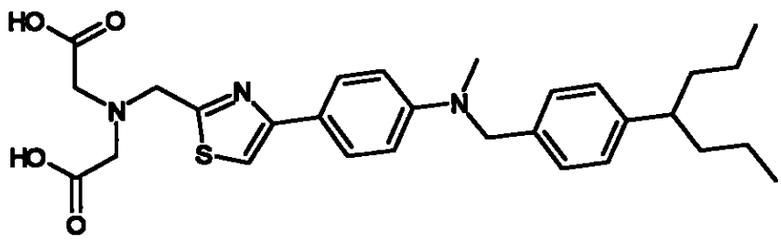
Example	Structural formula	m.p.(°C)
3-87		146
3-88		171 – 173
3-89		160 – 161
3-90		amorphous

Table 3-23

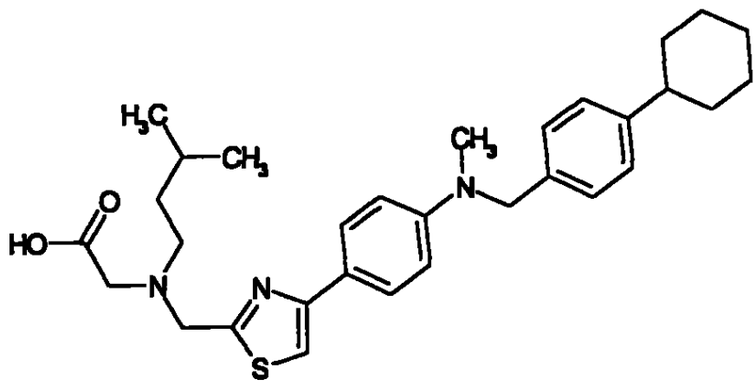
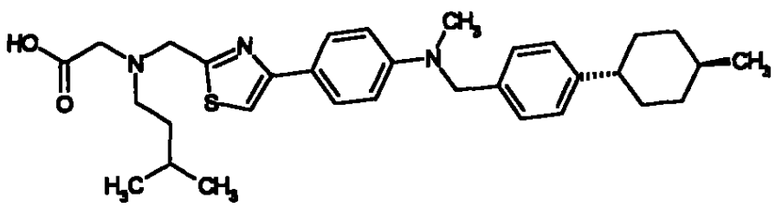
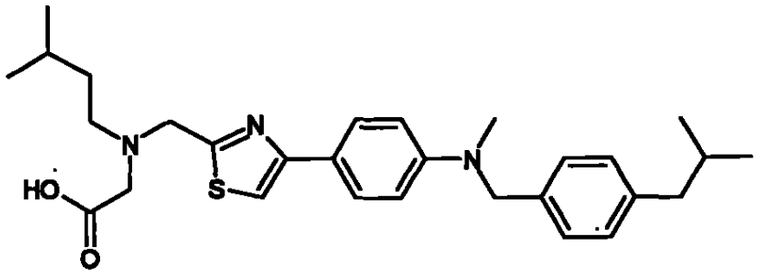
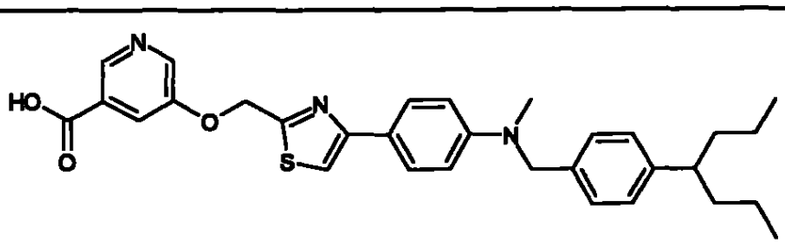
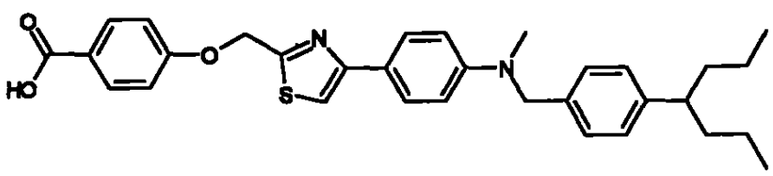
Example	Structural formula	m.p.(°C)
3-91		153 - 154
3-92		166 - 167
3-93		155 - 156
3-94		178 - 181
3-95		175 - 177

Table 3-24

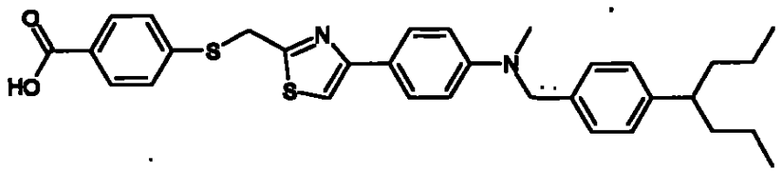
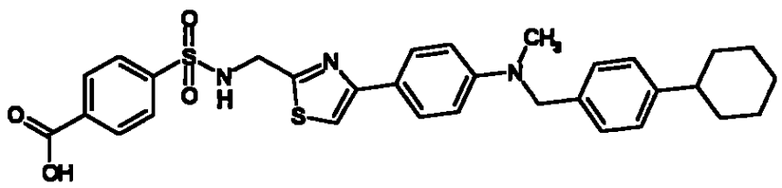
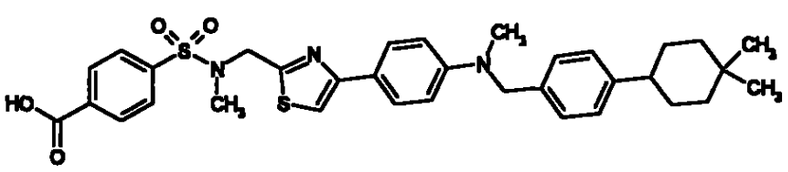
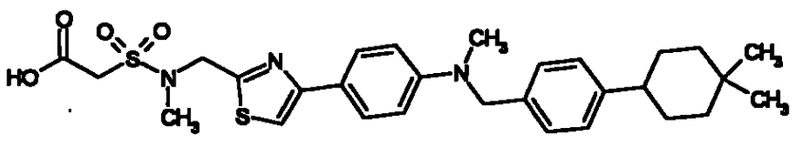
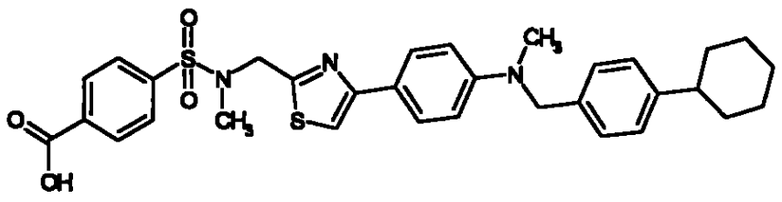
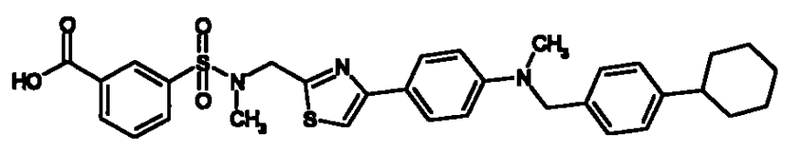
Example	Structural formula	m.p.(°C)
3-96		126 – 127
3-97		202 – 203
3-98		218 – 221
3-99		184 – 190
3-100		193 – 196
3-101		164 – 166

Table 3-25

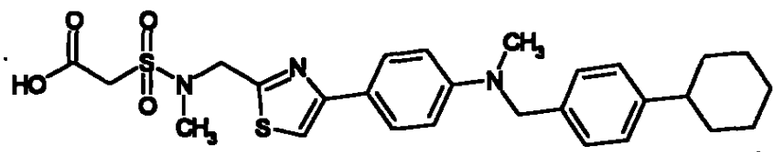
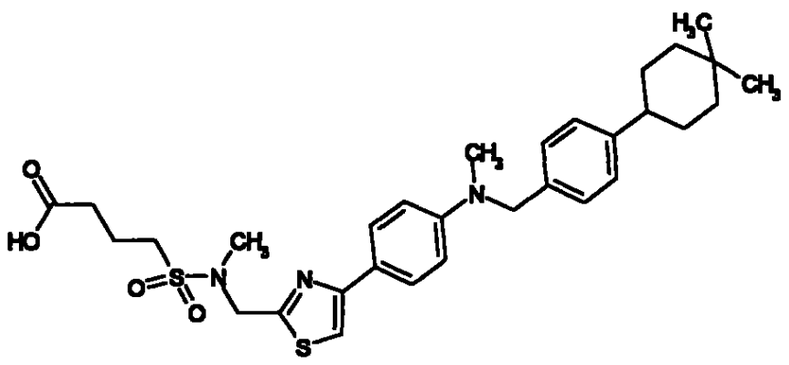
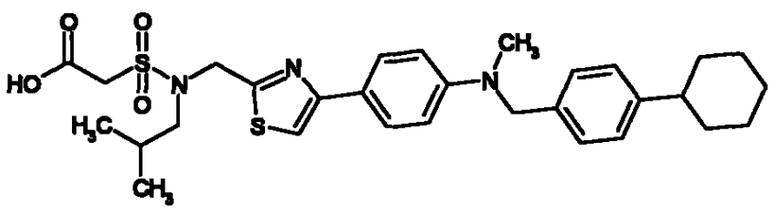
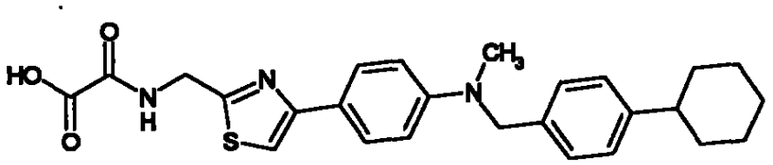
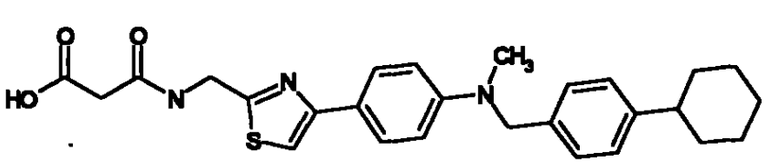
Example	Structural formula	m.p.(°C)
3-102		178 - 183
3-103		amorphous
3-104		104 - 110
3-105		amorphous
3-106		amorphous

Table 3-26

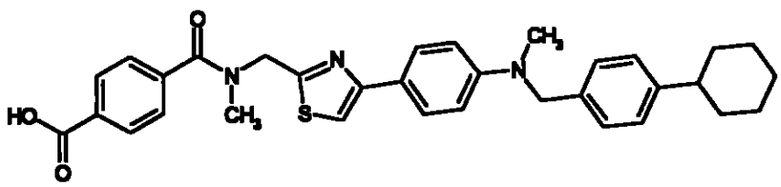
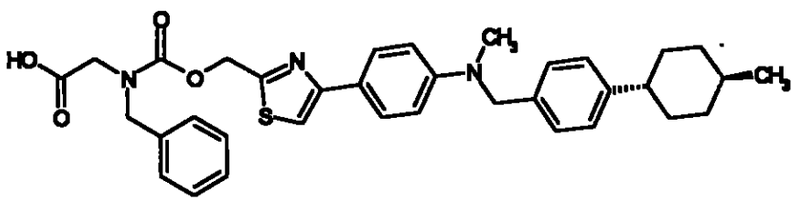
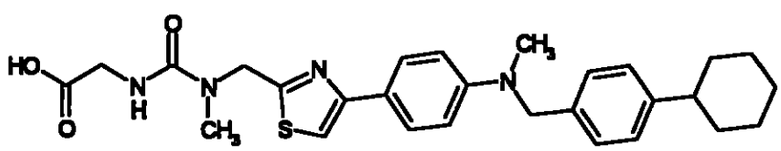
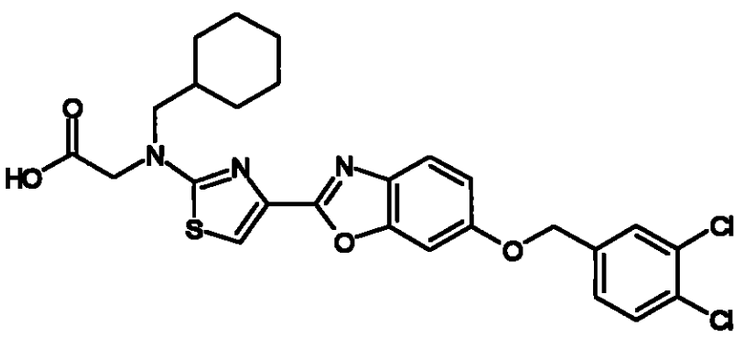
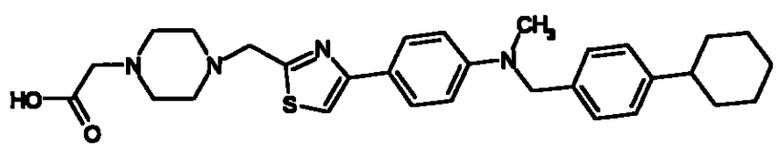
Example	Structural formula	m.p.(°C)
3-107		162 – 164
3-108		amorphous
3-109		149 – 150
3-110		198 – 200
3-111		190 – 191

Table 3-27

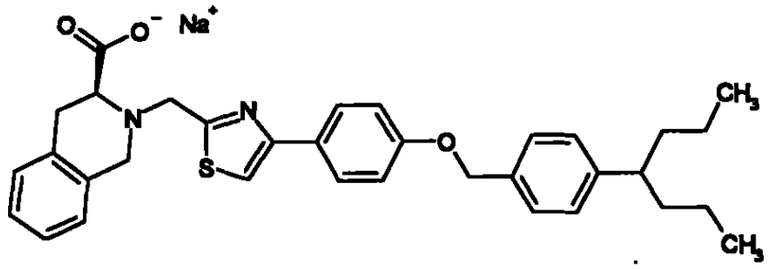
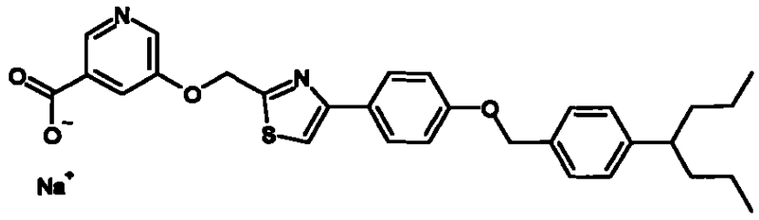
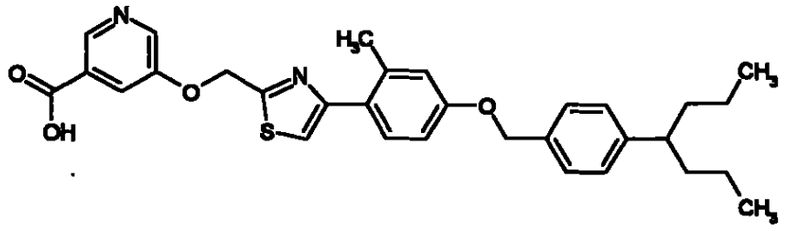
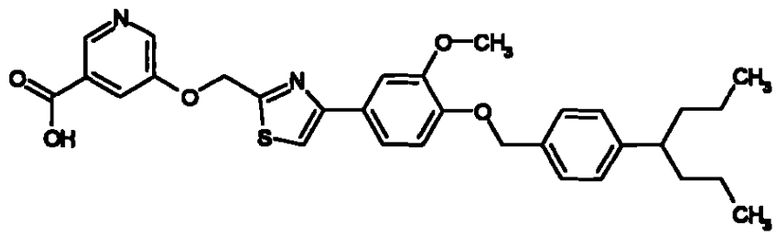
Example	Structural formula	m.p.(°C)
3-112		254 – 255
3-113		amorphous
3-114		148 – 150
3-115		156 – 158

Table 3-28

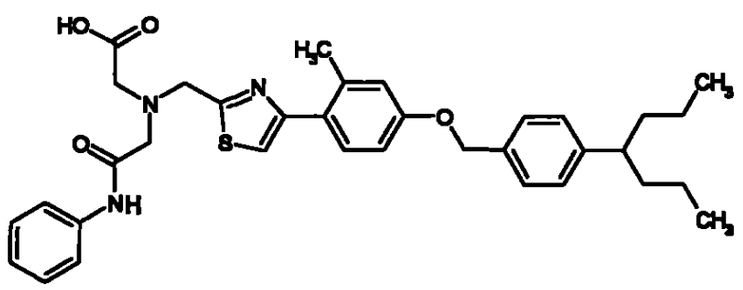
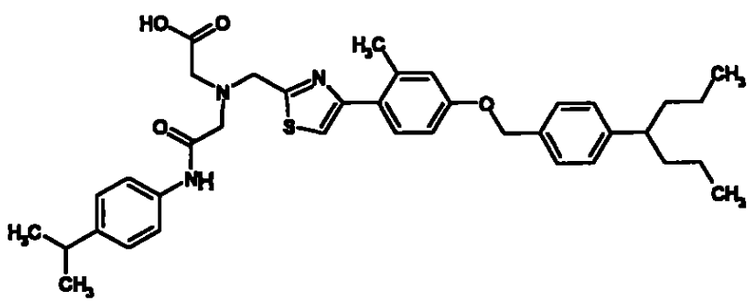
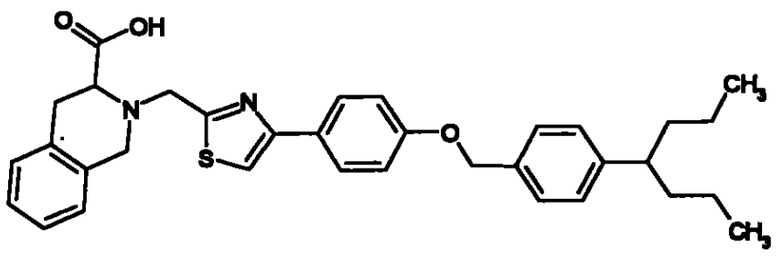
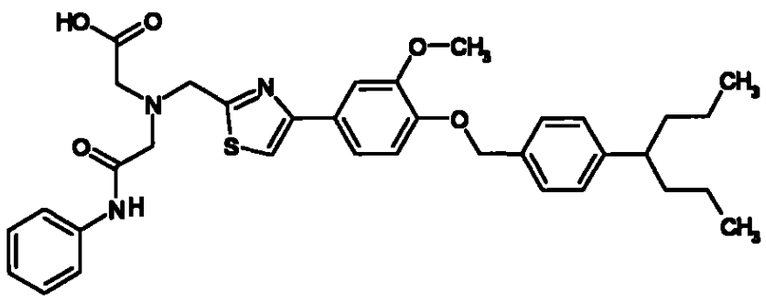
Example	Structural formula	m.p.(°C)
3-116		amorphous
3-117		amorphous
3-118		127 - 130
3-119		amorphous

Table 3-29

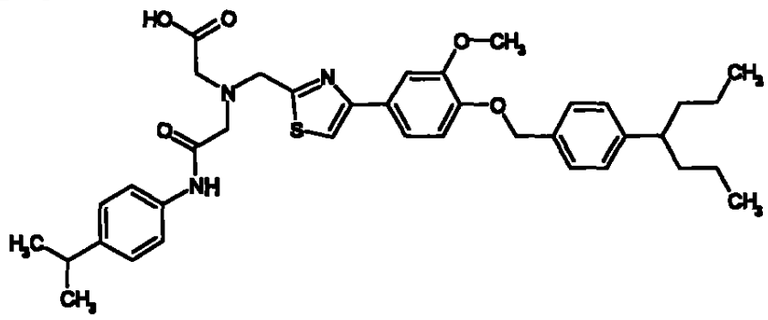
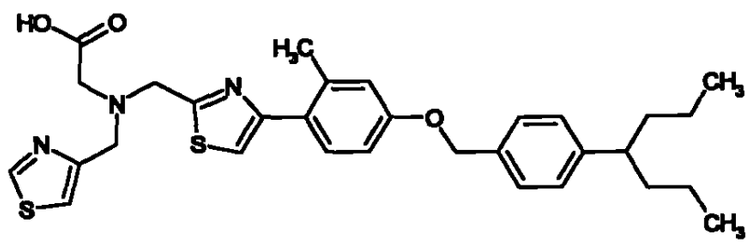
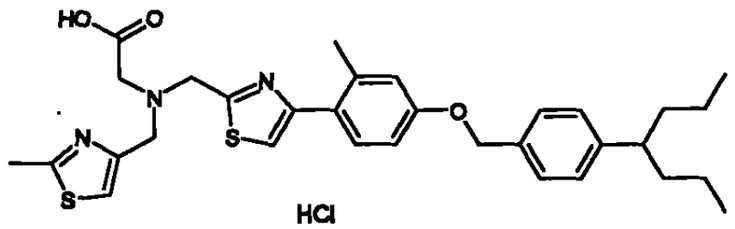
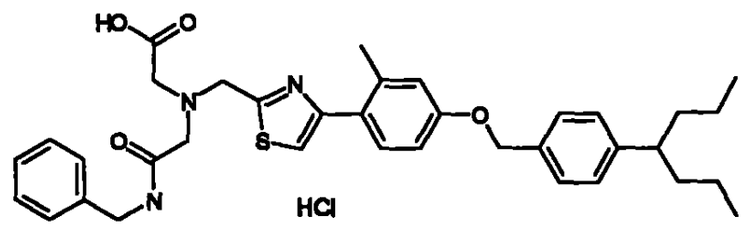
Example	Structural formula	m.p.(°C)
3-120		amorphous
3-121		103 – 104
3-122		98 – 103
3-123		amorphous

Table 3-30

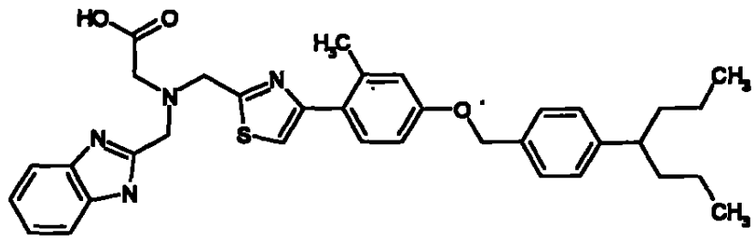
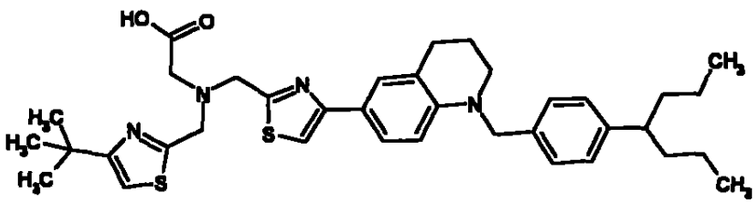
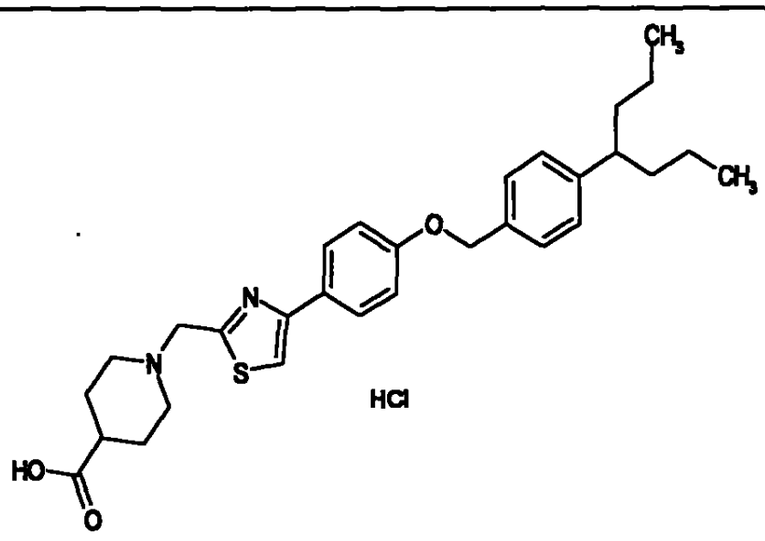
Example	Structural formula	m.p.(°C)
3-124		amorphous
3-125		132 - 135
3-126		amorphous

Table 3-31

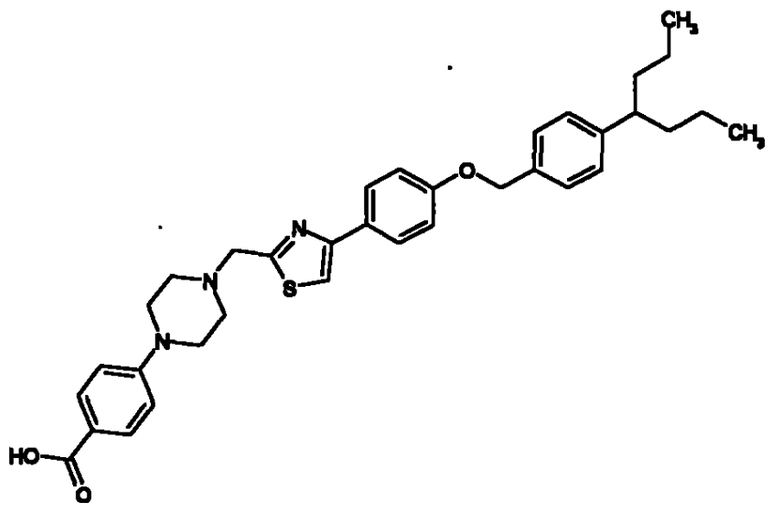
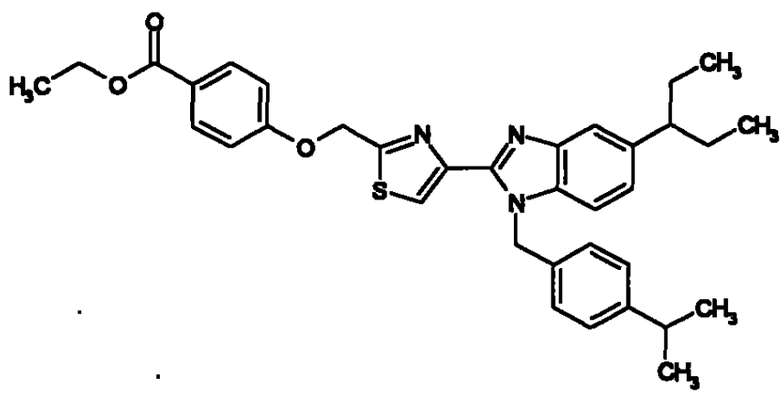
Example	Structural formula	m.p.(°C)
3-127		241 - 243
3-128		106 - 107

Table 3-32

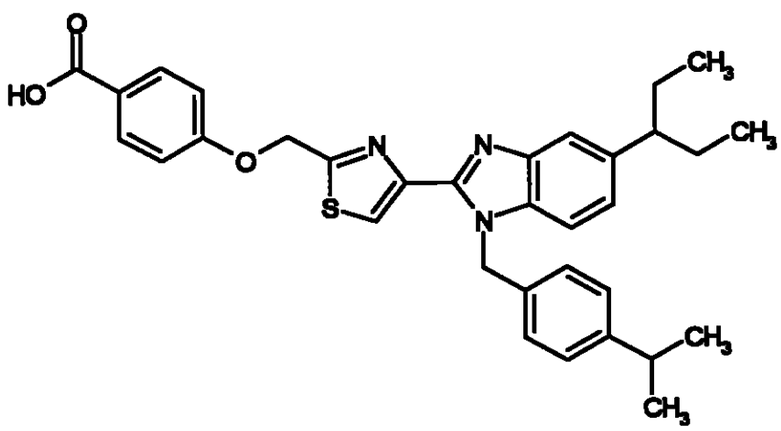
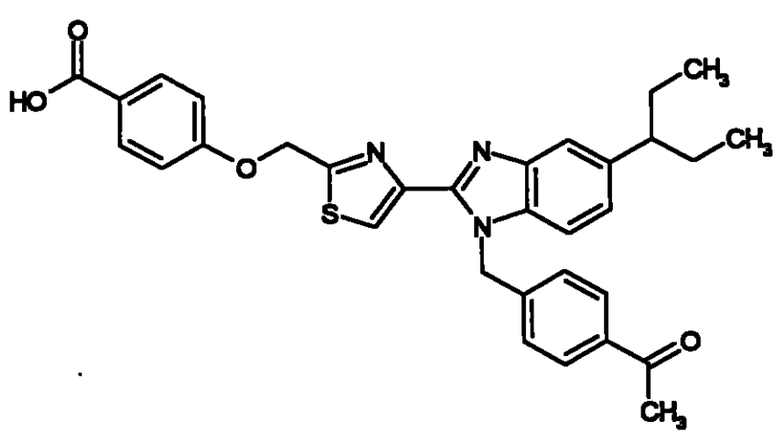
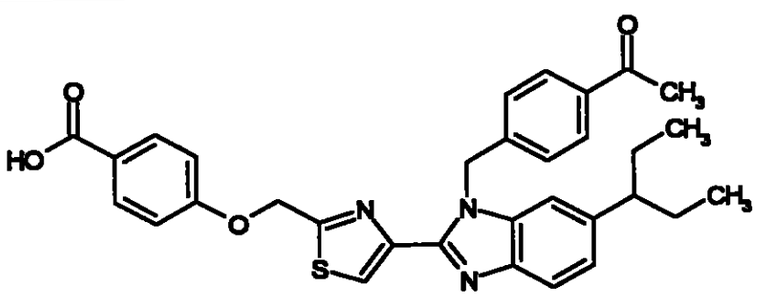
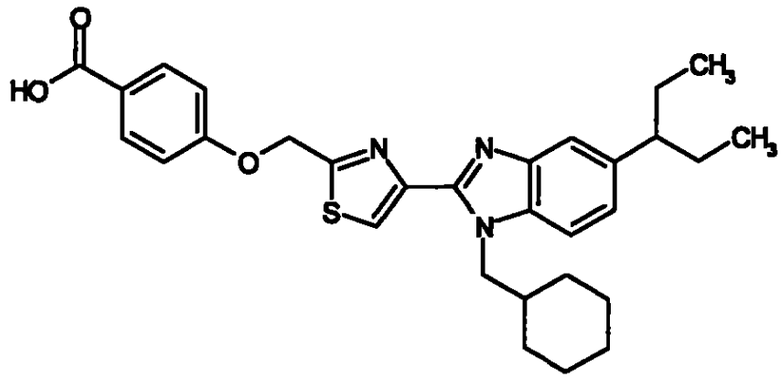
Example	Structural formula	m.p.(°C)
3-129		139 – 142
3-130		127 – 132
3-131		138 – 139

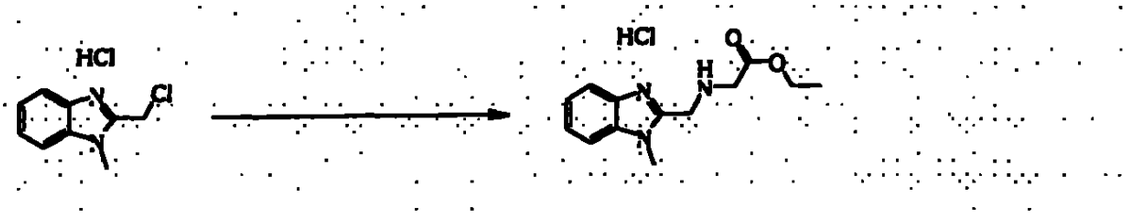
Table 3-33

Example	Structural formula	m.p.(°C)
3-132		176 - 183

Example 4-1

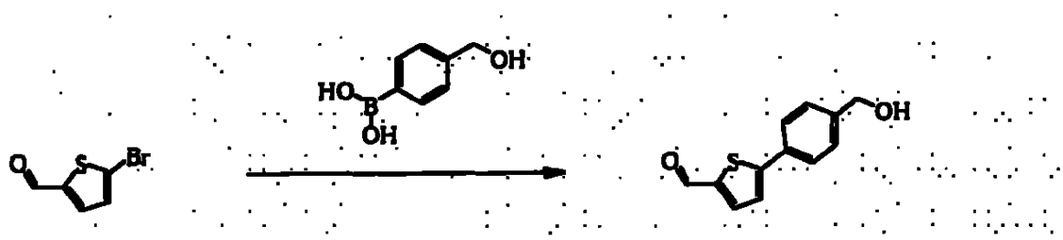
[(1-Methyl-1H-benzimidazol-2-ylmethyl)-5-{4-[4-(1-propyl-butyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl]amino]acetic acid

(1) N-(1-Methyl-1H-benzimidazol-2-ylmethyl)glycine ethyl ester hydrochloride



To a suspension of 2-chloromethyl-1-methyl-1H-benzimidazole hydrochloride (81.135 g, 0.374 mmol) in acetonitrile (800 ml) were added glycine ethyl ester hydrochloride (156.5 g, 1.12 mol), potassium carbonate (284.1 g, 2.06 mol) and potassium iodide (6.2 g, 0.037 mol) and the mixture was stirred at 75°C for 1.5 hr. After the completion of the reaction, ethyl acetate and water were added for extraction, and the organic layer was washed with water and saturated brine and dried over sodium sulfate. The solvent was evaporated, and the obtained residue was dissolved in ethyl acetate. A 4N-hydrochloric acid/ethyl acetate solution (93 ml) was added and the solvent was evaporated. Ethyl acetate was added to the obtained residue and the resulting solids were collected by filtration to give the title compound (74.4 g, 70%).

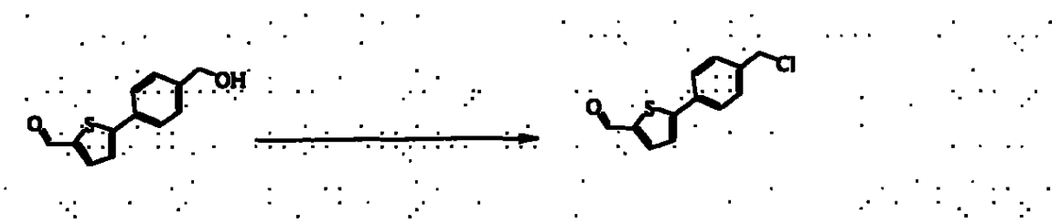
(2) 5-(4-Hydroxymethylphenyl)thiophene-2-carbaldehyde



To a suspension of 5-bromothiophene-2-carbaldehyde (125.7

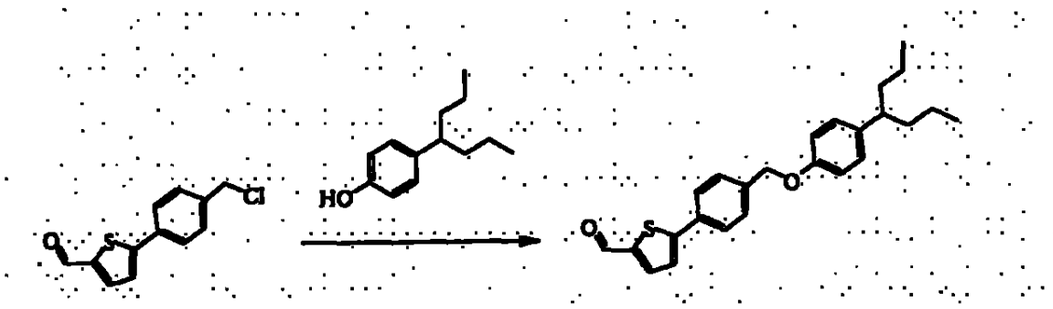
g, 0.658 mol), 4-hydroxymethylphenylboronic acid (100 g, 0.658 mol) and potassium carbonate (136.43 g, 0.987 mol) in 50% methanol (880 ml) was added bis(triphenylphosphine)palladium(II) dichloride (4.62 g, 6.58 mmol) and the mixture was stirred at 80°C for 1.5 hr. After the completion of the reaction, the resulting solids were collected by filtration. The obtained solid was dried under reduced pressure to give the title compound (137.2 g, 96%).

(3) 5-(4-Chloromethylphenyl)thiophene-2-carbaldehyde



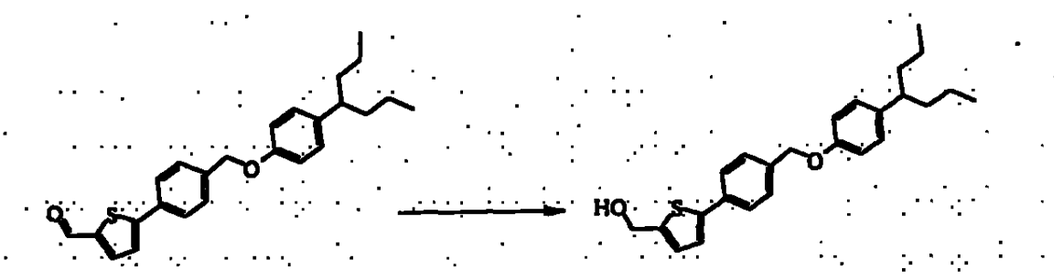
To a solution of 5-(4-hydroxymethylphenyl)thiophene-2-carbaldehyde (20 g, 91.6 mmol) obtained in Example 4-1(2) and triethylamine (15.3 ml, 110 mmol) in acetonitrile was added dropwise methanesulfonyl chloride (8.51 ml, 110 mmol) under ice-cooling and the mixture was stirred at room temperature for 1 hr. Lithium chloride (7.77 g, 183.3 mmol) was added to the reaction mixture and the mixture was stirred at 55°C for 1 hr. After the completion of the reaction, water was added at room temperature and the resulting solids were collected by filtration. The obtained solid was dried under reduced pressure to give the title compound (19.3 g, 89%).

(4) 5-(4-(4-(1-Propylbutyl)phenoxymethyl)phenyl)thiophene-2-carbaldehyde



To a solution of 4-(1-propylbutyl)phenol (15.6 g, 81.1 mmol) in N,N-dimethylacetamide (192 ml) were successively added 5-(4-chloromethylphenyl)thiophene-2-carbaldehyde (19.2 g, 81.1 mmol) obtained in Example 4-1(3), potassium carbonate (22.4 g, 162.2 mmol) and potassium iodide (2.69 g, 16.2 mmol) and the mixture was stirred at 90°C for 1.5 hr. After the completion of the reaction, ethyl acetate and water were added at room temperature and the mixture was extracted. The organic layer was washed successively with water and saturated brine and dried over magnesium sulfate. The solvent was evaporated and the obtained residue was stirred in hexane/diisopropyl ether=3/1. The resulting solids were collected by filtration and the obtained solid was dried under reduced pressure to give the title compound (25.9 g, 81%).

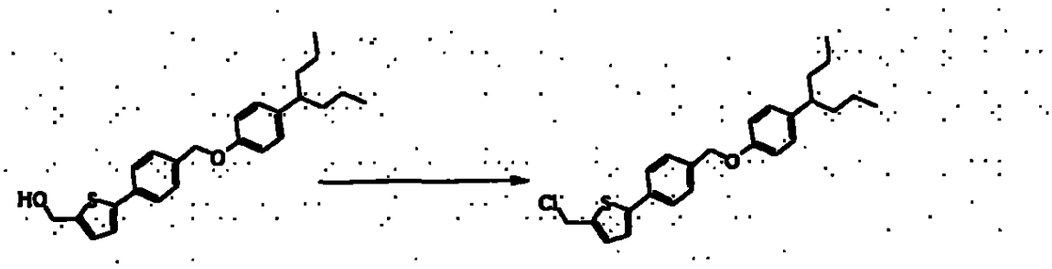
(5) (5-(4-(4-(1-Propylbutyl)phenoxymethyl)phenyl)thiophen-2-yl)methanol



To a solution of 5-(4-(4-(1-propylbutyl)phenoxymethyl)phenyl)thiophene-2-carbaldehyde (25.9 g, 66 mmol) obtained in Example 4-1(4) in tetrahydrofuran (260 ml) and ethanol (260 ml) was added sodium borohydride (2.5 g,

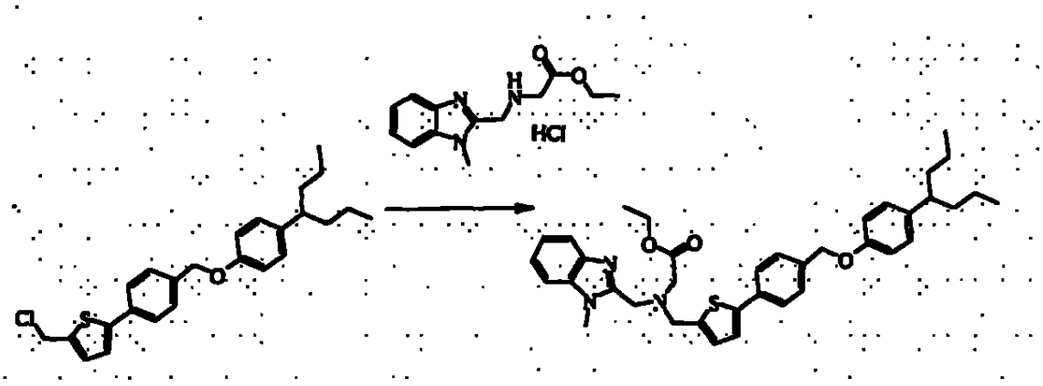
66 mmol) under ice-cooling and the mixture was stirred at room temperature for 0.5 hr. After the completion of the reaction, the solvent was partially concentrated. To the obtained residue were added ethyl acetate, a saturated aqueous sodium hydrogen carbonate solution and water and the mixture was stirred for 0.5 hr. The mixture was extracted and the organic layer was washed with saturated brine, and dried over magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (chloroform:methanol=50:1→10:1) to give the title compound (23.6 g, 91%).

(6) (5-(4-(4-(1-Propylbutyl)phenoxymethyl)phenyl)thiophen-2-yl)methyl chloride



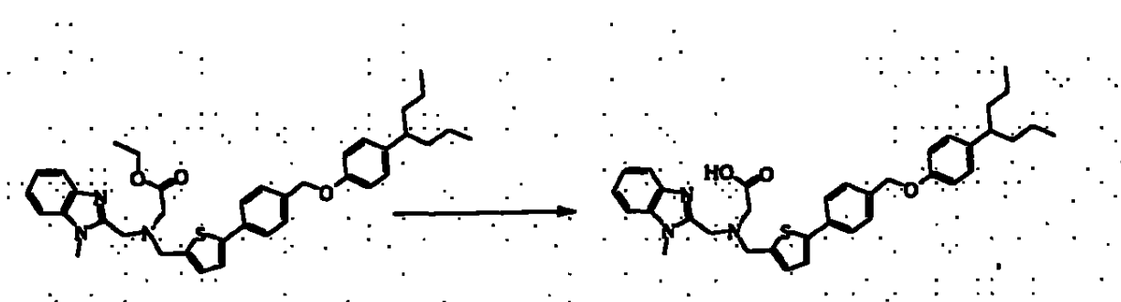
To a solution of (5-(4-(4-(1-propylbutyl)phenoxymethyl)phenyl)thiophen-2-yl)methanol (23.6 g, 59.8 mmol) obtained in Example 4-1(5) in chloroform (354 ml) was added thionyl chloride (8.73 ml, 119.6 mmol) at room temperature and the mixture was stirred at the same temperature for 1 hr. After the completion of the reaction, the solvent was evaporated and the obtained residue was concentrated by adding chloroform and dried under reduced pressure to give the title compound (24.6 g, 100%).

(7) [(1-Methyl-1H-benzimidazol-2-ylmethyl)-5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl]amino]acetic acid ethyl ester



To a solution of (5-(4-(4-(1-propylbutyl)phenoxymethyl)phenyl)thiophen-2-yl)methyl chloride (0.687 g, 1.66 mmol) obtained in Example 4-1(6) in acetonitrile were added N-(1-methyl-1H-benzimidazol-2-ylmethyl)glycine ethyl ester hydrochloride (0.674 g, 1.83 mmol) obtained in Example 4-1(1), potassium carbonate (0.69 g, 5.0 mmol) and potassium iodide (0.055 g, 0.33 mmol) and the mixture was stirred at 80°C for 1.5 hr. After the completion of the reaction, ethyl acetate and water were added. The mixture was extracted and the organic layer was washed with saturated brine and dried over magnesium sulfate. The solvent was evaporated, and the obtained residue was purified by silica gel column chromatography (chloroform:methanol=100:1→20:1) to give the title compound (0.633 g, 61%).

(8) [(1-Methyl-1H-benzimidazol-2-ylmethyl)-5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl]amino]acetic acid

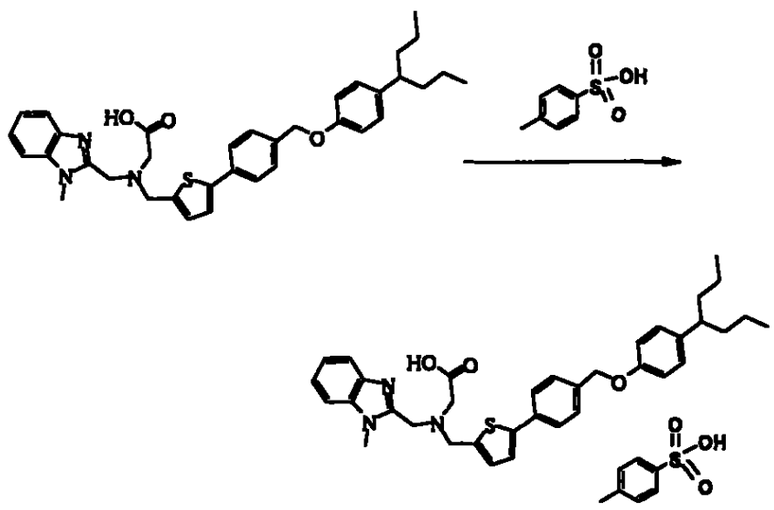


To a solution of [(1-methyl-1H-benzimidazol-2-ylmethyl)-

5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl]amino]acetic acid ethyl ester (5 g, 8.01 mmol) obtained in Example 4-1(7) in 50% tetrahydrofuran-ethanol (100 ml) was added a 1N-aqueous sodium hydroxide solution (16 ml) at room temperature, and the mixture was stirred at 80°C for 1 hr. After the completion of the reaction, a 1N-hydrochloric acid (16 ml) was added under ice-cooling, and the mixture was stirred at room temperature. The resulting solids were collected by filtration. The obtained solid was dried under reduced pressure to give the title compound (4.63 g, 97%).
^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.79(t, J=7.3Hz, 6H), 0.96-1.18(m, 4H), 1.34-1.60(m, 4H), 3.36(s, 2H), 3.88(s, 3H), 4.04(s, 2H), 4.16(s, 2H), 5.06(s, 2H), 6.92(d, J=8.7Hz, 2H), 7.01(d, J=3.4Hz, 1H), 7.07(d, J=8.7Hz, 2H), 7.14-7.26(m, 2H), 7.35(d, J=3.4Hz, 1H), 7.46(d, J=8.3Hz, 2H), 7.53(d, J=7.5Hz, 1H), 7.58-7.65(m, 3H), 12.52(br s, 1H)

Example 4-40

[(1-Methyl-1H-benzimidazol-2-ylmethyl)-5-{4-[4-(1-propyl-butyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl]amino]acetic acid p-toluenesulfonate



To a suspension of [(1-methyl-1H-benzimidazol-2-ylmethyl)-5-{4-[4-(1-propyl-butyl)phenoxymethyl]phenyl}-

thiophen-2-ylmethyl]amino]acetic acid (200 mg, 0.336 mmol) obtained in Example 4-1 in 2-butanone (5 ml) was added p-toluenesulfonic acid monohydrate (64 mg, 0.37 mmol) and the mixture was stirred at room temperature for 30 min. The crystals were collected by filtration and dried over to give the title compound (231 mg, 90%).

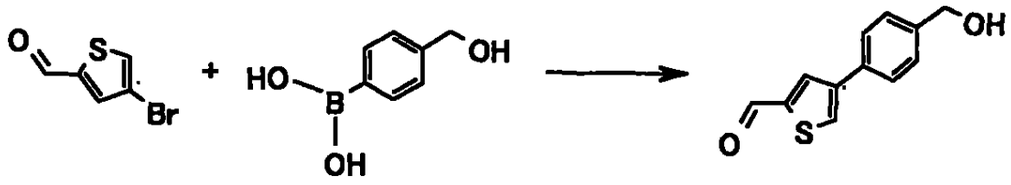
^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.79(t, J=7.3Hz, 6H), 0.95-1.20(m, 4H), 1.32-1.60(m, 4H), 2.28(s, 3H), 2.40-2.54(m, 1H), 3.62(s, 2H), 4.00(s, 3H), 4.19(s, 2H), 4.46(s, 2H), 5.05(s, 2H), 6.92(d, J=8.6Hz, 2H), 6.98-7.14(m, 5H), 7.25(d, J=3.6Hz, 1H), 7.36-7.58(m, 8H), 7.76(d, J=9.0Hz, 1H), 7.89(d, J=9.0Hz, 1H)

melting point: 100°C-135°C

Example 4-2

5-(4-{4-[4-(1-Propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinic acid

(1) 4-(4-Hydroxymethylphenyl)thiophene-2-carbaldehyde



To a solution of 4-bromothiophene-2-carbaldehyde (100 g, 0.523 mol) in tetrahydrofuran (500 ml) were added bis(triphenylphosphine)palladium(II) dichloride (3.67 g, 52.3 mmol), 4-hydroxymethylphenylboronic acid (79.5 g, 0.523 mol), sodium hydrogen carbonate (66.0 g, 0.786 mol) and water (1000 ml) and the mixture was stirred at an internal temperature of 62-63°C for 3 hr. After allowing to cool, ethyl acetate was added to the reaction mixture. The organic layer was washed with saturated brine and concentrated to give a crude product (140 g). To the obtained crude product were added toluene (400 ml) and hexane (100 ml) and the mixture was stirred. The

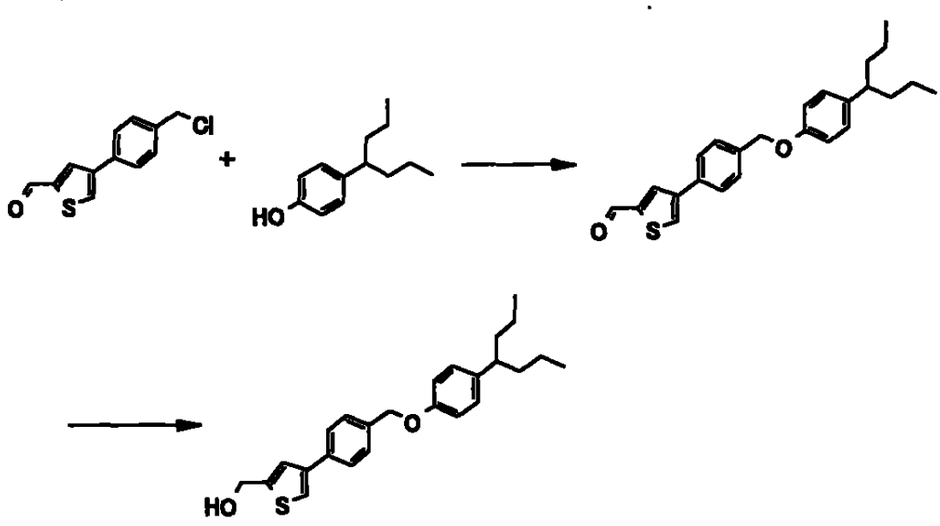
solids were collected by filtration and dried to give the title compound (95.4 g, 83%).

(2) 4-(4-Chloromethylphenyl)thiophene-2-carbaldehyde



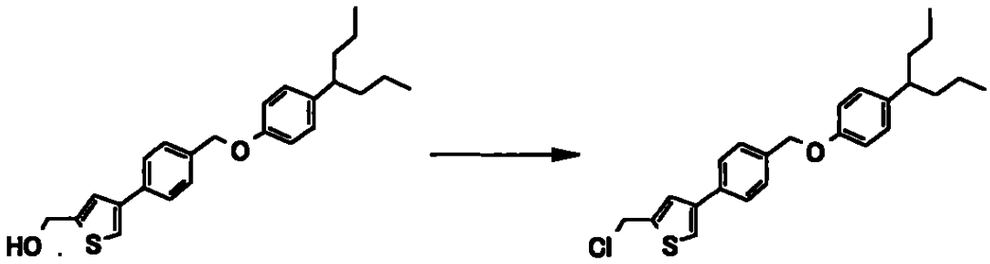
To a solution of 4-(4-hydroxymethylphenyl)thiophene-2-carbaldehyde (95.4 g, 0.437 mol) and triethylamine (73.1 ml, 0.524 mol) in N,N-dimethylformamide (763 ml) was added dropwise methanesulfonyl chloride (40.6 ml, 0.524 mol) under ice-cooling and the mixture was stirred at room temperature for 2 hr. Lithium chloride (37.1 g, 0.874 mol) was added to the reaction mixture and the mixture was stirred at 60°C for 1 hr. After allowing to cool, water was added and the resulting solids were collected by filtration. The obtained solid was suspended in diisopropyl ether (465 ml) and the mixture was stirred at an internal temperature of 60-65°C for 1.5 hr. After allowing to cool, the solids were collected by filtration and dried to give the title compound (83.2 g, 80%).

(3) (4-(4-(4-(1-Propylbutyl)phenoxymethyl)phenyl)thiophen-2-yl)methanol



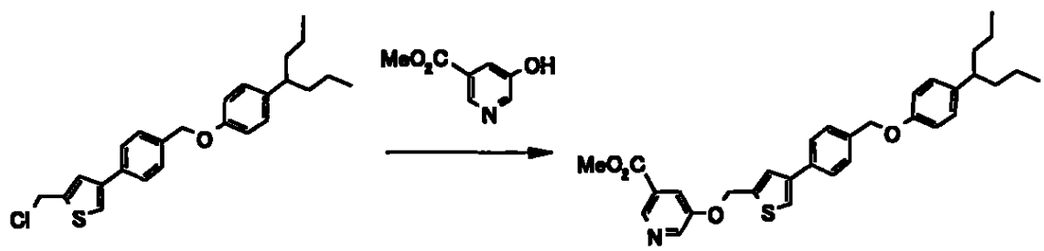
To a solution of 4-(4-chloromethylphenyl)thiophene-2-carbaldehyde (21.1 g, 88.9 mmol) in N,N-dimethylacetamide (105 ml) were successively added 4-(1-propylbutyl)phenol (18.7 g, 97.8 mmol), potassium carbonate (36.8 g, 267 mmol) and potassium iodide (1.47 g, 8.89 mmol) and the mixture was stirred at 90°C for 1.5 hr. After the completion of the reaction, ethyl acetate and water were added at room temperature. The mixture was extracted and the organic layer was washed successively with water and saturated brine and dried over magnesium sulfate. The solvent was evaporated and the obtained residue (68 g) was dissolved in ethanol (100 ml). Sodium borohydride (37.8 g, 88.9 mmol) was added under ice-cooling and the mixture was stirred at room temperature for 1 hr. Water and ethyl acetate were added to the reaction mixture and, the organic layer was washed successively with a 1N-aqueous sodium hydroxide solution, water and saturated brine and dried over magnesium sulfate. The solvent was evaporated and the obtained residue was purified by silica gel column chromatography (chloroform:methanol=100:1→50:1) to give a crude product (29.9 g). The crude product (14.5 g) was purified by silica gel column chromatography (ethyl acetate:hexane=1:5→1:4) to give the title compound (11.9 g).

(4) (4-(4-(4-(1-Propylbutyl)phenoxymethyl)phenyl)thiophen-2-yl)methyl chloride



To a solution of (4-(4-(4-(1-propylbutyl)phenoxymethyl)-phenyl)thiophen-2-yl)methanol (11.9 g, 30.2 mmol) in chloroform (60 ml) was added thionyl chloride (4.40 ml, 60.4 mmol) and the mixture was stirred at room temperature for 30 min. The solvent was evaporated and thionyl chloride (10.0 ml, 137 mmol) was added. The mixture was stirred at room temperature for 20 min. The reaction mixture was concentrated under pressure and the obtained residue was concentrated by adding chloroform to give the title compound (12.5 g, 100%).

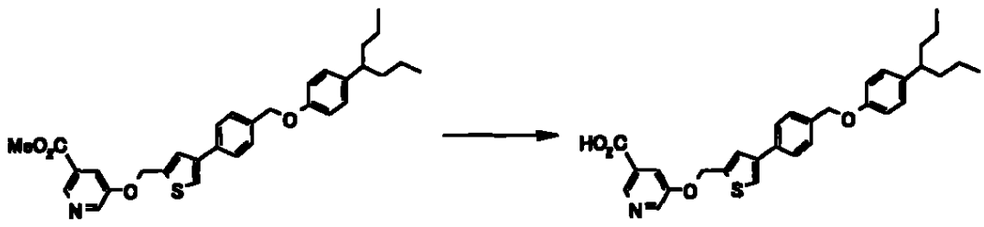
(5) 5-(4-{4-[4-(1-Propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinic acid methyl ester



To (4-(4-(4-(1-propylbutyl)phenoxymethyl)phenyl)thiophen-2-yl)methyl chloride (5.00 g, 12.1 mmol) were added N,N-dimethylacetamide (25 ml), 5-hydroxynicotinic acid methyl ester (2.04 g, 13.3 mmol), cesium carbonate (11.8 g, 36.3 mmol), potassium iodide (201 mg, 1.21 mmol) and tetra-n-butylammonium bromide (390 mg, 1.21 mmol) and the mixture was stirred at 60°C for 1.5 hr. After allowing to cool, ethyl acetate was added

and the mixture was washed successively with water and saturated brine. After concentration, the concentrate was purified by silica gel column chromatography (ethyl acetate:hexane=2:5→1:2) to give the title compound (5.19 g, 81%).

(6) 5-(4-{4-[4-(1-Propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinic acid



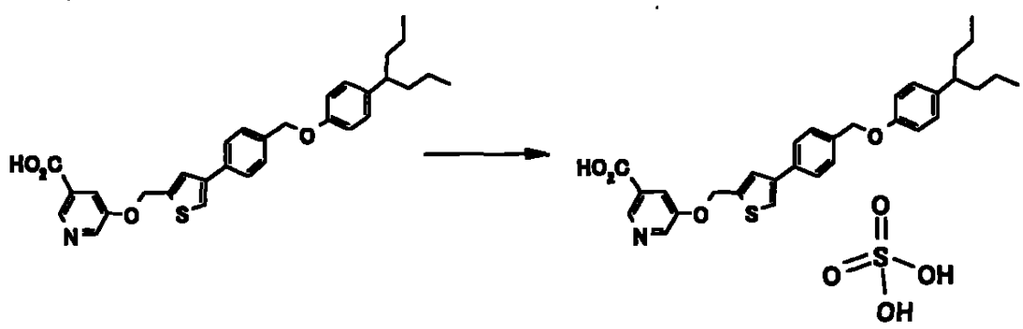
To 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}-thiophen-2-ylmethoxy)nicotinic acid methyl ester (5.04 g, 9.52 mmol) were added tetrahydrofuran (25 ml), ethanol (25 ml) and a 2N-aqueous sodium hydroxide solution (5.00 ml, 10 mmol) and the mixture was stirred at 60°C for 1.5 hr. After allowing to cool, 2N-hydrochloric acid (5.00 ml, 10 mmol) and water (30 ml) were added. The precipitated solids were collected by filtration and dried to give the title compound (4.77 g, yield 97%).

^{1}H NMR (DMSO-d_6, 300 MHz) δ 0.80(t, J=7.3Hz, 6H), 1.00-1.12(m, 4H), 1.38-1.57(m, 4H), 2.40-2.50(m, 1H), 5.07(s, 2H), 5.48(s, 2H), 6.93(d, J=8.6Hz, 2H), 7.07(d, J=8.6Hz, 2H), 7.49(d, J=7.9Hz, 2H), 7.70-7.70(m, 1H), 7.72(d, J=8.3Hz, 2H), 7.88-7.89(m, 1H), 7.91(d, J=1.5Hz, 1H), 8.56(d, J=2.6Hz, 1H), 8.69(d, J=1.5Hz, 1H), 13.41(brs, 1H)

melting point: 157-159°C

Example 4-41

5-(4-{4-[4-(1-Propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinic acid sulfate



To a suspension of 5-(4-{4-[4-(1-propylbutyl)-phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinic acid (200 mg, 0.388 mmol) obtained in Example 4-2 in 2-butanone (2 ml) was added concentrated sulfuric acid (0.0207 ml, 0.388 mmol) and the mixture was stirred at room temperature for 1 hr. The solids were collected by filtration and dried to give the title compound (224 mg, yield 94%).

^{1}H NMR (DMSO-d_6, 300 MHz) 0.80(t, J=7.3Hz, 6H), 0.98-1.15(m, 4H), 1.38-1.59(m, 4H), 2.39-2.54(m, 1H), 5.07(s, 2H), 5.52(s, 2H), 6.93(d, J=8.6Hz, 2H), 7.07(d, J=8.7Hz, 2H), 7.49(d, J=8.3Hz, 2H), 7.71(s, 1H), 7.72(d, J=6.4Hz, 2H), 7.93(d, J=1.5Hz, 1H), 8.00(brs, 1H), 8.65-8.67(m, 1H), 8.73-8.76(m, 1H)
melting point: 125°C (dec.)

Examples 4-3 to 4-39 and 4-42 to 4-107

In the same manner as in Examples 4-1, 4-2, 4-40 and 4-41 and using other conventional methods where necessary, the compounds of Examples 4-3 to 4-39 and Examples 4-42 to 4-107 were produced. The structural formulas and property values of the obtained compounds, as well as those of Examples 4-1, 4-2, 4-40 and 4-41, are shown in the following Tables.

Table 4-1

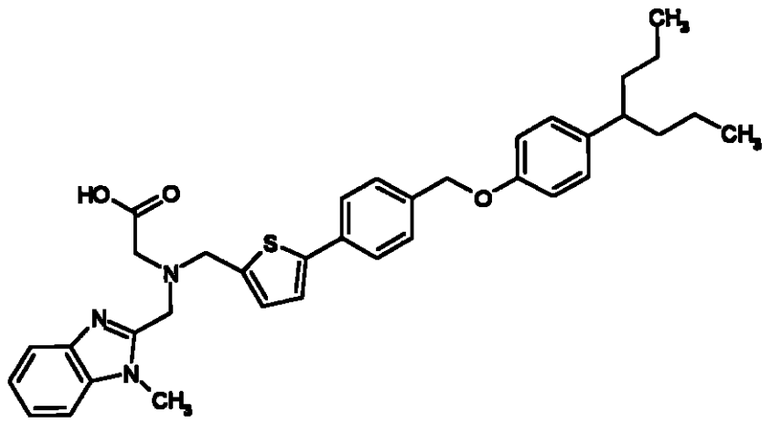
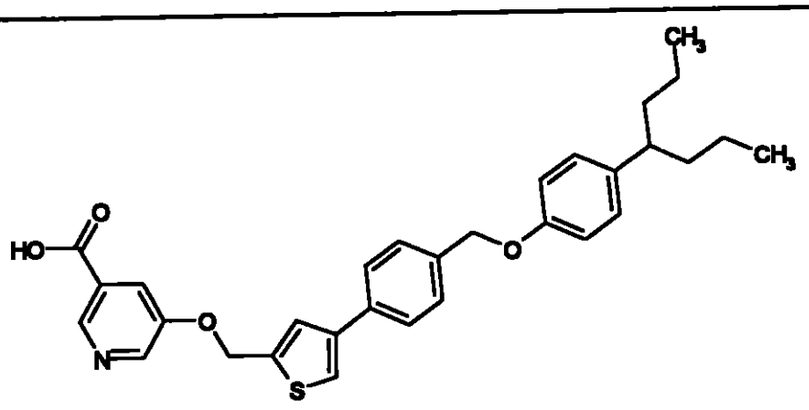
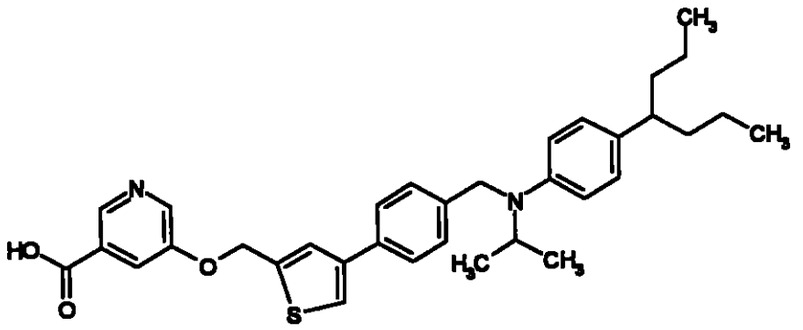
Example	Structural formula	m.p.(°C)
4-1		amorphous
4-2		157 – 159
4-3		156

Table 4-2

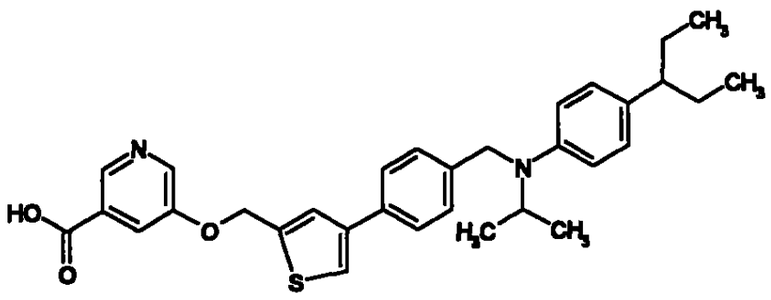
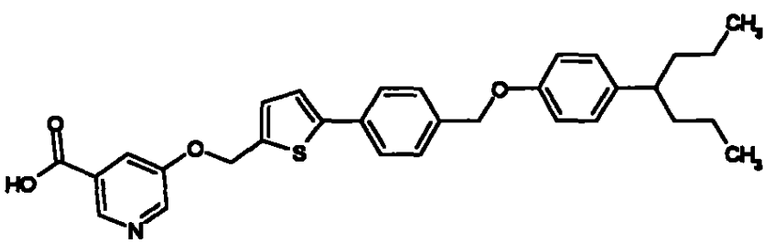
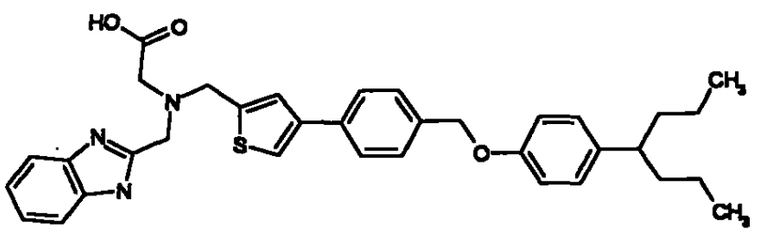
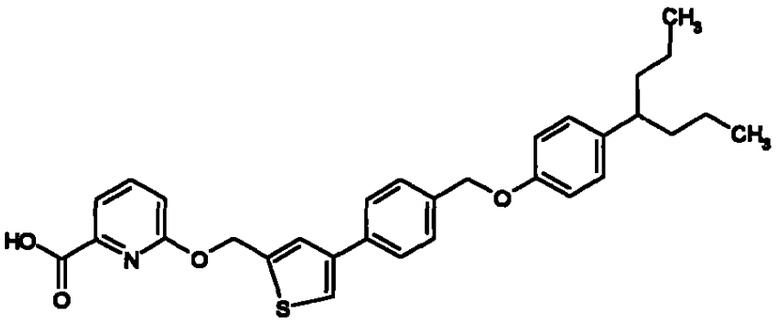
Example	Structural formula	m.p.(°C)
4-4		160
4-5		153 – 155
4-6		153 – 155
4-7		amorphous

Table 4-3

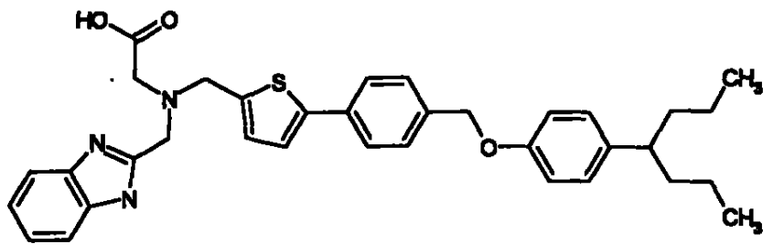
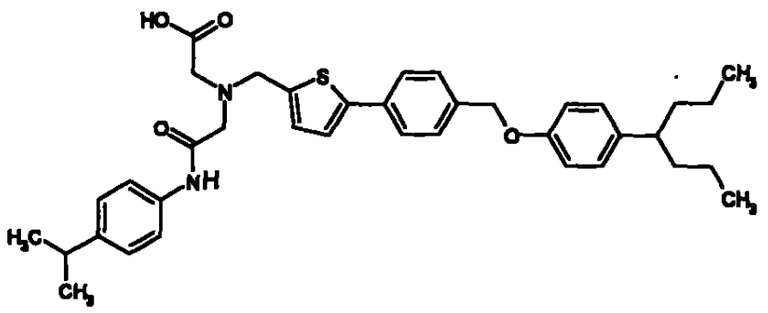
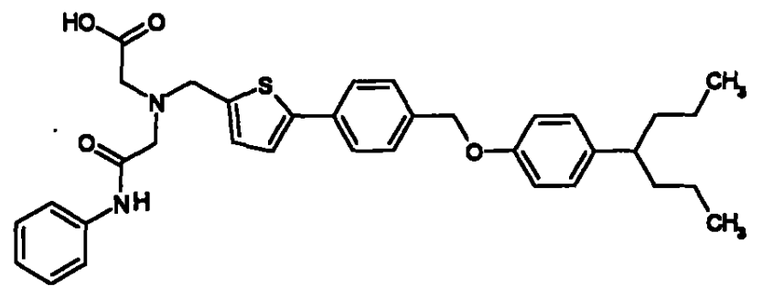
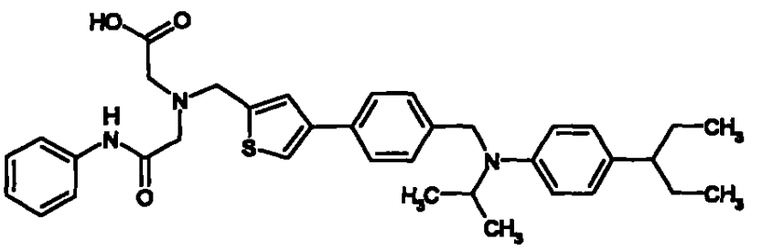
Example	Structural formula	m.p.(°C)
4-8		173 - 175
4-9		172 - 174
4-10		122 - 124
4-11		amorphous

Table 4-4

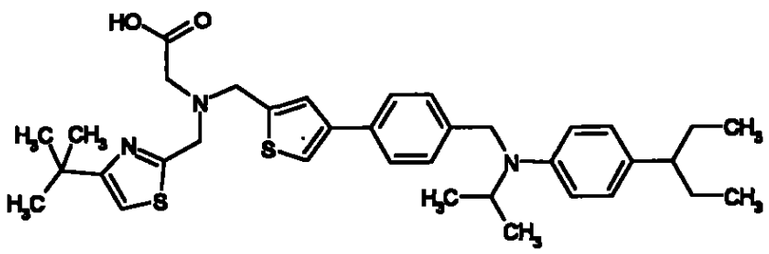
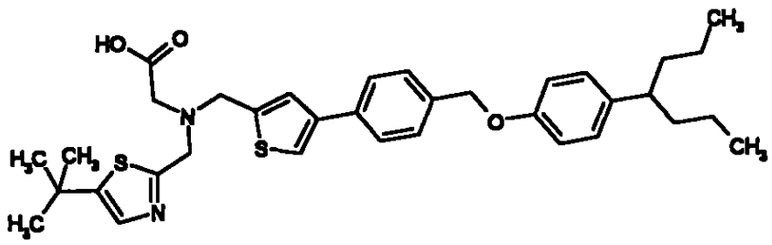
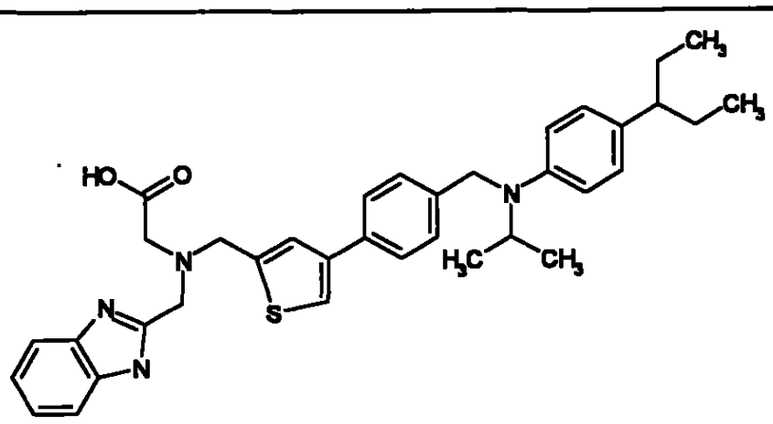
Example	Structural formula	m.p.(°C)
4-12		amorphous
4-13		amorphous
4-14		amorphous

Table 4-5

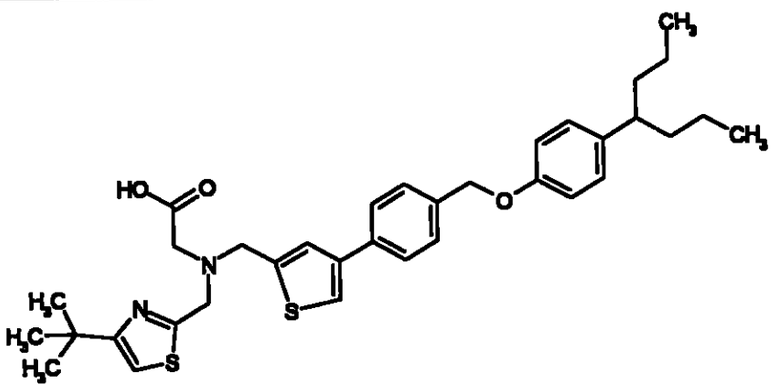
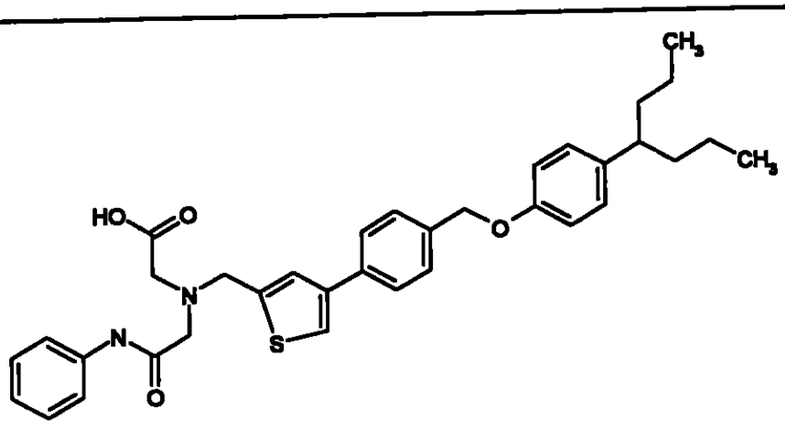
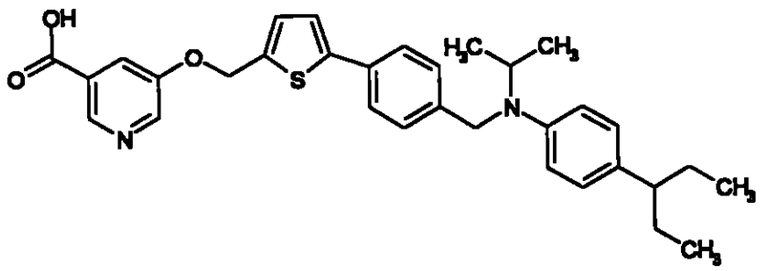
Example	Structural formula	m.p.(°C)
4-15		166
4-16		155
4-17		160 – 164

Table 4-6

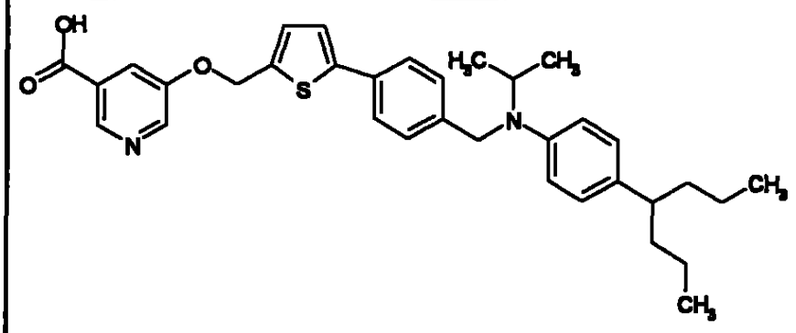
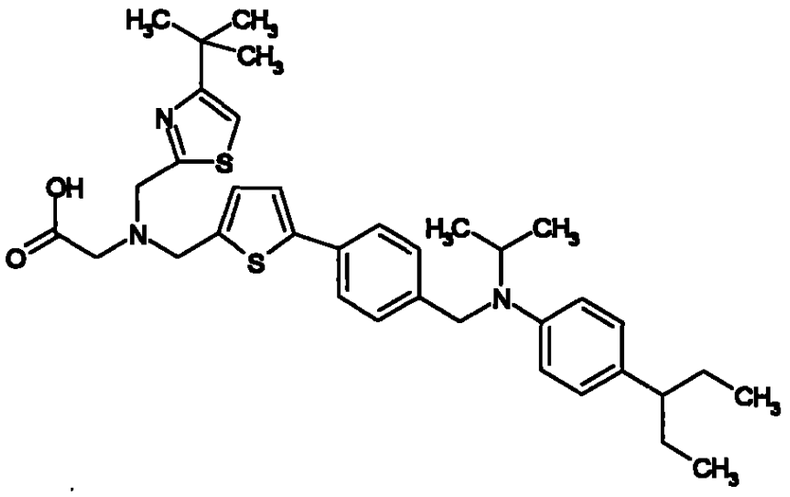
Example	Structural formula	m.p.(°C)
4-18		93 – 98
4-19		92 – 98

Table 4-7

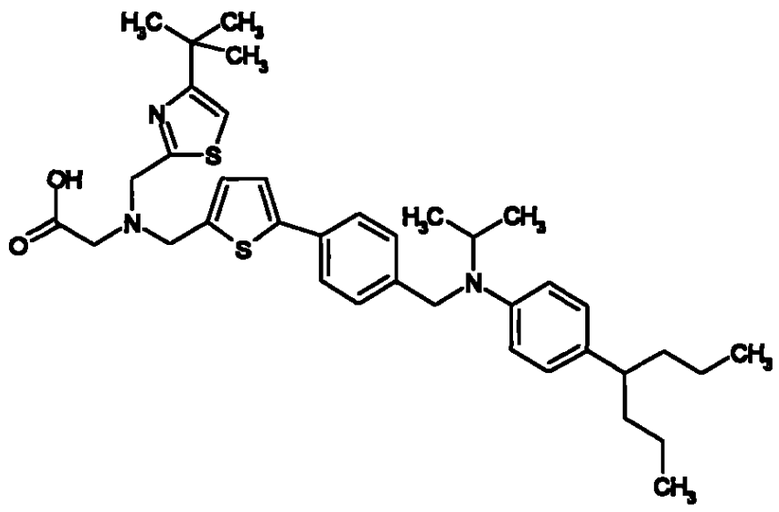
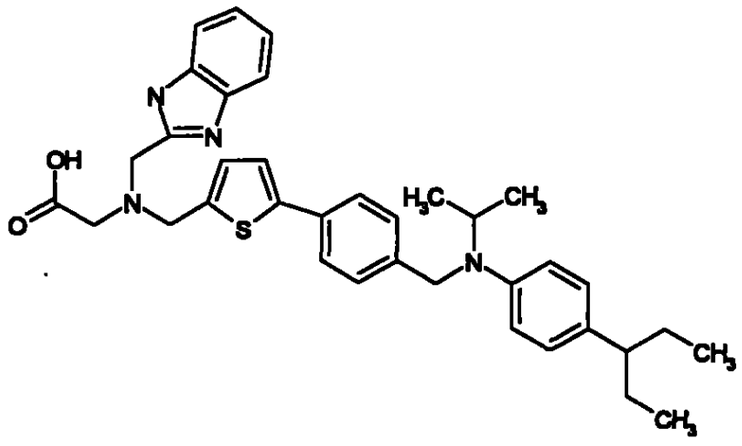
Example	Structural formula	m.p.(°C)
4-20		78 – 82
4-21		142 – 146

Table 4-8

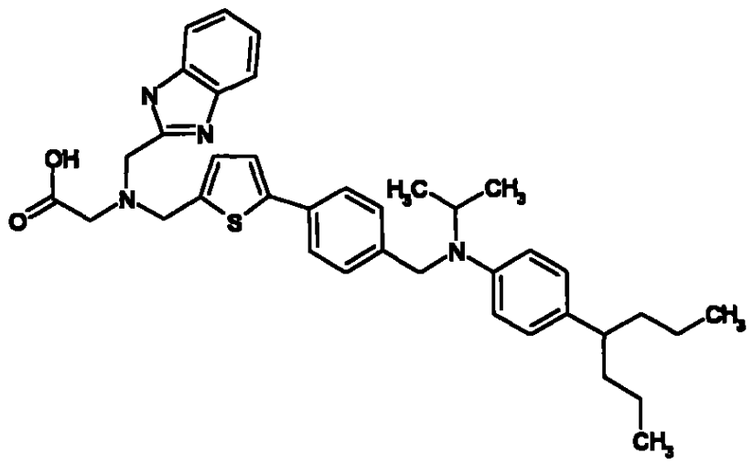
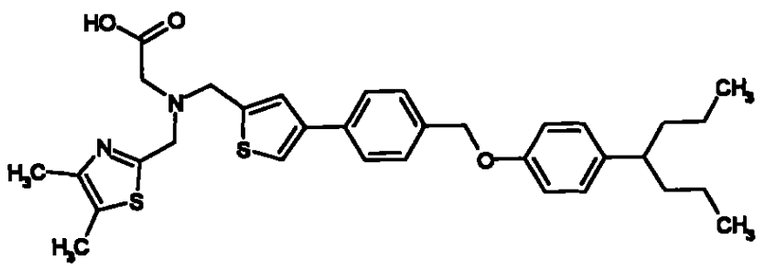
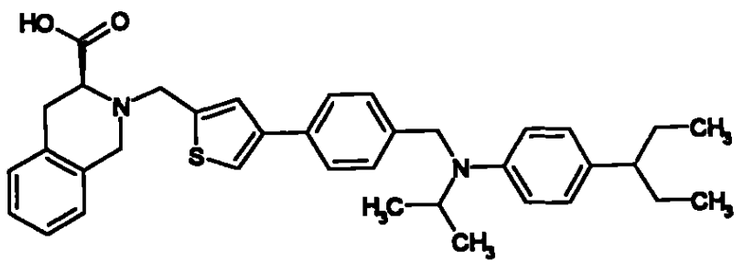
Example	Structural formula	m.p.(°C)
4-22		144 - 150
4-23		amorphous
4-24		amorphous

Table 4-9

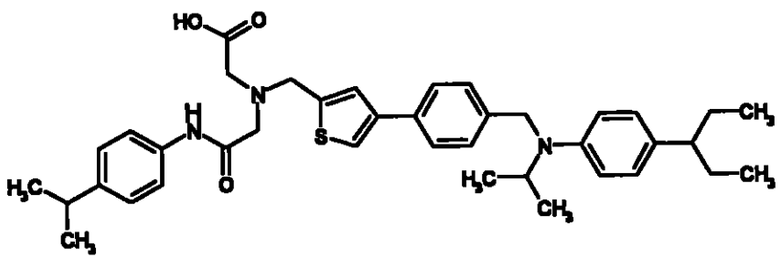
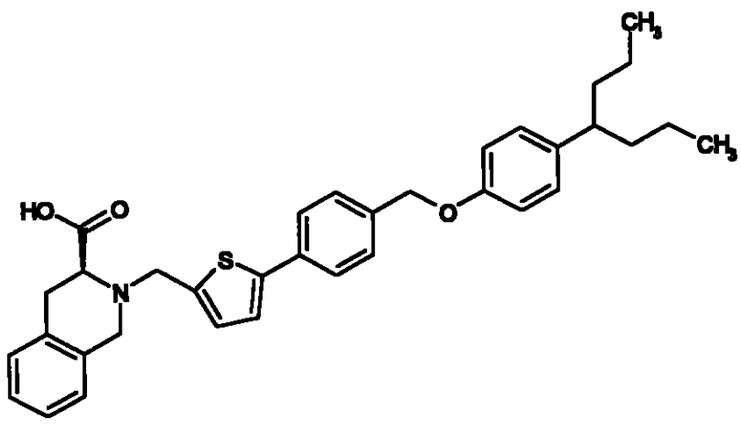
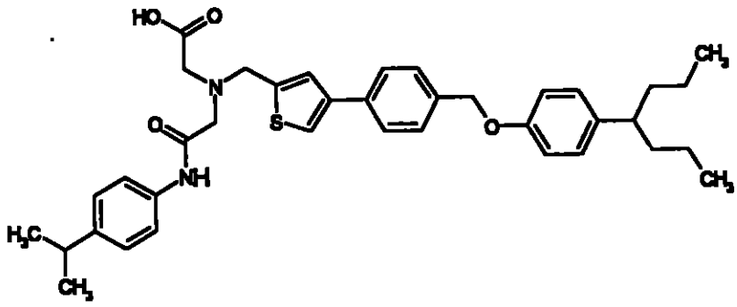
Example	Structural formula	m.p.(°C)
4-25		amorphous
4-26		amorphous
4-27		164 – 166

Table 4-10

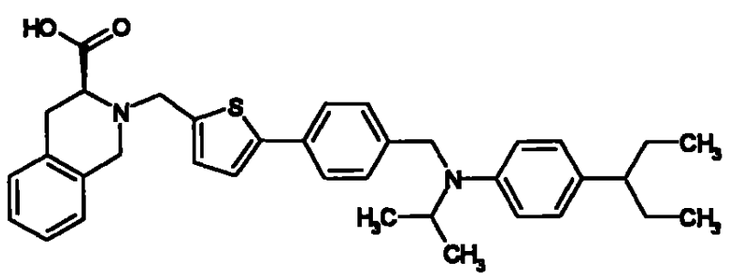
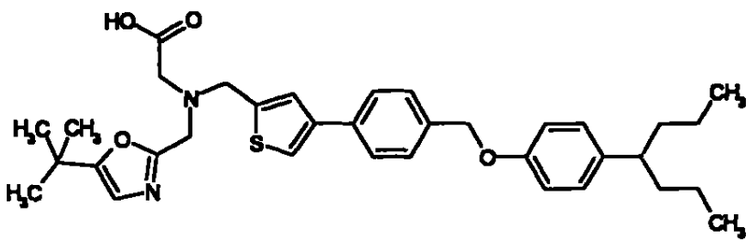
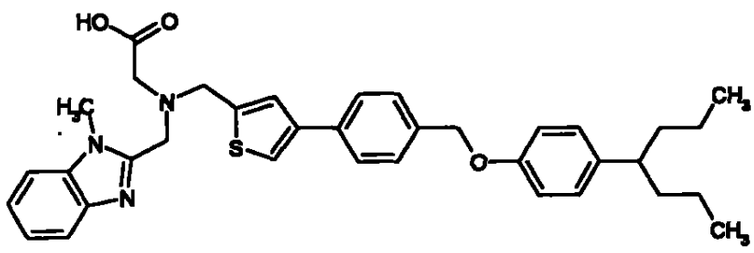
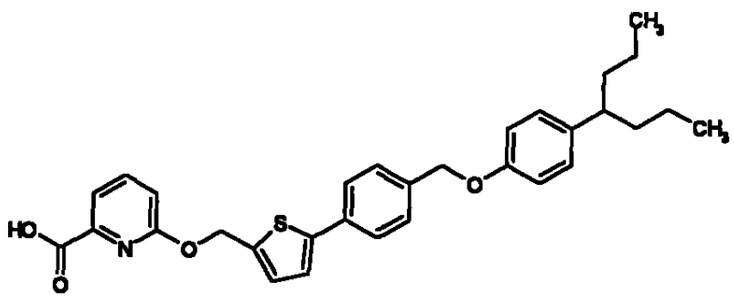
Example	Structural formula	m.p.(°C)
4-28		152
4-29		120.5
4-30		amorphous
4-31		amorphous

Table 4-11

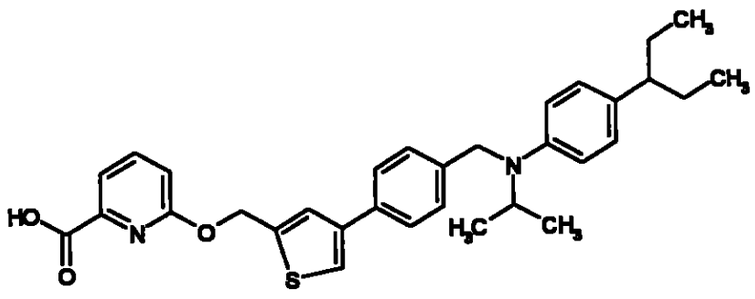
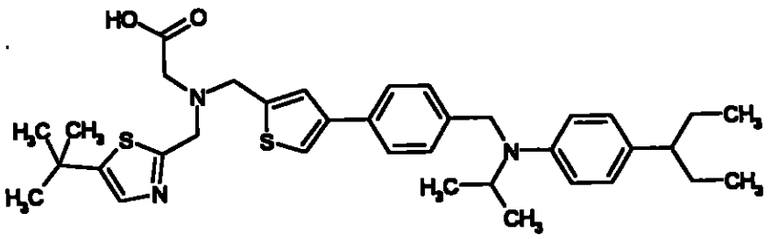
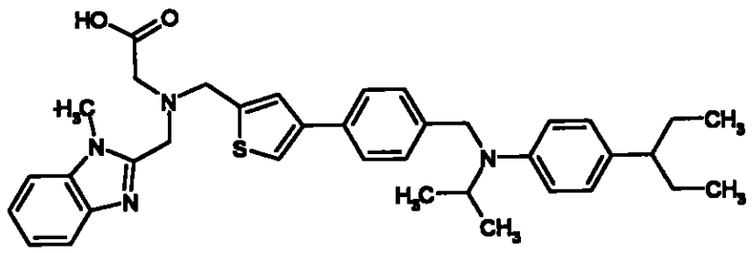
Example	Structural formula	m.p.(°C)
4-32		amorphous
4-33		amorphous
4-34		amorphous

Table 4-12

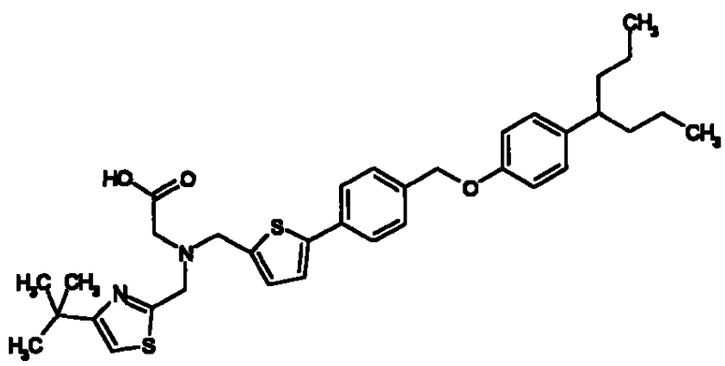
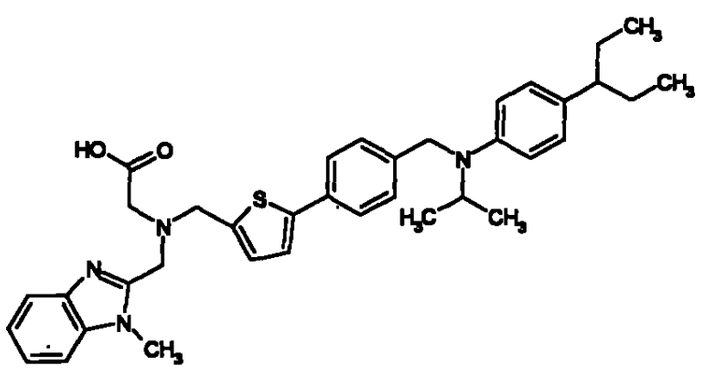
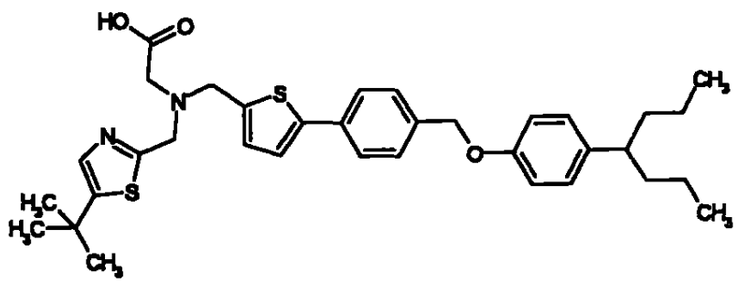
Example	Structural formula	m.p.(°C)
4-35		amorphous
4-36		amorphous
4-37		amorphous

Table 4-13

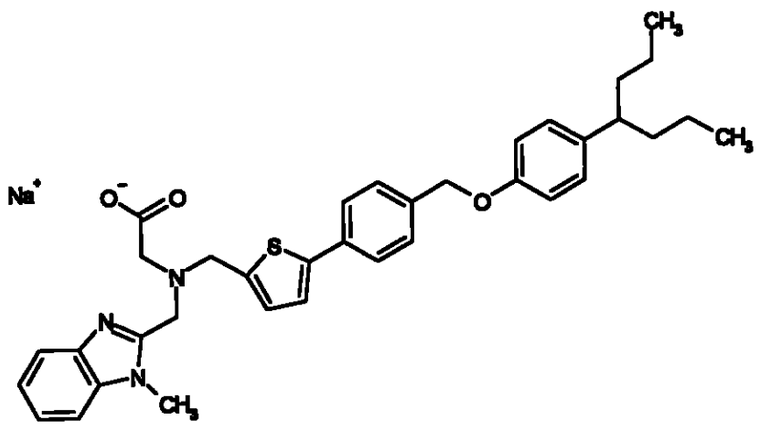
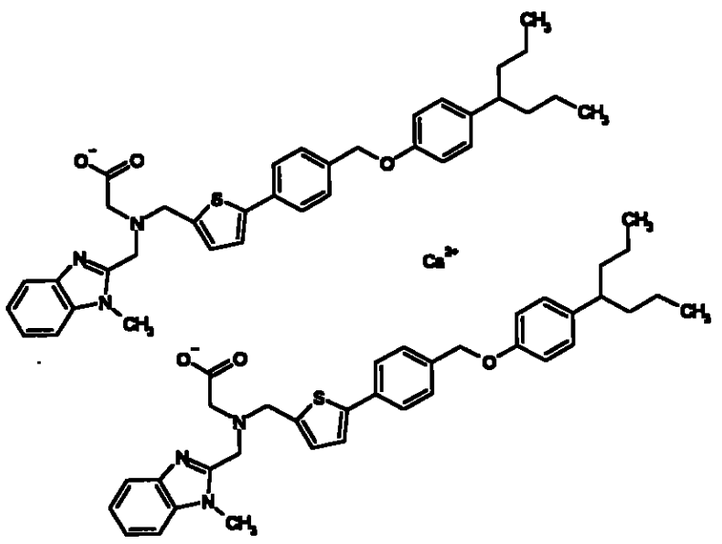
Example	Structural formula	m.p.(°C)
4-38		200 – 203
4-39		amorphous

Table 4-14

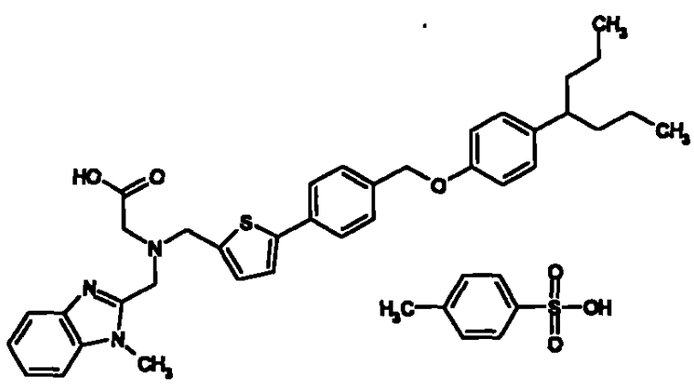
Example	Structural formula	m.p.(°C)
4-40		100- 135

Table 4-15

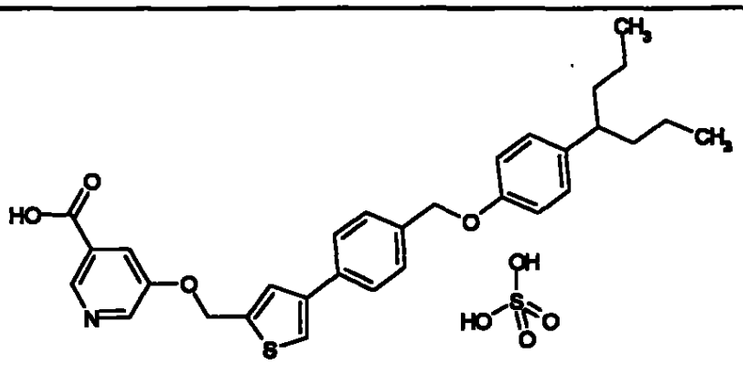
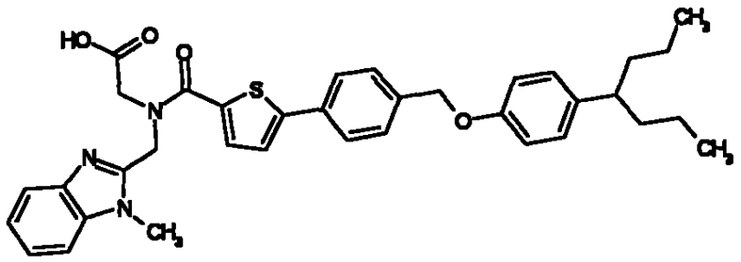
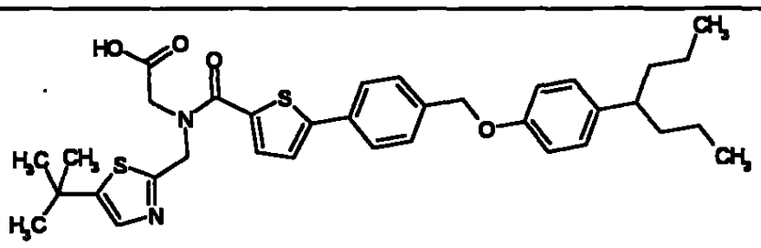
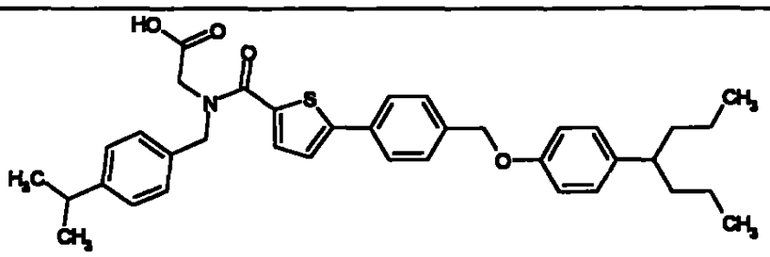
Example	Structural formula	m.p.(°C)
4-41		125 decomp.
4-42		185 - 188
4-43		amor-phous
4-44		134 - 136

Table 4-16

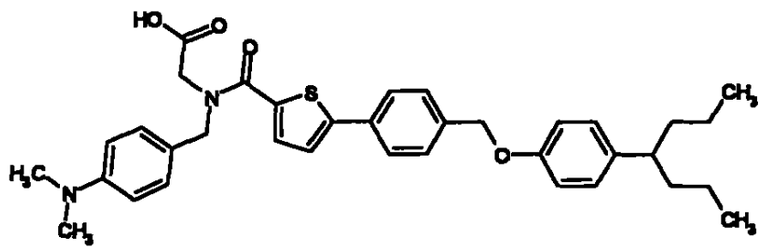
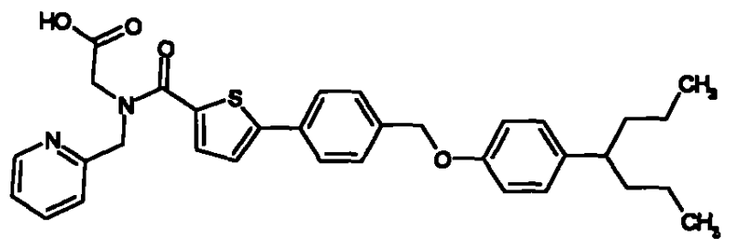
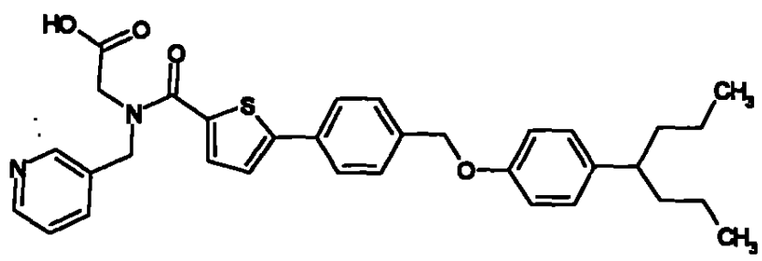
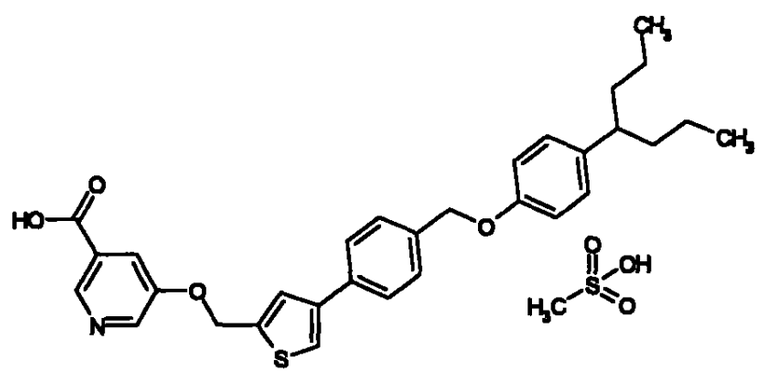
Example	Structural formula	m.p.(°C)
4-45		137 – 139
4-46		147 – 150
4-47		153 – 156
4-48		151 – 155 decomp.

Table 4-17

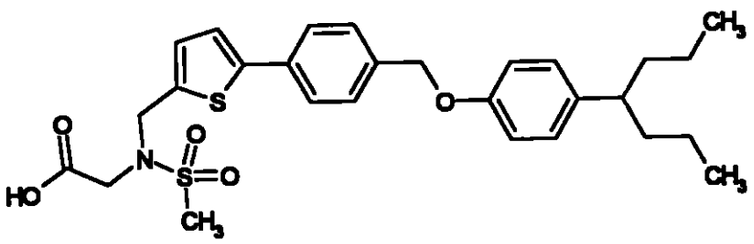
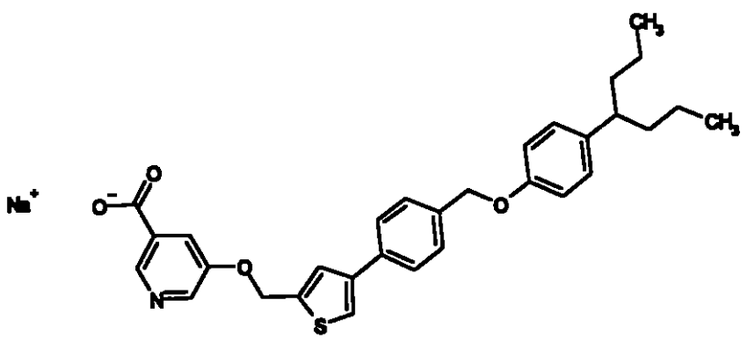
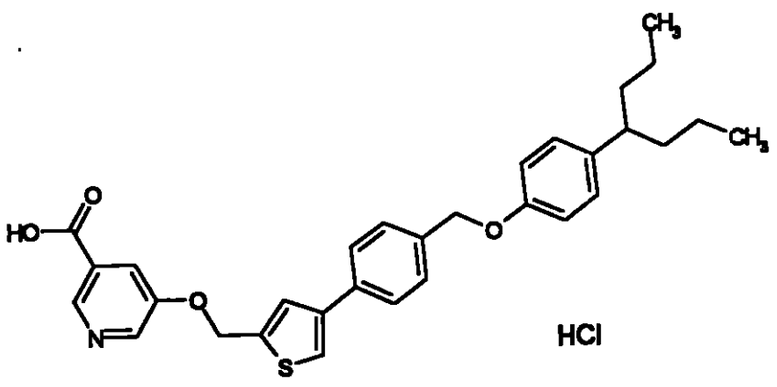
Example	Structural formula	m.p.(°C)
4-49		133.1 – 136.5
4-50		250~
4-51		170 – 173

Table 4-18

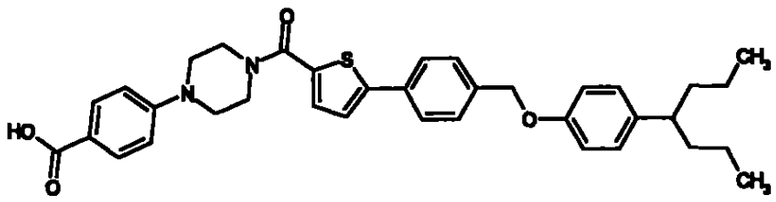
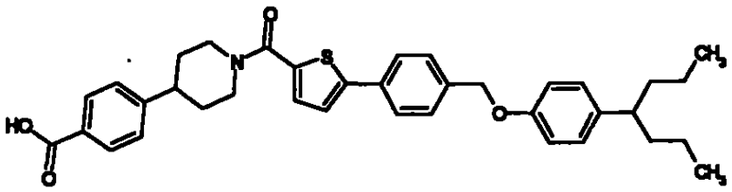
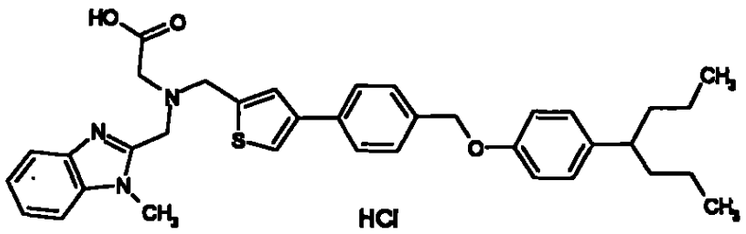
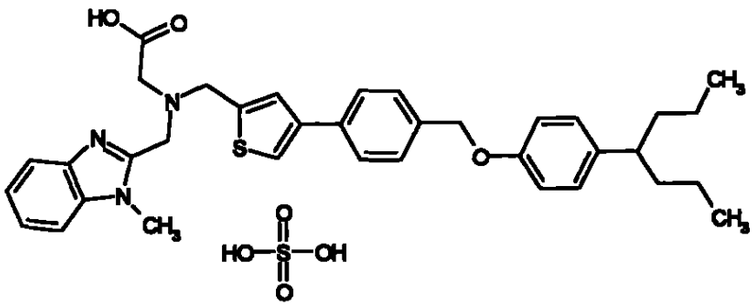
Example	Structural formula	m.p.(°C)
4-52		amor-phous
4-53		176 – 178
4-54		165.7 –166.8
4-55		137.5 – 141.5

Table 4-19

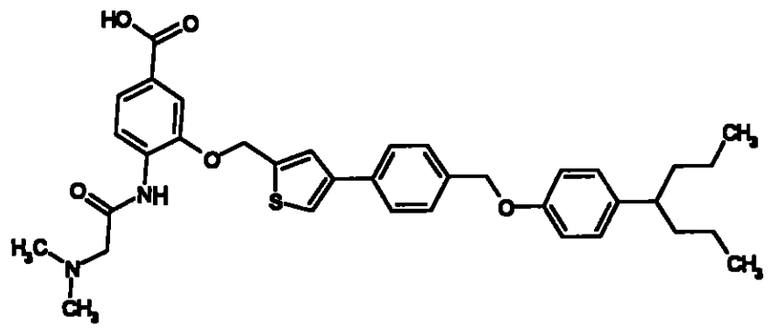
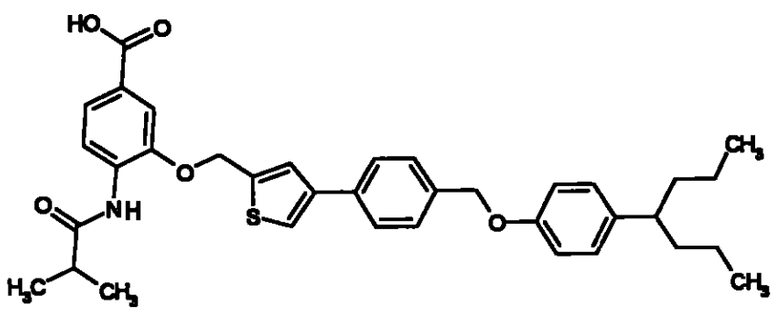
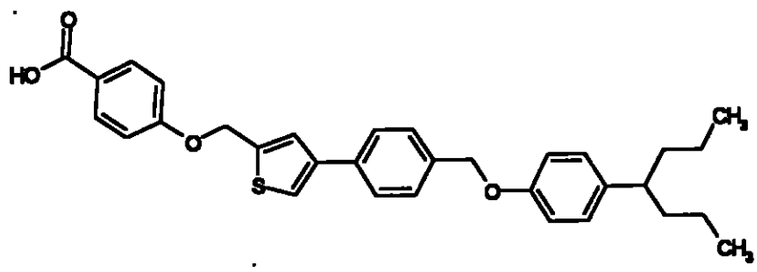
Example	Structural formula	m.p.(°C)
4-56		amor-phous
4-57		153.7 - 154.9
4-58		194.2 - 195.5

Table 4-20

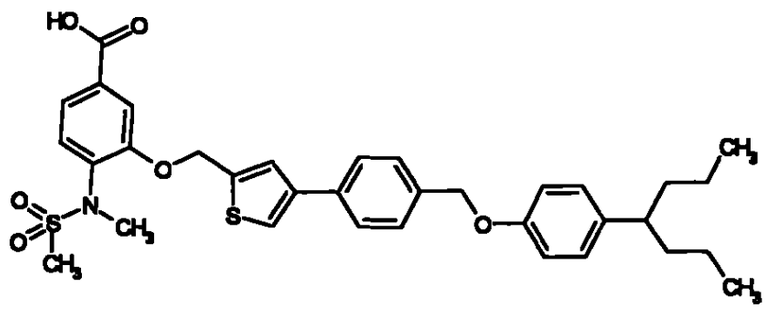
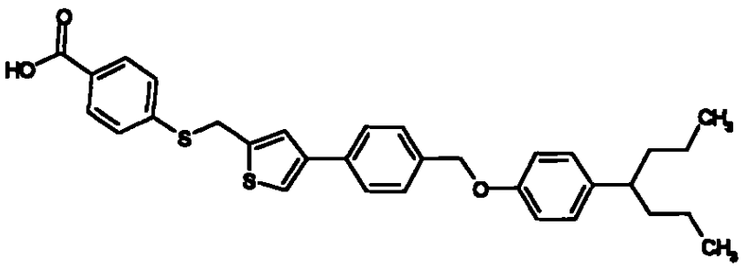
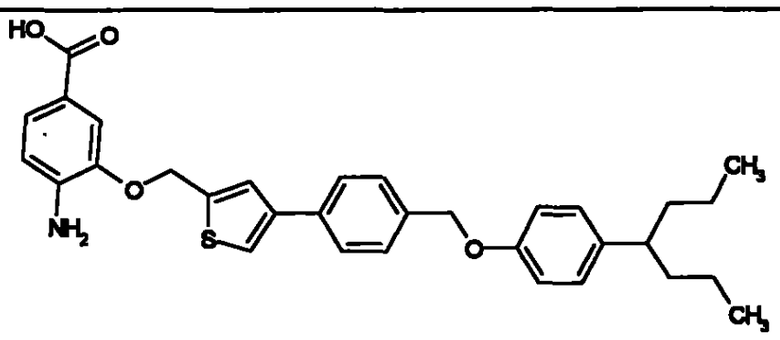
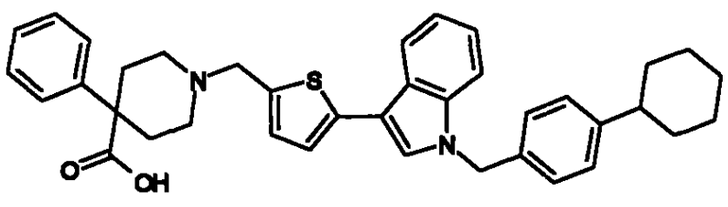
Example	Structural formula	m.p.(°C)
4-59		amor-phous
4-60		133.9 - 135.1
4-61		156.5 - 165.5
4-62	 HCl	227.3 - 233.6

Table 4-21

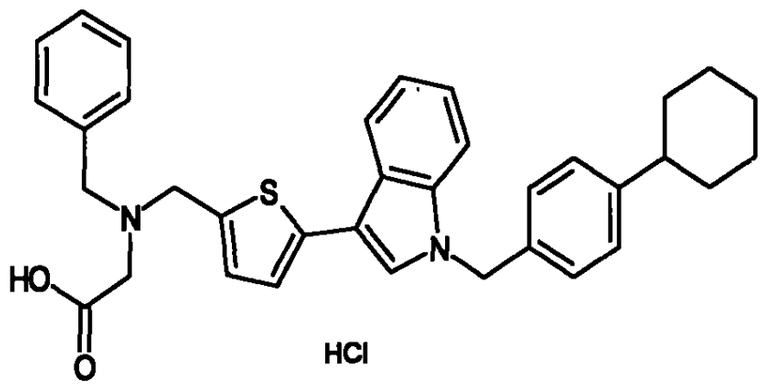
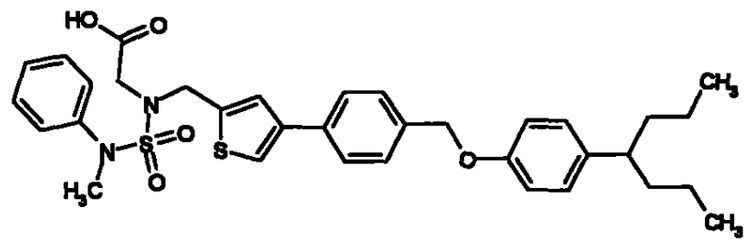
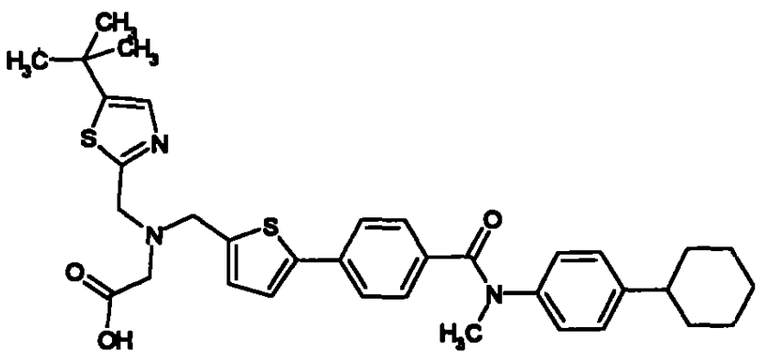
Example	Structural formula	m.p.(°C)
4-63	 HCl	161 – 164.3
4-64		139 – 140.2
4-65		amor-phous

Table 4-22

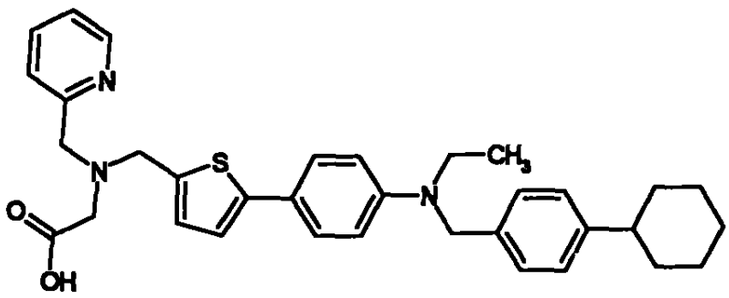
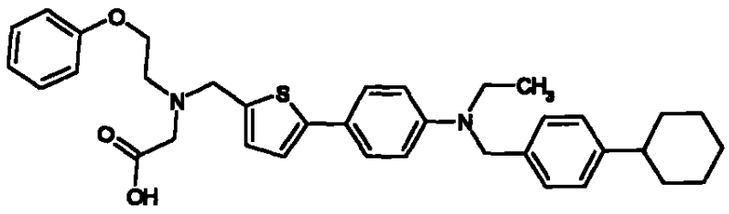
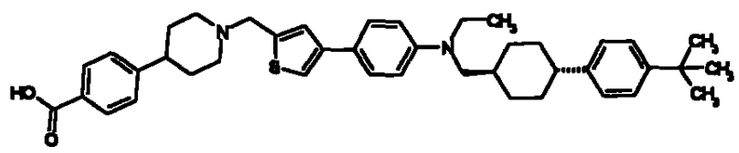
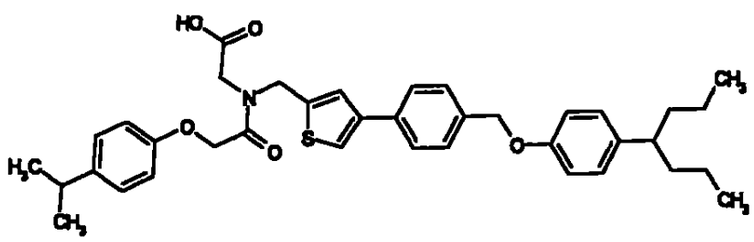
Example	Structural formula	m.p.(°C)
4-66		128 – 131
4-67		141 – 144
4-68		225 – 229 decomp.
4-69		146 – 152

Table 4-23

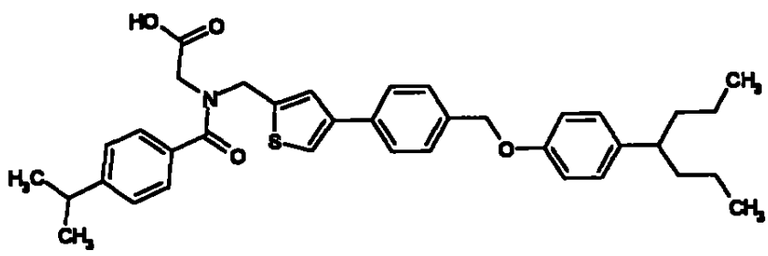
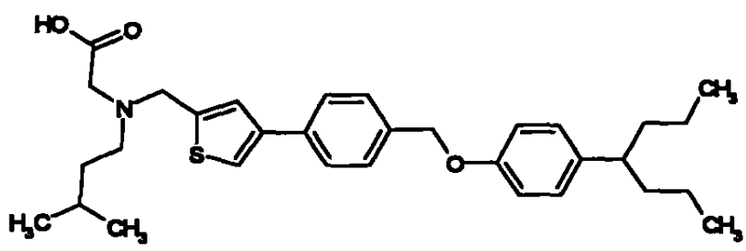
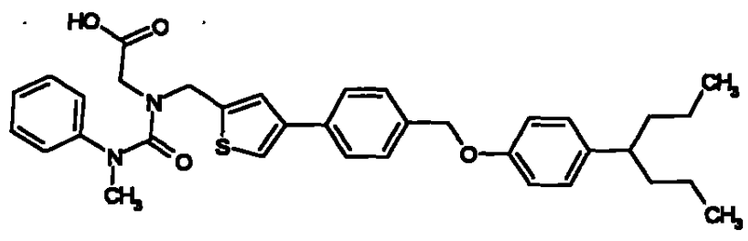
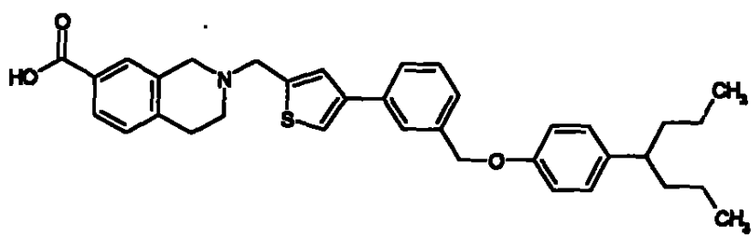
Example	Structural formula	m.p.(°C)
4-70		109 – 111
4-71		176 – 182
4-72		amor-phous
4-73		69.4 – 78.3

Table 4-24

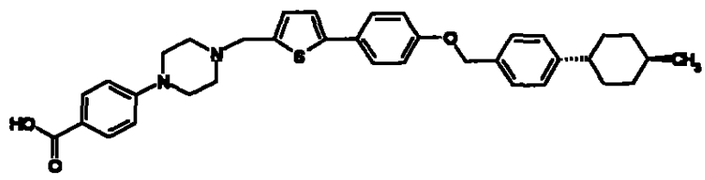
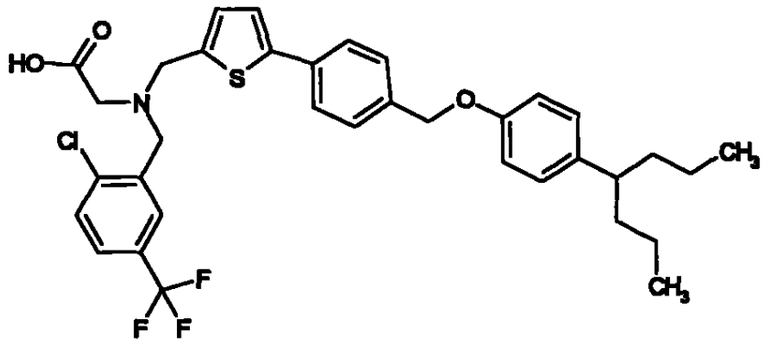
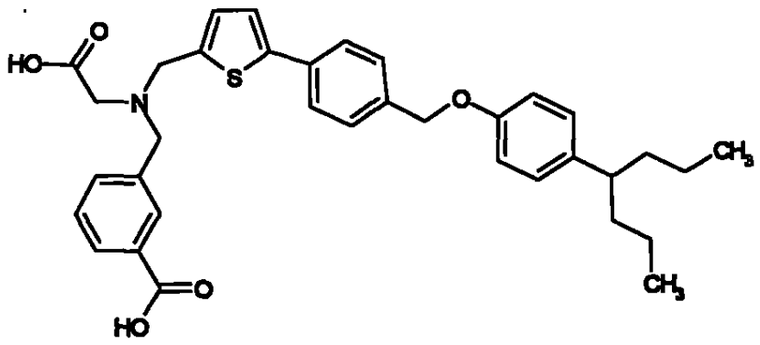
Example	Structural formula	m.p.(°C)
4-74		242.4 – 265.9
4-75		92.6 – 94.7
4-76		202.8 – 206.4

Table 4-25

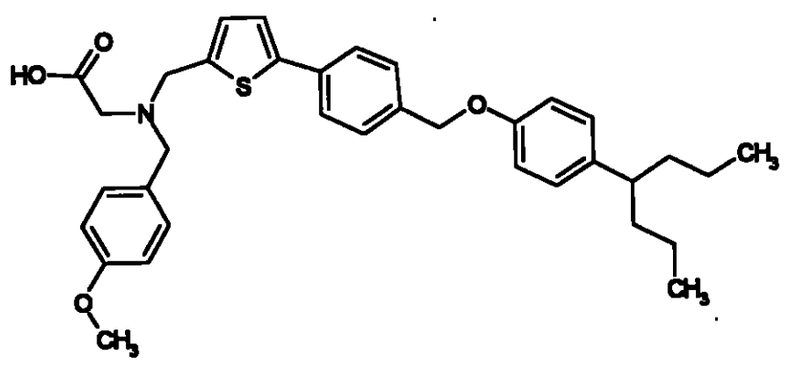
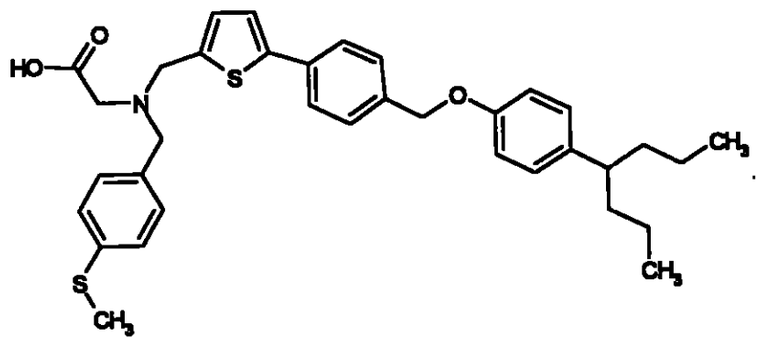
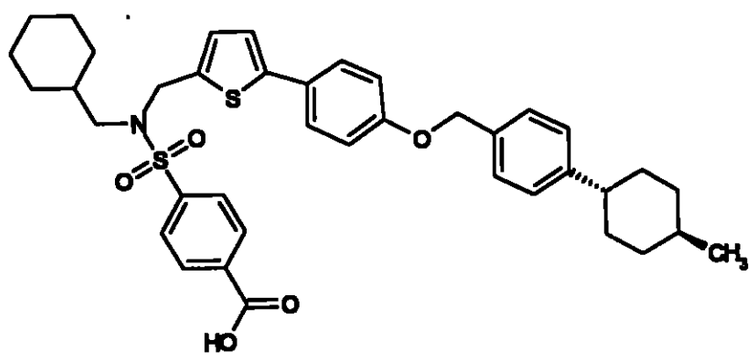
Example	Structural formula	m.p.(°C)
4-77		195.7 – 196.8
4-78		202.7 – 204.3
4-79		234 – 241.8

Table 4-26

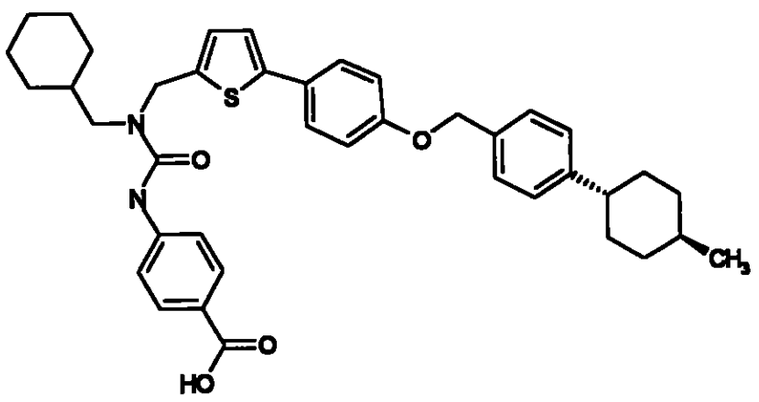
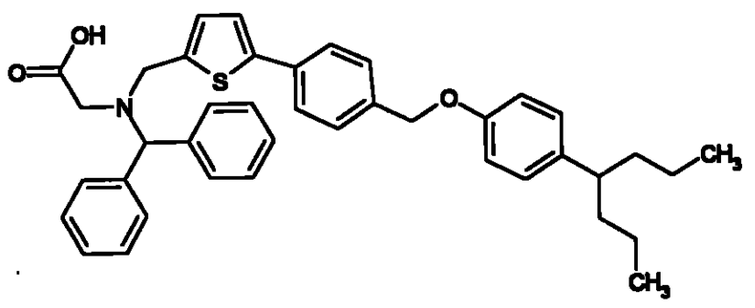
Example	Structural formula	m.p.(°C)
4-80		168 – 169.9
4-81		amor-phous

Table 4-27

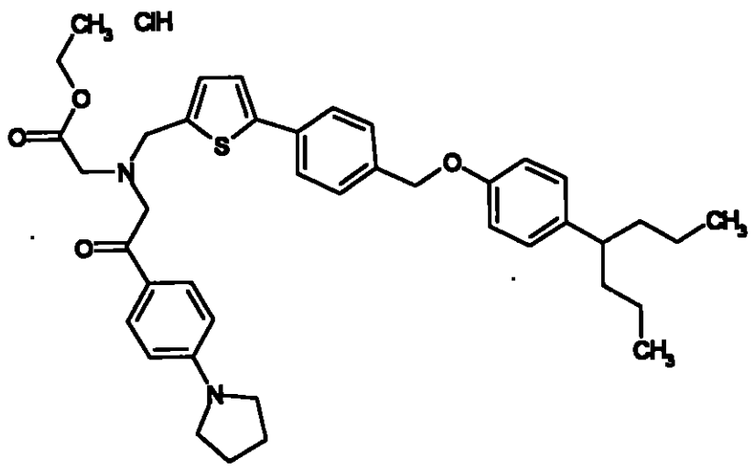
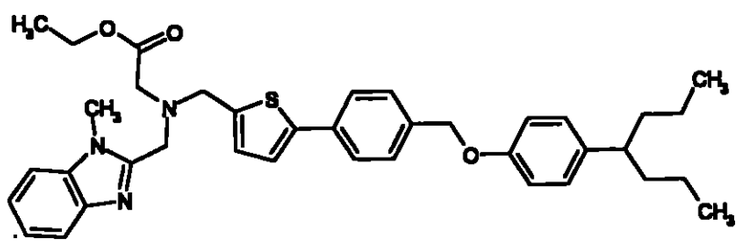
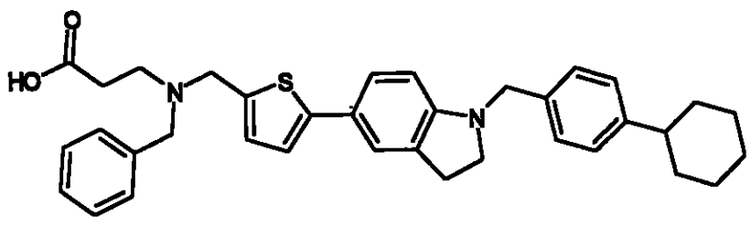
Example	Structural formula	m.p.(°C)
4-82		75.3 – 79.3
4-83		82 – 84
4-84		121 – 128

Table 4-28

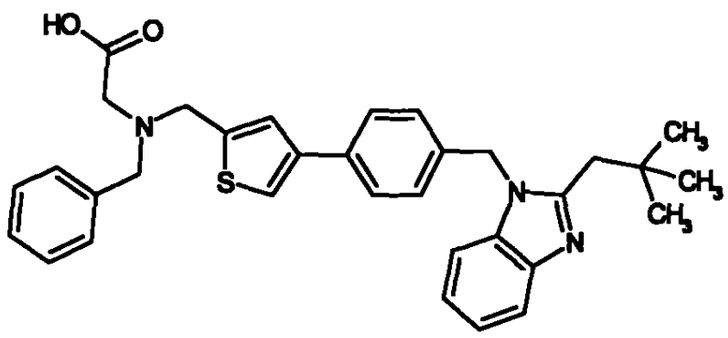
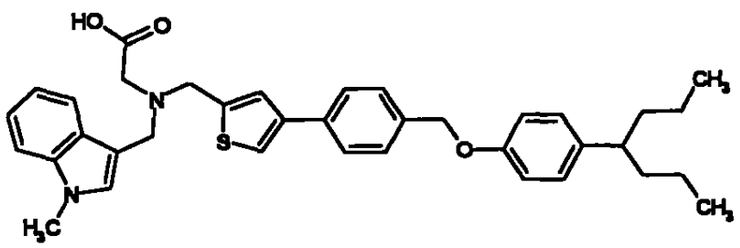
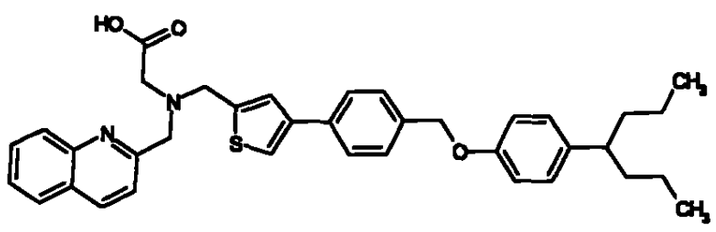
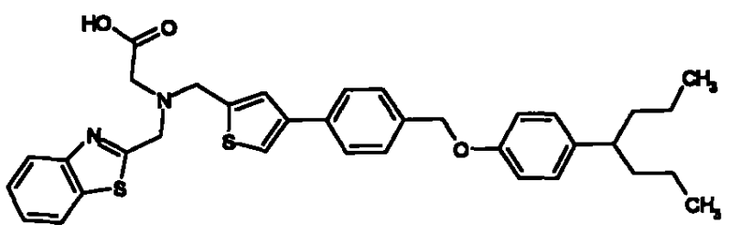
Example	Structural formula	m.p.(°C)
4-85		161 – 166
4-86		170.5 – 171.9
4-87		137.3 – 138.7
4-88		150.9 – 152.8

Table 4-29

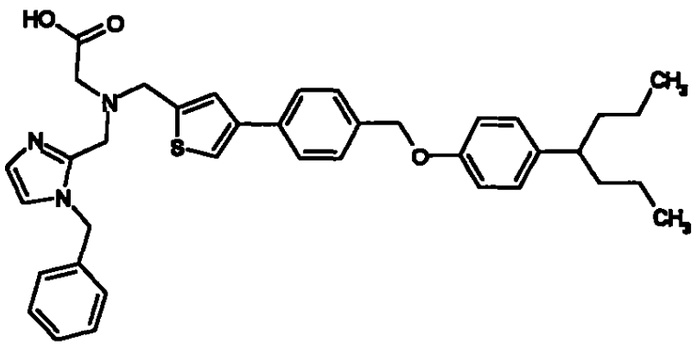
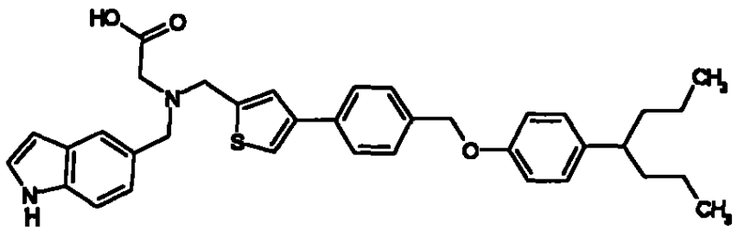
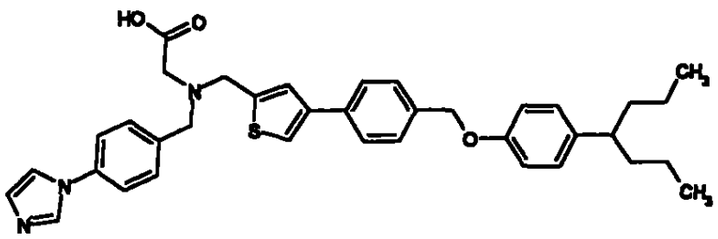
Example	Structural formula	m.p.(°C)
4-89		135.2 - 136
4-90		203.4 - 205.3
4-91		167.5 - 169.9

Table 4-30

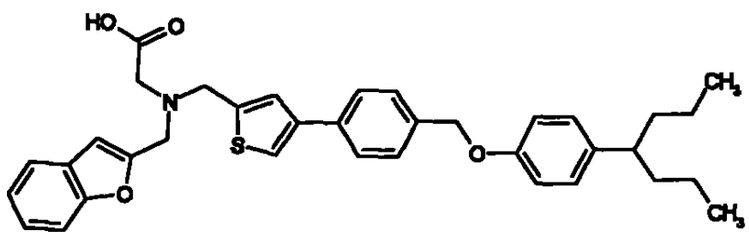
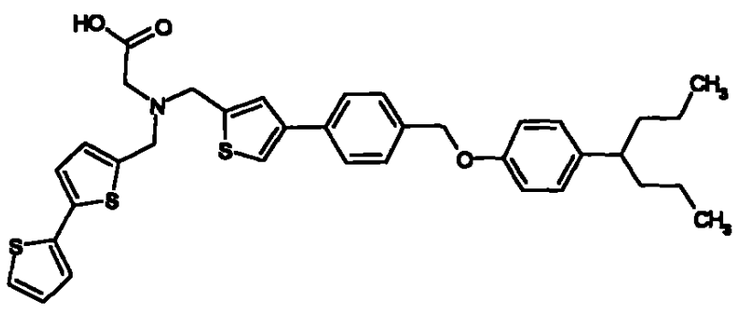
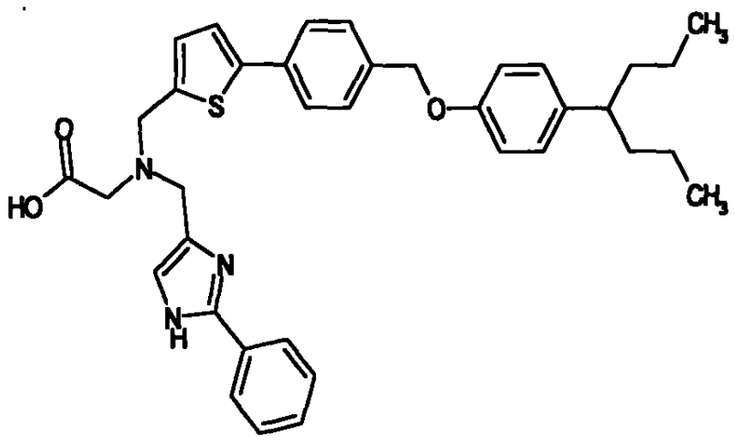
Example	Structural formula	m.p.(°C)
4-92		146.7 – 148.9
4-93		203.8 – 206.2
4-94		131.8 – 137.6

Table 4-31

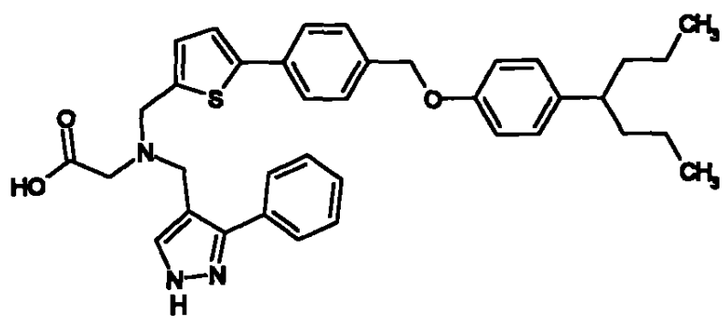
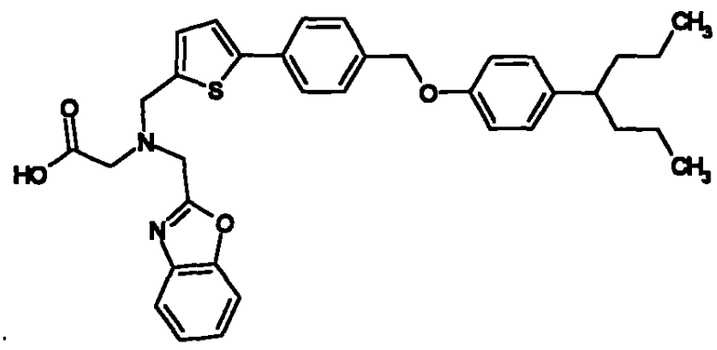
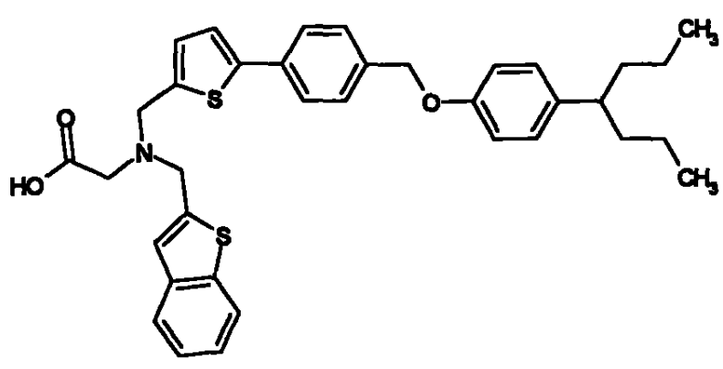
Example	Structural formula	m.p.(°C)
4-95		145.9 – 149.3
4-96		127.4 – 130
4-97		202.3 – 204.4

Table 4-32

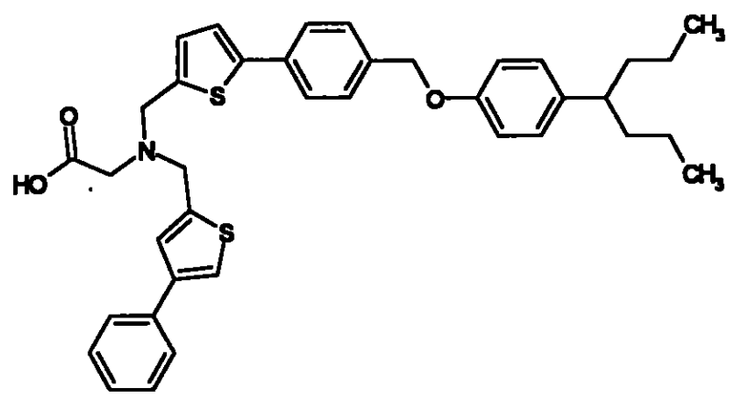
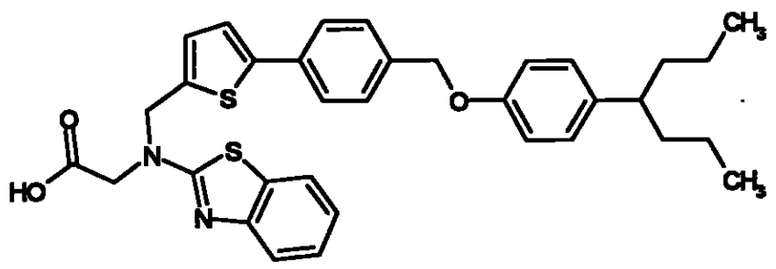
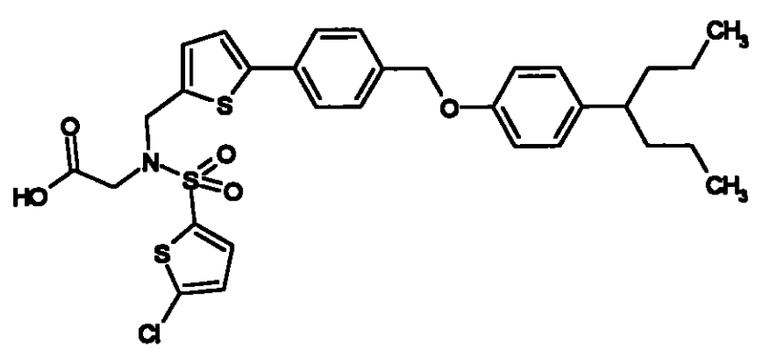
Example	Structural formula	m.p.(°C)
4-98		181.4 – 184.5
4-99		104.4 – 107.2
4-100		151.2 – 154.4

Table 4-33

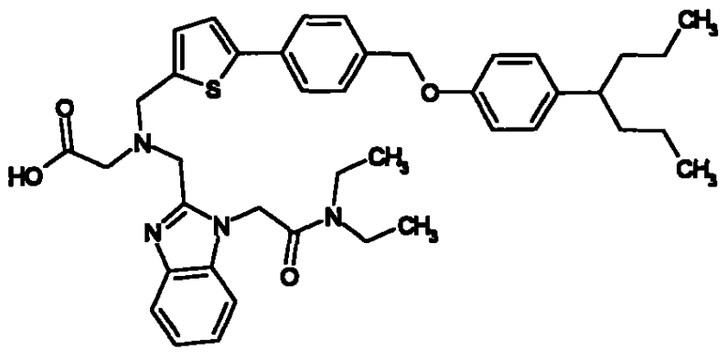
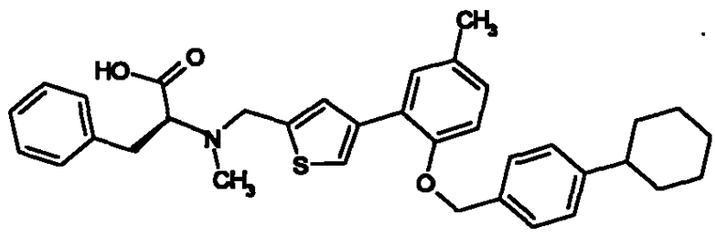
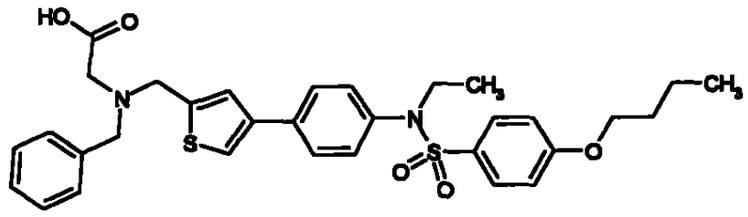
Example	Structural formula	m.p.(°C)
4-101		194.8 – 197
4-102		117 – 123.1
4-103		120.7 – 123.3

Table 4-34

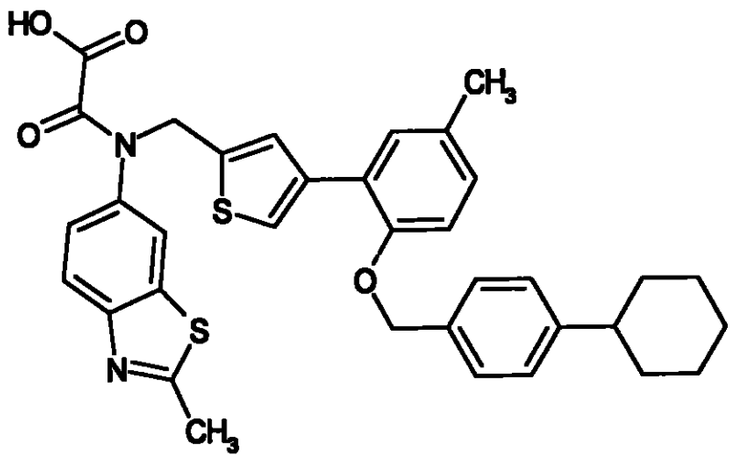
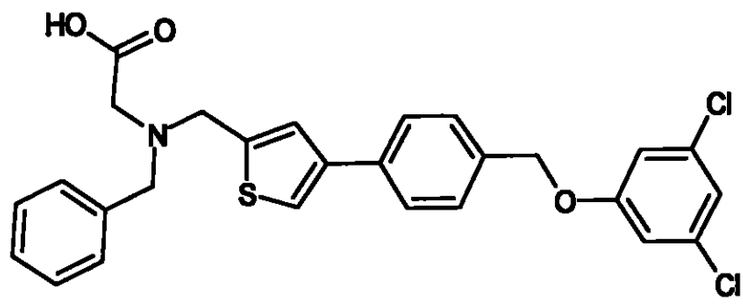
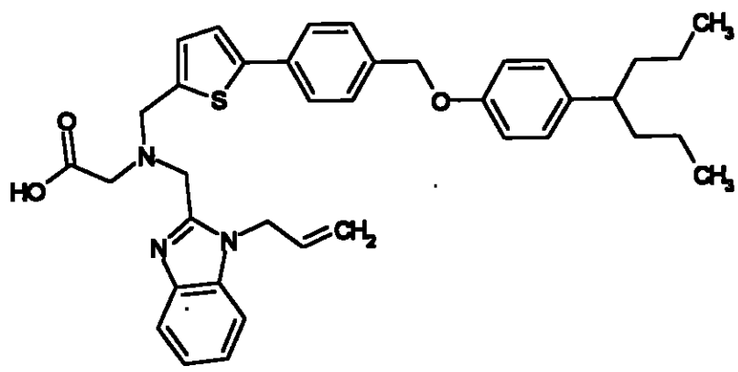
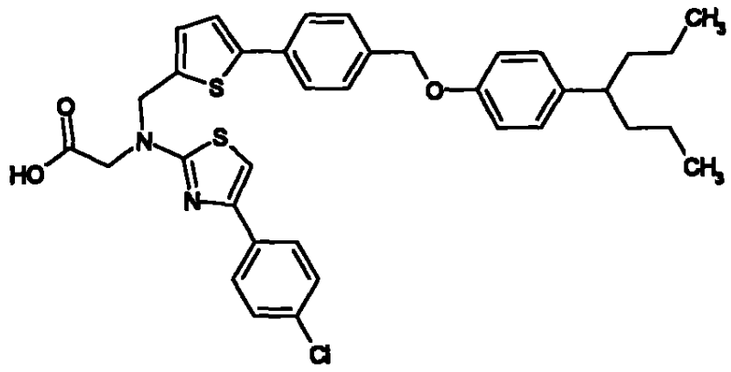
Example	Structural formula	m.p.(°C)
4-104		115.9 – 121.1
4-105		202.3 – 204.2
4-106		141.2 – 144.1

Table 4-35

Example	Structural formula	m.p.(°C)
4-107		116 – 117.6

The Formulation Examples are shown in the following, which are not to be construed as limiting the present invention.

Formulation Examples

(a)	compound of Ex. 1	10 g
(b)	lactose	50 g
(c)	cornstarch	15 g
(d)	sodium carboxymethylcellulose	44 g
(e)	magnesium stearate	1 g

The total amount of (a), (b) and (c) and 30 g of (d) were kneaded with water, dried in vacuo and granulated. The obtained granules were mixed with 14 g of (d) and 1 g of (e) and tableted with a tableting machine to give 1000 tablets containing 10 mg of (a) per tablet.

The test results of protein tyrosine phosphatase 1B inhibitory activity of the present invention are shown in the following.

Experimental Example 1 (protein tyrosine phosphatase 1B inhibitory activity)

Preparation of assay buffer:

A 50 mM Tris-HCl buffer (pH 7.5), 50 mM NaCl and 3 mM dithiothreitol (DTT) were prepared.

Preparation of sample:

10 mM DMSO solutions of 0.1, 0.3, 1, 3 and 10 μM of the test compound were prepared and diluted with the above-mentioned assay buffer to the final dimethyl sulfoxide (DMSO) concentration of not more than 1%. As the control, the assay buffer was used.

Preparation of substrate:

A synthetic peptide, wherein three tyrosines in 12 amino acids from 1142nd to 1153rd of the sequence of insulin receptor had been phosphorylated, was diluted with the above-mentioned assay buffer to 80 μM.

Preparation of enzyme:

Recombinant human protein tyrosine phosphatase 1B (manufactured by UBI) was diluted with the above-mentioned assay buffer (1.2 ng/25 μl).

(Evaluation method)

The sample (10 μl) prepared as mentioned above and a substrate (25 μl) were successively added to a 96 well plate, and the enzyme (25 μl) prepared as mentioned above was added and mixed. The mixture was incubated at room temperature for 60 min and a malachite green (120 μl, Biomol), which is a color reagent, was added. The mixture was further incubated at room temperature for 20 min to allow for color development. An absorbance at 650 nm was measured on a plate reader based on which the protein tyrosine phosphatase 1B inhibitory activity of the test compound was evaluated. The results are shown in Tables 5 and 6.

The T cell protein tyrosine phosphatase inhibitory activity of the compounds of Examples 1-1, 1-27, 1-48, 1-65, 1-66, 1-68, 1-71, 1-77, 1-78, 1-80, 1-86, 1-88, 1-89, 1-94, 1-97, 1-105, 1-109, 1-110, 1-111, 1-119, 1-120, 1-126, 1-130, 1-132, 1-138, 1-139, 1-140, 1-141, 1-146, 1-149, 1-153, 1-155, 1-156, 1-160, 1-161, 1-162, 3-1, 3-117, 3-120, 3-124, 4-1, 4-2, 4-6, 4-8, 4-9, 4-17, 4-18, 4-19, 4-21, 4-27, 4-30, 4-31, 4-34, 4-36 and 4-37 was evaluated and compared with the aforementioned protein tyrosine phosphatase 1B inhibitory activity. As a result, IC_{50} of protein tyrosine phosphatase 1B was as low as 1/60 or below of IC_{50} of T cell protein tyrosine phosphatase.

Experimental Example 2 (hypoglycemic activity)

A 0.5% methyl cellulose suspension of the test compound was orally administered to 6- to 9-week-old male ob/ob mice grouped according to the glucose level. Only a 0.5% methyl cellulose solution was administered to a control group.

Blood was drawn under fasting condition, which condition

was started simultaneously with the administration by means of removing the feed. The blood was drawn under anesthesia from the orbital vein 3 hours after the administration. The blood thus taken was centrifuged and the glucose level was measured from the obtained plasma by the hexokinase method (glucose measurement kit). For evaluation, the percentage (%) of decrease in the glucose level of the test compound-administered group relative to the control group is shown. The results are shown in Tables 5 to 9.

Table 5

Example	PTP1B inhibitory activity (IC50; μM)	blood glucose decreasing rate (%)	
		Dose (mg/kg)	3 hours later
1-1	0.28	1	45
1-15	0.13	1	35
1-19	0.10	1	35
1-25	0.13	1	25
1-37	0.14	3	26
1-39	0.19	1	32
1-44	0.22	1	20
1-45	0.066	1	32
1-48	0.23	1	46
1-50	0.14	---	
1-53	0.24	---	
1-78	0.18	3	24
1-141	0.35	---	
3-9	0.17	1	18
3-10	0.20	1	18
3-14	0.38	---	
3-15	0.27	1	25
3-21	0.45	1	27
3-25	0.14	1	20
3-26	0.11	---	
3-29	0.41	3	41
3-32	0.18	1	14
3-34	0.16	---	

Table 6

Example	PTP1B inhibitory activity (IC50; μM)	blood glucose decreasing rate (%)	
		dose (mg/kg)	3 hours later
3-35	0.073	---	
3-36	0.10	3	52
3-52	0.54	1	28
3-53	0.28	1	20
3-58	0.39	1	23
3-64	0.21	1	13
3-67	0.23	3	20
3-69	0.16	---	
3-70	0.16	---	
3-71	0.095	---	
3-73	0.20	1	14
3-76	0.48	1	33
3-86	0.20	1	16
3-87	0.21	---	
3-92	0.18	1	26
3-98	0.16	3	31
3-100	0.15	3	20
3-108	0.16	1	29
4-1	0.15	---	
4-6	0.092	---	
4-9	0.12	---	
4-30	0.17	---	
4-35	0.087	---	

Table 7

Example	PTP1B inhibitory activity (IC50; μM)	blood glucose decreasing rate (%)	
		dose (mg/kg)	3 hours later
1-155	0.37	---	
1-156	0.19	---	
1-157	0.17	---	
1-158	0.29	---	
1-160	0.31	---	
1-161	0.18	---	
1-162	0.21	---	
1-166	0.31	---	
1-167	0.41	---	
1-172	0.28	---	
1-178	0.44	---	
1-181	0.20	---	
1-182	0.19	---	
4-42	0.17	---	
4-43	0.16	---	
4-44	0.12	---	
4-45	0.27	---	
4-52	0.15	---	
4-53	0.07	---	
4-54	0.14	---	
4-55	0.17	---	
4-56	0.20	---	
4-57	0.17	---	

Table 8

Example	PTP1B inhibitory activity (IC50; μM)	blood glucose decreasing rate (%)	
		dose (mg/kg)	3 hours later
4-58	0.19	---	
4-59	0.18	---	
4-60	<0.1	---	
4-61	0.25	---	
4-62	0.45	---	
4-63	0.42	---	
4-64	0.24	---	
4-66	0.45	---	
4-67	0.23	---	
4-68	<0.1	---	
4-69	0.15	---	
4-70	0.17	---	
4-72	0.29	---	
4-73	0.19	---	
4-74	0.11	---	
4-75	<0.1	---	
4-77	0.40	---	
4-78	0.38	---	
4-79	<0.1	---	
4-80	<0.1	---	
4-81	<0.1	---	
4-82	0.48	---	
4-84	0.27	---	

Table 9

Example	PTP1B inhibitory activity (IC50; μM)	blood glucose decreasing rate (%)	
		dose (mg/kg)	3 hours later
4-87	0.12	---	
4-88	<0.1	---	
4-89	0.49	---	
4-90	0.16	---	
4-91	0.17	---	
4-92	<0.1	---	
4-93	<0.1	---	
4-94	0.12	---	
4-95	0.28	---	
4-96	0.12	---	
4-97	0.11	---	
4-98	<0.1	---	
4-99	<0.1	---	
4-100	<0.1	---	
4-101	0.10	---	
4-102	0.37	---	
4-104	0.20	---	
4-106	0.16	---	
4-107	<0.1	---	

Experimental Example 3 (effect of concomitant use with insulin on hypoglycemic activity)

A 0.5% methyl cellulose suspension of the test compound {note: Example 3-40 (30 mg/kg)} (test compound and insulin concomitant use group) or a 0.5% methyl cellulose solution alone (insulin administration group) was orally administered to 7-week-old, male SD rats once a day for 8 days, and 3 hours later, insulin (0.6 U/kg) was subcutaneously administered.

Blood was drawn on the day of the start of the administration, before administration of insulin on day 8 and 1 hour thereafter from the tail vein. For drawing blood, the animals were fasted after insulin administration. The blood thus taken was centrifuged and the glucose level was measured

from the obtained plasma by the hexokinase method (glucose measurement kit). For evaluation, the percentage (%) of decrease in the glucose level of the test compound and insulin concomitant use group and insulin administration group one hour later relative to before insulin administration is shown. The results are shown in Table 10.

Table 10

	dose of test compound (mg/kg)	blood glucose decreasing rate (%)	
		Day of start of administration	Day 8
Insulin administration group	------	29	17
test compound and insulin concomitant use group (Example 3-40)	30	43	36

Experimental Example 4 (effect of concomitant use with glibenclamide on hypoglycemic activity)

To 10-week-old female ob/ob mice grouped according to glucose level were orally administered a 0.5% methyl cellulose suspension of the test compound {note: Example 4-2 (1 mg/kg)} (test compound-administered group), a 0.5% methyl cellulose suspension of glibenclamide (3 mg/kg) (glibenclamide-administered group), simultaneously both a 0.5% methyl cellulose suspension of the test compound and a 0.5% methyl cellulose suspension (glibenclamide 3 mg/kg) (test compound and glibenclamide concomitant use group), or a 0.5% methyl cellulose solution alone (control group).

Blood was drawn under fasting condition, which condition was started simultaneously with the administration by means of removing the feed. The blood was drawn under anesthesia from the orbital vein 3 and 5 hours after the administration. The blood thus taken was centrifuged and the glucose level was

measured from the obtained plasma by the hexokinase method (glucose kit). For evaluation, the percentage (%) of decrease in the glucose level of each group other than the control group relative to the control group is shown. The results are shown in Table 11.

Table 11

	dose of test compound (mg/kg)	blood glucose decreasing rate (%)	
		3 hours later	5 hours later
Glibenclamide-administered group	-----	44	40
test compound-administered group (Example 4-2)	1	48	20
test compound and glibenclamide concomitant use group (Example 4-2)	1	64	60

Experimental Example 5 (effect of concomitant use with tolbutamide on hypoglycemic activity)

To 10-week-old male db/db mice grouped according to glucose level were orally administered a 0.5% methyl cellulose suspension of the test compound {note: Example 4-5 (5 mg/kg)} (test compound-administered group), a 0.5% methyl cellulose suspension of tolbutamide (30 mg/kg) (tolbutamide-administered group), simultaneously both a 0.5% methyl cellulose suspension of the test compound and a 0.5% methyl cellulose suspension (tolbutamide 30 mg/kg) (test compound and tolbutamide concomitant use group), or a 0.5% methyl cellulose solution alone (control group).

Blood was drawn under fasting condition, which condition was started simultaneously with the administration by means of removing the feed. The blood was drawn under anesthesia from the orbital vein 5 hours after the administration. The blood

thus taken was centrifuged and the glucose level was measured from the obtained plasma by the hexokinase method (glucose measurement kit). For evaluation, the percentage (%) of decrease in the glucose level of each group other than the control group relative to the control group is shown. The results are shown in Table 12.

Table 12

	dose of test compound (mg/kg)	blood glucose decreasing rate (%) 5 hours later
Tolbutamide-administered group	-----	26
test compound-administered group (Example 4-5)	5	26
test compound and tolbutamide concomitant use group (Example 4-5)	5	30

Experimental Example 6 (effect of concomitant use with nateglinide on hypoglycemic activity)

To 10-week-old male db/db mice grouped according to glucose level were orally administered a 0.5% methyl cellulose suspension of the test compound (note: Example 4-5 (5 mg/kg)) (test compound-administered group), a 0.5% methyl cellulose suspension of nateglinide (30 mg/kg) (nateglinide-administered group), simultaneously both a 0.5% methyl cellulose suspension of the test compound and a 0.5% methyl cellulose suspension (nateglinide 30 mg/kg) (test compound and nateglinide concomitant use group), or a 0.5% methyl cellulose solution alone (control group).

Blood was drawn under fasting condition, which condition was started simultaneously with the administration by means of removing the feed. The blood was drawn under anesthesia from

the orbital vein 2 hours after the administration. The blood thus taken was centrifuged and the glucose level was measured from the obtained plasma by the hexokinase method (glucose measurement kit). For evaluation, the percentage (%) of decrease in the glucose level of each group other than the control group relative to the control group is shown. The results are shown in Table 13.

Table 13

	dose of test compound (mg/kg)	blood glucose decreasing rate (%) 2 hours later
Nateglinide-administered group	-----	5
test compound-administered group (Example 4-5)	5	11
test compound and nateglinide concomitant use group (Example 4-5)	5	19

Experimental Example 7 (effect of concomitant use with metformin on hypoglycemic hydrochloride)

To 10-week-old female ob/ob mice grouped according to glucose level were orally administered a 0.5% methyl cellulose suspension of the test compound {note: Example 4-2 (1 mg/kg)} (test compound-administered group), a 0.5% methyl cellulose suspension of metformin chloride (30 mg/kg) (metformin-administered group), simultaneously both a 0.5% methyl cellulose suspension of the test compound and a 0.5% methyl cellulose suspension (metformin chloride 30 mg/kg) (test compound and metformin concomitant use group), or a 0.5% methyl cellulose solution alone (control group). The ob/ob mice were fasted for 3 hours before administration.

Blood was drawn under fasting condition, which condition was started simultaneously with the administration by means of

removing the feed. The blood was drawn under anesthesia from the orbital vein 3 and 5 hours after the administration. The blood thus taken was centrifuged and the glucose level was measured from the obtained plasma by the hexokinase method (glucose kit). For evaluation, the percentage (%) of decrease in the glucose level of each group other than the control group relative to the control group is shown. The results are shown in Table 14.

Table 14

	dose of test compound (mg/kg)	blood glucose decreasing rate (%)	
		3 hours later	5 hours later
Metformin-administered group	-----	17	39
test compound-administered group (Example 4-2)	1	19	20
test compound and metformin concomitant use group (Example 4-2)	1	40	51

Experimental Example 8 (effect of concomitant use with voglibose on hypoglycemic activity)

To 9-week-old female ob/ob mice grouped according to glucose level were orally administered a 0.5% methyl cellulose suspension of the test compound {note: Example 4-2 (1 mg/kg)} (test compound-administered group), a 0.5% methyl cellulose suspension of voglibose (0.3 mg/kg) (voglibose-administered group), simultaneously both a 0.5% methyl cellulose suspension of the test compound and a 0.5% methyl cellulose suspension (voglibose 0.3 mg/kg) (test compound and voglibose concomitant use group), or a 0.5% methyl cellulose solution alone (control group). One hour later, sucrose (2 g/5 mL/kg) was loaded.

Blood was drawn under fasting condition, which condition was started simultaneously with the loading by means of

removing the feed. The blood was drawn under anesthesia from the orbital vein 1 and 2 hours after the sucrose loading. The blood thus taken was centrifuged and the glucose level was measured from the obtained plasma by the hexokinase method (glucose kit). For evaluation, the percentage (%) of decrease in the glucose level of each group other than the control group relative to the control group is shown. The results are shown in Table 15.

Table 15

	dose of test compound (mg/kg)	blood glucose decreasing rate (%)	
		1 hour later	2 hours later
Voglibose-administered group	-----	35	38
test compound-administered group (Example 4-2)	1	32	40
test compound and voglibose concomitant use group (Example 4-2)	1	49	54

Experimental Example 9 (effect of concomitant use with Pioglitazone hydrochloride on hypoglycemic activity)

To 8-week-old male db/db mice grouped according to full feed glucose level were orally administered a 0.5% methyl cellulose suspension of the test compound {note: Example 4-5 (10 mg/kg)} (test compound-administered group), a 0.5% methyl cellulose suspension of Pioglitazone hydrochloride (3 mg/kg) (Pioglitazone-administered group), simultaneously both a 0.5% methyl cellulose suspension of the test compound and a 0.5% methyl cellulose suspension (Pioglitazone hydrochloride 3 mg/kg) (test compound and Pioglitazone concomitant use group), or a 0.5% methyl cellulose solution alone (control group), once a day for 3 days.

Blood was drawn under fasting condition, which condition was started simultaneously with the administration by means of removing the feed. The blood was drawn under anesthesia from the orbital vein on day 1 of administration and 3 hours after the administration on day 3. The blood thus taken was centrifuged and the glucose level was measured from the obtained plasma by the hexokinase method (glucose kit). For evaluation, the percentage (%) of decrease in the glucose level of each group other than the control group relative to the control group is shown. The results are shown in Table 16.

Table 16

	dose of test compound (mg/kg)	blood glucose decreasing rate (%)	
		Day of start of administration	Day 3
Pioglitazone-administered group	-----	11	44
test compound-administered group (Example 4-5)	10	24	32
test compound and Pioglitazone concomitant use group (Example 4-5)	10	30	48

The NMR data of the Example compounds are shown in the following Tables.

Table 17-1

Example	solvent, Hz	NMR(δ)
1-1	DMSO-d6, 300MHz	0.69 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.5 Hz, 6H), 1.48-1.31 (m, 2H), 1.64- 1.48 (m, 2H), 2.19- 2.06 (m, 1H), 4.23 (quint, J = 6.6 Hz, 1H), 5.67 (s, 2H), 6.62 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 7.36 (d, J = 8.2 Hz, 2H), 7.90 (d, J = 8.2 Hz, 2H), 7.99 (dd, J = 3.0, 1.5 Hz, 1H), 8.11 (s, 1H), 8.64 (d, J = 2.9 Hz, 1H), 8.72 (d, J = 1.5 Hz, 1H), 13.43 (br s, 1H).
1-2	DMSO-d6, 400MHz	0.68 (t, J = 7.4 Hz, 6 H), 1.14 (d, J = 8.0 Hz, 6 H), 1.32-1.46 (m, 2 H), 1.50- 1.62 (m, 2 H), 2.08- 2.17 (m, 1 H), 4.23 (quint, J = 6.6 Hz, 1 H), 4.37 (s, 2 H), 5.57 (s, 2 H), 6.62 (d, J = 8.8 Hz, 2 H), 6.88 (d, J = 8.8 Hz, 2 H), 7.17 (d, J = 9.2 Hz, 2 H), 7.36 (d, J = 8.3 Hz, 2 H), 7.89 (d, J = 8.8 Hz, 2 H), 7.91 (d, J = 9.0 Hz, 2 H), 8.09 (s, 1 H), 12.64 (br s, 1 H).
1-3	DMSO-d6, 400MHz	0.68(t, J=7.2Hz, 6H), 1.16(d, J=6.4Hz, 2H), 1.35-1.45(m, 2H), 1.50-1.60(m, 2H), 2.10-2.15(m, 1H), 4.20-4.25(m, 1H), 4.37(s, 2H), 5.75(s, 2H), 6.61(d, J=10.2Hz, 2H), 6.87(d, J=11.6Hz, 2H), 6.99(d, J=8.0Hz, 1H), 7.34(d, J=10.8Hz, 2H), 7.88(d, J=8.1Hz, 2H), 8.04(s, 1H), 8.18(d, J=8.0Hz, 1H), 8.70(s, 1H)
1-4	DMSO-d6, 400MHz	0.79(t, J=7.2Hz, 6H), 1.05-1.11(m, 4H), 1.39-1.50(m, 4H), 2.34-2.39(m, 1H), 2.97(s, 3H), 4.52(s, 2H), 5.65(s, 2H), 6.67(d, J=8.8Hz, 2H), 6.93(d, J=8.0Hz, 2H), 7.30(d, J=8.0Hz, 2H), 7.91(d, J=8.7Hz, 2H), 7.96-7.97(m, 1H), 8.12(s, 1H), 8.62(d, J=2.8Hz, 1H), 8.71(d, J=1.4Hz, 1H)
1-5	DMSO-d6, 400MHz	0.79(t, J=7.2Hz, 6H), 1.03-1.11(m, 4H), 1.39-1.50(m, 4H), 2.34-2.39(m, 1H), 2.97(s, 3H), 4.52(s, 2H), 5.56(s, 2H), , 6.67(d, J=8.8Hz, 2H), 6.93(d, J=8.8Hz, 2H), 7.15(d, J=8.8Hz, 2H), 7.30(d, J=8.8Hz, 2H), 7.91-7.93(m, 4H), 8.11(s, 1H)

Table 17-2

Example	solvent, Hz	NMR(δ)
1-6	DMSO-d6, 300MHz	0.85(t, J=7.3Hz, 6H), 1.10(d, J=6.8Hz, 6H), 1.25-1.64(m, 8H), 2.65-2.74(m, 1H), 3.84-3.91(m, 1H), 4.37(s, 2H), 5.77(s, 2H), 6.66(d, J=9.1Hz, 2H), 6.94(d, J=8.7Hz, 2H), 7.06(d, J=9.4Hz, 1H), 7.31(d, J=8.6Hz, 2H), 7.84(d, J=8.3Hz, 2H), 8.04(s, 1H), 8.22(dd, J=2.3, 8.7Hz, 1H), 8.75(dd, J=0.7, 2.6Hz, 1H), 13.05(brs, 1H)
1-7	DMSO-d6, 300MHz	0.85(t, J=7.2Hz, 6H), 1.11(d, J=6.8Hz, 6H), 1.25-1.64(m, 8H), 2.65-2.74(m, 1H), 3.83-3.92(m, 1H), 4.37(s, 2H), 5.65(s, 2H), 6.66(d, J=8.6Hz, 2H), 6.94(d, J=8.7Hz, 2H), 7.32(d, J=8.3Hz, 2H), 7.86(d, J=8.3Hz, 2H), 7.98-7.98(brs, 1H), 8.09(s, 1H), 8.63-8.63(brs, 1H), 8.72(s, 1H), 13.38(brs, 1H)
1-8	DMSO-d6, 300MHz	0.92(d, J=6.8Hz, 6H), 1.12(d, J=7.2Hz, 6H), 2.00-2.13(m, 1H), 2.67-2.78(m, 1H), 3.24(d, J=7.1Hz, 2H), 4.58(s, 2H), 5.66(s, 2H), 6.59(d, J=9.0Hz, 2H), 6.97(d, J=8.6Hz, 2H), 7.26(d, J=8.3Hz, 2H), 7.88(d, J=8.3Hz, 2H), 7.99-7.99(m, 1H), 8.10(s, 1H), 8.64(d, J=3.0Hz, 1H), 8.72(d, J=1.5Hz, 1H), 13.46(brs, 1H)
1-9	DMSO-d6, 300MHz	0.85(t, J=7.2Hz, 6H), 1.11(d, J=7.2Hz, 6H), 1.29-1.62(m, 8H), 2.65-2.74(m, 1H), 3.83-3.95(m, 1H), 4.37(s, 2H), 5.56(s, 2H), 6.66(d, J=8.6Hz, 2H), 6.94(d, J=8.7Hz, 2H), 7.17(d, J=9.1Hz, 2H), 7.32(d, J=8.3Hz, 2H), 7.85(d, J=8.3Hz, 2H), 7.92(d, J=9.0Hz, 2H), 8.07(s, 1H), 12.58(brs, 1H)
1-10	DMSO-d6, 300MHz	0.85(t, J=7.2Hz, 6H), 1.11(d, J=6.8Hz, 6H), 1.25-1.68(m, 8H), 2.65-2.75(m, 1H), 3.84-3.93(m, 1H), 4.37(s, 2H), 5.55(s, 2H), 6.66(d, J=8.7Hz, 2H), 6.94(d, J=8.7Hz, 2H), 7.32(d, J=8.3Hz, 2H), 7.35-7.36(m, 1H), 7.45(t, J=7.9Hz, 1H), 7.57-7.62(m, 2H), 7.86(d, J=8.3Hz, 2H), 8.06(s, 1H), 12.91(brs, 1H)

Table 17-3

Example	solvent, Hz	NMR(δ)
1-11	DMSO-d6, 300MHz	0.87(t, J = 6.0Hz, 6H), 1.09(d,J = 9.0Hz, 6H), 1.37-1.70(m,4H), 2.65-2.72(m,1H), 3.55-3.82(m,1H), 4.35(s,2H), 5.74(s,2H), 6.67(d,J = 9.0Hz, 2H), 6.92(d,J = 9.0Hz, 2H), 7.04(d,J = 9.0Hz, 1H), 7.31(d,J = 9.0Hz, 2H), 7.82(d,J = 9.0Hz, 2H), 8.01(s,1H), 8.20(d,J = 6.0Hz, 1H), 8.73(d,J = 3.0Hz, 1H)
1-12	DMSO-d6, 300MHz	0.88(t, J = 6.0Hz, 6H), 1.10(t, J = 6.0Hz, 6H), 1.37-1.72(m,4H), 2.53-2.76(m,1H), 3.57-3.84(m,1H), 4.36(s,2H), 5.63(s,2H), 6.45-6.76(m,2H), 6.83-7.07(m,2H), 7.19-7.42(m,2H), 7.80-7.86(m,2H), 7.92-7.95(m,1H), 8.04-8.08(m,1H), 8.59(m,1H), 8.7(m,1H)
1-13	DMSO-d6, 400MHz	0.68 (t, J = 7.3 Hz, 6 H), 1.16 (d, J = 6.7 Hz, 6 H), 1.33-1.46 (m, 2 H), 1.49- 1.62 (m, 2 H), 2.07- 2.17 (m, 1 H), 4.22 (quit, J = 6.5 Hz, 1 H), 4.36 (s, 2 H), 4.78 (s, 2 H), 6.61 (d, J = 8.8 Hz, 2 H), 6.88 (d, J = 8.6 Hz, 2 H), 7.33 (d, J = 8.3 Hz, 2 H), 7.50 (d, J = 8.8 Hz, 2 H), 7.84 (d, J = 8.6 Hz, 4 H), 7.92 (s, 1 H), 12.80 (br s, 1 H).
1-14	DMSO-d6, 400MHz	0.79(t, J=7.2Hz, 6H), 1.03-1.11(m, 4H), 1.39-1.50(m, 4H), 2.34-2.39(m, 1H), 2.97(s, 3H), 4.50(s, 2H), 4.78(s, 2H), , 6.66(d, J=8.8Hz, 2H), 6.93(d, J=8.4Hz, 2H), 7.28(d, J=8.0Hz, 2H), 7.50(d, J=8.0Hz, 2H), 7.82-7.85(m, 4H), 7.94(s, 1H)
1-15	DMSO-d6, 300MHz	0.79(t, J=7.1Hz, 6H), 1.02-1.16(m, 4H), 1.35-1.52(m, 4H), 2.32-2.42(m, 1H), 2.87(s, 3H), 2.96(s, 3H), 4.51(s, 2H), 4.68(s, 2H), 6.67(d, J=8.8Hz, 2H), 6.94(d, J=8.8Hz, 2H), 7.27(d, J=8.1Hz, 2H), 7.79(d, J=8.4Hz, 2H), 7.97(d, J=8.8Hz, 2H), 8.02(s, 1H), 8.13(d, J=8.8Hz, 2H), 13.20(brs, 1H)
1-16	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 1.02-1.15(m, 4H), 1.37-1.53(m, 4H), 1.78-1.88(m, 2H), 1.99(t, J=7.0Hz, 2H), 2.32-2.42(m, 1H), 2.89(s, 3H), 2.97(s, 3H), 3.21-3.26(m, 2H), 4.52(s, 2H), 4.67(s, 2H), 6.68(d, J=8.8Hz, 2H), 6.94(d, J=8.8Hz, 2H), 7.30(d, J=8.1Hz, 2H), 7.89(d, J=8.1Hz, 2H), 8.04(s, 1H)

Table 17-4

Example	solvent, Hz	NMR(δ)
1-17	DMSO-d6, 400MHz	1.11-1.37(m, 5H), 1.61-1.78(m, 5H), 2.23-2.33(m, 1H), 3.09(s, 3H), 4.22(s, 2H), 4.83(s, 2H), 5.97(brs, 1H), 6.48(d, J=8.4Hz, 2H), 6.87(d, J=8.4Hz, 2H), 7.12(s, 1H), 7.34(d, J=8.6Hz, 2H), 7.44(d, J=8.1Hz, 2H), 7.78(d, J=8.2Hz, 2H), 7.92(d, J=8.6Hz, 2H), 12.78(brs, 1H)
1-18	DMSO-d6, 400MHz	1.12-1.40(m, 5H), 1.63-1.82(m, 5H), 2.29-2.38(m, 1H), 2.96(s, 3H), 3.09(s, 3H), 4.49(s, 2H), 4.82(s, 2H), 6.65(d, J=8.6Hz, 2H), 6.99(d, J=8.6Hz, 2H), 7.12(s, 1H), 7.21(d, J=8.1Hz, 2H), 7.43(d, J=8.1Hz, 2H), 7.77(d, J=8.1Hz, 2H), 7.92(d, J=8.1Hz, 2H)
1-19	DMSO-d6, 300MHz	0.78(t, J=7.4Hz, 6H), 0.98-1.17(m, 4H), 1.32-1.54(m, 4H), 2.29-2.42(m, 1H), 2.95(s, 3H), 3.09(s, 3H), 4.49(s, 2H), 4.83(s, 2H), 6.66(d, J=8.7Hz, 2H), 6.93(d, J=8.7Hz, 2H), 7.14(s, 1H), 7.23(d, J=8.3Hz, 2H), 7.43(d, J=8.3Hz, 2H), 7.78(d, J=8.3Hz, 2H), 7.92(d, J=8.3Hz, 2H), 12.82(brs, 1H)
1-20	DMSO-d6, 300MHz	0.68(t, J=7.2Hz, 6H), 1.15(d, J=6.4Hz, 6H), 1.32-1.47(m, 2H), 1.49-1.64(m, 2H), 2.05-2.19(m, 1H), 3.09(s, 3H), 4.15-4.28(m, 1H), 4.34(s, 2H), 4.83(s, 2H), 6.61(d, J=8.6Hz, 2H), 6.87(d, J=8.6Hz, 2H), 7.12(s, 1H), 7.28(d, J=8.3Hz, 2H), 7.43(d, J=7.9Hz, 2H), 7.77(d, J=8.3Hz, 2H), 7.92(d, J=7.9Hz, 2H), 12.82(brs, 1H)
1-21	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6 H), 1.15 (d, J = 6.6 Hz, 6 H), 1.33-1.46 (m, 2 H), 1.48- 1.61 (m, 2 H), 2.06- 2.18 (m, 1 H), 2.34 (s, 3 H), 3.85 (d, J = 15.0 Hz, 1 H), 4.02 (d, J = 15.4 Hz, 1 H), 4.22 (quint, J = 6.6 Hz, 1 H), 4.36 (s, 2 H), 4.50 (s, 2 H), 6.62 (d, J = 8.4 Hz, 2 H), 6.88 (d, J = 8.8 Hz, 2 H), 7.32 (d, J = 8.0 Hz, 2 H), 7.34 (t, J = 7.1 Hz, 1 H), 7.40 (t, J = 7.0 Hz, 2 H), 7.47 (d, J = 7.0 Hz, 2 H), 7.84 (d, J = 8.1 Hz, 2 H), 7.93 (s, 1 H), 12.66 (br s, 1 H).

Table 17-5

Example	solvent, Hz	NMR(δ)
1-22	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6 H), 1.16 (d, J = 6.6 Hz, 6 H), 1.30-1.47 (m, 2 H), 1.48- 1.61 (m, 2 H), 2.07- 2.19 (m, 1 H), 2.37 (s, 3 H), 2.94 (dd, J = 14.1, 8.2 Hz, 1 H), 3.08 (dd, J = 13.9, 7.0 Hz, 1 H), 3.70 (t, J = 7.7 Hz, 1 H), 4.02 (d, J = 15.8 Hz, 1 H), 4.17 (d, J = 15.8 Hz, 1 H), 4.22 (t, J = 6.0 Hz, 1 H), 4.36 (s, 2 H), 6.62 (d, J = 8.8 Hz, 2 H), 6.88 (d, J = 8.8 Hz, 2 H), 7.16- 7.30 (m, 5 H), 7.32 (d, J = 8.4 Hz, 2 H), 7.83 (d, J = 8.4 Hz, 2 H), 7.86 (s, 1 H), 12.53 (br s, 1 H).
1-23	DMSO-d6, 300MHz	0.92 (d, J = 6.6 Hz, 6 H), 1.19 (s, 9 H), 2.05 (sept, J = 7.2 Hz, 1 H), 3.24 (d, J = 7.5 Hz, 2 H), 3.35 (s, 2 H), 3.86 (s, 2 H), 4.17 (s, 2 H), 4.57 (s, 2 H), 6.58 (d, J = 8.7 Hz, 2 H), 7.11 (d, J = 9.0 Hz, 2 H), 7.20- 7.45 (m, 5 H), 7.84 (d, J = 8.1 Hz, 2 H), 7.94 (s, 1 H), 13.38 (br s, 1 H).
1-24	DMSO-d6, 300MHz	0.92 (d, J = 6.6 Hz, 6 H), 2.05 (sept, J = 6.8 Hz, 1 H), 3.28 (d, J = 6.8 Hz, 2 H), 3.36 (s, 2 H), 3.86 (s, 2 H), 4.17 (s, 2 H), 4.61 (s, 2 H), 6.65 (d, J = 9.0 Hz, 2 H), 7.10 (d, J = 9.0 Hz, 2 H), 7.21 (d, J = 7.8 Hz, 2 H), 7.07- 7.43 (m, 5 H), 7.85 (d, J = 8.4 Hz, 2 H), 7.95 (s, 1 H), 12.37 (br s, 1 H).
1-25	DMSO-d6, 300MHz	0.79 (t, J = 7.1 Hz, 6 H), 1.00- 1.28 (m, 4 H), 1.34- 1.58 (m, 4 H), 2.30- 2.42 (m, 3 H), 2.97 (s, 3 H), 3.36 (s, 2 H), 3.87 (s, 2 H), 4.18 (s, 2 H), 4.51 (s, 2 H), 6.67 (d, J = 8.7 Hz, 2 H), 6.93 (d, J = 8.7 Hz, 2 H), 7.28 (d, J = 8.3 Hz, 2 H), 7.22- 7.43 (m, 5 H), 7.87 (d, J = 8.4 Hz, 2 H), 7.97 (s, 1 H), 12.38 (br s, 1 H).
1-26	MeOH-d4, 300MHz	0.70(t, J=7.3Hz, 6H), 1.26(d, J=6.4Hz, 6H), 1.36-1.53(m, 2H), 1.53-1.70(m, 2H), 2.11-2.24(m, 1H), 3.45(s, 2H), 3.97(s, 2H), 4.16-4.30(m, 3H), 4.50(s, 2H), 6.81(d, J=8.6Hz, 2H), 6.97(d, J=8.7Hz, 2H), 7.21-7.38(m, 5H), 7.44(d, J=6.7Hz, 2H), 7.68(s, 1H), 7.78(d, J=8.3Hz, 2H)

Table 17-6

Example	solvent, Hz	NMR(δ)
1-27	DMSO-d6, 300MHz	0.92 (d, J = 6.8 Hz, 6 H), 1.19 (s, 9 H), 2.05 (sept, J = 6.8 Hz, 1 H), 3.25 (d, J = 7.1 Hz, 2 H), 4.01 (s, 2 H), 4.58 (s, 2 H), 4.85 (s, 2 H), 6.60 (d, J = 8.7 Hz, 2 H), 6.93 (t, J = 7.3 Hz, 1 H), 7.11 (d, J = 9.1 Hz, 2 H), 7.23 (t, J = 7.9 Hz, 2 H), 7.24 (d, J = 8.7 Hz, 2 H), 7.43 (d, J = 7.5 Hz, 2 H), 7.85 (d, J = 8.3 Hz, 2 H), 7.94 (s, 1 H), 9.47 (br s, 1 H).
1-28	DMSO-d6, 300MHz	0.92 (d, J = 6.4 Hz, 6 H), 1.19 (s, 9 H), 2.05 (sept, J = 7.0 Hz, 1 H), 3.25 (d, J = 7.2 Hz, 2 H), 4.05- 4.25 (m, 2 H), 4.58 (s, 2 H), 4.76- 5.01 (m, 2 H), 6.59 (d, J = 8.7 Hz, 2 H), 7.11 (d, J = 8.7 Hz, 2 H), 7.26 (d, J = 7.9 Hz, 2 H), 7.33- 7.53 (m, 5 H), 7.81- 7.90 (m, 2 H), 7.97- 7.03 (m, 1 H), 12.84 (br s, 1 H).
1-29	DMSO-d6, 300MHz	0.91 (d, J = 6.6 Hz, 6 H), 1.22 (s, 9 H), 2.04 (sept, J = 6.8 Hz, 1 H), 3.19 (d, J = 7.0 Hz, 2 H), 4.36 (br s, 2 H), 4.54 (s, 2 H), 5.07 (s, 2 H), 6.67 (d, J = 8.8 Hz, 2 H), 7.13 (d, J = 8.8 Hz, 2 H), 7.26 (d, J = 8.4 Hz, 2 H), 7.47 (ddd, J = 7.6, 4.8, 1.2 Hz, 1 H), 7.70 (dt, J = 7.7, 1.1 Hz, 1 H), 7.81 (d, J = 8.1 Hz, 2 H), 7.82 (s, 1 H), 7.91 (td, J = 7.7, 1.8 Hz, 1 H), 8.56 (d, J = 4.8 Hz, 1 H).
1-30	DMSO-d6, 300MHz	0.92 (d, J = 6.6 Hz, 6 H), 1.22 (s, 9 H), 2.04 (sept, J = 6.8 Hz, 1 H), 3.20 (d, J = 7.0 Hz, 2 H), 4.18 (s, 2 H), 4.54 (s, 2 H), 4.93 (s, 2 H), 6.67 (d, J = 9.1 Hz, 2 H), 7.13 (d, J = 8.8 Hz, 2 H), 7.44 (ddd, J = 7.9, 5.0, 0.9 Hz, 1 H), 7.78- 7.86 (m, 4 H), 8.60- 8.65 (m, 2 H).
1-31	DMSO-d6, 300MHz	0.92 (d, J = 6.8 Hz, 6 H), 1.19 (s, 9 H), 2.05 (sept, J = 6.6 Hz, 1 H), 3.24 (d, J = 7.2 Hz, 2 H), 4.11 (s, 2 H), 4.58 (s, 2 H), 4.83 (s, 2 H), 6.58 (d, J = 9.0 Hz, 2 H), 7.11 (d, J = 8.7 Hz, 2 H), 7.23 (d, J = 8.3 Hz, 2 H), 7.55 (t, J = 7.5 Hz, 2 H), 7.63 (t, J = 7.3 Hz, 1 H), 7.76 (d, J = 8.3 Hz, 2 H), 7.86 (d, J = 7.5 Hz, 2 H), 7.95 (s, 1 H), 12.82 (br s, 1 H).

Table 17-7

Example	solvent, Hz	NMR(δ)
1-32	DMSO-d6, 300MHz	0.69 (t, J = 7.3 Hz, 6 H), 1.16 (d, J = 6.6 Hz, 6 H), 1.33-1.46 (m, 2 H), 1.47- 1.64 (m, 2 H), 2.07- 2.18 (m, 1 H), 3.09 (dd, J = 16.5, 3.3 Hz, 1 H), 3.18 (dd, J = 16.1, 6.2 Hz, 1 H), 3.94 (d, J = 16.1 Hz, 1 H), 3.97 (dd, J = 5.9, 3.6 Hz, 1 H), 4.09 (d, J = 15.8 Hz, 1 H), 4.21 (d, J = 6.2 Hz, 1 H), 4.26 (d, J = 8.4 Hz, 1 H), 4.37 (s, 2 H), 4.39 (d, J = 15.8 Hz, 1 H), 6.62 (d, J = 8.8 Hz, 2 H), 6.89 (d, J = 8.4 Hz, 2 H), 7.01- 7.17 (m, 4 H), 7.34 (d, J = 8.1 Hz, 2 H), 7.87 (d, J = 8.0 Hz, 2 H), 7.94 (s, 1 H), 12.51 (br s, 1 H).
1-33	DMSO-d6, 300MHz	0.69(t, J=7.3Hz, 6H), 1.16(d, J=6.4Hz, 6H), 1.32-1.48(m, 2H), 1.48-1.65(m, 2H), 2.06-2.20(m, 1H), 3.09(dd, J=3.4, 16.2Hz, 1H), 3.18(dd, J=6.0, 16.2Hz, 1H), 3.86-4.00(m, 2H), 4.09(d, J=15.4Hz, 1H), 4.16-4.45(m, 5H), 6.62(d, J=8.7Hz, 2H), 6.88(d, J=8.7Hz, 2H), 6.99-7.19(m, 4H), 7.34(d, J=8.3Hz, 2H), 7.87(d, J=8.3Hz, 2H), 7.94(s, 1H), 12.55(brs, 1H)
1-34	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 0.98-1.17(m, 4H), 1.33-1.58(m, 4H), 2.30-2.44(m, 1H), 2.98(s, 3H), 3.10(dd, J=2.6, 15.8Hz, 1H), 3.19(dd, J=6.0, 15.8Hz, 1H), 3.87-4.03(m, 2H), 4.10(d, J=15.5Hz, 1H), 4.26(d, J=15.8Hz, 1H), 4.41(d, J=15.8Hz, 1H), 4.52(s, 2H), 6.68(d, J=7.9Hz, 2H), 6.94(d, J=8.3Hz, 2H), 6.99-7.20(m, 4H), 7.29(d, J=8.3Hz, 2H), 7.88(d, J=7.9Hz, 2H), 7.97(s, 1H)
1-35	DMSO-d6, 300MHz	0.89(t, J = 9.0Hz, 6H), 1.09(t, J = 9.0Hz, 6H), 1.32-1.73(m,4H), 2.61-2.75(m,1H), 3.09(s,2H), 3.65-3.74(m,1H), 3.84-.89(m,2H), 4.06-4.19(m,1H), 4.24-4.25(m,1H), 4.33-4.40(m,3H), 6.68(d,J = 9.0Hz, 2H), 6.91-6.94(m,2H), 6.98-7.04(m,1H), 7.10-7.13(m,3H), 7.30(d,J = 6.0Hz, 2H), 7.81(d,J = 6.0Hz, 2H), 7.90(s,1H)
1-36	DMSO-d6, 400MHz	1.14-1.42(m, 5H), 1.64-1.82(m, 5H), 2.38-2.45(m, 1H), 3.60(s, 3H), 5.08(s, 2H), 6.92(d, J=8.6Hz, 2H), 7.12(d, J=8.6Hz, 2H), 7.41(s, 1H), 7.47(d, J=8.2Hz, 2H), 7.70(d, J=8.6Hz, 2H), 7.89(d, J=8.2Hz, 2H), 7.99(d, J=8.6Hz, 2H), 12.81(brs, 1H)

Table 17-8

Example	solvent, Hz	NMR(δ)
1-37	DMSO-d6, 400MHz	1.14-1.42(m, 5H), 1.64-1.81(m, 5H), 2.37-2.46(m, 1H), 3.10(s, 3H), 4.84(s, 2H), 5.06(s, 2H), 6.91(d, J=8.6Hz, 2H), 7.12(d, J=8.6Hz, 2H), 7.20(s, 1H), 7.43(d, J=5.4Hz, 2H), 7.45(d, J=5.4Hz, 2H), 7.86(d, J=8.1Hz, 2H), 7.93(d, J=8.1Hz, 2H)
1-38	DMSO-d6, 400MHz	0.61(t, J=7.4Hz, 3H), 1.20(s, 6H), 1.57(q, J=7.3Hz, 2H), 3.10(s, 3H), 4.83(s, 2H), 5.06(s, 2H), 6.92(d, J=8.8Hz, 2H), 7.20-7.22(m, 3H), 7.43(d, J=8.8Hz, 4H), 7.85(d, J=8.0Hz, 2H), 7.91(d, J=8.0Hz, 2H)
1-39	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 0.93-1.18(m, 4H), 1.32-1.59(m, 4H), 2.38-2.55(m, 1H), 3.11(s, 3H), 4.84(s, 2H), 5.06(s, 2H), 6.92(d, J=8.6Hz, 2H), 7.06(d, J=8.6Hz, 2H), 7.22(s, 1H), 7.45(d, J=8.2Hz, 4H), 7.87(d, J=8.2Hz, 2H), 7.93(d, J=8.2Hz, 2H), 12.83(brs, 1H)
1-40	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 0.99-1.17(m, 4H), 1.38-1.60(m, 4H), 2.40-2.52(m, 1H), 3.07(s, 3H), 4.73(s, 2H), 5.06(s, 2H), 6.93(d, J=8.7Hz, 2H), 7.06(d, J=8.7Hz, 2H), 7.19-7.23(m, 3H), 7.45(d, J=8.3Hz, 2H), 7.82(d, J=7.9Hz, 2H), 7.89(d, J=8.3Hz, 2H)
1-41	MeOH-d4, 300MHz	0.83(t, J=7.3Hz, 6H), 1.05-1.22(m, 4H), 1.40-1.64(m, 4H), 2.40-2.53(m, 1H), 2.61(s, 3H), 4.21(d, J=15.1Hz, 1H), 4.34(d, J=15.1Hz, 1H), 4.66(s, 1H), 5.08(s, 2H), 6.91(d, J=8.7Hz, 2H), 7.04(d, J=8.7Hz, 2H), 7.35-7.45(m, 3H), 7.46-7.59(m, 4H), 7.83(s, 1H), 7.93(d, J=8.3Hz, 2H)
1-42	DMSO-d6, 300MHz	0.79(t, J=7.4Hz, 6H), 0.99-1.17(m, 4H), 1.36-1.61(m, 4H), 2.40(s, 3H), 2.40-2.52(m, 1H), 2.95(dd, J=8.3, 13.9Hz, 1H), 3.08(dd, J=7.1, 13.9Hz, 1H), 3.73(t, J=7.5Hz, 1H), 4.05(d, J=15.8Hz, 1H), 4.21(d, J=15.8Hz, 1H), 5.07(s, 2H), 6.93(d, J=8.7Hz, 2H), 7.07(d, J=8.7Hz, 2H), 7.16-7.33(m, 5H), 7.49(d, J=8.3Hz, 2H), 7.81-8.05(m, 3H)

Table 17-9

Example	solvent, Hz	NMR(δ)
1-43	DMSO-d6, 300MHz	1.34 (s, 9 H), 2.23 (s, 3 H), 3.37 (s, 2 H), 3.88 (s, 2 H), 4.20 (s, 2 H), 5.12 (s, 2 H), 6.96 (s, 2 H), 7.04 (s, 1 H), 7.22- 7.45 (m, 5 H), 7.53 (d, J = 8.4 Hz, 2 H), 7.97 (d, J = 8.1 Hz, 2 H), 8.05 (s, 1 H), 12.38 (br s, 1 H).
1-44	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 0.95-1.18(m, 4H), 1.33-1.60(m, 4H), 2.40-2.54(m, 1H), 3.38(s, 2H), 3.88(s, 2H), 4.20(s, 2H), 5.08(s, 2H), 6.93(d, J=8.6Hz, 2H), 7.07(d, J=8.6Hz, 2H), 7.22-7.45(m, 5H), 7.50(d, J=8.2Hz, 2H), 7.96(d, J=8.2Hz, 2H), 8.05(s, 1H)
1-45	DMSO-d6, 300MHz	0.80(t, J=7.3Hz, 6H), 0.99-1.18(m, 4H), 1.37-1.61(m, 4H), 2.39-2.51(m, 1H), 3.10(dd, J=3.4, 16.2Hz, 1H), 3.19(dd, J=5.6, 15.8Hz, 1H), 3.88-4.03(m, 2H), 4.10(d, J=15.8Hz, 1H), 4.27(d, J=15.8Hz, 1H), 4.42(d, J=15.8Hz, 1H), 5.09(s, 2H), 6.94(d, J=8.6Hz, 2H), 7.01-7.20(m, 6H), 7.51(d, J=8.3Hz, 2H), 7.97(d, J=8.3Hz, 2H), 8.04(s, 1H), 12.56(brs, 1H)
1-46	DMSO-d6, 300MHz	0.80(t, J=7.3Hz, 6H), 0.99-1.18(m, 4H), 1.37-1.61(m, 4H), 2.39-2.51(m, 1H), 3.10(dd, J=3.4, 16.2Hz, 1H), 3.19(dd, J=5.6, 15.8Hz, 1H), 3.88-4.03(m, 2H), 4.10(d, J=15.8Hz, 1H), 4.27(d, J=15.8Hz, 1H), 4.42(d, J=15.8Hz, 1H), 5.09(s, 2H), 6.94(d, J=8.6Hz, 2H), 7.01-7.20(m, 6H), 7.51(d, J=8.3Hz, 2H), 7.97(d, J=8.3Hz, 2H), 8.04(s, 1H), 12.56(brs, 1H)
1-47	DMSO-d6, 300MHz	0.80(t, J=7.4Hz, 6H), 0.98-1.17(m, 4H), 1.36-1.60(m, 4H), 2.39-2.53(m, 1H), 3.10(dd, J=2.6, 15.8Hz, 1H), 3.19(dd, J=5.6, 16.2Hz, 1H), 3.88-4.02(m, 2H), 4.10(d, J=16.2Hz, 1H), 4.27(d, J=15.5Hz, 2H), 4.42(d, J=15.8Hz, 2H), 5.08(s, 2H), 6.94(d, J=8.3Hz, 2H), 7.01-7.21(m, 6H), 7.51(d, J=7.9Hz, 2H), 7.97(d, J=7.9Hz, 2H), 8.05(s, 1H), 12.59(brs, 1H)

Table 17-10

Example	solvent, Hz	NMR(δ)
1-48	DMSO-d6, 300MHz	0.80(t, J=7.2Hz, 6H), 1.02-1.15(m, 4H), 1.38-1.57(m, 4H), 2.41-2.48(m, 1H), 5.10(s, 2H), 5.69(s, 2H), 6.94(d, J=8.6Hz, 2H), 7.08(d, J=8.7Hz, 2H), 7.53(d, J=8.3Hz, 2H), 7.99-8.02(m, 3H), 8.21(s, 1H), 8.66(d, J=3.0Hz, 1H), 8.74(d, J=1.5Hz, 1H), 13.48(brs, 1H)
1-49	DMSO-d6, 300MHz	0.80(t, J=7.3Hz, 6H), 1.02-1.15(m, 4H), 1.38-1.58(m, 4H), 2.41-2.50(m, 1H), 5.10(s, 2H), 5.60(s, 2H), 6.94(d, J=8.7Hz, 2H), 7.07(d, J=9.0Hz, 2H), 7.19(d, J=9.1Hz, 2H), 7.53(d, J=8.3Hz, 2H), 7.93(d, J=9.1Hz, 2H), 8.00(d, J=8.3Hz, 2H), 8.19(s, 1H), 12.66(brs, 1H)
1-50	DMSO-d6, 300MHz	0.80(t, J=7.2Hz, 6H), 1.02-1.17(m, 4H), 1.38-1.56(m, 4H), 2.41-2.49(m, 1H), 2.88(s, 3H), 4.70(s, 2H), 5.08(s, 2H), 6.94(d, J=8.8Hz, 2H), 7.08(d, J=8.8Hz, 2H), 7.49(d, J=8.4Hz, 2H), 7.87(d, J=8.4Hz, 2H), 7.98(d, J=8.8Hz, 2H), 8.10(s, 1H), 8.14(d, J=8.8Hz, 2H), 13.38(brs, 1H)
1-51	DMSO-d6, 300MHz	0.80(t, J=7.3Hz, 6H), 1.02-1.15(m, 4H), 1.38-1.56(m, 4H), 1.88-1.98(m, 2H), 2.41(t, J=7.3Hz, 2H), 2.45-2.49(m, 1H), 2.92(s, 3H), 3.25-3.28(m, 2H), 4.72(s, 2H), 5.09(s, 2H), 6.94(d, J=8.8Hz, 2H), 7.08(d, J=8.8Hz, 2H), 7.52(d, J=8.4Hz, 2H), 7.97(d, J=8.1Hz, 2H), 8.13(s, 1H), 12.17(brs, 1H)
1-52	DMSO-d6, 400MHz	1.16-1.46(m, 5H), 1.67-1.85(m, 5H), 2.40-2.56(m, 1H), 3.62(s, 3H), 7.20(d, J=8.6Hz, 2H), 7.58(s, 1H), 7.68(d, J=8.6Hz, 2H), 7.71(d, J=9.2Hz, 2H), 7.95-8.05(m, 6H), 10.14(s, 1H), 12.75(brs, 1H)
1-53	DMSO-d6, 400MHz	1.17-1.45(m, 5H), 1.67-1.83(m, 5H), 2.43-2.52(m, 1H), 3.13(s, 3H), 4.86(s, 2H), 7.19(d, J=8.6Hz, 2H), 7.39(s, 1H), 7.46(d, J=8.6Hz, 2H), 7.67(d, J=8.6Hz, 2H), 7.94(d, J=8.6Hz, 2H), 7.96(d, J=9.2Hz, 2H), 7.99(d, J=9.2Hz, 2H), 10.11(s, 1H), 12.69(brs, 1H)

Table 17-11

Example	solvent, Hz	NMR(δ)
1-54	DMSO-d6, 300MHz	0.82(t, J=7.2Hz, 6H), 1.01-1.21(m, 4H), 1.41-1.63(m, 4H), 3.39(s, 2H), 3.89(s, 2H), 4.22(s, 2H), 7.14(d, J=8.6Hz, 2H), 7.24-7.46(m, 5H), 7.68(d, J=8.3Hz, 2H), 8.02(d, J=8.7Hz, 2H), 8.09(d, J=8.7Hz, 2H), 8.23(s, 1H), 10.19(s, 1H), 12.42(brs, 1H)
1-55	DMSO-d6, 300MHz	0.79(t, J = 6.0Hz, 6H), 1.04-1.12(m,4H), 1.45-1.56(m,4H), 2.43-2.48(m,1H), 3.38(s,2H), 3.88(s,2H), 4.21(s,2H), 4.47(d,J = 6.0Hz, 2H), 7.12(d,J = 9.0Hz, 2H), 7.23-7.45(m,8H), 7.97(d,J = 9.0Hz, 2H), 8.04(d,J = 9.0Hz, 2H), 8.19(s,1H), 9.03(t, J = 6.0Hz, 1H)
1-56	DMSO-d6, 300MHz	0.80(t, J = 6.0Hz, 6H), 1.06-1.18(m,4H), 1.47-1.54(m,4H), 2.88(s,3H), 3.37(s,2H), 3.88(s,2H), 4.20(s,2H), 4.50-4.64(m,2H), 7.17(d,J = 9.0Hz, 2H), 7.25-7.42(m,10H), 7.51(d,J = 6.0Hz, 2H), 8.00(d,J = 6.0Hz, 2H), 8.14(s,1H)
1-57	DMSO-d6, 300MHz	0.80(t, J = 6.0Hz, 6H), 0.93-1.24(m,10H), 1.40-1.67(m,4H), 3.37(s,2H), 3.88(s,2H), 4.20(s,2H), 4.48-4.65(m,1H), 7.15-7.49(m,12H), 8.00(d,J = 6.0Hz, 2H), 8.13(s,1H)
1-58	DMSO-d6, 300MHz	0.77(t, J=7.3Hz, 6H), 1.00-1.10(m, 4H), 1.19(s, 6H), 1.33-1.48(m, 4H), 2.27-2.37(m, 1H), 3.40(s, 2H), 4.45(brs, 1H), 4.72(s, 2H), 5.66(s, 2H), 6.66(d, J=8.6Hz, 2H), 6.84(d, J=8.8Hz, 2H), 7.27(d, J=8.0Hz, 2H), 7.87(d, J=8.3Hz, 2H), 7.98-7.99(m, 1H), 8.10(s, 1H), 8.64(d, J=2.9Hz, 1H), 8.73(d, J=1.4Hz, 1H)
1-59	DMSO-d6, 400MHz	0.92 (d, J = 6.5 Hz, 6 H), 1.19 (s, 9 H), 2.05 (sept, J = 6.7 Hz, 1 H), 3.19 (t, J = 4.5 Hz, 4 H), 3.24 (d, J = 7.2 Hz, 2 H), 3.57 (t, J = 4.5 Hz, 4 H), 3.92 (s, 2 H), 4.58 (s, 2 H), 4.68 (s, 2 H), 6.58 (d, J = 8.8 Hz, 2 H), 7.10 (d, J = 9.0 Hz, 2 H), 7.24 (d, J = 8.4 Hz, 2 H), 7.84 (d, J = 8.1 Hz, 2 H), 7.95 (s, 1 H), 12.69 (br s, 1 H).

Table 17-12

Example	solvent, Hz	NMR(δ)
1-60	DMSO-d6, 300MHz	0.69 (t, J = 7.4 Hz, 6 H), 1.16 (d, J = 6.8 Hz, 6 H), 1.31-1.48 (m, 2 H), 1.48- 1.64 (m, 2 H), 2.06- 2.19 (m, 1 H), 4.23 (sept, J = 6.6 Hz, 1 H), 4.38 (s, 2 H), 5.56 (s, 2 H), 6.62 (d, J = 8.7 Hz, 2 H), 6.89 (d, J = 8.6 Hz, 2 H), 7.36 (d, J = 8.3 Hz, 2 H), 7.80 (dd, J = 3.0, 1.5 Hz, 1 H), 7.90 (d, J = 8.3 Hz, 2 H), 8.08 (s, 1 H), 8.31 (d, J = 3.0 Hz, 1 H), 8.61 (d, J = 1.1 Hz, 1 H).
1-61	DMSO-d6, 300MHz	0.79(t, J = 9.0Hz, 6H), 1.02-1.11(m,4H), 1.40-1.56(m,4H), 2.40-2.51(m,1H), 2.95-3.00(m,1H), 3.14-3.22(m,1H), 3.31-3.36(m,2H), 3.69(d,J = 15.0Hz, 1H), 4.28-4.42(m,3H), 5.07(s,2H), 6.91-7.08(m,8H), 7.49(d,J = 9.0Hz, 2H), 7.96(d,J = 9.0Hz, 2H), 7.97(s,1H)
1-62	DMSO-d6, 300MHz	0.80 (t, J = 7.2 Hz, 6 H), 1.00- 1.17 (m, 4 H), 1.35- 1.62 (m, 4 H), 2.40- 2.53 (m, 1 H), 5.09 (s, 2 H), 5.58 (s, 2 H), 6.94 (d, J = 8.6 Hz, 2 H), 7.08 (d, J = 9.0 Hz, 2 H), 7.53 (d, J = 8.3 Hz, 2 H), 7.80 (dd, J = 3.0, 1.5 Hz, 1 H), 8.00 (d, J = 8.3 Hz, 2 H), 8.18 (s, 1 H), 8.32 (d, J = 3.0 Hz, 1 H), 8.61 (d, J = 1.1 Hz, 1 H).
1-63	DMSO-d6, 400MHz	0.68(t, J = 7.3 Hz, 6H), 1.16(d, J = 6.5 Hz, 6H), 1.34-1.45(m, 2H), 1.50-1.61(m, 2H), 2.09-2.16(m, 1H), 3.79 (s, 3H), 4.23(sep, J = 6.5 Hz, 1H), 4.37(s, 2H), 5.54 (s, 2H), 6.62(d, J = 8.6 Hz, 2H), 6.88(d, J = 8.6 Hz, 2H), 6.92(t, J = 2.4 Hz, 1H), 7.10(dd, J = 2.4, 1.2 Hz, 1H), 7.22(dd, J = 2.4, 1.2 Hz, 1H), 7.35 (d, J = 8.6 Hz, 2H), 7.89 (d, J = 8.6 Hz, 2H), 8.08(s, 1H), 13.03(brs, 1H)
1-64	DMSO-d6, 300MHz	0.68(t, J = 7.3 Hz, 6H), 1.16(d, J = 6.6 Hz, 6H), 1.32-1.47(m, 2H), 1.49-1.63(m, 2H), 2.08-2.17(m, 1H),4.05(s, 2H), 4.22(sep, J = 6.6 Hz, 1H), 4.37(s, 2H),4.87(s, 2H), 6.62(d, J = 8.4 Hz, 2H), 6.89(d, J = 8.4 Hz, 2H), 6.93(t,J = 7.3 Hz, 1H), 6.94(t, J = 7.3 Hz, 2H), 7.34(d,J = 8.4 Hz, 2H),7.44(d, J = 7.3 Hz, 2H), 7.87 (d, J = 8.4 Hz, 2H), 7.94(s, 1H), 9.49(brs, 1H)

Table 17-13

Example	solvent, Hz	NMR(δ)
1-65	DMSO-d6, 300MHz	0.68(t, J = 7.3 Hz, 6H), 1.16(d, J = 6.6 Hz, 6H), 1.32-1.47(m, 2H), 1.49-1.63(m, 2H), 2.08-2.18(m, 1H), 2.22(s, 3H), 4.19-4.28(m, 3H), 4.37(s, 2H), 4.89(s, 2H), 6.62(d, J = 8.4 Hz, 2H), 6.89(d, J = 8.4 Hz, 2H), 7.04(d, J = 8.4 Hz, 2H), 7.33(d, J = 8.4 Hz, 2H), 7.34(d, J = 8.4 Hz, 2H), 7.87(d, J = 8.4 Hz, 2H), 7.95(s, 1H), 8.80(brs, 1H), 12.70(brs, 1H)
1-66	DMSO-d6, 300MHz	0.68(t, J = 7.3 Hz, 6H), 1.16(d, J = 7.0 Hz, 12H), 1.33-1.47(m, 2H), 1.49-1.63(m, 2H), 2.06-2.17(m, 1H), 2.80(sep, J = 7.0 Hz, 1H), 4.04(s, 2H), 4.22(sep, J = 7.0 Hz, 1H), 4.37(s, 2H), 4.86(s, 2H), 6.62(d, J = 8.4 Hz, 2H), 6.88(d, J = 8.4 Hz, 2H), 7.09(d, J = 8.4 Hz, 2H), 7.34(d, J = 8.4 Hz, 4H), 7.87(d, J = 8.4 Hz, 2H), 7.93(s, 1H), 9.32(brs, 1H)
1-67	DMSO-d6, 300MHz	0.68(t, J = 7.3 Hz, 6H), 1.16(d, J = 6.6 Hz, 6H), 1.32-1.47(m, 2H), 1.49-1.63(m, 2H), 2.08-2.18(m, 1H), 3.08(s, 3H), 3.81(s, 2H), 4.22(sep, J = 6.6 Hz, 1H), 4.37(s, 2H), 4.63(s, 2H), 6.62 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8Hz, 2H), 7.10-7.15(m, 1H), 7.26-7.36(m, 6H), 7.84(d, J = 8.1 Hz, 2H), 7.93(s, 1H), 12.42(brs, 1H)
1-68	DMSO-d6, 400MHz	0.77(t, J = 7.3 Hz, 6H), 1.02-1.11(m, 4H), 1.16(d, J = 6.5Hz, 6H), 1.33-1.51(m, 4H), 2.29-2.37(m, 1H), 4.22(sep,J = 6.5 Hz,1H), 4.36(s, 2H), 5.66 (s, 2H), 6.59(d, J = 8.8 Hz, 2H), 6.87(d, J = 8.8 Hz, 2H), 7.35(d, J = 8.4 Hz, 2H), 7.89(d, J = 8.4 Hz, 4H), 7.98(dd, J = 3.0, 1.6Hz, 1H), 8.10(s, 1H),8.63(d, J = 3.0 Hz, 1H), 8.71(d, J = 1.6 Hz, 1H), 13.44(brs, 1H)
1-69	DMSO-d6, 300MHz	0.80(t, J=7.0Hz, 6H), 0.98-1.18(m, 4H), 1.36-1.60(m, 4H), 2.39-2.54(m, 1H), 4.18(s, 2H), 4.91(s, 2H), 5.09(s, 2H), 6.94(d, J=8.7Hz, 2H), 6.95(t, J=8.6Hz, 2H), 7.07(d, J=8.7Hz, 2H), 7.24(t, J=7.8Hz, 2H), 7.46(d, J=7.5Hz, 2H), 7.51(d, J=8.1Hz, 2H), 7.97(d, J=8.1Hz, 2H), 8.05(s, 1H), 9.11(brs, 1H)

Table 17-14

Example	solvent, Hz	NMR(δ)
1-70	DMSO-d6, 400MHz	0.68(t, J = 7.3 Hz, 6H), 1.16(d, J = 6.6 Hz, 6H), 1.33-1.47(m, 2H), 1.49-1.60(m, 2H), 2.08-2.17(m, 7H),4.18-4.25(m, 3H), 4.37(s, 2H), 4.90 (s, 2H), 6.62(d, J = 8.8 Hz, 2H), 6.88(d, J = 8.8 Hz, 2H), 7.02(s, 2H), 7.34(d, J = 8.4 Hz, 2H), 7.86(d, J = 8.4 Hz, 2H), 7.96(s, 1H), 8.16(brs, 1H), 12.70(brs, 1H)
1-71	DMSO-d6, 400MHz	0.68(t, J = 7.3 Hz, 6H), 1.16(d, J = 6.6 Hz, 6H), 1.33-1.47(m, 2H), 1.49-1.63(m, 2H), 2.08-2.18(m, 1H), 3.44(brs, 2H), 3.56(brs, 2H), 4.21(sep, J = 6.6 Hz,1H), 4.22(s, 2H), 4.36(s, 2H), 6.61(d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.01-7.04(m, 1H), 7.23-7.31(m, 4H), 7.61(d, J = 8.4 Hz, 2H), 7.84(d, J = 8.4 Hz, 2H), 7.94(s,1H), 10.94(brs,1H)
1-72	DMSO-d6, 300MHz	0.68(t, J=7.2Hz, 6H), 1.16(d, J=6.3Hz, 6H), 1.33(d, J=6.6Hz, 6H), 1.37-1.65(m, 4H), 2.06-2.21(m, 1H), 3.50-3.70(m, 1H), 4.06(s, 2H), 4.14-4.29(m, 1H), 4.37(s, 2H), 4.84(s, 2H), 6.62(d, J=8.4Hz, 2H), 6.88(d, J=8.4Hz, 2H), 7.35(d, J=7.8Hz, 2H), 7.86(d, J=8.1Hz, 2H), 8.01(s, 1H), 12.22(brs, 1H)
1-73	DMSO-d6, 400MHz	14.43(brs, 1H), 8.12(s, 1H), 7.88(d, J=8.4Hz, 2H), 7.35(d, J=8.4Hz, 2H), 7.07(s, 1H), 6.87(d, J=8.8Hz, 2H), 6.60(d, J=8.8Hz, 2H), 5.66(s, 2H), 4.37(s, 2H), 4.17-4.27(m, 1H), 2.27-2.39(m, 1H), 1.32-1.52(m, 4H), 1.16(d, J=6.4Hz, 6H), 0.99-1.12(m, 4H), 0.78(t, J=7.2Hz, 6H)
1-74	DMSO-d6, 300MHz	0.86 (t, J = 7.5 Hz, 6 H), 1.12 (d, J = 6.8 Hz, 6 H), 1.22-1.45 (m, 4 H), 1.70 (sept, J = 6.0 Hz, 1 H), 2.71 (sept, J = 6.8 Hz, 1 H), 3.33 (s, 2 H), 4.57 (s, 2 H), 5.66 (s, 2 H), 6.97 (d, J = 8.7 Hz, 2 H), 7.26 (d, J = 8.3 Hz, 2 H), 7.88 (d, J = 8.3 Hz, 2 H), 7.98 (dd, J = 3.0, 1.5 Hz, 1 H), 8.11 (s, 1 H), 8.64 (d, J = 3.0 Hz, 1 H), 8.72 (d, J = 1.9 Hz, 1 H), 13.44 (br s, 1 H).

Table 17-15

Example	solvent, Hz	NMR(δ)
1-75	DMSO-d6, 400MHz	0.68(t, J=7.4Hz, 6H), 1.15(d, J=6.4Hz, 6H), 1.32-1.66(m, 10H), 2.06-2.16(m, 1H), 2.92-2.98(m, 2H), 3.07-3.18(m, 2H), 3.31-3.48(m, 1H), 3.72(s, 1H), 4.01-4.09(m, 1H), 4.16-4.27(m, 1H), 4.36(s, 2H), 4.62(s, 1H), 6.60(d, J=8.8Hz, 2H), 6.87(d, J=8.4Hz, 2H), 7.32(d, J=7.6Hz, 2H), 7.84(d, J=8.0Hz, 2H), 7.91(s, 1H)
1-76	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6 H), 0.99- 1.18 (m, 4 H), 1.35- 1.61 (m, 4 H), 2.40- 2.55 (m, 1 H), 5.09 (s, 2 H), 5.79 (s, 2 H), 6.94 (d, J = 8.7 Hz, 2 H), 7.07 (d, J = 8.7 Hz, 2 H), 7.18 (dd, J = 7.4, 5.1 Hz, 1 H), 7.52 (d, J = 8.3 Hz, 2 H), 7.99 (d, J = 8.3 Hz, 2 H), 8.20 (dd, J = 7.3, 2.1 Hz, 1 H), 8.40 (dd, J = 4.9, 1.9 Hz, 1 H), 13.08 (br s, 1 H).
1-77	DMSO-d6, 400MHz	0.68 (t, J = 7.4 Hz, 6H), 1.15(d, J = 6.6 Hz, 6H), 1.34-1.45(m, 2H), 1.49-1.63(m, 2H), 2.08-2.15(m,1H), 2.22(s,3H), 3.41(brs, 2H), 3.53(brs, 2H), 4.18-4.23(m, 3H), 4.35(s, 2H), 6.60(d, J = 8.8 Hz, 2H), 6.87(d, J = 8.8 Hz, 2H), 7.06(d, J = 8.4 Hz, 2H), 7.32(d, J = 8.4 Hz, 2H), 7.51(d, J = 8.4 Hz, 2H), 7.84 (d, J = 8.4 Hz, 2H), 7.93(s, 1H), 10.91(brs, 1H)
1-78	DMSO-d6, 400MHz	0.68 (t, J = 7.3 Hz, 6H), 1.15(d, J = 6.5 Hz, 6H), 1.16(d, J = 6.5 Hz, 6H), 1.34-1.45(m, 2H), 1.50-1.60 (m, 2H), 2.08-2.16(m, 1H), 2.82(sep, J = 6.5 Hz, 1H), 3.55(s, 2H), 3.61(s, 2H), 4.22(sep, J = 6.5 Hz, 1H), 4.26(s, 2H), 4.36(s, 2H), 6.60(d, J = 8.8 Hz, 2H), 6.87(d, J = 8.8 Hz, 2H), 7.14(d, J = 8.3 Hz, 2H), 7.31(d, J = 8.3 Hz, 2H), 7.49(d, J = 8.3Hz, 2H), 7.84(d, J = 8.3 Hz, 2H), 7.95(s, 1H), 10.01(brs, 1H), 12.67(brs, 1H)
1-79	DMSO-d6, 300MHz	0.77(t, J = 7.3 Hz, 6H), 1.01-1.10(m,4H), 1.15(d, J = 6.6 Hz, 6H), 1.34-1.50(m, 4H), 2.28-2.38(m, 1H), 3.08(s, 3H), 3.67(s, 2H), 4.22(sep, J = 6.6 Hz, 1H), 4.36(s, 2H), 4.66(s, 2H), 6.61(d, J = 8.4 Hz, 2H), 6.88(d, J = 8.4 Hz, 2H), 7.06-7.11(m, 1H), 7.25-7.35(m, 6H), 7.84(d, J = 8.1 Hz, 2H), 7.92(s, 1H)

Table 17-16

Example	solvent, Hz	NMR(δ)
1-80	DMSO-d6, 300MHz	0.78(t, J = 7.3 Hz, 6H), 1.01-1.11(m,4H), 1.16(d, J = 6.6 Hz, 6H), 1.35-1.48(m, 4H), 2.23(s, 3H), 2.31-2.39(m, 1H), 4.19-4.26(m, 3H), 4.37(s, 2H), 4.89(s, 2H), 6.61(d, J = 8.4 Hz, 2H), 6.89(d, J = 8.4 Hz, 2H), 7.05(d, J = 8.4 Hz, 2H), 7.33(d, J = 8.4 Hz, 2H), 7.34(d, J = 8.4 Hz, 2H), 7.87(d, J = 8.1 Hz, 2H), 7.96(s, 1H), 8.76(brs, 1H), 12.71(brs, 1H)
1-81	DMSO-d6, 400MHz	0.77(t, J=7.4Hz, 6H), 0.99-1.11(m, 4H), 1.15(d, J=6.4Hz, 6H), 1.31-1.52(m, 4H), 2.27-2.37(m, 1H), 3.01(t, J=8.4Hz, 2H), 3.86(t, J=8.2Hz, 2H), 4.02(s, 2H), 4.16-4.26(m, 1H), 4.36(s, 2H), 4.82(s, 2H), 6.59(d, J=8.8Hz, 2H), 6.87(d, J=8.8Hz, 2H), 6.83-6.92(m, 1H), 7.11(t, J=8.2Hz, 1H), 7.19(d, J=7.6Hz, 1H), 7.25(d, J=8.0Hz, 1H), 7.33(d, J=8.4Hz, 2H), 7.86(d, J=8.4Hz, 2H), 7.97(s, 1H), 13.03(brs, 1H)
1-82	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6 H), 0.99- 1.19 (m, 4 H), 1.37- 1.60 (m, 4 H), 2.40- 2.53 (m, 1 H), 5.09 (s, 2 H), 5.63 (s, 2 H), 6.94 (d, J = 8.7 Hz, 2 H), 7.08 (d, J = 8.7 Hz, 2 H), 7.53 (d, J = 8.3 Hz, 2 H), 7.54 (dd, J = 8.5, 4.7 Hz, 1 H), 7.80 (dd, J = 8.7, 1.1 Hz, 1 H), 7.99 (d, J = 8.3 Hz, 2 H), 8.19 (s, 1 H), 8.23 (dd, J = 4.5, 1.1 Hz, 1 H), 13.22 (br s, 1 H).
1-83	DMSO-d6, 300MHz	0.86 (t, J = 7.3 Hz, 6 H), 1.12 (d, J = 6.8 Hz, 6 H), 1.23-1.44 (m, 4 H), 1.70 (sept, J = 6.4 Hz, 1 H), 2.71 (sept, J = 7.0 Hz, 1 H), 3.30 (d, J = 7.0 Hz, 2 H), 3.52- 3.69 (m, 4 H), 4.28 (s, 2 H), 4.53 (s, 2 H), 6.59 (d, J = 8.7 Hz, 2 H), 6.97 (d, J = 8.7 Hz, 2 H), 7.04 (t, J = 7.4 Hz, 1 H), 7.22 (d, J = 8.3 Hz, 2 H), 7.29 (t, J = 7.9 Hz, 2 H), 7.59 (d, J = 7.5 Hz, 2 H), 7.84 (d, J = 7.9 Hz, 2 H), 7.96 (s, 1 H), 10.05 (br s, 1 H), 12.54 (br s, 1 H).

Table 17-17

Example	solvent, Hz	NMR(δ)
1-84	DMSO-d6, 300MHz	0.86 (t, J = 7.4 Hz, 6 H), 1.12 (d, J = 6.8 Hz, 6 H), 1.17 (d, J = 6.8 Hz, 6 H), 1.26- 1.44 (m, 4 H), 1.63- 1.75 (m, 1 H), 2.71 (sept, J = 7.0 Hz, 1 H), 2.83 (sept, J = 7.0 Hz, 1 H), 3.30 (d, J = 7.0 Hz, 2 H), 3.50- 3.70 (m, 4 H), 4.27 (s, 2 H), 4.55 (s, 2 H), 6.59 (d, J = 8.7 Hz, 2 H), 6.97 (d, J = 8.6 Hz, 2 H), 7.15 (d, J = 8.3 Hz, 2 H), 7.22 (d, J = 8.3 Hz, 2 H), 7.49 (d, J = 8.7 Hz, 2 H), 7.84 (d, J = 7.9 Hz, 2 H), 7.97 (s, 1 H), 9.93 (br s, 1 H), 12.55 (br s, 1 H).
1-85	DMSO-d6, 300MHz	0.86 (t, J = 7.4 Hz, 6 H), 1.12 (d, J = 6.8 Hz, 6 H), 1.22- 1.45 (m, 4 H), 1.69 (sept, J = 6.6 Hz, 1 H), 2.71 (sept, J = 7.0 Hz, 1 H), 3.30 (d, J = 6.8 Hz, 2 H), 3.60- 3.69 (m, 4 H), 4.28 (s, 2 H), 6.59 (d, J = 8.7 Hz, 2 H), 6.97 (d, J = 8.6 Hz, 2 H), 7.22 (d, J = 8.3 Hz, 2 H), 7.70 (d, J = 9.0 Hz, 2 H), 7.83 (d, J = 8.3 Hz, 2 H), 7.88 (d, J = 8.7 Hz, 2 H), 7.95 (s, 1 H), 10.33 (s, 1 H), 12.66 (br s, 2 H).
1-86	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6 H), 0.98- 1.18 (m, 4 H), 1.36- 1.61 (m, 4 H), 2.40- 2.53 (m, 1 H), 5.09 (s, 2 H), 5.81 (s, 2 H), 6.94 (d, J = 8.7 Hz, 2 H), 7.07 (d, J = 8.7 Hz, 2 H), 7.22 (d, J = 7.5 Hz, 1 H), 7.52 (d, J = 8.3 Hz, 2 H), 7.75 (d, J = 7.5 Hz, 1 H), 7.96 (dd, J = 8.1, 7.3 Hz, 1 H), 7.99 (d, J = 8.3 Hz, 2 H), 8.15 (s, 1 H), 13.17 (br s, 1 H).
1-87	DMSO-d6, 300MHz	0.78(t, J=7.2Hz, 6H), 0.92(d, J=6.6Hz, 6H), 1.01-1.14(m, 4H), 1.33-1.56(m, 4H), 1.98-2.10(m, 1H), 2.27-2.40(m, 1H), 3.24(d, J=7.2Hz, 2H), 4.58(s, 2H), 5.55(s, 2H), 6.60(d, J=8.7Hz, 2H), 6.89(d, J=8.4Hz, 2H), 7.27(d, J=8.4Hz, 2H), 7.78(dd, J=3.0, 1.5Hz, 1H), 7.89(d, J=8.1Hz, 2H), 8.09(s, 1H), 8.30(d, J=3.3Hz, 1H), 8.60(d, J=0.9Hz, 1H)

Table 17-18

Example	solvent, Hz	NMR(δ)
1-88	DMSO-d6, 300MHz	0.78(t, J=7.2Hz, 6H), 0.92(d, J=6.9Hz, 6H), 1.00-1.16(m, 4H), 1.32-1.50(m, 4H), 1.97-2.11(m, 1H), 2.25-2.39(m, 1H), 3.23(d, J=7.2Hz, 2H), 3.97(brs, 2H), 4.57(s, 2H), 4.84(s, 2H), 6.59(d, J=9.3Hz, 2H), 6.86-6.97(m, 3H), 7.20-7.28(m, 4H), 7.42(d, J=8.4Hz, 2H), 7.86(d, J=7.8Hz, 2H), 7.95(s, 1H)
1-89	DMSO-d6, 300MHz	0.68(t, J=7.3Hz, 6H), 1.16(d, J=6.8Hz, 6H), 1.35-1.63(m, 4H), 2.08-2.18(m, 1H), 3.89(s, 3H), 4.19-4.28(m, 1H), 4.38(s, 2H), 5.68(s, 2H), 6.62(d, J=9.0Hz, 2H), 6.88(d, J=8.7Hz, 2H), 7.36(d, J=8.3Hz, 2H), 7.90(d, J=8.3Hz, 2H), 8.02-8.04(m, 1H), 8.11(s, 1H), 8.68(d, J=2.6Hz, 1H), 8.74(d, J=1.9Hz, 1H)
1-90	DMSO-d6, 300MHz	0.69 (t, J = 7.3 Hz, 6 H),1.16 (d, J = 6.5 Hz, 6 H),1.25-1.65 (m, 4 H),2.05- 2.20 (m, 1 H),4.15- 4.30 (m, 1 H),4.38 (s, 2 H),5.49 (s, 2 H),5.62 (s, 2 H),6.62 (d, J = 8.7 Hz, 2 H),6.68 (d, J = 8.2 Hz, 1 H),6.89 (d, J = 8.7 Hz, 2 H),7.35- 7.45 (m, 3 H),7.51 (br s, 1 H),7.90 (d, J = 8.2 Hz, 2 H),8.08 (s, 1 H).
1-91	DMSO-d6, 300MHz	0.69 (t, J = 7.3 Hz, 6 H),1.16 (d, J = 6.6 Hz, 6 H),1.30-1.65 (m, 4 H),2.05- 2.20 (m, 1 H),4.15- 4.30 (m, 1 H),4.38 (s, 2 H),5.56 (s, 2 H),6.62 (d, J = 8.3 Hz, 2 H),6.68 (d, J = 8.3 Hz, 2 H),7.30- 7.40 (m, 3 H),7.45 (t, J = 7.7 Hz, 1 H),7.58 (d, J = 7.7 Hz, 1 H),7.62 (br s, 1 H),7.90 (d, J = 8.7 Hz, 2 H),8.08 (s, 1 H).
1-92	DMSO-d6, 300MHz	0.69 (t, J = 7.3 Hz, 6 H),1.16 (d, J = 6.6 Hz, 6 H),1.30-1.65 (m, 4 H),2.05- 2.20 (m, 1 H),4.15- 4.30 (m, 1 H),4.37 (s, 2 H),4.65 (d, J = 6.0 Hz, 2 H),6.62 (d, J = 8.7 Hz, 2 H),6.70- 7.00 (m, 4 H),7.20- 7.30 (m, 3 H),7.34 (d, J = 8.4 Hz, 2 H),7.80- 7.90 (m, 3 H),12.66 (br s, 1 H).

Table 17-19

Example	solvent, Hz	NMR(δ)
1-93	DMSO-d6, 400MHz	0.68 (t, J = 7.3 Hz, 6 H),1.16 (d, J = 6.5 Hz, 6 H),1.35-1.65 (m, 4 H),2.10- 2.20 (m, 1 H),4.20- 4.30 (m, 1 H),4.37 (s, 2 H),5.78 (s, 2 H),6.61 (d, J = 8.8 Hz, 2 H),6.88 (d, J = 8.8 Hz, 2 H),7.35 (d, J = 8.4 Hz, 2 H),7.69 (dd, J = 8.3, 1.5 Hz, 1 H),7.89 (d, J = 8.4 Hz, 2 H),8.01 (d, J = 8.3 Hz, 1 H),8.05 (d, J = 1.5 Hz, 1 H),8.10 (s, 1 H).
1-94	DMSO-d6, 300MHz	0.77(t, J=7.3Hz, 6H), 0.98-1.21(m, 10H), 1.31-1.54(m, 4H), 2.25-2.41(m, 1H), 3.61(s, 2H), 4.14-4.43(m, 7H), 6.60(d, J=8.7Hz, 2H), 6.89(d, J=8.7Hz, 2H), 7.17-7.26(m, 2H), 7.32(d, J=8.3Hz, 2H), 7.52-7.61(m, 2H), 7.83(d, J=8.3Hz, 2H), 7.94(s, 1H)
1-95	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6 H), 0.99- 1.18 (m, 4 H), 1.35- 1.61 (m, 4 H), 2.40- 2.54 (m, 1 H), 3.60 (s, 2 H), 3.66 (s, 2 H), 4.30 (s, 2 H), 5.08 (s, 2 H), 6.93 (d, J = 9.0 Hz, 2 H), 7.05 (t, J = 7.3 Hz, 1 H), 7.07 (d, J = 8.7 Hz, 2 H), 7.30 (t, J = 7.9 Hz, 2 H), 7.49 (d, J = 8.3 Hz, 2 H), 7.60 (d, J = 7.6 Hz, 2 H), 7.95 (d, J = 8.7 Hz, 2 H), 8.06 (s, 1 H), 10.01 (s, 1 H), 12.65 (br s, 1 H).
1-96	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6 H), 0.96- 1.16 (m, 4 H), 1.36- 1.59 (m, 4 H), 2.38- 2.54 (m, 1 H), 3.66 (s, 2 H), 3.67 (s, 2 H), 4.31 (s, 2 H), 5.08 (s, 2 H), 6.93 (d, J = 8.7 Hz, 2 H), 7.07 (d, J = 8.7 Hz, 2 H), 7.34 (dd, J = 8.3, 4.5 Hz, 1 H), 7.49 (d, J = 8.3 Hz, 2 H), 7.95 (d, J = 8.3 Hz, 2 H), 8.05 (ddd, J = 8.5, 2.4, 1.5 Hz, 1 H), 8.05 (s, 1 H), 8.26 (dd, J = 4.9, 1.5 Hz, 1 H), 8.73 (d, J = 2.6 Hz, 1 H), 10.20 (s, 1 H), 12.63 (br s, 1 H).
1-97	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6 H), 0.99- 1.17 (m, 4 H), 1.37- 1.60 (m, 4 H), 2.39- 2.52 (m, 1 H), 2.84 (s, 6 H), 3.54 (s, 2 H), 3.64 (s, 2 H), 4.28 (s, 2 H), 5.08 (s, 2 H), 6.69 (d, J = 9.1 Hz, 2 H), 6.93 (d, J = 8.7 Hz, 2 H), 7.07 (d, J = 8.6 Hz, 2 H), 7.41 (d, J = 9.0 Hz, 2 H), 7.49 (d, J = 8.3 Hz, 2 H), 7.95 (d, J = 8.3 Hz, 2 H), 8.06 (s, 1 H), 9.70 (s, 1 H), 12.63 (br s, 1 H).

Table 17-20

Example	solvent, Hz	NMR(δ)
1-98	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6 H), 0.99- 1.16 (m, 4 H), 1.36- 1.60 (m, 4 H), 2.39- 2.52 (m, 1 H), 3.57 (s, 2 H), 3.65 (s, 2 H), 3.72 (s, 3 H), 4.29 (s, 2 H), 5.08 (s, 2 H), 6.88 (d, J = 9.0 Hz, 2 H), 6.93 (d, J = 8.6 Hz, 2 H), 7.07 (d, J = 8.6 Hz, 2 H), 7.49 (d, J = 8.3 Hz, 2 H), 7.51 (d, J = 9.1 Hz, 2 H), 7.95 (d, J = 8.3 Hz, 2 H), 8.06 (s, 1 H), 9.86 (s, 1 H), 12.63 (br s, 1 H).
1-99	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6 H), 0.96 (d, J = 6.8 Hz, 6 H), 1.00- 1.14 (m, 4 H), 1.36- 1.58 (m, 4 H), 2.38- 2.53 (m, 1 H), 3.16 (s, 2 H), 3.53 (s, 2 H), 4.17 (s, 2 H), 4.83 (t, J = 6.4 Hz, 1 H), 5.09 (s, 2 H), 6.94 (d, J = 8.7 Hz, 2 H), 7.07 (d, J = 8.7 Hz, 2 H), 7.10- 7.16 (m, 2 H), 7.33- 7.40 (m, 3 H), 7.51 (d, J = 8.3 Hz, 2 H), 7.93 (d, J = 8.3 Hz, 2 H), 8.01 (s, 1 H), 12.44 (br s, 1 H).
1-100	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6 H), 0.98- 1.16 (m, 4 H), 1.36- 1.61 (m, 4 H), 2.40- 2.54 (m, 1 H), 3.64 (s, 4 H), 4.30 (s, 2 H), 5.08 (s, 2 H), 6.93 (d, J = 8.3 Hz, 2 H), 7.07 (d, J = 8.7 Hz, 2 H), 7.11 (ddd, J = 7.2, 4.8, 1.0 Hz, 1 H), 7.49 (d, J = 8.3 Hz, 2 H), 7.78 (ddd, J = 8.4, 7.2, 1.0 Hz, 1 H), 7.97 (d, J = 7.9 Hz, 2 H), 8.06 (s, 1 H), 8.09 (d, J = 8.3 Hz, 1 H), 8.31 (ddd, J = 4.9, 1.9, 0.7 Hz, 1 H), 10.22 (s, 1 H), 12.61 (br s, 1 H).
1-101	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6 H), 0.99- 1.17 (m, 4 H), 1.35- 1.60 (m, 4 H), 1.71- 1.93 (m, 4 H), 2.40- 2.54 (m, 1 H), 3.11- 3.51 (m, 6 H), 3.78 (br s, 2 H), 4.28 (br s, 2 H), 5.09 (s, 2 H), 6.93 (d, J = 8.7 Hz, 2 H), 7.07 (d, J = 8.7 Hz, 2 H), 7.53 (d, J = 7.9 Hz, 2 H), 8.01 (d, J = 7.9 Hz, 2 H), 8.19 (s, 1 H).
1-102	DMSO-d6, 400MHz	0.79(t, J=7.4Hz, 6H), 0.99-1.14(m, 4H), 1.37-1.59(m, 4H), 2.32(s, 3H), 2.40-2.49(m, 1H), 3.50(s, 2H), 4.21(s, 2H), 4.28(s, 2H), 5.07(s, 2H), 6.92(d, J=8.8Hz, 2H), 7.06(d, J=8.4Hz, 2H), 7.20(brs, 1H), 7.49(d, J=8.4Hz, 2H), 7.94(d, J=8.4Hz, 2H), 8.06(s, 1H), 12.57(brs, 1H).

Table 17-21

Example	solvent, Hz	NMR(δ)
1-103	DMSO-d6, 300MHz	0.77(t, J = 7.3 Hz, 6H), 0.88-1.17(m,15H), 1.32-1.51(m, 4H), 1.56-1.72(m, 5H), 2.28-2.39(m, 1H), 3.38(d, J = 7.3 Hz, 2H), 4.22(sep, J = 6.6 Hz, 1H), 4.36(s, 2H), 4.90(s, 2H), 6.61(d, J = 8.8 Hz, 2H), 6.88(d, J = 8.8 Hz, 2H), 7.34(d, J = 8.4 Hz, 2H), 7.60(d, J = 8.4 Hz, 2H), 7.82-7.87 (m, 4H), 7.94(s, 1H), 8.88(brs, 1H), 12.54(brs, 1H)
1-104	DMSO(NaOD)-d6, 400MHz	0.77(t, J = 7.3 Hz, 6H), 0.77(d, J = 6.7 Hz, 6H), 1.02-1.11(m, 4H), 1.14(d, J = 6.5 Hz, 6H), 1.34-1.50(m, 4H), 1.94-2.01(m, 1H), 2.29-2.37(m, 1H), 3.31-3.38(m, 2H), 4.21(sep, J = 6.5 Hz, 1H), 4.36(s, 2H), 4.88(s, 2H), 6.59(d, J = 8.6 Hz, 2H), 6.87(d, J = 8.6 Hz, 2H), 7.33(d, J = 8.1 Hz, 2H), 7.38(d, J = 8.1 Hz, 2H), 7.75(d, J = 8.4 Hz, 2H), 7.86(d, J = 8.4 Hz, 2H), 7.93(s, 1H)
1-105	DMSO-d6, 300MHz	0.78(t, J=7.1Hz, 6H), 0.92(d, J=6.3Hz, 6H), 1.00-1.13(m, 4H), 1.31-1.55(m, 4H), 1.96-2.10(m, 1H), 2.26-2.39(m, 1H), 3.08(s, 3H), 3.23(d, J=7.5Hz, 2H), 3.78(s, 2H), 4.57(s, 2H), 4.63(s, 2H), 6.59(d, J=9.0Hz, 2H), 6.88(d, J=8.7Hz, 2H), 7.09-7.14(m, 1H), 7.24-7.36(m, 6H), 7.83(d, J=8.1Hz, 2H), 7.93(s, 1H)
1-106	DMSO-d6, 400MHz	0.78(t, J=7.4Hz, 6H), 0.92(d, J=6.4Hz, 6H), 1.02-1.12(m, 4H), 1.34-1.51(m, 4H), 2.00-2.07(m, 1H), 2.30-2.36(m, 1H), 3.22(d, J=6.4Hz, 2H), 3.42(brs, 2H), 3.51(s, 2H), 4.22(s, 2H), 4.56(s, 2H), 6.57(d, J=8.4Hz, 2H), 6.87(d, J=8.4Hz, 2H), 6.99-7.04(m, 1H), 7.22(d, J=8.0Hz, 2H), 7.26(dd, J=8.8, 7.2Hz, 2H), 7.65(d, J=8.8Hz, 2H), 7.82(d, J=8.8Hz, 2H), 7.93(s, 1H)
1-107	DMSO-d6, 400MHz	0.78(t, J=7.2Hz, 6H), 0.92(d, J=6.4Hz, 6H), 1.01-1.12(m, 4H), 1.17(d, J=6.8Hz, 6H), 1.33-1.51(m, 4H), 1.98-2.09(m, 1H), 2.28-2.37(m, 1H), 2.82(q, J=9.2Hz, 1H), 3.22(d, J=7.6Hz, 2H), 3.54(s, 2H), 3.59(s, 2H), 4.25(s, 2H), 4.56(s, 2H), 6.57(d, J=8.8Hz, 2H), 6.87(d, J=8.4Hz, 2H), 7.14(d, J=8.4Hz, 2H), 7.22(d, J=8.0Hz, 2H), 7.49(d, J=8.8Hz, 2H), 7.83(d, J=8.4Hz, 2H), 7.95(s, 1H)

Table 17-22

Example	solvent, Hz	NMR(δ)
1-108	DMSO-d6, 300MHz	0.78 (t, J = 7.4 Hz, 6 H),0.98- 1.14 (m, 4 H),1.16 (d, J = 6.4 Hz, 6 H),1.30- 1.55 (m, 4 H),2.15 (s, 3 H),2.25- 2.40 (m, 1 H),4.15- 4.30 (m, 1 H),4.37 (s, 2 H),5.64 (s, 2 H),6.61 (d, J = 8.7 Hz, 2 H),6.89 (d, J = 8.7 Hz, 2 H),7.38 (d, J = 8.1 Hz, 2 H),7.57 (dd, J = 8.6, 1.9 Hz, 1 H),7.78 (d, J = 1.9 Hz, 1 H),7.91 (d, J = 8.1 Hz, 2 H),8.09 (s, 1 H),8.14 (d, J = 8.6 Hz, 1 H),9.43 (s, 1 H),12.72 (br s, 1 H).
1-109	DMSO-d6, 300MHz	0.78 (t, J = 7.3 Hz, 6 H),1.00- 1.15 (m, 4 H),1.16 (d, J = 6.4 Hz, 6 H),1.30- 1.53 (m, 4 H),2.30 (s, 6 H),2.25- 2.40 (m, 1 H),3.14 (s, 2 H),4.15- 4.30 (m, 1 H),4.37 (s, 2 H),5.67 (s, 2 H),6.61 (d, J = 8.7 Hz, 2 H),6.88 (d, J = 8.7 Hz, 2 H),7.36 (d, J = 8.5 Hz, 2 H),7.65 (dd, J = 8.5, 1.5 Hz, 1 H),7.78 (d, J = 1.5 Hz, 1 H),7.91 (d, J = 8.5 Hz, 2 H),8.14 (s, 1 H),8.41 (d, J =8.5 Hz, 1 H),10.00 (s, 1 H),12.81 (br s, 1 H).
1-110	DMSO-d6, 300MHz	0.68(t, J=7.3Hz, 6H), 1.16(d, J=6.4Hz, 6H), 1.31-1.48(m, 2H), 1.49-1.64(m, 2H), 2.06-2.19(m, 1H), 3.58(s, 2H), 4.15-4.40(m, 7H), 6.62(d, J=8.7Hz, 2H), 6.88(d, J=8.7Hz, 2H), 7.14-7.22(m, 2H), 7.33(d, J=8.3Hz, 2H), 7.50-7.58(m, 2H), 7.84(d, J=8.3Hz, 2H), 7.95(s, 1H)
1-111	DMSO-d6, 300MHz	0.79(t, J=7.2Hz, 6H), 0.97-1.18(m, 4H), 1.36-1.61(m, 4H), 2.39-2.54(m, 1H), 3.59(s, 2H), 4.20(s, 2H), 4.33(s, 2H), 5.08(s, 2H), 6.93(d, J=8.6Hz, 2H), 7.07(d, J=8.7Hz, 2H), 7.12-7.21(m, 2H), 7.44-7.58(m, 4H), 7.95(d, J=8.3Hz, 2H), 8.05(s, 1H)
1-112	DMSO-d6, 300MHz	0.78 (t, J = 7.4 Hz, 6 H),1.00- 1.15 (m, 4 H),1.16 (d, J = 6.4 Hz, 6 H),1.30- 1.55 (m, 4 H),2.25- 2.40 (m, 1 H),3.08 (s, 3 H),4.15- 4.30 (m, 1 H),4.37 (s, 2 H),5.62 (s, 2 H),6.61 (d, J = 8.7 Hz, 2 H),6.89 (d, J = 8.7 Hz, 2 H),7.38 (d, J = 8.3 Hz, 2 H),7.45 (d, J = 8.3 Hz, 1 H),7.60 (dd, J = 8.3, 1.9 Hz, 1 H),7.81 (d, J = 1.9 Hz, 1 H),7.91 (d, J = 8.3 Hz, 2 H)8.10 (s, 1 H),9.33 (br s, 1 H),12.91 (br s, 1 H).

Table 17-23

Example	solvent, Hz	NMR(δ)
1-113	DMSO-d6, 300MHz	0.78 (t, J = 7.4 Hz, 6 H),0.98- 1.15 (m, 1 H),1.11 (d, J = 6.8 Hz, 6 H),1.16 (d, J = 6.4 Hz, 6 H),1.30- 1.55 (m, 1 H),2.25- 2.40 (m, 1 H),2.75- 2.90 (m, 1 H),4.15- 4.30 (m, 1 H),4.37 (s, 2 H),5.63 (s, 2 H),6.61 (d, J = 8.7 Hz, 2 H),6.89 (d, J = 8.7 Hz, 2 H),7.36 (d, J = 8.3 Hz, 2 H),7.59 (dd, J = 8.4, 1.5 Hz, 1 H),7.78 (d, J = 1.5 Hz, 1 H),7.90 (d, J = 8.3 Hz, 2 H),8.09 (s, 1 H),8.13 (d, J = 8.4 Hz, 1 H),9.24 (s, 1 H),12.77 (br s, 1 H).
1-114	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6 H), 1.16 (d, J = 6.4 Hz, 6 H), 1.32-1.46 (m, 2 H), 1.48- 1.63 (m, 2 H), 2.05- 2.21 (m, 1 H), 4.23 (sept, J = 6.8 Hz, 1 H), 4.37 (s, 2 H), 4.88 (s, 2 H), 5.47 (s, 2 H), 6.61 (d, J = 9.1 Hz, 2 H), 6.88 (d, J = 8.7 Hz, 2 H), 7.12 (d, J = 8.3 Hz, 1 H), 7.34 (d, J = 8.3 Hz, 2 H), 7.62 (dd, J = 8.3, 1.9 Hz, 1 H), 7.92 (d, J = 8.3 Hz, 2 H), 8.01 (s, 1 H), 8.18 (d, J = 1.9 Hz, 1 H), 12.84 (br s, 1 H).
1-115	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6 H), 1.15 (d, J = 6.4 Hz, 6 H), 1.32-1.47 (m, 2 H), 1.48- 1.64 (m, 2 H), 2.07- 2.18 (m, 1 H), 4.22 (sept, J = 6.6 Hz, 1 H), 4.37 (s, 2 H), 4.84 (s, 2 H), 5.49 (s, 2 H), 6.61 (d, J = 8.6 Hz, 2 H), 6.88 (d, J = 8.7 Hz, 2 H), 7.10 (t, J = 8.1 Hz, 1 H), 7.34 (d, J = 8.3 Hz, 2 H), 7.38 (dd, J = 7.9, 1.5 Hz, 1 H), 7.52 (dd, J = 8.1, 1.3 Hz, 1 H), 7.85 (d, J = 8.3 Hz, 2 H), 7.99 (s, 1 H), 12.91 (br s, 1 H).
1-116	DMSO-d6, 300MHz	0.77(t, J=7.3Hz, 6H), 1.01-1.10(m, 4H), 1.16(d, J=6.6Hz, 6H), 1.32-1.50(m, 4H), 2.29-2.38(m, 1H), 3.17(s, 3H), 4.02(s, 2H), 4.18-4.26(m, 1H), 4.37(s, 2H), 4.80(s, 2H), 6.61(d, J=8.8Hz, 2H), 6.88(d, J=8.8Hz, 2H), 7.25-7.43(m, 7H), 7.87(d, J=8.4Hz, 2H), 8.02(s, 1H), 12.96(brs, 1H)

Table 17-24

Example	solvent, Hz	NMR(δ)
1-117	DMSO-d6, 300MHz	0.77(t, J = 7.3 Hz, 6H), 1.00-1.14(m, 4H), 1.15(d, J = 6.6 Hz, 6H), 1.16(d, J = 6.6 Hz, 6H), 1.32-1.52(m, 4H), 2.27-2.39(m, 1H), 2.82(sep, J = 6.6 Hz, 1H), 3.51(brs, 2H), 3.55(brs, 2H), 4.17-4.28(m, 3H), 4.36(s, 2H), 6.60(d, J = 8.8 Hz, 2H), 6.88(d, J = 8.8 Hz, 2H), 7.15(d, J = 8.4 Hz, 2H), 7.32(d, J = 8.4 Hz, 2H), 7.52(d, J = 8.4 Hz, 2H), 7.85(d, J = 8.4 Hz, 2H), 7.95(s, 1H)
1-118	DMSO-d6, 400MHz	0.78(t, J = 7.3 Hz, 6H), 1.02-1.12(m, 4H), 1.15(d, J = 6.5 Hz, 6H), 1.34-1.51(m, 4H), 2.18(s, 6H), 2.30-2.37(m, 1H), 3.54(s, 2H), 3.60(s, 2H), 4.21(sep, J = 6.5 Hz, 1H), 4.25(s, 2H), 4.35(s, 2H), 6.59(d, J = 8.6 Hz, 2H), 6.66(s, 1H), 6.87(d, J = 8.6 Hz, 2H), 7.20(s, 2H), 7.31(d, J = 8.1 Hz, 2H), 7.84(d, J = 8.1 Hz, 2H), 7.95(s, 1H), 9.97(brs, 1H), 12.70(brs, 1H)
1-119	DMSO-d6, 400MHz	0.77(t, J = 7.3 Hz, 6H), 1.02-1.11(m, 4H), 1.15(d, J = 6.5 Hz, 6H), 1.30-1.50(m, 4H), 2.29-2.37(m, 1H), 2.83(s, 6H), 3.44(s, 2H), 3.52(s, 2H), 3.62(s, 2H), 4.21(sep, J = 6.5 Hz, 1H), 4.25(s, 2H), 4.35(s, 2H), 6.59(d, J = 8.6 Hz, 2H), 6.66(d, J = 9.0 Hz, 2H), 6.87(d, J = 8.6 Hz, 2H), 7.31(d, J = 8.4 Hz, 2H), 7.39(d, J = 9.0 Hz, 2H), 7.84(d, J = 8.4 Hz, 2H), 7.95(s, 1H), 9.68(s, 1H), 12.61(brs, 1H)
1-120	DMSO-d6, 400MHz	0.77(t, J = 7.3 Hz, 6H), 1.02-1.11(m, 4H), 1.15(d, J = 6.5 Hz, 6H), 1.34-1.51(m, 4H), 2.29-2.37(m, 1H), 3.44(s, 2H), 3.54(s, 2H), 4.18-4.25(m, 3H), 4.31(d, J = 6.0 Hz, 2H), 4.35(s, 2H), 6.59(d, J = 8.6 Hz, 2H), 6.87(d, J = 8.6 Hz, 2H), 7.17-7.28(m, 5H), 7.31(d, J = 8.4 Hz, 2H), 7.83(d, J = 8.4 Hz, 2H), 7.94(s, 1H), 8.40(t, J = 6.0 Hz, 1H), 12.59(brs, 1H)
1-121	DMSO-d6, 400MHz	0.77(t, J = 7.3 Hz, 6H), 1.02-1.11(m, 4H), 1.15(d, J = 6.5 Hz, 6H), 1.34-1.50(m, 4H), 2.29-2.37(m, 1H), 3.29-3.58(m, 10H), 3.67(s, 2H), 4.19(s, 2H), 4.21(sep, J = 6.5 Hz, 1H), 4.35(s, 2H), 6.59(d, J = 8.6 Hz, 2H), 6.87(d, J = 8.6 Hz, 2H), 7.32(d, J = 8.4 Hz, 2H), 7.84(d, J = 8.4 Hz, 2H), 7.94(s, 1H), 12.54(brs, 1H)

Table 17-25

Example	solvent, Hz	NMR(δ)
1-122	DMSO-d6, 300MHz	0.68(t, J=7.3Hz, 6H), 1.16(d, J=6.4Hz, 6H), 1.32-1.61(m, 4H), 2.05-2.17(m, 1H), 3.13(t, J=5.8Hz, 2H), 3.55(s, 2H), 4.09(t, J=5.8Hz, 2H), 4.17-4.30(m, 3H), 4.36(s, 2H), 6.62(d, J=8.6Hz, 2H), 6.87-6.93(m, 5H), 7.25(t, J=7.9Hz, 2H), 7.33(d, J=8.6Hz, 2H), 7.85(d, J=8.3Hz, 2H), 7.92(s, 1H)
1-123	DMSO-d6, 300MHz	0.67(t, J=7.4Hz, 6H), 1.14(d, J=6.4Hz, 6H), 1.31-1.62(m, 4H), 2.05-2.18(m, 1H), 2.90(t, J=6.4Hz, 2H), 3.13(t, J=6.4Hz, 2H), 3.32(s, 2H), 4.15-4.28(m, 3H), 4.34(s, 2H), 6.47-6.73(m, 5H), 6.87(d, J=8.6Hz, 2H), 7.05(t, J=7.9Hz, 2H), 7.31(d, J=8.3Hz, 2H), 7.83(d, J=7.9Hz, 2H), 7.91(s, 1H)
1-124	DMSO-d6, 300MHz	0.69 (t, J = 7.17 Hz, 6H), 1.16 (d, J = 6.39 Hz, 6H), 1.33-1.45 (m, 2H), 1.48- 1.62 (m, 2H), 2.08- 2.18 (m, 1H), 3.04 (s, 3H), 4.23 (quint, J = 6.39 Hz, 1H), 4.37 (s, 2H), 4.63 (s, 2H), 4.84 (s, 2H), 6.63 (d, J = 8.67 Hz, 2H), 6.89 (d, J = 8.67 Hz, 2H), 6.94 (d, J = 9.78 Hz, 1H), 6.99 (dd, J = 9.78, 2.64 Hz, 1H), 7.12 (d, J = 2.64 Hz, 1H), 7.34 (d, J = 8.28 Hz, 2H), 7.87 (d, J = 8.28 Hz, 2H), 7.90 (s, 1H)
1-125	DMSO-d6, 300MHz	0.80 (t, J = 7.15 Hz, 3H), 0.98-1.14 (m, 4H), 1.41-1.57 (m, 4H), 2.31-2.41 (m, 1H), 3.05 (s, 3H), 4.64 (s, 2H), 4.86 (s, 2H), 5.08 (s, 2H), 6.92-6.97 (m, 4H), 7.06-7.12 (m, 2H), 7.51 (d, J = 8.24 Hz, 2H), 7.97 (d, J = 8.24 Hz, 2H), 7.99 (s, 1H)
1-126	DMSO-d6, 300MHz	1HNMR(DMSO-d6,300MHz) δ .78 (t, J = 7.2 Hz, 6 H).95- 1.15 (m, 4 H),1.16 (d, J = 6.8 Hz, 6 H),1.30- 1.55 (m, 4 H),2.30- 2.40 (m, 1 H),2.34 (s, 3 H),3.27 (s, 2 H),4.15- 4.30 (m, 1 H),4.37 (s, 2 H),5.67 (s, 2 H),6.61 (d, J = 8.5 Hz, 2 H),6.89 (d, J = 8.5 Hz, 2 H),7.36 (d, J = 8.3 Hz, 2 H),7.63 (dd, J = 8.5, 1.5 Hz, 1 H),7.78 (d, J = 1.5 Hz, 1 H),7.91 (d, J = 8.3 Hz, 2 H),8.12 (s, 1 H),8.43 (d, J = 8.5 Hz, 1 H).

Table 17-26

Example	solvent, Hz	NMR(δ)
1-127	DMSO-d6, 400MHz	0.79(t, J=7.2Hz, 6H), 1.01-1.14(m, 4H), 1.26(s, 9H), 1.37-1.57(m, 4H), 2.41-2.49(m, 1H), 3.42(s, 2H), 4.22(s, 2H), 4.28(s, 2H), 5.07(s, 2H), 6.92(d, J=8.8Hz, 2H), 7.06(d, J=8.8Hz, 2H), 7.16(s, 1H), 7.48(d, J=8.0Hz, 2H), 7.94(d, J=8.4Hz, 2H), 8.04(s, 1H)
1-128	DMSO-d6, 400MHz	0.80(t, J=7.4Hz, 6H), 1.00-1.17(m, 4H), 1.38-1.57(m, 4H), 2.41-2.52(m, 1H), 4.28(s, 2H), 4.92(s, 2H), 5.08(s, 2H), 6.65-6.72(m, 1H), 6.68(d, J=8.0Hz, 2H), 6.93(d, J=8.8Hz, 2H), 7.06(d, J=8.4Hz, 2H), 7.16(dd, J=7.2, 7.2Hz, 2H), 7.51(d, J=8.4Hz, 2H), 7.97(d, J=8.0Hz, 2H), 7.99(s, 1H), 12.74(brs, 1H)
1-129	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6 H),0.95- 1.20 (m, 4 H),1.35- 1.60 (m, 4 H),2.40- 2.53 (m, 1 H),4.10 (s, 2 Hx0.4),4.37 (s, 2Hx0.6),4.80- 5.12 (m, 6H),6.85- 6.98 (m, 5H),7.07 (d, J = 8.6 Hz, 2Hx0.6),7.04- 7.31 (m, 2H),7.15- 7.31 (m, 2H),7.51 (d, J = 7.9 Hz, 2Hx0.4),7.96 (d, J = 8.3 Hz, 2Hx0.6),7.97 (d, J = 7.9 Hz, 2Hx0.4),8.06 (s, 1Hx0.6),8.13 (s, 1Hx0.4),12.73 (br s, 1Hx0.4),13.07 (br s, 1Hx0.6).
1-130	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6 H),0.95- 1.20 (m, 4 H),1.35- 1.60 (m, 4 H),2.19 (s, 3 Hx0.4),2.22 (s, 3 Hx0.6),2.40- 2.53 (m, 1 H),4.10 (s, 2 Hx0.4),4.36 (s, 2 Hx0.6),4.78 (s, 2 Hx0.6),4.84 (s, 2 Hx0.6),5.03 (s, 2 Hx0.4),5.05 (s, 2 Hx0.4),5.09 (s, 2 H),6.75- 7.10 (m, 8 H),7.51 (d, J = 8.3 Hz, 2 H),7.96 (d, J = 8.3 Hz, 2 H),8.06 (s, 1 Hx0.6),8.12 (s, 1 Hx0.4),12.73 (br s, 1 Hx0.4),13.05 (br s, 1 Hx0.6).
1-131	DMSO-d6, 400MHz	0.61-0.69(m, 6H), 0.74-0.97(m, 4H), 1.18(d, J = 6.3 Hz, 3H), 1.30-1.50(m, 4H), 1.63(d, J = 6.0 Hz, 3H), 2.39-2.48(m, 1H), 3.56(s, 2H), 3.65(s, 2H), 4.03-4.14(m, 3H), 4.21(s, 2H), 4.60-4.68(m, 1H), 4.96-5.02(m, 1H), 7.14(d, J = 8.1 Hz, 2H), 7.39(d, J = 8.1 Hz, 2H), 7.55(d, J = 8.1 Hz, 2H), 7.67(d, J = 8.1 Hz, 2H), 7.99(s, 1H), 12.63(brs, 1H)

Table 17-27

Example	solvent, Hz	NMR(δ)
1-132	DMSO-d6, 300MHz	0.68(t, J = 7.3 Hz, 6H), 1.16(d, J = 6.6 Hz, 6H), 1.26(s, 9H), 1.32-1.47(m, 2H), 1.49-1.63(m, 2H), 2.08-2.17(m, 1H), 3.45(s, 2H), 4.19-4.29(m, 5H), 4.36(s, 2H), 6.62(d, J = 8.8 Hz, 2H), 6.88(d, J = 8.8 Hz, 2H), 7.17(s, 1H), 7.33(d, J = 8.1 Hz, 2H), 7.85(d, J = 8.1 Hz, 2H), 7.96(s, 1H)
1-133	DMSO-d6, 300MHz	0.77(t, J = 7.3 Hz, 6H), 1.01-1.13(m, 4H), 1.16(d, J = 6.2 Hz, 6H), 1.35-1.51(m, 4H), 2.29-2.38(m, 1H), 4.22(sep, J = 6.2 Hz, 1H), 4.37(s, 2H), 5.79(s, 2H), 6.61(d, J = 8.8 Hz, 2H), 6.89(d, J = 8.8 Hz, 2H), 7.19(d, J = 8.1 Hz, 2H), 7.35(d, J = 8.1 Hz, 2H), 7.74(d, J = 7.3 Hz, 2H), 7.89(d, J = 8.4 Hz, 2H), 7.92-7.97(m, 1H), 8.05(s, 1H)
1-134	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6 H),0.95- 1.20 (m, 4 H),1.35- 1.60 (m, 4 H),2.40- 2.53 (m, 1 H),4.10 (s, 2 Hx0.4),4.23 (s, 2 Hx0.6),4.29 (s, 2 Hx0.6),4.41 (s, 2 Hx0.4),4.52 (s, 2 Hx0.6),4.54 (s, 2 Hx0.4),4.84 (s, 2 Hx0.6),4.97 (s, 2x0.4 H),5.09 (s, 2 H),6.94 (d, J = 8.7 Hz, 2 H),7.07 (d, J = 8.7 Hz, 2 H),7.25- 7.40 (m, 5 H),7.45- 7.55 (m, 2 H),7.92- 7.98 (m, 2 H),8.06 (s, 1 Hx0.6),8.08 (s, 1 Hx0.4),12.80 (br s, 1 H).
1-135	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6 H),0.96- 1.21 (m, 4 H),1.13 (d, J = 6.8 Hz, 6 Hx0.4),1.16 (d, J = 7.1 Hz, 6 Hx0.6),1.34- 1.62 (m, 4 H),2.39- 2.54 (m, 1 H),2.70- 2.89 (m, 1 H),4.10 (s, 2 Hx0.4),4.36 (s, 2 Hx0.6),4.79 (s, 2 Hx0.6),4.84 (s, 2 Hx0.6),5.04 (s, 2 Hx0.4),5.05 (s, 2 Hx0.4),5.09 (s, 2 H),6.77- 6.87 (m, 2 H),6.90- 6.98 (m, 2 H),7.02- 7.15 (m, 4 H),7.51 (d, J = 8.1 Hz, 2 H),7.97 (d, J = 8.1 Hz, 2 Hx0.6),7.98 (d, J = 8.1 Hz, 2 Hx04),8.06 (s, 1 Hx0.6),8.13 (s, 1 Hx0.4),12.75 (br.s, 1 Hx0.4),13.01 (br.s, 1 Hx0.6).
1-136	DMSO-d6, 400MHz	0.80(t, J=8.2Hz, 6H), 0.99-1.16(m, 4H), 1.37-1.58(m, 4H), 2.20(s, 3H), 2.30(s, 3H), 2.41-2.52(m, 1H), 3.46(s, 2H), 4.12(s, 2H), 4.26(s, 2H), 5.07(s, 2H), 6.93(d, J=8.8Hz, 2H), 7.06(d, J=8.8Hz, 2H), 7.49(d, J=8.4Hz, 2H), 7.94(d, J=8.0Hz, 2H), 8.05(s, 1H), 12.65(brs, 1H),

Table 17-28

Example	solvent, Hz	NMR(δ)
1-137	DMSO-d6, 400MHz	0.79(t, J=7.2Hz, 6H), 0.99-1.15(m, 4H), 1.38-1.58(m, 4H), 2.40-2.52(m, 1H), 5.24(s, 2H), 5.56(s, 2H), 5.56(s, 2H), 6.94(d, J=7.6Hz, 2H), 7.07(d, J=8.0Hz, 2H), 7.17(brs, 1H), 7.48(brs, 1H), 7.80(s, 1H), 8.01(s, 1H), 8.37(s, 1H), 8.63(s, 1H)
1-138	DMSO-d6, 300MHz	0.77(t, J = 6.0Hz, 6H), 1.03-1.09(m,4H), 1.18(d,J = 9.0Hz, 6H), 1.26(s,9H), 1.38-1.45(m,4H), 2.30-2.42(m,1H), 3.54(s,2H), 4.24(s,2H), 4.25-4.30(m,1H), 4.32(s,2H), 4.50(s,2H), 6.65(d,J = 9.0Hz, 2H), 6.90(d,J = 9.0Hz, 2H), 7.20(s,1H), 7.38(d,J = 9.0Hz, 1H), 7.62(s,1H), 7.73(d,J = 9.0Hz, 1H), 8.57(s,1H)
1-139	DMSO-d6, 300MHz	0.77(t, J = 6.0Hz, 6H), 1.02-1.10(m,4H), 1.18(d,J = 9.0Hz, 6H), 1.38-1.44(m,4H), 2.30-2.36(m,1H), 3.61(s,2H), 4.19(s,2H), 4.20-4.25(m,1H), 4.36(s,2H), 4.50(s,2H), 6.65(d,J = 9.0Hz, 2H), 6.90(d,J = 9.0Hz, 2H), 7.13(m,2H), 7.38(d,J = 9.0Hz, 1H), 7.53-7.56(m,2H), 7.62(s,1H), 7.73(d,J = 9.0Hz, 1H), 8.55(s,1H)
1-140	DMSO-d6, 300MHz	0.78(t, J = 6.0Hz, 6H), 1.02(m,4H), 1.19(d,J = 6.0Hz, 6H), 1.34-1.52(m,4H), 2.30-2.38(m,1H), 4.20(s,2H), 4.25-4.27(m,1H), 4.37(s,2H), 6.66(d,J = 9.0Hz, 2H), 7.03(d,J = 66.0Hz, 2H), 7.16-7.20(m,2H), 7.40-7.42(m,1H), 7.56-7.59(m,2H), 7.63(s,1H), 7.74(d,J = 9.0Hz, 1H), 8.56(s,1H)
1-141	DMSO-d6, 400MHz	0.79(t, J=7.2Hz, 6H), 0.99-1.14(m, 4H), 1.33(s, 9H), 1.37-1.57(m, 4H), 2.41-2.53(m, 1H), 3.43(s, 2H), 4.17(s, 2H), 4.27(s, 2H), 5.07(s, 2H), 6.92(d, J=8.4Hz, 2H), 7.06(d, J=8.4Hz, 2H), 7.41(s, 1H), 7.49(d, J=8.4Hz, 2H), 7.94(d, J=8.4Hz, 2H), 8.05(s, 1H)
1-142	DMSO-d6, 300MHz	0.76(t, J=7.2Hz, 6H), 0.99-1.09(m, 4H), 1.14(d, J=6.0Hz, 6H), 1.30-1.56(m, 10H), 2.25-2.38(m, 1H), 3.14(brs, 2H), 3.41(brs, 4H), 3.62(s, 2H), 4.12(s, 2H), 4.17-4.25(m, 1H), 4.34(s, 2H), 6.59(d, J=8.4Hz, 2H), 6.87(d, J=8.4Hz, 2H), 7.32(d, J=7.5Hz, 2H), 7.84(d, J=8.9Hz, 2H), 7.92(s, 1H)

Table 17-29

Example	solvent, Hz	NMR(δ)
1-143	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6 H),0.98- 1.18 (m, 4 H),1.35- 1.61 (m, 4 H),2.35- 2.53 (m, 1 H),3.18 (s, 3 H),5.08 (s, 2 H),5.22 (s, 2 H),6.94 (d, J = 8.7 Hz, 2 H),7.01 (d, J = 8.4 Hz, 1 H),7.07 (d, J = 8.7 Hz, 2 H),7.35 (d, J = 6.8 Hz, 1 H),7.51 (d, J = 7.9 Hz, 2 H),7.74 (dd, J = 8.4, 6.8 Hz, 1 H),7.96 (d, J = 7.9 Hz, 2 H),7.99 (s, 1 H),12.60 (br s, 1 H).
1-144	DMSO-d6, 300MHz	0.77(t, J = 6.0Hz, 6H), 1.02-1.10(m,4H), 1.18(d,J = 9.0Hz, 6H), 1.38-1.48(m,4H), 2.30-2.35(m,1H), 3.40(s,2H), 4.14(s,2H), 4.22-4.28(m,1H), 4.50(s,1H), 6.65(d,J = 9.0Hz, 2H), 6.90(d,J = 9.0Hz, 2H), 7.38(d,J = 9.0Hz, 1H), 7.62(s,1H), 7.73(d,J = 9.0Hz, 1H), 7.89(m,1H), 8.52(s,1H)
1-145	DMSO-d6, 300MHz	0.61-0.83(m, 6H), 1.00-1.24(m, 6H), 1.35-1.65(m, 8H), 2.27-2.39(m, 1H), 3.19-3.34(m, 2H), 4.03-4.26(m, 2H), 4.36(brs, 1H), 4.61-4.72(m, 1H), 4.83(brs, 1H), 4.96-5.06(m, 1H), 6.62(brs, 2H), 6.88(brs, 2H), 7.17(brd, J=8.4Hz, 2H), 7.28-7.53(m, 3H), 7.69(brd, J=7.2Hz, 2H), 7.79-7.87(m, 1H), 7.91-7.99(m, 2H)
1-146	DMSO-d6, 300MHz	0.78(t, J=7.3Hz, 6H), 1.01-1.22(m, 4H), 1.16(d, J=6.6Hz, 6H), 1.32-1.52(m, 4H), 2.20(s, 3H), 2.28-2.38(m, 1H), 2.30(s, 3H), 3.48(s, 2H), 4.11(s, 2H), 4.18-4.28(m, 1H), 4.25(s, 2H), 4.36(s, 2H), 6.61(d, J=8.4Hz, 2H), 6.88(d, J=8.4Hz, 2H), 7.34(d, J=8.0Hz, 2H), 7.86(d, J=8.0Hz, 2H), 7.97(s, 1H), 12.57(brs, 1H)
1-147	DMSO-d6, 400MHz	0.79(t, J=7.4Hz, 6H), 0.99-1.14(m, 4H), 1.23(s, 9H), 1.37-1.56(m, 4H), 2.39-2.49(m, 1H), 3.48(s, 2H), 4.03(s, 2H), 4.23(s, 2H), 5.07(s, 2H), 6.72(s, 1H), 6.92(d, J=8.8Hz, 2H), 7.06(d, J=8.8Hz, 2H), 7.48(d, J=8.4Hz, 2H), 7.93(d, J=8.0Hz, 2H), 8.02(s, 1H)
1-148	DMSO-d6, 300MHz	0.79(t, J=7.4Hz, 6H), 0.98-1.16(m, 4H), 1.35-1.60(m, 4H), 2.40-2.54(m, 1H), 3.65(s, 2H), 3.96(s, 3H), 4.36(s, 2H), 4.45(s, 2H), 5.07(s, 2H), 6.93(d, J=8.7Hz, 2H), 7.07(d, J=8.7Hz, 2H), 7.31-7.44(m, 2H), 7.47(d, J=8.3Hz, 2H), 7.64-7.77(m, 2H), 7.88(d, J=8.3Hz, 2H), 7.98(s, 1H)

Table 17-30

Example	solvent, Hz	NMR(δ)
1-149	DMSO-d6 +D2O+NaHCO3, 300MHz	0.78(t, J=7.4Hz, 6H), 0.87(d, J=6.4Hz, 6H), 0.99-1.13(m, 4H), 1.16(d, J=6.4Hz, 6H), 1.32-1.50(m, 4H), 1.78-1.90(m, 1H), 2.26-2.39(m, 1H), 3.08(s, 2H), 3.72(s, 2H), 3.82(d, J=6.4Hz, 2H), 4.16-4.26(m, 3H), 4.36(s, 2H), 6.60(d, J=8.7Hz, 2H), 6.88(d, J=8.7Hz, 2H), 7.32(d, J=8.3Hz, 2H), 7.84(d, J=8.3Hz, 2H), 7.89(s, 1H)
1-150	DMSO-d6 +D2O+NaHCO3, 300MHz	0.78(t, J=7.2Hz, 6H), 0.86(t, J=7.4Hz, 3H), 0.98-1.12(m, 4H), 1.16(d, J=6.4Hz, 6H), 1.30-1.63(m, 6H), 2.27-2.40(m, 1H), 3.98(t, J=6.6Hz, 2H), 4.17-4.25(m, 3H), 4.35(s, 2H), 6.60(d, J=8.6Hz, 2H), 6.88(d, J=8.6Hz, 2H), 7.33(d, J=8.3Hz, 2H), 7.84(d, J=8.3Hz, 2H), 7.88(s, 1H)
1-151	DMSO-d6, 300MHz	0.80(t, J=7.2Hz, 6H), 1.01-1.15(m, 4H), 1.37-1.58(m, 4H), 1.75-2.16(m, 5H), 2.43-2.46(m, 1H), 3.11(brs, 2H), 3.55(brs, 2H), 3.86(brs, 1H), 5.10(s, 2H), 6.94(d, J=8.7Hz, 2H), 7.08(d, J=8.7Hz, 2H), 7.54(d, J=9.0Hz, 2H), 8.01(d, J=9.0Hz, 2H), 8.32(brs, 1H), 11.54(brs, 1H), 12.45(brs, 1H)
1-152	DMSO-d6, 300MHz	0.69(t, J=7.3Hz, 6H), 1.16(d, J=6.8Hz, 6H), 1.33-1.65(m, 6H), 1.76-1.87(m, 2H), 2.08-2.30(m, 4H), 2.83-2.92(m, 2H), 3.84(s, 2H), 4.18-4.27(m, 1H), 4.36(s, 2H), 6.62(d, J=8.7Hz, 2H), 6.88(d, J=8.7Hz, 2H), 7.34(d, J=8.3Hz, 2H), 7.86(d, J=7.9Hz, 2H), 7.95(s, 1H), 12.15(s, 1H)
1-153	DMSO-d6, 300MHz	0.80(t, J=7.2Hz, 6H), 1.01-1.18(m, 4H), 1.38-1.58(m, 4H), 2.42-2.48(m, 1H), 2.70(brs, 4H), 3.35(brs, 4H), 3.96(s, 2H), 5.09(s, 2H), 6.94(d, J=9.1Hz, 2H), 6.98(d, J=9.4Hz, 2H), 7.08(d, J=8.7Hz, 2H), 7.51(d, J=8.3Hz, 2H), 7.78(d, J=9.0Hz, 2H), 7.98(d, J=8.3Hz, 2H), 8.08(s, 1H), 12.29(brs, 1H)

Table 17-31

Example	solvent, Hz	NMR(δ)
1-154	DMSO-d6, 300MHz	0.69(t, J=7.4Hz, 6H), 1.16(d, J=6.4Hz, 6H), 1.34-1.62(m, 4H), 2.08-2.18(m, 1H), 2.68(brs, 4H), 3.36(brs, 4H), 3.94(s, 2H), 4.18-4.27(m, 1H), 4.37(s, 2H), 6.62(d, J=8.6Hz, 2H), 6.89(d, J=8.6Hz, 2H), 6.97(d, J=9.0Hz, 2H), 7.34(d, J=7.9Hz, 2H), 7.77(d, J=9.0Hz, 2H), 7.87(d, J=8.3Hz, 2H), 7.98(s, 1H), 12.29(brs, 1H)
1-155	DMSO-d6, 300MHz	0.81(t, J=7.3Hz, 6H), 1.00-1.19(m, 4H), 1.43-1.59(m, 4H), 2.53-2.61(m, 1H), 2.81(brs, 4H), 3.13(brs, 4H), 4.01(s, 2H), 5.09(s, 2H), 7.07(d, J=12.7Hz, 2H), 7.19(d, J=8.3Hz, 2H), 7.35-7.42(m, 3H), 7.62-7.74(m, 2H), 7.89(d, J=9.0Hz, 2H), 7.92(s, 1H), 7.98-8.01(m, 1H), 12.81(brs, 1H)
1-156	DMSO-d6, 300MHz	0.81(t, J=7.2Hz, 6H), 1.02-1.18(m, 4H), 1.45-1.61(m, 4H), 2.55-2.60(m, 1H), 2.72(brs, 4H), 3.23(brs, 4H), 3.95(s, 2H), 5.09(s, 2H), 7.08(d, J=9.1Hz, 2H), 7.16-7.23(m, 3H), 7.31(d, J=7.5Hz, 2H), 7.34-7.42(m, 2H), 7.47(brs, 1H), 7.89(d, J=9.0Hz, 2H), 7.90(brs, 1H), 12.84(brs, 1H)
1-157	DMSO-d6, 300MHz	0.76(t, J = 7.3Hz, 6H), 0.93(m,4H), 1.36(m,4H), 5.45(s,2H), 5.60(s,2H), 7.09(m,9H), 7.57(d,J = 7.3Hz, 1H), 7.85(s,1H), 7.93(d,J = 8.4Hz, 2H), 8.06(s,1H), 8.11(d,J = 8.1Hz, 1H)
1-158	DMSO-d6, 300MHz	0.74(t, J = 7.5Hz, 6H), 0.98(m,4H), 1.06(d,J = 7.2Hz, 6H), 1.48(m,4H), 2.7(m,1H), 5.59(s,2H), 5.92(s,2H), 6.99(m,6H), 7.37(s,1H), 7.42(d,J = 8.3Hz, 1H), 7.80(d,J = 8.7Hz, 2H), 8.41(s,1H)
1-159	CDCl3, 300MHz	0.82(t, J = 7.2Hz, 6H), 1.09(m,4H), 1.53(s,3H), 1.54(m,4H), 2.53(m,1H), 0.82(s,1H), 6.99(d,J = 6.8Hz, 1H), 7.14(m,1H), 7.25(s,3H), 7.30(d,J = 8.3Hz, 1H), 7.38(s,1H), 8.04(brs,1H)

Table 17-32

Example	solvent, Hz	NMR(δ)
1-160	DMSO-d6, 300MHz	0.80(t, J=7.1Hz, 6H), 0.99-1.16(m, 4H), 1.38-1.59(m, 4H), 2.40-2.50(m, 1H), 2.82-2.98(m, 4H), 3.84(s, 2H), 4.09(s, 2H), 5.09(s, 2H), 6.94(d, J=8.8Hz, 2H), 7.08(d, J=8.4Hz, 2H), 7.26(d, J=8.1Hz, 1H), 7.52(d, J=8.4Hz, 2H), 7.66(s, 1H), 7.72(d, J=8.1Hz, 1H), 7.99(d, J=8.1Hz, 2H), 8.08(s, 1H), 12.79(s, 1H)
1-161	DMSO-d6, 300MHz	0.81(t, J=7.3Hz, 6H), 1.00-1.18(m, 4H), 1.43-1.60(m, 4H), 1.64-1.83(m, 4H), 2.29(t, J=11.1Hz, 3H), 2.55-2.67(m, 1H), 3.06(d, J=11.3Hz, 2H), 3.90(s, 2H), 5.08(s, 2H), 7.07(d, J=8.6Hz, 2H), 7.19(d, J=8.3Hz, 2H), 7.37-7.41(m, 4H), 7.86-7.89(m, 5H)
1-162	DMSO-d6, 300MHz	0.81(t, J=7.3Hz, 6H), 1.02-1.19(m, 4H), 1.43-1.60(m, 4H), 1.66-1.86(m, 4H), 2.30(t, J=10.5Hz, 2H), 2.53-2.68(m, 2H), 3.06(d, J=11.7Hz, 2H), 3.91(s, 2H), 5.09(s, 2H), 7.07(d, J=8.6Hz, 2H), 7.19(d, J=7.9Hz, 2H), 7.37-7.46(m, 3H), 7.54(d, J=7.9Hz, 1H), 7.78(d, J=7.5Hz, 1H), 7.83(s, 1H), 7.87-7.90(m, 3H), 12.93(brs, 1H)
1-163	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6 H),0.98- 1.18 (m, 4 H),1.36- 1.60 (m, 4 H),2.39- 2.53 (m, 1 H),4.85 (d, J = 6.3 Hz, 2 H),5.09 (s, 2 H),6.94 (d, J = 8.7 Hz, 2 H),7.07 (d, J = 8.7 Hz, 2 H),7.51 (d, J = 8.3 Hz, 2 H),7.97 (d, J = 8.3 Hz, 2 H),8.01 (s, 1 H),8.20 (dd, J = 8.1, .9 Hz, 1 H),8.48 (dd, J = 8.1, 2.1 Hz, 1 H),9.14 (dd, J = 2.1, .9 Hz, 1 H),9.88 (t, J = 6.3 Hz, 1 H),13.74 (br s, 1 H).
1-164	DMSO-d6, 300MHz	0.81(t, J=7.2Hz, 6H), 1.03-1.17(m, 4H), 1.48-1.59(m, 4H), 1.70-1.80(m, 4H), 2.19-2.30(m, 2H), 2.48-2.59(m, 2H), 3.06(d, J=10.9Hz, 2H), 3.90(s, 2H), 5.08(s, 2H), 7.07(d, J=9.0Hz, 2H), 7.19(d, J=8.3Hz, 2H), 7.24-7.31(m, 1H), 7.38(d, J=8.3Hz, 2H), 7.45-7.53(m, 2H), 7.66(d, J=8.3Hz, 1H), 7.87-7.89(m, 3H)
1-165	CDCl3, 300MHz	0.80(t, J = 7.2Hz, 6H), 1.06(m,4H), 1.43(m,4H), 2(m,4H), 2.42(m,2H), 2.64(m,1H), 3.17(m,2H), 4.17(s,2H), 5.31(s,2H), 7.02(m,4H), 7.21(m,5H), 7.33(m,2H), 7.69(s,1H), 7.99(m,1H)

Table 17-33

Example	solvent, Hz	NMR(δ)
1-166	CDCl3, 300MHz	0.80(t, J = 7.5Hz, 6H), 1.03(m,4H), 1.43(m,4H), 2.41(m,1H), 3.10-3.25(m,4H), 4.12(m,2H), 4.32(m,2H), 5.32(s,2H), 7.02-7.09(m,4H), 7.21(m,6H), 7.34(m,2H), 7.72(s,1H), 7.77(s,1H), 7.85(d,J = 6.4Hz, 1H), 8.01(t, J = 3.0Hz, 1H)
1-167	DMSO-d6, 300MHz	0.77(t, J = 7.3Hz, 6H), 1(m,4H), 1.42(m,4H), 4.68(s,2H), 5.44(s,2H), 6.86(m,1H), 7.1(m,9H), 7.56(d,J = 7.7Hz, 1H), 7.65(s,1H), 8.04(s,1H), 8.10(d,J = 7.3Hz, 1H)
1-168	DMSO-d6, 300MHz	0.80 (t, J = 7.2 Hz, 6 H),0.98- 1.19 (m, 4 H),1.36- 1.62 (m, 4 H),2.39- 2.53 (m, 1 H),3.07- 3.32 (m, 2 H),3.66- 4.10 (m, 2 H),5.02- 5.12 (m, 4 H),6.94 (d, J = 8.5 Hz, 2 H),7.08 (d, J = 8.5 Hz, 2 H),7.48- 7.58 (m, 2 H),7.84 (d, J = 7.9 Hz, 1 Hx0.5),7.89 (d, J = 8.3 Hz, 1 Hx0.5),7.92- 8.14 (m, 5 H),8.12 (s, 1 Hx0.5),8.13 (s, 1 Hx0.5),8.39- 8.48 (m, 1 H),9.04 (d, J = 1.5 Hz, 1 Hx0.5),9.15 (d, J = 1.5 Hz, 1 Hx0.5),13.67 (br s, 1 H).
1-169	DMSO-d6, 300MHz	0.72(t, J=7.4Hz, 6H), 0.87-1.08(m, 4H), 1.30-1.53(m, 4H), 2.36-2.47(m, 1H), 2.78-2.92(m, 4H), 3.80(s, 2H), 4.12(s, 2H), 6.05(s, 2H), 6.98-7.09(m, 4H), 7.20-7.30(m, 3H), 7.56-7.75(m, 4H), 8.40(s, 1H), 12.77(s, 1H)
1-170	DMSO-d6, 300MHz	0.73(t, J=7.2Hz, 6H), 0.89-1.09(m, 4H), 1.31-1.54(m, 4H), 2.37-2.50(m, 1H), 2.69(brs, 4H), 3.19(brs, 4H), 4.00(s, 2H), 6.04(s, 2H), 7.05(s, 4H), 7.16-7.41(m, 5H), 7.46(brs, 1H), 7.57-7.74(m, 2H), 8.42(s, 1H), 12.71(brs, 1H)
1-171	DMSO-d6, 300MHz	0.70(t, J=6.8Hz, 6H), 0.85-1.07(m, 4H), 1.30-1.51(m, 4H), 1.57-1.79(m, 4H), 2.20-2.63(m, 4H), 2.94-3.05(m, 2H), 3.96(s, 2H), 6.04(s, 2H), 7.03(s, 4H), 7.24(brs, 2H), 7.35(d, J=7.5Hz, 2H), 7.56-7.73(m, 2H), 7.87(d, J=7.5Hz, 2H), 8.39(s, 1H)

Table 17-34

Example	solvent, Hz	NMR(δ)
1-172	DMSO-d6, 300MHz	0.75(t, J = 7.5Hz, 6H), 0.96(m,4H), 1.4(m,4H), 2.72(m,4H), 3.22(m,4H), 3.95(s,2H), 5.42(s,2H), 7.07-7.20(m,7H), 7.31(m,1H), 7.45(s,1H), 7.54(d,J = 7.2Hz, 1H), 7.73(s,1H), 8.09(d,J = 6.0Hz, 1H)
1-173	DMSO-d6, 300MHz	1.64-1.85(m, 4H), 2.30(t, J=10.4Hz, 2H), 2.58-2.68(m, 1H), 3.06(d, J=11.7Hz, 2H), 3.90(s, 2H), 5.17(s, 2H), 7.08(d, J=9.0Hz, 2H), 7.40-7.54(m, 3H), 7.67(d, J=8.3Hz, 1H), 7.75(d, J=2.3Hz, 1H), 7.76-7.80(m, 1H), 7.81-7.84(m, 1H), 7.86-7.91(m, 3H)
1-174	DMSO-d6, 300MHz	1.72-2.12(m, 4H), 2.26-2.46(m, 2H), 2.80-3.03(m, 1H), 3.54-3.80(m, 2H), 4.82(s, 2H), 5.38(s, 2H), 7.16(d, J=8.3Hz, 2H), 7.42-7.53(m, 2H), 7.77-7.86(m, 2H), 7.96(d, J=7.9Hz, 2H), 8.11-8.19(m, 3H), 12.94(brs, 1H)
1-175	DMSO-d6, 300MHz	0.93(t, J=7.4Hz, 3H), 1.37-1.49(m, 2H), 1.65-1.85(m, 6H), 2.25-2.35(m, 2H), 3.02-3.10(m, 3H), 3.90(s, 2H), 3.97(t, J=6.4Hz, 2H), 5.05(s, 2H), 6.94(d, J=8.7Hz, 2H), 7.05(d, J=9.0Hz, 2H), 7.36-7.44(m, 3H), 7.49-7.54(m, 1H), 7.75-7.88(m, 5H)
1-176	DMSO-d6, 400MHz	0.80(t, J=7.3Hz, 6H), 1.02-1.13(m, 4H), 1.40-1.57(m, 4H), 2.21(s, 3H), 2.42-2.51(m, 1H), 5.08(s, 2H), 6.00(s, 2H), 6.72(s, 1H), 6.93(d, J=8.6Hz, 2H), 7.06(d, J=8.6Hz, 2H), 7.50(d, J=8.3Hz, 2H), 7.93(d, J=8.3Hz, 2H), 8.03(s, 1H), 13.52(brs, 1H)
1-177	DMSO-d6, 400MHz	0.79(t, J=7.3Hz, 6H), 1.02-1.13(m, 4H), 1.39-1.56(m, 4H), 2.39(s, 3H), 2.42-2.52(m, 1H), 5.08(s, 2H), 5.77(s, 2H), 6.56(s, 1H), 6.92(d, J=8.6Hz, 2H), 7.06(d, J=8.6Hz, 2H), 7.51(d, J=8.1Hz, 2H), 7.94(d, J=8.1Hz, 2H), 8.10(s, 1H), 12.67(brs, 1H)
1-178	DMSO-d6, 300MHz	0.80(t, J=7.3Hz, 6H), 1.01-1.15(m, 4H), 1.36(s, 9H), 1.40-1.59(m, 4H), 2.41-2.53(m, 1H), 5.09(s, 2H), 5.90(s, 2H), 6.54(s, 1H), 6.94(d, J=8.4Hz, 2H), 7.07(d, J=8.4Hz, 2H), 7.52(d, J=8.1Hz, 2H), 7.96(d, J=8.1Hz, 2H), 8.09(s, 1H), 12.74(brs, 1H)

Table 17-35

Example	solvent, Hz	NMR(δ)
1-179	DMSO-d6, 300MHz	0.80(t, J=7.1Hz, 6H), 1.02-1.15(m, 4H), 1.28(s, 9H), 1.38-1.56(m, 4H), 2.42-2.55(m, 1H), 5.09(s, 2H), 6.04(s, 2H), 6.81(s, 1H), 6.94(d, J=8.8Hz, 2H), 7.08(d, J=8.8Hz, 2H), 7.51(d, J=8.4Hz, 2H), 7.95(d, J=8.4Hz, 2H), 8.03(s, 1H)
1-180	DMSO-d6, 300MHz	0.76(t, J = 7.3Hz, 6H), 0.99(m,4H), 1.42(m,4H), 1.9(m,2H), 2.44(m,1H), 3.27(m,3H), 3.60(t, J = 8.1Hz, 1H), 4.04(d,J = 15.4Hz, 1H), 4.26(m,2H), 5.43(s,2H), 7.09(m,7H), 7.54(d,J = 7.0Hz, 1H), 7.70(s,1H), 8.01(s,1H), 8.11(d,J = 7.3Hz, 1H)
1-181	DMSO-d6 , 400MHz	0.77(t, J=7.3Hz, 6H), 1.00-1.11(m, 4H), 1.26-1.54(m, 6H), 1.77(brd, J=14.8Hz, 2H), 1.96-2.04(m, 1H), 2.39-2.45(m, 1H), 2.80(brt, J=12.3Hz, 2H), 2.98(d, J=6.9Hz, 2H), 3.87(brd, J=13.0Hz, 2H), 5.05(s, 2H), 6.90(d, J=8.6Hz, 4H), 7.04(d, J=8.6Hz, 2H), 7.47(d, J=8.1Hz, 2H), 7.70(d, J=9.0Hz, 2H), 7.93(d, J=8.1Hz, 2H), 7.95(s, 1H), 12.16(brs, 1H)
1-182	DMSO-d6, 300MHz	0.76(t, J = 7.3Hz, 6H), 0.97-1.09(m,4H), 1.39-1.52(m,4H), 2.44-2.50(m,1H), 5.44(s,2H), 5.95(s,2H), 7.10(d,J = 8.4Hz, 2H), 7.17(d,J = 8.4Hz, 2H), 7.21-7.28(m,3H), 7.54(d,J = 7.0Hz, 1H), 7.68(d,J = 7.0Hz, 1H), 7.70(s,1H), 8.03(s,1H), 8.04-8.10(m,2H), 8.29(s,1H)
1-183	DMSO-d6, 300MHz	0.74(t, J = 7.1Hz, 6H), 0.95-1.10(m,4H), 1.36-1.57(m,6H), 1.77-1.80(m,2H), 2.11-2.18(m,3H), 2.40-2.43(m,1H), 2.80-2.84(m,2H), 3.80(s,2H), 5.24(s,2H), 6.63(s,1H), 6.77(d,J = 7.9Hz, 2H), 6.97(d,J = 7.9Hz, 2H), 7.10-7.20(m,2H), 7.32-7.44(m,6H), 8.16(dd, J = 1.9, 9.0Hz, 1H)
1-184	DMSO-d6, 300MHz	1.63-1.85(m, 4H), 2.25-2.35(m, 2H), 2.52(s, 3H), 2.59-2.74(m, 1H), 3.06(d, J=12.8Hz, 2H), 3.90(s, 2H), 5.24(s, 2H), 7.09(d, J=9.0Hz, 2H), 7.42(t, J=7.7Hz, 1H), 7.51-7.58(m, 2H), 7.70-7.83(m, 3H), 7.86-7.92(m, 3H), 8.09(d, J=1.9Hz, 1H)

Table 17-36

Example	solvent, Hz	NMR(δ)
1-185	DMSO-d6, 300MHz	1.10(d, J=6.8Hz, 6H), 2.71-2.92(m, 5H), 3.11(brs, 4H), 3.71-3.82(m, 6H), 4.11(s, 2H), 6.00(s, 2H), 6.96-7.12(m, 6H), 7.24(d, J=7.9Hz, 1H), 7.53(d, J=9.1Hz, 1H), 7.61(s, 1H), 7.71(d, J=8.3Hz, 1H), 8.29(s, 1H), 12.78(brs, 1H)
1-186	DMSO-d6, 300MHz	1.11(d, J=6.4Hz, 6H), 2.66(brs, 4H), 2.72-2.83(m, 1H), 3.07-3.22(m, 8H), 3.75(brs, 4H), 3.98(s, 2H), 6.00(s, 2H), 6.95-7.23(m, 6H), 7.28-7.41(m, 3H), 7.45(s, 1H), 7.53(d, J=9.1Hz, 1H), 8.30(s, 1H), 12.82(brs, 1H)

Table 17-37

Example	solvent, Hz	NMR(δ)
2-1	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.95- 1.20 (m, 4H),1.40- 1.65 (m, 4H),2.40- 2.60 (m, 1H), 3.02 (s, 3H),3.81 (s, 2H),3.93 (s, 2H),4.57 (s, 2H),6.78 (d, J = 8.8 Hz, 2H),7.00- 7.40 (m, 9H),7.55 (d, J = 8.8 Hz, 2H),8.30 (s, 1H),12.30 (br s, 1H).

Table 17-38

Example	solvent, Hz	NMR(δ)
3-1	DMSO-d6, 400MHz	0.81(t, J = 7.3 Hz, 6H), 1.05-1.13(m, 4H), 1.48-1.57(m, 4H), 2.5-2.56(m, 1H), 5.09(s, 2H), 5.66(s, 2H), 7.09(d, J = 9.04 Hz, 2H), 7.19(d, J = 8.32 Hz, 2H), 7.38(d, J = 8.12 Hz, 2H), 7.91(d, J = 9.04 Hz, 2H), 7.98-7.99(m, 1H), 8.03(s, 1H), 8.64(d, J = 3 Hz, 1H), 8.72(d, J = 1.4 Hz, 1H), 13.52(s, 1H)
3-2	DMSO-d6, 400MHz	0.81(t,J=7.3Hz, 6H), 1.05-1.13(m, 4H), 1.48-1.57(m, 4H), 2.50-2.56(m, 1H), 5.09(s, 2H), 5.57(s, 2H), 7.09(d, J=9.2Hz, 2H), 7.17-7.19(m, 4H), 7.38(d, J=12.0Hz, 2H), 7.89-7.91(m, 4H), 8.01(s, 1H)
3-3	DMSO-d6, 400MHz	0.81(t,J=7.3Hz, 6H), 1.05-1.13(m, 4H), 1.48-1.57(m, 4H), 2.50-2.56(m, 1H), 4.78(s, 2H), 5.08(s, 2H), 7.07(d, J=8.8Hz, 2H), 7.18(d, J=8.1Hz, 2H), 7.37(d, J=8.0Hz, 2H), 7.51(d, J=8.0Hz, 2H), 7.82-7.86(m, 5H)
3-4	DMSO-d6, 300MHz	1.14-1.49(m, 5H), 1.64-1.84(m, 5H), 2.44-2.54(m, 1H), 4.77(s, 2H), 5.08(s, 2H), 7.06(d, J=9.0Hz, 2H), 7.24(d, J=8.3Hz, 2H), 7.37(d, J=8.3Hz, 2H), 7.50(d, J=8.7Hz, 2H), 7.82-7.86(m, 5H)
3-5	DMSO-d6, 400MHz	1.16-1.45(m, 5H), 1.67-1.83(m, 5H), 2.45-2.56(m, 1H), 5.07(s, 2H), 5.37(s, 2H), 7.00(d, J=9.0Hz, 2H), 7.24(d, J=8.1Hz, 2H), 7.36(d, J=8.1Hz, 2H), 7.65(d, J=9.0Hz, 2H), 7.94-7.96(m, 3H), 8.13(d, J=8.8Hz, 2H)
3-6	DMSO-d6, 300MHz	0.80(t, J=7.3Hz, 6H), 1.02-1.16(m, 4H), 1.46-1.60(m, 4H), 2.27(s, 3H), 2.54-2.58(m, 1H), 2.86(s, 3H), 4.68(s, 2H), 5.19(s, 2H), 7.10(d, J=0.8Hz, 2H), 7.18(d, J=8.3Hz, 2H), 7.39(d, J=8.3Hz, 2H), 7.78(s, 1H), 7.95-7.98(m, 3H), 8.13(d, J=8.3Hz, 2H), 13.39(brs, 1H)
3-7	DMSO-d6, 300MHz	0.78(t, J=7.4Hz, 6H), 0.97-1.16(m, 4H), 1.40-1.60(m, 4H), 2.30(s, 3H), 2.51-2.56(m, 1H), 3.17(s, 3H), 5.00(s, 2H), 5.19(s, 2H), 6.85(d, J=9.0Hz, 2H), 7.10(s, 1H), 7.11(s, 1H), 7.16(d, J=7.9Hz, 2H), 7.37(d, J=8.3Hz, 2H), 7.77(d, J=8.7Hz, 2H), 7.86(s, 1H), 7.96(s, 1H), 12.16(brs, 1H)

Table 17-39

Example	solvent, Hz	NMR(δ)
3-8	DMSO-d6, 300MHz	2.28(s, 3H), 3.36(s, 2H), 3.84(s, 2H), 4.19(s, 2H), 5.36(s, 2H), 7.07-7.08(m, 2H), 7.27-7.42(m, 5H), 7.67-7.77(m, 4H), 7.94-7.98(m, 2H)
3-9	DMSO-d6, 300MHz	0.80(t, J=7.3Hz, 6H), 1.02-1.14(m, 4H), 1.43-1.60(m, 4H), 2.29(s, 3H), 2.51-2.57(m, 1H), 3.35(s, 2H), 3.86(s, 2H), 4.19(s, 2H), 5.19(s, 2H), 7.10-7.10(m, 2H), 7.18(d, J=8.1Hz, 2H), 7.25-7.30(m, 1H), 7.33-7.42(m, 6H), 7.91(s, 1H), 7.94(br, 1H)
3-10	DMSO-d6, 400MHz	0.81(t,J=7.3Hz, 6H), 1.05-1.13(m, 4H), 1.48-1.57(m, 4H), 2.50-2.56(m, 1H), 3.40(s, 2H), 3.86(s, 2H), 4.17(s, 2H), 5.07(s, 2H), 7.06(d, J=9.2Hz, 2H), 7.19(d, J=6.0Hz, 2H), 7.26-7.68(m, 5H), 7.86-7.90(m, 3H)
3-11	DMSO-d6, 400MHz	0.72(t, J=7.4Hz, 6H), 1.48-1.55(m, 2H), 1.61-1.68(m, 2H), 2.30-2.33(m, 1H), 3.35(s, 2H), 3.86(s, 2H), 4.17(s, 2H), 5.08(s, 2H), 7.06(d, J=8.4Hz, 2H), 7.19(d, J=7.2Hz, 2H), 7.26-7.38(m, 7H), 7.86-7.87(m, 3H)
3-12	DMSO-d6, 300MHz	0.86(d, J=6.6Hz, 6H), 1.29(s, 9H), 1.79-1.88(m, 1H), 2.45(d, J=7.4Hz, 2H), 3.37(s, 2H), 3.87(s, 2H), 4.20(s, 2H), 5.21(s, 2H), 7.11-7.19(m, 3H), 7.25-7.44(m, 8H), 7.93(s, 1H), 8.18(d, J=2.6Hz, 1H), 12.41(brs, 1H)
3-13	DMSO-d6, 300MHz	0.80(t, J=7.3Hz, 6H), 1.02-1.16(m, 4H), 1.41-1.62(m, 4H), 2.52-2.59(m, 1H), 3.36(s, 2H), 3.86(s, 2H), 4.19(s, 2H), 5.26(s, 2H), 7.18-7.42(m, 11H), 8.00(s, 1H), 8.11(d, J=2.9Hz, 1H), 12.41(brs, 1H)
3-14	DMSO-d6, 400MHz	0.72(t, J=7.4Hz, 6H), 1.48-1.55(m, 2H), 1.61-1.68(m, 2H), 2.30-2.33(m, 1H), 3.37(s, 2H), 3.85(s, 2H), 4.16(s, 2H), 5.08(s, 2H), 7.06(d, J=8.8Hz, 2H), 7.18-7.28(m, 4H), 7.36-7.42(m, 4H), 7.86-7.89(m, 3H)

Table 17-40

Example	solvent, Hz	NMR(δ)
3-15	DMSO-d6, 300MHz	0.72(t, J=7.4Hz, 6H), 1.19(d, J=6.9Hz, 6H), 1.45-1.53(m, 2H), 1.63-1.66(m, 2H), 2.33-2.36(m, 1H), 2.85-2.88(m, 1H), 3.35(s, 2H), 3.83(s, 2H), 4.16(s, 2H), 5.09(s, 2H), 7.07(d, J=11.2Hz, 2H), 7.17-7.23(m, 4H), 7.31(d, J=8.1Hz, 2H), 7.39(d, J=8.1Hz, 2H), 7.85-7.87(m, 3H)
3-16	DMSO-d6, 400MHz	0.72(t, J=7.4Hz, 6H), 1.45-1.53(m, 2H), 1.63-1.66(m, 2H), 2.30-2.34(m, 1H),, 3.40(s, 2H), 3.97(s, 2H), 4.30(s, 2H), 5.09(s, 2H), 7.07(d, J=8.1Hz, 2H) , 7.08(d, J=8.0Hz, 2H), 7.18(d, J=8.0Hz, 2H), 7.38(d, J=8.0Hz, 2H), 7.65(d, J=8.0Hz, 2H), 7.72(d, J=8.0Hz, 2H), 7.84-7.87(m, 3H)
3-17	DMSO-d6, 400MHz	0.72(t, J=7.4Hz, 6H), 1.45-1.53(m, 2H), 1.63-1.66(m, 2H), 2.30-2.34(m, 1H), 3.37(s, 2H), 3.85(s, 2H), 4.30(s, 2H) , 5.09(s, 2H), 7.08(d, J=8.0Hz, 2H), 7.19(d, J=8.0Hz, 2H), 7.37-7.44(m, 6H), 7.86-7.90(m, 3H)
3-18	DMSO-d6, 400MHz	0.72(t, J=7.4Hz, 6H), 1.45-1.53(m, 2H), 1.63-1.66(m, 2H), , 2.26(s, 6H), 2.30-2.40(m, 1H), 3.48(s, 2H), 3.89(s, 2H), 4.25(s, 2H), 5.09(s, 2H), 6.92(s, 1H), 7.03-7.08(m, 4H), 7.20(d, J=8.0Hz, 2H), 7.38(d, J=8.0Hz, 2H), 7.86-7.91(m, 3H)
3-19	DMSO-d6, 400MHz	0.81(t,J=7.3Hz, 6H), 1.05-1.13(m, 4H), 1.48-1.57(m, 4H), 2.50-2.56(m, 1H),3.45(s, 2H), 4.00(s, 2H), 4.23(s, 2H), 5.07(s, 2H), 7.06(d, J=9.2Hz, 2H), 7.19(d, J=5.6Hz, 2H), 7.36-7.37(m, 1H), 7.35-7.37(m, 2H), 7.57-7.60(m, 1H), 7.81-7.85(m, 4H), 8.48-8.49(m, 1H)
3-20	DMSO-d6, 300MHz	0.72(t, J=7.4Hz, 6H), 1.48-1.55(m, 2H), 1.61-1.68(m, 2H), 2.30-2.33(m, 1H), 3.46(s, 2H), 4.02(s, 2H), 4.23(s, 2H), 5.09(s, 2H), 7.07(d, J=11.6Hz, 2H), 7.18(d, J=8.1Hz, 2H), 7.26-7.29(m, 1H), 7.39(d, J=9.0Hz, 2H), 7.57(d, J=9.0Hz, 1H), 7.80-7.87(m, 4H), 8.50(d, J=3.9Hz, 1H)

Table 17-41

Example	solvent, Hz	NMR(δ)
3-21	DMSO-d6, 300MHz	0.80(t, J=7.2Hz, 6H), 0.99-1.19(m, 4H), 1.42-1.62(m, 4H), 2.29(s, 3H), 2.46-2.58(m, 1H), 3.45(s, 2H), 4.01(s, 2H), 4.24(s, 2H), 5.19(s, 2H), 7.10(s, 2H), 7.18(d, J=8.1Hz, 2H), 7.25-7.30(m, 1H), 7.39(d, J=8.1Hz, 2H), 7.57(d, J=7.8Hz, 1H), 7.80(dt, J=1.9, 7.8Hz, 1H), 7.90(s, 1H), 7.93(s, 1H), 8.49-8.51(m, 1H)
3-22	DMSO-d6, 400MHz	0.81(t,J=7.3Hz, 6H), 1.05-1.13(m, 4H), 1.48-1.57(m, 4H), 2.50-2.56(m, 1H), 4.09(s, 2HX0.55),4.21(s,2HX0.45), 4.80(s,2HX0.45),4.97(s,2HX0.55), 5.09(s, 2H), 7.08(d, J=9.2Hz, 2H), 7.20(d, J=8.0Hz, 2H), 7.36-7.38(m, 3H), 7.46-7.48(m, 4H), 7.87-7.89(m, 3H)
3-23	DMSO-d6, 300MHz	0.72(t, J=7.4Hz, 6H), 1.45-1.53(m, 2H), 1.63-1.66(m, 2H), 2.33-2.36(m, 4H), 4.10(s, 1H), 4.20(s, 1H), 4.82(s, 1H), 4.94(s, 1H), 5.10(s, 2H), 7.09(d, J=9.0Hz, 2H), 7.18(d, J=8.1Hz, 2H), 7.26-7.28(m, 3H), 7.37-7.40(m, 3H), 7.86-7.91(m, 3H)
3-24	DMSO-d6, 400MHz	0.81(t,J=7.3Hz, 6H), 1.05-1.13(m, 4H), 1.48-1.57(m, 4H), 2.50-2.56(m, 1H),3.78(s, 3H), 4.11(s, 2H), 4.86-4.92(m, 2H), 5.08(s, 2H), 7.02(d, J=8.0Hz, 2H), 7.10(d, J=8.0Hz, 2H), 7.20(d, J=4.0Hz, 2H), 7.36-7.41(m, 4H), 7.86-7.96(m, 3H)
3-25	DMSO-d6, 300MHz	0.79(t, J=7.4Hz, 6H), 0.96-1.17(m, 4H), 1.41-1.62(m, 4H), 2.29(s, 3H), 2.46-2.57(m, 1H), 3.05-3.22(m, 2H), 3.91(d, J=15.5Hz, 1H), 3.95-3.99(m, 1H), 4.09(d, J=15.5Hz, 1H), 4.26(d, J=15.5Hz, 1H), 4.40(d, J=15.5Hz, 1H), 5.20(s, 2H), 7.02-7.19(m, 8H), 7.39(d, J=8.3Hz, 2H), 7.92(s, 1H)

Table 17-42

Example	solvent, Hz	NMR(δ)
3-26	DMSO-d6, 400MHz	0.81(t, J=7.3Hz, 6H), 1.04-1.15(m, 4H), 1.46-1.59(m, 4H), 2.52-2.57(m, 1H), 3.10(dd, J=3.5, 16.2Hz, 1H), 3.17(dd, J=6.0, 16.4Hz, 1H), 3.92(d, J=15.8Hz, 1H), 3.94-3.97(m, 1H), 4.09(d, J=15.8Hz, 1H), 4.25(d, J=15.8Hz, 1H), 4.39(d, J=15.8Hz, 1H), 5.08(s, 2H), 7.02-7.16(m, 6H), 7.18(d, J=8.1Hz, 2H), 7.38(d, J=8.1Hz, 2H), 7.86(s, 1H), 7.87(d, J=8.8Hz, 2H)
3-27	DMSO-d6, 400MHz	0.84 (s, 9 H), 2.42 (s, 3 H), 3.03 (s, 3 H), 3.35 (s, 2 H), 3.85 (s, 2 H), 4.15 (s, 2 H), 4.58 (s, 2 H), 6.76 (d, J = 8.8 Hz, 2 H), 7.05 (d, J = 7.9 Hz, 2 H), 7.11 (d, J = 8.1 Hz, 2 H), 7.26 (t, J = 6.9 Hz, 1 H), 7.34 (t, J = 7.4 Hz, 2 H), 7.39 (d, J = 7.0 Hz, 2 H), 7.85 (s, 1 H), 7.70 (d, J = 8.8 Hz, 2 H), 12.37 (br s, 1 H).
3-28	DMSO-d6, 300MHz	1.18-1.20(m,2H), 1.24(s,9H), 1.55-1.76(m,2H), 2.28-2.47(m,1H), 2.98(s,3H), 3.25(d,J = 6.0Hz, 2H), 3.36(s,2H), 3.87(s,2H), 4.16(s,2H), 6.72(d,J = 9.0Hz, 2H), 7.12(d,J = 9.0Hz, 2H), 7.23-7.28(m,3H), 7.31-7.44(m,4H), 7.65(s,1H), 7.73(d,J = 9.0Hz, 2H)
3-29	DMSO-d6, 300MHz	1.20-1.45(m, 5H), 1.65-1.80(m, 5H), 1.40-1.45(m, 1H), 3.03(s, 3H), 3.35(s, 2H), 3.86(s, 2H), 4.15(s, 2H), 4.56(s, 2H), 6.76(d, J=12.0Hz, 2H), 7.09-7.16(m, 4H), 7.26-7.39(m, 5H), 7.66-7.72(m, 3H)
3-30	DMSO-d6, 300MHz	1.20-1.40(m, 5H), 1.60-1.80(m, 5H), 2.45-2.50(m, 1H), 2.51(t, J=6.0Hz, 2H), 2.77(t, J=6.0Hz, 2H), 3.02(s, 3H), 3.69(s, 2H), 3.92(s, 2H), 4.56(s, 2H), 6.75(d, J=9.0Hz, 2H), 7.09-7.16(m, 4H), 7.31-7.41(m, 5H), 7.64(s, 1H), 7.71(d, J=9.0Hz, 2H)
3-31	DMSO-d6, 400MHz	0.84 (s, 9 H),2.42 (s, 2 H),2.87 (s, 3 H),3.31 (s, 2 H),3.35 (s, 2 H),3.86 (s, 2 H),4.15 (s, 2 H),6.72 (d, J = 9.0 Hz, 2 H),7.03 (d, J = 7.9 Hz, 2 H),7.14 (d, J = 7.9 Hz, 2 H),7.23- 7.29 (m, 1 H),7.32- 7.44 (m, 4 H),7.65 (s, 1 H),7.72 (d, J = 9.0 Hz, 2 H),12.40 (br s, 1 H).

Table 17-43

Example	solvent, Hz	NMR(δ)
3-32	DMSO-d6, 300MHz	0.89(d, J=6.5Hz, 3H), 1.01-1.05(m, 2H), 1.30-1.45(m, 3H), 1.70-1.75(m, 4H), 3.35(s, 2H), 3.86(s, 2H), 4.15(s, 2H), 4.55(s, 2H), 6.76(d, J=9.0Hz, 2H), 7.09-7.16(m, 4H), 7.26-7.29(m, 1H), 7.35-7.41(m, 4H), 7.65(s, 1H), 7.71(d, J=8.9Hz, 2H)
3-33	DMSO-d6, 300MHz	1.55-1.64(m,6H), 1.92-2.03(m,2H), 2.50-2.55(m,1H), 3.35(s,2H), 3.86(s,2H), 4.15(s,2H), 4.57(s,2H), 4.83(d,J = 15.0Hz, 1H), 6.77(d,J = 9.0Hz, 2H), 7.13-7.16(m,4H), 7.32-7.39(m,4H), 7.65(s,1H), 7.71(d,J = 8.8Hz, 2H)
3-34	DMSO-d6, 400MHz	1.12-1.21(m,2H), 1.32-1.43(m,2H), 1.78(d,J = 12.0Hz, 4H), 2.40-2.50(m,2H), 2.96(s,3H), 3.24(d,J = 4.0Hz, 2H), 3.35(s,2H), 3.85(s,2H), 4.14(s,2H), 6.69(d,J = 8.0Hz, 2H), 7.63(s,1H), 7.70(d,J = 8.0Hz, 2H)
3-35	DMSO-d6, 300MHz	0.92(s, 3H), 0.94(s, 3H), 1.23-1.63(m, 8H), 2.33-2.40(m, 1H), 3.02(s, 3H), 3.35(s, 2H), 3.85(s, 2H), 4.14(s, 2H), 4.55(s, 2H), 6.75(d, J=6.7Hz, 2H), 7.10(d, J=6.2Hz, 2H), 7.17(d, J=6.0Hz, 2H), 7.26(t, J=5.3Hz, 1H), 7.32-7.40(m, 4H), 7.64(s, 1H), 7.70(d, J=6.7Hz, 2H), 12.39(brs, 1H)
3-36	DMSO-d6, 300MHz	0.78 (t, J = 7.3 Hz, 6 H), 1.00- 1.18 (m, 4 H), 1.38- 1.59 (m, 4 H), 2.40- 2.58 (m, 1 H), 3.03 (s, 3 H), 3.32 (s, 2 H), 3.86 (s, 2 H), 4.15 (s, 2 H), 4.57 (s, 2 H), 6.77 (d, J = 8.9 Hz, 2 H), 7.06- 7.15 (m, 4 H), 7.21- 7.44 (m, 5 H), 7.66 (s, 1 H), 7.72 (d, J = 8.8 Hz, 2 H).
3-37	DMSO-d6, 300MHz	3.08(s, 3H), 3.35(s, 2H), 3.86(s, 2H), 4.15(s, 2H), 4.66(s, 2H), 6.79(d, J=8.6Hz, 2H), 7.22-7.46(m, 10H), 7.60-7.65(m, 4H), 7.67(s, 1H), 7.73(d, J=9.0Hz, 2H)

Table 17-44

Example	solvent, Hz	NMR(δ)
3-38	DMSO-d6, 300MHz	1.14-1.43(m, 5H), 1.63-1.82(m, 5H), 2.38-2.49(m, 1H), 2.94(s, 2H), 3.02(s, 3H), 3.90(s, 2H), 4.19(s, 2H), 4.55(s, 2H), 6.75(d, J=9.0Hz, 2H), 7.11(d, J=8.3Hz, 2H), 7.15(d, J=8.3Hz, 2H), 7.21(t, J=7.2Hz, 1H), 7.31(t, J=7.3Hz, 2H), 7.39(d, J=7.2Hz, 2H), 7.58(s, 1H), 7.70(d, J=9.0Hz, 2H)
3-39	DMSO-d6, 400MHz	0.85(d, J=6.8Hz, 6H), 1.75-1.81(m; 1H), 2.39(d, J=6.8Hz, 2H), 3.02(s, 3H), 3.34(s, 2H), 3.85(s, 2H), 4.14(s, 2H), 4.56(s, 2H), 6.76(d, J=8.0Hz, 2H), 7.08-7.10(m, 4H), 7.20-7.25(m, 1H), 7.33-7.40(m, 4H), 7.64(s, 1H), 7.69(d, J=8.0Hz, 2H)
3-40	DMSO-d6, 400MHz	0.78(t, J=7.3Hz, 6H), 0.99-1.15(m, 4H), 1.40-1.56(m, 4H), 2.43-2.52(m, 1H), 2.93(s, 2H), 3.02(s, 3H), 3.90(s, 2H), 4.19(s, 2H), 4.56(s, 2H), 6.75(d, J=9.1Hz, 2H), 7.08(d, J=8.3Hz, 2H), 7.11(d, J=8.3Hz, 2H), 7.20(t, J=7.3Hz, 1H), 7.30(t, J=7.3Hz, 2H), 7.38(d, J=7.3Hz, 2H), 7.58(s, 1H), 7.69(d, J=9.1Hz, 2H)
3-41	DMSO-d6, 300MHz	0.97 (s, 9H), 2.89 (s, 2H), 3.02 (s, 3H), 3.86 (s, 2H), 4.15 (s, 2H), 4.56 (s, 2H), 6.75 (d, J = 8.87 Hz, 2H), 7.13 (d, J = 8.25 Hz, 2H), 7.25-7.40 (m, 7H), 7.67 (s, 1H), 7.71 (d, J = 8.87, 2H)
3-42	DMSO-d6, 400MHz	0.86 (d, J = 6.72, 6H), 1.40-1.46 (m, 2H), 1.61-1.71 (m, 1H), 2.90 (d, J = 7.64 Hz, 1H), 2.92 (d, J = 7.64 Hz, 1H), 3.03 (s, 3H), 3.85 (s, 2H), 4.15 (s, 2H), 4.57 (s, 2H), 6.74 (d, J = 9.04 Hz, 2H), 7.14 (d, J = 8.36 Hz, 2H), 7.24-7.28 (m, 3H), 7.32-7.40 (m, 4H), 7.66 (s, 1H), 7.70 (d, J = 9.04, 2H)
3-43	DMSO-d6, 300MHz	0.81 (t, J = 7.2 Hz, 6 H), 1.44 (tq, J = 7.8, 7.2 Hz, 4 H), 3.19 (dd, J = 7.8, 7.8 Hz, 4 H), 3.34 (s, 3 H), 3.36 (s, 2 H), 3.86 (s, 2 H), 4.17 (s, 2 H), 6.40 (d, J = 8.7 Hz, 2 H), 7.12 (d, J = 9.0 Hz, 2 H), 7.17 (d, J = 8.7 Hz, 2 H), 7.21-7.43 (m, 5 H), 7.84 (d, J = 9.0 Hz, 2 H), 8.00 (s, 1 H), 12.38 (br s, 1 H).

Table 17-45

Example	solvent, Hz	NMR(δ)
3-44	DMSO-d6, 300MHz	1.12-1.20(m,15H), 2.80-2.89(m,2H), 3.24(s,2H), 3.15-3.52(m,2H), 3.82(s,2H), 4.15(s,2H), 4.52(s,2H), 6.70(d,J = 9.0Hz, 2H), 7.13-7.22(m,8H), 7.31(d,J = 9.0Hz, 2H), 7.61(s,1H), 7.68(d,J = 9.0Hz, 2H)
3-45	DMSO-d6, 300MHz	1.15-1.19(m,18H), 2.76-2.89(m,1H), 3.79(s,2H), 4.11(s,2H), 4.27-4.33(m,1H), 4.38(s,2H), 6.69(d,J = 9.0Hz, 2H), 7.15-7.32(m,8H), 7.60-7.66(m,3H)
3-46	DMSO-d6, 300MHz	1.14(d,J = 6.0Hz, 6H), 1.17(s,9H), 1.24(d,J = 6.0Hz, 6H), 2.74-2.90(m,1H), 3.79(s,2H), 4.12(s,2H), 4.23-4.36(m,1H), 4.38(s,2H), 6.68(d,J = 6.0Hz, 2H), 7.14-7.17(m,3H), 7.27-7.42(m,4H), 7.60-7.72(m,3H)
3-47	DMSO-d6, 400MHz	0.82(d, J=19.6Hz, 6H), 1.75-1.82(m, 1H), 2.40(d, J=14.4Hz, 2H), 3.03(s, 3H), 3.34(s, 2H), 3.84(s, 2H), 4.26(s, 2H), 4.56(s, 2H), 6.77(d, J=8.0Hz, 2H), 7.08-7.11(m, 4H), 7.40-7.41(m, 4H), 7.64(s, 1H), 7.69(d, J=8.0Hz, 2H)
3-48	DMSO-d6, 300MHz	0.79(t, J = 6.0Hz, 6H), 1.04-1.13(m,4H), 1.48-1.56(m,4H), 2.49-2.51(m,1H), 3.05(s,3H), 3.44(m,2H), 3.91(s,2H), 4.22(s,2H), 4.62(s,2H), 6.78(d,J = 9.0Hz, 1H), 7.15(d,J = 9.0Hz, 2H), 7.20-7.24(m,3H), 7.30-7.35(m,5H), 7.69-7.74(m,2H)
3-49	DMSO-d6, 300MHz	3.05(s,3H), 3.36(s,2H), 3.85(s,2H), 4.14(s,2H), 4.61(s,2H), 6.74-6.79(m,2H), 7.20-7.42(m,9H), 7.66(s,1H), 7.72(d,J = 6.0Hz, 2H)
3-50	DMSO-d6, 300MHz	3.04(s,3H), 3.42(s,2H), 4.02(s,2H), 4.22(s,2H), 4.61(s,2H), 6.76(d,J = 6.0Hz, 2H), 7.20-7.44(m,8H), 7.64-7.72(m,4H)
3-51	DMSO-d6, 300MHz	3.05(s,3H), 3.40(s,2H), 3.87(s,2H), 4.13(s,2H), 4.62(s,2H), 6.77(d,J = 9.0Hz, 2H), 7.20-7.45(m,6H), 7.58-7.74(m,6H)

Table 17-46

Example	solvent, Hz	NMR(δ)
3-52	DMSO-d6, 300MHz	0.89(d, J=6.0Hz, 3H), 1.00-1.80(m, 2H), 1.33-1.46(m, 3H), 1.72-1.75(m, 4H), 2.35-2.43(m, 1H), 2.95(s, 2H), 3.02(s, 3H), 4.10(s, 2H), 4.22(s, 2H), 4.55(s, 2H), 6.74(d, J=9.1Hz, 2H), 7.09-7.11(m, 4H), 7.16-7.22(m, 1H), 7.57-7.79(m, 5H), 8.45(d, J=4.1Hz, 2H)
3-53	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 0.97-1.16(m, 4H), 1.36-1.59(m, 4H), 2.43-2.53(m, 1H), 3.03(s, 3H), 3.44(s, 2H), 4.00(s, 2H), 4.21(s, 2H), 4.57(s, 2H), 6.77(d, J=9.1Hz, 2H), 7.09(d, J=8.7Hz, 2H), 7.12(d, J=8.7Hz, 2H), 7.28(dd, J=7.5, 4.5Hz, 1H), 7.57(d, J=7.5Hz, 1H), 7.65(s, 1H), 7.71(d, J=9.1Hz, 2H), 7.81(dt, J=1.9, 7.5Hz, 1H), 8.50(dd, J=4.5, 1.9Hz, 1H)
3-54	DMSO-d6, 300MHz	3.04(s,3H), 3.39(s,2H), 4.21(s,2H), 4.36(s,2H), 4.61(s,2H), 6.76(d,J = 9.0Hz, 2H), 7.20-7.35(m,5H), 7.44-7.72(m,9H), 7.85-7.91(m,2H), 8.41-8.444(m,1H)
3-55	DMSO-d6, 300MHz	3.05(s,3H), 3.51(s,2H), 4.22(s,2H), 4.27(s,2H), 4.61(s,2H), 6.76(d,J = 9.0Hz, 2H), 7.23(t, J = 9.0Hz, 3H), 7.32(t, J = 9.0Hz, 2H), 7.57-7.82(m,7H), 7.98(t, J = 6.0Hz, 2H), 8.42(d,J = 9.0Hz, 1H)
3-56	DMSO-d6, 300MHz	3.06(s,3H), 3.96(s,1H), 4.13(d,J = 12.0Hz, 2H), 4.44(s,1H), 4.63(s,2H), 4.82(s,1H), 5.10(s,1H), 6.78(d,J = 9.0Hz, 2H), 7.21-7.37(m,7H), 7.52(d,J = 6.0Hz, 1H), 7.66-7.76(m,4H), 7.96-7.98(m,1H)
3-57	DMSO-d6, 400MHz	0.84(t,J=7.3Hz, 6H), 1.73-1.78(m, 1H), 2.40(d, J=7.2Hz, 2H), 3.03(s, 3H), 3.70(s, 1H), 3.90(s, 1H), 4.07(s, 1H), 4.34(s, 1H), 4.57(s, 2H), 4.78(s, 1H), 5.02(s, 1H), 6.75-6.77(m, 2H), 7.10-7.12(m, 4H), 7.24-7.27(m, 2H), 7.33-7.36(m, 2H), 7.64-7.71(m, 3H)
3-58	DMSO-d6, 400MHz	0.846(t, J=7.4H, 6H), 1.18(t, J=8.4Hz, 6H), 1.76-1.81(m, 1H), 2.40(d, J=6.8Hz, 2H), 2.82-2.86(m, 1H), 3.03(s, 3H), 3.63(s, 1H), 3.83(s, 1H), 4.06(s, 1H), 4.30(s, 1H), 4.55(s, 2H), 4.78(s, 1H), 4.99(s, 1H), 6.75-6.77(m, 2H), 7.07-7.16(m, 8H), 7.64-7.72(m, 3H)

Table 17-47

Example	solvent, Hz	NMR(δ)
3-59	DMSO-d6, 400MHz	0.82-0.90(m, 12H), 1.74-1.81(m, 1H), 2.02-2.04(m, 1H), 2.15(d, J=8.0Hz, 1H), 2.33(d, J=8.0Hz, 1H), 2.39(d, J=7.0Hz, 2H), 3.02(s, 3H), 4.03(s, 1H), 4.24(s, 1H), 4.56(s, 2H), 4.74(s, 1H), 4.91(s, 1H), 6.72-6.76(m, 2H), 7.05-7.11(m, 4H), 7.61-7.70(m, 3H)
3-60	DMSO-d6, 300MHz	0.85 (s, 9 H), 2.43 (s, 2 H), 3.04 (s, 3 H), 4.21 (s, 2 H), 4.59 (s, 2 H), 4.90 (s, 2 H), 6.77 (d, J = 8.9 Hz, 2 H), 6.96 (d, J = 7.3 Hz, 1 H), 7.07 (d, J = 8.2 Hz, 2 H), 7.13 (d, J = 8.1 Hz, 2 H), 7.24 (dd, J = 7.9, 7.9 Hz, 2 H), 7.45 (d, J = 7.6 Hz, 2 H), 7.67 (s, 1 H), 7.73 (d, J = 8.8 Hz, 2 H), 8.79 (s, 1 H), 12.58 (br s, 1 H).
3-61	DMSO-d6, 400MHz	0.83(d, J=12.0Hz, 6H), 1.75-1.82(m, 1H) , 2.40(d, J=16.0Hz, 2H), 3.03(s, 3H), 4.07(s, 1H), 4.19(s, 1H), 4.57(s, 2H), 4.77(s, 1H), 4.93(s, 1H), 6.76(d, J=8.0Hz, 2H), 7.09-7.12(m, 4H), 7.36-7.37(m, 1H), 7.45-7.48(m, 4H), 7.67-7.71(m, 3H)
3-62	DMSO-d6, 400MHz	0.81(t,J=7.3Hz, 6H), 1.05-1.13(m, 4H), 1.48-1.57(m, 4H),2.31(s, 3H), 2.50-2.56(m, 1H), 3.00(s, 3H), 3.92(s, 2HX0.58), 4.15(s, 2HX0.42), 4.57 (s, 2H), 4.78 (s,2HX0.42), 4.90(s, 2HX0.58), 6.77(d, J=8.0Hz, 2H), 7.07-7.13(m, 4H), 7.23-7.39(m, 4H), 7.69-7.73(m, 3H)
3-63	DMSO-d6, 400MHz	0.81(t,J=7.3Hz, 6H), 1.05-1.13(m, 4H), 1.21(d, J=8.0Hz, 6H), 1.42-1.52(m, 4H), 2.48-2.50(m, 1H), 2.89-2.93(m, 1H), 3.20(s, 3H), 3.45(s, 2H), 4.57(s, 2H), 4.88(s, 2H), 6.77(d, J=8.0Hz, 2H), 7.08-7.13(m, 4H), 7.26(d, J=8.0Hz, 2H), 7.40(d, J=8.0Hz, 2H), 7.66(s, 1H), 7.73(d, J=8.0Hz, 2H)
3-64	DMSO-d6, 300MHz	0.79(t, J = 9.0Hz, 6H), 1.02-1.12(m,4H), 1.43-1.54(m,4H), 2.96-2.06(m,5H), 3.78(d,J = 15.0Hz, 1H), 4.16(d,J = 15.0Hz, 1H), 4.56(s,2H), 4.72-4.76(m,1H), 6.76(d,J = 9.0Hz, 2H), 7.05-7.12(m,7H), 7.48(s,1H), 7.68(d,J = 9.0Hz, 2H)

Table 17-48

Example	solvent, Hz	NMR(δ)
3-65	DMSO-d6, 300MHz	1.15-1.86(m, 13H), 2.12-2.29(m, 3H), 2.39-2.48(m, 1H), 2.82-2.91(m, 2H), 3.03(s, 3H), 3.81(s, 2H), 4.56(s, 2H), 6.75(d, J=9.1Hz, 2H), 7.11(d, J=8.4Hz, 2H), 7.16(d, J=8.4Hz, 2H), 7.64(s, 1H), 7.71(d, J=8.8Hz, 2H), 12.11(brs, 1H)
3-66	DMSO-d6, 300MHz	1.20-1.82(m, 14H), 2.00-2.12(m, 2H), 2.16-2.20(m, 1H), 2.45-2.50(m, 1H), 2.78-2.82(m, 1H), 2.90-2.95(m, 1H), 3.02(s, 3H), 3.78(s, 2H), 4.55(s, 2H), 6.75(d, J=9.0Hz, 2H), 7.09-7.16(m, 4H), 7.62(s, 1H), 7.70(d, J=12.0Hz, 2H)
3-67	DMSO-d6, 300MHz	1.20-1.40(m, 5H), 1.60-1.80(m, 7H), 2.20-2.50(m, 5H), 2.80-2.90(m, 2H), 3.03(s, 3H), 3.81(s, 2H), 4.56(s, 2H), 6.75(d, J=9.0Hz, 2H), 7.09-7.14(m, 4H), 7.25-7.28(m, 1H), 7.35-7.42(m, 4H), 7.63(s, 1H), 7.70(d, J=8.9Hz, 2H)
3-68	DMSO-d6, 300MHz	0.84(d, J=6.6Hz, 6H), 1.02-1.50(m, 12H), 1.65-1.81(m, 5H), 1.95-2.04(m, 2H), 2.15-2.26(m, 2H), 2.39-2.49(m, 1H), 2.69-2.79(m, 2H), 3.03(s, 3H), 3.78(s, 2H), 4.56(s, 2H), 6.75(d, J=9.1Hz, 2H), 7.10-7.17(m, 4H), 7.63(s, 1H), 7.70(d, J=8.8Hz, 2H)
3-69	DMSO-d6, 300MHz	0.89(d, J=6.0Hz, 3H), 1.00-1.10(m, 2H), 1.30-1.40(m, 3H), 1.72-1.95(m, 6H), 2.30-2.50(m, 5H), 2.80-2.90(m, 2H), 3.03(s, 3H), 3.81(s, 2H), 4.56(s, 2H), 6.75(d, J=9.0Hz, 2H), 7.09-7.17(m, 4H), 7.25-7.30(m, 1H), 7.32-7.37(m, 4H), 7.64(s, 1H), 7.70(d, J=11.7Hz, 2H)
3-70	DMSO-d6, 300MHz	1.08-1.19(m,2H), 1.30-1.44(m,2H), 1.57-1.67(m,2H), 2.35-2.44(m,2H), 2.75(d,J = 8.0Hz, 2H), 2.96(s,3H), 3.25-3.30(m,4H), 3.74(s,2H), 6.69(d,J = 8.0Hz, 2H), 7.08(t, J = 4.0Hz, 1H), 7.18-7.23(m,5H), 7.28(d,J = 8.0Hz, 2H), 7.37(d,J = 8.0Hz, 2H), 7.59(s,1H), 7.70(d,J = 12.0Hz, 2H)

Table 17-49

Example	solvent, Hz	NMR(δ)
3-71	DMSO-d6, 300MHz	0.89(d, J=4.8Hz, 3H), 1.01-1.10(m, 2H), 1.30-1.50(m, 3H), 1.70-1.80(m, 4H), 3.10-3.20(m, 1H), 3.10-3.20(m, 2H), 3.88-4.11(m, 3H), , 4.30(dd, J=37.7, 11.6Hz, 2H), 4.56(s, 2H), 6.76(d, J=9.0Hz, 2H), 7.04-7.17(m, 8H), 7.64(s, 1H), 7.72(d, J=8.8Hz, 2H)
3-72	DMSO-d6, 300MHz	0.84(d, J=6.8Hz, 6H), 1.70-1.80(m, 1H), 2.39(d, J=4.4Hz, 2H), 3.03(s, 3H), 3.10-3.20(m, 2H), 3.89-4.06(m, 3H), 4.22(d, J=15.6Hz, 1H), 4.36(d, J=15.6Hz, 1H), 4.57(s, 2H), 6.75(d, J=10.8Hz, 2H), 7.03-7.15(m, 8H), 7.64(s, 1H), 7.71(d, J=10.0Hz, 2H)
3-73	DMSO-d6, 300MHz	0.79(t, J=7.4Hz, 6H), 1.01-1.14(m, 4H), 1.39-1.56(m, 4H), 2.43-2.48(m, 1H), 3.03(s, 3H), 3.11-3.16(m, 2H), 4.00(ABq, J=15.6,41.6Hz, 2H), 3.95-3.97(m, 1H), 4.30(ABq, J=15.8, 50.1Hz, 2H), 4.57(s, 2H), 6.77(d, J=9.1Hz, 2H), 7.02-7.16(m, 8H), 7.65(s, 1H), 7.73(d, J=8.6Hz, 2H), 12.54(brs, 1H)
3-74	DMSO-d6, 300MHz	0.85 (s, 9 H), 2.43 (s, 2 H), 3.04 (s, 3 H), 3.10- 3.20 (m, 2 H), 3.92 (d, J = 16.1 Hz, 1 H), 3.90- 4.00 (m, 1 H), 4.10 (d, J = 7.7 Hz, 1 H), 4.23 (d, J = 15.7 Hz, 1 H), 4.37 (d, J = 15.7 Hz, 1 H), 4.59 (s, 2 H), 6.77 (d, J = 8.9 Hz, 2 H), 7.00- 7.20 (m, 8 H), 7.66 (s, 1 H), 7.72 (d, J = 8.8 Hz, 2 H), 12.50 (br s, 1 H).
3-75	DMSO-d6, 400MHz	1.21-1.34(m, 5H), 1.69-1.74(m, 5H), 2.44-2.54(m, 1H), 3.02(s, 3H), 3.70(s, 3H), 4.55(s, 2H), 4.77(s, 2H), 6.54(s, 1H), 6.71(d, J=8.0Hz, 2H), 6.87(s, 1H), 7.11-7.14(m, 5H), 7.64(d, J=8.0Hz, 2H)
3-76	DMSO-d6, 300MHz	1.20-1.45(m, 5H), 1.60-1.85(m, 5H), 2.45-2.50(m, 1H), 2.80-3.00(m, 2H), 3.35-3.38(m, 1H), 3.83(d, J=15.0Hz, 1H), 4.09(d, J=15.0Hz, 1H), 4.55(s, 2H), 6.74(d, J=9.0Hz, 2H), 7.09-7.25(m, 9H), 7.53(s, 1H), 7.67(d, J=9.0Hz, 2H)

Table 17-50

Example	solvent, Hz	NMR(δ)
3-77	DMSO-d6, 400MHz	1.21-1.40(m, 5H), 1.69-1.80(m, 5H), 2.44-2.50(m, 1H), 3.90-3.96(m, 2H), 4.34(s, 1H), 4.55(s, 2H), 6.75(d, J=8.8Hz, 2H), 7.12-7.14(m, 4H), 7.28-7.40(m, 5H), 7.60(s, 1H), 7.69(d, J=8.3Hz, 2H)
3-78	DMSO-d6, 400MHz	1.14(d, J=12.0Hz, 3H), 1.20-1.40(m, 5H), 1.65-1.80(m, 5H), 2.44-2.50(m, 1H), 3.05-3.08(m, 1H), 3.85(d, J=16.0Hz, 1H), 4.09(d, J=16.0Hz, 1H), 4.75(s, 2H), 6.74(d, J=8.0Hz, 2H), 7.09-7.15(m, 4H), 7.57(s, 1H), 7.70(d, J=8.8Hz, 2H)
3-79	DMSO-d6, 400MHz	0.83(d, J=14.0Hz, 6H), 1.78-1.90(m, 1H), 2.39(d, J=5.6Hz, 2H), 2.82-3.02(m, 2H), 3.02(s, 3H), 3.44-3.45(m, 1H), 3.87(d, J=16.0Hz, 1H), 4.11(d, J=16.0Hz, 1H), 4.56(s, 2H), 6.73(d, J=8.0Hz, 2H), 7.08-7.11(m, 4H), 7.27-7.30(m, 4H), 7.55(s, 1H), 7.67(d, J=10.8Hz, 2H)
3-80	DMSO-d6, 300MHz	1.08-1.35(m, 5H), 1.60-1.77(m, 5H), 2.44-2.54(m, 1H), 2.40(s, 3H), 2.44-2.50(m, 1H), 3.03(s, 3H), 3.38(s, 3H), 4.04(s, 2H), 4.56(s, 2H), 6.76(d, J=12.0Hz, 2H), 7.09-7.17(m, 5H), 7.66-7.72(m, 2H)
3-81	DMSO-d6, 300MHz	1.14-1.45(m, 5H), 1.63-1.83(m, 5H), 2.29(s, 3H), 2.39-2.49(m, 1H), 2.43(t, J=7.2Hz, 2H), 2.74(t, J=7.1Hz, 2H), 3.03(s, 3H), 3.87(s, 2H), 4.56(s, 2H), 6.76(d, J=8.8Hz, 2H), 7.10-7.17(m, 4H), 7.65(s, 1H), 7.71(d, J=8.8Hz, 2H)
3-82	DMSO-d6, 400MHz	1.19-1.41(m, 5H),1.67-1.77(m, 5H),2.26(s, 3H),2.44-2.47(m, 1H), 3.03(s, 3H), 3.66(s, 2H), 3.88(s, 2H), 4.56(s, 2H), 6.76(d, J=9.2, 2H), 7.10-7.16(m, 4H), 7.37(d, J=8.1, 2H), 7.66(s, 1H), 7.71(d, J=8.6, 2H), 7.87(d, J=9, 2H)
3-83	DMSO-d6, 300MHz	1.16-1.41(m, 5H), 1.67-1.81(m, 5H), 2.41-2.48(m, 1H), 3.03(s, 3H), 3.07(s, 3H), 4.56(s, 2H), 4.84(s, 2H), 6.68(d, J=8.9Hz, 2H), 6.76(d, J=6.5Hz, 2H), 7.10-7.17(m, 4H), 7.57(s, 1H), 7.68-7.73(m, 4H)

Table 17-51

Example	solvent, Hz	NMR(δ)
3-84	DMSO-d6, 400MHz	1.13-1.41(m, 5H), 1.65-1.81(m, 5H), 2.40-2.48(m, 1H), 3.03(s, 3H), 3.20(s, 3H), 4.56(s, 2H), 5.14(s, 2H), 6.75(d, J=9.0Hz, 2H), 6.80(d, J=9.0Hz, 1H), 7.09-7.15(m, 4H), 7.59(s, 1H), 7.70(d, J=9.0Hz, 2H), 7.97(dd, J=2.3, 9.0Hz, 1H), 8.64(dd, J=0.8, 2.4Hz, 1H), 12.46(brs, 1H)
3-85	DMSO-d6, 400MHz	0.83(d, J=13.6Hz, 6H), 1.70-1.80(m, 1H), 2.32-2.37(m, 5H), 2.90-3.00(m, 2H), 3.02(s, 3H), 3.60-3.70(m, 1H), 3.98(d, J=16.0Hz 1H), 4.14(d, J=16.0Hz,1H), 4.56(s, 2H), 6.74(d, J=9.2Hz, 2H), 7.08-7.11(m, 4H), 7.18-7.20(m, 1H), 7.25-7.27(m, 4H), 7.56(s, 1H), 7.67(d, J=8.0Hz, 2H)
3-86	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.96-1.15(m, 4H), 1.40-1.57(m, 4H), 2.37 (s, 3H), 2.41-2.5(m, 1H), 2.93 (dd, J = 14.1, 7.7, 1H), 3.02 (s, 3H), 3.06 (dd, J = 14.1, 7.7 Hz, 1H), 3.69 (t, J = 7.7 Hz, 1H), 4.00 (d, J = 15.8 Hz, 1H), 4.15 (d, J = 15.8 Hz, 1H), 4.56 (s, 2H), 6.76 (d, J = 8.9 Hz, 2H), 7.09 (d, J = 8.6 Hz, 2H), 7.12 (d, J = 8.6 Hz, 2H), 7.19-7.28 (m, 5H), 7.57 (s, 1H), 7.69 (d, J = 8.9 Hz, 2H)
3-87	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.96-1.15(m, 4H), 1.40-1.57(m, 4H), 2.34 (s, 3H), 2.42-2.5(m, 1H), 3.02 (s, 3H), 3.83 (d, J = 15.3 Hz, 1H), 3.98 (d, J = 15.3 Hz, 1H), 4.50 (s, 1H), 4.56 (s, 2H), 6.76 (d, J = 8.7 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 7.33-7.48 (m, 5H), 7.64 (s, 1H), 7.70 (d, J = 8.7 Hz, 2H)
3-88	DMSO-d6, 400MHz	0.84 (s, 9 H), 2.33 (s, 3 H), 2.42 (s, 2 H), 3.02 (s, 3 H), 3.82 (d, J = 15.2 Hz, 1 H), 3.96 (d, J = 15.6 Hz, 1 H), 4.48 (s, 1 H), .00 (s, 2 H), 6.74 (d, J = 8.8 Hz, 2 H), 7.05 (d, J = 7.6 Hz, 2 H), 7.10 (d, J = 7.6 Hz, 2 H), 7.32 (t, J = 7.2 Hz, 1 H), 7.39 (t, J = 7.4 Hz, 2 H), 7.45 (d, J = 8.9 Hz, 2 H), 7.63 (s, 1 H), 7.65 (d, J = 15.2 Hz, 2 H).

Table 17-52

Example	solvent, Hz	NMR(δ)
3-89	DMSO-d6, 400MHz	0.84 (s, 9 H), 2.36 (s, 3 H), 2.42 (s, 2 H), 2.93 (dd, J = 14.2, 8.1 Hz, 1 H), 3.02 (s, 3 H), 3.05 (dd, J = 14.1, 7.2 Hz, 1 H), 3.68 (t, J = 8.0 Hz, 1 H), 4.01 (d, J = 12.0 Hz, 1 H), 4.14 (d, J = 15.6 Hz, 1 H), 4.57 (s, 2 H), 6.74 (d, J = 9.0 Hz, 2 H), 7.05 (d, J = 8.1 Hz, 2 H), 7.10 (d, J = 8.1 Hz, 2 H), 7.19 (q, J = 4.4 Hz, 1 H), 7.26 (d, J = 4.6 Hz, 2 H), 7.56 (s, 1 H), 7.67 (d, J = 8.8 Hz, 2 H), 12.48 (br s, 1 H).
3-90	DMSO-d6, 400MHz	0.79(t, J=7.3Hz, 6H), 1.00-1.14(m, 4H), 1.41-1.57(m, 4H), 2.44-2.48(m, 1H), 3.03(s, 3H), 3.51(s, 4H), 4.16(s, 2H), 4.57(s, 2H), 6.76(d, J=9.0Hz, 2H), 7.09(d, J=8.6Hz, 2H), 7.12(d, J=8.4Hz, 2H), 7.64(s, 1H), 7.70(d, J=9.0Hz, 2H)
3-91	DMSO-d6, 300MHz	0.83(d, J=5.0Hz, 6H), 1.17-1.41(m, 7H), 1.54-1.62(m, 1H), 1.67-1.77(m, 5H), 2.41-2.49(m, 1H), 2.66-2.70(m, 2H), 3.02(s, 3H), 3.41(s, 2H), 4.10(s, 2H), 6.74(d, J=6.9Hz, 2H), 7.09-7.15(m, 4H), 7.61(s, 1H), 7.69(d, J=6.6Hz, 2H)
3-92	DMSO-d6, 300MHz	0.84(d, J=6.7Hz, 6H), 0.91(d, J=17.6Hz, 3H), 0.95-1.05(m, 2H), 1.30-1.42(m, 5H), 1.50-1.60(m, 1H), 1.72-1.76(m, 4H), 2.45-2.50(m, 1H), 2.60-2.70(m, 2H), 3.02(s, 3H), 3.41(s, 2H), 4.10(s, 2H), 4.56(s, 2H), 6.75(d, J=9.0Hz, 2H), 7.09-7.17(m, 4H), 7.62(s, 1H), 7.70(d, J=8.8Hz, 2H)
3-93	DMSO-d6, 400MHz	0.87-0.84(m, 12H), 1.33-1.37(m, 2H), 1.58-4.61(m, 1H), 1.75-1.78(m, 1H), 2.39(d, J=7.2Hz, 2H), 2.65-2.69(m, 2H), 3.02(s, 3H), 3.40(s, 2H), 4.09(s, 2H), 4.56(s, 2H), 6.74(d, J=9.2Hz, 2H), 7.06-7.11(m, 4H), 7.61(s, 1H), 7.68(d, J=11.6Hz, 2H)
3-94	DMSO-d6, 400MHz	0.81(t,J=7.3Hz, 6H), 1.05-1.13(m, 4H), 1.48-1.57(m, 4H), 2.50-2.56(m, 1H), 3.00(s, 3H), 4.56(s, 2H), 5.61(s, 2H), 6.78(d, J=8.8Hz, 2H), 7.10-7.13(m, 4H), 7.75(d, J=8.4Hz, 2H), 7.81(s, 1H), 7.97(s, 1H), 8.63(s, 1H), 8.71(s, 1H)

Table 17-53

Example	solvent, Hz	NMR(δ)
3-95	DMSO-d6, 400MHz	0.81(t,J=7.3Hz, 6H), 1.05-1.13(m, 4H), 1.48-1.57(m, 4H),2.50-2.56(m, 1H), 3.04(s, 3H), 4.58(s, 2H), 5.54(s, 2H), 6.78(d, J=8.8Hz, 2H), 7.10-7.13(m, 4H), 7.19(d, J=8.0Hz, 2H), 7.74(d, J=8.0Hz, 2H), 7.80(s, 1H), 7.91(d, J=9.2Hz, 2H)
3-96	DMSO-d6, 400MHz	0.81(t,J=7.3Hz, 6H), 1.05-1.13(m, 4H), 1.48-1.57(m, 4H),2.50-2.56(m, 1H), 3.03(s, 3H), 4.57(s, 2H), 4.74(s, 2H), 6.76(d, J=9.2Hz, 2H), 7.10-7.13(m, 4H), 7.52(d, J=8.0Hz, 2H) , 7.63(s, 1H), 7.69(d, J=9.2Hz, 2H), 7.83(d, J=8.0Hz, 2H)
3-97	DMSO-d6, 300MHz	1.20-1.40(m, 5H), 1.60-1.80(m, 5H), 1.45-1.50(m, 1H), 3.02(s, 3H), 4.39(d, J=6.3Hz, 2H), 4.55(s, 2H), 6.73(d, J=9.0Hz, 2H), 7.10-7.17(m, 4H), 7.61-7.64(m, 3H), 7.94(d, J=8.4Hz, 2H), 8.11(d, J=8.4Hz, 2H), 8.80(t, J=6.3Hz, 1H)
3-98	DMSO-d6, 400MHz	0.92 (s, 3H), 0.95 (s, 3H), 1.40-1.61 (m, 8H), 2.31-2.41 (m, 1H), 2.85 (s, 3H), 3.03 (s, 3H), 4.56 (s, 2H), 4.65 (s, 2H), 6.74 (d, J = 8.82 Hz, 2H), 7.12 (d, J = 8.10 Hz, 2H), 7.18 (d, J = 8.10 Hz, 2H), 7.61 (d, J = 8.82 Hz, 2H), 7.69 (s, 1H), 7.97 (d, J = 8.36 Hz, 2H), 8.13 (d, J = 8.36, 2H)
3-99	DMSO-d6, 400MHz	0.92 (s, 3H), 0.95 (s, 3H), 1.40-1.61 (m, 8H), 2.31-2.41 (m, 1H), 2.91 (s, 3H), 3.03 (s, 3H), 4.04 (s, 2H), 4.57 (s, 2H), 4.67 (s, 2H), 6.76 (d, J = 8.84 Hz, 2H), 7.12 (d, J = 8.12 Hz, 2H), 7.18 (d, J = 8.12 Hz, 2H), 7.70 (s, 1H), 7.72 (d, J = 8.84 Hz, 2H)
3-100	DMSO-d6, 300MHz	1.20-1.40(m, 5H), 1.60-1.77(m, 5H), 2.40-2.50(m, 1H), 2.84(s, 3H), 3.03(s, 3H), 4.55(s, 2H), 4.65(s, 2H), 6.73(d, J=9.0Hz, 2H), 7.90-7.16(m, 4H), 7.61(d, J=8.4Hz, 2H), 7.70(s, 1H), 7.97(d, J=8.1Hz, 2H), 8.13(d, J=8.1Hz, 2H)

Table 17-54

Example	solvent, Hz	NMR(δ)
3-101	DMSO-d6, 300MHz	1.20-1.40(m, 5H), 1.60-1.77(m, 5H), 2.40-2.50(m, 1H), 2.85(s, 3H), 3.03(s, 3H), 4.56(s, 2H), 4.65(s, 2H), 6.74(d, J=9.0Hz, 2H), 7.09-7.17(m, 4H), 7.62(d, J=8.7Hz, 2H), 7.69(s, 1H), 7.75(t, J=7.8Hz, 1H), 8.09(d, J=8.8Hz, 1H), 8.20(d, J=7.8Hz, 1H), 8.28(s, 1H)
3-102	DMSO-d6, 300MHz	1.20-1.40(m, 5H), 1.60-1.80(m, 5H), 1.45-1.50(m, 1H), 2.90(s, 3H), 3.03(s, 3H), 3.97(s, 2H), 4.56(s, 2H), 4.66(s, 2H), 6.76(d, J=8.7Hz, 2H), 7.09-7.16(m, 4H), 7.66-7.74(m, 3H)
3-103	DMSO-d6, 300MHz	0.92(s, 3H), 0.95(s, 3H), 1.24-1.60(m, 8H), 1.86-1.97(m, 2H), 2.34-2.42(m, 3H), 2.89(s, 3H), 3.04(s, 3H), 3.23-3.28(m, 2H), 4.57(s, 2H), 4.67(s, 2H), 6.77(d, J=8.8Hz, 2H), 7.12(d, J=8.4Hz, 2H), 7.19(d, J=8.1Hz, 2H), 7.70-7.74(m, 3H), 12.10(brs, 1H)
3-104	DMSO-d6, 300MHz	0.81(d, J=8.5Hz, 6H), 0.83-0.95(m, 1H), 1.20-1.45(m, 5H), 1.60-1.80(m, 5H), 2.40-2.50(m, 1H), 3.00-3.07(m, 5H), 4.22(s, 2H), 4.56(s, 2H), 4.73(s, 2H), 6.76(d, J=9.0Hz, 2H), 7.09-7.17(m, 4H), 7.70-7.73(m, 3H)
3-105	DMSO-d6, 300MHz	1.14-1.46(m, 5H), 1.64-1.85(m, 5H), 2.38-2.49(m, 1H), 3.03(s, 3H), 4.56(s, 2H), 4.61(d, J=6.0Hz, 2H), 6.76(d, J=9.1Hz, 2H), 7.10-7.17(m, 4H), 7.64(s, 1H), 7.71(d, J=9.1Hz, 2H), 9.61(t, J=6.2Hz, 1H)
3-106	DMSO-d6, 300MHz	1.19-1.43(m, 5H), 1.63-1.81(m, 5H), 2.40-2.47(m, 1H), 3.03(s, 3H), 3.23(s, 2H), 4.58(d, J=6.2Hz, 2H), 6.76(d, J=8.8Hz, 2H), 7.10-7.18(m, 4H), 7.63(s, 1H), 7.72(d, J=8.8Hz, 2H), 8.92(t, J=5.8Hz, 1H), 12.37(brs, 1H)
3-107	DMSO-d6, 300MHz-120℃	1.17-1.45(m, 5H), 1.66-1.85(m, 5H), 2.44-2.52(m, 1H), 3.01(s, 3H), 3.03(s, 3H), 4.52(s, 2H), 4.87(s, 2H), 6.80(d, J=8.8Hz, 2H), 7.14(s, 4H), 7.54(d, J=8.4Hz, 2H), 7.57(s, 1H), 7.71(d, J=8.8Hz, 2H), 7.99(d, J=8.4Hz, 2H)

Table 17-55

Example	solvent, Hz	NMR(δ)
3-108	DMSO-d6, 300MHz	0.89(d, J=6.6Hz, 3H), 1.00-1.50(m, 2H), 1.35-1.42(m, 3H), 1.72-1.76(m, 4H), 2.40-2.50(m, 1H), 3.04(s, 3H), 3.92(d, J=11.2Hz, 2H), 4.50-4.56(m, 4H), 5.40(d, J=6.0Hz, 2H), 6.77(d, J=9.0Hz, 2H), 7.09-7.17(m, 4H), 7.30-7.40(m, 5H), 7.70-7.76(m, 3H)
3-109	DMSO-d6, 400MHz	1.21-1.41(m, 5H), 1.65-1.80(m, 5H), 1.45-1.50(m, 1H), 2.93(s, 3H), 3.03(s, 3H), 3.69-3.80(m, 2H), 4.56(s, 2H), 4.71(s, 2H), 6.75(d, J=11.6Hz, 2H), 6.94-7.05(m, 1H), 7.12-7.16(m, 4H), 7.64(s, 1H), 7.71(d, J=8.0Hz, 2H)
3-110	DMSO-d6, 300MHz	1.15-1.25(m,4H), 162-1.76(m,6H), 3.68(s,4H), 4.39(s,2H), 5.21(s,2H), 7.09(dd, J = 1.5, 9.0Hz, 1H), 7.48-7.52(m,5H), 7.66-7.69(m,6H), 7.77(s,1H)
3-111	DMSO-d6, 300MHz	1.20-1.40(m, 5H), 1.60-1.80(m, 5H), 2.60-2.75(m, 4H), 2.80-2.95(m, 4H), 3.42(s, 2H), 3.91(s, 2H), 4.56(s, 2H), 6.76(d, J=9.0Hz, 2H), 7.09-7.16(m, 4H), 7.69(d, J=4.9Hz, 2H), 7.73(s, 1H)
3-112	DMSO-d6, 300MHz	0.81(t, J=7.3Hz, 6H), 0.99-1.21(m, 4H), 1.41-1.65(m, 4H), 2.48-2.61(m, 1H), 2.96(dd, J=6.4, 16.2Hz, 1H), 3.19(dd, J=3.8, 16.2Hz, 1H), 3.68(d, J=15.1Hz, 1H), 4.24-4.44(m, 3H), 5.08(s, 2H), 6.95(d, J=6.0Hz, 1H), 6.98-7.11(m, 6H), 7.19(d, J=8.3Hz, 2H), 7.38(d, J=7.9Hz, 2H), 7.80(s, 1H), 7.87(d, J=8.7Hz, 2H)
3-113	DMSO-d6, 300MHz	0.80(t, J=7.2Hz, 6H), 1.07-1.14(m, 4H), 1.48-1.58(m, 4H), 2.5-2.6(m, 1H), 5.09(s, 2H), 5.55(s, 2H), 7.09(d, J=9.0Hz, 2H), 7.19(d, J=7.8Hz, 2H), 7.39(d, J=8.1Hz, 2H), 7.77-7.79(m, 1H), 7.91(d, J=8.7Hz, 2H), 8.00(s, 1H), 8.29(d, J=3.0Hz, 1H), 8.60(d, J=1.5Hz, 1H)
3-114	DMSO-d6, 400MHz	0.80(t, J=7.2Hz, 6H), 1.04-1.14(m, 4H), 1.48-1.58(m, 4H),, 2.37(s, 3H), 2.49-2.53(m, 1H), 5.07(s, 2H), 5.65(s, 2H), 6.91(dd, J=8.6, 2.8Hz, 1H), 6.95(d, J=2.5Hz, 1H), 7.18(d, J=8.1Hz, 2H), 7.36(d, J=8.1Hz, 2H), 7.54(d, J=8.6Hz, 1H), 7.73(s, 1H), 7.95-7.96(m, 1H), 8.63(d, J=3.0Hz, 1H), 8.71(d, J=1.6Hz, 1H)

Table 17-56

Example	solvent, Hz	NMR(δ)
3-115	DMSO-d6, 400MHz	0.80(t, J=7.2Hz, 6H), 1.07-1.14(m, 4H), 1.48-1.58(m, 4H), 2.5-2.6(m, 1H), 3.83(s, 3H), 5.05(s, 2H), 5.66(s, 2H), 7.12(d, J=8.4Hz, 1H), 7.20(d, J=8.0Hz, 2H), 7.37(d, J=8.0Hz, 2H), 7.50-7.54(m, 2H), 7.99(s, 1H), 8.08(s, 1H), 8.63(s, 1H), 8.71(s, 1H)
3-116	DMSO-d6, 400MHz	0.80(t, J=7.2Hz, 6H), 1.05-1.14(m, 4H), 1.48-1.58(m, 4H), 2.37(s, 3H), 3.58(s, 2H), 3.63(s, 2H), 4.26(s, 2H), 5.07(s, 2H), 6.88(dd, J=8.0, 4.0Hz, 1H), 6.94(d, J=4.0Hz, 1H), 7.04(t, J=6.0Hz, 1H), 7.18(d, J=8.0Hz, 2H), 7.26(d, J=8.0Hz, 1H), 7.28(d, J=8.0Hz, 1H), 7.36(d, J=8.0Hz, 2H), 7.50(d, J=8.0Hz, 1H), 7.56-7.58(m, 3H)
3-117	DMSO-d6, 400MHz	0.80(t, J=7.2Hz, 6H), 1.05-1.14(m, 4H),1.16(d, t=7.0Hz, 6H), 1.48-1.58(m, 4H), 2.37(s, 3H), 2.50-2.55(m,1H),2.8-2.90(m,1H), 3.53(s, 4H), 4.23(s, 2H), 5.06(s, 2H), 6.88(dd, J=8.0, 4.0Hz, 1H), 6.94(d, J=4.0Hz, 1H), 7.05-7.19(m, 4H), 7.36(d, J=8.0Hz, 2H), 7.50-7.60(m, 4H)
3-118	DMSO-d6, 300MHz	0.81(t, J=7.4Hz, 6H), 0.99-1.20(m, 4H), 1.41-1.64(m, 4H), 2.48-2.61(m, 1H), 3.10(dd, J=2.6, 16.2Hz, 1H), 3.18(dd, J=5.7, 16.9Hz, 1H), 3.87-4.01(m, 2H), 4.09(d, J=15.8Hz, 1H), 4.25(d, J=15.8Hz, 1H), 4.40(d, J=15.5Hz, 1H), 5.09(s, 2H), 7.00-7.23(m, 8H), 7.38(d, J=8.3Hz, 2H), 7.84-7.93(m, 3H), 12.65(brs, 1H)
3-119	DMSO-d6, 400MHz	0.80(t, J=7.2Hz, 6H), 1.05-1.14(m, 4H),1.48-1.58(m, 4H), 2.50-2.54(m, 1H), 3.58(s, 2H), 3.64(s, 2H), 3.80(s, 3H), 4.27(s, 2H), 5.40(s, 2H), 7.04(t, J=8.0Hz, 1H), 7.08(d, J=8.0Hz, 1H), 7.18(d, J=8.0Hz, 2H), 7.28(d, J=8.0Hz, 1H), 7.30(d, J=8.0Hz, 1H), 7.36(d, J=8.0Hz, 2H), 7.46(dd, J=8.0, 4.0Hz, 1H), 7.50(d, J=4.0Hz, 1H), 7.59(d, J=8.0Hz, 2H), 7.93(s, 1H)

Table 17-57

Example	solvent, Hz	NMR(δ)
3-120	DMSO-d6, 400MHz	0.80(t, J=7.2Hz, 6H), 1.05-1.14(m, 4H),1.16(d, t=7.0Hz, 6H), 1.48-1.58(m, 4H), 2.50-2.55(m,1H), 2.80-2.90(m,1H), 3.56(s, 2H), 3.63(s, 2H), 3.80(s, 3H), 4.26(s, 2H), 5.03(s, 2H), 7.08(d, J=8.0Hz, 1H), 7.15-7.19(m, 4H), 7.36(d, J=8.0Hz, 2H), 7.44-7.50(m, 4H), 7.93(s, 1H)
3-121	DMSO-d6, 400MHz	0.80(t, J=7.2Hz, 6H), 1.05-1.14(m, 4H), 1.48-1.58(m, 4H), 2.38(s, 3H), 2.50-2.54(m, 1H), 3.45(s, 2H), 4.05(s, 2H), 4.19(s, 2H), 5.02(s, 2H), 6.89(d, J=8.0Hz, 1H), 6.94(d, J=4.0Hz, 1H), 7.18(d, J=8.0Hz, 2H), 7.36(d, J=8.0Hz, 2H), 7.51-7.56(m, 3H), 9.07(d, J=4.0Hz, 2H)
3-122	DMSO-d6, 400MHz	0.81(t, J=7.3Hz, 6H), 1.02-1.05(m, 4H), 1.40-1.50(m, 4H), 2.40(s, 3H), 2.49-2.53(m, 1H), 2.66(s, 3H), 3.85(s, 2H), 4.29(s, 2H), 4.51(s, 2H), 5.07(s, 2H), 6.91(dd, J=8.0, 4.0Hz, 1H), 6.96(d, J=4.0Hz, 1H), 7.18(d, J=8.0Hz, 2H), 7.36(d, J=8.0Hz, 2H), 7.53(d, J=8.0Hz, 1H), 7.55(s, 1H), 7.70(s, 1H)
3-123	DMSO-d6, 400MHz	0.81(t, J=7.3Hz, 6H), 1.05-1.15(m, 4H), 1.40-1.50(m, 4H), 2.38(s, 3H), 2.45-2.55(m, 1H), 3.58(s, 2H), 3.68(s, 2H), 4.30(s, 2H), 4.31(s, 2H), 5.07(s, 2H), 6.88(dd, J=12.0, 4.0Hz, 1H), 6.94(d, J=2.0Hz, 1H), 7.18(d, J=8.0Hz, 2H), 7.22-7.30(m, 5H), 7.36(d, J=8.0Hz, 2H), 7.51(d, J=8.0Hz, 1H), 7.62(s, 1H)
3-124	DMSO-d6, 400MHz	0.80(t, J=7.2Hz, 6H), 1.05-1.14(m, 4H),1.48-1.58(m, 4H), 2.38(s, 3H), 2.50-2.54(m, 1H), 3.54(s, 2H), 4.17(s, 2H), 4.28(s, 2H), 5.06(s, 2H), 6.89(d, J=8.0Hz, 1H), 6.94(d, J=4.0Hz, 1H), 7.14-7.18(m, 4H), 7.35(d,J=8Hz,2H), 7.49-7.56(m, 4H)
3-125	DMSO-d6, 300MHz	0.79(t, J=7.2Hz, 6H), 1.00-1.14(m, 4H), 1.26(s, 9H), 1.40-1.58(m, 4H), 1.89-1.98(m, 2H), 2.42-2.55(m, 1H), 2.75-2.82(m, 2H), 3.35-3.42(m, 2H), 3.49(s, 2H), 4.19(s, 2H), 4.21(s, 2H), 4.49(s, 2H), 6.53(d, J=9.0Hz, 1H), 7.09-7.18(m, 5H), 7.45(d, J=9.0Hz, 1H), 7.49(s, 1H), 7.61(s, 1H), 12.58(brs, 1H)

Table 17-58

Example	solvent, Hz	NMR(δ)
3-126	DMSO-d6, 300MHz	0.81(t, J=7.2Hz, 6H), 1.00-1.19(m, 4H), 1.43-1.63(m, 4H), 1.98(brm, 4H), 2.53-2.59(m, 1H), 3.13(brs, 2H), 3.61(brs, 2H), 4.73(brs, 2H), 5.10(s, 2H), 7.12(d, J=9.1Hz, 2H), 7.20(d, J=7.9Hz, 2H), 7.38(d, J=8.3Hz, 2H), 7.93(d, J=8.7Hz, 2H), 8.14(brs, 1H), 10.74(brs, 1H), 12.52(brs, 1H)
3-127	DMSO-d6, 300MHz	0.81(t, J=7.3Hz, 6H), 1.02-1.19(m, 4H), 1.46-1.61(m, 4H), 2.52-2.59(m, 1H), 2.69(brs, 4H), 3.35(brs, 4H), 3.94(s, 2H), 5.09(s, 2H), 6.98(d, J=9.1Hz, 2H), 7.08(d, J=9.0Hz, 2H), 7.19(d, J=8.3Hz, 2H), 7.38(d, J=7.9Hz, 2H), 7.77(d, J=9.0Hz, 2H), 7.89(d, J=9.0Hz, 2H), 7.90(s, 1H), 12.27(brs, 1H)
3-128	DMSO-d6, 300MHz	0.71(t, J = 9.0Hz, 6H), 1.11(d,J = 6.0Hz, 6H), 1.29(t, J = 6.0Hz, 3H), 1.56-1.71(m,4H), 2.38-2.42(m,1H), 2.76-2.83(m,1H), 4.26(q, J = 6.0, 2H), 5.66(s,2H), 5.97(s,2H), 7.05-7.20(m,5H), 7.43(s,1H), 7.49(d,J = 9.0Hz, 1H), 7.87(d,J = 9.0Hz, 2H), 8.47(s,1H)
3-129	DMSO-d6, 300MHz	0.72(t, J = 6.0Hz, 6H), 1.11(d,J = 0.9Hz, 6H), 1.52-1.74(m,4H), 2.42-2.46(m,1H), 2.75-2.84(m,1H), 5.66(s,2H), 5.99(s,2H), 7.06-7.18(m,9H), 7.44(s,1H), 7.50(d,J = 9.0Hz, 1H), 7.87(d,J = 9.0Hz, 2H), 8.48(s,1H)
3-130	DMSO-d6, 300MHz	0.79(t, J = 6.0Hz, 6H), 1.15(s,3H), 1.57-1.89(m,4H), 2.42-2.52(m,1H), 5.43(s,2H), 6.10(s,2H), 6.99-7.09(m,3H), 7.24-7.33(m,15H), 7.65(t, J = 9.0Hz, 1H), 7.90(d,J = 6.3Hz, 1H), 7.99-8.03(m,3H)
3-131	DMSO-d6, 300MHz	0.68(t, J = 6.0Hz, 6H), 1.48-1.76(m,4H), 2.35-2.42(m,1H), 5.61(s,2H), 6.14(s,2H), 7.07(s,1H), 7.10(d,J = 9.0Hz, 2H), 7.20(d,J = 6.0Hz, 2H), 7.35(s,1H), 7.62(d,J = 6.0Hz, 1H), 7.82(d,J = 6.0Hz, 2H), 7.83(d,J = 9.0Hz, 2H), 8.47(s,1H)

Table 17-59

Example	solvent, Hz	NMR(δ)
3-132	DMSO-d6, 300MHz	0.74(t, J = 6.0Hz, 6H), 0.89-1.10(m,9H), 1.42-1.778(m,13H), 2.38-2.45(m,1H), 4.58(d,J = 6.0Hz, 2H), 5.65(s,2H), 7.08-7.16(m,3H), 7.41(s,1H), 7.53(d,J = 9.0Hz, 1H), 7.91(d,J = 9.0Hz, 2H), 8.42(s,1H)

Table 17-60

Example	solvent, Hz	NMR(δ)
4-1	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.96- 1.18 (m, 4H), 1.34- 1.60 (m, 4H), 3.36 (s, 2H), 3.88 (s, 3H), 4.04 (s, 2H), 4.16 (s, 2H), 5.06 (s, 2H), 6.92 (d, J = 8.7 Hz, 2H), 7.01 (d, J = 3.4 Hz, 1H), 7.07 (d, J = 8.7 Hz, 2H), 7.14- 7.26 (m, 2H), 7.35 (d, J = 3.4 Hz, 1H), 7.46 (d, J = 8.3 Hz, 2H), 7.53 (d, J = 7.5 Hz, 1H), 7.58- 7.65 (m, 3H), 12.52 (br s, 1H)
4-2	DMSO-d6, 300MHz	0.80(t, J=7.3Hz, 6H), 1.00-1.12(m, 4H), 1.38-1.57(m, 4H), 2.40-2.50(m, 1H), 5.07(s, 2H), 5.48(s, 2H), 6.93(d, J=8.6Hz, 2H), 7.07(d, J=8.6Hz, 2H), 7.49(d, J=7.9Hz, 2H), 7.69-7.71(m, 1H), 7.72(d, J=8.3Hz, 2H), 7.88-7.89(m, 1H), 7.91(d, J=1.5Hz, 1H), 8.56(d, J=2.6Hz, 1H), 8.69(d, J=1.5Hz, 1H), 13.41(brs, 1H)
4-3	DMSO-d6, 300MHz	0.78 (t, J = 7.4 Hz, 6 H), 1.00- 1.12 (m, 4 H), 1.15 (d, J = 6.4 Hz, 6 H), 1.30- 1.53 (m, 4 H), 2.27- 2.41 (m, 1 H), 4.22 (sept, J = 6.8 Hz, 1 H), 4.35 (s, 2 H), 5.48 (s, 2 H), 6.60 (d, J = 8.6 Hz, 2 H), 6.88 (d, J = 9.0 Hz, 2 H), 7.32 (d, J = 8.3 Hz, 2 H), 7.62 (d, J = 8.7 Hz, 2 H), 7.65 (d, J = 1.5 Hz, 1 H), 7.83 (d, J = 1.5 Hz, 1 H), 7.89 (dd, J = 3.0, 1.5 Hz, 1 H), 8.59 (d, J = 2.6 Hz, 1 H), 8.69 (d, J = 1.5 Hz, 1 H), 13.48 (br s, 1 H).
4-4	DMSO-d6, 300MHz	0.69 (t, J = 7.4 Hz, 6 H), 1.16 (d, J = 6.4 Hz, 6 H), 1.32-1.47 (m, 2 H), 1.48- 1.64 (m, 2 H), 2.06- 2.18 (m, 1 H), 4.23 (sept, J = 6.6 Hz, 1 H), 4.36 (s, 2 H), 5.48 (s, 2 H), 6.62 (d, J = 8.7 Hz, 2 H), 6.88 (d, J = 9.0 Hz, 2 H), 7.32 (d, J = 8.3 Hz, 2 H), 7.62 (d, J = 8.3 Hz, 2 H), 7.65 (d, J = 1.1 Hz, 1 H), 7.83 (d, J = 1.5 Hz, 1 H), 7.89 (dd, J = 2.8, 1.7 Hz, 1 H), 8.59 (d, J = 3.0 Hz, 1 H), 8.69 (d, J = 1.5 Hz, 1 H), 13.48 (br s, 1 H).

Table 17-61

Example	solvent, Hz	NMR(δ)
4-5	DMSO-d6, 300MHz	0.79(t, J=7.2Hz, 6H), 1.01-1.14(m, 4H), 1.37-1.58(m, 4H), 2.41-2.48(m, 1H), 5.07(s, 2H), 5.48(s, 2H), 6.93(d, J=8.7Hz, 2H), 7.07(d, J=8.7Hz, 2H), 7.26(d, J=3.8Hz, 1H), 7.45(d, J=3.8Hz, 1H), 7.49(d, J=8.3Hz, 2H), 7.67(d, J=8.3Hz, 2H), 7.88-7.90(m, 1H), 8.58(d, J=2.6Hz, 1H), 8.70(d, J=1.5Hz, 1H), 13.53(brs, 1H)
4-6	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 0.97-1.17(m, 4H), 1.35-1.60(m, 4H), 2.38-2.53(m, 1H), 3.45(s, 2H), 4.12(s, 4H), 5.06(s, 2H), 6.93(d, J=8.7Hz, 2H), 7.07(d, J=8.7Hz, 2H), 7.11-7.20(m, 2H), 7.41-7.59(m, 5H), 7.69(d, J=8.3Hz, 2H), 7.75-7.80(m, 1H)
4-7	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6 H), 0.99- 1.17 (m, 4 H), 1.36- 1.59 (m, 4 H), 2.38- 2.53 (m, 1 H), 5.07 (s, 2 H), 5.63 (s, 2 H), 6.93 (d, J = 8.6 Hz, 2 H), 7.07 (d, J = 8.6 Hz, 2 H), 7.10 (dd, J = 8.3, 0.7 Hz, 1 H), 7.48 (d, J = 8.3 Hz, 2 H), 7.71 (d, J = 7.6 Hz, 2 H), 7.72 (d, J = 0.8 Hz, 1 H), 7.79 (d, J = 1.5 Hz, 1 H), 7.87 (d, J = 1.5 Hz, 1 H), 7.90 (dd, J = 8.3, 7.2 Hz, 1 H), 13.17 (br s, 1 H).
4-8	DMSO-d6, 400MHz	0.80(t, J=7.2Hz, 6H), 1.05-1.14(m, 4H),1.48-1.58(m, 4H), 2.45-2.50(m, 1H), 3.42(s, 2H), 4.07(s, 4H), 5.06(s, 2H), 6.89(d, J=8.0Hz, 2H), 7.00-7.05(m, 3H), 7.11-7.13(m, 2H), 7.35(d, J=4.0Hz, 1H), 7.44(d, J=12.0Hz, 2H), 7.48-7.50(m, 2H), 7.60(d, J=8.0Hz, 2H)
4-9	DMSO-d6, 400MHz	0.77(t, J=7.3Hz, 6H), 1.02-1.05(m, 4H), 1.15(d, J=4.0Hz, 6H), 1.40-1.51(m, 4H), 2.40-2.45(m, 1H), 2.79-2.84(m, 1H), 3.44(s, 2H), 3.51(s, 2H), 4.04(s, 2H), 5.03(s, 2H), 6.89(d, J=8.0Hz, 2H), 6.99(d, J=4.0Hz, 1H), 7.03(d, J=8.0Hz, 2H), 7.14(d, J=8.0Hz, 2H), 7.33(d, J=4.0Hz, 1H), 7.43(d, J=8.0Hz, 2H), 7.48(d, J=8.0Hz, 2H), 7.58(d, J=8.0Hz, 2H)

Table 17-62

Example	solvent, Hz	NMR(δ)
4-10	DMSO-d6, 400MHz	0.77(t, J=7.3Hz, 6H), 1.02-1.05(m, 4H), 1.40-1.51(m, 4H), 2.40-2.45(m, 1H), 3.47(s, 2H), 3.51(s, 2H), 4.70(s, 2H), 5.05(s, 2H), 6.91(d, J=8.0Hz, 2H), 7.01(d, J=2.0Hz, 1H), 7.03-7.07(m, 3H), 7.28-7.31(m, 2H), 7.35(d, J=3.0Hz, 1H), 7.45(d, J=8.0Hz, 2H), 7.59-7.62(m, 4H)
4-11	DMSO-d6, 400MHz	0.68(t, J = 7.3 Hz, 6H), 1.15(d, J = 6.5 Hz, 6H), 1.34-1.45(m, 2H), 1.50-1.60(m, 2H), 2.08-2.15(m, 1H), 3.46(s, 2H), 3.50(s, 2H), 4.07(s, 2H), 4.21(sep, J = 6.5Hz, 1H), 4.34(s, 2H), 6.60(d, J = 8.8 Hz, 2H), 6.87(d, J = 8.8 Hz, 2H), 7.03(t, J = 7.3 Hz, 1H), 7.26-7.31(m, 4H), 7.40(s, 1H), 7.56-7.61(m, 4H), 7.69(s, 1H), 10.11(brs, 1H), 12.64(brs, 1H)
4-12	DMSO-d6, 400MHz	0.68(t, J = 7.3 Hz, 6H), 1.15(d, J = 6.5 Hz, 6H), 1.34-1.45(m, 2H), 1.50-1.60(m, 2H), 2.08-2.15(m, 1H), 3.41(s, 2H), 4.07(s, 2H), 4.11(s, 2H), 4.21(sep, J = 6.5Hz, 1H), 4.34(s, 2H), 6.60(d, J = 8.8 Hz, 2H), 6.88(d, J = 8.8 Hz, 2H), 7.15(s, 1H), 7.16(d, J = 8.6 Hz, 2H), 7.28(d, J = 8.1 Hz, 2H), 7.38(s, 1H), 7.58(d, J = 8.1 Hz, 2H), 7.70(s, 1H), 12.48(brs, 1H)
4-13	DMSO-d6, 400MHz	0.79(t, J=7.2Hz, 6H), 1.01-1.14(m, 4H), 1.33(s, 9H), 1.37-1.58(m, 4H), 2.41-2.51(m, 1H), 3.37(s, 2H), 4.09(s, 4H), 5.05(s, 2H), 6.91(d, J=8.4Hz, 2H), 7.05(d, J=8.4Hz, 2H), 7.39(s, 1H), 7.42(brs, 1H), 7.45(d, J=8.4Hz, 2H), 7.68(d, J=8.0Hz, 2H), 7.77(d, J=1.2Hz, 1H)
4-14	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6 H), 1.15 (d, J = 6.7 Hz, 6 H), 1.32-1.46 (m, 2 H), 1.48- 1.64 (m, 2 H), 2.05- 2.18 (m, 1 H), 3.43 (s, 2 H), 4.10 (s, 4 H), 4.22 (sept, J = 6.6 Hz, 1 H), 4.35 (s, 2 H), 6.61 (d, J = 8.7 Hz, 2 H), 6.88 (d, J = 8.7 Hz, 2 H), 7.14 (dd, J = 6.0, 3.0 Hz, 2 H), 7.29 (d, J = 8.3 Hz, 2 H), 7.41 (d, J = 1.1 Hz, 1 H), 7.52 (dd, J = 5.8, 3.2 Hz, 1 H), 7.59 (d, J = 8.3 Hz, 2 H), 7.69 (d, J = 1.5 Hz, 1 H), 12.43 (br s, 1 H).

Table 17-63

Example	solvent, Hz	NMR(δ)
4-15	DMSO-d6, 300MHz	0.76 (t, J = 7.17 Hz, 6H), 0.98-1.16 (m, 4H), 1.23 (s, 9H), 1.34-1.56 (m, 4H), 2.38-2.46(m, 1H), 3.39 (s, 2H), 4.05 (s, 2H), 4.10 (s, 2H), 5.02 (s, 2H), 6.89 (d, J = 8.60 Hz, 2H), 7.03 (d, J = 8.60 Hz, 2H), 7.14 (s, 1H), 7.41 (s, 1H), 7.43 (d, J = 8.31 Hz, 2H), 7.66 (d, J = 8.31 Hz, 2H), 7.76 (s, 1H)
4-16	DMSO-d6, 300MHz	0.76 (t, J = 7.14 Hz, 6H), 0.97-1.11 (m, 4H), 1.34-1.55 (m, 4H), 2.36-2.46(m, 1H), 3.45 (s, 2H), 3.52 (s, 2H), 4.07 (s, 2H), 5.02 (s, 2H), 6.89 (d, J = 8.67 Hz, 2H), 7.01(d, J = 6.39 Hz, 1H), 7.03 (d, J = 8.67 Hz, 2H), 7.28 (dd, J = 8.28, 7.53 Hz, 2H), 7.42 (d, J = 8.28 Hz, 2H), 7.43 (d, J = 1.5 Hz, 1H), 7.57 (d, J = 7.53 Hz, 2H), 7.65 (d, J = 8.31 Hz, 2H), 7.75 (d, J = 1.5 Hz, 1H), 9.93 (s, 1H)
4-17	DMSO-d6, 300MHz	0.67(t, J = 4.0Hz, 6H), 1.14(d,J = 8.0Hz, 6H), 1.39-1.43(m,2H), 1.50-1.60(m,2H), 2.08-2.15(m,1H), 4.34(s,2H), 5.44(s,2H), 6.59(d,J = 8.0Hz, 2H), 6.87(d,J = 12.0Hz, 2H), 7.22(d,J = 4.0Hz, 1H), 7.30(d,J = 8.0Hz, 2H), 7.36(d,J = 4.0Hz, 1H), 7.56(d,J = 8.0Hz, 2H), 7.85(s,1H), 8.82(s,1H), 8.66(s,1H)
4-18	DMSO-d6, 400MHz	0.77(t, J = 8.0Hz, 6H), 1.02-1.10(m,4H), 1.14(d,J = 4.0Hz, 6H), 1.31-1.50(m,4H), 2.29-2.37(m,1H), 4.15-4.26(m,1H), 4.33(s,2H), 5.43(s,2H), 6.58(d,J = 12.0Hz, 2H), 6.87(d,J = 12.0Hz, 2H), 7.22(s,1H), 7.30(d,J = 8.0Hz, 1H), 7.36(d,J = 4.0Hz, 2H), 7.56(d,J = 8.0Hz, 2H), 7.84(s,1H), 8.51(s,1H), 8.65(s,1H)
4-19	DMSO-d6, 400MHz	0.63(t, J = 8.0Hz, 6H), 1.10(d,J = 8.0Hz, 6H), 1.21(s,9H), 1.33-1.38(m,2H), 1.45-1.52(m,2H), 2.27(m,1H), 3.25-3.60(m,1H), 3.98(s,2H), 4.06(s,2H), 4.29(s,2H), 6.55(d,J = 8.0Hz, 2H), 6.82(d,J = 8.0Hz, 2H), 6.92(d,J = 4.0Hz, 1H), 7.10(s,1H), 7.25(d,J = 12.0Hz, 2H), 7.24(s,1H), 7.49(d,J = 8.0Hz, 2H)

Table 17-64

Example	solvent, Hz	NMR(δ)
4-20	DMSO-d6, 300MHz	0.78(t, J = 9.0Hz, 6H), 1.01-1.13(m,4H), 1.15(d,J = 6.0Hz, 6H), 1.26(s,9H), 1.38-1.49(m,4H), 2.28-2.35(m,1H), 3.33(s,2H), 4.06(s,2H), 4.13(s,2H), 4.14-4.24(m,1H), 4.34(s,2H), 6.60(d,J = 9.0Hz, 2H), 6.89(d,J = 9.0Hz, 2H), 6.96(d,J = 6.0Hz, 1H), 7.13(s,1H), 7.29(d,J = 12.0Hz, 2H), 7.29(s,1H), 7.54(d,J = 6.0Hz, 2H)
4-21	DMSO-d6, 300MHz	0.67(t, J = 4.0Hz, 6H), 1.14(d,J = 8.0Hz, 6H), 1.30-1.43(m,2H), 1.48-1.60(m,2H), 2.06-2.14(m,1H), 3.40(s,2H), 4.06(s,2H), 4.07(s,2H), 4.18-4.25(m,1H), 4.33(s,2H), 6.59(d,J = 8.0Hz, 2H), 6.86(d,J = 8.0Hz, 2H), 7.00(d,J = 4.0Hz, 1H), 7.12-7.14(m,2H), 7.28(m,3H), 7.48-7.54(m,3H)
4-22	DMSO-d6, 300MHz	0.78(t, J = 9.0Hz, 6H), 1.01-1.14(m,4H), 1.15(d,J = 6.0Hz, 6H), 1.36-1.48(m,4H), 2.24-2.40(m,1H), 4.07(s,4H), 4.17-4.25(m,1H), 4.34(s,2H), 6.60(d,J = 6.0Hz, 2H), 6.89(d,J = 9.0Hz, 2H), 6.97-7.43(m,6H), 7.43-7.69(m,3H)
4-23	DMSO-d6, 400MHz	0.79(t, J = 7.3 Hz, 6H), 1.01-1.14(m, 4H), 1.39-1.56(m, 4H), 2.20(s, 3H), 2.29(s, 3H), 2.41-2.49(m, 1H), 3.37(s, 2H), 4.04(s, 2H), 4.08(s, 2H), 5.05(s, 2H), 6.91(d, J = 8.6 Hz, 2H), 7.05(d, J = 8.6 Hz, 2H), 7.42(s, 1H), 7.45(d, J = 8.1 Hz, 2H), 7.68(d, J = 8.1 Hz, 2H), 7.77(s, 1H)
4-24	DMSO-d6, 400MHz	0.68(t, J = 7.2 Hz, 6H), 1.15(d, J = 6.3 Hz, 6H), 1.34-1.45(m, 2H), 1.51-1.61(m, 2H), 2.09-2.16(m, 1H), 3.04-3.17(m, 2H), 3.83-3.96(m, 2H), 4.00-4.09(m, 1H), 4.16-4.27(m, 3H), 4.34(s, 2H), 6.60(d, J = 8.6 Hz, 2H), 6.87(d, J = 8.6 Hz, 2H), 7.00-7.16(m, 4H), 7.29(d, J = 8.1 Hz, 2H), 7.45(brs, 3H), 7.61(d, J = 8.1 Hz, 2H), 7.71(brs, 1H)

Table 17-65

Example	solvent, Hz	NMR(δ)
4-25	DMSO-d6, 400MHz	0.68(t, J = 7.3 Hz, 6H), 1.15(d, J = 7.0 Hz, 6H), 1.17(d, J = 7.0 Hz, 6H), 1.34-1.45(m, 2H), 1.50-1.60(m, 2H), 2.08-2.16(m, 1H), 2.82(sep, J = 7.0 Hz, 1H), 3.45(s, 2H), 3.53(s, 2H), 4.08(s, 2H), 4.21(sep, J = 7.0 Hz, 1H), 4.34(s, 2H), 6.60(d, J = 8.6 Hz, 2H), 6.87(d, J = 8.6 Hz, 2H), 7.16(d, J = 8.6 Hz, 2H), 7.28(d, J = 8.4 Hz, 2H), 7.41(s, 1H), 7.50(d, J = 8.6 Hz, 2H), 7.57(d, J = 8.4 Hz, 2H), 7.69(s, 1H), 9.85(s, 1H), 12.58(brs, 1H)
4-26	DMSO-d6, 400MHz	0.79(t, J=7.4Hz, 6H),.1.00-1.14(m, 4H), 1.39-1.56(m, 4H), 2.42-2.48(m, 1H), 3.17-3.43(m, 2H), 4.15-4.63(m, 5H), 5.07(s, 2H), 6.92(d, J=8.8Hz, 2H), 7.06(d, J=8.8Hz, 2H), 7.18-7.28(m, 5H), 7.48-7.50(m, 3H), 7.67(d, J=8.4Hz, 2H)
4-27	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6 H),0.99- 1.18 (m, 4 H),1.18 (d, J = 6.8 Hz, 6 H),1.32- 1.60 (m, 4 H),2.39- 2.55 (m, 1 H),2.75-2.91 (m, 1 H),3.47 (s, 2 H),3.55 (s, 2 H),4.10 (s, 2 H),5.06 (s, 2 H),6.93 (d, J = 8.7 Hz, 2 H),7.07 (d, J = 8.7 Hz, 2 H),7.18 (d, J = 8.7 Hz, 2 H),7.42- 7.53 (m, 5 H),7.68 (d, J = 8.3 Hz, 2 H),7.79 (d, J = 1.5 Hz, 1 H),9.87 (s, 1 H),12.50 (br s, 1 H).
4-28	DMSO-d6, 300MHz	0.68(t, J = 7.3 Hz, 6H), 1.14(d, J = 6.6 Hz, 6H), 1.32-1.47(m, 2H), 1.49-1.62(m, 2H), 2.08-2.17(m, 1H), 3.04(dd, J = 16.3, 3.5 Hz, 1H), 3.11(dd, J = 16.3, 6.2 Hz, 1H), 3.81-3.86(m, 2H), 4.00(d, J = 15.8 Hz, 1H), 4.14-4.26(m, 3H), 4.34(s, 2H), 6.60(d, J = 8.4 Hz, 2H), 6.88(d, J = 8.4 Hz, 2H), 7.00-7.14(m, 5H), 7.28-7.31(m, 3H), 7.54(d, J = 8.0 Hz, 2H), 12.47(brs, 1H)
4-29	DMSO-d6, 300MHz	0.79(t, J = 7.1 Hz, 6H), 1.01-1.14(m, 4H), 1.25(s, 9H), 1.38-1.58(m, 4H), 2.41-2.50(m, 1H), 3.39(s, 2H), 3.95(s, 2H), 4.03(s, 2H), 5.06(s, 2H), 6.75(s, 1H), 6.93(d, J = 8.4 Hz, 2H), 7.07(d, J = 8.4 Hz, 2H), 7.40(s, 1H), 7.47(d, J = 8.4 Hz, 2H), 7.69(d, J = 8.4 Hz, 2H), 7.78(s, 1H), 12.40(brs, 1H)

Table 17-66

Example	solvent, Hz	NMR(δ)
4-30	DMSO-d6, 400MHz	0.79(t, J = 7.3 Hz, 6H), 1.00-1.14(m, 4H), 1.39-1.56(m, 4H), 2.41-2.49(m, 1H), 3.36(s, 2H), 3.86(s, 3H), 4.06(s, 2H), 4.17(s, 2H), 5.05(s, 2H), 6.91(d, J = 8.6 Hz, 2H), 7.05(d, J = 8.8 Hz, 2H), 7.16(t, J = 7.4 Hz, 1H), 7.23(t, J = 7.4 Hz, 1H), 7.41(s, 1H), 7.44(d, J = 8.1 Hz, 2H), 7.52(d, J = 7.4 Hz, 1H), 7.59(d, J = 7.4 Hz, 1H), 7.65(d, J = 8.1 Hz, 2H), 7.75(s, 1H)
4-31	DMSO-d6, 300MHz	0.79(t, J=7.2Hz, 6H), 0.99-1.14(m, 4H), 1.38-1.59(m, 4H), 2.41-2.46(m, 1H), 5.06(s, 2H), 5.62(s, 2H), 6.92(d, J=8.4Hz, 2H), 7.05-7.11(m, 3H), 7.30(d, J=3.6Hz, 1H), 7.42(d, J=3.3Hz, 1H), 7.48(d, J=8.1Hz, 2H), 7.65(d, J=7.8Hz, 2H), 7.71(d, J=7.2Hz, 1H), 7.90(dd, J=8.1, 7.2Hz, 1H)
4-32	DMSO-d6, 300MHz	0.69 (t, J = 7.17 Hz, 6H), 1.16 (d, J = 6.59 Hz, 6H), 1.35-1.47 (m, 2H), 1.48-1.63 (m, 2H), 2.07-2.18 (m, 1H), 4.22 (quint, J = 6.59 Hz, 1H), 4.35 (s, 2H), 5.53 (s, 2H), 6.62 (d, J = 8.66 Hz, 2H), 6.68 (dd, J = 8.10, 0.75 Hz, 1H), 6.88 (d, J = 8.66 Hz, 2H), 7.30 (d, J = 8.28 Hz, 2H), 7.41 (dd, J = 7.14, 0.75 Hz, 1H), 7.61 (dd, J = 8.10, 7.14 Hz, 1H), 7.64 (d, J = 8.28 Hz, 2H), 7.76 (d, J = 1.5 Hz, 1H), 7.78 (d, J = 1.5 Hz, 1H)
4-33	DMSO-d6, 300MHz	0.68(t, J = 7.1 Hz, 6H), 1.14(d, J = 6.8 Hz, 6H), 1.33(s, 9H), 1.35-1.60(m, 4H), 2.07-2.18(m, 1H), 3.41(s, 2H), 4.08(s, 4H), 4.22(sep, J = 6.6 Hz, 1H), 4.35(s, 2H), 6.61(d, J = 8.8 Hz, 2H), 6.88(d, J = 8.8 Hz, 2H), 7.30(d, J = 8.4 Hz, 2H), 7.39(s, 1H), 7.41(s, 1H), 7.60(d, J = 8.4 Hz, 2H), 7.72(s, 1H), 12.48(brs, 1H)
4-34	DMSO-d6, 300MHz	0.68(t, J = 7.3 Hz, 6H), 1.15(d, J = 6.6 Hz, 6H), 1.32-1.47(m, 2H), 1.49-1.62(m, 2H), 2.08-2.17(m, 1H), 3.37(s, 2H), 3.86(s, 3H), 4.06(s, 2H), 4.17(s, 2H), 4.22(sep, J = 6.6 Hz, 1H), 4.34(s, 2H), 6.61(d, J = 8.8 Hz, 2H), 6.88(d, J = 8.8 Hz, 2H), 7.16-7.30(m, 4H), 7.38(brs, 1H), 7.52-7.61(m, 4H), 7.67(brs, 1H)

Table 17-67

Example	solvent, Hz	NMR(δ)
4-35	DMSO-d6, 400MHz	0.79(t, J=7.4Hz, 6H), 1.01-1.14(m, 4H), 1.27(s, 9H), 1.39-1.56(m, 4H), 2.41-2.48(m, 1H), 3.42(s, 2H), 4.13(s, 2H), 5.06(s, 2H), 6.92(d, J=8.8Hz, 2H), 7.00(d, J=3.6Hz, 1H), 7.06(d, J=8.4Hz, 2H), 7.16(s, 1H), 7.36(d, J=3.6Hz, 1H), 7.46(d, J=8.4Hz, 2H), 7.63(d, J=8.4Hz, 2H)
4-36	DMSO-d6, 300MHz	0.69(t, J=7.2Hz, 6H), 1.15(d, J=6.6Hz, 6H), 1.32-1.63(m, 4H), 2.07-2.18(m, 1H), 3.36(s, 2H), 3.87(s, 3H), 4.03(s, 2H), 4.16(s, 2H), 4.18-4.26(m, 1H), 4.34(s, 2H), 6.61(d, J=8.7Hz, 2H), 6.89(d, J=8.4Hz, 2H), 6.99(d, J=3.6Hz, 1H), 7.16-7.31(m, 5H), 7.53(brd, J=8.4Hz, 3H), 7.60(d, J=7.2Hz, 1H)
4-37	DMSO-d6, 300MHz	0.80(t, J=7.3Hz, 6H), 0.98-1.16(m, 4H), 1.34(s, 9H), 1.37-1.59(m, 4H), 2.39-2.53(m, 1H), 3.41(s, 2H), 4.06(s, 2H), 4.10(s, 2H), 5.07(s, 2H), 6.93(d, J=7.9Hz, 2H), 7.01(d, J=3.0Hz, 1H), 7.07(d, J=8.3Hz, 2H), 7.37(d, J=3.4Hz, 1H), 7.41-7.43(m, 1H), 7.48(d, J=7.9Hz, 2H), 7.64(d, J=7.9Hz, 2H), 12.51(brs, 1H)
4-38	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 0.98-1.17(m, 4H), 1.36-1.59(m, 4H), 2.39-2.54(m, 1H), 2.94(s, 2H), 3.91(s, 2H), 4.03(s, 3H), 4.16(s, 2H), 5.05(s, 2H), 6.86-6.98(m, 3H), 7.06(d, J=8.7Hz, 2H), 7.12-7.26(m, 2H), 7.30(d, J=3.4Hz, 1H), 7.44(d, J=8.3Hz, 2H), 7.51(d, J=7.2Hz, 1H), 7.55-7.63(m, 3H)
4-39	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 0.97-1.17(m, 4H), 1.34-1.60(m, 4H), 2.37-2.55(m, 1H), 3.02(brs, 2H), 3.95(brs, 5H), 4.14(brs, 2H), 5.04(brs, 2H), 6.91(brd, J=8.3Hz, 3H), 7.06(d, J=8.6Hz, 2H), 7.10-7.27(m, 2H), 7.27-7.35(m, 1H), 7.35-7.68(m, 6H)

Table 17-68

Example	solvent, Hz	NMR(δ)
4-40	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 0.95-1.20(m, 4H), 1.32-1.60(m, 4H), 2.28(s, 3H), 2.40-2.54(m, 1H), 3.62(s, 2H), 4.00(s, 3H), 4.19(s, 2H), 4.46(s, 2H), 5.05(s, 2H), 6.92(d, J=8.6Hz, 2H), 6.98-7.14(m, 5H), 7.25(d, J=3.6Hz, 1H), 7.36-7.58(m, 8H), 7.76(d, J=9.0Hz, 1H), 7.89(d, J=9.0Hz, 1H)
4-41	DMSO-d6, 300MHz	0.80(t, J=7.3Hz, 6H), 0.98-1.15(m, 4H), 1.38-1.59(m, 4H), 2.39-2.54(m, 1H), 5.07(s, 2H), 5.52(s, 2H), 6.93(d, J=8.6Hz, 2H), 7.07(d, J=8.7Hz, 2H), 7.49(d, J=8.3Hz, 2H), 7.71(s, 1H), 7.72(d, J=6.4Hz, 2H), 7.93(d, J=1.5Hz, 1H), 8.00(brs, 1H), 8.65-8.67(m, 1H), 8.73-8.76(m, 1H)
4-42	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 1.00-1.14(m, 4H), 1.37-1.60(m, 4H), 2.40-2.54(m, 1H), 3.80(brs, 3H), 4.08-4.62(m, 2H), 4.92-5.36(m, 4H), 6.92(d, J=8.6Hz, 2H), 7.07(d, J=8.7Hz, 2H), 7.16-7.80(m, 10H)
4-43	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 0.93-1.15(m, 4H), 1.16-1.60(m, 13H), 2.36-2.55(m, 1H), 4.16(brs, 2Hx0.45), 4.43(brs, 2Hx0.55), 4.70-5.25(m, 4H), 6.93(d, J=8.4Hz, 2H), 7.07(d, J=8.4Hz, 2H), 7.29-7.62(m, 5H), 7.72-7.75(m, 2H)
4-44	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 0.97-1.15(m, 4H), 1.20(d, J=6.8Hz, 6H), 1.35-1.59(m, 4H), 2.39-2.54(m, 1H), 2.81-2.96(m, 1H), 4.01(brs, 2Hx0.60), 4.23(brs, 2Hx0.40), 4.63(brs, 2Hx0.40), 4.88(brs, 2Hx0.60), 5.08(s, 2H), 6.92(d, J=8.7Hz, 2H), 7.06(d, J=8.7Hz, 2H), 7.16-7.40(m, 5H), 7.41-7.56(m, 3H), 7.71(d, J=7.9Hz, 2H)
4-45	DMSO-d6, 300MHz	0.79(t, J=7.2Hz, 6H), 0.97-1.19(m, 4H), 1.35-1.60(m, 4H), 2.37-2.56(m, 1H), 2.89(s, 6H), 3.84-4.30(m, 2H), 4.40-4.93(m, 2H), 5.09(s, 2H), 6.73(brd, J=7.2Hz, 2H), 6.93(d, J=8.6Hz, 2H), 7.07(d, J=8.7Hz, 2H), 7.15(brd, J=7.9Hz, 2H), 7.31(d, J=3.8Hz, 1H), 7.44-7.57(m, 3H), 7.72(d, J=8.3Hz, 2H)
4-46	DMSO-d6, 300MHz	0.79(t, J=7.2Hz, 6H), 0.95-1.18(m, 4H), 1.35-1.61(m, 4H), 2.39-2.55(m, 1H), 4.11(brs, 2Hx0.62), 4.46(brs, 2Hx0.38), 4.77(brs, 2Hx0.38), 4.99(brs, 2Hx0.62), 5.08(s, 2H), 6.92(d, J=8.7Hz, 2H), 7.07(d, J=8.7Hz, 2H), 7.25-7.60(m, 6H), 7.61-7.92(m, 3H), 8.42-8.72(m, 1H)

Table 17-69

Example	solvent, Hz	NMR(δ)
4-47	DMSO-d6, 300MHz	0.79(t, J=7.4Hz, 6H), 0.97-1.18(m, 4H), 1.34-1.60(m, 4H), 2.37-2.55(m, 1H), 3.94-4.50(m, 2H), 4.59-5.07(m, 2H), 5.09(s, 2H), 6.93(d, J=8.7Hz, 2H), 7.07(d, J=8.7Hz, 2H), 7.19-7.58(m, 5H), 7.72(d, J=7.9Hz, 2H), 7.79(d, J=7.5Hz, 1H), 8.51(d, J=4.5Hz, 1H), 8.58(s, 1H)
4-48	DMSO-d6, 300MHz	0.80(t, J=7.3Hz, 6H), 1.00-1.15(m, 4H), 1.38-1.58(m, 4H), 2.40(s, 3H), 2.42-2.50(m, 1H), 5.07(s, 2H), 5.53(s, 2H), 6.93(d, J=8.6Hz, 2H), 7.07(d, J=8.6Hz, 2H), 7.49(d, J=8.3Hz, 2H), 7.71-7.75(m, 3H), 7.93(d, J=1.5Hz, 1H), 8.04(brs, 1H), 8.69(d, J=2.6Hz, 1H), 8.76(d, J=1.5Hz, 1H)
4-49	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6 H),0.97- 1.18 (m, 4 H),1.35- 1.61 (m, 4 H),2.39- 2.53 (m, 1 H),3.09 (s, 3 H),3.91 (s, 2 H),4.62 (s, 2 H),5.07 (s, 2 H),6.93 (d, J = 8.7 Hz, 2 H),7.03- 7.12 (m, 3 H),7.39 (d, J = 3.8 Hz, 1 H),7.48 (d, J = 8.5 Hz, 2 H),7.66 (d, J = 8.5 Hz, 2 H),12.95 (br s, 1 H).
4-50	DMSO-d6, 300MHz	0.80(t, J=7.3Hz, 6H), 0.99-1.17(m, 4H), 1.37-1.58(m, 4H), 2.40-2.54(m, 1H), 5.07(s, 2H), 5.39(s, 2H), 6.93(d, J=8.3Hz, 2H), 7.07(d, J=8.6Hz, 2H), 7.48(d, J=8.3Hz, 2H), 7.67(brs, 1H), 7.72(d, J=8.3Hz, 2H), 7.79(dd, J=1.5, 3.0Hz, 1H), 7.89(d, J=1.5Hz, 1H), 8.26(d, J=3.0Hz, 1H), 8.60(d, J=1.1Hz, 1H)
4-51	DMSO-d6, 300MHz	0.80(t, J=7.3Hz, 6H), 1.00-1.15(m, 4H), 1.38-1.58(m, 4H), 2.39-2.54(m, 1H), 5.07(s, 2H), 5.52(s, 2H), 6.93(d, J=8.6Hz, 2H), 7.07(d, J=8.6Hz, 2H), 7.49(d, J=8.3Hz, 2H), 7.71(s, 1H), 7.72(d, J=6.8Hz, 2H), 7.93(d, J=1.5Hz, 1H), 7.99(brs, 1H), 8.65-8.67(m, 1H), 8.73-8.75(m, 1H)
4-52	DMSO-d6, 300MHz	0.80(t, J=7.3Hz, 6H), 0.97-1.19(m, 4H), 1.36-1.62(m, 4H), 2.40-2.55(m, 1H), 3.45(brs, 4H), 3.84(brs, 4H), 5.10(s, 2H), 6.96(dd, J=8.7, 12.8Hz, 4H), 7.08(d, J=8.3Hz, 2H), 7.46-7.59(m, 4H), 7.78(dd, J=8.3, 15.5Hz, 4H)
4-53	DMSO-d6, 300MHz	0.79(t, J=7.2Hz, 6H), 0.98-1.19(m, 4H), 1.36-1.59(m, 4H), 1.60-1.80(m, 2H), 1.88(brd, J=11.3Hz, 2H), 2.40-2.54(m, 1H), 2.88-3.02(m, 1H), 3.03-3.22(m, 2H), 4.46(brd, J=13.2Hz, 2H), 5.09(s, 2H), 6.93(d, J=8.7Hz, 2H), 7.07(d, J=8.7Hz, 2H), 7.38-7.58(m, 6H), 7.74(d, J=8.3Hz, 2H), 7.89(d, J=8.3Hz, 2H)

Table 17-70

Example	solvent, Hz	NMR(δ)
4-54	DMSO-d6, 300MHz	0.79 (t, J = 7.4 Hz, 6 H),0.98- 1.18 (m, 4 H),1.36- 1.60 (m, 4 H),2.39- 2.53 (m, 1 H),3.64 (s, 2 H),3.99 (s, 3 H),4.21 (s, 2 H),4.48 (s, 2 H),5.06 (s, 2 H),6.93 (d, J = 8.7 Hz, 2 H),7.07 (d, J = 8.7 Hz, 2 H),7.40- 7.68 (m, 8 H),7.71- 7.76 (m, 1 H),7.85- 7.91 (m, 1 H).
4-55	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 0.98-1.18(m, 4H), 1.36-1.59(m, 4H), 2.40-2.50(m, 1H), 3.64(s, 2H), 3.99(s, 3H), 4.22(s, 2H), 4.48(s, 2H), 5.06(s, 2H), 6.93(d, J=8.8Hz, 2H), 7.07(d, J=8.8Hz, 2H), 7.42-7.63(m, 7H), 7.66(s, 1H), 7.75(d, J=8.0Hz, 1H), 7.89(d, J=8.8Hz, 1H)
4-56	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6 H),0.96- 1.18 (m, 4 H),1.35- 1.60 (m, 4 H),2.33 (s, 6 H),2.38- 2.54 (m, 1 H),5.07 (s, 2 H),5.51 (s, 2 H),6.93 (d, J = 8.7 Hz, 2 H),7.07 (d, J = 8.7 Hz, 2 H),7.49 (d, J = 7.9 Hz, 2 H),7.60- 7.78 (m, 5 H),7.93 (d, J = 1.1 Hz, 1 H),8.35 (d, J = 8.3 Hz, 1 H),9.99 (s, 1 H),12.76 (br s, 1 H).
4-57	DMSO-d6, 300MHz	0.80 (t, J = 7.2 Hz, 6 H),0.97- 1.16 (m, 4 H),1.10 (d, J = 6.8 Hz, 6 H),1.35- 1.60 (m, 4 H),2.39- 2.53 (m, 1 H),2.71- 2.87 (m, 1 H),5.07 (s, 2 H),5.48 (s, 2 H),6.93 (d, J = 8.6 Hz, 2 H),7.07 (d, J = 8.6 Hz, 2 H),7.49 (d, J = 8.3 Hz, 2 H),7.56 (dd, J = 8.6, 1.4 Hz, 1 H),7.66- 7.73 (m, 4 H),7.90 (d, J = 1.4 Hz, 1 H),8.11 (d, J = 8.6 Hz, 1 H),9.10 (s, 1 H),12.85 (br s, 1 H).
4-58	DMSO-d6, 300MHz	0.80 (t, J = 7.2 Hz, 6 H),0.97- 1.18 (m, 4 H),1.34- 1.61 (m, 4 H),2.38- 2.54 (m, 1 H),5.07 (s, 2 H),5.40 (s, 2 H),6.93 (d, J = 8.7 Hz, 2 H),7.07 (d, J = 8.7 Hz, 2 H),7.14 (d, J = 8.7 Hz, 2 H),7.49 (d, J = 7.9 Hz, 2 H),7.68- 7.75 (m, 3 H),7.87- 7.94 (m, 3 H),12.66 (br s, 1 H).
4-59	DMSO-d6, 300MHz	0.80 (t, J = 7.2 Hz, 6 H),0.98- 1.18 (m, 4 H),1.36- 1.59 (m, 4 H),2.39- 2.54 (m, 1 H),2.99 (s, 3 H),3.18 (s, 3 H),5.07 (s, 2 H),5.51 (s, 2 H),6.93 (d, J = 8.5 Hz, 2 H),7.07 (d, J = 8.5 Hz, 2 H),7.43 (d, J = 8.0 Hz, 1 H),7.49 (d, J = 8.1 Hz, 2 H),7.58 (dd, J = 8.0, 1.5 Hz, 1 H),7.70 (s, 1 H),7.71 (d, J = 8.1 Hz, 2 H),7.78 (d, J = 1.5 Hz, 1 H),7.92 (s, 1 H),13.17 (br s, 1 H).

Table 17-71

Example	solvent, Hz	NMR(δ)
4-60	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6 H),0.98- 1.18 (m, 4 H),1.35- 1.60 (m, 4 H),2.39- 2.54 (m, 1 H),4.63 (s, 2 H),5.06 (s, 2 H),6.93 (d, J = 8.7 Hz, 2 H),7.06 (d, J = 8.7 Hz, 2 H),7.42- 7.54 (m, 5 H),7.66 (d, J = 8.3 Hz, 2 H),7.73 (d, J = 1.1 Hz, 1 H),7.86 (d, J = 8.3 Hz, 2 H),12.90 (br s, 1 H).
4-61	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6 H),0.99- 1.19 (m, 4 H),1.36- 1.60 (m, 4 H),2.40- 2.54 (m, 1 H),5.07 (s, 2 H),5.33 (s, 2 H),5.54 (s, 2 H),6.67 (d, J = 8.0 Hz, 1 H),6.93 (d, J = 8.7 Hz, 2 H),7.07 (d, J = 8.7 Hz, 2 H),7.39 (dd, J = 8.0, 1.6 Hz, 1 H),7.45- 7.52 (m, 3 H),7.65- 7.76 (m, 3 H),7.88 (d, J = 1.6 Hz, 1 H),12.11 (br s, 1 H).
4-62	DMSO-d6, 400MHz	1.11-1.41(m, 5H), 1.61-1.81(m, 5H), 2.00-3.68(m, 9H), 4.30-4.76(m, 2H), 5.41(s, 2H), 7.09-7.44(m, 13H), 7.57(d, J=7.9Hz, 1H), 7.88(d, J=7.9Hz, 1H), 7.96(s, 1H)
4-63	DMSO-d6, 300MHz	1.12-1.44(m, 5H), 1.60-1.83(m, 5H), 2.37-2.48(m, 1H), 3.28(s, 2H), 3.83(s, 2H), 4.00(s, 2H), 5.40(s, 2H), 6.97(d, J=3.7Hz, 1H), 7.11-7.44(m, 12H), 7.52-7.57(m, 1H), 7.85-7.90(m, 1H), 7.88(s, 1H), 12.35(brs, 1H)
4-64	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 0.99-1.15(m, 4H), 1.38-1.59(m, 4H), 2.39-2.53(m, 1H), 3.18(s, 3H), 3.85(s, 2H), 4.65(s, 2H), 5.07(s, 2H), 6.93(d, J=8.7Hz, 2H), 7.07(d, J=8.6Hz, 2H), 7.25-7.35(m, 1H), 7.39-7.43(m, 4H), 7.45-7.51(m, 3H), 7.68(d, J=8.2Hz, 2H), 7.84(d, J=1.6Hz, 1H)
4-65	DMSO-d6, 300MHz	1.08-1.39(m, 5H), 1.27(s, 9H), 1.61-1.77(m, 5H), 2.34-2.47(m, 1H), 3.16(brs, 2H), 3.35(brs, 3H), 4.01(brs, 2H), 4.08(brs, 2H), 6.97(brd, J=2.6Hz, 1H), 7.06(brd, J=8.7Hz, 2H), 7.10(brd, J=8.7Hz, 2H), 7.24(brd, J=8.7Hz, 2H), 7.32(brd, J=3.0Hz, 1H), 7.37-7.43(m, 3H)

Table 17-72

Example	solvent, Hz	NMR(δ)
4-66	DMSO-d6, 300MHz	1.08-1.45(m, 5H), 1.13(t, J=7.0Hz, 3H), 1.62-1.84(m, 5H), 2.38-2.54(m, 1H), 3.32(s, 2H), 3.48(q, J=6.9Hz, 2H), 3.92(s, 2H), 3.97(s, 2H), 4.51(s, 2H), 6.67(d, J=8.7Hz, 2H), 6.88(d, J=3.4Hz, 2H), 7.04(d, J=3.8Hz, 2H), 7.12(d, J=8.7Hz, 2H), 7.16(d, J=8.3Hz, 2H), 7.24-7.28(m, 1H), 7.36(d, J=8.7Hz, 2H), 7.54(d, J=7.5Hz, 1H), 7.77-7.83(m, 1H), 8.48(d, J=4.1Hz, 1H), 12.45(brs, 1H)
4-67	DMSO-d6, 300MHz	1.09-1.44(m, 5H), 1.13(t, J=7.0Hz, 3H), 1.64-1.82(m, 5H), 2.38-2.51(m, 1H), 3.03(t, J=5.8Hz, 2H), 3.47(q, J=7.1Hz, 2H), 3.44(s, 2H), 4.05(t, J=7.2Hz, 2H), 4.03(s, 2H), 4.51(s, 2H), 6.65(s, 2H), 6.68(s, 2H), 6.85-6.94(m, 4H), 7.03(d, J=3.4Hz, 1H), 7.12(d, J=8.3Hz, 2H), 7.16(d, J=8.3Hz, 2H), 7.26(t, J=7.9Hz, 2H), 7.35(d, J=8.7Hz, 2H), 12.31(brs, 1H)
4-68	DMSO-d6, 300MHz	1.02-1.47(m, 4H), 1.08(t, J=6.8Hz, 3H), 1.24(s, 9H), 1.61-1.87(m, 9H), 2.05-2.16(m, 2H), 2.38-2.47(m, 1H), 2.53-2.65(m, 1H), 3.02(brd, J=11.3Hz, 2H), 3.16(brd, J=6.4Hz, 2H), 3.41(q, J=6.9Hz, 2H), 3.72(s, 2H), 6.68(d, J=8.7Hz, 2H), 7.12(d, J=8.3Hz, 2H), 7.23-7.30(m, 3H), 7.38(d, J=7.9Hz, 2H), 7.42(s, 1H), 7.46(d, J=8.3Hz, 2H), 7.87(d, J=8.3Hz, 2H), 12.78(brs, 1H)
4-69	DMSO-d6, 300MHz	0.79(t, J=7.4Hz, 6H), 1.01-1.21(m, 4H), 1.15(d, J=7.2Hz, 6H), 1.37-1.59(m, 4H), 2.40-2.51(m, 1H), 2.72-2.87(m, 1H), 3.95(s, 2H), 4.65(s, 2Hx0.75), 4.74(s, 2Hx0.75), 4.85(s, 2Hx0.25), 4.91(s, 2Hx0.25), 5.05(s, 2H), 6.79-6.86(m, 2H), 6.92(d, J=8.3Hz, 2H), 7.03-7.13(m, 4H), 7.42-7.57(m, 3H), 7.62-7.85(m, 3H)
4-70	DMSO-d6, 300MHz	0.79(t, J=7.2Hz, 6H), 0.99-1.15(m, 4H), 1.21(d, J=6.8Hz, 6H), 1.37-1.58(m, 4H), 2.40-2.51(m, 1H), 2.86-3.00(m, 1H), 3.93(s, 2Hx0.5), 4.08(s, 2Hx0.5), 4.69(s, 2Hx0.5), 4.81(s, 2Hx0.5), 5.07(s, 2H), 6.93(d, J=8.7Hz, 2H), 7.07(d, J=8.7Hz, 2H), 7.26-7.61(m, 7H), 7.71(d, J=7.9Hz, 2H), 7.81(s, 1H)
4-71	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 0.84(d, J=6.8Hz, 6H), 1.00-1.17(m, 4H), 1.29-1.65(m, 7H), 2.41-2.51(m, 1H), 2.63(t, J=7.3Hz, 2H), 3.30(s, 2H), 3.99(s, 2H), 5.06(s, 2H), 6.93(d, J=8.7Hz, 2H), 7.07(d, J=8.7Hz, 2H), 7.40(brs, 1H), 7.46(d, J=8.3Hz, 2H), 7.69(d, J=8.3Hz, 2H), 7.76(d, J=1.1Hz, 1H), 12.22(brs, 1H)

Table 17-73

Example	solvent, Hz	NMR(δ)
4-72	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 0.97-1.16(m, 4H), 1.37-1.58(m, 4H), 2.39-2.50(m, 1H), 3.11(s, 3H), 3.70(s, 2H), 4.46(s, 2H), 5.06(s, 2H), 6.93(d, J=8.7Hz, 2H), 7.06(d, J=8.3Hz, 2H), 7.14(t, J=7.2Hz, 1H), 7.25-7.41(m, 5H), 7.47(d, J=8.3Hz, 2H), 7.66(d, J=8.3Hz, 2H), 7.75(d, J=1.1Hz, 1H), 11.96(brs, 1H)
4-73	DMSO-d6, 300MHz	0.79(t, J=7.4Hz, 6H), 1.00-1.15(m, 4H), 1.36-1.58(m, 4H), 2.41-2.50(m, 1H), 2.74(br, 2H), 2.85(br, 2H), 3.72(s, 2H), 3.91(s, 2H), 5.09(s, 2H), 6.95(d, J=8.3Hz, 2H), 7.07(d, J=8.3Hz, 2H), 7.23(d, J=7.9Hz, 1H), 7.34-7.46(m, 3H), 7.48(s, 1H), 7.61-7.73(m, 3H), 7.79(s, 2H), 12.74(br, 1H)
4-74	DMSO-d6, 300MHz	0.91(d, J=6.4Hz, 3H), 0.98-1.13(m, 2H), 1.34-1.52(m, 3H), 1.71-1.82(m, 4H), 2.38-2.49(m, 1H), 2.51(br, 4H), 3.27(br, 4H), 3.72(s, 2H), 5.07(s, 2H), 6.92-6.98(m, 3H), 7.03(d, J=9.0Hz, 2H), 7.21(s, 1H), 7.23(d, J=8.3Hz, 2H), 7.35(d, J=8.3Hz, 2H), 7.54(d, J=8.7Hz, 2H), 7.76(d, J=8.7Hz, 2H), 12.25(s, 1H)
4-75	DMSO-d6, 300MHz	0.79(t, J=7.2Hz, 6H), 1.01-1.14(m, 4H), 1.38-1.58(m, 4H), 2.41-2.49(m, 1H), 3.41(s, 2H), 4.04(s, 2H), 5.06(s, 2H), 6.92(d, J=8.7Hz, 2H), 6.98(d, J=3.8Hz, 1H), 7.07(d, J=8.7Hz, 2H), 7.34(d, J=3.8Hz, 1H), 7.47(d, J=8.3Hz, 2H), 7.60(d, J=8.3Hz, 2H), 7.63-7.69(m, 2H), 8.06(s, 1H), 12.47(br, 1H)
4-76	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 1.00-1.14(m, 4H), 1.38-1.57(m, 4H), 2.39-2.50(m, 1H), 3.29(s, 2H), 3.88(s, 2H), 4.00(s, 2H), 5.07(s, 2H), 6.93(d, J=8.7Hz, 2H), 7.00(d, J=3.4Hz, 1H), 7.07(d, J=8.7Hz, 2H), 7.37(d, J=3.4Hz, 1H), 7.47(d, J=8.3Hz, 2H), 7.51(d, J=8.3Hz, 2H), 7.65(d, J=8.3Hz, 2H), 7.93(d, J=8.3Hz, 2H), 12.52(br, 2H)
4-77	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 1.01-1.16(m, 4H), 1.38-1.58(m, 4H), 2.40-2.50(m, 1H), 3.23(s, 2H), 3.70(br, 5H), 3.97(s, 2H), 5.07(s, 2H), 6.88-6.96(m, 4H), 6.98(d, J=3.8Hz, 1H), 7.07(d, J=8.7Hz, 2H), 7.28(d, J=8.7Hz, 2H), 7.36(d, J=3.4Hz, 1H), 7.47(d, J=8.7Hz, 2H), 7.65(d, J=8.3Hz, 2H), 12.11(br, 1H)

Table 17-74

Example	solvent, Hz	NMR(δ)
4-78	DMSO-d6, 300MHz	0.79(t, J=7.4Hz, 6H), 1.01-1.16(m, 4H), 1.38-1.58(m, 4H), 2.46(s, 3H), 3.25(s, 2H), 3.75(s, 2H), 3.98(s, 2H), 5.07(s, 2H), 6.93(d, J=8.7Hz, 2H), 6.99(d, J=3.4Hz, 1H), 7.07(d, J=8.7Hz, 2H), 7.24(d, J=8.3Hz, 2H), 7.32(d, J=8.3Hz, 2H), 7.36(d, J=3.4Hz, 1H), 7.47(d, J=8.3Hz, 2H), 7.65(d, J=8.3Hz, 2H), 12.28(br, 1H)
4-79	DMSO-d6, 300MHz-120℃	0.73-0.96(m, 5H), 0.98-1.31(m, 5H), 1.34-1.89(m, 13H), 3.20(d, J=7.0Hz, 2H), 4.70(s, 2H), 5.08(s, 2H), 6.93(d, J=3.7Hz, 1H), 7.02(d, J=8.8Hz, 2H), 7.13(d, J=3.7Hz, 1H), 7.22(d, J=8.1Hz, 2H), 7.26-7.37(m, 4H), 7.50(d, J=8.8Hz, 2H), 7.69(d, J=8.4Hz, 2H)
4-80	DMSO-d6, 300MHz	0.87-1.25(m, 10H), 1.32-1.53(m, 3H), 1.55-1.82(m, 10H), 2.38-2.49(m, 1H), 3.25(d, J=6.8Hz, 2H), 4.71(s, 2H), 5.06(s, 2H), 6.98-7.03(m, 3H), 7.18-7.25(m, 3H), 7.34(d, J=8.3Hz, 2H), 7.50(d, J=8.7Hz, 2H), 7.61(d, J=9.0Hz, 2H), 7.83(d, J=8.7Hz, 2H), 8.70(s, 1H), 12.35(br, 1H)
4-81	DMSO-d6, 300MHz	0.80(t, J=7.3Hz, 6H), 1.00-1.17(m, 4H), 1.37-1.58(m, 4H), 2.40-2.50(m, 1H), 3.22(s, 2H), 3.97(s, 2H), 5.07(s, 2H), 5.33(s, 1H), 6.90-6.98(m, 3H), 7.07(d, J=8.7Hz, 2H), 7.19-7.27(m, 2H), 7.30-7.39(m, 5H), 7.45-7.56(m, 6H), 7.68(d, J=8.3Hz, 2H), 12.29(br, 1H)
4-82	DMSO-d6, 300MHz	0.79(t, J=7.2Hz, 6H), 1.00-1.27(m, 7H), 1.34-1.61(m, 4H), 1.97(brs, 4H), 3.34(brs, 4H), 4.07-4.19(m, 2H), 4.60(brs, 2H), 4.76(brs, 2H), 5.08(s, 2H), 6.59(d, J=9.0Hz, 2H), 6.92(d, J=8.7Hz, 2H), 7.07(d, J=8.7Hz, 2H), 7.30(brs, 1H), 7.41-7.53(m, 3H), 7.65(d, J=7.5Hz, 2H), 7.76(d, J=7.9Hz, 2H)
4-83	DMSO-d6, 300MHz	0.79(t, J=7.3Hz, 6H), 1.00-1.20(m, 4H), 1.15(t, J=7.2Hz, 3H), 1.38-1.58(m, 4H), 2.40-2.54(m, 1H), 3.44(s, 2H), 3.88(s, 3H), 4.04(q, J=7.2Hz, 2H), 4.02(s, 2H), 4.14(s, 2H), 5.06(s, 2H), 6.92(d, J=8.6Hz, 2H), 7.02(d, J=3.8Hz, 1H), 7.07(d, J=9.0Hz, 2H), 7.17(t, J=7.5Hz, 1H), 7.24(t, J=7.7Hz, 1H), 7.36(d, J=3.8Hz, 1H), 7.46(d, J=8.3Hz, 2H), 7.53(d, J=9.1Hz, 1H), 7.57-7.65(m, 3H)

Table 17-75

Example	solvent, Hz	NMR(δ)
4-84	DMSO-d6, 300MHz	1.16-1.45(m, 5H), 1.65-1.83(m, 5H), 2.39-2.49(m, 3H), 2.70(t, J=7.2Hz, 2H), 2.93(t, J=8.1Hz, 2H), 3.31(t, J=8.5Hz, 2H), 3.61(s, 2H), 3.73(s, 2H), 4.27(s, 2H), 6.59(d, J=8.3Hz, 1H), 6.88(d, J=3.8Hz, 1H), 7.06(d, J=3.8Hz, 1H), 7.16-7.40(m, 11H), 12.17(brs, 1H)
4-85	DMSO-d6, 300MHz	1.03(s, 9H), 2.79(s, 2H), 3.24(s, 2H), 3.78(s, 2H), 4.00(s, 2H), 5.54(s, 2H), 7.05-7.18(m, 4H), 7.21-7.45(m, 7H), 7.58-7.64(m, 3H), 7.71(d, J=1.5Hz, 1H), 12.37(brs, 1H)
4-86	DMSO-d6, 300MHz	0.79 (t, J = 7.4 Hz, 6 H),0.97- 1.17 (m, 4 H),1.34- 1.59 (m, 4 H),2.39- 2.55 (m, 1 H),3.26 (s, 2 H),3.76 (s, 3 H),3.96 (s, 2 H),4.03 (s, 2 H),5.06 (s, 2 H),6.93 (d, J = 8.7 Hz, 2 H),6.99- 7.20 (m, 4 H),7.26 (s, 1 H),7.36- 7.51 (m, 4 H),7.66- 7.80 (m, 4 H),12.22 (br s, 1 H).
4-87	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6 H),0.98- 1.17 (m, 4 H),1.36- 1.58 (m, 4 H),2.38- 2.53 (m, 1 H),3.41 (s, 2 H),4.11 (s, 2 H),4.12 (s, 2 H),5.06 (s, 2 H),6.92 (d, J = 8.7 Hz, 2 H),7.07 (d, J = 8.7 Hz, 2 H),7.43- 7.48 (m, 3 H),7.54- 7.61 (m, 1 H),7.66- 7.79 (m, 5 H),7.94- 8.00 (m, 2 H),8.37 (d, J = 8.3 Hz, 1 H),12.54 (br s, 1 H).
4-88	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6 H),0.97- 1.19 (m, 4 H),1.35- 1.60 (m, 4 H),2.39- 2.54 (m, 1 H),3.51 (s, 2 H),4.18 (s, 2 H),4.33 (s, 2 H),5.06 (s, 2 H),6.93 (d, J = 8.9 Hz, 2 H),7.07 (d, J = 8.9 Hz, 2 H),7.37- 7.53 (m, 5 H),7.70 (d, J = 8.3 Hz, 2 H),7.82 (d, J = 1.5 Hz, 1 H),7.90- 7.96 (m, 1 H),8.07- 8.13 (m, 1 H),12.58 (br s, 1 H).
4-89	DMSO-d6, 300MHz	0.79 (t, J = 7.1 Hz, 6 H),0.98- 1.19 (m, 4 H),1.36- 1.60 (m, 4 H),2.38- 2.55 (m, 1 H),3.28 (s, 2 H),3.84 (s, 2 H),3.98 (s, 2 H),5.07 (s, 2 H),5.29 (s, 2 H),6.86 (d, J = 1.1 Hz, 1 H),6.93 (d, J = 8.4 Hz, 2 H),7.03- 7.31 (m, 8 H),7.40- 7.43 (m, 1 H),7.47 (d, J = 8.0 Hz, 2 H),7.68 (d, J = 8.0 Hz, 2 H),7.78 (d, J = 1.1 Hz, 1 H),12.62 (br s, 1 H).

Table 17-76

Example	solvent, Hz	NMR(δ)
4-90	DMSO-d6, 300MHz	0.79 (t, J = 7.1 Hz, 6 H),0.97- 1.17 (m, 4 H),1.36- 1.59 (m, 4 H),2.39- 2.53 (m, 1 H),3.25 (s, 2 H),3.85 (s, 2 H),4.05 (s, 2 H),5.06 (s, 2 H),6.38- 6.41 (m, 1 H),6.93 (d, J = 8.8 Hz, 2 H),7.03- 7.15 (m, 3 H),7.29- 7.39 (m, 2 H),7.41- 7.52 (m, 4 H),7.70 (d, J = 8.1 Hz, 2 H),7.78 (d, J = 1.1 Hz, 1 H),11.04 (br s, 1 H),12.30 (br s, 1 H).
4-91	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6 H),0.99- 1.16 (m, 4 H),1.36- 1.58 (m, 4 H),2.38- 2.54 (m, 1 H),3.31 (s, 2 H),3.85 (s, 2 H),4.05 (s, 2 H),5.07 (s, 2 H),6.93 (d, J = 8.8 Hz, 2 H),7.04- 7.12 (m, 3 H),7.42- 7.55 (m, 5 H),7.60- 7.75 (m, 5 H),7.79 (d, J = 1.4 Hz, 1 H),8.23- 8.26 (m, 1 H),12.42 (br s, 1 H).
4-92	DMSO-d6, 300MHz	0.79 (t, J = 7.1 Hz, 6 H),0.98- 1.18 (m, 4 H),1.36- 1.59 (m, 4 H),2.39- 2.53 (m, 1 H),3.38 (s, 2 H),4.05 (s, 2 H),4.10 (s, 2 H),5.07 (s, 2 H),6.82 (s, 1 H),6.93 (d, J = 8.6 Hz, 2 H),7.07 (d, J = 8.6 Hz, 2 H),7.19- 7.32 (m, 2 H),7.44- 7.64 (m, 5 H),7.70 (d, J = 8.4 Hz, 2 H),7.79 (d, J = 1.4 Hz, 1 H),12.44 (br s, 1 H).
4-93	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6 H),0.97- 1.17 (m, 4 H),1.35- 1.59 (m, 4 H),2.39- 2.53 (m, 1 H),3.37 (s, 2 H),4.02 (s, 2 H),4.07 (s, 2 H),5.06 (s, 2 H),6.89- 6.98 (m, 3 H),7.03- 7.10 (m, 3 H),7.14 (d, J = 3.7 Hz, 1 H),7.27 (dd, J = 3.3, 1.1 Hz, 1 H),7.42- 7.51 (m, 4 H),7.70 (d, J = 8.1 Hz, 2 H),7.79 (d, J = 1.1 Hz, 1 H),12.46 (br s, 1 H).
4-94	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6 H),0.97- 1.17 (m, 4 H),1.35- 1.59 (m, 4 H),2.38- 2.54 (m, 1 H),3.34 (s, 2 H),3.83 (s, 2 H),4.01 (s, 2 H),5.06 (s, 2 H),6.93 (d, J = 8.7 Hz, 2 H),6.99- 7.11 (m, 4 H),7.27- 7.50 (m, 6 H),7.64 (d, J = 8.3 Hz, 2 H),7.93 (d, J = 7.9 Hz, 2 H),12.42 (br s, 1 H).
4-95	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6 H),0.98- 1.18 (m, 4 H),1.34- 1.59 (m, 4 H),2.38- 2.54 (m, 1 H),3.27 (s, 2 H),3.83 (s, 2 H),4.03 (s, 2 H),5.06 (s, 2 H),6.89- 6.97 (m, 3 H),7.07 (d, J = 8.7 Hz, 2 H),7.26- 7.51 (m, 6 H),7.58- 7.66 (m, 3 H),7.79 (d, J = 7.1 Hz, 2 H),12.66 (br s, 2 H).

Table 17-77

Example	solvent, Hz	NMR(δ)
4-96	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6 H),0.97- 1.17 (m, 4 H),1.33- 1.60 (m, 4 H),2.38- 2.53 (m, 1 H),3.51 (s, 2 H),4.15 (s, 2 H),4.21 (s, 2 H),5.06 (s, 2 H),6.93 (d, J = 8.7 Hz, 2 H),6.98- 7.11 (m, 3 H),7.32- 7.50 (m, 5 H),7.62 (d, J = 7.9 Hz, 2 H),7.68- 7.77 (m, 2 H),12.49 (br s, 1 H).
4-97	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6 H),0.97- 1.18 (m, 4 H),1.36- 1.61 (m, 4 H),2.40- 2.54 (m, 1 H),3.40 (s, 2 H),4.08 (s, 2 H),4.16 (s, 2 H),5.07 (s, 2 H),6.88- 7.12 (m, 2 H),7.28- 7.41 (m, 3 H),7.48 (d, J = 8.3 Hz, 5 H),7.66 (d, J = 8.3 Hz, 2 H),7.73- 7.81 (m, 2 H),7.90- 7.97 (m, 1 H),12.48 (br s, 1 H).
4-98	DMSO-d6, 400MHz	0.80 (t, J = 7.3 Hz, 6 H),0.98- 1.16 (m, 4 H),1.37- 1.58 (m, 4 H),2.41- 2.53 (m, 1 H),3.39 (s, 2 H),4.05 (s, 2 H),4.09 (s, 2 H),5.07 (s, 2 H),6.93 (d, J = 8.7 Hz, 2 H),7.02 (d, J = 3.7 Hz, 1 H),7.07 (d, J = 8.7 Hz, 2 H),7.25- 7.31 (m, 1 H),7.36- 7.50 (m, 6 H),7.63- 7.70 (m, 4 H),7.78 (d, J = 1.4 Hz, 1 H),12.46 (br s, 1 H).
4-99	DMSO-d6, 400MHz	0.79 (t, J = 7.3 Hz, 6 H),1.00- 1.15 (m, 4 H),1.36- 1.57 (m, 4 H),2.40- 2.52 (m, 1 H),4.32 (s, 2 H),4.96 (s, 2 H),5.05 (s, 2 H),6.91 (d, J = 8.6 Hz, 2 H),7.02- 7.13 (m, 3 H),7.21 (d, J = 3.7 Hz, 1 H),7.28- 7.34 (m, 1 H),7.39- 7.54 (m, 4 H),7.63 (d, J = 8.3 Hz, 2 H),7.77- 7.82 (m, 1 H),12.95 (br s, 1 H).
4-100	DMSO-d6, 400MHz	0.80 (t, J = 7.3 Hz, 6 H),0.99- 1.17 (m, 4 H),1.38- 1.58 (m, 4 H),2.40- 2.52 (m, 1 H),3.96 (s, 2 H),4.68 (s, 2 H),5.07 (s, 2 H),6.93 (d, J = 8.8 Hz, 2 H),7.03- 7.12 (m, 3 H),7.32 (d, J = 4.0 Hz, 1 H),7.37 (d, J = 3.7 Hz, 1 H),7.48 (d, J = 8.5 Hz, 2 H),7.62 (d, J = 8.5 Hz, 2 H),7.67 (d, J = 4.0 Hz, 1 H),12.97 (br s, 1 H).
4-101	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6 H),0.96 (t, J = 7.0 Hz, 3 H),1.00- 1.17 (m, 4 H),1.23 (t, J = 7.0 Hz, 3 H),1.35- 1.61 (m, 4 H),2.37- 2.55 (m, 1 H),3.16- 3.50 (m, 6 H),3.96 (s, 2 H),4.02 (s, 2 H),5.07 (s, 2 H),5.43 (s, 2 H),6.93 (d, J = 8.7 Hz, 2 H),7.00- 7.24 (m, 5 H),7.31- 7.41 (m, 2 H),7.48 (d, J = 8.6 Hz, 2 H),7.58- 7.68 (m, 3 H),12.08 (br s, 1 H).

Table 17-78

Example	solvent, Hz	NMR(δ)
4-102	DMSO-d6, 300MHz	1.14-1.48(m, 5H), 1.64-1.85(m, 5H), 2.26(s, 3H), 2.27(s, 3H), 2.38-2.54(m, 1H), 2.87(dd, J=7.7, 14.1Hz, 1H), 3.02(dd, J=7.6, 13.9Hz, 1H), 3.59(t, J=7.5Hz, 1H), 3.81(d, J=14.3Hz, 1H), 3.96(d, J=14.3Hz, 1H), 5.07(s, 2H), 7.05(d, J=1.1Hz, 2H), 7.14-7.35(m, 11H), 7.57(d, J=1.5Hz, 1H), 12.48(brs, 1H)
4-103	DMSO-d6, 300MHz	0.93(t, J=7.3Hz, 3H), 0.97(t, J=7.0Hz, 3H), 1.36-1.51(m, 2H), 1.65-1.77(m, 2H), 3.26(s, 2H), 3.57(q, J=7.1Hz, 2H), 3.81(s, 2H), 4.00-4.08(m, 4H), 7.07(t, J=8.5Hz, 4H), 7.23-7.44(m, 6H), 7.48(d, J=8.7Hz, 2H), 7.66(d, J=8.4Hz, 2H), 7.80(d, J=1.1Hz, 1H)
4-104	CDCl3-300MHz	1.17-1.51(m, 5H), 1.67-1.95(m, 5H), 2.30(s, 3H), 2.43-2.57(m, 1H), 2.78(s, 3H), 4.99(s, 2H), 5.19(s, 2H), 6.88(d, J=8.3Hz, 1H), 7.00(dd, J=1.8, 8.4Hz, 1H), 7.14-7.36(m, 7H), 7.53(d, J=1.5Hz, 1H), 7.70(d, J=8.6Hz, 1H), 7.79(d, J=1.9Hz, 1H)
4-105	DMSO-d6, 400MHz	3.27(s, 2H), 3.81(s, 2H), 4.03(s, 2H), 5.17(s, 2H), 7.13-7.18(m, 3H), 7.24-7.29(m, 1H), 7.32-7.40(m, 4H), 7.42-7.49(m, 3H), 7.71(d, J=8.3Hz, 2H), 7.79(d, J=1.6Hz, 1H), 12.40(brs, 1H)
4-106	DMSO-d6, 400MHz	0.79 (t, J = 7.3 Hz, 6 H),0.99- 1.16 (m, 4 H),1.38- 1.58 (m, 4 H),2.40- 2.53 (m, 1 H),3.35 (s, 2 H),4.04 (s, 2 H),4.10 (s, 2 H),4.94- 5.17 (m, 6 H),5.92- 6.04 (m, 1 H),6.92 (d, J = 8.8 Hz, 2 H),7.02- 7.10 (m, 3 H),7.16- 7.27 (m, 2 H),7.37 (d, J = 3.5 Hz, 1 H),7.44- 7.53 (m, 3 H),7.59- 7.65 (m, 3 H),12.60 (br s, 1 H).
4-107	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6 H),0.97- 1.16 (m, 4 H),1.36- 1.60 (m, 4 H),2.39- 2.56 (m, 1 H),4.26 (s, 2 H),4.90 (s, 2 H),5.05 (s, 2 H),6.91 (d, J = 8.7 Hz, 2 H),7.06 (d, J = 8.7 Hz, 2 H),7.19 (d, J = 3.6 Hz, 1 H),7.34 (s, 1 H),7.40 (d, J = 3.6 Hz, 1 H),7.42- 7.49 (m, 4 H),7.62 (d, J = 8.3 Hz, 2 H),7.86- 7.92 (m, 2 H),12.88 (br s, 1 H).

Industrial Applicability

As is clear from the foregoing test results and the like, compound [I] of the present invention has been shown to have a superior PTP1B inhibitory activity and a hypoglycemic activity. That is, the compound [I] of the present invention is expected to provide a new type of drug for the prophylaxis or treatment of diabetes, which directly improves the action of insulin and ameliorates hyperglicemic state. In addition, the compound [I] of the present invention is expected to provide a drug for the prophylaxis or treatment of diabetic complications (retinopathy, nephropathy, neuropathy, syndrome X or metabolic syndrome, ischemic heart diseases (cardiac infarction, angina pectoris etc.), strokes (cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage etc.) etc.), hyperlipidemia, obesity and the like, and further a drug for the prophylaxis or treatment of diseases mediated by PTP1B.

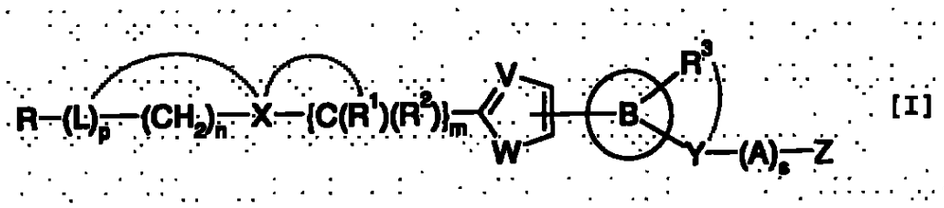
Moreover, the compound [I] of the present invention enhances hypoglycemic activity, as shown in the foregoing test results, by administration in combination with each of insulin, glibenclamide, tolbutamide, nateglinide, metformin hydrochloride, voglibose and Pioglitazone hydrochloride. Therefore, the compound [I] is expected to have an activity to mutually enhance and/or complement blood glucose (fasting, postprandial) lowering ability that the compound [I] of the present invention and therapeutic agents for diabetes individually have, by the use in combination with other therapeutic agents for diabetes (particularly the corresponding therapeutic agents other than therapeutic agents for diabetic complications) including insulin preparation, insulin secretagogue, biguanide, α-glucosidase inhibitor and insulin sensitivity enhancer. Furthermore, the compound [I] of the present invention is expected to simultaneously realize improvement of hyperglycemia and prophylaxis or treatment of

diabetic complications (particularly, microangio complications), by the use in combination with other therapeutic agents for diabetes (particularly, therapeutic agents for diabetic complications). Moreover, the compound [I] of the present invention is expected to ameliorate hyperglycemia, high blood lipid and obesity, and further, prevent transition into diabetic complications (particularly, large artery complications) and/or suppress progression thereof, by a use in combination with other therapeutic agents for hyperlipidemia, therapeutic agents for obesity, therapeutic agents for hypertension and/or therapeutic agents for thrombosis. In other words, the compound [I] of the present invention is expected to exhibit a high prophylactic or therapeutic effect for diabetes and diabetic complications, by the use in combination with other therapeutic agents for diabetes, other therapeutic agents for hyperlipidemia, other therapeutic agents for obesity, therapeutic agents for hypertension or therapeutic agents for thrombosis, which effect is unavailable by independent use of each therapeutic agent.

This application is based on a patent application Nos. 2003-105267 and 2003-157590 filed in Japan, the contents of which are hereby incorporated by reference. The references cited herein, including patents and patent applications, are hereby incorporated in their entireties by reference, to the extent that they have been disclosed herein.

WHAT IS CLAIMED IS:

1. A 5-membered heteroaromatic ring compound represented by the formula [I]



[I]

wherein

V is =N- or =CH-;

W is -S- or -O-;

m is 0, 1 or 2;

R^1 and R^2 are each independently a hydrogen atom or a C_{1-4} alkyl group;

X is $-N(R^4)-$, $-N(R^5)-CO-O-$, $-SO_2-N(R^5)-$, $-N(R^5)-SO_2-$, $-N(R^6)-SO_2-N(R^5)-$, $-CO-N(R^7)-$, $-N(R^8)-CO-$, $-N(R^9)-CO-N(R^5)-$, $-N(R^{10})-(CH_2)_k-N(R^5)-$, $-N(R^{10})-(CH_2)_k-N(R^5)-CO-$, $-C(R^{10})=N-N(R^7)-$, $-N(R^{10})-(CH_2)_k-CH(R^6)-$, -O-, -S- or $-SO_2-$

wherein

k is 0 or an integer of 1 to 4,

R^4, R^5, R^6, R^7, R^8, R^9 and R^{10} are each independently

(1) a hydrogen atom,

(2) a C_{1-6} alkyl group

wherein said C_{1-6} alkyl group is optionally substituted by

(a) an optionally substituted aryl group,

(b) an optionally substituted heteroaromatic ring group,

(c) a carboxy group,

(d) a C_{1-4} alkoxycarbonyl group,

(e) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom, an optionally substituted aryl group, an optionally substituted heteroaromatic ring group, a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by substituent(s) selected from the group consisting of an optionally substituted

aryl group, an optionally substituted heteroaromatic ring group, a C_{1-4} alkoxy group optionally substituted by an aryl group and an optionally substituted aryloxy group, or, together with the nitrogen atom bonded thereto, may form an indoline ring or may form a 5- to 7-membered hetero ring optionally further containing at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom,

(f) $-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are as defined above,

(g) $-O-R^{17}$

wherein R^{17} is a hydrogen atom, an optionally substituted aryl group, an optionally substituted heteroaromatic ring group or a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by substituent(s) selected from the group consisting of an optionally substituted aryl group, an optionally substituted heteroaromatic ring group, a C_{1-4} alkoxy group optionally substituted by an aryl group and an optionally substituted aryloxy group,

(h) $-CO-R^{17}$

wherein R^{17} is as defined above,

(i) $-SO_2-R^{17}$

wherein R^{17} is as defined above or

(j) a C_{3-7} cycloalkyl group,

(3) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are as defined above,

(4) $-SO_2-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are as defined above,

(5) $-CO-R^{17}$

wherein R^{17} is as defined above,

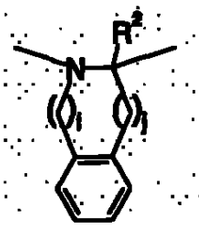
(6) $-SO_2-R^{17}$

wherein R^{17} is as defined above,

(7) an optionally substituted aryl group,

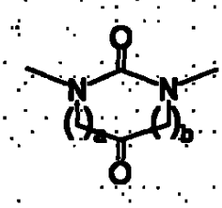
(8) an optionally substituted heteroaromatic ring group, or

(9) R^4 and R^1 are optionally linked to form



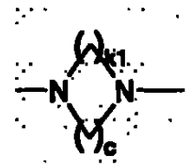
wherein i and j are each independently 0, 1 or 2 and R^2 is as defined above,

(10) R^5 and R^9 are optionally linked to form



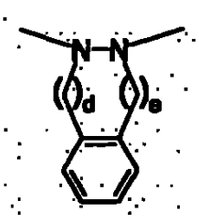
wherein a and b are each independently 0, 1 or 2,

(11) R^5 and R^{10} are optionally linked to form



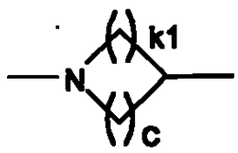
wherein k1 and c are each independently 0 or an integer of 1 to 4,

(12) R^5 and R^{10} are optionally linked to form



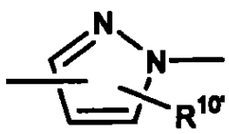
wherein d and e are each independently 0, 1 or 2,

(13) R^6 and R^{10} are optionally linked to form



wherein k1 and c are as defined above, or

(14) R^7 and R^{10} are optionally linked to form



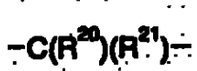
wherein $R^{10'}$ is a hydrogen atom or a C_{1-6} alkyl group;

n is 0 or an integer of 1 to 4;

p is 0 or 1;

L is

(1)



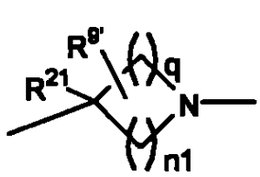
wherein

R^{20} is

(a) a hydrogen atom,

(b) a C_{1-6} alkyl group, or

(c) optionally linked with R^4 or R^8 to form



wherein n1 and q are each independently 0 or an integer of 1 to 4, $R^{9'}$ is a hydrogen atom, a hydroxyl group, a C_{1-6} alkyl group, a carboxy group or a C_{1-6} alkoxy group, or

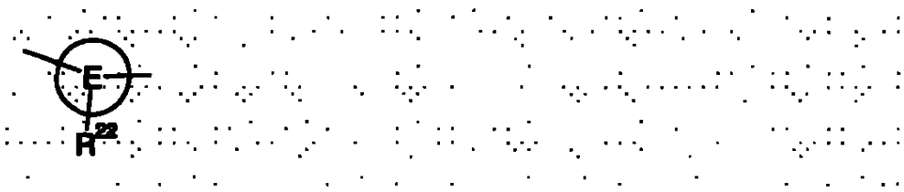
(d) optionally linked with R^4 to form



wherein u and v are each independently 0, 1 or 2,

R^{21} is a hydrogen atom, a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by an optionally substituted aryl group or an optionally substituted heteroaromatic ring group, an optionally substituted aryl group or an optionally substituted heteroaromatic ring group,

(2)



wherein

E is an aryl group or a heteroaromatic ring group,

R^{22} is

(a) a hydrogen atom,

(b) a halogen atom,

(c) a C_{1-4} alkyl group,

(d) a C_{1-4} alkoxy group optionally substituted by a carboxy group,

(e) a C_{1-6} alkylthio group,

(f) a nitro group,

(g) $-N(R^{23})(R^{24})$

wherein R^{23} and R^{24} are each independently a hydrogen atom, a C_{1-6} alkyl group, a C_{1-4} alkylcarbonyl group wherein said C_{1-4} alkylcarbonyl group is optionally substituted by an amino group, a C_{1-4} alkylamino group or a di(C_{1-4} alkyl)amino group, or a C_{1-4} alkylsulfonyl group, or

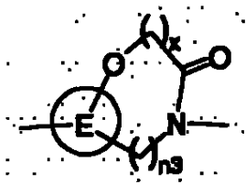
(h) optionally linked with R^4 to form



wherein n2 and w are each independently 0 or an integer of 1 to

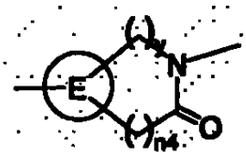
3 and E is as defined above,

(i) optionally linked with R^4 to form



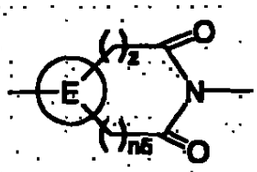
wherein n3 and x are each independently 0 or 1 and E is as defined above,

(j) optionally linked with R^7 to form



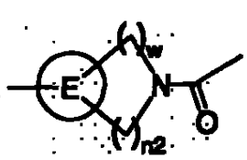
wherein n4 and y are each independently 0, 1 or 2 and E is as defined above,

(k) optionally linked with R^7 to form



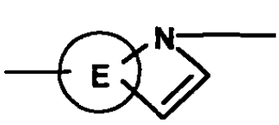
wherein n5 and z are each independently 0 or 1 and E is as defined above,

(l) optionally linked with R^8 to form



wherein n2 and w are each independently 0 or an integer of 1 to 3 and E is as defined above, or

(m) optionally linked with R^4 to form



wherein E is as defined above

or

(3)



wherein

R^{20}, R^{21} and E are as defined above,

R^{25} is

(a) a hydrogen atom,

(b) a halogen atom,

(c) a C_{1-4} alkyl group,

(d) a C_{1-4} alkoxy group optionally substituted by a carboxy group,

(e) a C_{1-6} alkylthio group,

(f) a nitro group or

(g) $-N(R^{23})(R^{24})$

wherein R^{23} and R^{24} are as defined above;

R is $-COO(R^{19})$, $-A^1-COO(R^{19})$ or $-O-A^1-COO(R^{19})$

wherein A^1 is a C_{1-4} alkylene group and R^{19} is a hydrogen atom or a C_{1-4} alkyl group;

B is an aryl group or a heteroaromatic ring group;

R^3 is

(1) a hydrogen atom,

(2) a halogen atom,

(3) a C_{1-8} alkyl group,

(4) a C_{1-6} alkoxy group,

(5) a C_{1-6} alkylamino group,

(6) a di(C_{1-6} alkyl)amino group,

(7) a cyano group,

(8) a nitro group,

(9) a C_{1-4} haloalkyl group,

(10) $-S-R^{18}$ wherein R^{18} is a C_{1-6} alkyl group or an aryl group,

(11) $-SO-R^{18}$ wherein R^{18} is a C_{1-6} alkyl group or an aryl group,

(12) $-SO_2-R^{18}$ wherein R^{18} is a C_{1-6} alkyl group or an aryl group,

(13) an aryl group or

(14) a heterocyclic group;

Y is $-O-$, $-S-$, $-SO-$, $-SO_2-$, $-N(R^{11})-$, $-N(R^{12})-CO-$, $-N(R^{12})-SO_2-$, $-SO_2-N(R^{12})-$, $-C(R^{13})(R^{14})-$, $-CO-$, $-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$

wherein

R^{11} is

(1) a hydrogen atom,

(2) a C_{1-8} alkyl group

wherein said C_{1-8} alkyl group is optionally substituted by substituent(s) selected from the group consisting of

(a) a C_{3-7} cycloalkyl group,

(b) an optionally substituted aryl group,

(c) an optionally substituted heterocyclic group,

(d) a hydroxyl group,

(e) a C_{1-4} alkylamino group and

(f) a di(C_{1-4} alkyl)amino group,

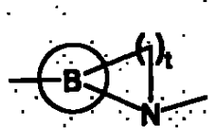
(3) a C_{2-4} alkenyl group,

(4) a C_{1-4} alkylsulfonyl group,

(5) a C_{1-4} alkylcarbonyl group

wherein said C_{1-4} alkylcarbonyl group is optionally substituted by a hydroxyl group or a C_{1-4} alkoxy group, or

(6) optionally linked with R^3 to form



wherein t is an integer of 1 to 4 and B is as defined above,

R^{12} is

(1) a hydrogen atom,

(2) a C_{1-8} alkyl group

wherein said C_{1-8} alkyl group is optionally substituted by substituent(s) selected from the group consisting of

(a) a C_{3-7} cycloalkyl group,

(b) an optionally substituted aryl group,

(c) an optionally substituted heterocyclic group,

(d) a hydroxyl group,

(e) a C_{1-4} alkylamino group and

(f) a di(C_{1-4} alkyl)amino group,

(3) a C_{2-4} alkenyl group,

(4) a C_{1-4} alkylsulfonyl group or

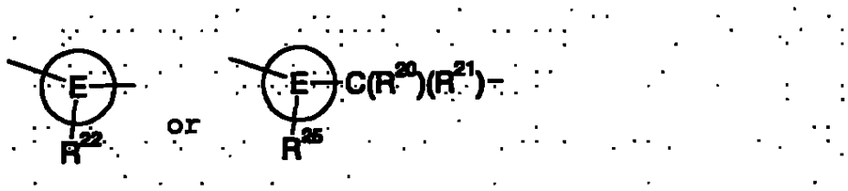
(5) a C_{1-4} alkylcarbonyl group

wherein said C_{1-4} alkylcarbonyl group is optionally substituted by a hydroxyl group or a C_{1-4} alkoxy group,

R^{13} and R^{14} are each independently a hydrogen atom, a C_{1-4} alkyl group, or optionally form a C_{3-7} cycloalkane together with the carbon atom bonded thereto, or optionally form, together with the carbon atom bonded thereto, a 5- to 7-membered hetero ring optionally having at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom,

provided that,

when m is 0, p is 1 and L is



wherein R^{20} and R^{21} are each a hydrogen atom, E is a phenyl group, R^{22} is a hydrogen atom, a halogen atom, a C_{1-4} alkyl group, a C_{1-4} alkoxy group or a nitro group, and R^{25} is a hydrogen atom, a halogen atom, a C_{1-4} alkyl group, a C_{1-4} alkoxy group or a nitro group,

Y should be

$-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$ wherein R^{12}, R^{13} and R^{14} are as defined above;

s is 0 or 1;

A is a C_{1-4} alkylene group optionally substituted by a C_{3-7} cycloalkyl group;

Z is

(1) a C_{3-7} cycloalkyl group

wherein said C_{3-7} cycloalkyl group is optionally substituted by an aryl group wherein said aryl group is optionally substituted by a halogen atom or a C_{1-6} alkyl group, or a heteroaromatic ring group wherein said heteroaromatic ring group is optionally substituted by a halogen atom or a C_{1-6} alkyl group,

(2) an aryl group

wherein said aryl group is optionally substituted by substituent(s) selected from the group consisting of

(a) a heterocyclic group optionally substituted by a C_{1-4} alkyl group or a C_{1-4} alkylcarbonyl group,

(b) a C_{3-7} cycloalkyl group optionally substituted by a hydroxyl group, an oxo group, a halogen atom or a C_{1-6} alkyl group,

(c) a carboxy group,

(d) a halogen atom,

(e) a C_{1-8} alkyl group,

(f) a C_{1-4} haloalkyl group,

(g) a C_{1-4} alkylamino group,

(h) a di(C_{1-4} alkyl)amino group,

(i) a C_{1-6} alkylthio group,

(j) a C_{1-4} alkoxy group,

(k) a C_{1-4} alkylcarbonyl group and

(l) a nitro group,

(3) a heteroaromatic ring group

wherein said heteroaromatic ring group is optionally substituted by substituent(s) selected from the group consisting of

(a) a heterocyclic group optionally substituted by a C_{1-4} alkyl

group or a C_{1-4} alkylcarbonyl group,

(b) a C_{3-7} cycloalkyl group optionally substituted by a hydroxyl group, an oxo group, a halogen atom or a C_{1-6} alkyl group,

(c) a carboxy group,

(d) a halogen atom,

(e) a C_{1-8} alkyl group,

(f) a C_{1-4} haloalkyl group,

(g) a C_{1-4} alkylamino group,

(h) a di(C_{1-4} alkyl)amino group,

(i) a C_{1-6} alkylthio group,

(j) a C_{1-4} alkoxy group,

(k) a C_{1-4} alkylcarbonyl group and

(l) an aryl group optionally substituted by a halogen atom or a C_{1-4} haloalkyl group,

(4) an indanyl group or

(5) a piperazinyl group

wherein said piperazinyl group is optionally substituted by substituent(s) selected from the group consisting of

(a) a phenyl group,

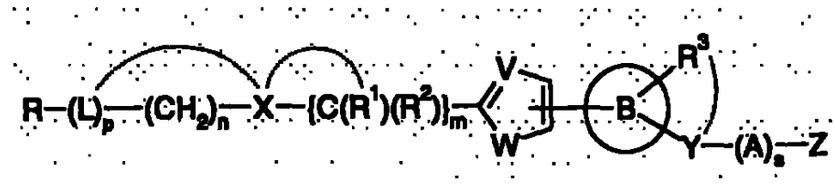
(b) a phenyl C_{1-4} alkyl group,

(c) a benzoyl group optionally substituted by a halogen atom and

(d) a phenyl C_{1-4} alkoxycarbonyl group

or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

2. The 5-membered heteroaromatic ring compound of claim 1, which is represented by the formula [I]



[I]

wherein

V is =N- or =CH-;

W is -S- or -O-;

m is 0, 1 or 2;

R^1 and R^2 are each independently a hydrogen atom or a C_{1-4} alkyl group;

X is $-N(R^4)-$, $-N(R^5)-CO-O-$, $-SO_2-N(R^5)-$, $-N(R^5)-SO_2-$, $-N(R^6)-SO_2-N(R^5)-$, $-CO-N(R^7)-$, $-N(R^8)-CO-$, $-N(R^9)-CO-N(R^5)-$, $-N(R^{10})-(CH_2)_k-N(R^5)-$, -O-, -S- or $-SO_2-$

wherein

k is 0 or an integer of 1 to 4,

R^4, R^5, R^6, R^7, R^8, R^9 and R^{10} are each independently

(1) a hydrogen atom,

(2) a C_{1-6} alkyl group

wherein said C_{1-6} alkyl group is optionally substituted by

(a) an optionally substituted aryl group,

(b) an optionally substituted heteroaromatic ring group,

(c) a carboxy group,

(d) a C_{1-4} alkoxycarbonyl group,

(e) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom, an optionally substituted aryl group, an optionally substituted heteroaromatic ring group, a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by substituent(s) selected from the group consisting of an optionally substituted aryl group, an optionally substituted heteroaromatic ring group, a C_{1-4} alkoxy group optionally substituted by an aryl group and an optionally substituted aryloxy group, or, together with the nitrogen atom bonded thereto, may form an indoline ring or may form a 5- to 7-membered hetero ring optionally further containing at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom,

(f) $-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are as defined above,

(g) $-O-R^{17}$

wherein R^{17} is a hydrogen atom, an optionally substituted aryl group, an optionally substituted heteroaromatic ring group or a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by substituent(s) selected from the group consisting of an optionally substituted aryl group, an optionally substituted heteroaromatic ring group, a C_{1-4} alkoxy group optionally substituted by an aryl group and an optionally substituted aryloxy group,

(h) $-CO-R^{17}$

wherein R^{17} is as defined above,

(i) $-SO_2-R^{17}$

wherein R^{17} is as defined above or

(j) a C_{3-7} cycloalkyl group,

(3) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are as defined above,

(4) $-SO_2-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are as defined above,

(5) $-CO-R^{17}$

wherein R^{17} is as defined above,

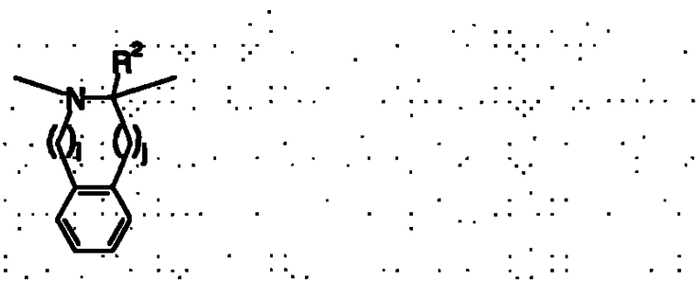
(6) $-SO_2-R^{17}$

wherein R^{17} is as defined above,

(7) an optionally substituted aryl group,

(8) an optionally substituted heteroaromatic ring group, or

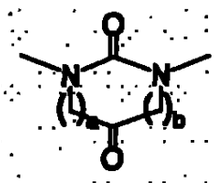
(9) R^4 and R^1 are optionally linked to form



wherein i and j are each independently 0, 1 or 2 and R^2 is as

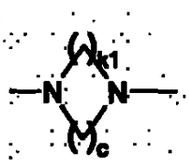
defined above,

(10) R^5 and R^9 are optionally linked to form



wherein a and b are each independently 0, 1 or 2,

(11) R^5 and R^{10} are optionally linked to form



wherein k1 and c are each independently 0 or an integer of 1 to 4, or

(12) R^5 and R^{10} are optionally linked to form



wherein d and e are each independently 0, 1 or 2;

n is 0 or an integer of 1 to 4;

p is 0 or 1;

L is

(1)



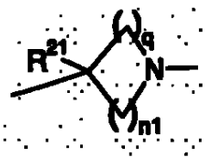
wherein

R^{20} is

(a) a hydrogen atom,

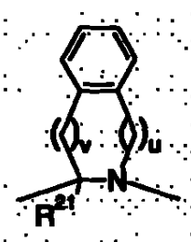
(b) a C_{1-6} alkyl group, or

(c) optionally linked with R^4 to form



wherein n1 and q are each independently 0 or an integer of 1 to 4, or

(d) optionally linked with R^4 to form



wherein u and v are each independently 0, 1 or 2,

R^{21} is a hydrogen atom, a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by an optionally substituted aryl group or an optionally substituted heteroaromatic ring group, an optionally substituted aryl group or an optionally substituted heteroaromatic ring group,

(2)



wherein

E is an aryl group or a heteroaromatic ring group,

R^{22} is

(a) a hydrogen atom,

(b) a halogen atom,

(c) a C_{1-4} alkyl group,

(d) a C_{1-4} alkoxy group optionally substituted by a carboxy group,

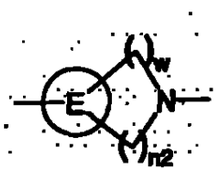
(e) a C_{1-6} alkylthio group,

(f) a nitro group,

(g) $-N(R^{23})(R^{24})$

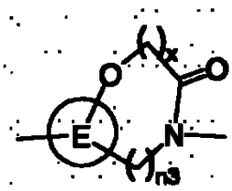
wherein R^{23} and R^{24} are each independently a hydrogen atom, a C_{1-6} alkyl group, a C_{1-4} alkylcarbonyl group wherein said C_{1-4} alkylcarbonyl group is optionally substituted by an amino group, a C_{1-4} alkylamino group or a di(C_{1-4} alkyl)amino group, or a C_{1-4} alkylsulfonyl group, or

(h) optionally linked with R^4 to form



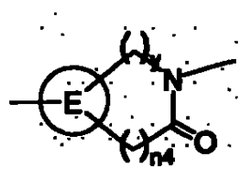
wherein n2 and w are each independently 0 or an integer of 1 to 3 and E is as defined above,

(i) optionally linked with R^4 to form



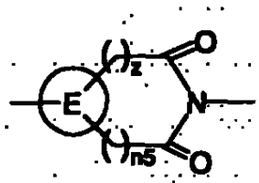
wherein n3 and x are each independently 0 or 1 and E is as defined above,

(j) optionally linked with R^7 to form



wherein n4 and y are each independently 0, 1 or 2 and E is as defined above,

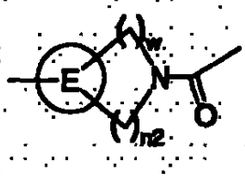
(k) optionally linked with R^7 to form



wherein n5 and z are each independently 0 or 1 and E is as

defined above, or

(1) optionally linked with R^8 to form



wherein n2 and w are each independently 0 or an integer of 1 to 3 and E is as defined above, or

(3)



wherein

R^{20}, R^{21} and E are as defined above,

R^{25} is

(a) a hydrogen atom,

(b) a halogen atom,

(c) a C_{1-4} alkyl group,

(d) a C_{1-4} alkoxy group optionally substituted by a carboxy group,

(e) a C_{1-6} alkylthio group,

(f) a nitro group or

(g) $-N(R^{23})(R^{24})$

wherein R^{23} and R^{24} are as defined above;

R is $-COO(R^{19})$, $-A^1-COO(R^{19})$ or $-O-A^1-COO(R^{19})$

wherein A^1 is a C_{1-4} alkylene group and R^{19} is a hydrogen atom or a C_{1-4} alkyl group;

B is an aryl group or a heteroaromatic ring group;

R^3 is

(1) a hydrogen atom,

(2) a halogen atom,

(3) a C_{1-8} alkyl group,

(4) a C_{1-6} alkoxy group,

(5) a C_{1-6} alkylamino group,

(6) a di(C_{1-6} alkyl)amino group,

(7) a cyano group,

(8) a nitro group,

(9) a C_{1-4} haloalkyl group,

(10) $-S-R^{18}$ wherein R^{18} is a C_{1-6} alkyl group or an aryl group,

(11) $-SO-R^{18}$ wherein R^{18} is a C_{1-6} alkyl group or an aryl group, or

(12) $-SO_2-R^{18}$ wherein R^{18} is a C_{1-6} alkyl group or an aryl group;

Y is $-O-$, $-S-$, $-SO-$, $-SO_2-$, $-N(R^{11})-$, $-N(R^{12})-CO-$, $-N(R^{12})-SO_2-$, $-SO_2-N(R^{12})-$, $-C(R^{13})(R^{14})-$, $-CO-$, $-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$

wherein

R^{11} is

(1) a hydrogen atom,

(2) a C_{1-8} alkyl group

wherein said C_{1-8} alkyl group is optionally substituted by substituent(s) selected from the group consisting of

(a) a C_{3-7} cycloalkyl group,

(b) an optionally substituted aryl group,

(c) an optionally substituted heterocyclic group,

(d) a hydroxyl group,

(e) a C_{1-4} alkylamino group and

(f) a di(C_{1-4} alkyl)amino group,

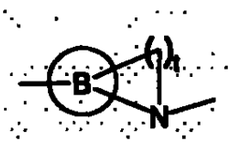
(3) a C_{2-4} alkenyl group,

(4) a C_{1-4} alkylsulfonyl group,

(5) a C_{1-4} alkylcarbonyl group

wherein said C_{1-4} alkylcarbonyl group is optionally substituted by a hydroxyl group or a C_{1-4} alkoxy group, or

(6) optionally linked with R^3 to form



wherein t is an integer of 1 to 4 and B is as defined above,

R^{12} is

(1) a hydrogen atom,

(2) a C_{1-8} alkyl group

wherein said C_{1-8} alkyl group is optionally substituted by substituent(s) selected from the group consisting of

(a) a C_{3-7} cycloalkyl group,

(b) an optionally substituted aryl group,

(c) an optionally substituted heterocyclic group,

(d) a hydroxyl group,

(e) a C_{1-4} alkylamino group and

(f) a di(C_{1-4} alkyl)amino group,

(3) a C_{2-4} alkenyl group,

(4) a C_{1-4} alkylsulfonyl group or

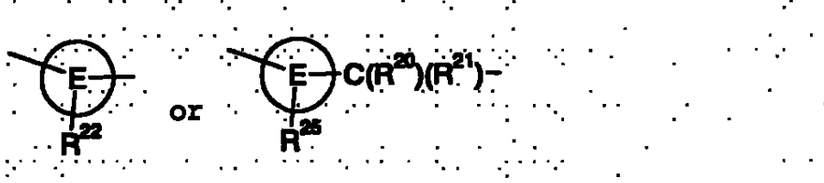
(5) a C_{1-4} alkylcarbonyl group

wherein said C_{1-4} alkylcarbonyl group is optionally substituted by a hydroxyl group or a C_{1-4} alkoxy group,

R^{13} and R^{14} are each independently a hydrogen atom, a C_{1-4} alkyl group, or optionally form a C_{3-7} cycloalkane together with the carbon atom bonded thereto, or optionally form, together with the carbon atom bonded thereto, a 5- to 7-membered hetero ring optionally having at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom,

provided that,

when m is 0, p is 1 and L is



wherein R^{20} and R^{21} are each a hydrogen atom, E is a phenyl

group, R^{22} is a hydrogen atom, a halogen atom, a C_{1-4} alkyl group, a C_{1-4} alkoxy group or a nitro group, and R^{25} is a hydrogen atom, a halogen atom, a C_{1-4} alkyl group, a C_{1-4} alkoxy group or a nitro group,

Y should be

$-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$ wherein R^{12}, R^{13} and R^{14} are as defined above;

s is 0 or 1;

A is a C_{1-4} alkylene group optionally substituted by a C_{3-7} cycloalkyl group;

Z is

(1) a C_{3-7} cycloalkyl group

wherein said C_{3-7} cycloalkyl group is optionally substituted by an aryl group wherein said aryl group is optionally substituted by a halogen atom or a C_{1-6} alkyl group, or a heteroaromatic ring group wherein said heteroaromatic ring group is optionally substituted by a halogen atom or a C_{1-6} alkyl group,

(2) an aryl group

wherein said aryl group is optionally substituted by substituent(s) selected from the group consisting of

(a) a heterocyclic group optionally substituted by a C_{1-4} alkyl group or a C_{1-4} alkylcarbonyl group,

(b) a C_{3-7} cycloalkyl group optionally substituted by a hydroxyl group, an oxo group, a halogen atom or a C_{1-6} alkyl group,

(c) a carboxy group,

(d) a halogen atom,

(e) a C_{1-6} alkyl group,

(f) a C_{1-4} haloalkyl group,

(g) a C_{1-4} alkylamino group,

(h) a di(C_{1-4} alkyl)amino group,

(i) a C_{1-6} alkylthio group,

(j) a C_{1-4} alkoxy group, and

(k) a C_{1-4} alkylcarbonyl group,

(3) a heteroaromatic ring group

wherein said heteroaromatic ring group is optionally substituted by substituent(s) selected from the group consisting of

(a) a heterocyclic group optionally substituted by a C_{1-4} alkyl group or a C_{1-4} alkylcarbonyl group,

(b) a C_{3-7} cycloalkyl group optionally substituted by a hydroxyl group, an oxo group, a halogen atom or a C_{1-6} alkyl group,

(c) a carboxy group,

(d) a halogen atom,

(e) a C_{1-8} alkyl group,

(f) a C_{1-4} haloalkyl group,

(g) a C_{1-4} alkylamino group,

(h) a di(C_{1-4} alkyl)amino group,

(i) a C_{1-6} alkylthio group,

(j) a C_{1-4} alkoxy group,

(k) a C_{1-4} alkylcarbonyl group and

(l) an aryl group optionally substituted by a halogen atom or a C_{1-4} haloalkyl group,

(4) an indanyl group or

(5) a piperazinyl group

wherein said piperazinyl group is optionally substituted by substituent(s) selected from the group consisting of

(a) a phenyl group,

(b) a phenyl C_{1-4} alkyl group,

(c) a benzoyl group optionally substituted by a halogen atom and

(d) a phenyl C_{1-4} alkoxycarbonyl group

or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

3. The 5-membered heteroaromatic ring compound of claim 1, wherein, in the formula [I],

R^3 is

(1) a hydrogen atom,

(2) a halogen atom,

(3) a C_{1-6} alkyl group or

(4) a C_{1-4} alkoxy group;

Y is $-O-$, $-N(R^{11})-$, $-N(R^{12})-CO-$, $-C(R^{13})(R^{14})-$, $-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$

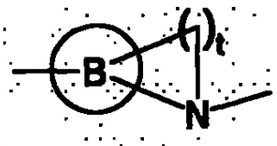
wherein

R^{11} is

(1) a hydrogen atom,

(2) a C_{1-8} alkyl group, or

(3) optionally linked with R^3 to form



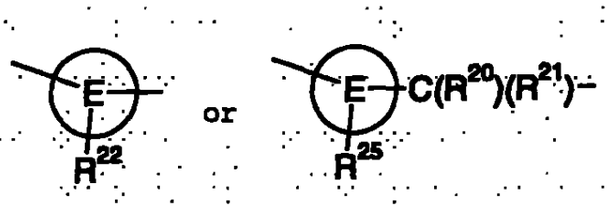
wherein t is 3 and B is as defined in claim 2 above,

R^{12} is a hydrogen atom or a C_{1-8} alkyl group,

R^{13} and R^{14} are each a hydrogen atom

provided that

when m is 0, p is 1, and L is



wherein R^{20} and R^{21} are each a hydrogen atom, E is a phenyl group, R^{22} is a hydrogen atom, a C_{1-4} alkoxy group or a nitro group, and R^{25} is a hydrogen atom, a C_{1-4} alkoxy group or a nitro group,

Y should be

$-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$ wherein R^{12}, R^{13} and R^{14} are as defined above;

s is 0 or 1;

A is a C_{1-4} alkylene group;

Z is an aryl group substituted by substituent(s) selected from the group consisting of

(a) a C_{3-7} cycloalkyl group optionally substituted by 1 to 3 substituent(s) selected from the group consisting of a halogen atom and a C_{1-6} alkyl group,

(b) a halogen atom,

(c) C_{1-8} alkyl group,

(d) a C_{1-4} haloalkyl group,

(e) a di(C_{1-4} alkyl)amino group,

(f) a C_{1-6} alkylthio group and

(g) a C_{1-4} alkylcarbonyl group,

or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

4. The 5-membered heteroaromatic ring compound of claim 3, wherein V is =N- and W is -S- or -O-, or V is =CH- and W is -S-, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

5. The 5-membered heteroaromatic ring compound of claim 4, wherein Z is a phenyl group substituted by a C_{1-8} alkyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

6. The 5-membered heteroaromatic ring compound of claim 5, wherein Y is $-C(R^{13})(R^{14})-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$ wherein R^{12}, R^{13} and R^{14} are as defined in claim 3 and s is 0, or Y is -O- or $-N(R^{11})-$ wherein R^{11} is as defined in claim 3, s is 1, and A is a methylene group, or a prodrug thereof, or a pharmaceutically

acceptable salt thereof.

7. The 5-membered heteroaromatic ring compound of claim 6, wherein V is =CH-, W is -S-, and the position of substitution of B on the thiophene ring formed by V together with W is the 4-position or 5-position, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

8. The 5-membered heteroaromatic ring compound of claim 7, wherein B is a phenyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

9. The 5-membered heteroaromatic ring compound of claim 8, wherein

m is 1;

R^1 and R^2 are each a hydrogen atom;

X is $-N(R^4)-$ or $-O-$

wherein R^4 is a C_{1-6} alkyl group optionally substituted by

(a) an aryl group,

(b) an heteroaromatic ring group optionally substituted by 1 to 3 C_{1-8} alkyl groups or

(c) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom or an aryl group wherein said aryl group is optionally substituted by 1 to 3 C_{1-8} alkyl groups;

n is 0 or 1;

p is 0 or 1;

L is

(1)

$-C(R^{20})(R^{21})-$

wherein R^{20} is linked with R^4 to form



wherein u is 1, v is 1 and R^2 is as defined above,

R^{21} is a hydrogen atom, or

(2)



wherein E is an heteroaromatic ring group and R^{22} is a hydrogen atom;

R is $-COO(R^{19})$

wherein R^{19} is a hydrogen atom, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

10. The 5-membered heteroaromatic ring compound of claim 9, wherein X is $-N(R^4)$ wherein R^4 is as defined in claim 9, n is 1 and p is 0, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

11. The 5-membered heteroaromatic ring compound of claim 10, wherein R^4 is a methyl group substituted by a heteroaromatic ring group optionally substituted by one C_{1-8} alkyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

12. The 5-membered heteroaromatic ring compound of claim 11, wherein the heteroaromatic ring defined in claim 11 is a thiazolyl group, an oxazolyl group or a benzimidazolyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

13. The 5-membered heteroaromatic ring compound of claim 10, wherein R^4 is a methyl group substituted by $-CO-N(R^{15})(R^{16})$ wherein R^{15} is a hydrogen atom and R^{16} is an aryl group optionally substituted by one C_{1-8} alkyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

14. The 5-membered heteroaromatic ring compound of claim 6, wherein V is =N-, W is -S-, and the position of substitution of B on the thiazole ring formed by V together with W is the 4-position, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

15. The 5-membered heteroaromatic ring compound of claim 14, wherein B is a phenyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

16. The 5-membered heteroaromatic ring compound of claim 15, wherein

m is 0 or 1;

R^1 and R^2 are each independently a hydrogen atom or a C_{1-4} alkyl group;

X is $-N(R^4)-$, $-N(R^5)-CO-O-$, $-SO_2-N(R^5)-$, $-CO-N(R^7)-$, $-N(R^9)-CO-N(R^5)-$, $-N(R^{10})-(CH_2)_k-N(R^5)-$, $-O-$, $-S-$ or $-SO_2-$

wherein

R^4 is

(1) a hydrogen atom,

(2) a C_{1-6} alkyl group

wherein said C_{1-6} alkyl group is optionally substituted by

(a) an aryl group optionally substituted by 1 to 3 substituent(s) selected from the group consisting of a halogen atom, a C_{1-8} alkyl group and a C_{1-4} haloalkyl group,

(b) a heteroaromatic ring group optionally substituted by 1 to

3 C_{1-8} alkyl group,

(c) a carboxy group,

(d) a C_{1-4} alkoxycarbonyl group,

(e) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom, an aryl group wherein said aryl group is optionally substituted by 1 to 3 substituent(s) selected from the group consisting of a C_{1-8} alkyl group, a C_{1-4} alkoxy group, a carboxy group and a di(C_{1-4} alkyl)amino group, a heteroaromatic ring group, a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by an aryl group, or, together with the nitrogen atom bonded thereto, may form a 5- to 7-membered hetero ring optionally further containing at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom,

(f) $-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom or an aryl group,

(g) $-O-R^{17}$

wherein R^{17} is an aryl group, or

(h) a C_{3-7} cycloalkyl group,

(3) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom, an aryl group wherein said aryl group is optionally substituted by 1 to 3 C_{1-8} alkyl groups, a C_{1-6} alkyl group, or, together with the nitrogen atom bonded thereto, may form an indoline ring or may form a 5- to 7-membered hetero ring optionally further containing at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom,

(4) $-SO_2-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently an aryl group or a C_{1-6} alkyl group,

(5) $-CO-R^{17}$

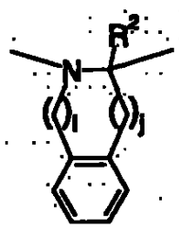
wherein R^{17} is an aryl group wherein said aryl group is optionally substituted by 1 to 3 substituent(s) selected from the group consisting of a C_{1-8} alkyl group and a C_{1-4} alkoxy group, a heteroaromatic ring group or a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by an aryl group optionally substituted by 1 to 3 substituent(s) selected from the group consisting of a halogen atom and a C_{1-8} alkyl group, a heteroaromatic ring group, a C_{1-4} alkoxy group optionally substituted by an aryl group or an aryloxy group optionally substituted by 1 to 3 C_{1-8} alkyl groups,

(6) $-SO_2-R^{17}$

wherein R^{17} is an aryl group,

(7) an aryl group, or

(8) optionally linked with R^1 to form



wherein i and j are each 1 and R^2 is as defined above,

R^5 is a hydrogen atom or a C_{1-6} alkyl group optionally substituted by an aryl group or a C_{3-7} cycloalkyl group,

R^7 is a hydrogen atom or a C_{1-6} alkyl group,

R^9 is a hydrogen atom or a C_{1-6} alkyl group,

k is 2,

R^{10} is

(1) a hydrogen atom,

(2) a C_{1-6} alkyl group, or

(3) optionally linked with R^5 to form



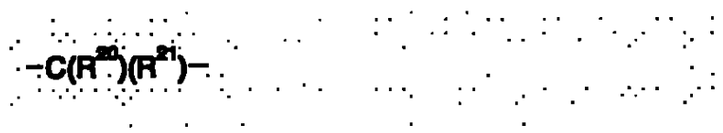
wherein k1 and c are each 2;

n is 0 or an integer of 1 to 3;

p is 0 or 1;

L is

(1)



wherein

R^{20} is

(a) a hydrogen atom,

(b) a C_{1-6} alkyl group, or

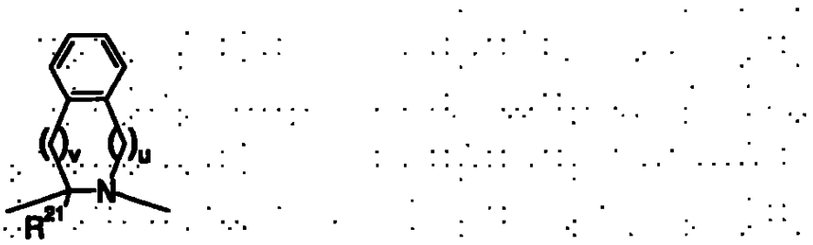
(c) optionally linked with R^4 to form



wherein n1 and q are each independently an integer of 1 to 3,

or

(d) optionally linked with R^4 to form



wherein u is 1 and v is 1,

R^{21} is a hydrogen atom, a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by an aryl group optionally substituted by 1 to 3 halogen atoms, or an aryl

group or

(2)



wherein

E is an aryl group or a heteroaromatic ring group,

R^{22} is

(a) a hydrogen atom,

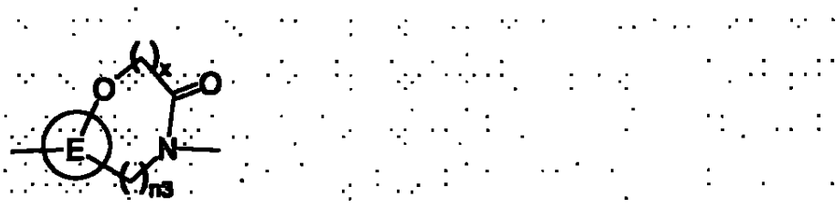
(b) a C_{1-4} alkoxy group optionally substituted by a carboxy group,

(c) a nitro group,

(d) $-N(R^{23})(R^{24})$

wherein R^{23} and R^{24} are each independently a hydrogen atom, a C_{1-4} alkylcarbonyl group wherein said C_{1-4} alkylcarbonyl group is optionally substituted by a C_{1-4} alkylamino group or a di(C_{1-4} alkyl)amino group or a C_{1-4} alkylsulfonyl group, or

(e) optionally linked with R^4 to form



wherein n3 is 0, x is 1 and E is as defined above;

R is $-COO(R^{19})$

wherein R^{19} is a hydrogen atom or a C_{1-4} alkyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

17. The 5-membered heteroaromatic ring compound of claim 16, wherein m is 1 and R^1 and R^2 are each a hydrogen atom, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

18. The 5-membered heteroaromatic ring compound of claim 17, wherein X is $-N(R^4)$ wherein R^4 is as defined in claim 16, n is 1 and p is 0, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

19. The 5-membered heteroaromatic ring compound of claim 18, wherein

R^4 is a C_{1-6} alkyl group optionally substituted by

(a) an aryl group optionally substituted by 1 to 3 substituent(s) selected from the group consisting of a halogen atom, a C_{1-8} alkyl group and a C_{1-4} haloalkyl group,

(b) a heteroaromatic ring group optionally substituted by 1 to 3 C_{1-8} alkyl groups,

(c) a carboxy group,

(d) a C_{1-4} alkoxycarbonyl group,

(e) $-CO-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom, an aryl group wherein said aryl group is optionally substituted by 1 to 3 substituent(s) selected from the group consisting of a C_{1-8} alkyl group, a C_{1-4} alkoxy group, a carboxy group and a di(C_{1-4} alkyl)amino group, a heteroaromatic ring group, a C_{1-6} alkyl group wherein said C_{1-6} alkyl group is optionally substituted by an aryl group, or, together with the nitrogen atom bonded thereto, may form a 5- to 7-membered hetero ring optionally further containing at least one heteroatom selected from the group consisting of nitrogen atom, oxygen atom and sulfur atom,

(f) $-N(R^{15})(R^{16})$

wherein R^{15} and R^{16} are each independently a hydrogen atom or an aryl group,

(g) $-O-R^{17}$

wherein R^{17} is an aryl group, or

(h) a C_{3-7} cycloalkyl group,

or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

20. The 5-membered heteroaromatic ring compound of claim 19, wherein R^4 is a methyl group substituted by a heteroaromatic ring group optionally substituted by one C_{1-8} alkyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

21. The 5-membered heteroaromatic ring compound of claim 20, wherein the heteroaromatic ring defined in claim 20 is a thiazolyl group, an oxazolyl group, a benzimidazolyl group, a pyridyl group or a quinolyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

22. The 5-membered heteroaromatic ring compound of claim 19, wherein R^4 is a methyl group substituted by $-CO-N(R^{15})(R^{16})$ wherein R^{15} is a hydrogen atom and R^{16} is an aryl group optionally substituted by one C_{1-8} alkyl group, or a prodrug thereof, or a pharmaceutically acceptable salt thereof.

23. The 5-membered heteroaromatic ring compound of any of claims 1 to 22, which is selected from the group consisting of the following compounds, or a prodrug thereof, or a pharmaceutically acceptable salt thereof:

(1) 5-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}nicotinic acid;

(2) 4-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}benzoic acid;

(3) 6-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}nicotinic acid;

(4) 5-{4-[4-({methyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}nicotinic acid;

(5) 4-{4-[4-({methyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}benzoic acid;

(6) 6-[4-(4-{[(4-isopropylphenyl)(1-propylbutyl)amino]methyl}phenyl)thiazol-2-ylmethoxy]nicotinic acid;

(7) 5-[4-(4-{[(4-isopropylphenyl)(1-propylbutyl)amino]methyl}phenyl)thiazol-2-ylmethoxy]nicotinic acid;

(8) 5-[4-(4-{[isobutyl(4-isopropylphenyl)amino]methyl}phenyl)thiazol-2-ylmethoxy]nicotinic acid;

(9) 4-[4-(4-{[(4-isopropylphenyl)(1-propylbutyl)amino]methyl}phenyl)thiazol-2-ylmethoxy]benzoic acid;

(10) 3-[4-(4-{[(4-isopropylphenyl)(1-propylbutyl)amino]methyl}phenyl)thiazol-2-ylmethoxy]benzoic acid;

(11) 6-[4-(4-{[(1-ethylpropyl)(4-isopropylphenyl)amino]methyl}phenyl)thiazol-2-ylmethoxy]nicotinic acid;

(12) 5-[4-(4-{[(1-ethylpropyl)(4-isopropylphenyl)amino]methyl}phenyl)thiazol-2-ylmethoxy]nicotinic acid;

(13) 4-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethylthio}benzoic acid;

(14) 4-{4-[4-({methyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethylthio}benzoic acid;

(15) 4-(methyl-{4-[4-({methyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}sulfamoyl)benzoic acid;

(16) sodium 4-(methyl{4-[4-({methyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}sulfamoyl)butyrate;

(17) 4-{[(4-{4-[(4-cyclohexylphenylamino)methyl]phenyl}thiazol-2-yl)methylamino]methyl}benzoic acid;

(18) 4-({[4-(4-[[(4-cyclohexylphenyl)methylamino]methyl}phenyl)thiazol-2-yl]methylamino}methyl)benzoic acid;

(19) 4-[(methyl-{4-[4-({methyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-yl}amino)methyl]benzoic acid;

(20) 4-[({4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-yl}methylamino)methyl]benzoic acid;

(21) (S)-({4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}methylamino)phenylacetic acid;

(22) (S)-2-({4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}methylamino)-3-phenylpropionic acid;

(23) {benzyl[4-(4-{[(4-tert-butylphenyl)isobutylamino]methyl}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(24) {benzyl[4-(4-{[(4-chloro-phenyl)isobutylamino]methyl}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(25) (benzyl{4-[4-({methyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(26) (benzyl{4-[4-({[4-(1-

ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(27) {1-[4-(4-{[(4-tert-butylphenyl)isobutylamino]methyl}phenyl)thiazol-2-ylmethyl]-3-phenylureido}acetic acid;

(28) {benzoyl-[4-(4-{[(4-tert-butylphenyl)isobutylamino]methyl}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(29) [[4-(4-{[(4-tert-butylphenyl)isobutylamino]methyl}phenyl)thiazol-2-ylmethyl]-(pyridin-2-ylcarbonyl)amino]acetic acid;

(30) [[4-(4-{[(4-tert-butylphenyl)isobutylamino]methyl}phenyl)thiazol-2-ylmethyl]-(pyridin-3-ylcarbonyl)amino]acetic acid;

(31) {benzenesulfonyl-[4-(4-{[(4-tert-butylphenyl)isobutylamino]methyl}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(32) 2-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(33) (S)-2-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(34) (S)-2-{4-[4-({methyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(35) (S)-2-[4-(4-{[(1-ethylpropyl)-(4-isopropylphenyl)amino]methyl}phenyl)thiazol-2-ylmethyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(36) 4-({4-[4-(4-cyclohexylphenoxymethyl)phenyl]thiazol-2-yl}methylamino)benzoic acid;

(37) 4-[({4-[4-(4-cyclohexylphenoxymethyl)phenyl]thiazol-2-yl}methylamino)methyl]benzoic acid;

(38) 4-{[(4-{4-[4-(1,1-dimethylpropyl)phenoxymethyl]phenyl}thiazol-2-yl)methylamino]methyl}benzoic acid;

(39) 4-{[methyl-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-yl)amino]methyl}benzoic acid;

(40) sodium 4-{[methyl(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-yl)amino]methyl}-benzoate;

(41) (S)-[methyl-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]phenylacetic acid;

(42) (S)-2-[methyl-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]-3-phenylpropionic acid;

(43) (benzyl{4-[4-(2-tert-butyl-4-methyl-phenoxymethyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(44) [benzyl(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(45) 2-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(46) (S)-2-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(47) (R)-2-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(48) 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethoxy)nicotinic acid;

(49) 4-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethoxy)benzoic acid;

(50) 4-[methyl-(4-{4-[4-(1-

propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)sulfamoyl]benzoic acid;

(51) 4-[methyl-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)sulfamoyl]butyric acid;

(52) 4-({4-[4-(4-cyclohexylphenylcarbamoyl)phenyl]thiazol-2-yl}methylamino)benzoic acid;

(53) 4-[({4-[4-(4-cyclohexylphenylcarbamoyl)phenyl]thiazol-2-yl}methylamino)methyl]benzoic acid;

(54) [benzyl(4-{4-[4-(1-propylbutyl)phenylcarbamoyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(55) [benzyl(4-{4-[4-(1-propylbutyl)benzylcarbamoyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(56) {benzyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]-carbamoyl}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(57) {benzyl[4-(4-{ethyl-[4-(1-propylbutyl)benzyl]-carbamoyl}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(58) 5-{4-[4-({(2-hydroxy-2-methylpropyl)-[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}nicotinic acid;

(59) [[4-(4-{[(4-tert-butyl-phenyl)isobutylamino]methyl}phenyl)thiazol-2-ylmethyl]-(morpholine-4-carbonyl)amino]acetic acid;

(60) sodium 5-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}-nicotinate;

(61) sodium (S)-2-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylate;

(62) sodium 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-

ylmethoxy)nicotinate;

(63) 3-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}-5-methoxy-benzoic acid;

(64) (1-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-3-phenylureido)acetic acid;

(65) (1-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-3-p-tolylureido)acetic acid;

(66) [1-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-3-(4-isopropylphenyl)ureido]acetic acid;

(67) (1-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-3-methyl-3-phenylureido)acetic acid;

(68) 5-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}nicotinic acid;

(69) [3-phenyl-1-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)ureido]acetic acid;

(70) (3-(2,6-dimethylphenyl)-1-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}ureido)acetic acid;

(71) ({4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}phenylcarbamoylmethylamino)acetic acid;

(72) (1-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-3-isopropyl-ureido)acetic acid;

(73) 3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}-

isoxazole-5-carboxylic acid;

(74) 5-[4-(4-{[(2-ethylbutyl)-(4-isopropylphenyl)amino]methyl}phenyl)thiazol-2-ylmethoxy]nicotinic acid;

(75) [{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-(piperidine-1-carbonyl)amino]acetic acid;

(76) 2-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethoxy)nicotinic acid;

(77) [{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-(p-tolylcarbamoylmethyl)amino]acetic acid;

(78) {{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-[(4-isopropylphenylcarbamoyl)methyl]amino}acetic acid;

(79) (1-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-3-methyl-3-phenylureido)acetic acid;

(80) (1-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-3-p-tolylureido)acetic acid;

(81) {(2,3-dihydro-indole-1-carbonyl)-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(82) 3-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethoxy)pyridine-2-carboxylic acid;

(83) {[4-(4-{[(2-ethylbutyl)-(4-isopropylphenyl)amino]methyl}phenyl)thiazol-2-ylmethyl]phenylcarbamoylmethylamino}acetic acid;

(84) {[4-(4-{[(2-ethylbutyl)-(4-isopropylphenyl)amino]methyl}phenyl)thiazol-2-ylmethyl]-[(4-isopropylphenylcarbamoyl)methyl]amino}acetic acid;

(85) 4-(2-{carboxymethyl[4-(4-{[(2-ethylbutyl)-(4-isopropylphenyl)amino]methyl}phenyl)thiazol-2-ylmethyl]amino}-acetylamino)benzoic acid;

(86) 6-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethoxy)pyridine-2-carboxylic acid;

(87) 5-{4-[4-({isobutyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}nicotinic acid;

(88) (1-{4-[4-({isobutyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-3-phenylureido)acetic acid;

(89) 5-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}nicotinic acid methyl ester;

(90) 4-amino-3-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}benzoic acid;

(91) 3-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}benzoic acid;

(92) 3-({4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}amino)benzoic acid;

(93) 3-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethoxy}-4-nitro-benzoic acid;

(94) ((1H-benzimidazol-2-ylmethyl)-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(95) [phenylcarbamoylmethyl(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(96) [(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-

ylmethyl)-(pyridin-3-ylcarbamoylmethyl)amino]acetic acid;
(97) [[(4-dimethylaminophenylcarbamoyl)methyl]-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;
(98) [[(4-methoxyphenylcarbamoyl)methyl]-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;
(99) [[(isopropylphenylcarbamoyl)methyl]-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;
(100) [(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-(pyridin-2-ylcarbamoylmethyl)amino]acetic acid;
(101) [(2-oxo-2-pyrrolidin-1-yl-ethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;
(102) [(4-methylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;
(103) 4-(3-cyclohexylmethyl-3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}ureido)benzoic acid;
(104) 4-(3-isobutyl-3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}ureido)benzoic acid;
(105) (1-{4-[4-({isobutyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-3-methyl-3-phenylureido)acetic acid;
(106) ({4-[4-({isobutyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}phenylcarbamoylmethylamino)acetic acid;
(107) {{4-[4-({isobutyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-[(4-isopropylphenylcarbamoyl)methyl]amino}acetic acid;

(108) 4-acetylamino-3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}benzoic acid;

(109) 4-(2-dimethylaminoacetylamino)-3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}benzoic acid;

(110) ((1H-benzimidazol-2-ylmethyl)-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(111) [(1H-benzimidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(112) 3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}-4-methanesulfonylaminobenzoic acid;

(113) 4-isobutyrylamino-3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}benzoic acid;

(114) 4-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazine-6-carboxylic acid;

(115) 4-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-3-oxo-3,4-dihydro-2H-benzo[1,4]oxazine-8-carboxylic acid;

(116) ({4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-{methylphenylaminosulfonyl}amino)acetic acid;

(117) ([(4-isopropylphenylcarbamoyl)methyl]-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(118) ([(3,5-dimethylphenylcarbamoyl)methyl]-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(119) ([(4-dimethylaminophenylcarbamoyl)methyl]-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(120) ((benzylcarbamoylmethyl)-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(121) [{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-[2-(morpholin-4-yl)-2-oxo-ethyl]amino]acetic acid;

(122) [{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-(2-phenoxyethyl)amino]acetic acid;

(123) [{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-(2-phenylamino-ethyl)amino]acetic acid;

(124) 2-carboxymethoxy-5-({4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}methylamino)benzoic acid;

(125) 2-carboxymethoxy-5-[methyl(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]benzoic acid;

(126) 3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}-4-(2-methylamino-acetylamino)benzoic acid;

(127) [(4-tert-butylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(128) [phenyl(4-{4-[4-(1-

propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(129) [(2-phenoxyacetyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(130) [(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-(2-p-tolyloxy-acetyl)amino]acetic acid;

(131) (ethoxycarbonylmethyl{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid dihydrochloride;

(132) ((4-tert-butylthiazol-2-ylmethyl)-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(133) 6-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethoxy}-pyridine-2-carboxylic acid;

(134) [(2-benzyloxy-acetyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(135) [[2-(4-isopropylphenoxy)acetyl]-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(136) [(4,5-dimethylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(137) 5-(4-{5-[4-(1-propylbutyl)phenoxymethyl]thiophen-2-yl}thiazol-2-ylmethoxy)nicotinic acid;

(138) ((4-tert-butylthiazol-2-ylmethyl)-{4-[6-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)benzoxazol-2-yl]thiazol-2-ylmethyl}amino)acetic acid;

(139) ((1H-benzimidazol-2-ylmethyl)-{4-[6-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)benzoxazol-2-yl]thiazol-2-ylmethyl}amino)acetic acid;

(140) 5-{4-[6-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)benzoxazol-2-yl]thiazol-2-ylmethoxy}nicotinic acid;

(141) [(5-tert-butylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(142) [{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-(2-oxo-2-piperidin-1-yl-ethyl)amino]acetic acid;

(143) 6-[methyl-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]pyridine-2-carboxylic acid;

(144) ({4-[6-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)benzoxazol-2-yl]thiazol-2-ylmethyl}amino)acetic acid;

(145) (S)-(carboxymethyl{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)phenylacetic acid;

(146) ((4,5-dimethylthiazol-2-ylmethyl)-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(147) [(5-tert-butyloxazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(148) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(149) (isobutoxycarbonylmethyl{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid dihydrochloride;

(150) ({4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}-propoxycarbonylmethylamino)acetic acid dihydrochloride;

(151) 1-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)piperidine-4-carboxylic acid hydrochloride;

(152) 1-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}piperidine-4-carboxylic acid;

(153) 4-[4-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)piperazin-1-yl]benzoic acid;

(154) 4-(4-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-piperazin-1-yl)benzoic acid;

(155) 2-[4-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)piperazin-1-yl]benzoic acid;

(156) 3-[4-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)piperazin-1-yl]benzoic acid;

(157) 4-(4-{1-[4-(1-propylbutyl)benzyl]-1H-indol-3-yl}thiazol-2-ylmethoxy)benzoic acid;

(158) 4-{4-[1-(4-isopropylbenzyl)-5-(1-propylbutyl)-1H-benzimidazol-2-yl]thiazol-2-ylmethoxy}benzoic acid;

(159) 4-{4-[1-(6-methylpyridin-2-ylmethyl)-5-(1-propylbutyl)-1H-benzimidazol-2-yl]thiazol-2-ylmethoxy}benzoic acid;

(160) 2-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid;

(161) 4-[1-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)piperidin-4-yl]benzoic acid;

(162) 3-[1-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)piperidin-4-yl]benzoic acid;

(163) 6-[(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)carbamoyl]nicotinic acid;

(164) 2-[1-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)piperidin-4-yl]benzoic acid;

(165) 1-(4-{1-[4-(1-propylbutyl)benzyl]-1H-indol-3-yl}thiazol-2-ylmethyl)piperidine-4-carboxylic acid;

(166) 2-(4-{1-[4-(1-propylbutyl)benzyl]-1H-indol-3-yl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid;

(167) 3-[(4-{1-[4-(1-propylbutyl)benzyl]-1H-indol-3-yl}thiazol-2-ylmethyl)amino]benzoic acid;

(168) 6-[(2-aminoethyl)(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)carbamoyl]nicotinic acid hydrochloride;

(169) 2-(4-{1-[4-(1-propylbutyl)benzyl]-1H-benzimidazol-2-yl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid;

(170) 3-[4-(4-{1-[4-(1-propylbutyl)benzyl]-1H-benzimidazol-2-yl}thiazol-2-ylmethyl)piperazin-1-yl]benzoic acid;

(171) 4-[1-(4-{1-[4-(1-propylbutyl)benzyl]-1H-benzimidazol-2-yl}thiazol-2-ylmethyl)piperidin-4-yl]benzoic acid;

(172) 3-[4-(4-{1-[4-(1-propylbutyl)benzyl]-1H-indol-3-yl}thiazol-2-ylmethyl)piperazin-1-yl]benzoic acid;

(173) 3-(1-{4-[4-(3,4-dichloro-benzyloxy)phenyl]thiazol-2-ylmethyl}piperidin-4-yl)benzoic acid;

(174) 3-(1-{4-[4-(3,5-bis-trifluoromethylbenzyloxy)phenyl]thiazol-2-ylmethyl}piperidin-4-yl)benzoic acid;

(175) 3-(1-{4-[4-(4-butoxy-benzyloxy)phenyl]thiazol-2-ylmethyl}piperidin-4-yl)benzoic acid;

(176) 5-methyl-2-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-2H-pyrazole-3-carboxylic acid;

(177) 5-methyl-1-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-1H-pyrazole-3-carboxylic acid;

(178) 5-tert-butyl-1-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-1H-pyrazole-3-carboxylic acid;

(179) 5-tert-butyl-2-(4-{4-[4-(1-

propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-2H-pyrazole-3-carboxylic acid;

(180) (2S,4R)-4-hydroxy-1-(4-{1-[4-(1-propylbutyl)benzyl]-1H-indol-3-yl}thiazol-2-ylmethyl)pyrrolidine-2-carboxylic acid;

(181) 4-[4-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)piperidin-1-yl]benzoic acid;

(182) 1-(4-{1-[4-(1-propylbutyl)benzyl]-1H-indol-3-yl}thiazol-2-ylmethyl)-1H-indole-3-carboxylic acid;

(183) 1-(4-{2-phenyl-1-[4-(1-propylbutyl)benzyl]-1H-indol-3-yl}thiazol-2-ylmethyl)piperidine-4-carboxylic acid;

(184) 3-(1-{4-[4-(4-methyl-3-nitrobenzyloxy)phenyl]thiazol-2-ylmethyl}piperidin-4-yl)benzoic acid;

(185) 2-{4-[1-(4-isopropylbenzyl)-6-(morpholin-4-yl)-1H-benzimidazol-2-yl]thiazol-2-ylmethyl}-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid;

(186) 3-(4-{4-[1-(4-isopropylbenzyl)-6-(morpholin-4-yl)-1H-benzimidazol-2-yl]thiazol-2-ylmethyl}-piperazin-1-yl)benzoic acid;

(187) {benzyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)oxazol-2-ylmethyl]amino}acetic acid;

(188) 5-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethoxy)nicotinic acid;

(189) 4-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethoxy)benzoic acid;

(190) 4-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethylthio)benzoic acid;

(191) 4-{4-[4-(4-cyclohexylbenzyloxy)phenyl]thiazol-2-ylmethylthio}benzoic acid;

(192) 4-{4-[4-(4-cyclohexylbenzyloxy)phenyl]thiazol-2-ylmethanesulfonyl}benzoic acid;

(193) 4-[methyl-(4-{5-methyl-2-[4-(1-

propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)sulfamoyl]benzoic acid;

(194) 4-[methyl-(4-{5-methyl-2-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]benzoic acid;

(195) (benzyl{4-[5-methyl-2-(4-trifluoromethylbenzyloxy)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(196) [benzyl(4-{5-methyl-2-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(197) [benzyl(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(198) [benzyl(4-{4-[4-(1-ethylpropyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(199) (benzyl{4-[5-tert-butyl-2-(4-isobutylbenzyloxy)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(200) [benzyl(4-{5-chloro-2-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(201) [(4-{4-[4-(1-ethylpropyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-(4-fluoro-benzyl)amino]acetic acid;

(202) [(4-{4-[4-(1-ethylpropyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-(4-isopropylbenzyl)amino]acetic acid;

(203) [(4-{4-[4-(1-ethylpropyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-(4-trifluoromethylbenzyl)amino]acetic acid;

(204) [(4-chlorobenzyl)-(4-{4-[4-(1-ethylpropyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(205) [(3,5-dimethylbenzyl)-(4-{4-[4-(1-ethylpropyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(206) [(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-

ylmethyl)-pyridin-2-ylmethylamino]acetic acid;

(207) [(4-{4-[4-(1-ethylpropyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-pyridin-2-ylmethylamino]acetic acid;

(208) [(4-{5-methyl-2-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-pyridin-2-ylmethylamino]acetic acid;

(209) [benzoyl-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(210) [(4-{4-[4-(1-ethylpropyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-(4-methylbenzoyl)amino]acetic acid;

(211) [(4-methoxybenzoyl)-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(212) 2-(4-{5-methyl-2-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(213) (S)-2-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(214) {benzyl[4-(4-{[4-(2,2-dimethylpropyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(215) {benzyl[4-(4-{[trans-4-(4-tert-butylphenyl)-cyclohexylmethyl]methylamino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(216) [benzyl(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(217) 3-[benzyl(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]propionic acid;

(218) (benzyl{4-[4-({2-[4-(2,2-dimethylpropyl)phenyl]-ethyl}methylamino)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(219) {benzyl[4-(4-{methyl[4-(trans-4-methyl-cyclohexyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(220) {benzyl[4-(4-{[4-(cis-4-fluoro-cyclohexyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(221) {benzyl[4-(4-{[trans-4-(4-chlorophenyl)-cyclohexylmethyl]methylamino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(222) {benzyl[4-(4-{[4-(4,4-dimethyl-cyclohexyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(223) {benzyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(224) (benzyl{4-[4-(biphenyl-4-ylmethylmethylamino)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(225) sodium [benzyl(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]-acetate;

(226) [benzyl(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(227) sodium {benzyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}-acetate;

(228) {benzyl[4-(4-{[4-(2,2-dimethylpropylthio)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(229) {benzyl[4-(4-{methyl[4-(3-methylbutylthio)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(230) [benzyl(4-{4-[(4-dipropylamino-benzoyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(231) [(4-{4-[ethyl(4-isopropylbenzyl)amino]phenyl}thiazol-2-ylmethyl)-(4-isopropylbenzyl)amino]acetic acid;

(232) [(4-isopropylbenzyl)-(4-{4-[isopropyl-(4-isopropylbenzyl)amino]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(233) [(4-tert-butylbenzyl)-(4-{4-[isopropyl-(4-isopropylbenzyl)amino]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(234) [(4-chlorobenzyl)-(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(235) {{4-[4-(benzylmethylamino)phenyl]thiazol-2-ylmethyl}-[4-(1-propylbutyl)benzyl]amino}acetic acid;

(236) [{4-[4-(benzylmethylamino)phenyl]thiazol-2-ylmethyl}-(4-chloro-benzyl)amino]acetic acid;

(237) [{4-[4-(benzylmethylamino)phenyl]thiazol-2-ylmethyl}-(2-chloro-benzyl)amino]acetic acid;

(238) [{4-[4-(benzylmethylamino)phenyl]thiazol-2-ylmethyl}-(3,4-dichloro-benzyl)amino]acetic acid;

(239) {[4-(4-{methyl[4-(trans-4-methyl-cyclohexyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]pyridin-2-ylmethylamino}acetic acid;

(240) {[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]pyridin-2-ylmethylamino}acetic acid;

(241) ({4-[4-(benzylmethylamino)phenyl]thiazol-2-ylmethyl}-naphthalen-1-ylmethylamino)acetic acid;

(242) ({4-[4-(benzylmethylamino)phenyl]thiazol-2-ylmethyl}-quinolin-2-ylmethylamino)acetic acid;

(243) ((2-benzo[b]thiophen-3-yl-acetyl)-{4-[4-

(benzylmethylamino)phenyl]thiazol-2-ylmethyl}amino)acetic acid;
(244) [[2-(4-chlorophenyl)acetyl]-(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]acetic acid;
(245) {(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-[2-(4-isopropylphenyl)acetyl]amino}acetic acid;
(246) [(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-(3-methyl-butyryl)amino]acetic acid;
(247) {1-[4-(4-{[4-(2,2-dimethylpropyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]-3-phenylureido}acetic acid;
(248) [benzoyl-(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]acetic acid;
(249) {(4-methylbenzoyl)-[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;
(250) sodium {(4-isopropylbenzoyl)-[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}-acetate;
(251) sodium (S)-{3-[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-yl]-3,4-dihydro-1H-isoquinolin-2-yl}-acetate;
(252) 1-(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)piperidine-4-carboxylic acid;
(253) 1-(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)piperidine-3-carboxylic acid;
(254) 1-(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-4-phenylpiperidine-4-carboxylic acid;
(255) 1-(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-4-(3-methylbutyl)piperidine-4-carboxylic acid;
(256) 1-[4-(4-{methyl[4-(trans-4-methyl-cyclohexyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]-4-

phenylpiperidine-4-carboxylic acid;

(257) 1-[4-(4-{[trans-4-(4-chloro-phenyl)-cyclohexylmethyl]methylamino}phenyl)thiazol-2-ylmethyl]-4-phenylpiperidine-4-carboxylic acid;

(258) 2-[4-(4-{methyl[4-(trans-4-methyl-cyclohexyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(259) 2-(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(260) 2-[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(261) 2-[4-(4-{[4-(2,2-dimethylpropyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(262) 5-{[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-yl)methylamino]methyl}furan-2-carboxylic acid;

(263) 2-[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]-3-phenylpropionic acid;

(264) [(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]phenylacetic acid;

(265) 2-[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]propionic acid;

(266) 3-(4-chlorophenyl)-2-[(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)amino]propionic acid;

(267) [(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylamino]acetic acid;

(268) 3-[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylamino]propionic acid;

(269) 4-{[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-

ylmethyl)methylamino]methyl}benzoic acid;

(270) 4-[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylamino]benzoic acid;

(271) 6-[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylamino]nicotinic acid;

(272) 2-[(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylamino]-3-phenylpropionic acid;

(273) (S)-2-{methyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}-3-phenylpropionic acid;

(274) (S)-{methyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}phenylacetic acid;

(275) {[4-(4-{[4-(2,2-dimethylpropyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]methylamino}phenylacetic acid;

(276) 2-{[4-(4-{[4-(2,2-dimethylpropyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]methylamino}-3-phenylpropionic acid;

(277) {carboxymethyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(278) [(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-(3-methylbutyl)amino]acetic acid;

(279) {(3-methylbutyl)-[4-(4-{methyl[4-(trans-4-methylcyclohexyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(280) [(4-{4-[(4-isobutylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-(3-methylbutyl)amino]acetic acid;

(281) 5-[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethoxy]nicotinic acid;

(282) 4-[4-(4-{methyl[4-(1-

propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethoxy]benzoic acid;

(283) 4-[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethylthio]benzoic acid;

(284) 4-[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)sulfamoyl]benzoic acid;

(285) 4-{[4-(4-{[4-(4,4-dimethyl-cyclohexyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]methylsulfamoyl}benzoic acid;

(286) {[4-(4-{[4-(4,4-dimethyl-cyclohexyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]methylsulfamoyl}acetic acid;

(287) 4-[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylsulfamoyl]benzoic acid;

(288) 3-[(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylsulfamoyl]benzoic acid;

(289) [(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)methylsulfamoyl]acetic acid;

(290) 4-{[4-(4-{[4-(4,4-dimethyl-cyclohexyl)benzyl]methylamino}phenyl)thiazol-2-ylmethyl]methylsulfamoyl}butyric acid;

(291) [(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)isobutyl-sulfamoyl]acetic acid;

(292) N-(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)oxamic acid;

(293) {benzyl[4-(4-{[4-(1-propylbutyl)benzyl]methylamino-carbonyl}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(294) N-(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-N-methylterephthalamic acid;

(295) {benzyl[4-(4-{methyl[4-(trans-4-methyl-cyclohexyl)benzyl]amino}phenyl)thiazol-2-ylmethoxycarbonyl]amino}acetic acid;

(296) [3-(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)-3-methyl-ureido]acetic acid;

(297) (cyclohexylmethyl{4-[6-(3,4-dichlorobenzyloxy)benzoxazol-2-yl]thiazol-2-yl}amino)acetic acid;

(298) [4-(4-{4-[(4-cyclohexylbenzyl)methylamino]phenyl}thiazol-2-ylmethyl)piperazin-1-yl]acetic acid;

(299) sodium (S)-2-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylate;

(300) sodium 5-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethoxy)nicotinate;

(301) 5-(4-{2-methyl-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethoxy)nicotinic acid;

(302) 5-(4-{3-methoxy-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethoxy)nicotinic acid;

(303) [(4-{2-methyl-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)phenylcarbamoylmethylamino]acetic acid;

(304) [[(4-isopropylphenylcarbamoyl)methyl]-(4-{2-methyl-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(305) 2-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(306) [(4-{3-methoxy-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)phenylcarbamoylmethylamino]acetic acid;

(307) [[(4-isopropylphenylcarbamoyl)methyl]-(4-{3-methoxy-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(308) [(4-{2-methyl-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)thiazol-4-

ylmethylamino]acetic acid;

(309) [(4-{2-methyl-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)-(2-methylthiazol-4-ylmethyl)amino]acetic acid hydrochloride;

(310) [(benzylcarbamoylmethyl)-(4-{2-methyl-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid hydrochloride;

(311) [(1H-benzimidazol-2-ylmethyl)-(4-{2-methyl-4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(312) [(4-tert-butylthiazol-2-ylmethyl)-(4-{1-[4-(1-propylbutyl)benzyl]-1,2,3,4-tetrahydroquinolin-6-yl}thiazol-2-ylmethyl)amino]acetic acid;

(313) 1-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)piperidine-4-carboxylic acid hydrochloride;

(314) 4-[4-(4-{4-[4-(1-propylbutyl)benzyloxy]phenyl}thiazol-2-ylmethyl)piperazin-1-yl]benzoic acid;

(315) 4-{4-[5-(1-ethylpropyl)-1-(4-isopropylbenzyl)-1H-benzimidazol-2-yl]thiazol-2-ylmethoxy}benzoic acid ethyl ester;

(316) 4-{4-[5-(1-ethylpropyl)-1-(4-isopropylbenzyl)-1H-benzimidazol-2-yl]thiazol-2-ylmethoxy}benzoic acid;

(317) 4-{4-[1-(4-acetylbenzyl)-5-(1-ethylpropyl)-1H-benzimidazol-2-yl]thiazol-2-ylmethoxy}benzoic acid;

(318) 4-{4-[1-(4-acetylbenzyl)-6-(1-ethylpropyl)-1H-benzimidazol-2-yl]thiazol-2-ylmethoxy}benzoic acid;

(319) 4-{4-[1-cyclohexylmethyl-5-(1-ethylpropyl)-1H-benzimidazol-2-yl]thiazol-2-ylmethoxy}benzoic acid;

(320) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(321) 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinic acid;

(322) 5-{4-[4-({isopropyl[4-(1-

propylbutyl)phenyl]amino}methyl)phenyl]thiophen-2-ylmethoxy}nicotinic acid;

(323) 5-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethoxy}nicotinic acid;

(324) 5-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinic acid;

(325) [(1H-benzimidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(326) 6-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)pyridine-2-carboxylic acid;

(327) [(1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(328) [[(4-isopropylphenylcarbamoyl)methyl]-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(329) [phenylcarbamoylmethyl(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(330) ({4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}phenylcarbamoylmethylamino)acetic acid;

(331) ((4-tert-butylthiazol-2-ylmethyl)-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}amino)acetic acid;

(332) [(5-tert-butylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)-amino]acetic acid;

(333) ((1H-benzimidazol-2-ylmethyl)-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}amino)acetic acid;

(334) [(4-tert-butylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(335) [phenylcarbamoylmethyl(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(336) 5-{5-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethoxy}nicotinic acid;

(337) 5-{5-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiophen-2-ylmethoxy}nicotinic acid;

(338) ((4-tert-butylthiazol-2-ylmethyl)-{5-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}amino)acetic acid;

(339) ((4-tert-butylthiazol-2-ylmethyl)-{5-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiophen-2-ylmethyl}amino)acetic acid;

(340) ((1H-benzimidazol-2-ylmethyl)-{5-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}amino)acetic acid;

(341) ((1H-benzimidazol-2-ylmethyl)-{5-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiophen-2-ylmethyl}amino)acetic acid;

(342) [(4,5-dimethylthiazol-2-ylmethyl)- (4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(343) (S)-2-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(344) {{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}-[(4-isopropylphenylcarbamoyl)methyl]amino}acetic

acid;

(345) (S)-2-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(346) [[(4-isopropylphenylcarbamoyl)methyl]-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(347) (S)-2-{5-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(348) [(5-tert-butyloxazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(349) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(350) 6-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)pyridine-2-carboxylic acid;

(351) 6-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethoxy}-pyridine-2-carboxylic acid;

(352) ((5-tert-butylthiazol-2-ylmethyl)-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}amino)acetic acid;

(353) [{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}-(1-methyl-1H-benzimidazol-2-ylmethyl)amino]acetic acid;

(354) [(4-tert-butylthiazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(355) [{5-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-

ylmethyl}-(1-methyl-1H-benzimidazol-2-ylmethyl)amino]acetic acid;

(356) [(5-tert-butylthiazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(357) sodium [(1-methyl-1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]-acetate;

(358) calcium bis{[(1-methyl-1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]-acetate};

(359) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid toluene-4-sulfonate;

(360) 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinic acid sulfate;

(361) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophene-2-carbonyl)amino]acetic acid;

(362) [(5-tert-butylthiazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophene-2-carbonyl)amino]acetic acid;

(363) [(4-isopropylbenzyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophene-2-carbonyl)amino]acetic acid;

(364) [(4-dimethylaminobenzyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophene-2-carbonyl)amino]acetic acid;

(365) [(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophene-2-carbonyl)-pyridin-2-ylmethylamino]acetic acid;

(366) [(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophene-2-carbonyl)-pyridin-3-ylmethylamino]acetic acid;

(367) 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-

2-ylmethoxy)nicotinic acid methanesulfonate;

(368) [methanesulfonyl-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(369) sodium 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinate;

(370) 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)nicotinic acid hydrochloride;

(371) 4-[4-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophene-2-carbonyl)piperazin-1-yl]benzoic acid;

(372) 4-[1-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophene-2-carbonyl)piperidin-4-yl]benzoic acid;

(373) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid hydrochloride;

(374) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid sulfate;

(375) 4-(2-dimethylaminoacetylamino)-3-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)benzoic acid;

(376) 4-isobutyrylamino-3-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)benzoic acid;

(377) 4-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)benzoic acid;

(378) 4-(methanesulfonylmethylamino)-3-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)benzoic acid;

(379) 4-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-

2-ylmethylthio)benzoic acid;

(380) 4-amino-3-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy)benzoic acid;

(381) 1-{5-[1-(4-cyclohexylbenzyl)-1H-indol-3-yl]thiophen-2-ylmethyl}-4-phenylpiperidine-4-carboxylic acid hydrochloride;

(382) (benzyl{5-[1-(4-cyclohexylbenzyl)-1H-indol-3-yl]thiophen-2-ylmethyl}amino)acetic acid hydrochloride;

(383) [(methylphenylsulfamoyl)(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(384) [(5-tert-butylthiazol-2-ylmethyl)-(5-{4-[(4-cyclohexylphenyl)methylcarbamoyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(385) [(5-{4-[(4-cyclohexylbenzyl)ethylamino]phenyl}thiophen-2-ylmethyl)pyridin-2-ylmethylamino]acetic acid;

(386) [(5-{4-[(4-cyclohexylbenzyl)ethylamino]phenyl}thiophen-2-ylmethyl)-(2-phenoxyethyl)amino]acetic acid;

(387) 4-{1-[4-(4-{[trans-4-(4-tert-butylphenyl)-cyclohexylmethyl]ethylamino}phenyl)thiophen-2-ylmethyl]piperidin-4-yl}benzoic acid;

(388) [[2-(4-isopropylphenoxy)acetyl]-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(389) [(4-isopropylbenzoyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(390) [(3-methylbutyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(391) [3-methyl-3-phenyl-1-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)ureido]acetic acid;

(392) 2-(4-{3-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid;

(393) 4-[4-(5-{4-[4-(trans-4-methylcyclohexyl)benzyloxy]phenyl}thiophen-2-ylmethyl)piperazin-1-yl]benzoic acid;

(394) [(2-chloro-5-trifluoromethylbenzyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(395) 3-{[carboxymethyl(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]methyl}benzoic acid;

(396) [(4-methoxybenzyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(397) [(4-methylthiobenzyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(398) 4-[cyclohexylmethyl(5-{4-[4-(trans-4-methylcyclohexyl)benzyloxy]phenyl}thiophen-2-ylmethyl)sulfamoyl]benzoic acid;

(399) 4-[3-cyclohexylmethyl-3-(5-{4-[4-(trans-4-methylcyclohexyl)benzyloxy]phenyl}thiophen-2-ylmethyl)ureido]benzoic acid;

(400) [benzhydryl-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(401) [[2-oxo-2-(4-pyrrolidin-1-yl-phenyl)ethyl]-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid ethyl ester hydrochloride;

(402) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid ethyl ester;

(403) 3-(benzyl{5-[1-(4-cyclohexylbenzyl)-2,3-dihydro-1H-indol-

5-yl]thiophen-2-ylmethyl}amino)propionic acid;

(404) [benzyl(4-{4-[2-(2,2-dimethylpropyl)benzimidazol-1-ylmethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(405) [(1-methyl-1H-indol-3-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(406) [(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)quinolin-2-ylmethylamino]acetic acid;

(407) [benzothiazol-2-ylmethyl(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(408) [(1-benzyl-1H-imidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(409) [(1H-indol-5-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(410) [(4-imidazol-1-ylbenzyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(411) [benzofuran-2-ylmethyl(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(412) [[2,2']bithiophenyl-5-ylmethyl(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(413) [(2-phenyl-1H-imidazol-4-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(414) [(3-phenyl-1H-pyrazol-4-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(415) [benzoxazol-2-ylmethyl(5-{4-[4-(1-

propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(416) [benzo[b]thiophen-2-ylmethyl(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(417) [(4-phenylthiophen-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(418) [benzothiazol-2-yl-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(419) [(5-chlorothiophene-2-sulfonyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(420) [(1-diethylcarbamoylmethyl-1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(421) (S)-({4-[2-(4-cyclohexylbenzyloxy)-5-methylphenyl]thiophen-2-ylmethyl}methylamino)-3-phenylpropionic acid;

(422) [benzyl(4-{4-[(4-butoxy-benzenesulfonyl)ethylamino]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(423) N-{4-[2-(4-cyclohexylbenzyloxy)-5-methylphenyl]thiophen-2-ylmethyl}-N-(2-methylbenzothiazol-6-yl)oxamic acid;

(424) (benzyl{4-[4-(3,5-dichlorophenoxymethyl)phenyl]thiophen-2-ylmethyl}amino)acetic acid;

(425) [(1-allyl-1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid; and

(426) [[4-(4-chlorophenyl)thiazol-2-yl]-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid.

24. The 5-membered heteroaromatic ring compound of any of claims 1 to 23, which is selected from the group consisting of the following compounds, or a prodrug thereof, or a pharmaceutically acceptable salt thereof:

(1) (S)-2-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(2) {{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiazol-2-ylmethyl}-[(4-isopropylphenylcarbamoyl)methyl]amino}acetic acid;

(3) 4-(3-isobutyl-3-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}ureido)benzoic acid;

(4) ({4-[4-({isobutyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}phenylcarbamoylmethylamino)acetic acid;

(5) ([(4-isopropylphenylcarbamoyl)methyl]-{4-[4-({isopropyl[4-(1-propylbutyl)phenyl]amino}methyl)phenyl]thiazol-2-ylmethyl}amino)acetic acid;

(6) [(4-tert-butylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(7) [(4,5-dimethylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(8) [(5-tert-butylthiazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(9) [[2-(4-isopropylphenoxy)acetyl]-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-2-ylmethyl)amino]acetic acid;

(10) 4-[4-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiazol-

2-ylmethyl)piperazin-1-yl]benzoic acid;

(11) {benzyl[4-(4-{methyl[4-(1-propylbutyl)benzyl]amino}phenyl)thiazol-2-ylmethyl]amino}acetic acid;

(12) [(1-methyl-1H-benzimidazol-2-ylmethyl)-5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(13) 5-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethoxy}nicotinic acid;

(14) [(1H-benzimidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(15) [(1H-benzimidazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

(16) [[(4-isopropylphenylcarbamoyl)methyl]-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid;

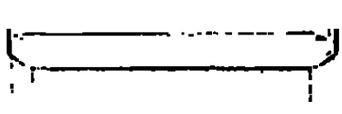
(17) (S)-2-{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid;

(18) {{4-[4-({[4-(1-ethylpropyl)phenyl]isopropylamino}methyl)phenyl]thiophen-2-ylmethyl}-[(4-isopropylphenylcarbamoyl)methyl]amino}acetic acid;

(19) [(1-methyl-1H-benzimidazol-2-ylmethyl)-(4-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid; and

(20) [(4-tert-butylthiazol-2-ylmethyl)-(5-{4-[4-(1-propylbutyl)phenoxymethyl]phenyl}thiophen-2-ylmethyl)amino]acetic acid.

25. A pharmaceutical composition comprising the 5-membered



heteroaromatic ring compound of any of claims 1 to 24, or a prodrug thereof, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

26. A pharmaceutical composition for inhibition of a receptor tyrosine kinase negative regulator, which comprises a 5-membered heteroaromatic ring compound of any of claims 1 to 24, or a prodrug thereof, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

27. A pharmaceutical composition for inhibition of protein tyrosine phosphatase 1B, which comprises a 5-membered heteroaromatic ring compound of any of claims 1 to 24, or a prodrug thereof, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

28. A pharmaceutical composition for the prophylaxis or treatment of diabetes, which comprises a 5-membered heteroaromatic ring compound of any of claims 1 to 24, or a prodrug thereof, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

29. A pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia, which comprises a 5-membered heteroaromatic ring compound of any of claims 1 to 24, or a prodrug thereof, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

30. A pharmaceutical composition for the prophylaxis or treatment of obesity, which comprises a 5-membered heteroaromatic ring compound of any of claims 1 to 24, or a prodrug thereof, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

31. A pharmaceutical composition for the prophylaxis or treatment of diabetic complications, which comprises a 5-membered heteroaromatic ring compound of any of claims 1 to 24, or a prodrug thereof, or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

32. The pharmaceutical composition of claim 25, which is used in combination with a therapeutic agent for hyperlipidemia.

33. The pharmaceutical composition of claim 32, wherein the therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of HMG-CoA reductase inhibitors (statins), fibrates, TNFSF6 expression inhibitors, HDL-cholesterol increasing agents, ApoA1 expression enhancers, SPP1 (osteopontin) expression inhibitors, drugs acting on peroxisome proliferator-activated receptors (PPAR), PPAR-alpha agonists, lipase clearing factor stimulants, cholesterol antagonists, platelet aggregation antagonists, antioxidants, cholesterol biosynthesis inhibitors, LDL-receptor up-regulators, bile acid sequestrants, cholesterol absorption inhibitors and nicotinic acids.

34. The pharmaceutical composition of claim 33, wherein the therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of lovastatin, pravastatin (eptastatin) sodium, fluvastatin (fluindostainin) sodium, rosuvastatin calcium, atorvastatin calcium, simvastatin (synvinolin), pitavastatin (itavastatin, nisvastatin) calcium, ronifibrate (ronifibrato), binifibrate (binifibrato), clinofibrate, ciprofibrate, clofibrate, etofibrate, fenofibrate, bezafibrate, gemfibrozil, acipimox, eicosapentaenoic acid (icosapent, icopenate, icosapentate)

ethyl ester, probucol, policosanol, colesevelam hydrochloride, colestyramine (cholestyramine resin), colestipol hydrochloride, colestimide (colestilan), ezetimibe and niacin (nicotinic acid).

35. The pharmaceutical composition of claim 25, which is used in combination with a therapeutic agent for diabetes.

36. The pharmaceutical composition of claim 35, wherein the therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of insulin secretagogues, biguanides, α-glucosidase inhibitors, insulin preparations, insulin analogs, insulin sensitivity enhancers, IL-11, anti-CD25 (IL-2 Receptor) agents, angiotensin (AT1) antagonists, angiotensin-converting enzyme (ACE) inhibitors, aldose reductase inhibitors, antioxidants, carnitine acetyltransferase stimulant, antidepressants, glucocorticoids, retilin, radical formation agonists and transketolase activators.

37. The pharmaceutical composition of claim 36, wherein the therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of nateglinide, glimepiride, glibenclamide, gliclazide, acetohexamide, tolbutamide, glyclopyramide, tolazamide, glybuzole, glipizide, glibornuride, gliquidone, repaglinide, metformin hydrochloride, buformin hydrochloride, voglibose, acarbose, epalrestat, miglitol, insulin, pioglitazone hydrochloride, rosiglitazone maleate, chromium picolinate/biotin, V-411, recombinant human interleukin-11, dacliximab (daclizumab), losartan potassium, captopril, imidapril hydrochloride, alpha-lipoic acid, levacecarnine (acetyl-L-carnitine, levocarnitine acetyl) hydrochloride, captopril, retilin, verteporfin, benfotiamine and fluocinolone acetonide.

38. The pharmaceutical composition of claim 25, which is used in combination with a therapeutic agent for obesity.

39. The pharmaceutical composition of claim 38, wherein the therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, lipase inhibitors, 5-HT/norepinephrine reuptake dual inhibitors, 5-HT reuptake inhibitors, supplements containing herbal ephedrine and caffeine, human chorionic gonadotropins, adrenoceptor agonists, methamphetamine, phentermine and amfepramone.

40. The pharmaceutical composition of claim 39, wherein the therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, orlistat, sibutramine hydrochloride monohydrate, fluoxetine hydrochloride, chorionic gonadotropin (human), VNS therapy using NCP System, metaraminol, d-methamphetamine hydrochloride, phentermine, amfepramone hydrochloride (diethylpropion), benzfetamine hydrochloride and phendimetrazine tartrate.

41. The pharmaceutical composition of claim 25, which is used in combination with a therapeutic agent for hypertension.

42. The pharmaceutical composition of claim 41, wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of thiazides, aldosterone antagonists, adrenergic neuron blockers, calcium channel blockers; dopamine D2 antagonists, beta-adrenoceptor antagonists, alpha2-adrenoceptor agonists, guanylate cyclase activators, beta1-adrenoceptor antagonists, alpha1-adrenoceptor antagonists, antioxidants, angiotensin-I converting enzyme (ACE) inhibitors, Na+/H+ exchange inhibitors,

alpha-adrenoceptor antagonists, nitric oxide donors, 5-HT2 antagonists, K(ATP) channel activators, potassium sparing diuretic prostaglandin synthase stimulants, imidazoline I1 receptor agonists, angiotensin AT1 antagonists, dopamine D1 agonists, guanylate cyclase stimulants, endothelin ETA receptor antagonists, endothelin ETB receptor antagonists, NOS3 expression enhancers, prostacyclin analogs, prostaglandins, angiotensin II antagonists, electrolyte absorption agonists, nicotinic antagonists, dopamine D2 agonists, prolactin inhibitors, platelet-activating factor (PAF) antagonists, platelet aggregation antagonists, tumor necrosis factor antagonists, Rho kinase inhibitors, PPAR-alpha agonists, AMPA receptor modulators, GABA(A) receptor antagonists and phosphodiesterase V (PDE5A) inhibitors.

43. The pharmaceutical composition of claim 42, wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of chlorothiazide, hydrochlorothiazide, hydroflumethiazide, methyclothiazide, polythiazide, xipamide, cyclopenthiazide, bendroflumethiazide (bendrofluazide), spironolactone, epoxymexrenone (eplerenone), guanethidine monosulfate, guanadrel sulfate, verapamil, propranolol hydrochloride, alprenolol hydrochloride, pindolol, oxprenolol hydrochloride, timolol maleate, sotalol hydrochloride, acebutolol hydrochloride, carteolol hydrochloride, mepindolol sulfate, arotinolol hydrochloride, indenolol hydrochloride, tertatolol hydrochloride, celiprolol hydrochloride, tilisolol hydrochloride, nebivolol, penbutolol sulfate, nadolol, cloranolol hydrochloride, bevantol (bevantolol) hydrochloride, clonidine, guanfacine hydrochloride, diltiazem hydrochloride, nicardipine hydrochloride, nitrendipine, felodipine, nilvadipine; nivadipine, nisoldipine, benidipine hydrochloride,

amlodipine besylate, franidipine (manidipine) hydrochloride, lacidipine, isradipine, barnidipine (mepirodipine) hydrochloride, efonidipine hydrochloride ethanol, cinaldipine (cilnidipine), aranidipine, lercanidipine (masnidipine) hydrochloride, azelnidipine, amlodipine, manidipine (franidipine), sodium nitroprusside, atenolol, metoprolol tartrate, betaxolol hydrochloride, bopindolol, bisoprolol fumarate, esmolol hydrochloride, carvedilol, metoprolol succinate, talinolol, prazosin hydrochloride, urapidil, indoramin hydrochloride, bunazosin hydrochloride, terazosin hydrochloride, doxazosin mesylate, urapidil, nifedipine, captopril, enalapril maleate, lisinopril, perindopril, alacepril, ramipril, quinapril hydrochloride, delapril hydrochloride, benazepril hydrochloride, cilazapril, fosinoprilat, fosinopril sodium, trandolapril, spirapril, temocapril hydrochloride, moexipril hydrochloride, imidapril hydrochloride, zofenopril calcium, enalaprilat, zofenoprilat, amiloride hydrochloride, labetalol hydrochloride, nipradilol (nipradolol), linsidomine, ketanserin, pinacidil, cicletanine (cycletanide), amosulalol hydrochloride, moxonidine hydrochloride hydrate, losartan potassium, valsartan, eprosartan mesylate, candesartan cilexetil (hexetil), irbesartan, telmisartan, olmesartan medoxomil, fenoldopam mesilate, cadralazine, rilmenidine dihydrogen phosphate, bosentan, beraprost sodium, limaprost alfadex (alpha-cyclodextrin), uniprost (treprostinil sodium), iloprost (ciloprost), mecamylamine hydrochloride, metergoline, guanabenz acetate, cloricromene, fasudil, doconexent (docosahexaenoic acid), cyclothiazide, sildenafil citrate, chlortalidone (chlorthalidone), quinethazone, indapamide, metolazone, phenoxybenzamine hydrochloride, metirosine (metyrosine), diazoxide, torasemide (torsemide), clopamide, hydralazine hydrochloride, reserpine and methyldopa.

44. The pharmaceutical composition of claim 25, which is used in combination with a therapeutic agent for thrombosis.

45. The pharmaceutical composition of claim 44, wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin preparations, low molecular weight heparins, heparin analogs, anticoagulants, thrombin inhibitors, anti-thrombin preparations, antiplatelet agents and thrombolytic agents.

46. The pharmaceutical composition of claim 45, wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin calcium, heparin sodium, dalteparin sodium, parnaparin sodium, reviparin sodium, danaparoid sodium, warfarin potassium, argatroban, gabexate mesylate, nafamostat mesylate, human anti-thrombin III, aspirin, dipyridamole, ticlopidine hydrochloride, cilostazol, limaprost alfadex, sodium ozagrel, sarpogrelate hydrochloride, ethyl icosapentate, beraprost sodium, urokinase, tisokinase, alteplase, nasaruplase, nateplase, monteplase, pamiteplase, batroxobin, sodium citrate and protein C.

47. The pharmaceutical composition for the prophylaxis or treatment of diabetes according to claim 28, which is used in combination with a therapeutic agent for hyperlipidemia.

48. The pharmaceutical composition for the prophylaxis or treatment of diabetes according to claim 47, wherein the therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of HMG-CoA reductase inhibitors (statins), fibrates, TNFSF6 expression inhibitors, HDL-cholesterol increasing agents, ApoA1

expression enhancers, SPP1 (osteopontin) expression inhibitors, drugs acting on peroxisome proliferator-activated receptors (PPAR), PPAR-alpha agonists, lipase clearing factor stimulants, cholesterol antagonists, platelet aggregation antagonists, antioxidants, cholesterol biosynthesis inhibitors, LDL-receptor up-regulators, bile acid sequestrants, cholesterol absorption inhibitors and nicotinic acids.

49. The pharmaceutical composition for the prophylaxis or treatment of diabetes according to claim 48, wherein the therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of lovastatin, pravastatin (eptastatin) sodium, fluvastatin (fluindostainin) sodium, rosuvastatin calcium, atorvastatin calcium, simvastatin (synvinolin), pitavastatin (itavastatin, nisvastatin) calcium, ronifibrate (ronifibrato), binifibrate (binifibrato), clinofibrate, ciprofibrate, clofibrate, etofibrate, fenofibrate, bezafibrate, gemfibrozil, acipimox, eicosapentaenoic acid (icosapent, icopenate, icosapentate) ethyl ester, probucol, policosanol, colesevelam hydrochloride, colestyramine (cholestyramine resin), colestipol hydrochloride, colestimide (colestilan), ezetimibe and niacin (nicotinic acid).

50. The pharmaceutical composition for the prophylaxis or treatment of diabetes according to claim 28, which is used in combination with a different therapeutic agent for diabetes.

51. The pharmaceutical composition for the prophylaxis or treatment of diabetes according to claim 50, wherein the different therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of insulin secretagogues, biguanides, α-glucosidase inhibitors, insulin preparations, insulin analogs, insulin sensitivity

enhancers, IL-11, anti-CD25 (IL-2 Receptor) agents, angiotensin (AT1) antagonists, angiotensin-converting enzyme (ACE) inhibitors, aldose reductase inhibitors, antioxidants, carnitine acetyltransferase stimulant, antidepressants, glucocorticoids, retilin, radical formation agonists and transketolase activators.

52. The pharmaceutical composition for the prophylaxis or treatment of diabetes according to claim 51, wherein the different therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of nateglinide, glimepiride, glibenclamide, gliclazide, acetohexamide, tolbutamide, glyclopyramide, tolazamide, glybuzole, glipizide, glibornuride, gliquidone, repaglinide, metformin hydrochloride, buformin hydrochloride, voglibose, acarbose, epalrestat, miglitol, insulin, pioglitazone hydrochloride, rosiglitazone maleate, chromium picolinate/biotin, V-411, recombinant human interleukin-11, dacliximab (daclizumab), losartan potassium, captopril, imidapril hydrochloride, alpha-lipoic acid, levacecarnine (acetyl-L-carnitine, levocarnitine acetyl) hydrochloride, captopril, retilin, verteporfin, benfotiamine and fluocinolone acetonide.

53. The pharmaceutical composition for the prophylaxis or treatment of diabetes according to claim 28, which is used in combination with a therapeutic agent for obesity.

54. The pharmaceutical composition for the prophylaxis or treatment of diabetes according to claim 53, wherein the therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, lipase inhibitors, 5-HT/norepinephrine reuptake dual inhibitors, 5-HT

reuptake inhibitors, supplements containing herbal ephedrine and caffeine, human chorionic gonadotropins, adrenoceptor agonists, methamphetamine, phentermine and amfepramone.

55. The pharmaceutical composition for the prophylaxis or treatment of diabetes according to claim 54, wherein the therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, orlistat, sibutramine hydrochloride monohydrate, fluoxetine hydrochloride, chorionic gonadotropin (human), VNS therapy using NCP System, metaraminol, d-methamphetamine hydrochloride, phentermine, amfepramone hydrochloride (diethylpropion), benzfetamine hydrochloride and phendimetrazine tartrate.

56. The pharmaceutical composition for the prophylaxis or treatment of diabetes according to claim 28, which is used in combination with a therapeutic agent for hypertension.

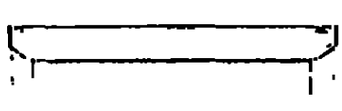
57. The pharmaceutical composition for the prophylaxis or treatment of diabetes according to claim 56, wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of thiazides, aldosterone antagonists, adrenergic neuron blockers, calcium channel blockers; dopamine D2 antagonists, beta-adrenoceptor antagonists, alpha2-adrenoceptor agonists, guanylate cyclase activators, beta1-adrenoceptor antagonists, alpha1-adrenoceptor antagonists, antioxidants, angiotensin-I converting enzyme (ACE) inhibitors, Na+/H+ exchange inhibitors, alpha-adrenoceptor antagonists, nitric oxide donors, 5-HT2 antagonists, K(ATP) channel activators, potassium sparing diuretic prostaglandin synthase stimulants, imidazoline I1 receptor agonists, angiotensin AT1 antagonists, dopamine D1 agonists, guanylate cyclase stimulants, endothelin ETA receptor

antagonists, endothelin ETB receptor antagonists, NOS3 expression enhancers, prostacyclin analogs, prostaglandins, angiotensin II antagonists, electrolyte absorption agonists, nicotinic antagonists, dopamine D2 agonists, prolactin inhibitors, platelet-activating factor (PAF) antagonists, platelet aggregation antagonists, tumor necrosis factor antagonists, Rho kinase inhibitors, PPAR-alpha agonists, AMPA receptor modulators, GABA(A) receptor antagonists and phosphodiesterase V (PDE5A) inhibitors.

58. The pharmaceutical composition for the prophylaxis or treatment of diabetes according to claim 57, wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of chlorothiazide, hydrochlorothiazide, hydroflumethiazide, methyclothiazide, polythiazide, xipamide, cyclopenthiazide, bendroflumethiazide (bendrofluazide), spironolactone, epoxymexrenone (eplerenone), guanethidine monosulfate, guanadrel sulfate, verapamil, propranolol hydrochloride, alprenolol hydrochloride, pindolol, oxprenolol hydrochloride, timolol maleate, sotalol hydrochloride, acebutolol hydrochloride, carteolol hydrochloride, mepindolol sulfate, arotinolol hydrochloride, indenolol hydrochloride, tertatolol hydrochloride, celiprolol hydrochloride, tilisolol hydrochloride, nebivolol, penbutolol sulfate, nadolol, cloranolol hydrochloride, bevantol (bevantolol) hydrochloride, clonidine, guanfacine hydrochloride, diltiazem hydrochloride, nicardipine hydrochloride, nitrendipine, felodipine, nilvadipine; nivadipine, nisoldipine, benidipine hydrochloride, amlodipine besylate, franidipine (manidipine) hydrochloride, lacidipine, isradipine, barnidipine (mepirodipine) hydrochloride, efonidipine hydrochloride ethanol, cinaldipine (cilnidipine), aranidipine, lercanidipine (masnidipine)

hydrochloride, azelnidipine, amlodipine, manidipine (franidipine), sodium nitroprusside, atenolol, metoprolol tartrate, betaxolol hydrochloride, bopindolol, bisoprolol fumarate, esmolol hydrochloride, carvedilol, metoprolol succinate, talinolol, prazosin hydrochloride, urapidil, indoramin hydrochloride, bunazosin hydrochloride, terazosin hydrochloride, doxazosin mesylate, urapidil, nifedipine, captopril, enalapril maleate, lisinopril, perindopril, alacepril, ramipril, quinapril hydrochloride, delapril hydrochloride, benazepril hydrochloride, cilazapril, fosinoprilat, fosinopril sodium, trandolapril, spirapril, temocapril hydrochloride, moexipril hydrochloride, imidapril hydrochloride, zofenopril calcium, enalaprilat, zofenoprilat, amiloride hydrochloride, labetalol hydrochloride, nipradilol (nipradolol), linsidomine, ketanserin, pinacidil, cicletanine (cycletanide), amosulalol hydrochloride, moxonidine hydrochloride hydrate, losartan potassium, valsartan, eprosartan mesylate, candesartan cilexetil (hexetil), irbesartan, telmisartan, olmesartan medoxomil, fenoldopam mesilate, cadralazine, rilmenidine dihydrogen phosphate, bosentan, beraprost sodium, limaprost alfadex (alpha-cyclodextrin), uniprost (treprostinil sodium), iloprost (ciloprost), mecamylamine hydrochloride, metergoline, guanabenz acetate, cloricromene, fasudil, doconexent (docosahexaenoic acid), cyclothiazide, sildenafil citrate, chlortalidone (chlorthalidone), quinethazone, indapamide, metolazone, phenoxybenzamine hydrochloride, metirosine (metyrosine), diazoxide, torasemide (torsemide), clopamide, hydralazine hydrochloride, reserpine and methyldopa.

59. The pharmaceutical composition for the prophylaxis or treatment of diabetes according to claim 28, which is used in combination with a therapeutic agent for thrombosis.



60. The pharmaceutical composition for the prophylaxis or treatment of diabetes according to claim 59, wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin preparations, low molecular weight heparins, heparin analogs, anticoagulants, thrombin inhibitors, anti-thrombin preparations, antiplatelet agents and thrombolytic agents.

61. The pharmaceutical composition for the prophylaxis or treatment of diabetes according to claim 60, wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin calcium, heparin sodium, dalteparin sodium, parnaparin sodium, reviparin sodium, danaparoid sodium, warfarin potassium, argatroban, gabexate mesylate, nafamostat mesylate, human anti-thrombin III, aspirin, dipyridamole, ticlopidine hydrochloride, cilostazol, limaprost alfadex, sodium ozagrel, sarpogrelate hydrochloride, ethyl icosapentate, beraprost sodium, urokinase, tisokinase, alteplase, nasaruplase, nateplase, monteplase, pamiteplase, batroxobin, sodium citrate and protein C.

62. The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to claim 29, which is used in combination with a different therapeutic agent for hyperlipidemia.

63. The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to claim 62, wherein the different therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of HMG-CoA reductase inhibitors (statins), fibrates, TNFSF6 expression inhibitors, HDL-cholesterol increasing agents, ApoA1

expression enhancers, SPP1 (osteopontin) expression inhibitors, drugs acting on peroxisome proliferator-activated receptors (PPAR), PPAR-alpha agonists, lipase clearing factor stimulants, cholesterol antagonists, platelet aggregation antagonists, antioxidants, cholesterol biosynthesis inhibitors, LDL-receptor up-regulators, bile acid sequestrants, cholesterol absorption inhibitors and nicotinic acids.

64. The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to claim 63, wherein the different therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of lovastatin, pravastatin (eptastatin) sodium, fluvastatin (fluindostainin) sodium, rosuvastatin calcium, atorvastatin calcium, simvastatin (synvinolin), pitavastatin (itavastatin, nisvastatin) calcium, ronifibrate (ronifibrato), binifibrate (binifibrato), clinofibrate, ciprofibrate, clofibrate, etofibrate, fenofibrate, bezafibrate, gemfibrozil, acipimox, eicosapentaenoic acid (icosapent, icopenate, icosapentate) ethyl ester, probucol, policosanol, colesevelam hydrochloride, colestyramine (cholestyramine resin), colestipol hydrochloride, colestimide (colestilan), ezetimibe and niacin (nicotinic acid).

65. The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to claim 29, which is used in combination with a therapeutic agent for diabetes.

66. The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to claim 65, wherein the therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of insulin secretagogues, biguanides, α-glucosidase inhibitors, insulin preparations, insulin analogs, insulin sensitivity enhancers,

IL-11, anti-CD25 (IL-2 Receptor) agents, angiotensin (AT1) antagonists, angiotensin-converting enzyme (ACE) inhibitors, aldose reductase inhibitors, antioxidants, carnitine acetyltransferase stimulant, antidepressants, glucocorticoids, retilin, radical formation agonists and transketolase activators.

67. The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to claim 66, wherein the therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of nateglinide, glimepiride, glibenclamide, gliclazide, acetohexamide, tolbutamide, glyclopyramide, tolazamide, glybuzole, glipizide, glibornuride, gliquidone, repaglinide, metformin hydrochloride, buformin hydrochloride, voglibose, acarbose, epalrestat, miglitol, insulin, pioglitazone hydrochloride, rosiglitazone maleate, chromium picolinate/biotin, V-411, recombinant human interleukin-11, dacliximab (daclizumab), losartan potassium, captopril, imidapril hydrochloride, alpha-lipoic acid, levacecarnine (acetyl-L-carnitine, levocarnitine acetyl) hydrochloride, captopril, retilin, verteporfin, benfotiamine and fluocinolone acetonide.

68. The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to claim 29, which is used in combination with a therapeutic agent for obesity.

69. The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to claim 68, wherein the therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, lipase inhibitors, 5-HT/norepinephrine reuptake dual inhibitors, 5-HT reuptake inhibitors, supplements containing herbal ephedrine

and caffeine, human chorionic gonadotropins, adrenoceptor agonists, methamphetamine, phentermine and amfepramone.

70. The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to claim 69, wherein the therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, orlistat, sibutramine hydrochloride monohydrate, fluoxetine hydrochloride, chorionic gonadotropin (human), VNS therapy using NCP System, metaraminol, d-methamphetamine hydrochloride, phentermine, amfepramone hydrochloride (diethylpropion), benzfetamine hydrochloride and phendimetrazine tartrate.

71. The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to claim 29, which is used in combination with a therapeutic agent for hypertension.

72. The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to claim 71, wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of thiazides, aldosterone antagonists, adrenergic neuron blockers, calcium channel blockers; dopamine D2 antagonists, beta-adrenoceptor antagonists, alpha2-adrenoceptor agonists, guanylate cyclase activators, beta1-adrenoceptor antagonists, alpha1-adrenoceptor antagonists, antioxidants, angiotensin-I converting enzyme (ACE) inhibitors, Na+/H+ exchange inhibitors, alpha-adrenoceptor antagonists, nitric oxide donors, 5-HT2 antagonists, K(ATP) channel activators, potassium sparing diuretic prostaglandin synthase stimulants, imidazoline I1 receptor agonists, angiotensin AT1 antagonists, dopamine D1 agonists, guanylate cyclase stimulants, endothelin ETA receptor antagonists, endothelin ETB receptor antagonists, NOS3

expression enhancers, prostacyclin analogs, prostaglandins, angiotensin II antagonists, electrolyte absorption agonists, nicotinic antagonists, dopamine D2 agonists, prolactin inhibitors, platelet-activating factor (PAF) antagonists, platelet aggregation antagonists, tumor necrosis factor antagonists, Rho kinase inhibitors, PPAR-alpha agonists, AMPA receptor modulators, GABA(A) receptor antagonists and phosphodiesterase V (PDE5A) inhibitors.

73. The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to claim 72, wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of chlorothiazide, hydrochlorothiazide, hydroflumethiazide, methyclothiazide, polythiazide, xipamide, cyclopenthiazide, bendroflumethiazide (bendrofluazide), spironolactone, epoxymexrenone (eplerenone), guanethidine monosulfate, guanadrel sulfate, verapamil, propranolol hydrochloride, alprenolol hydrochloride, pindolol, oxprenolol hydrochloride, timolol maleate, sotalol hydrochloride, acebutolol hydrochloride, carteolol hydrochloride, mepindolol sulfate, arotinolol hydrochloride, indenolol hydrochloride, tertatolol hydrochloride, celiprolol hydrochloride, tilisolol hydrochloride, nebivolol, penbutolol sulfate, nadolol, cloranolol hydrochloride, bevantol (bevantolol) hydrochloride, clonidine, guanfacine hydrochloride, diltiazem hydrochloride, nicardipine hydrochloride, nitrendipine, felodipine, nilvadipine; nivadipine, nisoldipine, benidipine hydrochloride, amlodipine besylate, franidipine (manidipine) hydrochloride, lacidipine, isradipine, barnidipine (mepirodipine) hydrochloride, efonidipine hydrochloride ethanol, cinaldipine (cilnidipine), aranidipine, lercanidipine (masnidipine) hydrochloride, azelnidipine, amlodipine, manidipine

(franidipine), sodium nitroprusside, atenolol, metoprolol tartrate, betaxolol hydrochloride, bopindolol, bisoprolol fumarate, esmolol hydrochloride, carvedilol, metoprolol succinate, talinolol, prazosin hydrochloride, urapidil, indoramin hydrochloride, bunazosin hydrochloride, terazosin hydrochloride, doxazosin mesylate, urapidil, nifedipine, captopril, enalapril maleate, lisinopril, perindopril, alacepril, ramipril, quinapril hydrochloride, delapril hydrochloride, benazepril hydrochloride, cilazapril, fosinoprilat, fosinopril sodium, trandolapril, spirapril, temocapril hydrochloride, moexipril hydrochloride, imidapril hydrochloride, zofenopril calcium, enalaprilat, zofenoprilat, amiloride hydrochloride, labetalol hydrochloride, nipradilol (nipradolol), linsidomine, ketanserin, pinacidil, cicletanine (cycletanide), amosulalol hydrochloride, moxonidine hydrochloride hydrate, losartan potassium, valsartan, eprosartan mesylate, candesartan cilexetil (hexetil), irbesartan, telmisartan, olmesartan medoxomil, fenoldopam mesilate, cadralazine, rilmenidine dihydrogen phosphate, bosentan, beraprost sodium, limaprost alfadex (alpha-cyclodextrin), uniprost (treprostinil sodium), iloprost (ciloprost), mecamylamine hydrochloride, metergoline, guanabenz acetate, cloricromene, fasudil, doconexent (docosahexaenoic acid), cyclothiazide, sildenafil citrate, chlortalidone (chlorthalidone), quinethazone, indapamide, metolazone, phenoxybenzamine hydrochloride, metirosine (metyrosine), diazoxide, torasemide (torsemide), clopamide, hydralazine hydrochloride, reserpine and methyldopa.

74. The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to claim 29, which is used in combination with a therapeutic agent for thrombosis.

75. The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to claim 74, wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin preparations, low molecular weight heparins, heparin analogs, anticoagulants, thrombin inhibitors, anti-thrombin preparations, antiplatelet agents and thrombolytic agents.

76. The pharmaceutical composition for the prophylaxis or treatment of hyperlipidemia according to claim 75, wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin calcium, heparin sodium, dalteparin sodium, parnaparin sodium, reviparin sodium, danaparoid sodium, warfarin potassium, argatroban, gabexate mesylate, nafamostat mesylate, human anti-thrombin III, aspirin, dipyridamole, ticlopidine hydrochloride, cilostazol, limaprost alfadex, sodium ozagrel, sarpogrelate hydrochloride, ethyl icosapentate, beraprost sodium, urokinase, tisokinase, alteplase, nasaruplase, nateplase, monteplase, pamiteplase, batroxobin, sodium citrate and protein C.

77. The pharmaceutical composition for the prophylaxis or treatment of obesity according to claim 30, which is used in combination with a therapeutic agent for hyperlipidemia.

78. The pharmaceutical composition for the prophylaxis or treatment of obesity according to claim 77, wherein the therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of HMG-CoA reductase inhibitors (statins), fibrates, TNFSF6 expression inhibitors, HDL-cholesterol increasing agents, ApoA1 expression enhancers, SPP1 (osteopontin) expression inhibitors, drugs acting on peroxisome proliferator-activated receptors

(PPAR), PPAR-alpha agonists, lipase clearing factor stimulants, cholesterol antagonists, platelet aggregation antagonists, antioxidants, cholesterol biosynthesis inhibitors, LDL-receptor up-regulators, bile acid sequestrants, cholesterol absorption inhibitors and nicotinic acids.

79. The pharmaceutical composition for the prophylaxis or treatment of obesity according to claim 78, wherein the therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of lovastatin, pravastatin (eptastatin) sodium, fluvastatin (fluindostainin) sodium, rosuvastatin calcium, atorvastatin calcium, simvastatin (synvinolin), pitavastatin (itavastatin, nisvastatin) calcium, ronifibrate (ronifibrato), binifibrate (binifibrato), clinofibrate, ciprofibrate, clofibrate, etofibrate, fenofibrate, bezafibrate, gemfibrozil, acipimox, eicosapentaenoic acid (icosapent, icopenate, icosapentate) ethyl ester, probucol, policosanol, colesevelam hydrochloride, colestyramine (cholestyramine resin), colestipol hydrochloride, colestimide (colestilan), ezetimibe and niacin (nicotinic acid).

80. The pharmaceutical composition for the prophylaxis or treatment of obesity according to claim 30, which is used in combination with a therapeutic agent for diabetes.

81. The pharmaceutical composition for the prophylaxis or treatment of obesity according to claim 80, wherein the therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of insulin secretagogues, biguanides, α-glucosidase inhibitors, insulin preparations, insulin analogs, insulin sensitivity enhancers, IL-11, anti-CD25 (IL-2 Receptor) agents, angiotensin (AT1) antagonists, angiotensin-converting enzyme (ACE) inhibitors,

aldose reductase inhibitors, antioxidants, carnitine acetyltransferase stimulant, antidepressants, glucocorticoids, retilin, radical formation agonists and transketolase activators.

82. The pharmaceutical composition for the prophylaxis or treatment of obesity according to claim 81, wherein the therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of nateglinide, glimepiride, glibenclamide, gliclazide, acetohexamide, tolbutamide, glyclopyramide, tolazamide, glybuzole, glipizide, glibornuride, gliquidone, repaglinide, metformin hydrochloride, buformin hydrochloride, voglibose, acarbose, epalrestat, miglitol, insulin, pioglitazone hydrochloride, rosiglitazone maleate, chromium picolinate/biotin, V-411, recombinant human interleukin-11, dacliximab (daclizumab), losartan potassium, captopril, imidapril hydrochloride, alpha-lipoic acid, levacecarnine (acetyl-L-carnitine, levocarnitine acetyl) hydrochloride, captopril, retilin, verteporfin, benfotiamine and fluocinolone acetonide.

83. The pharmaceutical composition for the prophylaxis or treatment of obesity according to claim 30, which is used in combination with a different therapeutic agent for obesity.

84. The pharmaceutical composition for the prophylaxis or treatment of obesity according to claim 83, wherein the different therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, lipase inhibitors, 5-HT/norepinephrine reuptake dual inhibitors, 5-HT reuptake inhibitors, supplements containing herbal ephedrine and caffeine, human chorionic gonadotropins, adrenoceptor agonists, methamphetamine, phentermine and

amfepramone.

85. The pharmaceutical composition for the prophylaxis or treatment of obesity according to claim 84, wherein the different therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, orlistat, sibutramine hydrochloride monohydrate, fluoxetine hydrochloride, chorionic gonadotropin (human), VNS therapy using NCP System, metaraminol, d-methamphetamine hydrochloride, phentermine, amfepramone hydrochloride (diethylpropion), benzfetamine hydrochloride and phendimetrazine tartrate.

86. The pharmaceutical composition for the prophylaxis or treatment of obesity according to claim 30, which is used in combination with a therapeutic agent for hypertension.

87. The pharmaceutical composition for the prophylaxis or treatment of obesity according to claim 86, wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of thiazides, aldosterone antagonists, adrenergic neuron blockers, calcium channel blockers; dopamine D2 antagonists, beta-adrenoceptor antagonists, alpha2-adrenoceptor agonists, guanylate cyclase activators, beta1-adrenoceptor antagonists, alpha1-adrenoceptor antagonists, antioxidants, angiotensin-I converting enzyme (ACE) inhibitors, Na+/H+ exchange inhibitors, alpha-adrenoceptor antagonists, nitric oxide donors, 5-HT2 antagonists, K(ATP) channel activators, potassium sparing diuretic prostaglandin synthase stimulants, imidazoline I1 receptor agonists, angiotensin AT1 antagonists, dopamine D1 agonists, guanylate cyclase stimulants, endothelin ETA receptor antagonists, endothelin ETB receptor antagonists, NOS3

expression enhancers, prostacyclin analogs, prostaglandins, angiotensin II antagonists, electrolyte absorption agonists, nicotinic antagonists, dopamine D2 agonists, prolactin inhibitors, platelet-activating factor (PAF) antagonists, platelet aggregation antagonists, tumor necrosis factor antagonists, Rho kinase inhibitors, PPAR-alpha agonists, AMPA receptor modulators, GABA(A) receptor antagonists and phosphodiesterase V (PDE5A) inhibitors.

88. The pharmaceutical composition for the prophylaxis or treatment of obesity according to claim 87, wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of chlorothiazide, hydrochlorothiazide, hydroflumethiazide, methyclothiazide, polythiazide, xipamide, cyclopenthiazide, bendroflumethiazide (bendrofluazide), spironolactone, epoxymexrenone (eplerenone), guanethidine monosulfate, guanadrel sulfate, verapamil, propranolol hydrochloride, alprenolol hydrochloride, pindolol, oxprenolol hydrochloride, timolol maleate, sotalol hydrochloride, acebutolol hydrochloride, carteolol hydrochloride, mepindolol sulfate, arotinolol hydrochloride, indenolol hydrochloride, tertatolol hydrochloride, celiprolol hydrochloride, tilisolol hydrochloride, nebivolol, penbutolol sulfate, nadolol, cloranolol hydrochloride, bevantol (bevantolol) hydrochloride, clonidine, guanfacine hydrochloride, diltiazem hydrochloride, nicardipine hydrochloride, nitrendipine, felodipine, nilvadipine; nivadipine, nisoldipine, benidipine hydrochloride, amlodipine besylate, franidipine (manidipine) hydrochloride, lacidipine, isradipine, barnidipine (mepirodipine) hydrochloride, efonidipine hydrochloride ethanol, cinaldipine (cilnidipine), aranidipine, lercanidipine (masnidipine) hydrochloride, azelnidipine, amlodipine, manidipine

(franidipine), sodium nitroprusside, atenolol, metoprolol tartrate, betaxolol hydrochloride, bopindolol, bisoprolol fumarate, esmolol hydrochloride, carvedilol, metoprolol succinate, talinolol, prazosin hydrochloride, urapidil, indoramin hydrochloride, bunazosin hydrochloride, terazosin hydrochloride, doxazosin mesylate, urapidil, nifedipine, captopril, enalapril maleate, lisinopril, perindopril, alacepril, ramipril, quinapril hydrochloride, delapril hydrochloride, benazepril hydrochloride, cilazapril, fosinoprilat, fosinopril sodium, trandolapril, spirapril, temocapril hydrochloride, moexipril hydrochloride, imidapril hydrochloride, zofenopril calcium, enalaprilat, zofenoprilat, amiloride hydrochloride, labetalol hydrochloride, nipradilol (nipradolol), linsidomine, ketanserin, pinacidil, cicletanine (cycletanide), amosulalol hydrochloride, moxonidine hydrochloride hydrate, losartan potassium, valsartan, eprosartan mesylate, candesartan cilexetil (hexetil), irbesartan, telmisartan, olmesartan medoxomil, fenoldopam mesilate, cadralazine, rilmenidine dihydrogen phosphate, bosentan, beraprost sodium, limaprost alfadex (alpha-cyclodextrin), uniprost (treprostinil sodium), iloprost (ciloprost), mecamylamine hydrochloride, metergoline, guanabenz acetate, cloricromene, fasudil, doconexent (docosahexaenoic acid), cyclothiazide, sildenafil citrate, chlortalidone (chlorthalidone), quinethazone, indapamide, metolazone, phenoxybenzamine hydrochloride, metirosine (metyrosine), diazoxide, torasemide (torsemide), clopamide, hydralazine hydrochloride, reserpine and methyldopa.

89. The pharmaceutical composition for the prophylaxis or treatment of obesity according to claim 30, which is used in combination with a therapeutic agent for thrombosis.

90. The pharmaceutical composition for the prophylaxis or treatment of obesity according to claim 89, wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin preparations, low molecular weight heparins, heparin analogs, anticoagulants, thrombin inhibitors, anti-thrombin preparations, antiplatelet agents and thrombolytic agents.

91. The pharmaceutical composition for the prophylaxis or treatment of obesity according to claim 90, wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin calcium, heparin sodium, dalteparin sodium, parnaparin sodium, reviparin sodium, danaparoid sodium, warfarin potassium, argatroban, gabexate mesylate, nafamostat mesylate, human anti-thrombin III, aspirin, dipyridamole, ticlopidine hydrochloride, cilostazol, limaprost alfadex, sodium ozagrel, sarpogrelate hydrochloride, ethyl icosapentate, beraprost sodium, urokinase, tisokinase, alteplase, nasaruplase, nateplase, monteplase, pamiteplase, batroxobin, sodium citrate and protein C.

92. The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to claim 31, which is used in combination with a therapeutic agent for hyperlipidemia.

93. The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to claim 92, wherein the therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of HMG-CoA reductase inhibitors (statins), fibrates, TNFSF6 expression inhibitors, HDL-cholesterol increasing agents, ApoA1 expression enhancers, SPP1 (osteopontin) expression inhibitors,

drugs acting on peroxisome proliferator-activated receptors (PPAR), PPAR-alpha agonists, lipase clearing factor stimulants, cholesterol antagonists, platelet aggregation antagonists, antioxidants, cholesterol biosynthesis inhibitors, LDL-receptor up-regulators, bile acid sequestrants, cholesterol absorption inhibitors and nicotinic acids.

94. The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to claim 93, wherein the therapeutic agent for hyperlipidemia is one or more pharmaceutical agents selected from the group consisting of lovastatin, pravastatin (eptastatin) sodium, fluvastatin (fluindostainin) sodium, rosuvastatin calcium, atorvastatin calcium, simvastatin (synvinolin), pitavastatin (itavastatin, nisvastatin) calcium, ronifibrate (ronifibrato), binifibrate (binifibrato), clinofibrate, ciprofibrate, clofibrate, etofibrate, fenofibrate, bezafibrate, gemfibrozil, acipimox, eicosapentaenoic acid (icosapent, icopenate, icosapentate) ethyl ester, probucol, policosanol, colesevelam hydrochloride, colestyramine (cholestyramine resin), colestipol hydrochloride, colestimide (colestilan), ezetimibe and niacin (nicotinic acid).

95. The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to claim 31, which is used in combination with a therapeutic agent for diabetes.

96. The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to claim 95, wherein the therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of insulin secretagogues, biguanides, α-glucosidase inhibitors, insulin preparations, insulin analogs, insulin sensitivity

enhancers, IL-11, anti-CD25 (IL-2 Receptor) agents, angiotensin (AT1) antagonists, angiotensin-converting enzyme (ACE) inhibitors, aldose reductase inhibitors, antioxidants, carnitine acetyltransferase stimulant, antidepressants, glucocorticoids, retilin, radical formation agonists and transketolase activators.

97. The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to claim 96, wherein the therapeutic agent for diabetes is one or more pharmaceutical agents selected from the group consisting of nateglinide, glimepiride, glibenclamide, gliclazide, acetohexamide, tolbutamide, glyclopyramide, tolazamide, glybuzole, glipizide, glibornuride, gliquidone, repaglinide, metformin hydrochloride, buformin hydrochloride, voglibose, acarbose, epalrestat, miglitol, insulin, pioglitazone hydrochloride, rosiglitazone maleate, chromium picolinate/biotin, V-411, recombinant human interleukin-11, dacliximab (daclizumab), losartan potassium, captopril, imidapril hydrochloride, alpha-lipoic acid, levacecarnine (acetyl-L-carnitine, levocarnitine acetyl) hydrochloride, captopril, retilin, verteporfin, benfotiamine and fluocinolone acetonide.

98. The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to claim 31, which is used in combination with a therapeutic agent for obesity.

99. The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to claim 98, wherein the therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of

mazindol, lipase inhibitors, 5-HT/norepinephrine reuptake dual inhibitors, 5-HT reuptake inhibitors, supplements containing herbal ephedrine and caffeine, human chorionic gonadotropins, adrenoceptor agonists, methamphetamine, phentermine and amfepramone.

100. The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to claim 99, wherein the therapeutic agent for obesity is one or more pharmaceutical agents selected from the group consisting of mazindol, orlistat, sibutramine hydrochloride monohydrate, fluoxetine hydrochloride, chorionic gonadotropin (human), VNS therapy using NCP System, metaraminol, d-methamphetamine hydrochloride, phentermine, amfepramone hydrochloride (diethylpropion), benzfetamine hydrochloride and phendimetrazine tartrate.

101. The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to claim 31, which is used in combination with a therapeutic agent for hypertension.

102. The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to claim 101, wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of thiazides, aldosterone antagonists, adrenergic neuron blockers, calcium channel blockers; dopamine D2 antagonists, beta-adrenoceptor antagonists, alpha2-adrenoceptor agonists, guanylate cyclase activators, beta1-adrenoceptor antagonists, alpha1-adrenoceptor antagonists, antioxidants, angiotensin-I converting enzyme (ACE) inhibitors, Na+/H+ exchange inhibitors, alpha-adrenoceptor antagonists, nitric oxide donors, 5-HT2

antagonists, K(ATP) channel activators, potassium sparing diuretic prostaglandin synthase stimulants, imidazoline I1 receptor agonists, angiotensin AT1 antagonists, dopamine D1 agonists, guanylate cyclase stimulants, endothelin ETA receptor antagonists, endothelin ETB receptor antagonists, NOS3 expression enhancers, prostacyclin analogs, prostaglandins, angiotensin II antagonists, electrolyte absorption agonists, nicotinic antagonists, dopamine D2 agonists, prolactin inhibitors, platelet-activating factor (PAF) antagonists, platelet aggregation antagonists, tumor necrosis factor antagonists, Rho kinase inhibitors, PPAR-alpha agonists, AMPA receptor modulators, GABA(A) receptor antagonists and phosphodiesterase V (PDE5A) inhibitors.

103. The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to claim 102, wherein the therapeutic agent for hypertension is one or more pharmaceutical agents selected from the group consisting of chlorothiazide, hydrochlorothiazide, hydroflumethiazide, methyclothiazide, polythiazide, xipamide, cyclopenthiazide, bendroflumethiazide (bendrofluazide), spironolactone, epoxymexrenone (eplerenone), guanethidine monosulfate, guanadrel sulfate, verapamil, propranolol hydrochloride, alprenolol hydrochloride, pindolol, oxprenolol hydrochloride, timolol maleate, sotalol hydrochloride, acebutolol hydrochloride, carteolol hydrochloride, mepindolol sulfate, arotinolol hydrochloride, indenolol hydrochloride, tertatolol hydrochloride, celiprolol hydrochloride, tilisolol hydrochloride, nebivolol, penbutolol sulfate, nadolol, cloranolol hydrochloride, bevantol (bevantolol) hydrochloride, clonidine, guanfacine hydrochloride, diltiazem hydrochloride, nicardipine hydrochloride, nitrendipine, felodipine, nilvadipine; nivadipine, nisoldipine, benidipine hydrochloride,

amlodipine besylate, franidipine (manidipine) hydrochloride, lacidipine, isradipine, barnidipine (mepirodipine) hydrochloride, efonidipine hydrochloride ethanol, cinaldipine (cilnidipine), aranidipine, lercanidipine (masnidipine) hydrochloride, azelnidipine, amlodipine, manidipine (franidipine), sodium nitroprusside, atenolol, metoprolol tartrate, betaxolol hydrochloride, bopindolol, bisoprolol fumarate, esmolol hydrochloride, carvedilol, metoprolol succinate, talinolol, prazosin hydrochloride, urapidil, indoramin hydrochloride, bunazosin hydrochloride, terazosin hydrochloride, doxazosin mesylate, urapidil, nifedipine, captopril, enalapril maleate, lisinopril, perindopril, alacepril, ramipril, quinapril hydrochloride, delapril hydrochloride, benazepril hydrochloride, cilazapril, fosinoprilat, fosinopril sodium, trandolapril, spirapril, temocapril hydrochloride, moexipril hydrochloride, imidapril hydrochloride, zofenopril calcium, enalaprilat, zofenoprilat, amiloride hydrochloride, labetalol hydrochloride, nipradilol (nipradolol), linsidomine, ketanserin, pinacidil, cicletanine (cycletanide), amosulalol hydrochloride, moxonidine hydrochloride hydrate, losartan potassium, valsartan, eprosartan mesylate, candesartan cilexetil (hexetil), irbesartan, telmisartan, olmesartan medoxomil, fenoldopam mesilate, cadralazine, rilmenidine dihydrogen phosphate, bosentan, beraprost sodium, limaprost alfadex (alpha-cyclodextrin), uniprost (treprostinil sodium), iloprost (ciloprost), mecamylamine hydrochloride, metergoline, guanabenz acetate, cloricromene, fasudil, doconexent (docosahexaenoic acid), cyclothiazide, sildenafil citrate, chlortalidone (chlorthalidone), quinethazone, indapamide, metolazone, phenoxybenzamine hydrochloride, metirosine (metyrosine), diazoxide, torasemide (torsemide), clopamide, hydralazine hydrochloride, reserpine and methyldopa.

104. The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to claim 31, which is used in combination with a therapeutic agent for thrombosis.

105. The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to claim 104, wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin preparations, low molecular weight heparins, heparin analogs, anticoagulants, thrombin inhibitors, anti-thrombin preparations, antiplatelet agents and thrombolytic agents.

106. The pharmaceutical composition for the prophylaxis or treatment of diabetic complications according to claim 105, wherein the therapeutic agent for thrombosis is one or more pharmaceutical agents selected from the group consisting of heparin calcium, heparin sodium, dalteparin sodium, parnaparin sodium, reviparin sodium, danaparoid sodium, warfarin potassium, argatroban, gabexate mesylate, nafamostat mesylate, human anti-thrombin III, aspirin, dipyridamole, ticlopidine hydrochloride, cilostazol, limaprost alfadex, sodium ozagrel, sarpogrelate hydrochloride, ethyl icosapentate, beraprost sodium, urokinase, tisokinase, alteplase, nasaruplase, nateplase, monteplase, pamiteplase, batroxobin, sodium citrate and protein C.

107. A pharmaceutical composition for inhibition of a receptor tyrosine kinase negative regulator, which is used in combination with a therapeutic agent for hyperlipidemia.

108. A pharmaceutical composition for inhibition of a receptor tyrosine kinase negative regulator, which is used in

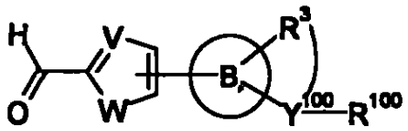
combination with a therapeutic agent for diabetes.

109. A pharmaceutical composition for inhibition of a receptor tyrosine kinase negative regulator, which is used in combination with a therapeutic agent for obesity.

110. A pharmaceutical composition for inhibition of a receptor tyrosine kinase negative regulator, which is used in combination with a therapeutic agent for hypertension.

111. A pharmaceutical composition for inhibition of a receptor tyrosine kinase negative regulator, which is used in combination with a therapeutic agent for thrombosis.

112. A 5-membered heteroaromatic ring compound represented by the formula [II]



[II]

wherein

Y^{100} is $-C(R^{13})(R^{14})-$ (R^{13} and R^{14} are each as defined in claim 1);

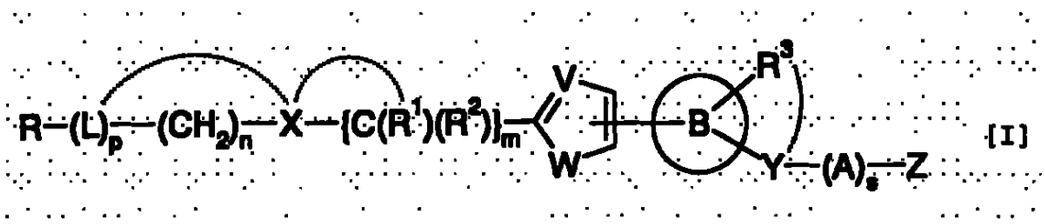
R^{100} is a hydroxyl group or a halogen atom, and

V, W and R^3 are each as defined in claim 1, or a pharmaceutically acceptable salt thereof.

113. The 5-membered heteroaromatic ring compound of claim 112, wherein, in the formula [II], R^{13} and R^{14} are each a hydrogen atom, V is =CH- and W is -S-, or a pharmaceutically acceptable salt thereof.

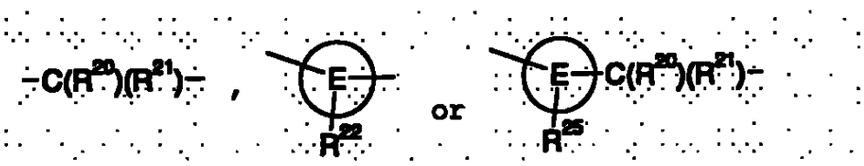
ABSTRACT

A 5-membered heteroaromatic ring compound represented by the formula [I]



[I]

wherein V is CH or N; W is S or O; R^1 and R^2 are each H etc.; X is $-N(R^4)-$, $-O-$, $-S-$, $-SO_2-N(R^5)-$, $-CO-N(R^7)-$ etc.; L is



wherein R^{20}, R^{21}, R^{22} and R^{25} are each H etc.; E is aryl or heteroaromatic ring group; R is -COOH etc.; B is aryl etc.; R^3 is H etc.; Y is $-C(R^{13})(R^{14})-N(R^{12})-$, $-C(R^{13})(R^{14})-O-$, $-N(R^{11})-$, $-O-$ etc.; A is alkylene; and Z is aryl etc., a prodrug thereof and a pharmaceutically acceptable salt thereof.

The compound [I] has a superior protein tyrosine phosphatase 1B inhibitory activity and is useful as a therapeutic agent for diabetes, diabetic complications, hyperlipidemia, obesity and the like.

577

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COMPUESTO PENTACICLICO HETEROAROMATICO Y USO MEDICINAL DEL MISMO

CAMPO TECNICO DE LA INVENCION

La presente invención se relaciona con un compuesto anular heteroaromático de 5 miembros, novedoso. Más particularmente, la presente invención se relaciona con un compuesto anular heteroaromático de 5 miembros que tiene una actividad inhibidora de la proteína tirosina fosfatasa 1B (PTP1B), una a sal farmacéuticamente aceptable del mismo, y una composición farmacéutica que contiene el mismo.

ANTECEDENTES DE LA INVENCION

La diabetes causa varios disbolismos, caracterizados principalmente por un estado crónico del nivel elevado de glucosa en sangre. Esta muestra un amplio intervalo de síntomas basados en el nivel elevado de glucosa en sangre, tal como boca seca, polidipsia, diuresis, pérdida de peso corporal y lo similar. Cuando tal estado de nivel elevado de glucosa en sangre dura un largo tiempo, se sabe que causa todo tipo de complicaciones tales como retinopatía, nefropatía, neuropatía, infarto cardiaco e infarto cerebral basados en la arteriosclerosis y lo similar.

La diabetes se clasifica generalmente en cuatro tipos: diabetes tipo I (IDDM; diabetes mellitus dependiente de insulina) que acompaña la deficiencia absoluta de la insulina, debida al daño o a la destrucción de las células β pancreáticas; diabetes del tipo II (NIDDM; diabetes mellitus no dependiente de insulina), que acompaña la deficiencia relativa de la insulina debida a la resistencia a la insulina y a la disminución de la secreción de insulina; diabetes especial, desarrollada de manera secundaria por una anormalidad en los genes, otras enfermedades y lo similar; y la diabetes gestacional. En algunos casos, los pacientes diagnosticados con la diabetes del tipo II poco después del inicio, pueden mostrar una secreción disminuida de la insulina con el progreso de la enfermedad y finalmente conduce a la diabetes del tipo I.

Para tratar la diabetes, es esencial mejorar los estados mencionados anteriormente de niveles elevados de glucosa en sangre y evitar el inicio y la progresión de las complicaciones. Para este fin, se ha tratado la terapia con dieta, la terapia con ejercicio y lo similar, así como tratamientos utilizando una variedad de agentes farmacéuticos con el propósito de controlar el nivel de glucosa en sangre, para que esté dentro del intervalo normal. Como agentes farmacéuticos existentes, representativos, se mencionan las preparaciones de insulina, los secretagogos de la insulina (agente de sulfonilurea, agente de sulfonamida, derivado de fenilalanina, etc.), que fomentan la secreción de insulina de las células β pancreáticas, inhibidores de

la α-glucosidasa que retardan la absorción del azúcar, agentes de biguanida considerados como que tienen una acción inhibidora de la gluconeogénesis en el hígado, en donde el detalle del mecanismo se desconoce, mejoradores de la sensibilidad a la insulina (derivado de tiazolidindiona, etc.), que fomentan la diferenciación del fibroblasto a la célula adiposa vía una acción agonista del receptor activado por el proliferador de la peroxisoma (PPAR), para incrementar el número de células sensibles a la insulina, y lo similar. Sin embargo, todos estos son problemáticos en términos de la efectividad y la seguridad (por ejemplo, falla secundaria debida a la fatiga de las células β pancreáticas, riesgo de hipoglucemia y fomento de la obesidad, asociada con el secretagogo de la insulina, edema e influencia adversa en el corazón, basado en el mismo, anemia, sobrealimentación, fomento de la obesidad, falta de respuesta asociada con el mejorador de la sensibilidad a la insulina y lo similar) y fallan en alcanzar un control suficiente de la glucosa en sangre.

Refiriéndose al metabolismo de la glucosa en el organismo viviente, los materiales que son para la fuente de energía y los componentes que constituyen el organismo viviente se han tomado de manera intermitente en el cuerpo, y en contraste, por ejemplo, el cerebro consume glucosa continuamente. En esta situación, el nivel de glucosa en sangre se mantiene a un nivel constante, y el control de la glucosa en sangre es habilitado por la interacción entre la hormona involucrada en el control de la glucosa en sangre, el metabolismo en el órgano y el intercambio de sacáridos y lo similar

entre los órganos. De éstos, la acción de la insulina, que es una hormona responsable particularmente del control de la glucosa en sangre, es significativa, y los trastornos de la misma, en otras palabras, resistencia a al insulina y secreción disminuida de la insulina, se consideran profundamente involucradas en la diabetes.

La insulina se secreta de las células β pancreáticas y se une con el receptor de la insulina, el cual es un receptor del tipo de la tirosina cinasa, presente en la superficie de la membrana de su célula objetivo o la célula del músculo esquelético y una célula adiposa, después de lo cual, el residuo de tirosina en el dominio intracelular se autofosforila. Posteriormente, el residuo de tirosina del IRS (sustrato del receptor de la insulina), la APS (proteína adaptadora que contiene el dominio PH y SH2) y lo similar, que es un sustrato de un receptor de la insulina, se fosforilan y se activa la trayectoria PI_3 cinasa-Akt, lo cual, a su vez, transfiere un transportador de glucosa en la membrana celular, causando la captación de la glucosa y la disminución de la concentración de la glucosa en sangre. Por otra parte, también está presente la tirosina fosfatasa, la cual realiza la desfosforilación de la tirosina para controlar de manera negativa la señalización intracelular, por la insulina, suprimiendo por lo tanto, la activación. Como se mencionó anteriormente, la fosforilación de la tirosina juega un papel principal en la acción de la insulina. Considerando el hecho de que la fosforilación de la tirosina se determina por el equilibrio de la actividad de la tirosina cinasa (enzima de la fosforilación) y la

de la tirosina fosfatasa (enzima de la desfosforilación), se considera que la tirosina fosfatasa juega directamente un papel significativo en el control de la señalización de la insulina, junto con la tirosina cinasa.

En la actualidad, la tirosina fosfatasa forma una gran familia de genes, y se ha reportado más de siete docenas de clases de isozimas. De éstas, se considera que la proteína tirosina fosfatasa 1B (PTP1B) es una fosfatasa principal involucrada en la señalización de la insulina. Particularmente, debido a que la expresión génica de la PTP1B se incrementa en cultivos con alta glucosa y los cambios en la localización intracelular de la misma disminuye la fosforilación de la tirosina del receptor de la insulina y el IRS-1 e induce la resistencia a la insulina (J. Biol. Chem., 1995, Vol. 270, pp. 7724-7730; J. Biochem. (Tokyo), 1998, Vol. 123, pp. 813-820), la introducción de la PTP1B del tipo silvestre inhibe la translocación del transportador de la glucosa GLUT4, tal efecto no se encontró en los mutantes defectuosos para la actividad de la fosfatasa, y la sensibilidad a la insulina se mejoró en ratones bloqueados para la PTP1B y los ratones se volvieron resistentes a la obesidad con una dieta alta en grasas (Science, 1999, Vol. 283, pp. 1544-1548), existe la posibilidad de que esta enzima pueda volverse un objetivo para mejorar la acción de la activación del receptor de la insulina a la captación de la glucosa, de la cual es responsable la insulina. De hecho, el ácido vanádico, conocido convencionalmente como un inhibidor de la tirosina fosfatasa, muestra una acción similar a la insulina en los animales de prueba y lo similar.

En consecuencia, un fármaco que suprima y/o inhiba la activación de tal tirosina fosfatasa, particularmente la PTP1B, mejora la acción hasta la captación de la glucosa, inhibiendo que una señal activada por el receptor de la insulina, sea controlada negativamente a través de la desfosforilación, y puede ser un nuevo tipo de agente terapéutico para la diabetes, que disminuya la glucosa en sangre, basado en la mejora directa de la acción de la insulina. Además, se espera la aplicación de varios agentes terapéuticos para las enfermedades tales como la obesidad, enfermedad neurodegenerativa y lo similar.

Hay varios reportes en años recientes sobre compuestos dirigidos al tratamiento de enfermedades, tales como la diabetes y lo similar, mediante la inhibición de tal proteína tirosina fosfatasa.

Por ejemplo, la WO00/17211, describe un derivado de ácido fosfónico que tiene una actividad inhibidora de la PTP1B. Sin embargo, esta publicación no describe un compuesto que tiene una estructura del compuesto de la presente invención, ni menciona ninguna descripción sugestiva de lo mismo.

La JP-T-11-508919 (Patente de E.U.A. No. 5,770,620), describe un derivado de ácido arilacrílico útil como un inhibidor de la proteína tirosina fosfatasa. Sin embargo, esta publicación no describe un compuesto que tiene una estructura del compuesto de la presente invención, ni menciona ninguna descripción sugestiva de lo mismo.

La WO98/27092 (Patente de E.U.A. No. 6,080,772), describe un compuesto de tiazol que tiene una acción inhibidora de la proteína tirosina fosfatasa. Sin embargo, esta publicación no describe un compuesto que tiene una estructura del compuesto de la presente invención, ni menciona ninguna descripción sugestiva de lo mismo.

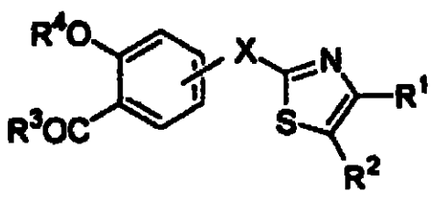
La WO99/58522 describe un derivado de nafto[2,3-B]heteroar-4-ilo, la WO99/58511 describe un derivado del ácido oxa/tiazol-aril-carboxílico; la WO99/58521 y la Patente de E.U.A. No. 6,110,962, describen derivados de 11-aril-benzo[B]nafto[2,3-D]furano y 11-aril-benzo[B]nafto[2,3-D]tiofeno; la WO99/58518 describe un derivado del ácido bifenil-oxo-acético; la WO99/61419 describe un derivado de bifenilo 2,3,5 sustituido; la WO99/58520 describe un derivado del ácido bifenil-sulfonil-aril-carboxílico; la WO99/61435 describe derivados de benzotiofeno, benzofurano e indol; la Patente de E.U.A. No. 6,103,708, describe derivados de furano, benzofurano y tiofeno; la Patente de E.U.A. No. 6,110,963, describe un derivado del ácido aril-oxo-acético; la Patente de E.U.A. No. 6,001,867, describe un derivado del 1-aril-dibenzotiofeno; la Patente de E.U.A. No. 6,057,316, describe un derivado del 4-aril-1-oxa-9-tia-ciclopenta[B]fluoreno; la Patente de E.U.A. No. 6,063,815, describe un derivado de benzofenona, cada uno de los cuales tiene una acción inhibidora de la proteína tirosina fosfatasa. Sin embargo, estas publicaciones no describen un compuesto que tiene una estructura del compuesto de la presente invención, ni menciona ninguna descripción sugestiva de lo mismo.

Como un compuesto que tiene una estructura de tiazol, tiofeno u oxazol, se ha reportado lo siguiente.

La WO00/45635 describe un derivado de tiazol 2 sustituido. Sin embargo, este compuesto tiene un grupo carbamoilo en el extremo del sustituyente de la posición 2 de un anillo de tiazol, y esta publicación no describe un compuesto que tiene una estructura del compuesto de la presente invención, ni menciona ninguna descripción sugestiva de lo mismo. El compuesto de esta publicación es útil como un agente antibacteriano o un agente analgésico, y esta publicación no describe la utilidad como un inhibidor de la PTP1B, ni menciona ninguna descripción sugestiva de lo mismo.

La JP-T-2000-504039 describe un derivado de 2-anilino-4-feniltiazol. Sin embargo, el compuesto de esta publicación tiene un grupo anilino sustituido por un grupo hidroxilo o un grupo carboxilo en la posición 2 del anillo de tiazol, y el grupo fenilo en la posición 4, en donde el grupo fenilo en la posición 4 tiene un sustituyente en la posición 2. Esta publicación no describe un compuesto que tiene una estructura del compuesto de la presente invención, ni menciona ninguna descripción sugestiva de lo mismo. Además, el compuesto de esta publicación es útil como un antagonista del CRF (factor de liberación de la corticotropina). Esta publicación no describe la utilidad como un inhibidor de la PTP1B, ni menciona ninguna descripción sugestiva de lo mismo.

La JP-A-4-154773 describe un derivado de tiazol de la fórmula

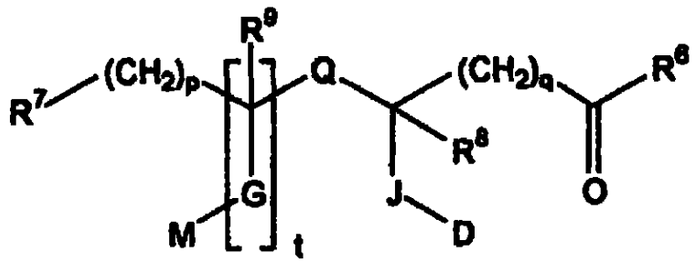


en donde R^1 y R^2 son los mismos o diferentes, y cada uno es un átomo de hidrógeno, un átomo de halógeno, un grupo alquilo inferior, un grupo fenilo, un grupo fenilo sustituido, un grupo piridilo o un grupo piridilo sustituido, R^3 es un grupo hidroxilo, un grupo alcoxi inferior o un grupo representado por $-N(R^5)(R^6)$, en donde R^5 y R^6 son los mismos o diferentes y cada uno es un átomo de hidrógeno o un grupo alquilo inferior, R^4 es un átomo de hidrógeno o un grupo alquilo inferior, y X es un grupo amino, un grupo amida, un grupo carbonilo, un grupo alquileno, un átomo de oxígeno o un átomo de azufre. Sin embargo, esta publicación no describe un compuesto que tiene una estructura del compuesto de la presente invención, ni menciona ninguna descripción sugestiva de lo mismo. Además, el compuesto de esta publicación es útil como un agente antiinflamatorio. Esta publicación no describe la utilidad como un inhibidor de la PTP1B, ni menciona ninguna descripción sugestiva de lo mismo.

La WO94/08982 describe un derivado de 4-feniltiazol. Sin embargo, el compuesto de esta publicación tiene un grupo fenilo en la posición 4 del anillo de tiazol, y un grupo fenilo en la posición 4, en donde el grupo fenilo en la posición 4 tiene un sustituyente en la posición 2. Esta publicación no describe un compuesto que tiene una estructura del compuesto de la presente invención, ni menciona ninguna descripción sugestiva de lo

mismo. Además, el compuesto de esta publicación es útil como un eliminador de organismos dañinos. Esta publicación no describe la utilidad como un inhibidor de la PTP1B, ni menciona ninguna descripción sugestiva de lo mismo.

La WO02/39997 describe un compuesto representado por la fórmula

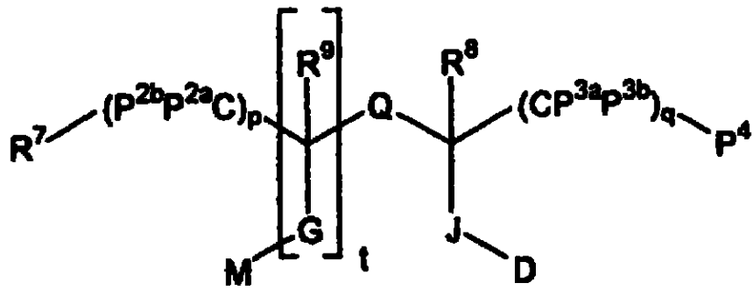


en donde R^6 es un grupo hidroxilo o una porción protectora de profármaco, R^7 es un átomo de hidrógeno, un grupo carboxi, un grupo arilaminocarbonilo, un grupo aroilo, un grupo arilo, un grupo alquilaminocarbonilo, un grupo aminocarbonilo, un grupo alquenilaminocarboxi, un grupo hidroxilo, un grupo alcoxi, éter, tiol, un grupo heteroanular que contiene un grupo amino o una porción protectora de profármaco, R^8 es un átomo de hidrógeno o un grupo alquilo que puede estar unido con D para formar un anillo, R^9 es un grupo alquilo inferior o un átomo de hidrógeno, Q es un enlace, un átomo de oxígeno, un átomo de azufre, CR^3OH, CR^3SH, $CR^3NR^{3a}R^{3b}$, NR^3, $(CR^3R^{3a})_n$, $O(CR^3R^{3b})_n$ o $(CR^3R^{3a})_nO(CR^{3b}R^{3c})_n$, en donde n es 0 o un entero de 1 a 3, R^3, R^{3a}, R^{3b} y R^{3c} son cada uno de manera independiente, un átomo de hidrógeno, una cadena

lineal sustituida opcionalmente, un grupo alquilo de C_{1-6} de cadena cíclica o ramificada, un grupo alquenilo de C_{2-6}, un grupo acilo, un grupo arilalquilo, un grupo ariloxicarbonilo, un grupo arilaminocarbonilo, un grupo arilalquilsulfonilo o un grupo arilo), G es una porción enlazante, M es una porción de anclaje, J es un enlace, un grupo alquileno, un grupo alquenileno o un grupo alquinileno, D es un átomo de hidrógeno, un grupo alcoxi, una amina, un grupo alquilo, un grupo alquenilo, un grupo alquinilo, un grupo arilo o un grupo heteroarilo que está unido con G, M o Q para formar un anillo, t es 0 ó 1, p es 0 o un entero de 1 a 5, y q es 0 o un entero de 1 a 3],

y

un compuesto representado por la fórmula

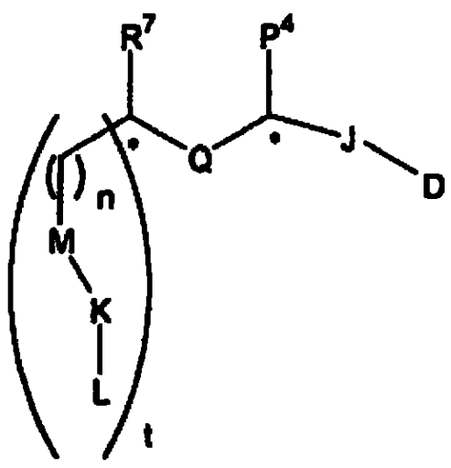


en donde P^4 es un grupo carboxi, una porción escindible del profármaco, $COOP^{4'}$, $(CH_2)_{1-4}SP^{4'}$ o $C(O)NP^{4'}P^{4''}$, R^7 es un átomo de hidrógeno, un grupo carboxi, un éster de alquilo inferior sustituido opcionalmente, un éster de alquenilo inferior, un éster agregado con una amina secundaria sustituida con un alquilo inferior, un grupo arilaminocarbonilo, un grupo aroilo, un grupo arilo, un grupo

alquilaminocarbonilo, un grupo aminocarbonilo, $COOR^{7'}$, $CONR^{7'}R^{7''}$, un grupo hidroxilo, éter, tiol, un grupo amino, $(CH_2)_{1-4}SR^{7'}$, un grupo heteroanular o una porción escindible del profármaco, $P^{4'}$, $P^{4''}$, $R^{7'}$ y $R^{7''}$ son cada uno de manera independiente, un átomo de hidrógeno, un grupo alquilo de C_{1-6}, un grupo alquenilo de C_{2-6}, un grupo alquinilo de C_{2-6} o un grupo arilo sustituido opcionalmente, R^8 es un átomo de hidrógeno, un grupo alquilo o un enlace covalente con D, R^9 es un grupo alquilo inferior o un átomo de hidrógeno, Q es un enlace, un átomo de oxigeno, un átomo de azufre, CR^3OH, CR^3SH, $CR^3NR^{3a}R^{3b}$, NR^3, $(CR^3R^{3a})_n$, $O(CR^3R^{3b})_n$ o $(CR^3R^{3a})_nO(CR^{3b}R^{3c})_n$, en donde n es 0 o un entero de 1 a 3, R^3, R^{3a}, R^{3b} y R^{3c} son cada uno de manera independiente, un átomo de hidrógeno, un grupo alquilo de C_{1-6} de cadena lineal o de cadena ramificada sustituido opcionalmente, un grupo alquenilo de C_{2-6} de cadena lineal o de cadena ramificada, un grupo ariloxicarbonilo, un grupo arilaminocarbonilo, un grupo arilalquilsulfonilo, un grupo arilalquilo, un grupo acilo sustituido opcionalmente, un grupo arilo o un anillo de C_{3-6} sustituido opcionalmente por 4 heteroátomos como máximo, P^{2a}, P^{2b}, P^{3a} y P^{3b} son cada uno de manera independiente, un átomo de hidrógeno o una cadena lineal sustituida opcionalmente, una cadena ramificada o un grupo alquilo de C_{1-5} cíclico, G es una porción enlazante, M es una porción de anclaje, J es un enlace, un grupo alquileno, un grupo alquenileno o un grupo alquinileno, D es un átomo de hidrógeno, un grupo alquilo, un grupo alquenilo, un grupo alquinilo o un grupo arilo o puede estar unida con G, M o Q para formar un anillo, t es 0 ó 1, p es 0 o un entero de 1 a 5, y q es 0 o un entero de 1 a 3, y

como ejemplos de la porción de anclaje en cada fórmula, un grupo tiazol y un grupo oxazol que tienen, como un sustituyente, un grupo arilo o un grupo heteroarilo sustituido por $-NR'R''$, $-CONR'R''$, $-S(O)_2NR'R''$, $-S(O)_{0-2}R'$, $-NR'R''$, $-O(CR'R'')_{0-2}CF_3$, $-COR'$, $-CO_2R'$ y $-OR'$, en donde R' y R'' son cada uno de manera independiente, un átomo de hidrógeno, un grupo alquilo de C_{1-6}, un grupo alquenilo de C_{2-6}, un grupo alquinilo de C_{2-6} o un grupo arilo sustituido opcionalmente, y como ejemplos de la porción enlazante, se describe un enlace covalente y un grupo alquilo de C_{1-6}.

Además, se describe un compuesto representado por la fórmula



en donde M es un grupo anular de carbono, un grupo heteroanular o $CONR'R''$, en donde R' y R'' son cada uno de manera independiente, un átomo de hidrógeno, un grupo alquilo de C_{1-6}, un grupo alquenilo de C_{2-6}, un grupo alquinilo de C_{2-6} o un grupo arilo sustituido opcionalmente, Q es un enlace, un átomo de oxígeno, un átomo de azufre, CR^3OH, CR^3SH, $CR^3NR^{3a}R^{3b}$, NR^3, $(CR^3R^{3a})_n$, $O(CR^3R^{3b})_n$ o

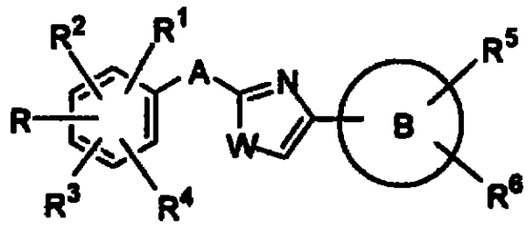
$(CR^3R^{3a})_nO(CR^{3b}R^{3c})_n$, en donde n es 0 o un entero de 1 a 3, R^3, R^{3a}, R^{3b} y R^{3c} son cada uno de manera independiente, un átomo de hidrógeno, una cadena ramificada sustituida opcionalmente, un grupo alquilo de C_{1-6} de cadena cíclica o lineal, un grupo alquenilo de C_{2-6}, un grupo acilo, un grupo arilalquilo, un grupo ariloxicarbonilo, un grupo arilaminocarbonilo, un grupo arilalquilsulfonilo o un grupo arilo, K es una porción enlazante secundaria seleccionada de manera independiente, L es una porción de anclaje secundaria seleccionada de manera independiente, P^4 es un átomo de hidrógeno, un grupo carboxi, $(CH_2)_{1-4}SP^{4'}$, una porción escindible del profármaco, $COOP^{4'}$ o $CONP^{4'}P^{4''}$, R^7 es un átomo de hidrógeno, un grupo carboxi, un grupo aroilo, un grupo arilo, $COOR^{7'}$, $C(O)NR^{7'}R^{7''}$, un grupo hidroxilo, éter, tiol, $(CH_2)_{1-4}SR^{7'}$, un grupo heteroanular o una porción escindible del profármaco, $P^{4'}$, $P^{4''}$, $R^{7'}$ y $R^{7''}$ son cada uno de manera independiente, un átomo de hidrógeno, un grupo alquilo de C_{1-6}, un grupo alquenilo de C_{2-6}, un grupo alquinilo de C_{2-6} o un grupo arilo sustituido opcionalmente, n es 0 o un entero de 1 a 4, D es un átomo de hidrógeno, un grupo alquilo, un grupo alcoxi, un grupo alquenilo, una amina, un grupo hidroxilo, un grupo alquinilo, un grupo arilo o un grupo heteroarilo, y t es 0 ó 1, y se describe que la porción enlazante secundaria tiene un enlace covalente, y la porción de anclaje secundaria tiene un grupo arilo sustituido opcionalmente.

Sin embargo, esta publicación no describe un compuesto que tiene una estructura del compuesto de la presente invención, ni menciona ninguna descripción sugestiva de lo mismo.

Además, el compuesto de esta publicación es útil como un agente que regula la enzima que convierte la angiotensina (ACE)-2. Esta publicación no describe la utilidad como un inhibidor de la PTP1B, ni menciona ninguna descripción sugestiva de lo mismo.

Como reportes de un compuesto que tiene una estructura de tiazol u oxazol, que está dirigido al tratamiento no sólo de la diabetes, sino también de la hiperlipidemia mediante la inhibición de la PTP1B, puede mencionarse lo siguiente.

La JP-A-2003-231679 describe un compuesto de azol representado por la fórmula



[I]

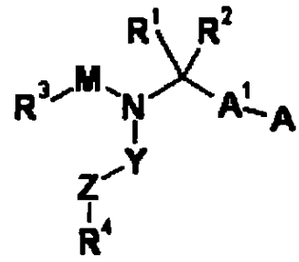
que tiene una actividad inhibidora de la PTP1B, y enseña que este compuesto es útil como un agente terapéutico para la hiperlipidemia. Sin embargo, el compuesto de esta publicación está caracterizado esencialmente en que el átomo de nitrógeno o el grupo carbonilo en el sustituyente A debe estar adyacente al átomo de carbono en la posición 2 del tiazol u oxazol, o A es un alquileno; un enlace entre A y el anillo de benceno es esencial; y un átomo de nitrógeno, átomo de oxígeno, átomo de azufre o grupo carbonilo en el sustituyente R^6 debe estar adyacente al anillo B, o R^6 está unido a la

estructura anular vía un alquileno o es esencial un enlace sencillo, y esta publicación no describe un compuesto que tiene una estructura del compuesto de la presente invención. Además, esta publicación no describe que la actividad inhibidora de la PTP1B de este compuesto sea más alta que la actividad de otras proteínas tirosina fosfatasas.

Como reportes de un método que utiliza varios profármacos terapéuticos para la diabetes u otras enfermedades en combinación, pueden mencionarse lo siguiente.

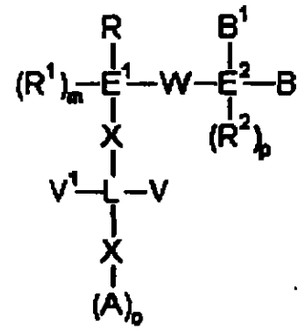
La JP-A-9-67271 describe una combinación de un mejorador de la sensitividad de la insulina con una preparación de insulina, un secretagogo de insulina, un inhibidor de α-glucosidasa, un agente de biguanida y lo similar. Sin embargo, esta publicación no describe un inhibidor de la PTP1B o un inhibidor del regulador negativo del receptor de tirosina cinasa tal como un compuesto de la presente invención, ni menciona ninguna descripción sugestiva de lo mismo.

La WO02/100846 describe un compuesto derivado de tiofeno que tiene la fórmula



en donde M se selecciona de $-SO_2-$, -C=O-, -C=S-, etc.; A^1 se selecciona de un enlace, un alquilo de C_{1-6}, un alquenilo de C_{2-6}, etc.; A se selecciona de $COOR^5$, $CO-COOR^5$, $PO_3R^5R^5$, etc., en donde cada R^5 se selecciona de manera independiente de un átomo de hidrógeno y alquilo de C_{1-6}; R^1 y R^2 se seleccionan de manera independiente de un átomo de hidrógeno, un alquilo de C_{1-6}, un arilo de C_{6-12}, etc.; R^3 se selecciona de un arilo de C_{6-12}, un heterociclo de C_{3-10}, un aralquilo de C_{6-12}, etc.; Y se selecciona de un enlace, $-CH_2-$, -CO-, etc.; Z se selecciona de un alquilo de C_{1-6}, un alquenilo de C_{2-6}, un alquinilo de C_{2-6}, etc.; R^4 se selecciona de un átomo de hidrógeno, halógeno, CN, NO_2, etc.; o una sal del mismo.

La WO 02/34711 describe un compuesto derivado de tiofeno que tiene la fórmula

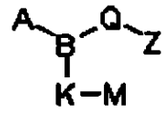


en donde

E^1 y L se seleccionan cada uno de manera independiente de un anillo de carbono de 5 a 7 miembros, saturado o no saturado, un heteroanillo de 5 a 7 miembros saturado o no saturado, un anillo de carbono bicíclico, saturado o no saturado, etc.; R se selecciona de $-CH=CH-R^2$, $-C\equiv C-R^2$,

-C(R^2)=CH, etc.; R^1 se selecciona de un átomo de hidrógeno, -R, -NO_2, etc.; m es 1 o mayor; R^2 se selecciona de un átomo de hidrógeno, un halógeno, un alquilo, etc.; W se selecciona de un enlace directo, -CHR^2-, -$CH=CR^2$-, etc.; E^2 se selecciona de un anillo de carbono de 5 a 7 miembros, saturado o no saturado, un heteroanillo de 5 a 7 miembros saturado o no saturado, un sistema anular bicíclico, etc.; cada X se selecciona de manera independiente de un enlace directo, una cadena de metileno de C_{1-4} sustituida o no sustituida, O, etc., en donde la X en las diferentes ubicaciones puede ser el mismo o diferente; B se selecciona de un átomo de hidrógeno, -halo, -CN, etc.; B^1 se selecciona de B, en donde B^1 y B pueden ser los mismos o diferentes; p es 1 o mayor, dependiendo del tamaño del anillo; A se selecciona de R^1 cuando o es 1, excepto que cuando L es un anillo cíclico de más que 5 átomos, o es 1 o mayor dependiendo del tamaño del anillo; V y V^1 se seleccionan cada uno de manera independiente de R^1 y carboxamidilo sustituido con N-alquilo (CONHR), en donde el grupo alquilo puede ser lineal, ramificado, cíclico o bicíclico, etc.; y n es 0 a 4.

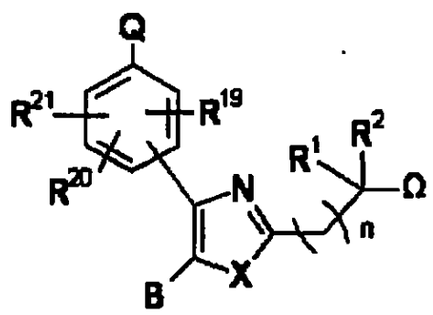
La WO 98/28264 describe un compuesto derivado de tiofeno que tiene la siguiente fórmula



en donde B es N; A se selecciona de un alquilsulfonilo de C_{1-6}, un cicloalquilsulfonilo de C_{3-7}, un cicloalquil de C_{3-7}-alquilsulfonilo de C_{1-6}, cada

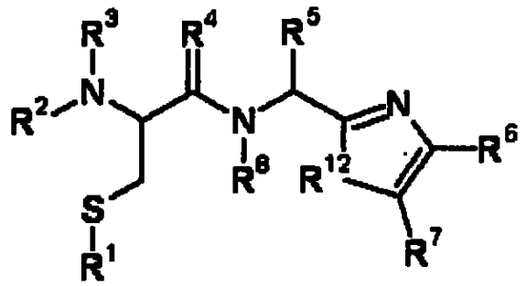
uno de los cuales está mono, di o trisustituido con un grupo hidroxi, un alquilo de C_{1-4} o un átomo de halógeno; Q es un -alquilen de C_{2-8}-W-alquileno de C_{1-3}- o un -alquileno de C_{3-8} -, el -alquileno de C_{3-8} - está sustituido opcionalmente con hasta cuatro sustituyentes seleccionados de manera independiente de un átomo de flúor, un alquilo de C_{1-4}, -X-alquileno de C_{1-5}-, etc., en donde X es un anillo aromático de 5 ó 6 miembros que tiene opcionalmente uno o dos heteroátomos seleccionados de manera independiente de un átomo de oxígeno, un átomo de nitrógeno y un átomo de azufre; Z es carboxilo, un alcoxicarbonilo de C_{1-6}, tetrazolilo, etc.; K es un enlace, un alquileno de C_{1-8}, un tioalquileno de (C_{1-4}), etc., en donde el alquileno de C_{1-8} está opcionalmente monoinsaturado y K está opcionalmente mono, di o trisustituido con un átomo de flúor, un metilo o un átomo de cloro; y M es -Ar, -Ar^1-V-AP, -Ar^1-S-AP, etc., en donde Ar, Ar^1 y AP se seleccionan cada uno de manera independiente de un anillo de 5 a 8 miembros parcialmente saturado, completamente saturado o completamente no saturado, que tiene opcionalmente uno a cuatro heteroátomos seleccionados de un átomo de oxígeno, un átomo de azufre y un átomo de nitrógeno, etc.; o una sal farmacéuticamente aceptable del mismo o un profármaco del mismo.

Además, la WO 01/26656 (JP-A-2003-511416) describe un compuesto que tiene la siguiente fórmula



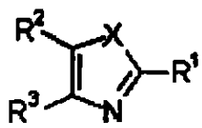
en donde Ω es $-NR^{46}R^{47}$ o $-OR^{46}$, en donde R^{46} y R^{47} se seleccionan cada uno de manera independiente de un átomo de hidrógeno, un alquilo, un cicloalquilo, etc., y R^{48} se selecciona de un átomo de hidrógeno, un alquilo, un alquinilo, etc.; B es un átomo de hidrógeno o un alquilo; Q se selecciona de un átomo de hidrógeno, $-OR^{22}$, $-SR^{22}$, etc., en donde R^{22} se selecciona de un átomo de hidrógeno, un alquilo, un arilo sustituido opcionalmente con un alquilo, un grupo hidroxilo, un átomo de halógeno, etc., etc.; R^{19}, R^{20} y R^{21} se seleccionan cada uno de manera independiente de un átomo de hidrógeno, un átomo de halógeno, un grupo hidroxi, etc.; X es NH o S; N es 0 a 6; R^1 y R^2 se seleccionan cada uno de un átomo de hidrógeno, un alquilo y un cicloalquilo.

La WO 97/30053 describe un compuesto que tiene la siguiente fórmula



en donde R^1 es un átomo de hidrógeno, un alquilo inferior, un cicloalquiltio o un alquiltio inferior, y R^2 y R^3 son cada uno de manera independiente, un átomo de hidrógeno o un alquilo inferior; o R^1 y R^2 pueden formar $-CH_2-$, -CO- o $-C(CH_3)_2-$; R^4 es H2 u O; R^5 se selecciona de un átomo de hidrógeno, un alquilo inferior sustituido o no sustituido, un alquenilo inferior, etc.; R^6 y R^7 se seleccionan cada uno de manera independiente de un átomo de hidrógeno, $-C(O)NHCHR^{13}CO_2R^{14}$, un alquilo inferior sustituido o no sustituido, etc., en donde R^{13} se selecciona de un alquilo inferior sustituido o no sustituido, etc., y R^{14} es un átomo de hidrógeno o un alquilo inferior, o R^6 y R^7 pueden formar un arilo o un heterociclilo; R^8 y R^9 se seleccionan cada uno de manera independiente de un átomo de hidrógeno, un alquilo inferior sustituido o no sustituido, un cicloalquilo, etc.; y R^{12} es NR^9, S u O; o una sal farmacéuticamente aceptable del mismo.

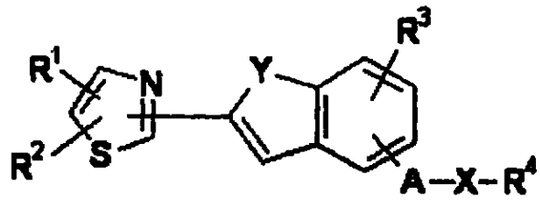
La WO 99/21555 y la JP-A-2000-302680 describen un compuesto que tiene la siguiente fórmula



en donde R^1 se selecciona de un átomo de hidrógeno, un grupo hidrocarburo el cual puede estar sustituido, un grupo heterocíclico que puede estar sustituido, etc.; al menos uno de R^2 y R^3 es un átomo de hidrógeno, un piridilo que puede estar sustituido o un grupo hidrocarburo aromático que puede estar sustituido, y el otro es un piridilo que puede estar sustituido; y X

es un átomo de azufre el cual puede estar oxidado, un átomo de oxígeno o un grupo representado por la fórmula NR^4, en donde R^4 es un átomo de hidrógeno, un grupo hidrocarburo que puede estar sustituido o un acilo; o una sal del mismo, el cual puede estar N oxidado.

La JP-A-5-202040 describe un compuesto que tiene la siguiente fórmula



en donde R^1 es un alquilo el cual puede estar sustituido, o un grupo cicloalquilo, tricicloalquilo o arilheterocíclico que puede estar sustituido; y R^2 es un átomo de hidrógeno o un átomo de halógeno, o R^1 y R^2, junto con el átomo adyacente, forman un anillo de cicloalqueno o un anillo heterocíclico que contiene N; R^3 se selecciona de un átomo de hidrógeno, un átomo de halógeno, OH, etc.; R^4 se selecciona de un átomo de hidrógeno, un grupo acilo, CN, etc.; A es un alquileno, un alquenileno o un enlace sencillo; X es un enlace sencillo, O o S; y

Y es O o S, o una sal del mismo.

Sin embargo, estas publicaciones no describen un compuesto que tiene una estructura del compuesto de la presente invención, ni menciona ninguna descripción sugestiva de lo mismo.

BREVE DESCRIPCION DE LA INVENCION

La presente invención está dirigida a proporcionar un compuesto que tiene una actividad inhibidora selectiva superior de la PTP1B y una actividad inhibidora del regulador negativo del receptor de la tirosina cinasa basada la misma, que es útil como un agente terapéutico para la diabetes, un agente terapéutico para la hiperlipidemia, la obesidad o complicación diabética, y un agente terapéutico para una enfermedad, tal como una enfermedad neurodegenerativa y lo similar.

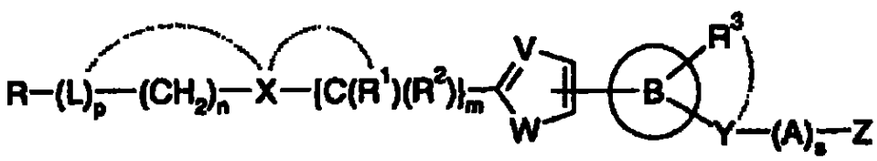
Es un objeto de la presente invención proporcionar un inhibidor de la PTP1B, un agente terapéutico para la diabetes, un agente terapéutico para la hiperlipidemia, un agente terapéutico para la obesidad o un agente terapéutico para las complicaciones diabéticas.

Los presentes inventores han realizado estudios extensos con el propósito de alcanzar el objeto mencionado anteriormente y han encontrado que un compuesto anular heteroaromático de 5 miembros, representado por la siguiente fórmula [I], tiene una alta actividad inhibidora de la PTP1B, pero una baja actividad inhibidora contra otras proteínas tirosina fosfatasas, a saber, una actividad inhibidora selectiva superior de la PTP1B, ausente en los compuestos convencionales, y útil como un inhibidor de la PTP1B, un agente terapéutico para la diabetes, un agente terapéutico para la hiperlipidemia, un agente terapéutico para la obesidad o un agente terapéutico para las

complicaciones diabéticas, lo cual resultó en la terminación de la presente invención.

La presente invención se relaciona con compuestos y el uso farmacéutico de los mismos, representados por lo siguiente [1] a [113].

[1] Un compuesto anular heteroaromático de 5 miembros, representado por la fórmula [I]



[I]

en donde

V es =N- o =CH-;

W es -S- u -O-;

m es 0, 1 ó 2;

R^1 y R^2 son cada uno de manera independiente, un átomo de hidrógeno o un grupo alquilo de C_{1-4};

X es $-N(R^4)-$, $-N(R^5)-CO-O-$, $-SO_2-N(R^5)-$, $-N(R^5)-SO_2-$, $-N(R^6)-SO_2-N(R^5)-$, $-CO-N(R^7)-$, $-N(R^8)-CO-$, $-N(R^9)-CO-N(R^5)-$, $-N(R^{10})-(CH_2)_k-N(R^5)-$, $-N(R^{10})-(CH_2)_k-N(R^5)-CO-$, $-C(R^{10})=N-N(R^7)-$, $-N(R^{10})-(CH_2)_k-CH(R^6)-$, -O-, -S- o $-SO_2-$

en donde

k es 0 o un entero de 1 a 4,

R^4, R^5, R^6, R^7, R^8, R^9 y R^{10} son cada uno de manera independiente

(1) un átomo de hidrógeno,

(2) un grupo alquilo de C_{1-6}

en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por

(a) un grupo arilo sustituido opcionalmente,

(b) un grupo anular heteroaromático sustituido opcionalmente,

(c) un grupo carboxi,

(d) un grupo alcoxicarbonilo de C_{1-4},

(e) $-CO-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son cada uno de manera independiente, un átomo de hidrógeno, un grupo arilo sustituido opcionalmente, un grupo anular heteroaromático sustituido opcionalmente, un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de un grupo arilo sustituido opcionalmente, un grupo anular heteroaromático sustituido opcionalmente, un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo arilo y un grupo ariloxi sustituido opcionalmente, o, junto con el átomo de nitrógeno unido al mismo, puede formar un anillo de indolina o puede formar un heteroanillo de 5 a 7 miembros que contiene opcionalmente además, al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre,

(f) $-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son como se definió anteriormente,

(g) $-O-R^{17}$

en donde R^{17} es un átomo de hidrógeno, un grupo arilo sustituido opcionalmente, un grupo anular heteroaromático sustituido opcionalmente o un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de un grupo arilo sustituido opcionalmente, un grupo anular heteroaromático sustituido opcionalmente, un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo arilo y un grupo ariloxi sustituido opcionalmente,

(h) $-CO-R^{17}$

en donde R^{17} es como se definió anteriormente,

(i) $-SO_2-R^{17}$

en donde R^{17} es como se definió anteriormente o

(j) un grupo cicloalquilo de C_{3-7},

(3) $-CO-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son como se definió anteriormente,

(4) $-SO_2-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son como se definió anteriormente,

(5) $-CO-R^{17}$

en donde R^{17} es como se definió anteriormente,

(6) $-SO_2-R^{17}$

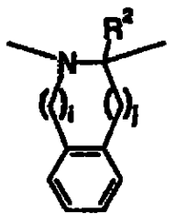
en donde R^{17} es como se definió anteriormente,

(7) un grupo arilo sustituido opcionalmente,

(8) un grupo anular heteroaromático sustituido opcionalmente,

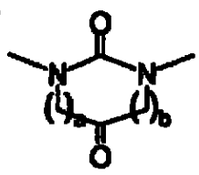
o

(9) R^4 y R^1 están unidos opcionalmente para formar



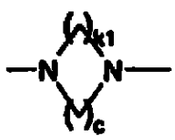
en donde i y j son cada uno de manera independiente 0, 1 ó 2 y R^2 es como se definió anteriormente,

(10) R^5 y R^9 están unidos opcionalmente para formar



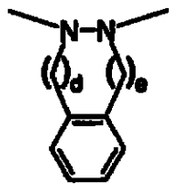
en donde a y b son cada uno de manera independiente 0, 1 ó 2,

(11) R^5 y R^{10} están unidos opcionalmente para formar



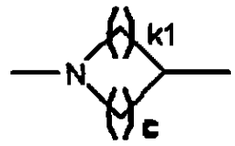
en donde k1 y c son cada uno de manera independiente 0 o un entero de 1 a 4,

(12) R^5 y R^{10} están unidos opcionalmente para formar



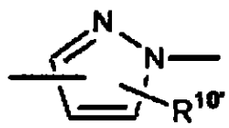
en donde d y e son cada uno de manera independiente 0, 1 ó 2,

(13) R^6 y R^{10} están unidos opcionalmente para formar



en donde k1 y c son como se definió anteriormente, o

(14) R^7 y R^{10} están unidos opcionalmente para formar



en donde $R^{10'}$ es un átomo de hidrógeno o un grupo alquilo de C_{1-6};

n es 0 o un entero de 1 a 4;

p es 0 ó 1;

L es

(1)

$-C(R^{20})(R^{21})-$

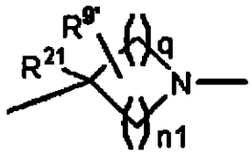
en donde

R^{20} es

(a) un átomo de hidrógeno,

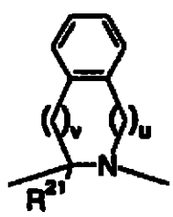
(b) un grupo alquilo de C_{1-6}, o

(c) unido opcionalmente con R^4 o R^8 para formar



en donde n1 y q son cada uno de manera independiente 0 o un entero de 1 a 4, $R^{9'}$ es un átomo de hidrógeno, un grupo hidroxilo, un grupo alquilo de C_{1-6}, un grupo carboxi o un grupo alcoxi de C_{1-6}, o

(d) unido opcionalmente con R^4 para formar



en donde u y v son cada uno de manera independiente 0, 1 ó 2,

R^{21} es un átomo de hidrógeno, un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por un grupo arilo sustituido opcionalmente o un grupo anular heteroaromático sustituido opcionalmente, un grupo arilo sustituido opcionalmente o un grupo anular heteroaromático sustituido opcionalmente,

(2)



en donde

E es un grupo arilo o un grupo anular heteroaromático,

R^{22} es

(a) un átomo de hidrógeno,

(b) un átomo de halógeno,

(c) un grupo alquilo de C_{1-4},

(d) un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo carboxi,

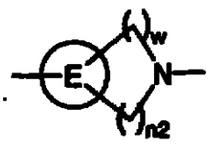
(e) un grupo alquiltio de C_{1-6},

(f) un grupo nitro,

(g) $-N(R^{23})(R^{24})$

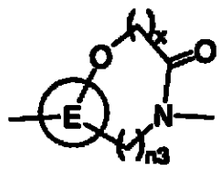
en donde R^{23} y R^{24} son cada uno de manera independiente, un átomo de hidrógeno, un grupo alquilo de C_{1-6}, un grupo alquilcarbonilo de C_{1-4} en donde el grupo alquilcarbonilo de C_{1-4} está sustituido opcionalmente por un grupo amino, un grupo alquilamino de C_{1-4} o un grupo di(alquil de C_{1-4})amino, o un grupo alquilsulfonilo de C_{1-4}, o

(h) unido opcionalmente con R^4 para formar



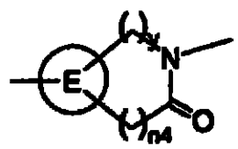
en donde n2 y w son cada uno de manera independiente 0 o un entero de 1 a 3 y E es como se definió anteriormente,

(i) unido opcionalmente con R^4 para formar



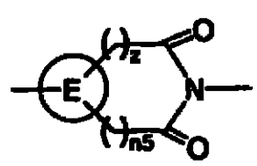
en donde n3 y x son cada uno de manera independiente 0 ó 1 y E es como se definió anteriormente,

(j) unido opcionalmente con R^7 para formar



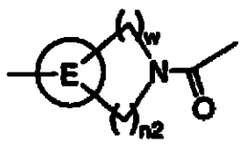
en donde n4 y y son cada uno de manera independiente 0, 1 ó 2 y E es como se definió anteriormente,

(k) unido opcionalmente con R^7 para formar



en donde n5 y z son cada uno de manera independiente 0 ó 1 y E es como se definió anteriormente,

(l) unido opcionalmente con R^8 para formar



en donde n2 y w son cada uno de manera independiente 0 o un entero de 1 a 3 y E es como se definió anteriormente, o

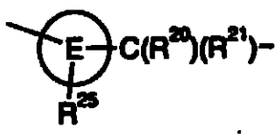
(m) unido opcionalmente con R^4 para formar



en donde E es como se definió anteriormente

o

(3)



en donde

R^{20}, R^{21} y E son como se definió anteriormente,

R^{25} es

(a) un átomo de hidrógeno,

(b) un átomo de halógeno,

(c) un grupo alquilo de C_{1-4},

(d) un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo carboxi,

(e) un grupo alquiltio de C_{1-6},

(f) un grupo nitro o

(g) $-N(R^{23})(R^{24})$

en donde R^{23} y R^{24} son como se definió anteriormente;

R es $-COO(R^{19})$, $-A^1-COO(R^{19})$ o $-O-A^1-COO(R^{19})$

en donde A^1 es un grupo alquileno de C_{1-4} y R^{19} es un átomo de hidrógeno o un grupo alquilo de C_{1-4};

B es un grupo arilo o un grupo anular heteroaromático;

R^3 es

(1) un átomo de hidrógeno,

(2) un átomo de halógeno,

(3) un grupo alquilo de C_{1-6},

(4) un grupo alcoxi de C_{1-6},

(5) un grupo alquilamino de C_{1-6},

(6) un grupo di(alquil de C_{1-6})amino,

(7) un grupo ciano,

(8) un grupo nitro,

(9) un grupo haloalquilo de C_{1-4},

(10) $-S-R^{18}$ en donde R^{18} es un grupo alquilo de C_{1-6} o un grupo arilo,

(11) $-SO-R^{18}$ en donde R^{18} es un grupo alquilo de C_{1-6} o un grupo arilo,

(12) $-SO_2-R^{18}$ en donde R^{18} es un grupo alquilo de C_{1-6} o un grupo arilo,

(13) un grupo arilo o

(14) un grupo heterocíclico;

Y es -O-, -S-, -SO-, $-SO_2-$, $-N(R^{11})-$, $-N(R^{12})-CO-$, $-N(R^{12})-SO_2-$, $-SO_2-N(R^{12})-$, $-C(R^{13})(R^{14})-$, -CO-, $-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ o $-C(R^{13})(R^{14})-O-$

en donde

R^{11} es

(1) un átomo de hidrógeno,

(2) un grupo alquilo de C_{1-6}

en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de

(a) un grupo cicloalquilo de C_{3-7},

(b) un grupo arilo sustituido opcionalmente,

(c) un grupo heterocíclico sustituido opcionalmente,

(d) un grupo hidroxilo,

(e) un grupo alquilamino de C_{1-4} y

(f) un grupo di(alquil de C_{1-4})amino,

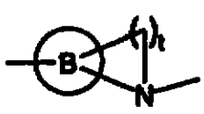
(3) un grupo alquenilo de C_{2-4},

(4) un grupo alquilsulfonilo de C_{1-4},

(5) un grupo alquilcarbonilo de C_{1-4}

en donde el grupo alquilcarbonilo de C_{1-4} está sustituido opcionalmente por un grupo hidroxilo o un grupo alcoxi de C_{1-4}, o

(6) unido opcionalmente con R^3 para formar



en donde t es un entero de 1 a 4 y B es como se definió anteriormente,

R^{12} es

(1) un átomo de hidrógeno,

(2) un grupo alquilo de C_{1-8}

en donde el grupo alquilo de C_{1-8} está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de

(a) un grupo cicloalquilo de C_{3-7},

(b) un grupo arilo sustituido opcionalmente,

(c) un grupo heterocíclico sustituido opcionalmente,

(d) un grupo hidroxilo,

(e) un grupo alquilamino de C_{1-4} y

(f) un grupo di(alquil de C_{1-4})amino,

(3) un grupo alquenilo de C_{2-4},

(4) un grupo alquilsulfonilo de C_{1-4} o

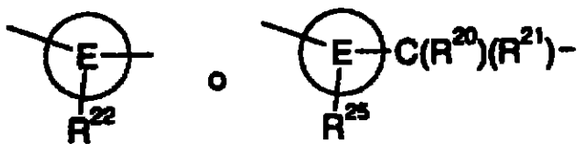
(5) un grupo alquilcarbonilo de C_{1-4}

en donde el grupo alquilcarbonilo de C_{1-4} está sustituido opcionalmente por un grupo hidroxilo o un grupo alcoxi de C_{1-4},

R^{13} y R^{14} son cada uno de manera independiente, un átomo de hidrógeno, un grupo alquilo de C_{1-4}, u opcionalmente forman un cicloalcano de C_{3-7} junto con el átomo de carbono unido al mismo, u opcionalmente forman, junto con el átomo de carbono unido al mismo, un heteroanillo de 5 a 7 miembros que tiene opcionalmente al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre,

con la condición de que,

cuando m es 0, p es 1 y L es



en donde R^{20} y R^{21} son cada uno un átomo de hidrógeno, E es un grupo fenilo, R^{22} es un átomo de hidrógeno, un átomo de halógeno, un grupo alquilo de C_{1-4}, un grupo alcoxi de C_{1-4} o un grupo nitro, y R^{25} es un átomo de hidrógeno, un átomo de halógeno, un grupo alquilo de C_{1-4}, un grupo alcoxi de C_{1-4} o un grupo nitro,

Y puede ser

$-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ o $-C(R^{13})(R^{14})-O-$, en donde R^{12}, R^{13} y R^{14} son como se definió anteriormente;

s es 0 ó 1;

A es un grupo alquileno de C_{1-4} sustituido opcionalmente por un grupo cicloalquilo de C_{3-7};

Z es

(1) un grupo cicloalquilo de C_{3-7}

en donde el grupo cicloalquilo de C_{3-7} está sustituido opcionalmente por un grupo arilo, en donde el grupo arilo está sustituido opcionalmente por un átomo de halógeno o un grupo alquilo de C_{1-6}, o un grupo anular heteroaromático, en donde el grupo anular heteroaromático está sustituido opcionalmente por un átomo de halógeno o un grupo alquilo de C_{1-6},

(2) un grupo arilo

en donde el grupo arilo está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de

(a) un grupo heterocíclico sustituido opcionalmente por un grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4},

(b) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por un grupo hidroxilo, un grupo oxo, un átomo de halógeno o un grupo alquilo de C_{1-6},

(c) un grupo carboxi,

(d) un átomo de halógeno,

(e) un grupo alquilo de C_{1-6},

(f) un grupo haloalquilo de C_{1-4},

(g) un grupo alquilamino de C_{1-4},

(h) un grupo di(alquil de C_{1-4})amino,

(i) un grupo alquiltio de C_{1-6},

(j) un grupo alcoxi de C_{1-4},

(k) un grupo alquilcarbonilo de C_{1-4} y

(l) un grupo nitro,

(3) un grupo anular heteroaromático

en donde el grupo anular heteroaromático está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de

(a) un grupo heterocíclico sustituido opcionalmente por un grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4},

(b) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por un grupo hidroxilo, un grupo oxo, un átomo de halógeno o un grupo alquilo de C_{1-6},

(c) un grupo carboxi,

(d) un átomo de halógeno,

(e) un grupo alquilo de C_{1-6},

(f) un grupo haloalquilo de C_{1-4},

(g) un grupo alquilamino de C_{1-4},

(h) un grupo di(alquil de C_{1-4})amino,

(i) un grupo alquiltio de C_{1-6},

(j) un grupo alcoxi de C_{1-4},

(k) un grupo alquilcarbonilo de C_{1-4} y

(l) un grupo arilo sustituido opcionalmente por un átomo de halógeno o un grupo haloalquilo de C_{1-4},

(4) un grupo indanilo o

(5) un grupo piperacinilo

en donde el grupo piperacinilo está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de

(a) un grupo fenilo,

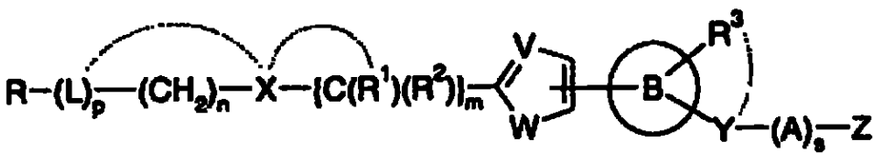
(b) un grupo fenilalquilo de C_{1-4},

(c) un grupo benzoilo sustituido opcionalmente por un átomo de halógeno y

(d) un grupo fenilalcoxicarbonilo de C_{1-4}

o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[2] El compuesto anular heteroaromático de 5 miembros de [1], el cual está representado por la fórmula [I]



[I]

en donde

V es =N- o =CH-;

W es -S- u -O-;

m es 0, 1 ó 2;

R^1 y R^2 son cada uno de manera independiente, un átomo de hidrógeno o un grupo alquilo de C_{1-4};

X es $-N(R^4)-$, $-N(R^5)-CO-O-$, $-SO_2-N(R^5)-$, $-N(R^5)-SO_2-$, $-N(R^6)-SO_2-N(R^5)-$, $-CO-N(R^7)-$, $-N(R^8)-CO-$, $-N(R^9)-CO-N(R^5)-$, $-N(R^{10})-(CH_2)_k-N(R^5)-$, -O-, -S- o $-SO_2-$

en donde

k es 0 o un entero de 1 a 4,

R^4, R^5, R^6, R^7, R^8, R^9 y R^{10} son cada uno de manera independiente

(1) un átomo de hidrógeno,

(2) un grupo alquilo de C_{1-6}

en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por

(a) un grupo arilo sustituido opcionalmente,

(b) un grupo anular heteroaromático sustituido opcionalmente,

(c) un grupo carboxi,

(d) un grupo alcoxicarbonilo de C_{1-4},

(e) $-CO-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son cada uno de manera independiente, un átomo de hidrógeno, un grupo arilo sustituido opcionalmente, un grupo anular heteroaromático sustituido opcionalmente, un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de un grupo arilo sustituido

opcionalmente, un grupo anular heteroaromático sustituido opcionalmente, un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo arilo y un grupo ariloxi sustituido opcionalmente, o, junto con el átomo de nitrógeno unido al mismo, puede formar un anillo de indolina o puede formar un heteroanillo de 5 a 7 miembros que contiene opcionalmente además al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre,

(f) $-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son como se definió anteriormente,

(g) $-O-R^{17}$

en donde R^{17} es un átomo de hidrógeno, un grupo arilo sustituido opcionalmente, un grupo anular heteroaromático sustituido opcionalmente o un grupo alquilo de C_{1-8}, en donde el grupo alquilo de C_{1-8} está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de un grupo arilo sustituido opcionalmente, un grupo anular heteroaromático sustituido opcionalmente, un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo arilo y un grupo ariloxi sustituido opcionalmente,

(h) $-CO-R^{17}$

en donde R^{17} es como se definió anteriormente,

(i) $-SO_2-R^{17}$

en donde R^{17} es como se definió anteriormente o

(j) un grupo cicloalquilo de C_{3-7},

(3) $-CO-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son como se definió anteriormente,

(4) $-SO_2-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son como se definió anteriormente,

(5) $-CO-R^{17}$

en donde R^{17} es como se definió anteriormente,

(6) $-SO_2-R^{17}$

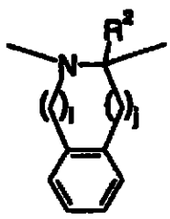
en donde R^{17} es como se definió anteriormente,

(7) un grupo arilo sustituido opcionalmente,

(8) un grupo anular heteroaromático sustituido opcionalmente,

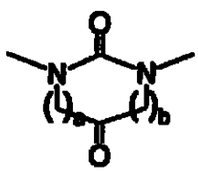
o

(9) R^4 y R^1 están unidos opcionalmente para formar



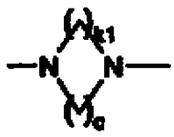
en donde i y j son cada uno de manera independiente 0, 1 ó 2 y R^2 es como se definió anteriormente,

(10) R^5 y R^9 están unidos opcionalmente para formar



en donde a y b son cada uno de manera independiente 0, 1 ó 2,

(11) R^5 y R^{10} están unidos opcionalmente para formar



en donde k1 y c son cada uno de manera independiente 0 o un entero de 1 a 4, o

(12) R^5 y R^{10} están unidos opcionalmente para formar



en donde d y e son cada uno de manera independiente 0, 1 ó 2;

n es 0 o un entero de 1 a 4;

p es 0 ó 1;

L es

(1) $-C(R^{20})(R^{21})-$

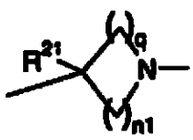
en donde

R^{20} es

(a) un átomo de hidrógeno,

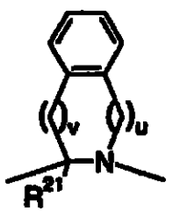
(b) un grupo alquilo de C_{1-8}, o

(c) unido opcionalmente con R^4 para formar



en donde n1 y q son cada uno de manera independiente 0 o un entero de 1 a 4, o

(d) unido opcionalmente con R^4 para formar



en donde u y v son cada uno de manera independiente 0, 1 ó 2,

R^{21} es un átomo de hidrógeno, un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por un grupo arilo sustituido opcionalmente o un grupo anular heteroaromático sustituido opcionalmente, un grupo arilo sustituido opcionalmente o un grupo anular heteroaromático sustituido opcionalmente,

(2)



en donde

E es un grupo arilo o un grupo anular heteroaromático,

R^{22} es

(a) un átomo de hidrógeno,

(b) un átomo de halógeno,

(c) un grupo alquilo de C_{1-4},

(d) un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo carboxi,

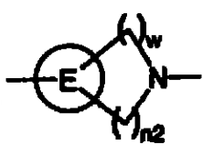
(e) un grupo alquiltio de C_{1-6},

(f) un grupo nitro,

(g) $-N(R^{23})(R^{24})$

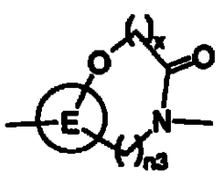
en donde R^{23} y R^{24} son cada uno de manera independiente, un átomo de hidrógeno, un grupo alquilo de C_{1-6}, un grupo alquilcarbonilo de C_{1-4} en donde el grupo alquilcarbonilo de C_{1-4} está sustituido opcionalmente por un grupo amino, un grupo alquilamino de C_{1-4} o un grupo di(alquil de C_{1-4})amino, o un grupo alquilsulfonilo de C_{1-4}, o

(h) unido opcionalmente con R^4 para formar



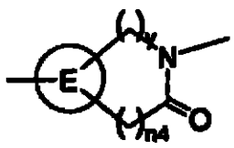
en donde n2 y w son cada uno de manera independiente 0 o un entero de 1 a 3 y E es como se definió anteriormente,

(i) unido opcionalmente con R^4 para formar



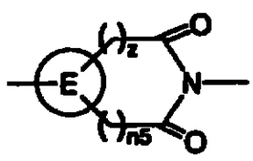
en donde n3 y x son cada uno de manera independiente 0 ó 1 y E es como se definió anteriormente,

(j) unido opcionalmente con R^7 para formar



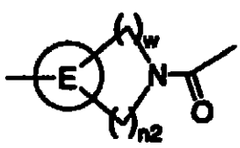
en donde n4 y y son cada uno de manera independiente 0, 1 ó 2 y E es como se definió anteriormente,

(k) unido opcionalmente con R^7 para formar



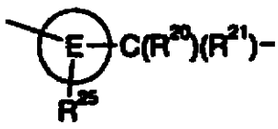
en donde n5 y z son cada uno de manera independiente 0 ó 1 y E es como se definió anteriormente, o

(l) unido opcionalmente con R^8 para formar



en donde n2 y w son cada uno de manera independiente 0 o un entero de 1 a 3 y E es como se definió anteriormente, o

(3)



en donde

R^{20}, R^{21} y E son como se definió anteriormente,

R^{25} es

(a) un átomo de hidrógeno,

(b) un átomo de halógeno,

(c) un grupo alquilo de C_{1-4},

(d) un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo carboxi,

(e) un grupo alquiltio de C_{1-6},

(f) un grupo nitro o

(g) $-N(R^{23})(R^{24})$

en donde R^{23} y R^{24} son como se definió anteriormente;

R es $-COO(R^{19})$, $-A^1-COO(R^{19})$ o $-O-A^1-COO(R^{19})$

en donde A^1 es un grupo alquileno de C_{1-4} y R^{19} es un átomo de hidrógeno o un grupo alquilo de C_{1-4};

B es un grupo arilo o un grupo anular heteroaromático;

R^3 es

(1) un átomo de hidrógeno,

(2) un átomo de halógeno,

(3) un grupo alquilo de C_{1-6},

(4) un grupo alcoxi de C_{1-6},

(5) un grupo alquilamino de C_{1-6},

(6) un grupo di(alquil de C_{1-6})amino,

(7) un grupo ciano,

(8) un grupo nitro,

(9) un grupo haloalquilo de C_{1-4},

(10) $-S-R^{18}$ en donde R^{18} es un grupo alquilo de C_{1-6} o un grupo arilo,

(11) $-SO-R^{18}$ en donde R^{18} es un grupo alquilo de C_{1-6} o un grupo arilo, o

(12) $-SO_2-R^{18}$ en donde R^{18} es un grupo alquilo de C_{1-6} o un grupo arilo;

Y es -O-, -S-, -SO-, $-SO_2-$, $-N(R^{11})-$, $-N(R^{12})-CO-$, $-N(R^{12})-SO_2-$, $-SO_2-N(R^{12})-$, $-C(R^{13})(R^{14})-$, -CO-, $-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ o $-C(R^{13})(R^{14})-O-$

en donde

R^{11} es

(1) un átomo de hidrógeno,

(2) un grupo alquilo de C_{1-6}

en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de

(a) un grupo cicloalquilo de C_{3-7},

(b) un grupo arilo sustituido opcionalmente,

(c) un grupo heterocíclico sustituido opcionalmente,

(d) un grupo hidroxilo,

(e) un grupo alquilamino de C_{1-4} y

(f) un grupo di(alquil de C_{1-4})amino,

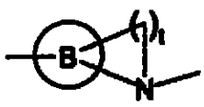
(3) un grupo alquenilo de C_{2-4},

(4) un grupo alquilsulfonilo de C_{1-4},

(5) un grupo alquilcarbonilo de C_{1-4}

en donde el grupo alquilcarbonilo de C_{1-4} está sustituido opcionalmente por un grupo hidroxilo o un grupo alcoxi de C_{1-4}, o

(6) unido opcionalmente con R^3 para formar



en donde t es un entero de 1 a 4 y B es como se definió anteriormente,

R^{12} es

(1) un átomo de hidrógeno,

(2) un grupo alquilo de C_{1-8}

en donde el grupo alquilo de C_{1-8} está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de

(a) un grupo cicloalquilo de C_{3-7},

(b) un grupo arilo sustituido opcionalmente,

(c) un grupo heterocíclico sustituido opcionalmente,

(d) un grupo hidroxilo,

(e) un grupo alquilamino de C_{1-4} y

(f) un grupo di(alquil de C_{1-4})amino,

(3) un grupo alquenilo de C_{2-4},

(4) un grupo alquilsulfonilo de C_{1-4} o

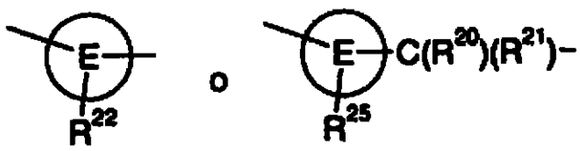
(5) un grupo alquilcarbonilo de C_{1-4}

en donde el grupo alquilcarbonilo de C_{1-4} está sustituido opcionalmente por un grupo hidroxilo o un grupo alcoxi de C_{1-4},

R^{13} y R^{14} son cada uno de manera independiente, un átomo de hidrógeno, un grupo alquilo de C_{1-4}, u opcionalmente forman un cicloalcano de C_{3-7} junto con el átomo de carbono unido al mismo, u opcionalmente forman, junto con el átomo de carbono unido al mismo, un heteroanillo de 5 a 7 miembros que tiene opcionalmente al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre,

con la condición de que,

cuando m es 0, p es 1 y L es



en donde R^{20} y R^{21} son cada uno un átomo de hidrógeno, E es un grupo fenilo, R^{22} es un átomo de hidrógeno, un átomo de halógeno, un

grupo alquilo de C_{1-4}, un grupo alcoxi de C_{1-4} o un grupo nitro, y R^{25} es un átomo de hidrógeno, un átomo de halógeno, un grupo alquilo de C_{1-4}, un grupo alcoxi de C_{1-4} o un grupo nitro,

Y debe ser

$-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ o $-C(R^{13})(R^{14})-O-$, en donde R^{12}, R^{13} y R^{14} son como se definió anteriormente;

s es 0 ó 1;

A es un grupo alquileno de C_{1-4} sustituido opcionalmente por un grupo cicloalquilo de C_{3-7};

Z es

(1) un grupo cicloalquilo de C_{3-7}

en donde el grupo cicloalquilo de C_{3-7} está sustituido opcionalmente por un grupo arilo, en donde el grupo arilo está sustituido opcionalmente por un átomo de halógeno o un grupo alquilo de C_{1-6}, o un grupo anular heteroaromático en donde el grupo anular heteroaromático está sustituido opcionalmente por un átomo de halógeno o un grupo alquilo de C_{1-6},

(2) un grupo arilo

en donde el grupo arilo está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de

(a) un grupo heterocíclico sustituido opcionalmente por un grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4},

(b) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por un grupo hidroxilo, un grupo oxo, un átomo de halógeno o un grupo alquilo de C_{1-6},

(c) un grupo carboxi,

(d) un átomo de halógeno,

(e) un grupo alquilo de C_{1-6},

(f) un grupo haloalquilo de C_{1-4},

(g) un grupo alquilamino de C_{1-4},

(h) un grupo di(alquil de C_{1-4})amino,

(i) un grupo alquiltio de C_{1-6},

(j) un grupo alcoxi de C_{1-4}, y

(k) un grupo alquilcarbonilo de C_{1-4},

(3) un grupo anular heteroaromático

en donde el grupo anular heteroaromático está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de

(a) un grupo heterocíclico sustituido opcionalmente por un grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4},

(b) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por un grupo hidroxilo, un grupo oxo, un átomo de halógeno o un grupo alquilo de C_{1-6},

(c) un grupo carboxi,

(d) un átomo de halógeno,

(e) un grupo alquilo de C_{1-6},

(f) un grupo haloalquilo de C_{1-4},

(g) un grupo alquilamino de C_{1-4},

(h) un grupo di(alquil de C_{1-4})amino,

(i) un grupo alquiltio de C_{1-6},

(j) un grupo alcoxi de C_{1-4},

(k) un grupo alquilcarbonilo de C_{1-4} y

(l) un grupo arilo sustituido opcionalmente por un átomo de halógeno o un grupo haloalquilo de C_{1-4},

(4) un grupo indanilo o

(5) un grupo piperacinilo

en donde el grupo piperacinilo está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de

(a) un grupo fenilo,

(b) un grupo fenilalquilo de C_{1-4},

(c) un grupo benzoilo sustituido opcionalmente por un átomo de halógeno y

(d) un grupo fenilalcoxicarbonilo de C_{1-4}

o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[3] El compuesto anular heteroaromático de 5 miembros de [1],

en donde, en la fórmula [I],

R^3 es

(1) un átomo de hidrógeno,

(2) un átomo de halógeno,

(3) un grupo alquilo de C_{1-6} o

(4) un grupo alcoxi de C_{1-4};

Y es -O-, -N(R^{11})-, -N(R^{12})-CO-, -C(R^{13})(R^{14})-, -C(R^{13})(R^{14})-N(R^{12})-, -CO-N(R^{12})- o -C(R^{13})(R^{14})-O-

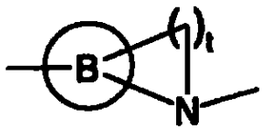
en donde

R^{11} es

(1) un átomo de hidrógeno,

(2) un grupo alquilo de C_{1-6}, o

(3) unido opcionalmente con R^3 para formar



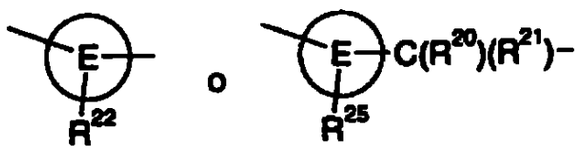
en donde t es 3 y B es como se definió en [2] anteriormente,

R^{12} es un átomo de hidrógeno o un grupo alquilo de C_{1-6},

R^{13} y R^{14} son cada uno un átomo de hidrógeno

con la condición de que

cuando m es 0, p es 1, y L es



en donde R^{20} y R^{21} son cada uno un átomo de hidrógeno, E es un grupo fenilo, R^{22} es un átomo de hidrógeno, un grupo alcoxi de C_{1-4} o un grupo nitro, y R^{25} es un átomo de hidrógeno, un grupo alcoxi de C_{1-4} o un grupo nitro,

Y puede ser

$-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ o $-C(R^{13})(R^{14})-O-$, en donde R^{12}, R^{13} y R^{14} son como se definió anteriormente;

s es 0 ó 1;

A es un grupo alquileno de C_{1-4};

Z es un grupo arilo sustituido por sustituyentes seleccionados del grupo que consiste de

(a) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un átomo de halógeno y un grupo alquilo de C_{1-6},

(b) un átomo de halógeno,

(c) un grupo alquilo de C_{1-6},

(d) un grupo haloalquilo de C_{1-4},

(e) un grupo di(alquil de C_{1-4})amino,

(f) un grupo alquiltio de C_{1-6} y

(g) un grupo alquilcarbonilo de C_{1-4},

o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[4] El compuesto anular heteroaromático de 5 miembros de [3], en donde V es =N- y W es -S- u -O-, o V es =CH- y W es -S-, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[5] El compuesto anular heteroaromático de 5 miembros de [4], en donde Z es un grupo fenilo sustituido por un grupo alquilo de C_{1-6}, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[6] El compuesto anular heteroaromático de 5 miembros de [5], en donde Y es $-C(R^{13})(R^{14})-N(R^{12})-$ o $-C(R^{13})(R^{14})-O-$, en donde R^{12}, R^{13} y R^{14} son como se definió en [3] y s es 0, o Y es -O- o $-N(R^{11})-$ en donde R^{11} es como se definió en [3], s es 1, y A es un grupo metileno, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[7] El compuesto anular heteroaromático de 5 miembros de [6], en donde V es =CH-, W es -S-, y la posición de la sustitución de B en el anillo de tiofeno formado por V junto con W está en la posición 4 o la posición 5, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[8] El compuesto anular heteroaromático de 5 miembros de [7], en donde B es un grupo fenilo, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[9] El compuesto anular heteroaromático de 5 miembros de [8], en donde

m es 1;

R^1 y R^2 son cada uno un átomo de hidrógeno;

X es -N(R^4)- u -O-

en donde R^4 es un grupo alquilo de C_{1-6} sustituido opcionalmente por

(a) un grupo arilo,

(b) un grupo anular heteroaromático sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-6} o

(c) -CO-N(R^{15})(R^{16})

en donde R^{15} y R^{16} son cada uno de manera independiente, un átomo de hidrógeno o un grupo arilo, en donde el grupo arilo está sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-6};

n es 0 ó 1;

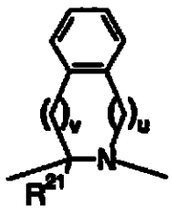
p es 0 ó 1;

L es

(1)

-C(R^{20})(R^{21})-

en donde R^{20} está enlazado con R^4 para formar



en donde u es 1, v es 1 y R^2 es como se definió anteriormente,

R^{21} es un átomo de hidrógeno, o

(2)



en donde E es un grupo anular heteroaromático y R^{22} es un átomo de hidrógeno;

R es -COO(R^{19})

en donde R^{19} es un átomo de hidrógeno, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[10] El compuesto anular heteroaromático de 5 miembros de [9], en donde X es -N(R^4), en donde R^4 es como se definió en [9], n es 1 y p es 0, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[11] El compuesto anular heteroaromático de 5 miembros de [10], en donde R^4 es un grupo metilo sustituido por un grupo anular heteroaromático sustituido opcionalmente por un grupo alquilo de C_{1-6}, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[12] El compuesto anular heteroaromático de 5 miembros de [11], en donde el anillo heteroaromático definido en [11] es un grupo tiazolilo, un grupo oxazolilo o un grupo bencimidazolilo, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[13] El compuesto anular heteroaromático de 5 miembros de [10], en donde R^4 es un grupo metilo sustituido por -CO-N(R^{15})(R^{16}), en donde R^{15} es un átomo de hidrógeno y R^{16} es un grupo arilo sustituido opcionalmente

por un grupo alquilo de C_{1-6}, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[14] El compuesto anular heteroaromático de 5 miembros de [6], en donde V es =N-, W es -S-, y la posición de la sustitución de B en el anillo de tiazol formado por V junto con W está en la posición 4, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[15] El compuesto anular heteroaromático de 5 miembros de [14], en donde B es un grupo fenilo, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[16] El compuesto anular heteroaromático de 5 miembros de [15], en donde

m es 0 ó 1;

R^1 y R^2 son cada uno de manera independiente, un átomo de hidrógeno o un grupo alquilo de C_{1-4};

X es $-N(R^4)-$, $-N(R^5)-CO-O-$, $-SO_2-N(R^5)-$, $-CO-N(R^7)-$, $-N(R^9)-CO-N(R^5)-$, $-N(R^{10})-(CH_2)_k-N(R^5)-$, -O-, -S- o $-SO_2-$

en donde

R^4 es

(1) un átomo de hidrógeno,

(2) un grupo alquilo de C_{1-6}

en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por

(a) un grupo arilo sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un átomo de halógeno, un grupo alquilo de C_{1-6} y un grupo haloalquilo de C_{1-4},

(b) un grupo anular heteroaromático sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-6},

(c) un grupo carboxi,

(d) un grupo alcoxicarbonilo de C_{1-4},

(e) $-CO-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son cada uno de manera independiente, un átomo de hidrógeno, un grupo arilo, en donde el grupo arilo está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un grupo alquilo de C_{1-6}, un grupo alcoxi de C_{1-4}, un grupo carboxi y un grupo di(alquil de C_{1-4})amino, un grupo anular heteroaromático, un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por un grupo arilo, o, junto con el átomo de nitrógeno unido al mismo, puede formar un heteroanillo de 5 a 7 miembros que contiene además, opcionalmente al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre,

(f) $-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son cada uno de manera independiente, un átomo de hidrógeno o un grupo arilo,

(g) $-O-R^{17}$

en donde R^{17} es un grupo arilo, o

(h) un grupo cicloalquilo de C_{3-7},

(3) $-CO-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son cada uno de manera independiente, un átomo de hidrógeno, un grupo arilo, en donde el grupo arilo está sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-6}, un grupo alquilo de C_{1-6}, o, junto con el átomo de nitrógeno unido al mismo, puede formar un anillo de indolina o puede formar un heteroanillo de 5 a 7 miembros que contiene opcionalmente además, al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre,

(4) $-SO_2-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son cada uno de manera independiente un grupo arilo o un grupo alquilo de C_{1-6},

(5) $-CO-R^{17}$

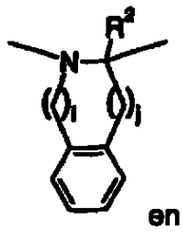
en donde R^{17} es un grupo arilo, en donde el grupo arilo está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un grupo alquilo de C_{1-6} y un grupo alcoxi de C_{1-4}, un grupo anular heteroaromático o un grupo alquilo de C_{1-6}, en dónde el grupo alquilo de C_{1-6} está sustituido opcionalmente por un grupo arilo sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un átomo de halógeno y un grupo alquilo de C_{1-6}, un grupo anular heteroaromático, un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo arilo o un grupo ariloxi sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-6},

(6) $-SO_2-R^{17}$

en donde R^{17} es un grupo arilo,

(7) un grupo arilo, o

(8) unido opcionalmente con R^1 para formar



en donde i y j son cada uno 1 y R^2 es como se definió anteriormente,

R^5 es un átomo de hidrógeno o un grupo alquilo de C_{1-6} sustituido opcionalmente por un grupo arilo o un grupo cicloalquilo de C_{3-7},

R^7 es un átomo de hidrógeno o un grupo alquilo de C_{1-6},

R^9 es un átomo de hidrógeno o un grupo alquilo de C_{1-6},

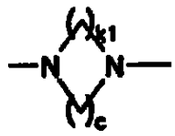
k es 2,

R^{10} es

(1) un átomo de hidrógeno,

(2) un grupo alquilo de C_{1-6}, o

(3) unido opcionalmente con R^5 para formar



en donde k1 y c son cada uno 2;

n es 0 o un entero de 1 a 3;

p es 0 ó 1;

L es

(1)

$-C(R^{20})(R^{21})-$

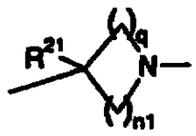
en donde

R^{20} es

(a) un átomo de hidrógeno,

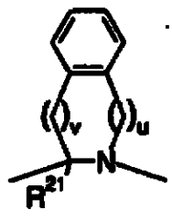
(b) un grupo alquilo de C_{1-6}, o

(c) unido opcionalmente con R^4 para formar



en donde n1 y q son cada uno de manera independiente un entero de 1 a 3, o

(d) unido opcionalmente con R^4 para formar



en donde u es 1 y v es 1,

R^{21} es un átomo de hidrógeno, un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por un grupo arilo sustituido opcionalmente por 1 a 3 átomos de halógeno, o un grupo arilo o

(2)



en donde

E es un grupo arilo o un grupo anular heteroaromático,

R^{22} es

(a) un átomo de hidrógeno,

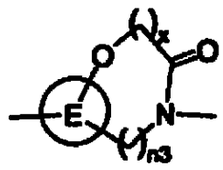
(b) un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo carboxi,

(c) un grupo nitro,

(d) $-N(R^{23})(R^{24})$

en donde R^{23} y R^{24} son cada uno de manera independiente, un átomo de hidrógeno, un grupo alquilcarbonilo de C_{1-4}, en donde el grupo alquilcarbonilo de C_{1-4} está sustituido opcionalmente por un grupo alquilamino de C_{1-4} o un grupo di(alquil de C_{1-4})amino o un grupo alquilsulfonilo de C_{1-4}, o

(e) unido opcionalmente con R^4 para formar



en donde n3 es 0, x es 1 y E es como se definió anteriormente;

R es $-COO(R^{19})$

en donde R^{19} es un átomo de hidrógeno o un grupo alquilo de C_{1-4}, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[17] El compuesto anular heteroaromático de 5 miembros de [16], en donde m es 1 y R^1 y R^2 son cada uno un átomo de hidrógeno, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[18] El compuesto anular heteroaromático de 5 miembros de [17], en donde X es -N(R^4), en donde R^4 es como se definió en [16], n es 1 y p es 0, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[19] El compuesto anular heteroaromático de 5 miembros de [18], en donde

R^4 es un grupo alquilo de C_{1-6} sustituido opcionalmente por

(a) un grupo arilo sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un átomo de halógeno, un grupo alquilo de C_{1-6} y un grupo haloalquilo de C_{1-4},

(b) un grupo anular heteroaromático sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-6},

(c) un grupo carboxi,

(d) un grupo alcoxicarbonilo de C_{1-4},

(e) -CO-N(R^{15})(R^{16})

en donde R^{15} y R^{16} son cada uno de manera independiente, un átomo de hidrógeno, un grupo arilo, en donde el grupo arilo está sustituido

opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un grupo alquilo de C_{1-6}, un grupo alcoxi de C_{1-4}, un grupo carboxi y un grupo di(alquil de C_{1-4})amino, un grupo anular heteroaromático, un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por un grupo arilo, o, junto con el átomo de nitrógeno unido al mismo, puede formar un heteroanillo de 5 a 7 miembros que contiene además, opcionalmente al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre,

(f) $-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son cada uno de manera independiente, un átomo de hidrógeno o un grupo arilo,

(g) $-O-R^{17}$

en donde R^{17} es un grupo arilo, o

(h) un grupo cicloalquilo de C_{3-7},

o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[20] El compuesto anular heteroaromático de 5 miembros de [19], en donde R^4 es un grupo metilo sustituido por un grupo anular heteroaromático sustituido opcionalmente por un grupo alquilo de C_{1-6}, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[21] El compuesto anular heteroaromático de 5 miembros de [20], en donde el anillo heteroaromático definido en [20] es un grupo tiazolilo, un grupo oxazolilo, un grupo bencimidazolilo, un grupo piridilo o un grupo

quinolilo, o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos.

[22] El compuesto anular heteroaromático de 5 miembros de [19], en donde R^4 es un grupo metilo sustituido por -CO-N(R^{15})(R^{16}), en donde R^{15} es un átomo de hidrógeno y R^{16} es un grupo arilo sustituido opcionalmente por un grupo alquilo de C_{1-6}, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

[23] El compuesto anular heteroaromático de 5 miembros de cualquiera de [1] a [22], que se selecciona del grupo que consiste de los siguientes compuestos, o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos:

(1) ácido 5-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetoxi}nicotínico;

(2) ácido 4-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetoxi}benzoico;

(3) ácido 6-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetoxi}nicotínico;

(4) ácido 5-{4-[4-({metil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetoxi}nicotínico;

(5) ácido 4-{4-[4-({metil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetoxi}benzoico;

(6) ácido 6-[4-(4-[[(4-isopropilfenil)(1-propilbutil)amino]metil]-fenil)tiazol-2-ilmetoxi]nicotínico;

(7) ácido 5-[4-(4-[[(4-isopropilfenil)(1-propilbutil)amino]metil}-fenil)tiazol-2-ilmetoxi]nicotínico;

(8) ácido 5-[4-(4-[[isobutil(4-isopropilfenil)amino]metil}fenil)-tiazol-2-ilmetoxi]nicotínico;

(9) ácido 4-[4-(4-[[(4-isopropilfenil)(1-propilbutil)amino]metil}-fenil)tiazol-2-ilmetoxi]benzoico;

(10) ácido 3-[4-(4-[[(4-isopropilfenil)(1-propilbutil)amino]metil}-fenil)tiazol-2-ilmetoxi]benzoico;

(11) ácido 6-[4-(4-[[(1-etilpropil)(4-isopropilfenil)amino]metil}-fenil)tiazol-2-ilmetoxi]nicotínico;

(12) ácido 5-[4-(4-[[(1-etilpropil)(4-isopropilfenil)amino]metil}-fenil)tiazol-2-ilmetoxi]nicotínico;

(13) ácido 4-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetiltio}benzoico;

(14) ácido 4-{4-[4-({metil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetiltio}benzoico;

(15) ácido 4-(metil-{4-[4-({metil[4-(1-propilbutil)fenil]amino}-metil)fenil]tiazol-2-ilmetil}sulfamoil)benzoico;

(16) 4-(metil{4-[4-({metil[4-(1-propilbutil)fenil]amino}metil)fenil]-tiazol-2-ilmetil}sulfamoil)butirato de sodio;

(17) ácido 4-{[(4-{4-[(4-ciclohexilfenilamino)metil]fenil}tiazol-2-il)metilamino]metil}benzoico;

(18) ácido 4-({[4-(4-[[(4-ciclohexilfenil)metilamino]metil}fenil)-tiazol-2-il]metilamino}metil)benzoico;

(19) ácido 4-[(metil-{4-[4-({metil[4-(1-propilbutil)fenil]amino}-metil)fenil]tiazol-2-il}amino)metil]benzoico;

(20) ácido 4-[({4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-il}metilamino)metil]benzoico;

(21) ácido (S)-({4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}metilamino)fenilacético;

(22) ácido (S)-2-({4-[4-({[4-(1-etilpropil)fenil]isopropilamino}-metil)fenil]tiazol-2-ilmetil}metilamino)-3-fenilpropiónico;

(23) ácido {bencil[4-(4-[[(4-ter-butilfenil)isobutilamino]metil}-fenil)-tiazol-2-ilmetil]amino}acético;

(24) ácido {bencil[4-(4-[[(4-cloro-fenil)isobutilamino]metil}fenil)-tiazol-2-ilmetil]amino}acético;

(25) ácido (bencil{4-[4-({metil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}amino)acético;

(26) ácido (bencil{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}-metil)fenil]tiazol-2-ilmetil}amino)acético;

(27) ácido {1-[4-(4-[[(4-ter-butil-fenil)isobutilamino]metil}fenil)-tiazol-2-ilmetil]-3-fenilureido}acético;

(28) ácido {benzoil-[4-(4-[[(4-ter-butilfenil)isobutilamino]metil}-fenil)tiazol-2-ilmetil]amino}acético;

(29) ácido [[4-(4-{[(4-ter-butil-fenil)isobutilamino]metil}fenil)-tiazol-2-ilmetil]-(piridin-2-ilcarbonil)amino]acético;

(30) ácido [[4-(4-{[(4-ter-butil-fenil)isobutilamino]metil}fenil)-tiazol-2-ilmetil]-(piridin-3-ilcarbonil)amino]acético;

(31) ácido {bencensulfonil-[4-(4-{[(4-ter-butilfenil)isobutilamino]-metil}fenil)tiazol-2-ilmetil]amino}acético;

(32) ácido 2-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(33) ácido (S)-2-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}-metil)fenil]tiazol-2-ilmetil}-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(34) ácido (S)-2-{4-[4-({metil[4-(1-propilbutil)fenil]amino}-metil)fenil]tiazol-2-ilmetil}-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(35) ácido (S)-2-[4-(4-{[(1-etilpropil)-(4-isopropilfenil)amino]-metil}fenil)tiazol-2-ilmetil]-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(36) ácido 4-({4-[4-(4-ciclohexilfenoximetil)fenil]tiazol-2-il}metilamino)benzoico;

(37) ácido 4-[({4-[4-(4-ciclohexilfenoximetil)fenil]tiazol-2-il}metilamino)metil]benzoico;

(38) ácido 4-{[(4-{4-[4-(1,1-dimetilpropil)fenoximetil]fenil}tiazol-2-il)metilamino]metil}benzoico;

(39) ácido 4-{[metil-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-il)amino]metil}benzoico;

(40) 4-{[metil(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-il)amino]metil}-benzoato de sodio;

(41) ácido (S)-[metil-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiazol-2-ilmetil)amino]fenilacético;

(42) ácido (S)-2-[metil-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiazol-2-ilmetil)amino]-3-fenilpropiónico;

(43) ácido (bencil{4-[4-(2-ter-butil-4-metil-fenoximetil)fenil]-tiazol-2-ilmetil}amino)acético;

(44) ácido [bencil(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(45) ácido 2-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(46) ácido (S)-2-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(47) ácido (R)-2-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(48) ácido 5-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetoxi)nicotínico;

(49) ácido 4-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetoxi)benzoico;

(50) ácido 4-[metil-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)sulfamoil]benzoico;

(51) ácido 4-[metil-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)sulfamoil]butírico;

(52) ácido 4-({4-[4-(4-ciclohexilfenilcarbamoil)fenil]tiazol-2-il}metilamino)benzoico;

(53) ácido 4-[({4-[4-(4-ciclohexilfenilcarbamoil)fenil]tiazol-2-il}metilamino)metil]benzoico;

(54) ácido [bencil(4-{4-[4-(1-propilbutil)fenilcarbamoil]fenil}-tiazol-2-ilmetil)amino]acético;

(55) ácido [bencil(4-{4-[4-(1-propilbutil)bencilcarbamoil]fenil}-tiazol-2-ilmetil)amino]acético;

(56) ácido {bencil[4-(4-{metil[4-(1-propilbutil)bencil]-carbamoil}-fenil)tiazol-2-ilmetil]amino}acético;

(57) ácido {bencil[4-(4-{etil-[4-(1-propilbutil)bencil]-carbamoil}-fenil)tiazol-2-ilmetil]amino}acético;

(58) ácido 5-{4-[4-({(2-hidroxi-2-metilpropil)-[4-(1-propilbutil)-fenil]amino}metil)fenil]tiazol-2-ilmetoxi}nicotínico;

(59) ácido [[4-(4-{[(4-ter-butil-fenil)isobutilamino]metil}fenil)-tiazol-2-ilmetil]-(morfolin-4-carbonil)amino]acético;

(60) 5-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)fenil]tiazol-2-ilmetoxi}-nicotinato de sodio;

(61) (S)-2-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxilato de sodio;

(62) 5-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetoxi)-nicotinato de sodio;

(63) ácido 3-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetoxi}-5-metoxi-benzoico;

(64) ácido (1-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-3-fenilureido)acético;

(65) ácido (1-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-3-p-tolilureido)acético;

(66) ácido [1-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-3-(4-isopropilfenil)ureido]acético;

(67) ácido (1-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-3-metil-3-fenilureido)acético;

(68) ácido 5-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetoxi}nicotínico;

(69) ácido [3-fenil-1-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiazol-2-ilmetil)ureido]acético;

(70) ácido (3-(2,6-dimetilfenil)-1-{4-[4-({[4-(1-etilpropil)fenil]-isopropilamino}metil)fenil]tiazol-2-ilmetil}ureido)acético;

(71) ácido ({4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}fenilcarbamoilmetilamino)acético;

(72) ácido (1-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-3-isopropil-ureido)acético;

(73) ácido 3-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetoxi}-isoxazol-5-carboxílico;

(74) ácido 5-[4-(4-{[(2-etilbutil)-(4-isopropilfenil)amino]metil}-fenil)tiazol-2-ilmetoxi]nicotínico;

(75) ácido [{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-(piperidin-1-carbonil)amino]acético;

(76) ácido 2-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetoxi)nicotínico;

(77) ácido [{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-(p-tolilcarbamoilmetil)amino]acético;

(78) ácido {{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-[(4-isopropilfenilcarbamoil)metil]amino}acético;

(79) ácido (1-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}-3-metil-3-fenilureido)acético;

(80) ácido (1-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}-3-p-tolilureido)acético;

(81) ácido ((2,3-dihidro-indol-1-carbonil)-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}amino)acético;

(82) ácido 3-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetoxi)piridin-2-carboxílico;

(83) ácido {[4-(4-{[(2-etilbutil)-(4-isopropilfenil)amino]metil}-fenil)tiazol-2-ilmetil]fenilcarbamoilmetilamino}acético;

(84) ácido {[4-(4-[[(2-etilbutil)-(4-isopropilfenil)amino]metil}fenil)-tiazol-2-ilmetil]-[(4-isopropilfenilcarbamoil)metil]amino}acético;

(85) ácido 4-(2-{carboximetil[4-(4-[[(2-etilbutil)-(4-isopropilfenil)-amino]metil}fenil)tiazol-2-ilmetil]amino}-acetilamino)benzoico;

(86) ácido 6-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetoxi)piridin-2-carboxílico;

(87) ácido 5-{4-[4-({isobutil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetoxi}nicotínico;

(88) ácido (1-{4-[4-({isobutil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}-3-fenilureido)acético;

(89) éster metílico del ácido 5-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)fenil]tiazol-2-ilmetoxi}nicotínico;

(90) ácido 4-amino-3-{4-[4-({[4-(1-etilpropil)fenil]-isopropilamino}metil)fenil]tiazol-2-ilmetoxi}benzoico;

(91) ácido 3-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetoxi}benzoico;

(92) ácido 3-({4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}amino)benzoico;

(93) ácido 3-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetoxi}-4-nitro-benzoico;

(94) ácido ((1H-bencimidazol-2-ilmetil)-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}amino)acético;

(95) ácido [fenilcarbamoilmetil(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiazol-2-ilmetil)amino]acético;

(96) ácido [(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)-(piridin-3-ilcarbamoilmetil)amino]acético;

(97) ácido [[(4-dimetilaminofenilcarbamoil)metil]-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(98) ácido [[(4-metoxifenilcarbamoil)metil]-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(99). ácido [[(isopropilfenilcarbamoil)metil]-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(100) ácido [(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)-(piridin-2-ilcarbamoilmetil)amino]acético;

(101) ácido [(2-oxo-2-pirrolidin-1-il-etil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(102) ácido [(4-metiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(103) ácido 4-(3-ciclohexilmetil-3-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}ureido)benzoico;

(104) ácido 4-(3-isobutil-3-{4-[4-({isopropil[4-(1-propilbutil)fenil]-amino}metil)fenil]tiazol-2-ilmetil}ureido)benzoico;

(105) ácido (1-{4-[4-({isobutil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}-3-metil-3-fenilureido)acético;

(106) ácido ({4-[4-({isobutil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}fenilcarbamoilmetilamino)acético;

(107) ácido {{4-[4-({isobutil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}-[(4-isopropilfenilcarbamoil)metil]amino}acético;

(108) ácido 4-acetilamino-3-{4-[4-({isopropil[4-(1-propilbutil)fenil]-amino}metil)fenil]tiazol-2-ilmetoxi}benzoico;

(109) ácido 4-(2-dimetilaminoacetilamino)-3-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetoxi}benzoico;

(110) ácido ((1H-bencimidazol-2-ilmetil)-{4-[4-({[4-(1-etilpropil)-fenil]isopropilamino}metil)fenil]tiazol-2-ilmetil}amino)acético;

(111) ácido [(1H-bencimidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(112) ácido 3-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetoxi}-4-metansulfonilaminobenzoico;

(113) ácido 4-isobutirilamino-3-{4-[4-({isopropil[4-(1-propilbutil)-fenil]amino}metil)fenil]tiazol-2-ilmetoxi}benzoico;

(114) ácido 4-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-3-oxo-3,4-dihidro-2H-benzo[1,4]oxacin-6-carboxílico;

(115) ácido 4-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-3-oxo-3,4-dihidro-2H-benzo[1,4]oxacin-8-carboxílico;

(116) ácido ({4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}-{metilfenilaminosulfonil}amino)acético;

(117) ácido [[(4-isopropilfenilcarbamoil)metil]-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}amino)acético;

(118) ácido [[(3,5-dimetilfenilcarbamoil)metil]-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}amino)acético;

(119) ácido [[(4-dimetilaminofenilcarbamoil)metil]-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}amino)acético;

(120) ácido ((bencilcarbamoilmetil)-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}amino)acético;

(121) ácido [{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}-[2-(morfolin-4-il)-2-oxo-etil]amino]acético;

(122) ácido [{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-(2-fenoxietil)amino]acético;

(123) ácido [{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-(2-fenilamino-etil)amino]acético;

(124) ácido 2-carboximetoxi-5-({4-[4-({[4-(1-etilpropil)fenil]-isopropilamino}metil)fenil]tiazol-2-ilmetil}metilamino)benzoico;

(125) ácido 2-carboximetoxi-5-[metil(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]benzoico;

(126) ácido 3-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetoxi}-4-(2-metilamino-acetilamino)benzoico;

(127) ácido [(4-ter-butiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(128) ácido [fenil(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(129) ácido [(2-fenoxiacetil)-(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiazol-2-ilmetil)amino]acético;

(130) ácido [(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)-(2-p-toliloxi-acetil)amino]acético;

(131) diclorhidrato del ácido (etoxicarbonilmetil{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}amino)acético;

(132) ácido ((4-ter-butiltiazol-2-ilmetil)-{4-[4-({[4-(1-etilpropil)-fenil]isopropilamino}metil)fenil]tiazol-2-ilmetil}amino)acético;

(133) ácido 6-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetoxi}-piridin-2-carboxílico;

(134) ácido [(2-benciloxi-acetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(135) ácido [[2-(4-isopropilfenoxi)acetil]-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(136) ácido [(4,5-dimetiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(137) ácido 5-(4-{5-[4-(1-propilbutil)fenoximetil]tiofen-2-il}tiazol-2-ilmetoxi)nicotínico;

(138) ácido ((4-ter-butiltiazol-2-ilmetil)-{4-[6-({isopropil[4-(1-propilbutil)fenil]amino}metil)benzoxazol-2-il]tiazol-2-ilmetil}amino)acético;

(139) ácido ((1H-bencimidazol-2-ilmetil)-{4-[6-({isopropil[4-(1-propilbutil)fenil]amino}metil)benzoxazol-2-il]tiazol-2-ilmetil}amino)acético;

(140) ácido 5-{4-[6-({isopropil[4-(1-propilbutil)fenil]amino}metil)-benzoxazol-2-il]tiazol-2-ilmetoxi}nicotínico;

(141) ácido [(5-ter-butiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(142) ácido [{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}-(2-oxo-2-piperidin-1-il-etil)amino]acético;

(143) ácido 6-[metil-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)amino]piridin-2-carboxílico;

(144) ácido ({4-[6-({isopropil[4-(1-propilbutil)fenil]amino}metil)-benzoxazol-2-il]tiazol-2-ilmetil}amino)acético;

(145) ácido (S)-(carboximetil{4-[4-({isopropil[4-(1-propilbutil)-fenil]amino}metil)fenil]tiazol-2-ilmetil}amino)fenilacético;

(146) ácido ((4,5-dimetiltiazol-2-ilmetil)-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}amino)acético;

(147) ácido [(5-ter-butiloxazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(148) ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(149) diclorhidrato del ácido (isobutoxicarbonilmetil{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}amino)acético;

(150) diclorhidrato del ácido ({4-[4-({isopropil[4-(1-propilbutil)-fenil]amino}metil)fenil]tiazol-2-ilmetil}-propoxicarbonilmetilamino)acético;

(151) clorhidrato del ácido 1-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)piperidin-4-carboxílico;

(152) ácido 1-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}piperidin-4-carboxílico;

(153) ácido 4-[4-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)piperacin-1-il]benzoico;

(154) ácido 4-(4-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-piperacin-1-il)benzoico;

(155) ácido 2-[4-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)piperacin-1-il]benzoico;

(156) ácido 3-[4-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)piperacin-1-il]benzoico;

(157) ácido 4-(4-{1-[4-(1-propilbutil)bencil]-1H-indol-3-il}tiazol-2-ilmetoxi)benzoico;

(158) ácido 4-{4-[1-(4-isopropilbencil)-5-(1-propilbutil)-1H-bencimidazol-2-il]tiazol-2-ilmetoxi}benzoico;

(159) ácido 4-{4-[1-(6-metilpiridin-2-ilmetil)-5-(1-propilbutil)-1H-bencimidazol-2-il]tiazol-2-ilmetoxi}benzoico;

(160) ácido 2-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-7-carboxílico;

(161) ácido 4-[1-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)piperidin-4-il]benzoico;

(162) ácido 3-[1-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)piperidin-4-il]benzoico;

(163) ácido 6-[(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)carbamoil]nicotínico;

(164) ácido 2-[1-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)piperidin-4-il]benzoico;

(165) ácido 1-(4-{1-[4-(1-propilbutil)bencil]-1H-indol-3-il}tiazol-2-ilmetil)piperidin-4-carboxílico;

(166) ácido 2-(4-{1-[4-(1-propilbutil)bencil]-1H-indol-3-il}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-7-carboxílico;

(167) ácido 3-[(4-{1-[4-(1-propilbutil)bencil]-1H-indol-3-il}tiazol-2-ilmetil)amino]benzoico;

(168) clorhidrato del ácido 6-[(2-aminoetil)(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)carbamoil]nicotínico;

(169) ácido 2-(4-{1-[4-(1-propilbutil)bencil]-1H-bencimidazol-2-il}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-7-carboxílico;

(170) ácido 3-[4-(4-{1-[4-(1-propilbutil)bencil]-1H-bencimidazol-2-il}tiazol-2-ilmetil)piperacin-1-il]benzoico;

(171) ácido 4-[1-(4-{1-[4-(1-propilbutil)bencil]-1H-bencimidazol-2-il}tiazol-2-ilmetil)piperidin-4-il]benzoico;

(172) ácido 3-[4-(4-{1-[4-(1-propilbutil)bencil]-1H-indol-3-il}tiazol-2-ilmetil)piperacin-1-il]benzoico;

(173) ácido 3-(1-{4-[4-(3,4-dicloro-benciloxi)fenil]tiazol-2-ilmetil}-piperidin-4-il)benzoico;

(174) ácido 3-(1-{4-[4-(3,5-bis-trifluorometilbenciloxi)fenil]tiazol-2-ilmetil}piperidin-4-il)benzoico;

(175) ácido 3-(1-{4-[4-(4-butoxi-benciloxi)fenil]tiazol-2-ilmetil}-piperidin-4-il)benzoico;

(176) ácido 5-metil-2-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiazol-2-ilmetil)-2H-pirazol-3-carboxílico;

(177) ácido 5-metil-1-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiazol-2-ilmetil)-1H-pirazol-3-carboxílico;

(178) ácido 5-ter-butil-1-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiazol-2-ilmetil)-1H-pirazol-3-carboxílico;

(179) ácido 5-ter-butil-2-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiazol-2-ilmetil)-2H-pirazol-3-carboxílico;

(180) ácido (2S,4R)-4-hidroxi-1-(4-{1-[4-(1-propilbutil)bencil]-1H-indol-3-il}tiazol-2-ilmetil)pirrolidin-2-carboxílico;

(181) ácido 4-[4-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)piperidin-1-il]benzoico;

(182) ácido 1-(4-{1-[4-(1-propilbutil)bencil]-1H-indol-3-il}tiazol-2-ilmetil)-1H-indol-3-carboxílico;

(183) ácido 1-(4-{2-fenil-1-[4-(1-propilbutil)bencil]-1H-indol-3-il}tiazol-2-ilmetil)piperidin-4-carboxílico;

(184) ácido 3-(1-{4-[4-(4-metil-3-nitrobenciloxi)fenil]tiazol-2-ilmetil}piperidin-4-il)benzoico;

(185) ácido 2-{4-[1-(4-isopropilbencil)-6-(morfolin-4-il)-1H-bencimidazol-2-il]tiazol-2-ilmetil}-1,2,3,4-tetrahidroisoquinolin-7-carboxílico;

(186) ácido 3-(4-{4-[1-(4-isopropilbencil)-6-(morfolin-4-il)-1H-bencimidazol-2-il]tiazol-2-ilmetil}-piperacin-1-il)benzoico;

(187) ácido {bencil[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)-oxazol-2-ilmetil]amino}acético;

(188) ácido 5-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetoxi)nicotínico;

(189) ácido 4-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetoxi)benzoico;

(190) ácido 4-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetiltio)benzoico;

(191) ácido 4-{4-[4-(4-ciclohexilbenciloxi)fenil]tiazol-2-ilmetiltio}-benzoico;

(192) ácido 4-{4-[4-(4-ciclohexilbenciloxi)fenil]tiazol-2-ilmetansulfonil}benzoico;

(193) ácido 4-[metil-(4-{5-metil-2-[4-(1-propilbutil)benciloxi]fenil}-tiazol-2-ilmetil)sulfamoil]benzoico;

(194) ácido 4-[metil-(4-{5-metil-2-[4-(1-propilbutil)benciloxi]fenil}-tiazol-2-ilmetil)amino]benzoico;

(195) ácido (bencil{4-[5-metil-2-(4-trifluorometilbenciloxi)fenil]-tiazol-2-ilmetil}amino)acético;

(196) ácido [bencil(4-{5-metil-2-[4-(1-propilbutil)benciloxi]fenil}-tiazol-2-ilmetil)amino]acético;

(197) ácido [bencil(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)amino]acético;

(198) ácido [bencil(4-{4-[4-(1-etilpropil)benciloxi]fenil}tiazol-2-ilmetil)amino]acético;

(199) ácido (bencil{4-[5-ter-butil-2-(4-isobutilbenciloxi)fenil]tiazol-2-ilmetil}amino)acético;

(200) ácido [bencil(4-{5-cloro-2-[4-(1-propilbutil)benciloxi]fenil}-tiazol-2-ilmetil)amino]acético;

(201) ácido [(4-{4-[4-(1-etilpropil)benciloxi]fenil}tiazol-2-ilmetil)-(4-fluoro-bencil)amino]acético;

(202) ácido [(4-{4-[4-(1-etilpropil)benciloxi]fenil}tiazol-2-ilmetil)-(4-isopropilbencil)amino]acético;

(203) ácido [(4-{4-[4-(1-etilpropil)benciloxi]fenil}tiazol-2-ilmetil)-(4-trifluorometilbencil)amino]acético;

(204) ácido [(4-clorobencil)-(4-{4-[4-(1-etilpropil)benciloxi]fenil}-tiazol-2-ilmetil)amino]acético;

(205) ácido [(3,5-dimetilbencil)-(4-{4-[4-(1-etilpropil)benciloxi]-fenil}tiazol-2-ilmetil)amino]acético;

(206) ácido [(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)-piridin-2-ilmetilamino]acético;

(207) ácido [(4-{4-[4-(1-etilpropil)benciloxi]fenil}tiazol-2-ilmetil)-piridin-2-ilmetilamino]acético;

(208) ácido [(4-{5-metil-2-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)-piridin-2-ilmetilamino]acético;

(209) ácido [benzoil-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)amino]acético;

(210) ácido [(4-{4-[4-(1-etilpropil)benciloxi]fenil}tiazol-2-ilmetil)-(4-metilbenzoil)amino]acético;

(211) ácido [(4-metoxibenzoil)-(4-{4-[4-(1-propilbutil)benciloxi]-fenil}tiazol-2-ilmetil)amino]acético;

(212) ácido 2-(4-{5-metil-2-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(213) ácido (S)-2-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(214) ácido {bencil[4-(4-{[4-(2,2-dimetilpropil)bencil]metilamino}-fenil)tiazol-2-ilmetil]amino}acético;

(215) ácido {bencil[4-(4-{[trans-4-(4-ter-butilfenil)-ciclohexilmetil]-metilamino}fenil)tiazol-2-ilmetil]amino}acético;

(216) ácido [bencil(4-{4-[(4-ciclohexilbencil)metilamino]fenil}-tiazol-2-ilmetil)amino]acético;

(217) ácido 3-[bencil(4-{4-[(4-ciclohexilbencil)metilamino]fenil}-tiazol-2-ilmetil)amino]propiónico;

(218) ácido (bencil{4-[4-({2-[4-(2,2-dimetilpropil)fenil]-etil}-metilamino)fenil]tiazol-2-ilmetil}amino)acético;

(219) ácido {bencil[4-(4-{metil[4-(trans-4-metil-ciclohexil)bencil]-amino}fenil)tiazol-2-ilmetil]amino}acético;

(220) ácido {bencil[4-(4-{[4-(cis-4-fluoro-ciclohexil)bencil]-metilamino}fenil)tiazol-2-ilmetil]amino}acético;

(221) ácido {bencil[4-(4-{[trans-4-(4-clorofenil)-ciclohexilmetil]-metilamino}fenil)tiazol-2-ilmetil]amino}acético;

(222) ácido {bencil[4-(4-{[4-(4,4-dimetil-ciclohexil)bencil]-metilamino}fenil)tiazol-2-ilmetil]amino}acético;

(223) ácido {bencil[4-(4-{metil[4-(1-propilbutil)bencil]amino}-fenil)tiazol-2-ilmetil]amino}acético;

(224) ácido (bencil{4-[4-(bifenil-4-ilmetilmetilamino)fenil]tiazol-2-ilmetil}amino)acético;

(225) [bencil(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)amino]-acetato de sodio;

(226) ácido [bencil(4-{4-[(4-isobutilbencil)metilamino]fenil}tiazol-2-ilmetil)amino]acético;

(227) {bencil[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)tiazol-2-ilmetil]amino}-acetato de sodio;

(228) ácido {bencil[4-(4-[[4-(2,2-dimetilpropiltio)bencil]-metilamino}fenil)tiazol-2-ilmetil]amino}acético;

(229) ácido {bencil[4-(4-{metil[4-(3-metilbutiltio)bencil]amino}-fenil)tiazol-2-ilmetil]amino}acético;

(230) ácido [bencil(4-{4-[(4-dipropilamino-benzoil)metilamino]-fenil}tiazol-2-ilmetil)amino]acético;

(231) ácido [(4-{4-[etil(4-isopropilbencil)amino]fenil}tiazol-2-ilmetil)-(4-isopropilbencil)amino]acético;

(232) ácido [(4-isopropilbencil)-(4-{4-[isopropil-(4-isopropilbencil)amino]fenil}tiazol-2-ilmetil)amino]acético;

(233) ácido [(4-ter-butilbencil)-(4-{4-[isopropil-(4-isopropilbencil)-amino]fenil}tiazol-2-ilmetil)amino]acético;

(234) ácido [(4-clorobencil)-(4-{4-[(4-isobutilbencil)metilamino]-fenil}tiazol-2-ilmetil)amino]acético;

(235) ácido {{4-[4-(bencilmetilamino)fenil]tiazol-2-ilmetil}-[4-(1-propilbutil)bencil]amino}acético;

(236) ácido [{4-[4-(bencilmetilamino)fenil]tiazol-2-ilmetil}-(4-cloro-bencil)amino]acético;

(237) ácido [{4-[4-(bencilmetilamino)fenil]tiazol-2-ilmetil}-(2-cloro-bencil)amino]acético;

(238) ácido [{4-[4-(bencilmetilamino)fenil]tiazol-2-ilmetil}-(3,4-dicloro-bencil)amino]acético;

(239) ácido {[4-(4-{metil[4-(trans-4-metil-ciclohexil)bencil]amino}-fenil)tiazol-2-ilmetil]piridin-2-ilmetilamino}acético;

(240) ácido {[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)tiazol-2-ilmetil]piridin-2-ilmetilamino}acético;

(241) ácido ({4-[4-(bencilmetilamino)fenil]tiazol-2-ilmetil}-naftalen-1-ilmetilamino)acético;

(242) ácido ({4-[4-(bencilmetilamino)fenil]tiazol-2-ilmetil}-quinolin-2-ilmetilamino)acético;

(243) ácido ((2-benzo[b]tiofen-3-il-acetil)-{4-[4-(bencilmetilamino)fenil]tiazol-2-ilmetil}amino)acético;

(244) ácido [[2-(4-clorofenil)acetil]-(4-{4-[(4-isobutilbencil)-metilamino]fenil}tiazol-2-ilmetil)amino]acético;

(245) ácido {(4-{4-[(4-isobutilbencil)metilamino]fenil}tiazol-2-ilmetil)-[2-(4-isopropilfenil)acetil]amino}acético;

(246) ácido [(4-{4-[(4-isobutilbencil)metilamino]fenil}tiazol-2-ilmetil)-(3-metil-butiril)amino]acético;

(247) ácido {1-[4-(4-{[4-(2,2-dimetilpropil)bencil]metilamino}fenil)-tiazol-2-ilmetil]-3-fenilureido}acético;

(248) ácido [benzoil-(4-{4-[(4-isobutilbencil)metilamino]fenil}-tiazol-2-ilmetil)amino]acético;

(249) ácido {(4-metilbenzoil)-[4-(4-{metil[4-(1-propilbutil)bencil]-amino}fenil)tiazol-2-ilmetil]amino}acético;

(250) {(4-isopropilbenzoil)-[4-(4-{metil[4-(1-propilbutil)bencil]-amino}fenil)tiazol-2-ilmetil]amino}-acetato de sodio;

(251) (S)-{3-[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)tiazol-2-il]-3,4-dihidro-1H-isoquinolin-2-il}-acetato de sodio;

(252) ácido 1-(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)piperidin-4-carboxílico;

(253) ácido 1-(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)piperidin-3-carboxílico;

(254) ácido 1-(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)-4-fenilpiperidin-4-carboxílico;

(255) ácido 1-(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)-4-(3-metilbutil)piperidin-4-carboxílico;

(256) ácido 1-[4-(4-{metil[4-(trans-4-metil-ciclohexil)-bencil]-amino}-fenil)tiazol-2-ilmetil]-4-fenilpiperidin-4-carboxílico;

(257) ácido 1-[4-(4-[[trans-4-(4-cloro-fenil)-ciclohexilmetil]-metilamino}fenil)tiazol-2-ilmetil]-4-fenilpiperidin-4-carboxílico;

(258) ácido 2-[4-(4-{metil[4-(trans-4-metil-ciclohexil)bencil]-amino}fenil)tiazol-2-ilmetil]-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(259) ácido 2-(4-{4-[(4-isobutilbencil)metilamino]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(260) ácido 2-[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)-tiazol-2-ilmetil]-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(261) ácido 2-[4-(4-{[4-(2,2-dimetilpropil)bencil]metilamino}fenil)-tiazol-2-ilmetil]-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(262) ácido 5-{[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-il)metilamino]metil}furan-2-carboxílico;

(263) ácido 2-[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)amino]-3-fenilpropiónico;

(264) ácido [(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)amino]fenilacético;

(265) ácido 2-[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)amino]propiónico;

(266) ácido 3-(4-clorofenil)-2-[(4-{4-[(4-isobutilbencil)metilamino]-fenil}tiazol-2-ilmetil)amino]propiónico;

(267) ácido [(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)metilamino]acético;

(268) ácido 3-[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)metilamino]propiónico;

(269) ácido 4-{[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)metilamino]metil}benzoico;

(270) ácido 4-[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)metilamino]benzoico;

(271) ácido 6-[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)metilamino]nicotínico;

(272) ácido 2-[(4-{4-[(4-isobutilbencil)metilamino]fenil}tiazol-2-ilmetil)metilamino]-3-fenilpropiónico;

(273) ácido (S)-2-{metil[4-(4-{metil[4-(1-propilbutil)bencil]amino}-fenil)tiazol-2-ilmetil]amino}-3-fenilpropiónico;

(274) ácido (S)-{metil[4-(4-{metil[4-(1-propilbutil)bencil]amino}-fenil)tiazol-2-ilmetil]amino}fenilacético;

(275) ácido {[4-(4-{[4-(2,2-dimetilpropil)bencil]metilamino}fenil)-tiazol-2-ilmetil]metilamino}fenilacético;

(276) ácido 2-{[4-(4-{[4-(2,2-dimetilpropil)bencil]metilamino}fenil)-tiazol-2-ilmetil]metilamino}-3-fenilpropiónico;

(277) ácido {carboximetil[4-(4-{metil[4-(1-propilbutil)bencil]-amino}fenil)tiazol-2-ilmetil]amino}acético;

(278) ácido [(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)-(3-metilbutil)amino]acético;

(279) ácido {(3-metilbutil)-[4-(4-{metil[4-(trans-4-metil-ciclohexil)-bencil]amino}fenil)tiazol-2-ilmetil]amino}acético;

(280) ácido [(4-{4-[(4-isobutilbencil)metilamino]fenil}tiazol-2-ilmetil)-(3-metilbutil)amino]acético;

(281) ácido 5-[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)-tiazol-2-ilmetoxi]nicotínico;

(282) ácido 4-[4-(4-{metil[4-(1-propilbutil)benzil]amino}fenil)-tiazol-2-ilmetoxi]benzoico;

(283) ácido 4-[4-(4-{metil[4-(1-propilbutil)benzil]amino}fenil)-tiazol-2-ilmetiltio]benzoico;

(284) ácido 4-[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)sulfamoil]benzoico;

(285) ácido 4-{[4-(4-{[4-(4,4-dimetil-ciclohexil)bencil]metilamino}-fenil)tiazol-2-ilmetil]metilsulfamoil}benzoico;

(286) ácido {[4-(4-{[4-(4,4-dimetil-ciclohexil)bencil]metilamino}-fenil)tiazol-2-ilmetil]metilsulfamoil}acético;

(287) ácido 4-[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)metilsulfamoil]benzoico;

(288) ácido 3-[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)metilsulfamoil]benzoico;

(289) ácido [(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)metilsulfamoil]acético;

(290) ácido 4-{[4-(4-{[4-(4,4-dimetil-ciclohexil)bencil]metilamino}-fenil)tiazol-2-ilmetil]metilsulfamoil}butírico;

(291) ácido [(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)isobutil-sulfamoil]acético;

(292) ácido N-(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)oxámico;

(293) ácido {bencil[4-(4-[[4-(1-propilbutil)bencil]metilamino-carbonil}fenil)tiazol-2-ilmetil]amino}acético;

(294) ácido N-(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)-N-metiltereftalámico;

(295) ácido {bencil[4-(4-{metil[4-(trans-4-metil-ciclohexil)bencil]-amino}fenil)tiazol-2-ilmetoxicarbonil]amino}acético;

(296) ácido [3-(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)-3-metil-ureido]acético;

(297) ácido (ciclohexilmetil{4-[6-(3,4-diclorobenciloxi)-benzoxazol-2-il]tiazol-2-il}amino)acético;

(298) ácido [4-(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)piperacin-1-il]acético;

(299) (S)-2-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxilato de sodio;

(300) 5-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetoxi)-nicotinato de sodio;

(301) ácido 5-(4-{2-metil-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetoxi)nicotínico;

(302) ácido 5-(4-{3-metoxi-4-[4-(1-propilbutil)benciloxi]fenil}-tiazol-2-ilmetoxi)nicotínico;

(303) ácido [(4-{2-metil-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)fenilcarbamoilmetilamino]acético;

(304) ácido [[(4-isopropilfenilcarbamoil)metil]-(4-{2-metil-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)amino]acético;

(305) ácido 2-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(306) ácido [(4-{3-metoxi-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)fenilcarbamoilmetilamino]acético;

(307) ácido [[(4-isopropilfenilcarbamoil)metil]-(4-{3-metoxi-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)amino]acético;

(308) ácido [(4-{2-metil-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)tiazol-4-ilmetilamino]acético;

(309) clorhidrato del ácido [(4-{2-metil-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)-(2-metiltiazol-4-ilmetil)amino]acético;

(310) clorhidrato del ácido [(bencilcarbamoilmetil)-(4-{2-metil-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)amino]acético;

(311) ácido [(1H-bencimidazol-2-ilmetil)-(4-{2-metil-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)amino]acético;

(312) ácido [(4-ter-butiltiazol-2-ilmetil)-(4-{1-[4-(1-propilbutil)-bencil]-1,2,3,4-tetrahidroquinolin-6-il}tiazol-2-ilmetil)amino]acético;

(313) clorhidrato del ácido 1-(4-{4-[4-(1-propilbutil)benciloxi]-fenil}tiazol-2-ilmetil)piperidin-4-carboxílico;

(314) ácido 4-[4-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)piperacin-1-il]benzoico;

(315) éster etílico del ácido 4-{4-[5-(1-etilpropil)-1-(4-isopropilbencil)-1H-bencimidazol-2-il]tiazol-2-ilmetoxi}benzoico;

(316) ácido 4-{4-[5-(1-etilpropil)-1-(4-isopropilbencil)-1H-bencimidazol-2-il]tiazol-2-ilmetoxi}benzoico;

(317) ácido 4-{4-[1-(4-acetilbencil)-5-(1-etilpropil)-1H-bencimidazol-2-il]tiazol-2-ilmetoxi}benzoico;

(318) ácido 4-{4-[1-(4-acetilbencil)-6-(1-etilpropil)-1H-bencimidazol-2-il]tiazol-2-ilmetoxi}benzoico;

(319) ácido 4-{4-[1-ciclohexilmetil-5-(1-etilpropil)-1H-bencimidazol-2-il]tiazol-2-ilmetoxi}benzoico;

(320) ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(321) ácido 5-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi)nicotínico;

(322) ácido 5-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiofen-2-ilmetoxi}nicotínico;

(323) ácido 5-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiofen-2-ilmetoxi}nicotínico;

(324) ácido 5-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi)nicotínico;

(325) ácido [(1H-bencimidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(326) ácido 6-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi)piridin-2-carboxílico;

(327) ácido [(1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(328) ácido [[(4-isopropilfenilcarbamoil)metil]-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(329) ácido [fenilcarbamoilmetil(5-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]acético;

(330) ácido ({4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiofen-2-ilmetil}fenilcarbamoilmetilamino)acético;

(331) ácido ((4-ter-butiltiazol-2-ilmetil)-{4-[4-({[4-(1-etilpropil)-fenil]isopropilamino}metil)fenil]tiofen-2-ilmetil}amino)acético;

(332) ácido [(5-ter-butiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)-amino]acético;

(333) ácido ((1H-bencimidazol-2-ilmetil)-{4-[4-({[4-(1-etilpropil)-fenil]isopropilamino}metil)fenil]tiofen-2-ilmetil}amino)acético;

(334) ácido [(4-ter-butiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(335) ácido [fenilcarbamoilmetil(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]acético;

(336) ácido 5-{5-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiofen-2-ilmetoxi}nicotínico;

(337) ácido 5-{5-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiofen-2-ilmetoxi}nicotínico;

(338) ácido ((4-ter-butiltiazol-2-ilmetil)-{5-[4-({[4-(1-etilpropil)-fenil]isopropilamino}metil)fenil]tiofen-2-ilmetil}amino)acético;

(339) ácido ((4-ter-butiltiazol-2-ilmetil)-{5-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiofen-2-ilmetil}amino)acético;

(340) ácido ((1H-bencimidazol-2-ilmetil)-{5-[4-({[4-(1-etilpropil)-fenil]isopropilamino}metil)fenil]tiofen-2-ilmetil}amino)acético;

(341) ácido ((1H-bencimidazol-2-ilmetil)-{5-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiofen-2-ilmetil}amino)acético;

(342) ácido [(4,5-dimetiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(343) ácido (S)-2-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}-metil)fenil]tiofen-2-ilmetil}-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(344) ácido {{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiofen-2-ilmetil}-[(4-isopropilfenilcarbamoil)metil]amino}acético;

(345) ácido (S)-2-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(346) ácido [[(4-isopropilfenilcarbamoil)metil]-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(347) ácido (S)-2-{5-[4-({[4-(1-etilpropil)fenil]isopropilamino}-metil)fenil]tiofen-2-ilmetil}-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(348) ácido [(5-ter-butiloxazol-2-ilmetil)-(4-[4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(349) ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(350) ácido 6-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi)piridin-2-carboxílico;

(351) ácido 6-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiofen-2-ilmetoxi}-piridin-2-carboxílico;

(352) ácido ((5-ter-butiltiazol-2-ilmetil)-{4-[4-({[4-(1-etilpropil)-fenil]isopropilamino}metil)fenil]tiofen-2-ilmetil}amino)acético;

(353) ácido [{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiofen-2-ilmetil}-(1-metil-1H-bencimidazol-2-ilmetil)amino]acético;

(354) ácido [(4-ter-butiltiazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(355) ácido [{5-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiofen-2-ilmetil}-(1-metil-1H-bencimidazol-2-ilmetil)amino]acético;

(356) ácido [(5-ter-butiltiazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(357) [(1-metil-1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]-acetato de sodio;

(358) bis{[(1-metil-1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]-acetato} de calcio;

(359) toluen-4-sulfonato del ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(360) sulfato del ácido 5-(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetoxi)nicotínico;

(361) ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-carbonil)amino]acético;

(362) ácido [(5-ter-butiltiazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-carbonil)amino]acético;

(363) ácido [(4-isopropilbencil)-(5-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-carbonil)amino]acético;

(364) ácido [(4-dimetilaminobencil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-carbonil)amino]acético;

(365) ácido [(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-carbonil)-piridin-2-ilmetilamino]acético;

(366) ácido [(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-carbonil)-piridin-3-ilmetilamino]acético;

(367) metansulfonato del ácido 5-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetoxi)nicotínico;

(368) ácido [metansulfonil-(5-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]acético;

(369) 5-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi)-nicotinato de sodio;

(370) clorhidrato del ácido 5-(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetoxi)nicotínico;

(371) ácido 4-[4-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-carbonil)piperacin-1-il]benzoico;

(372) ácido 4-[1-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-carbonil)piperidin-4-il]benzoico;

(373) clorhidrato del ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(374) sulfato del ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(375) ácido 4-(2-dimetilaminoacetilamino)-3-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi)benzoico;

(376) ácido 4-isobutirilamino-3-(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetoxi)benzoico;

(377) ácido 4-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi)benzoico;

(378) ácido 4-(metansulfonilmetilamino)-3-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetoxi)benzoico;

(379) ácido 4-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetiltio)benzoico;

(380) ácido 4-amino-3-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiofen-2-ilmetoxi)benzoico;

(381) clorhidrato del ácido 1-{5-[1-(4-ciclohexilbencil)-1H-indol-3-il]tiofen-2-ilmetil}-4-fenilpiperidin-4-carboxílico;

(382) clorhidrato del ácido (bencil{5-[1-(4-ciclohexilbencil)-1H-indol-3-il]tiofen-2-ilmetil}amino)acético;

(383) ácido [(metilfenilsulfamoil)(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(384) ácido [(5-ter-butiltiazol-2-ilmetil)-(5-{4-[(4-ciclohexil-fenil)metilcarbamoil]fenil}tiofen-2-ilmetil)amino]acético;

(385) ácido [(5-{4-[(4-ciclohexilbencil)etilamino]fenil}tiofen-2-ilmetil)piridin-2-ilmetilamino]acético;

(386) ácido [(5-{4-[(4-ciclohexilbencil)etilamino]fenil}tiofen-2-ilmetil)-(2-fenoxietil)amino]acético;

(387) ácido 4-{1-[4-(4-{[trans-4-(4-ter-butilfenil)-ciclohexilmetil]-etilamino}fenil)tiofen-2-ilmetil]piperidin-4-il}benzoico;

(388) ácido [[2-(4-isopropilfenoxi)acetil]-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(389) ácido [(4-isopropilbenzoil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(390) ácido [(3-metilbutil)-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiofen-2-ilmetil)amino]acético;

(391) ácido [3-metil-3-fenil-1-(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)ureido]acético;

(392) ácido 2-(4-{3-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-7-carboxílico;

(393) ácido 4-[4-(5-{4-[4-(trans-4-metil-ciclohexil)benciloxi]fenil}-tiofen-2-ilmetil)piperacin-1-il]benzoico;

(394) ácido [(2-cloro-5-trifluorometilbencil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(395) ácido 3-{[carboximetil(5-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]metil}benzoico;

(396) ácido [(4-metoxibencil)-(5-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]acético;

(397) ácido [(4-metiltiobencil)-(5-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]acético;

(398) ácido 4-[ciclohexilmetil(5-{4-[4-(trans-4-metil-ciclohexil)-benciloxi]fenil}tiofen-2-ilmetil)sulfamoil]benzoico;

(399) ácido 4-[3-ciclohexilmetil-3-(5-{4-[4-(trans-4-metil-ciclohexil)benciloxi]fenil}tiofen-2-ilmetil)ureido]benzoico;

(400) ácido [benzhidril-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiofen-2-ilmetil)amino]acético;

(401) clorhidrato del éster etílico del ácido [[2-oxo-2-(4-pirrolidin-1-il-fenil)etil]-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]-acético;

(402) éster etílico del ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(403) ácido 3-(bencil{5-[1-(4-ciclohexilbencil)-2,3-dihidro-1H-indol-5-il]tiofen-2-ilmetil}amino)propiónico;

(404) ácido [bencil(4-{4-[2-(2,2-dimetilpropil)bencimidazol-1-ilmetil]fenil}tiofen-2-ilmetil)amino]acético;

(405) ácido [(1-metil-1H-indol-3-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(406) ácido [(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)quinolin-2-ilmetilamino]acético;

(407) ácido [benzotiazol-2-ilmetil(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(408) ácido [(1-bencil-1H-imidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(409) ácido [(1H-indol-5-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(410) ácido [(4-imidazol-1-ilbencil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(411) ácido [benzofuran-2-ilmetil(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(412) ácido [[2,2']bitiofenil-5-ilmetil(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(413) ácido [(2-fenil-1H-imidazol-4-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(414) ácido [(3-fenil-1H-pirazol-4-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(415) ácido [benzoxazol-2-ilmetil(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(416) ácido [benzo[b]tiofen-2-ilmetil(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(417) ácido [(4-feniltiofen-2-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(418) ácido [benzotiazol-2-il-(5-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]acético;

(419) ácido [(5-clorotiofen-2-sulfonil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(420) ácido [(1-dietilcarbamoilmetil-1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(421) ácido (S)-({4-[2-(4-ciclohexilbenciloxi)-5-metilfenil]tiofen-2-ilmetil}metilamino)-3-fenilpropiónico;

(422) ácido [bencil(4-{4-[(4-butoxi-bencensulfonil)etilamino]-fenil}tiofen-2-ilmetil)amino]acético;

(423) ácido N-{4-[2-(4-ciclohexilbenciloxi)-5-metilfenil]tiofen-2-ilmetil}-N-(2-metilbenzotiazol-6-il)oxámico;

(424) ácido (bencil{4-[4-(3,5-diclorofenoximetil)fenil]tiofen-2-ilmetil}amino)acético;

(425) ácido [(1-alil-1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; y

(426) ácido [[4-(4-clorofenil)tiazol-2-il]-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético.

[24] El compuesto anular heteroaromático de 5 miembros de cualquiera de [1] a [23], que se selecciona del grupo que consiste de los siguientes compuestos, o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos:

(1) ácido (S)-2-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(2) ácido {{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-[(4-isopropilfenilcarbamoil)metil]amino}acético;

(3) ácido 4-(3-isobutil-3-{4-[4-({isopropil[4-(1-propilbutil)fenil]-amino}metil)fenil]tiazol-2-ilmetil}ureido)benzoico;

(4) ácido ({4-[4-({isobutil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}fenilcarbamoilmetilamino)acético;

(5) ácido ([(4-isopropilfenilcarbamoil)metil]-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}amino)acético;

(6) ácido [(4-ter-butiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(7) ácido [(4,5-dimetiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(8) ácido [(5-ter-butiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(9) ácido [[2-(4-isopropilfenoxi)acetil]-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético;

(10) ácido 4-[4-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)piperacin-1-il]benzoico;

(11) ácido {bencil[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)-tiazol-2-ilmetil]amino}acético;

(12) ácido [(1-metil-1H-bencimidazol-2-ilmetil)-5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(13) ácido 5-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi}nicotínico;

(14) ácido [(1H-bencimidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(15) ácido [(1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(16) ácido [[(4-isopropilfenilcarbamoil)metil]-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético;

(17) ácido (S)-2-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}-metil)fenil]tiofen-2-ilmetil}-1,2,3,4-tetrahidroisoquinolin-3-carboxílico;

(18) ácido {{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiofen-2-ilmetil}-[(4-isopropilfenilcarbamoil)metil]amino}acético;

(19) ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; y

(20) ácido [(4-ter-butiltiazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético.

[25] Una composición farmacéutica que comprende el compuesto anular heteroaromático de 5 miembros de cualquiera de [1] a [24], o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos y un portador farmacéuticamente aceptable.

[26] Una composición farmacéutica para la inhibición de un regulador negativo del receptor de la tirosina cinasa, que comprende un compuesto anular heteroaromático de 5 miembros de cualquiera de [1] a [24], o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos y un portador farmacéuticamente aceptable.

[27] Una composición farmacéutica para la inhibición de la proteína tirosina fosfatasa 1B, que comprende un compuesto anular heteroaromático de 5 miembros de cualquiera de [1] a [24], o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos y un portador farmacéuticamente aceptable.

[28] Una composición farmacéutica para la profilaxis o el tratamiento de la diabetes, que comprende un compuesto anular heteroaromático de 5 miembros de cualquiera de [1] a [24], o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos y un portador farmacéuticamente aceptable.

[29] Una composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia, que comprende un compuesto anular heteroaromático de 5 miembros de cualquiera de [1] a [24], o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos y un portador farmacéuticamente aceptable.

[30] Una composición farmacéutica para la profilaxis o el tratamiento de la obesidad, que comprende un compuesto anular heteroaromático de 5 miembros de cualquiera de [1] a [24], o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos y un portador farmacéuticamente aceptable.

[31] Una composición farmacéutica para la profilaxis o el tratamiento de las complicaciones diabéticas, que comprende un compuesto anular heteroaromático de 5 miembros de cualquiera de [1] a [24], o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos y un portador farmacéuticamente aceptable.

[32] La composición farmacéutica de [25], que se utiliza en combinación con un agente terapéutico para la hiperlipidemia.

[33] La composición farmacéutica de [32], en donde el agente terapéutico para la hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de inhibidores de la HMG-CoA reductasa (estatinas), fibratos, inhibidores de la expresión de TNFSF6, agentes que incrementan el colesterol de HDL, mejoradores de la expresión de ApoA1, inhibidores de la expresión de SPP1 (osteopontina), fármacos que

actúan sobre los receptores activados por el proliferador de la peroxisoma (PPAR), antagonistas del PPAR-alfa, estimulantes del factor de eliminación de la lipasa, antagonistas del colesterol, antagonistas de agregación de las plaquetas, antioxidantes, inhibidores de la biosíntesis del colesterol, sobrerreguladores del receptor de LDL, secuestrantes del ácido biliar, inhibidores de la absorción del colesterol y ácidos nicotínicos.

[34] La composición farmacéutica de [33], en donde el agente terapéutico para hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de lovastatina, pravastatina (eptastatina) sódica, fluvastatina (fluindostainina) sódica, rosuvastatina cálcica, atorvastatina cálcica, simvastatina (sinvinolina), pitavastatina (itavastatina, nisvastatina) cálcica, ronifibrato (ronifibrato), binifibrato (binifibrato), clinofibrato, ciprofibrato, clofibrato, etofibrato, fenofibrato, bezafibrato, gemfibrozil, acipimox, éster etílico del ácido eicosapentaenoico (icosapent, icopenato, icosapentato), probucol, policosanol, clorhidrato de colesevelam, colestiramina (resina de colestiramina), clorhidrato de colestipol, colestimida (colestilan), ezetimibe y niacina (ácido nicotínico).

[35] La composición farmacéutica de [25], que se utiliza en combinación con un agente terapéutico para la diabetes.

[36] La composición farmacéutica de [35], en donde el agente terapéutico para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de secretagogos de la insulina, biguanidas, inhibidores de la α-glucosidasa, preparaciones de insulina, análogos de la insulina,

mejoradores de la sensitividad de la insulina, IL-11, agentes anti-CD25 (Receptor IL-2), antagonistas de la angiotensina (AT1), inhibidores de la enzima que convierte la angiotensina (ACE), inhibidores de la aldosa reductasa, antioxidantes, estimulante de la carnitina acetiltransferasa, antidepresivos, glucocorticoides, retilina, agonistas de la formación de radicales y activadores de la transcetolasa.

[37] La composición farmacéutica de [36], en donde el agente terapéutico para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de nateglinida, glimepirida, glibenclamida, gliclazida, acetohexamida, tolbutamida, gliclopiramida, tolazamida, glibuzol, glipizida, glibornurida, gliquidona, repaglinida, clorhidrato de metformina, clorhidrato de buformina, voglibosa, acarbosa, epalrestat, miglitol, insulina, clorhidrato de pioglitazona, maleato de rosiglitazona, picolinato de cromo/biotina, V-411, interleucina-11 humana recombinante, daclixímab (daclizumab), losartan potásico, captopril, clorhidrato de imidapril, ácido alfa-lipoico, clorhidrato de levacecarnina (acetil-L-carnitina, levocarnitin acetilo), captopril, retilina, verteporfin, benfotiamina y fluocinolon acetónido.

[38] La composición farmacéutica de [25], que se utiliza en combinación con un agente terapéutico para la obesidad.

[39] La composición farmacéutica de [38], en donde el agente terapéutico para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, inhibidores de la lipasa, inhibidores dobles de la recaptación de 5-HT/norepinefrina, inhibidores de la

recaptación de 5-HT, suplementos herbales que contienen efedrina y cafeína, gonadotropinas coriónicas humanas, agonistas de adrenoceptores, metamfetamina, fentermina y amfepramona.

[40] La composición farmacéutica de [39], en donde el agente terapéutico para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, orlistat, monohidrato del clorhidrato de sibutramina, clorhidrato de fluoxetina, gonadotropina coriónica (humana), terapia VNS utilizando el Sistema NCP, metaraminol, clorhidrato de d-metamfetamina, fentermina, clorhidrato de amfepramona (dietilpropion), clorhidrato de benzfetamina y tartrato de fendimetracina.

[41] La composición farmacéutica de [25], que se utiliza en combinación con un agente terapéutico para la hipertensión.

[42] La composición farmacéutica de [41], en donde el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de tiazidas, antagonistas de la aldosterona, bloqueadores adrenérgicos de las neuronas, bloqueadores del canal del calcio; antagonistas de la dopamina D2, antagonistas del aadrenoceptor beta, agonistas del adrenoceptor alfa2, activadores de la guanilato ciclasa, antagonistas del adrenoceptor beta1, antagonistas del adrenoceptor alfa1, antioxidantes, inhibidores de la enzima que convierten la angiotensina-I (ACE), inhibidores de intercambio de Na+/H+, antagonistas del adrenoceptor alfa, donadores de óxido nítrico, antagonistas de 5-HT2, activadores del canal de K(ATP), estimulantes de la prostaglandina sintasa

diurética del potasio sobrante, agonistas del receptor de la imidazolina I1, antagonistas de la angiotensina AT1, agonistas de la dopamina D1, estimulantes de la guanilato ciclasa, antagonistas del receptor de la endotelina ETA, antagonistas del receptor de la endotelina ETB, mejoradores de la expresión de NOS3, análogos de la prostaciclina, prostaglandinas, antagonistas de la angiotensina II, agonistas de la absorción del electrolito, antagonistas nicotínicos, agonistas de la dopamina D2, inhibidores de la prolactina, antagonistas del factor de activación de las plaquetas (PAF), antagonistas de agregación de las plaquetas, antagonistas del factor de necrosis del tumor, inhibidores de la Rho cinasa, antagonistas del PPAR-alfa, moduladores del receptor AMPA, antagonistas del receptor GABA(A) e inhibidores de la fosfodiesterasa V (PDE5A).

[43] La composición farmacéutica de [42], en donde el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de clorotiazida, hidroclorotiazida, hidroflumetiazida, meticlotiazida, politiazida, xipamida, ciclopentiazida, bendroflumetiazida (bendrofluazida), espironolactona, epoximexrenona (eplerenona), monosulfato de guanetidina, sulfato de guanadrel, verapamil, clorhidrato de propranolol, clorhidrato alprenolol, pindolol, clorhidrato de oxprenolol, maleato de timolol, clorhidrato de sotalol, clorhidrato de acebutolol, clorhidrato de carteolol, sulfato de mepindolol, clorhidrato de arotinolol, clorhidrato de indenolol, clorhidrato de tertatolol, clorhidrato de celiprolol, clorhidrato de tilisolol, nebivolol, sulfato de penbutolol, nadolol, clorhidrato de

cloranolol, clorhidrato de bevantol (bevantolol), clonidina, clorhidrato de guanfacina, clorhidrato de diltiazem, clorhidrato de nicardipina, nitrendipina, felodipina, nilvadipina; nivadipina, nisoldipina, clorhidrato de benidipina, besilato de amlodipina, clorhidrato de franidipina (manidipina), lacidipina, isradipina, clorhidrato de barnidipina (mepirodipina), clorhidrato etanólico de efonidipina, cinaldipina (cilnidipina), aranidipina, clorhidrato de lercanidipina (masnidipina), azelnidipina, amlodipina, manidipina (franidipina), nitroprussida sódica, atenolol, tartrato de metoprolol, clorhidrato de betaxolol, bopindolol, fumarato de bisoprolol, clorhidrato de esmolol, carvedilol, succinato de metoprolol, talinolol, clorhidrato de prazosina, urapidil, clorhidrato de indoramina, clorhidrato de bunazosina, clorhidrato de terazosina, mesilato de doxazosina, urapidil, nifedipina, captopril, maleato de enalapril, lisinopril, perindopril, alacepril, ramipril, clorhidrato de quinapril, clorhidrato de delapril, clorhidrato de benazepril, cilazapril, fosinoprilat, fosinopril sódico, trandolapril, espirapril, clorhidrato de temocapril, clorhidrato de moexipril, clorhidrato de imidapril, zofenopril cálcico, enalaprilat, zofenoprilat, clorhidrato de amilorida, clorhidrato de labetalol, nipradilol (nipradolol), linsidomina, quetanserina, pinacidil, cicletanina (cicletanida), clorhidrato de amosulalol, hidrato del clorhidrato de moxonidina, losartan potásico, valsartan, mesilato de eprosartan, candesartan cilexetilo (hexetilo), irbesartan, telmisartan, olmesartan medoxomilo, mesilato de fenoldopam, cadralacina, fosfato diácido de rilmenidina, bosentan, beraprost sódico, limaprost alfadex (alfa-ciclodextrina), uniprost (treprostinilo sódico), iloprost (ciloprost), clorhidrato de

mecamilamina, metergolina, acetato de guanabenz, cloricromeno, fasudilo, doconexent (ácido docosahexaenoico), ciclotiazida, citrato de sildenafil, clortalidona (clortalidona), quinetazona, indapamida, metolazona, clorhidrato de fenoxibenzamina, metirosina (metirosina), diazóxido, torasemida (torsemida), clopamida, clorhidrato de hidralacina, reserpina y metildopa.

[44] La composición farmacéutica de [25], que se utiliza en combinación con un agente terapéutico para la trombosis.

[45] La composición farmacéutica de [44], en donde el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste preparaciones de heparina, heparinas de bajo peso molecular, análogos de heparina, anticoagulantes, inhibidores de la trombina, preparaciones antitrombina, agentes antiplaquetarios y agentes trombolíticos.

[46] La composición farmacéutica de [45], en donde el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste de heparina cálcica, heparina sódica, dalteparina sódica, parnaparina sódica, reviparina sódica, danaparoid sódico, warfarina potásica, argatroban, mesilato de gabexato, mesilato de nafamostat, antitrombina III humana, aspirina, dipiridamol, clorhidrato de ticlopidina, cilostazol, limaprost alfadex, ozagrel sódico, clorhidrato de sarpogrelato, icosapentato de etilo, beraprost sódico, urocinasa, tisocinasa, alteplasa, nasaruplasa, nateplasa, monteplasa, pamiteplasa, batroxobina, citrato de sodio y proteína C.

[47] La composición farmacéutica para la profilaxis o el tratamiento de la diabetes de acuerdo con [28], que se utiliza en combinación con un agente terapéutico para la hiperlipidemia.

[48] La composición farmacéutica para la profilaxis o el tratamiento de la diabetes de acuerdo con [47], en donde el agente terapéutico para hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de inhibidores de la HMG-CoA reductasa (estatinas), fibratos, inhibidores de la expresión de TNFSF6, agentes que incrementan el colesterol de HDL, mejoradores de la expresión de ApoA1, inhibidores de la expresión de SPP1 (osteopontina), fármacos que actúan sobre los receptores activados por el proliferador de la peroxisoma (PPAR), antagonistas del PPAR-alfa, estimulantes del factor de eliminación de la lipasa, antagonistas del colesterol, antagonistas de agregación de las plaquetas, antioxidantes, inhibidores de la biosíntesis del colesterol, sobrerreguladores del receptor de LDL, secuestrantes del ácido biliar, inhibidores de la absorción del colesterol y ácidos nicotínicos.

[49] La composición farmacéutica para la profilaxis o el tratamiento de la diabetes de acuerdo con [48], en donde el agente terapéutico para hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de lovastatina, pravastatina (eptastatina) sódica, fluvastatina (fluindostainina) sódica, rosuvastatina cálcica, atorvastatina cálcica, simvastatina (sinvinolina), pitavastatina (itavastatina, nisvastatina) cálcica, ronifibrato (ronifibrato), binifibrato

(binifibrato), clinofibrato, ciprofibrato, clofibrato, etofibrato, fenofibrato, bezafibrato, gemfibrozil, acipimox, éster etílico del ácido eicosapentaenoico (icosapent, icopenato, icosapentato), probucol, policosanol, clorhidrato de colesevelam, colestiramina (resina de colestiramina), clorhidrato de colestipol, colestimida (colestilan), ezetimibe y niacina (ácido nicotínico).

[50] La composición farmacéutica para la profilaxis o el tratamiento de la diabetes de acuerdo con [28], que se utiliza en combinación con un agente terapéutico diferente para la diabetes.

[51] La composición farmacéutica para la profilaxis o el tratamiento de la diabetes de acuerdo con [50], en donde el agente terapéutico diferente para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de secretagogos de la insulina, biguanidas, inhibidores de la α-glucosidasa, preparaciones de insulina, análogos de la insulina, mejoradores de la sensitividad de la insulina, IL-11, agentes anti-CD25 (Receptor IL-2), antagonistas de la angiotensina (AT1), inhibidores de la enzima que convierte la angiotensina (ACE), inhibidores de la aldosa reductasa, antioxidantes, estimulante de la carnitina acetiltransferasa, antidepresivos, glucocorticoides, retilina, agonistas de la formación de radicales y activadores de la transcetolasa.

[52] La composición farmacéutica para la profilaxis o el tratamiento de la diabetes de acuerdo con [51], en donde el agente terapéutico diferente para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de nateglinida, glimepirida,

glibenclamida, gliclazida, acetohexamida, tolbutamida, gliclopiramida, tolazamida, glibuzol, glipizida, glibornurida, gliquidona, repaglinida, clorhidrato de metformina, clorhidrato de buformina, voglibosa, acarbosa, epalrestat, miglitol, insulina, clorhidrato de pioglitazona, maleato de rosiglitazona, picolinato de cromo/biotina, V-411, interleucina-11 humana recombinante, daclixímab (daclizumab), losartan potásico, captopril, clorhidrato de imidapril, ácido alfa-lipoico, clorhidrato de levacecarnina (acetil-L-carnitina, levocarnitin acetilo), captopril, retilina, verteporfin, benfotiamina y fluocinolon acetónido.

[53] La composición farmacéutica para la profilaxis o el tratamiento de la diabetes de acuerdo con [28], que se utiliza en combinación con un agente terapéutico para la obesidad.

[54] La composición farmacéutica para la profilaxis o el tratamiento de la diabetes de acuerdo con [53], en donde el agente terapéutico para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, inhibidores de la lipasa, inhibidores dobles de la recaptación de 5-HT/norepinefrina, inhibidores de la recaptación de 5-HT, suplementos herbales que contienen efedrina y cafeína, gonadotropinas coriónicas humanas, agonistas de adrenoceptores, metamfetamina, fentermina y anfepramona.

[55] La composición farmacéutica para la profilaxis o el tratamiento de la diabetes de acuerdo con [54], en donde el agente terapéutico para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, orlistat, monohidrato del

clorhidrato de sibutramina, clorhidrato de fluoxetina, gonadotropina coriónica (humana), terapia VNS utilizando el Sistema NCP, metaraminol, clorhidrato de d-metamfetamina, fentermina, clorhidrato de amfepramona (dietilpropion), clorhidrato de benzfetamina y tartrato de fendimetracina.

[56] La composición farmacéutica para la profilaxis o el tratamiento de la diabetes de acuerdo con [28], que se utiliza en combinación con un agente terapéutico para la hipertensión.

[57] La composición farmacéutica para la profilaxis o el tratamiento de la diabetes de acuerdo con [56], en donde el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de tiazidas, antagonistas de la aldosterona, bloqueadores adrenérgicos de las neuronas, bloqueadores del canal del calcio; antagonistas de la dopamina D2, antagonistas del aadrenoceptor beta, agonistas del adrenoceptor alfa2, activadores de la guanilato ciclasa, antagonistas del adrenoceptor beta1, antagonistas del adrenoceptor alfa1, antioxidantes, inhibidores de la enzima que convierten la angiotensina-I (ACE), inhibidores de intercambio de Na+/H+, antagonistas del adrenoceptor alfa, donadores de óxido nítrico, antagonistas de 5-HT2, activadores del canal de K(ATP), estimulantes de la prostaglandina sintasa diurética del potasio sobrante, agonistas del receptor de la imidazolina I1, antagonistas de la angiotensina AT1, agonistas de la dopamina D1, estimulantes de la guanilato ciclasa, antagonistas del receptor de la endotelina ETA, antagonistas del receptor de la endotelina ETB, mejoradores de la

expresión de NOS3, análogos de la prostaciclina, prostaglandinas, antagonistas de la angiotensina II, agonistas de la absorción del electrolito, antagonistas nicotínicos, agonistas de la dopamina D2, inhibidores de la prolactina, antagonistas del factor de activación de las plaquetas (PAF), antagonistas de agregación de las plaquetas, antagonistas del factor de necrosis del tumor, inhibidores de la Rho cinasa, antagonistas del PPAR-alfa, moduladores del receptor AMPA, antagonistas del receptor GABA(A) e inhibidores de la fosfodiesterasa V (PDE5A).

[58] La composición farmacéutica para la profilaxis o el tratamiento de la diabetes de acuerdo con [57], en donde el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de clorotiazida, hidroclorotiazida, hidroflumetiazida, meticlotiazida, politiazida, xipamida, ciclopentiazida, bendroflumetiazida (bendrofluazida), espironolactona, epoximexrenona (eplerenona), monosulfato de guanetidina, sulfato de guanadrel, verapamil, clorhidrato de propranolol, clorhidrato alprenolol, pindolol, clorhidrato de oxprenolol, maleato de timolol, clorhidrato de sotalol, clorhidrato de acebutolol, clorhidrato de carteolol, sulfato de mepindolol, clorhidrato de arotinolol, clorhidrato de indenolol, clorhidrato de tertatolol, clorhidrato de celiprolol, clorhidrato de tilisolol, nebivolol, sulfato de penbutolol, nadolol, clorhidrato de cloranolol, clorhidrato de bevantol (bevantolol), clonidina, clorhidrato de guanfacina, clorhidrato de diltiazem, clorhidrato de nicardipina, nitrendipina, felodipina, nilvadipina; nivadipina, nisoldipina, clorhidrato de benidipina,

besilato de amlodipina, clorhidrato de franidipina (manidipina), lacidipina, isradipina, clorhidrato de barnidipina (mepirodipina), clorhidrato etanólico de efonidipina, cinaldipina (cilnidipina), aranidipina, clorhidrato de lercanidipina (masnidipina), azelnidipina, amlodipina, manidipina (franidipina), nitroprussida sódica, atenolol, tartrato de metoprolol, clorhidrato de betaxolol, bopindolol, fumarato de bisoprolol, clorhidrato de esmolol, carvedilol, succinato de metoprolol, talinolol, clorhidrato de prazosina, urapidil, clorhidrato de indoramina, clorhidrato de bunazosina, clorhidrato de terazosina, mesilato de doxazosina, urapidil, nifedipina, captopril, maleato de enalapril, lisinopril, perindopril, alacepril, ramipril, clorhidrato de quinapril, clorhidrato de delapril, clorhidrato de benazepril, cilazapril, fosinoprilat, fosinopril sódico, trandolapril, espirapril, clorhidrato de temocapril, clorhidrato de moexipril, clorhidrato de imidapril, zofenopril cálcico, enalaprilat, zofenoprilat, clorhidrato de amilorida, clorhidrato de labetalol, nipradilol (nipradolol), linsidomina, quetanserina, pinacidil, cicletanina (cicletanida), clorhidrato de amosulalol, hidrato del clorhidrato de moxonidina, losartan potásico, valsartan, mesilato de eprosartan, candesartan cilexetilo (hexetilo), irbesartan, telmisartan, olmesartan medoxomilo, mesilato de fenoldopam, cadralacina, fosfato diácido de rilmenidina, bosentan, beraprost sódico, limaprost alfadex (alfa-ciclodextrina), uniprost (treprostinilo sódico), iloprost (ciloprost), clorhidrato de mecamilamina, metergolina, acetato de guanabenz, cloricromeno, fasudilo, doconexent (ácido docosahexaenoico), ciclotiazida, citrato de sildenafil, clortalidona (clortalidona), quinetazona, indapamida, metolazona, clorhidrato

de fenoxibenzamina, metirosina (metirosina), diazóxido, torasemida (torsemida), clopamida, clorhidrato de hidralacina, reserpina y metildopa.

[59] La composición farmacéutica para la profilaxis o el tratamiento de la diabetes de acuerdo con [28], que se utiliza en combinación con un agente terapéutico para la trombosis.

[60] La composición farmacéutica para la profilaxis o el tratamiento de la diabetes de acuerdo con [59], en donde el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste preparaciones de heparina, heparinas de bajo peso molecular, análogos de heparina, anticoagulantes, inhibidores de la trombina, preparaciones antitrombina, agentes antiplaquetarios y agentes trombolíticos.

[61] La composición farmacéutica para la profilaxis o el tratamiento de la diabetes de acuerdo con [60], en donde el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste de heparina cálcica, heparina sódica, dalteparina sódica, parnaparina sódica, reviparina sódica, danaparoid sódico, warfarina potásica, argatroban, mesilato de gabexato, mesilato de nafamostat, antitrombina III humana, aspirina, dipiridamol, clorhidrato de ticlopidina, cilostazol, limaprost alfadex, ozagrel sódico, clorhidrato de sarpogrelato, icosapentato de etilo, beraprost sódico, urocinasa, tisocinasa, alteplasa, nasaruplasa, nateplasa, monteplasa, pamiteplasa, batroxobina, citrato de sodio y proteína C.

[62] La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia de acuerdo con [29], que se utiliza en combinación con un agente terapéutico diferente para la hiperlipidemia.

[63] La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia de acuerdo con [62], en donde el agente terapéutico diferente para la hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de inhibidores de la HMG-CoA reductasa (estatinas), fibratos, inhibidores de la expresión de TNFSF6, agentes que incrementan el colesterol de HDL, mejoradores de la expresión de ApoA1, inhibidores de la expresión de SPP1 (osteopontina), fármacos que actúan sobre los receptores activados por el proliferador de la peroxisoma (PPAR), antagonistas del PPAR-alfa, estimulantes del factor de eliminación de la lipasa, antagonistas del colesterol, antagonistas de agregación de las plaquetas, antioxidantes, inhibidores de la biosíntesis del colesterol, sobrerreguladores del receptor de LDL, secuestrantes del ácido biliar, inhibidores de la absorción del colesterol y ácidos nicotínicos.

[64] La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia de acuerdo con [63], en donde el agente terapéutico diferente para la hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de lovastatina, pravastatina (eptastatina) sódica, fluvastatina (fluindostainina) sódica, rosuvastatina cálcica, atorvastatina cálcica, simvastatina (sinvinolina), pitavastatina (itavastatina, nisvastatina) cálcica, ronifibrato (ronifibrato), binifibrato

(binifibrato), clinofibrato, ciprofibrato, clofibrato, etofibrato, fenofibrato, bezafibrato, gemfibrozil, acipimox, éster etílico del ácido eicosapentaenoico (icosapent, icopenato, icosapentato), probucol, policosanol, clorhidrato de colesevelam, colestiramina (resina de colestiramina), clorhidrato de colestipol, colestimida (colestilan), ezetimibe y niacina (ácido nicotínico).

[65] La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia de acuerdo con [29], que se utiliza en combinación con un agente terapéutico para la diabetes.

[66] La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia de acuerdo con [65], en donde el agente terapéutico para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de secretagogos de la insulina, biguanidas, inhibidores de la α-glucosidasa, preparaciones de insulina, análogos de la insulina, mejoradores de la sensitividad de la insulina, IL-11, agentes anti-CD25 (Receptor IL-2), antagonistas de la angiotensina (AT1), inhibidores de la enzima que convierte la angiotensina (ACE), inhibidores de la aldosa reductasa, antioxidantes, estimulante de la carnitina acetiltransferasa, antidepresivos, glucocorticoides, retilina, agonistas de la formación de radicales y activadores de la transcetolasa.

[67] La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia de acuerdo con [66], en donde el agente terapéutico para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de nateglinida, glimepirida, glibenclamida, gliclazida,

acetohexamida, tolbutamida, gliclopiramida, tolazamida, glibuzol, glipizida, glibornurida, gliquidona, repaglinida, clorhidrato de metformina, clorhidrato de buformina, voglibosa, acarbosa, epalrestat, miglitol, insulina, clorhidrato de pioglitazona, maleato de rosiglitazona, picolinato de cromo/biotina, V-411, interleucina-11 humana recombinante, daclximab (daclizumab), losartan potásico, captopril, clorhidrato de imidapril, ácido alfa-lipoico, clorhidrato de levacecarnina (acetil-L-carnitina, levocarnitin acetilo), captopril, retilina, verteporfin, benfotiamina y fluocinolon acetónido.

[68] La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia de acuerdo con [29], que se utiliza en combinación con un agente terapéutico para la obesidad.

[69] La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia de acuerdo con [68], en donde el agente terapéutico para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, inhibidores de la lipasa, inhibidores dobles de la recaptación de 5-HT/norepinefrina, inhibidores de la recaptación de 5-HT, suplementos herbales que contienen efedrina y cafeína, gonadotropinas coriónicas humanas, agonistas de adrenoceptores, metamfetamina, fentermina y amfepramona.

[70] La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia de acuerdo con [69], en donde el agente terapéutico para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, orlistat, monohidrato del

clorhidrato de sibutramina, clorhidrato de fluoxetina, gonadotropina coriónica (humana), terapia VNS utilizando el Sistema NCP, metaraminol, clorhidrato de d-metamfetamina, fentermina, clorhidrato de amfepramona (dietilpropion), clorhidrato de benzfetamina y tartrato de fendimetracina.

[71] La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia de acuerdo con [29], que se utiliza en combinación con un agente terapéutico para la hipertensión.

[72] La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia de acuerdo con [71], en donde el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de tiazidas, antagonistas de la aldosterona, bloqueadores adrenérgicos de las neuronas, bloqueadores del canal del calcio; antagonistas de la dopamina D2, antagonistas del aadrenoceptor beta, agonistas del adrenoceptor alfa2, activadores de la guanilato ciclasa, antagonistas del adrenoceptor beta1, antagonistas del adrenoceptor alfa1, antioxidantes, inhibidores de la enzima que convierten la angiotensina-I (ACE), inhibidores de intercambio de Na+/H+, antagonistas del adrenoceptor alfa, donadores de óxido nítrico, antagonistas de 5-HT2, activadores del canal de K(ATP), estimulantes de la prostaglandina sintasa diurética del potasio sobrante, agonistas del receptor de la imidazolina I1, antagonistas de la angiotensina AT1, agonistas de la dopamina D1, estimulantes de la guanilato ciclasa, antagonistas del receptor de la endotelina ETA, antagonistas del receptor de la endotelina ETB, mejoradores de la

expresión de NOS3, análogos de la prostaciclina, prostaglandinas, antagonistas de la angiotensina II, agonistas de la absorción del electrolito, antagonistas nicotínicos, agonistas de la dopamina D2, inhibidores de la prolactina, antagonistas del factor de activación de las plaquetas (PAF), antagonistas de agregación de las plaquetas, antagonistas del factor de necrosis del tumor, inhibidores de la Rho cinasa, antagonistas del PPAR-alfa, moduladores del receptor AMPA, antagonistas del receptor GABA(A) e inhibidores de la fosfodiesterasa V (PDE5A).

[73] La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia de acuerdo con [72], en donde el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de clorotiazida, hidroclorotiazida, hidroflumetiazida, meticlotiazida, politiazida, xipamida, ciclopentiazida, bendroflumetiazida (bendrofluazida), espironolactona, epoximexrenona (eplerenona), monosulfato de guanetidina, sulfato de guanadrel, verapamil, clorhidrato de propranolol, clorhidrato alprenolol, pindolol, clorhidrato de oxprenolol, maleato de timolol, clorhidrato de sotalol, clorhidrato de acebutolol, clorhidrato de carteolol, sulfato de mepindolol, clorhidrato de arotinolol, clorhidrato de indenolol, clorhidrato de tertatolol, clorhidrato de celiprolol, clorhidrato de tilisolol, nebivolol, sulfato de penbutolol, nadolol, clorhidrato de cloranolol, clorhidrato de bevantol (bevantolol), clonidina, clorhidrato de guanfacina, clorhidrato de diltiazem, clorhidrato de nicardipina, nitrendipina, felodipina, nilvadipina; nivadipina, nisoldipina, clorhidrato de benidipina,

besilato de amlodipina, clorhidrato de franidipina (manidipina), lacidipina, isradipina, clorhidrato de barnidipina (mepirodipina), clorhidrato etanólico de efonidipina, cinaldipina (cilnidipina), aranidipina, clorhidrato de lercanidipina (masnidipina), azelnidipina, amlodipina, manidipina (franidipina), nitroprussida sódica, atenolol, tartrato de metoprolol, clorhidrato de betaxolol, bopindolol, fumarato de bisoprolol, clorhidrato de esmolol, carvedilol, succinato de metoprolol, talinolol, clorhidrato de prazosina, urapidil, clorhidrato de indoramina, clorhidrato de bunazosina, clorhidrato de terazosina, mesilato de doxazosina, urapidil, nifedipina, captopril, maleato de enalapril, lisinopril, perindopril, alacepril, ramipril, clorhidrato de quinapril, clorhidrato de delapril, clorhidrato de benazepril, cilazapril, fosinoprilat, fosinopril sódico, trandolapril, espirapril, clorhidrato de temocapril, clorhidrato de moexipril, clorhidrato de imidapril, zofenopril cálcico, enalaprilat, zofenoprilat, clorhidrato de amilorida, clorhidrato de labetalol, nipradilol (nipradolol), linsidomina, quetanserina, pinacidil, cicletanina (cicletanida), clorhidrato de amosulalol, hidrato del clorhidrato de moxonidina, losartan potásico, valsartan, mesilato de eprosartan, candesartan cilexetilo (hexetilo), irbesartan, telmisartan, olmesartan medoxomilo, mesilato de fenoldopam, cadralacina, fosfato diácido de rilmenidina, bosentan, beraprost sódico,. limaprost alfadex (alfa-ciclodextrina), uniprost (treprostinilo sódico), iloprost (ciloprost), clorhidrato de mecamilamina, metergolina, acetato de guanabenz, cloricromeno, fasudilo, doconexent (ácido docosahexaenoico), ciclotiazida, citrato de sildenafil, clortalidona (clortalidona), quinetazona, indapamida, metolazona, clorhidrato

de fenoxibenzamina, metirosina (metirosina), diazóxido, torasemida (torsemida), clopamida, clorhidrato de hidralacina, reserpina y metildopa.

[74] La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia de acuerdo con [29], que se utiliza en combinación con un agente terapéutico para la trombosis.

[75] La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia de acuerdo con [74], en donde el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste preparaciones de heparina, heparinas de bajo peso molecular, análogos de heparina, anticoagulantes, inhibidores de la trombina, preparaciones antitrombina, agentes antiplaquetarios y agentes trombolíticos.

[76] La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia de acuerdo con [75], en donde el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste de heparina cálcica, heparina sódica, dalteparina sódica, parnaparina sódica, reviparina sódica, danaparoid sódico, warfarina potásica, argatroban, mesilato de gabexato, mesilato de nafamostat, antitrombina III humana, aspirina, dipiridamol, clorhidrato de ticlopidina, cilostazol, limaprost alfadex, ozagrel sódico, clorhidrato de sarpogrelato, icosapentato de etilo, beraprost sódico, urocinasa, tisocinasa, alteplasa, nasaruplasa, nateplasa, monteplasa, pamiteplasa, batroxobina, citrato de sodio y proteína C.

[77] La composición farmacéutica para la profilaxis o el tratamiento de la obesidad de acuerdo con [30], que se utiliza en combinación con un agente terapéutico para la hiperlipidemia.

[78] La composición farmacéutica para la profilaxis o el tratamiento de la obesidad de acuerdo con [77], en donde el agente terapéutico para hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de inhibidores de la HMG-CoA reductasa (estatinas), fibratos, inhibidores de la expresión de TNFSF6, agentes que incrementan el colesterol de HDL, mejoradores de la expresión de ApoA1, inhibidores de la expresión de SPP1 (osteopontina), fármacos que actúan sobre los receptores activados por el proliferador de la peroxisoma (PPAR), antagonistas del PPAR-alfa, estimulantes del factor de eliminación de la lipasa, antagonistas del colesterol, antagonistas de agregación de las plaquetas, antioxidantes, inhibidores de la biosíntesis del colesterol, sobrerreguladores del receptor de LDL, secuestrantes del ácido biliar, inhibidores de la absorción del colesterol y ácidos nicotínicos.

[79] La composición farmacéutica para la profilaxis o el tratamiento de la obesidad de acuerdo con [78], en donde el agente terapéutico para hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de lovastatina, pravastatina (eptastatina) sódica, fluvastatina (fluindostainina) sódica, rosuvastatina cálcica, atorvastatina cálcica, simvastatina (sinvinolina), pitavastatina (itavastatina, nisvastatina) cálcica, ronifibrato (ronifibrato), binifibrato

(binifibrato), clinofibrato, ciprofibrato, clofibrato, etofibrato, fenofibrato, bezafibrato, gemfibrozil, acipimox, éster etílico del ácido eicosapentaenoico (icosapent, icopenato, icosapentato), probucol, policosanol, clorhidrato de colesevelam, colestiramina (resina de colestiramina), clorhidrato de colestipol, colestimida (colestilan), ezetimibe y niacina (ácido nicotínico).

[80] La composición farmacéutica para la profilaxis o el tratamiento de la obesidad de acuerdo con [30], que se utiliza en combinación con un agente terapéutico para la diabetes.

[81] La composición farmacéutica para la profilaxis o el tratamiento de la obesidad de acuerdo con [80], en donde el agente terapéutico para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de secretagogos de la insulina, biguanidas, inhibidores de la α-glucosidasa, preparaciones de insulina, análogos de la insulina, mejoradores de la sensitividad de la insulina, IL-11, agentes anti-CD25 (Receptor IL-2), antagonistas de la angiotensina (AT1), inhibidores de la enzima que convierte la angiotensina (ACE), inhibidores de la aldosa reductasa, antioxidantes, estimulante de la carnitina acetiltransferasa, antidepresivos, glucocorticoides, retilina, agonistas de la formación de radicales y activadores de la transcetolasa.

[82] La composición farmacéutica para la profilaxis o el tratamiento de la obesidad de acuerdo con [81], en donde el agente terapéutico para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de nateglinida, glimepirida, glibenclamida, gliclazida,

acetohexamida, tolbutamida, gliclopiramida, tolazamida, glibuzol, glipizida, glibornurida, gliquidona, repaglinida, clorhidrato de metformina, clorhidrato de buformina, voglibosa, acarbosa, epalrestat, miglitol, insulina, clorhidrato de pioglitazona, maleato de rosiglitazona, picolinato de cromo/biotina, V-411, interleucina-11 humana recombinante, daclixímab (daclizumab), losartan potásico, captopril, clorhidrato de imidapril, ácido alfa-lipoico, clorhidrato de levacecarnina (acetil-L-carnitina, levocarnitin acetilo), captopril, retilina, verteporfin, benfotiamina y fluocinolon acetónido.

[83] La composición farmacéutica para la profilaxis o el tratamiento de la obesidad de acuerdo con [30], que se utiliza en combinación con un agente terapéutico diferente para la obesidad.

[84] La composición farmacéutica para la profilaxis o el tratamiento de la obesidad de acuerdo con [83], en donde el agente terapéutico diferente para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, inhibidores de la lipasa, inhibidores dobles de la recaptación de 5-HT/norepinefrina, inhibidores de la recaptación de 5-HT, suplementos herbales que contienen efedrina y cafeína, gonadotropinas coriónicas humanas, agonistas de adrenoceptores, metamfetamina, fentermina y amfepramona.

[85] La composición farmacéutica para la profilaxis o el tratamiento de la obesidad de acuerdo con [84], en donde el agente terapéutico diferente para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, orlistat, monohidrato del

clorhidrato de sibutramina, clorhidrato de fluoxetina, gonadotropina coriónica (humana), terapia VNS utilizando el Sistema NCP, metaraminol, clorhidrato de d-metamfetamina, fentermina, clorhidrato de amfepramona (dietilpropion), clorhidrato de benzfetamina y tartrato de fendimetracina.

[86] La composición farmacéutica para la profilaxis o el tratamiento de la obesidad de acuerdo con [30], que se utiliza en combinación con un agente terapéutico para la hipertensión.

[87] La composición farmacéutica para la profilaxis o el tratamiento de la obesidad de acuerdo con [86], en donde el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de tiazidas, antagonistas de la aldosterona, bloqueadores adrenérgicos de las neuronas, bloqueadores del canal del calcio; antagonistas de la dopamina D2, antagonistas del aadrenoceptor beta, agonistas del adrenoceptor alfa2, activadores de la guanilato ciclasa, antagonistas del adrenoceptor beta1, antagonistas del adrenoceptor alfa1, antioxidantes, inhibidores de la enzima que convierten la angiotensina-I (ACE), inhibidores de intercambio de Na+/H+, antagonistas del adrenoceptor alfa, donadores de óxido nítrico, antagonistas de 5-HT2, activadores del canal de K(ATP), estimulantes de la prostaglandina sintasa diurética del potasio sobrante, agonistas del receptor de la imidazolina I1, antagonistas de la angiotensina AT1, agonistas de la dopamina D1, estimulantes de la guanilato ciclasa, antagonistas del receptor de la endotelina ETA, antagonistas del receptor de la endotelina ETB, mejoradores de la

expresión de NOS3, análogos de la prostaciclina, prostaglandinas, antagonistas de la angiotensina II, agonistas de la absorción del electrolito, antagonistas nicotínicos, agonistas de la dopamina D2, inhibidores de la prolactina, antagonistas del factor de activación de las plaquetas (PAF), antagonistas de agregación de las plaquetas, antagonistas del factor de necrosis del tumor, inhibidores de la Rho cinasa, antagonistas del PPAR-alfa, moduladores del receptor AMPA, antagonistas del receptor GABA(A) e inhibidores de la fosfodiesterasa V (PDE5A).

[88] La composición farmacéutica para la profilaxis o el tratamiento de la obesidad de acuerdo con [87], en donde el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de clorotiazida, hidroclorotiazida, hidroflumetiazida, meticlotiazida, politiazida, xipamida, ciclopentiazida, bendroflumetiazida (bendrofluazida), espironolactona, epoximexrenona (eplerenona), monosulfato de guanetidina, sulfato de guanadrel, verapamil, clorhidrato de propranolol, clorhidrato alprenolol, pindolol, clorhidrato de oxprenolol, maleato de timolol, clorhidrato de sotalol, clorhidrato de acebutolol, clorhidrato de carteolol, sulfato de mepindolol, clorhidrato de arotinolol, clorhidrato de indenolol, clorhidrato de tertatolol, clorhidrato de celiprolol, clorhidrato de tilisolol, nebivolol, sulfato de penbutolol, nadolol, clorhidrato de cloranolol, clorhidrato de bevantol (bevantolol), clonidina, clorhidrato de guanfacina, clorhidrato de diltiazem, clorhidrato de nicardipina, nitrendipina, felodipina, nilvadipina; nivadipina, nisoldipina, clorhidrato de benidipina,

besilato de amlodipina, clorhidrato de franidipina (manidipina), lacidipina, isradipina, clorhidrato de barnidipina (mepirodipina), clorhidrato etanólico de efonidipina, cinaldipina (cilnidipina), aranidipina, clorhidrato de lercanidipina (masnidipina), azelnidipina, amlodipina, manidipina (franidipina), nitroprussida sódica, atenolol, tartrato de metoprolol, clorhidrato de betaxolol, bopindolol, fumarato de bisoprolol, clorhidrato de esmolol, carvedilol, succinato de metoprolol, talinolol, clorhidrato de prazosina, urapidil, clorhidrato de indoramina, clorhidrato de bunazosina, clorhidrato de terazosina, mesilato de doxazosina, urapidil, nifedipina, captopril, maleato de enalapril, lisinopril, perindopril, alacepril, ramipril, clorhidrato de quinapril, clorhidrato de delapril, clorhidrato de benazepril, cilazapril, fosinoprilat, fosinopril sódico, trandolapril, espirapril, clorhidrato de temocapril, clorhidrato de moexipril, clorhidrato de imidapril, zofenopril cálcico, enalaprilat, zofenoprilat, clorhidrato de amilorida, clorhidrato de labetalol, nipradilol (nipradolol), linsidomina, quetanserina, pinacidil, cicletanina (cicletanida), clorhidrato de amosulalol, hidrato del clorhidrato de moxonidina, losartan potásico, valsartan, mesilato de eprosartan, candesartan cilexetilo (hexetilo), irbesartan, telmisartan, olmesartan medoxomilo, mesilato de fenoldopam, cadralacina, fosfato diácido de rilmenidina, bosentan, beraprost sódico, limaprost alfadex (alfa-ciclodextrina), uniprost (treprostinilo sódico), iloprost (ciloprost), clorhidrato de mecamilamina, metergolina, acetato de guanabenz, cloricromeno, fasudilo, doconexent (ácido docosahexaenoico), ciclotiazida, citrato de sildenafil, clortalidona (clortalidona), quinetazona, indapamida, metolazona, clorhidrato

de fenoxibenzamina, metirosina (metirosina), diazóxido, torasemida (torsemida), clopamida, clorhidrato de hidralacina, reserpina y metildopa.

[89] La composición farmacéutica para la profilaxis o el tratamiento de la obesidad de acuerdo con [30], que se utiliza en combinación con un agente terapéutico para la trombosis.

[90] La composición farmacéutica para la profilaxis o el tratamiento de la obesidad de acuerdo con [89], en donde el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste preparaciones de heparina, heparinas de bajo peso molecular, análogos de heparina, anticoagulantes, inhibidores de la trombina, preparaciones antitrombina, agentes antiplaquetarios y agentes trombolíticos.

[91] La composición farmacéutica para la profilaxis o el tratamiento de la obesidad de acuerdo con [90], en donde el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste de heparina cálcica, heparina sódica, dalteparina sódica, parnaparina sódica, reviparina sódica, danaparoid sódico, warfarina potásica, argatroban, mesilato de gabexato, mesilato de nafamostat, antitrombina III humana, aspirina, dipiridamol, clorhidrato de ticlopidina, cilostazol, limaprost alfadex, ozagrel sódico, clorhidrato de sarpogrelato, icosapentato de etilo, beraprost sódico, urocinasa, tisocinasa, alteplasa, nasaruplasa, nateplasa, monteplasa, pamiteplasa, batroxobina, citrato de sodio y proteína C.

[92] La composición farmacéutica para la profilaxis o el tratamiento de complicaciones diabéticas de acuerdo con [31], que se utiliza en combinación con un agente terapéutico para la hiperlipidemia.

[93] La composición farmacéutica para la profilaxis o el tratamiento de complicaciones diabéticas de acuerdo con [92], en donde el agente terapéutico para hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de inhibidores de la HMG-CoA reductasa (estatinas), fibratos, inhibidores de la expresión de TNFSF6, agentes que incrementan el colesterol de HDL, mejoradores de la expresión de ApoA1, inhibidores de la expresión de SPP1 (osteopontina), fármacos que actúan sobre los receptores activados por el proliferador de la peroxisoma (PPAR), antagonistas del PPAR-alfa, estimulantes del factor de eliminación de la lipasa, antagonistas del colesterol, antagonistas de agregación de las plaquetas, antioxidantes, inhibidores de la biosíntesis del colesterol, sobrerreguladores del receptor de LDL, secuestrantes del ácido biliar, inhibidores de la absorción del colesterol y ácidos nicotínicos.

[94] La composición farmacéutica para la profilaxis o el tratamiento de complicaciones diabéticas de acuerdo con [93], en donde el agente terapéutico para hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de lovastatina, pravastatina (eptastatina) sódica, fluvastatina (fluindostalnina) sódica, rosuvastatina cálcica, atorvastatina cálcica, simvastatina (sinvinolina), pitavastatina (itavastatina, nisvastatina) cálcica, ronifibrato (ronifibrato), binifibrato

(binifibrato), clinofibrato, ciprofibrato, clofibrato, etofibrato, fenofibrato, bezafibrato, gemfibrozil, acipimox, éster etílico del ácido eicosapentaenoico (icosapent, icopenato, icosapentato), probucol, policosanol, clorhidrato de colesevelam, colestiramina (resina de colestiramina), clorhidrato de colestipol, colestimida (colestilan), ezetimibe y niacina (ácido nicotínico).

[95] La composición farmacéutica para la profilaxis o el tratamiento de complicaciones diabéticas de acuerdo con [31], que se utiliza en combinación con un agente terapéutico para la diabetes.

[96] La composición farmacéutica para la profilaxis o el tratamiento de complicaciones diabéticas de acuerdo con [95], en donde el agente terapéutico para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de secretagogos de la insulina, biguanidas, inhibidores de la α-glucosidasa, preparaciones de insulina, análogos de la insulina, mejoradores de la sensitividad de la insulina, IL-11, agentes anti-CD25 (Receptor IL-2), antagonistas de la angiotensina (AT1), inhibidores de la enzima que convierte la angiotensina (ACE), inhibidores de la aldosa reductasa, antioxidantes, estimulante de la carnitina acetiltransferasa, antidepresivos, glucocorticoides, retilina, agonistas de la formación de radicales y activadores de la transcetolasa.

[97] La composición farmacéutica para la profilaxis o el tratamiento de complicaciones diabéticas de acuerdo con [96], en donde el agente terapéutico para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de nateglinida, glimepirida,

glibenclamida, gliclazida, acetohexamida, tolbutamida, gliclopiramida, tolazamida, glibuzol, glipizida, glibornurida, gliquidona, repaglinida, clorhidrato de metformina, clorhidrato de buformina, voglibosa, acarbosa, epalrestat, miglitol, insulina, clorhidrato de pioglitazona, maleato de rosiglitazona, picolinato de cromo/biotina, V-411, interleucina-11 humana recombinante, daclixímab (daclizumab), losartan potásico, captopril, clorhidrato de imidapril, ácido alfa-lipoico, clorhidrato de levacecarnina (acetil-L-carnitina, levocarnitin acetilo), captopril, retilina, verteporfin, benfotiamina y fluocinolon acetónido.

[98] La composición farmacéutica para la profilaxis o el tratamiento de complicaciones diabéticas de acuerdo con [31], que se utiliza en combinación con un agente terapéutico para la obesidad.

[99] La composición farmacéutica para la profilaxis o el tratamiento de complicaciones diabéticas de acuerdo con [98], en donde el agente terapéutico para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, inhibidores de la lipasa, inhibidores dobles de la recaptación de 5-HT/norepinefrina, inhibidores de la recaptación de 5-HT, suplementos herbales que contienen efedrina y cafeína, gonadotropinas coriónicas humanas, agonistas de adrenoceptores, metamfetamina, fentermina y amfepramona.

[100] La composición farmacéutica para la profilaxis o el tratamiento de complicaciones diabéticas de acuerdo con [99], en donde el agente terapéutico para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, orlistat, monohidrato del

clorhidrato de sibutramina, clorhidrato de fluoxetina, gonadotropina coriónica (humana), terapia VNS utilizando el Sistema NCP, metaraminol, clorhidrato de d-metamfetamina, fentermina, clorhidrato de amfepramona (dietilpropion), clorhidrato de benzfetamina y tartrato de fendimetracina.

[101] La composición farmacéutica para la profilaxis o el tratamiento de complicaciones diabéticas de acuerdo con [31], que se utiliza en combinación con un agente terapéutico para la hipertensión.

[102] La composición farmacéutica para la profilaxis o el tratamiento de complicaciones diabéticas de acuerdo con [101], en donde el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de tiazidas, antagonistas de la aldosterona, bloqueadores adrenérgicos de las neuronas, bloqueadores del canal del calcio; antagonistas de la dopamina D2, antagonistas del aadrenoceptor beta, agonistas del adrenoceptor alfa2, activadores de la guanilato ciclasa, antagonistas del adrenoceptor beta1, antagonistas del adrenoceptor alfa1, antioxidantes, inhibidores de la enzima que convierten la angiotensina-I (ACE), inhibidores de intercambio de Na+/H+, antagonistas del adrenoceptor alfa, donadores de óxido nítrico, antagonistas de 5-HT2, activadores del canal de K(ATP), estimulantes de la prostaglandina sintasa diurética del potasio sobrante, agonistas del receptor de la imidazolina I1, antagonistas de la angiotensina AT1, agonistas de la dopamina D1, estimulantes de la guanilato ciclasa, antagonistas del receptor de la endotelina ETA, antagonistas del receptor de la endotelina ETB, mejoradores de la

expresión de NOS3, análogos de la prostaciclina, prostaglandinas, antagonistas de la angiotensina II, agonistas de la absorción del electrolito, antagonistas nicotínicos, agonistas de la dopamina D2, inhibidores de la prolactina, antagonistas del factor de activación de las plaquetas (PAF), antagonistas de agregación de las plaquetas, antagonistas del factor de necrosis del tumor, inhibidores de la Rho cinasa, antagonistas del PPAR-alfa, moduladores del receptor AMPA, antagonistas del receptor GABA(A) e inhibidores de la fosfodiesterasa V (PDE5A).

[103] La composición farmacéutica para la profilaxis o el tratamiento de complicaciones diabéticas de acuerdo con [102], en donde el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de clorotiazida, hidroclorotiazida, hidroflumetiazida, meticlotiazida, politiazida, xipamida, ciclopentiazida, bendroflumetiazida (bendrofluazida), espironolactona, epoximexrenona (eplerenona), monosulfato de guanetidina, sulfato de guanadrel, verapamil, clorhidrato de propranolol, clorhidrato alprenolol, pindolol, clorhidrato de oxprenolol, maleato de timolol, clorhidrato de sotalol, clorhidrato de acebutolol, clorhidrato de carteolol, sulfato de mepindolol, clorhidrato de arotinolol, clorhidrato de indenolol, clorhidrato de tertatolol, clorhidrato de celiprolol, clorhidrato de tilisolol, nebivolol, sulfato de penbutolol, nadolol, clorhidrato de cloranolol, clorhidrato de bevantol (bevantolol), clonidina, clorhidrato de guanfacina, clorhidrato de diltiazem, clorhidrato de nicardipina, nitrendipina, felodipina, nilvadipina; nivadipina, nisoldipina, clorhidrato de benidipina,

besilato de amlodipina, clorhidrato de franidipina (manidipina), lacidipina, isradipina, clorhidrato de barnidipina (mepirodipina), clorhidrato etanólico de efonidipina, cinaldipina (cilnidipina), aranidipina, clorhidrato de lercanidipina (masnidipina), azelnidipina, amlodipina, manidipina (franidipina), nitroprussida sódica, atenolol, tartrato de metoprolol, clorhidrato de betaxolol, bopindolol, fumarato de bisoprolol, clorhidrato de esmolol, carvedilol, succinato de metoprolol, talinolol, clorhidrato de prazosina, urapidil, clorhidrato de indoramina, clorhidrato de bunazosina, clorhidrato de terazosina, mesilato de doxazosina, urapidil, nifedipina, captopril, maleato de enalapril, lisinopril, perindopril, alacepril, ramipril, clorhidrato de quinapril, clorhidrato de delapril, clorhidrato de benazepril, cilazapril, fosinoprilat, fosinopril sódico, trandolapril, espirapril, clorhidrato de temocapril, clorhidrato de moexipril, clorhidrato de imidapril, zofenopril cálcico, enalaprilat, zofenoprilat, clorhidrato de amilorida, clorhidrato de labetalol, nipradilol (nipradolol), linsidomina, quetanserina, pinacidil, cicletanina (cicletanida), clorhidrato de amosulalol, hidrato del clorhidrato de moxonidina, losartan potásico, valsartan, mesilato de eprosartan, candesartan cilexetilo (hexetilo), irbesartan, telmisartan, olmesartan medoxomilo, mesilato de fenoldopam, cadralacina, fosfato diácido de rilmenidina, bosentan, beraprost sódico, limaprost alfadex (alfa-ciclodextrina), uniprost (treprostinilo sódico), iloprost (ciloprost), clorhidrato de mecamilamina, metergolina, acetato de guanabenz, cloricromeno, fasudilo, doconexent (ácido docosahexaenoico), ciclotiazida, citrato de sildenafil, clortalidona (clortalidona), quinetazona, indapamida, metolazona, clorhidrato

de fenoxibenzamina, metirosina (metirosina), diazóxido, torasemida (torsemida), clopamida, clorhidrato de hidralacina, reserpina y metildopa.

[104] La composición farmacéutica para la profilaxis o el tratamiento de complicaciones diabéticas de acuerdo con [31], que se utiliza en combinación con un agente terapéutico para la trombosis.

[105] La composición farmacéutica para la profilaxis o el tratamiento de complicaciones diabéticas de acuerdo con [104], en donde el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste preparaciones de heparina, heparinas de bajo peso molecular, análogos de heparina, anticoagulantes, inhibidores de la trombina, preparaciones antitrombina, agentes antiplaquetarios y agentes trombolíticos.

[106] La composición farmacéutica para la profilaxis o el tratamiento de complicaciones diabéticas de acuerdo con [105] en donde el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste de heparina cálcica, heparina sódica, dalteparina sódica, parnaparina sódica, reviparina sódica, danaparoid sódico, warfarina potásica, argatroban, mesilato de gabexato, mesilato de nafamostat, antitrombina III humana, aspirina, dipiridamol, clorhidrato de ticlopidina, cilostazol, limaprost alfadex, ozagrel sódico, clorhidrato de sarpogrelato, icosapentato de etilo, beraprost sódico, urocinasa, tisocinasa, alteplasa, nasaruplasa, nateplasa, monteplasa, pamiteplasa, batroxobina, citrato de sodio y proteína C.

[107] Una composición farmacéutica para la inhibición de un regulador negativo del receptor de la tirosina cinasa, que se utiliza en combinación con un agente terapéutico para la hiperlipidemia.

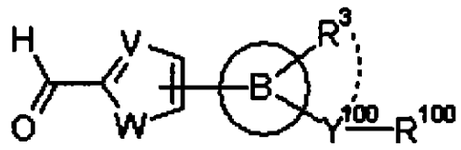
[108] Una composición farmacéutica para la inhibición de un regulador negativo del receptor de la tirosina cinasa, que se utiliza en combinación con un agente terapéutico para la diabetes.

[109] Una composición farmacéutica para la inhibición de un regulador negativo del receptor de la tirosina cinasa, que se utiliza en combinación con un agente terapéutico para la obesidad.

[110] Una composición farmacéutica para la inhibición de un regulador negativo del receptor de la tirosina cinasa, que se utiliza en combinación con un agente terapéutico para la hipertensión.

[111] Una composición farmacéutica para la inhibición de un regulador negativo del receptor de la tirosina cinasa, que se utiliza en combinación con un agente terapéutico para la trombosis.

[112] Un compuesto anular heteroaromático de 5 miembros, representado por la fórmula [II]



[II]

en donde

Y^{100} es $-C(R^{13})(R^{14})-$ (R^{13} y R^{14} son cada uno como se definió en [1]);

R^{100} es un grupo hidroxilo o un átomo de halógeno, y

V, W y R^3 son cada uno como se definió en [1], o una sal farmacéuticamente aceptable del mismo.

[113] El compuesto anular heteroaromático de 5 miembros de [112], en donde, en la fórmula [II], R^{13} y R^{14} son cada uno un átomo de hidrógeno, V es =CH- y W es -S-, o una sal farmacéuticamente aceptable del mismo.

DESCRIPCION DETALLADA DE LA INVENCION

La definición de cada sustituyente y cada porción utilizada en la presente especificación es como sigue.

El "átomo de halógeno" es un átomo de flúor, un átomo de cloro, un átomo de bromo o un átomo de yodo, de manera preferida, un átomo de flúor o un átomo de cloro.

El "grupo alquilo de C_{1-4}" es un grupo alquilo de cadena lineal o de cadena ramificada que tiene de 1 a 4 átomos de carbono, el cual se ejemplifica específicamente por un grupo metilo, un grupo etilo, un grupo propilo, un grupo isopropilo, un grupo butilo, un grupo isobutilo, un grupo sec-butilo y un grupo ter-butilo.

Es de manera preferida un grupo metilo para R^1 o R^2, y un grupo metilo o un grupo etilo para R^{13}, R^{14}, R^{19}, R^{22} o R^{25}.

El "grupo alquilo de C_{1-6}" es un grupo alquilo de cadena lineal o de cadena ramificada que tiene de 1 a 6 átomos de carbono, el cual se ejemplifica específicamente por un grupo metilo, un grupo etilo, un grupo propilo, un grupo isopropilo, un grupo butilo, un grupo isobutilo, un grupo sec-butilo, un grupo ter-butilo, un grupo pentilo, un grupo isopentilo, un grupo neopentilo, un grupo ter-pentilo, un grupo 1-etilpropilo, un grupo un grupo hexilo y lo similar. Los preferidos son el grupo alquilo, el grupo metilo y el grupo etilo de cadena ramificada, cada uno tiene de 3 a 6 átomos de carbono, tal como un grupo isopropilo, un grupo isobutilo, un grupo ter-butilo, un grupo isopentilo, un grupo neopentilo, un grupo ter-pentilo, un grupo 1-etilpropilo y lo similar.

De manera preferida, es un grupo metilo, un grupo etilo o un grupo isopentilo para R^4, un grupo metilo o un grupo isobutilo para R^5, R^6, R^7, R^8, R^9 o R^{10}, un grupo metilo, un grupo etilo o un grupo isopropilo para R^{15} o R^{16}, un grupo metilo o un grupo isobutilo para R^{17}, un grupo metilo o un grupo isopentilo para R^{20} o R^{21}, y un grupo metilo, un grupo isobutilo, un grupo ter-butilo, un grupo isopentilo, un grupo neopentilo, un grupo ter-pentilo o un grupo 1-etilpropilo para R^{18}, R^{23} o R^{24}.

El "grupo alquilo de C_{1-8}" es un grupo alquilo de cadena lineal o de cadena ramificada que tiene de 1 a 8 átomos de carbono, el cual se ejemplifica específicamente por un grupo metilo, un grupo etilo, un grupo

propilo, un grupo isopropilo, un grupo butilo, un grupo isobutilo, un grupo sec-butilo, un grupo ter-butilo, un grupo pentilo, un grupo isopentilo, un grupo neopentilo, un grupo ter-pentilo, un grupo 1-etilpropilo, un grupo hexilo, un grupo 2-etilbutilo, un grupo 3,3-dimetilbutilo, un grupo heptilo, un grupo 1-propilbutilo, un grupo 3-etilpentilo, un grupo octilo y lo similar. De manera preferida, es un grupo metilo, un grupo etilo, un grupo propilo, un grupo isopropilo o un grupo alquilo de cadena ramificada que tiene de 4 a 8 átomos de carbono, tal como un grupo isobutilo, un grupo sec-butilo, un grupo ter-butilo, un grupo isopentilo, un grupo neopentilo, un grupo ter-pentilo, un grupo 1-etilpropilo, un grupo 2-etilbutilo, un grupo 1-propilbutilo y lo similar.

De manera preferida, es un grupo metilo, un grupo ter-butilo o un grupo 1-etilpropilo para R^3, y un grupo metilo, un grupo etilo, un grupo propilo, un grupo isopropilo, un grupo isobutilo, un grupo sec-butilo, un grupo ter-butilo, un grupo isopentilo, un grupo neopentilo, un grupo ter-pentilo, un grupo 1-etilpropilo, un grupo 2-etilbutilo o un grupo 1-propilbutilo para R^{11} o R^{12}. Es particularmente, de manera preferida, un grupo isopropilo para R^{11} o R^{12}.

El "grupo haloalquilo de C_{1-4}" es un grupo haloalquilo en donde un grupo alquilo de cadena lineal o de cadena ramificada que tiene de 1 a 4 átomos de carbono, está sustituido por el "átomo de halógeno" definido anteriormente, el cual se ejemplifica específicamente por un grupo fluorometilo, un grupo difluorometilo, un grupo trifluorometilo, un grupo bromometilo, un grupo clorometilo, un grupo 1,2-diclorometilo, un grupo 2,2-

diclorometilo, un grupo 2,2,2-trifluoroetilo y lo similar, se le da preferencia a un grupo trifluorometilo.

Es de manera preferida un grupo trifluorometilo para R^3.

El "grupo alquileno de C_{1-4}" es un grupo alquileno de cadena lineal o de cadena ramificada que tiene de 1 a 4 átomos de carbono, el cual se ejemplifica específicamente por un grupo metileno, un grupo un grupo etileno, un grupo trimetileno, un grupo propileno, un grupo tetrametileno y lo similar. De manera preferida, es un grupo metileno o un grupo etileno, de manera más preferida, un grupo metileno.

De manera preferida, es un grupo metileno o un grupo etileno para A, y un grupo metileno para A^1.

El "grupo alcoxi de C_{1-4}" es un grupo alcoxi de cadena lineal o de cadena ramificada que tiene de 1 a 4 átomos de carbono, el cual se ejemplifica específicamente por un grupo metoxi, un grupo etoxi, un grupo propoxi, un grupo isopropoxi, un grupo butoxi, un grupo isobutoxi, un grupo ter-butoxi y lo similar. De manera preferida, es un grupo metoxi.

De manera preferida, es un grupo metoxi para R^{22} o R^{25}.

El "grupo alcoxi de C_{1-6}" es un grupo alcoxi de cadena lineal o de cadena ramificada que tiene de 1 a 6 átomos de carbono, el cual se ejemplifica específicamente por un grupo metoxi, un grupo etoxi, un grupo propoxi, un grupo isopropoxi, un grupo butoxi, un grupo isobutoxi, un grupo ter-butoxi, un grupo pentiloxi, un grupo isopentiloxi, un grupo neopentiloxi, un grupo ter-pentiloxi, un grupo 1-etilpropoxi, un grupo hexiloxi y lo similar. Es de

manera preferida un grupo metoxi, un grupo etoxi o un grupo alcoxi de cadena ramificada que tiene de 3 a 6 átomos de carbono (por ejemplo, un grupo isopropoxi, un grupo isobutoxi, un grupo ter-butoxi, un grupo isopentiloxi, un grupo neopentiloxi, un grupo ter-pentiloxi, un grupo 1-etilpropoxi, etc.).

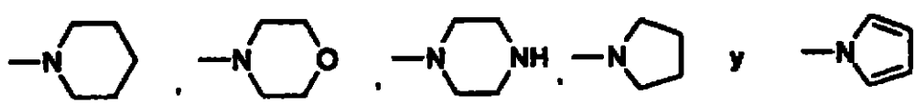
De manera preferida, es un grupo metoxi, un grupo etoxi, un grupo isopropoxi, un grupo Isobutoxi, un grupo ter-butoxi, un grupo isopentiloxi, un grupo neopentiloxi, un grupo ter-pentiloxi o un grupo 1-etilpropoxi para R^3.

El "grupo arilo" es un grupo hidrocarburo aromático que tiene de 6 a 14 átomos de carbono, el cual se ejemplifica específicamente por un grupo fenilo, un grupo naftilo, un grupo bifenililo (por ejemplo, un grupo 2-bifenililo, un grupo 3-bifenililo, un grupo 4-bifenililo, etc.), un grupo antrilo y lo similar. De manera preferida, es un grupo fenilo, un grupo naftilo o un grupo bifenililo, de manera más preferida, un grupo fenilo.

De manera preferida, es un grupo fenilo o un grupo bifenililo para Z, un grupo fenilo para B o E, un grupo fenilo o un grupo naftilo para R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{15}, R^{16}, R^{17}, R^{18} o R^{21}. Es particularmente de manera preferida, un grupo fenilo para Z.

El "grupo heterocíclico" es un "un grupo heterocíclico de 5 a 7 miembros, saturado o no saturado, que contiene de 1 a 3 heteroátomos seleccionados del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre", el cual se ejemplifica específicamente por un grupo furilo, un grupo tienilo, un grupo pirrolilo, un grupo oxazolilo, un grupo

isoxazolilo, un grupo tiazolilo, un grupo isotiazolilo, un grupo imidazolilo, un grupo pirazolilo, un grupo piridilo, un grupo piridacinilo, un grupo pirimidinilo, un grupo piracinilo, un grupo tetrahidrofurilo, un grupo tetrahidrotienilo, un grupo pirrolidinilo, un grupo pirazolidinilo, un grupo imidazolidinilo, un grupo oxazolidinilo, un grupo tiazolidinilo, un grupo tetrahidropiranilo, un grupo dioxanilo, un grupo piperidinilo, un grupo piperacinilo, un grupo morfolinilo y lo similar, de manera preferida, un grupo heterocíclico seleccionado del grupo que consiste de



El "grupo anular heteroaromático" es "un grupo anular heteroaromático de 5 a 14 miembros mono o fusionado, que contiene de 1 a 3 heteroátomos seleccionados del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre, el cual se ejemplifica específicamente por un grupo furilo, un grupo tienilo, un grupo pirrolilo, un grupo oxazolilo, un grupo isoxazolilo, un grupo tiazolilo, un grupo isotiazolilo, un grupo imidazolilo, un grupo pirazolilo, un grupo 1,3,4-tiadiazolilo, un grupo piridilo, un grupo piridacinilo, un grupo pirimidinilo, un grupo piracinilo, un grupo indolilo, un grupo isoindolilo, un grupo benzofuranilo, un grupo benzotienilo, un grupo bencimidazolilo, un grupo benzotiazolilo, un grupo benzoxazolilo, un grupo indolicinilo, un grupo quinolilo, un grupo isoquinolilo, un grupo quinazolinilo, un grupo cinnolinilo, un grupo quinoxalinilo, un grupo

ftalacinilo, un grupo acridinilo, un grupo fenacinilo, un grupo naftiridinilo y lo similar. De manera preferida, "un grupo anular heteroaromático de 5 a 10 miembros mono o fusionado que contiene de 1 a 3 heteroátomos seleccionados del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre", el cual se ejemplifica específicamente por un grupo furilo, un grupo tienilo, un grupo pirrolilo, un grupo oxazolilo, un grupo isoxazolilo, un grupo tiazolilo, un grupo isotiazolilo, un grupo imidazolilo, un grupo pirazolilo, un grupo 1,3,4-tiadiazolilo, un grupo piridilo, un grupo piridacinilo, un grupo pirimidinilo, un grupo piracinilo, un grupo indolilo, un grupo isoindolilo, un grupo benzofuranilo, un grupo benzotienilo, un grupo bencimidazolilo, un grupo benzotiazolilo, un grupo benzoxazolilo, un grupo indolicinilo, un grupo quinolilo, un grupo isoquinolilo y lo similar.

De manera preferida, es un grupo tienilo, un grupo tiazolilo, un grupo pirazolilo, un grupo 1,3,4-tiadiazolilo, un grupo piridilo, un grupo piridacinilo, un grupo pirimidinilo, un grupo indolilo, un grupo bencimidazolilo, un grupo benzotiazolilo o un grupo benzoxazolilo para B, un grupo furilo, un grupo isoxazolilo o un grupo piridilo para E, un grupo tienilo o un grupo piridilo para Z, y un grupo oxazolilo, un grupo tiazolilo, un grupo piridilo, un grupo benzotienilo, un grupo bencimidazolilo o un grupo quinolilo para R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{15}, R^{16}, R^{17} o R^{21}.

El "grupo cicloalquilo de C_{3-7}" es un grupo cicloalquilo que tiene de 3 a 7 átomos de carbono, el cual se ejemplifica específicamente por un grupo ciclopropilo, un grupo ciclobutilo, un grupo ciclopentilo, un grupo

ciclohexilo y un grupo cicloheptilo. De manera preferida, es un grupo cicloalquilo que tiene de 5 a 7 átomos de carbono, particularmente de manera preferida, un grupo ciclohexilo.

De manera preferida, es un grupo ciclohexilo para Z.

El "grupo alquenilo de C_{2-4}" es un grupo alquenilo de cadena lineal o de cadena ramificada que tiene de 2 a 4 átomos de carbono, el cual se ejemplifica específicamente por vinilo, un grupo 1-propenilo, un grupo alilo, un grupo 1-metil-2-propenilo, un grupo 1-butenilo, un grupo 2-butenilo, un grupo 3-butenilo y lo similar.

De manera preferida, es un grupo alilo para R^{11} o R^{12}.

El "grupo alquilsulfonilo de C_{1-4}", es aquél en donde la porción "alquilo" es un grupo alquilsulfonilo que tiene el "grupo alquilo de C_{1-4}" definido anteriormente, el cual se ejemplifica específicamente por un grupo metilsulfonilo, un grupo etilsulfonilo, un grupo propilsulfonilo, un grupo isopropilsulfonilo, un grupo butilsulfonilo, un grupo isobutilsulfonilo, un grupo sec-butilsulfonilo y un grupo ter-butilsulfonilo.

De manera preferida, es un grupo metilsulfonilo (es decir, un grupo mesilo), para R^{11}, R^{12}, R^{23} o R^{24}.

El "grupo alquilcarbonilo de C_{1-4}", es aquél en donde la porción "alquilo" es un grupo alquilcarbonilo que tiene el "grupo alquilo de C_{1-4}" definido anteriormente, se le da preferencia a un grupo acetilo, un grupo propionilo, un grupo butirilo, un grupo isobutirilo, un grupo valerilo, un grupo isovalerilo, un grupo pivaloilo y lo similar.

De manera preferida, es un grupo acetilo para R^{11} o R^{12}, y un grupo acetilo o un grupo isobutirilo para R^{23} o R^{24}.

El "grupo alcoxicarbonilo de C_{1-4}", es un grupo alcoxicarbonilo en donde la porción "alcoxi" es el "grupo alcoxi de C_{1-4}" definido anteriormente, el cual se ejemplifica específicamente por un grupo metoxicarbonilo, un grupo etoxicarbonilo, un grupo propoxicarbonilo, un grupo isopropoxicarbonilo, un grupo butoxicarbonilo, un grupo isobutoxicarbonilo, un grupo ter-butoxicarbonilo y lo similar.

El "grupo ariloxi" es un grupo ariloxi en donde la porción "arilo" es el "grupo arilo" definido anteriormente, el cual se ejemplifica específicamente por un grupo fenoxi, un grupo naftiloxi y lo similar.

El "grupo aralquilo" es un "grupo alquilo de C_{1-4}" sustituido por un "grupo arilo", en donde el "grupo arilo" y el "grupo alquilo de C_{1-4}" son como se definió anteriormente. El "grupo aralquilo" es, ejemplificado específicamente por un grupo bencilo y lo similar.

El "grupo alquilamino de C_{1-4}" es un grupo alquilamino en donde la porción "alquilo" es el "grupo alquilo de C_{1-4}" definido anteriormente, el cual se ejemplifica específicamente por un grupo metilamino, un grupo etilamino, un grupo propilamino, un grupo isopropilamino, un grupo butilamino, un grupo isobutilamino, un grupo sec-butilamino, un grupo ter-butilamino y lo similar.

El "grupo alquilamino de C_{1-6}", es un grupo alquilamino en donde la porción "alquilo" es el "grupo alquilo de C_{1-6}" definido anteriormente, el cual se ejemplifica específicamente por un grupo metilamino, un grupo etilamino,

un grupo propilamino, un grupo isopropilamino, un grupo butilamino, un grupo isobutilamino, un grupo sec-butilamino, un grupo ter-butilamino, un grupo pentilamino, un grupo isopentilamino, un grupo neopentilamino, un grupo ter-pentilamino, un grupo hexilamino y lo similar.

De manera preferida, es un grupo metilamino, un grupo etilamino, un grupo isopropilamino, un grupo isobutilamino, un grupo sec-butilamino, un grupo ter-butilamino, un grupo isopentilamino, un grupo neopentilamino o un grupo ter-pentilamino para R^{22} o R^{25}.

El "grupo di(alquil de C_{1-4})amino" es un grupo di(alquil)amino en donde la porción "alquilo" es el "grupo alquilo de C_{1-4}" definido anteriormente, el cual se ejemplifica específicamente por un grupo dimetilamino, un grupo dietilamino, un grupo dipropilamino, un grupo diisopropilamino, un grupo dibutilamino, un grupo diisobutilamino, un grupo di(sec-butil)amino, un grupo di(ter-butil)amino, un grupo N-etil-N-metilamino, un grupo N-metil-N-propilamino, un grupo N-etil-N-propilamino y lo similar.

El "grupo di(alquil de C_{1-8})amino" es un grupo di(alquil)amino en donde la porción "alquilo" es el "grupo alquilo de C_{1-4}" definido anteriormente, el cual se ejemplifica específicamente por un grupo dimetilamino, un grupo dietilamino, un grupo dipropilamino, un grupo diisopropilamino, un grupo dibutilamino, un grupo diisobutilamino, un grupo di(sec-butil)amino, un grupo di(ter-butil)amino, un grupo dipentilamino, un grupo diisopentilamino, un grupo di(ter-pentil)amino, un grupo dihexilamino, un grupo N-etil-N-metilamino, un grupo N-metil-N-propilamino, un grupo N-etil-N-propilamino y lo similar.

De manera preferida, es un grupo dimetilamino, un grupo dietilamino, un grupo dipropilamino, un grupo dibutilamino, un grupo dipentilamino, un grupo diisopentilamino, un grupo dihexilamino, un grupo N-etil-N-metilamino, un grupo N-metil-N-propilamino o un grupo N-etil-N-propilamino para R^{22} o R^{25}.

El "grupo alquiltio de C_{1-6}" es un grupo alquiltio en donde la porción "alquilo" es el "grupo alquilo de C_{1-6}" definido anteriormente, el cual se ejemplifica específicamente por un grupo metiltio, un grupo etiltio, un grupo propiltio, un grupo isopropiltio, un grupo butiltio, un grupo isobutiltio, un grupo sec-butiltio, un grupo ter-butiltio, un grupo pentiltio, un grupo isopentiltio, un grupo neopentiltio, un grupo ter-pentiltio, un grupo 1-etilpropiltio, un grupo hexiltio y lo similar.

De manera preferida, es un grupo metiltio para R^{22} o R^{25}.

El "grupo di(alquil de C_{1-6})aminocarbonilo" es un grupo di(alquil)aminocarbonilo en donde la porción "di(alquil de C_{1-6})amino" es el "grupo di(alquil de C_{1-6})amino" definido anteriormente, el cual se ejemplifica específicamente por un grupo dimetilaminocarbonilo, un grupo dietilaminocarbonilo, un grupo dipropilaminocarbonilo, un grupo diisopropilaminocarbonilo, un grupo dibutilaminocarbonilo, un grupo diisobutilaminocarbonilo, un grupo di(sec-butil)aminocarbonilo, un grupo di(ter-butil)aminocarbonilo, un grupo dipentilaminocarbonilo, un grupo diisopentilaminocarbonilo, un grupo di(ter-pentil)aminocarbonilo, un grupo dihexilaminocarbonilo, un grupo N-etil-N-metilaminocarbonilo, un grupo N-

metil-N-propilaminocarbonilo, un grupo N-etil-N-propilaminocarbonilo y lo similar.

Cuando R^{19} de la porción -COO(R^{19}) para R es un átomo de hidrógeno, este grupo carboxi puede formar una sal. Como la sal, pueden mencionarse las sales de metales alcalinos (por ejemplo, sal de potasio, sal de sodio, etc.), las sales de metales alcalinotérreos (por ejemplo, sal de calcio, sal de magnesio, etc.) y lo similar, se le da preferencia a la sal de sodio y la sal de calcio.

El "grupo alquilo de C_{1-6}" para R^4, R^5, R^6, R^7, R^8, R^9 o R^{10} está sustituido opcionalmente por un grupo arilo sustituido opcionalmente, un anillo heteroaromático sustituido opcionalmente, un grupo carboxi, un grupo alcoxicarbonilo de C_{1-4}, un grupo -CO-N(R^{15})(R^{16}), -N(R^{15})(R^{16}), -O-R^{17}, -CO-R^{17}, -SO_2-R^{17} o un grupo cicloalquilo de C_{3-7}. Tal "grupo alquilo de C_{1-6}" puede ser un grupo alquilo de C_{1-6} sustituido por varios sustituyentes tales como, por ejemplo, un grupo benzhidrilo. De manera preferida, el número de sustituyentes es 1. Cuando el "grupo alquilo de C_{1-6}" está sustituido, la porción "grupo alquilo de C_{1-6}" es, de manera preferida, un grupo metilo.

La porción "grupo arilo" del "grupo arilo sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^4, R^5, R^6, R^7, R^8, R^9 o R^{10}, es el "grupo arilo" definido anteriormente, de manera preferida, un grupo fenilo o un grupo naftilo.

El "grupo arilo sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^4, R^5, R^6, R^7, R^8, R^9 o R^{10}, está sustituido

opcionalmente por 1 a 3 sustituyentes seleccionados de los siguiente. Como tal sustituyente, puede mencionarse un átomo de halógeno, un grupo alquilo de C_{1-6}, un grupo alquilo de C_{1-6} sustituido por un grupo di(alquil de C_{1-6})aminocarbonilo, un grupo haloalquilo de C_{1-4}, un grupo alcoxi de C_{1-4}, un grupo alquenilo de C_{2-4}, un grupo carboxi, un grupo hidroxilo, un grupo ciano, un grupo nitro, un grupo amino, un grupo alquilamino de C_{1-4}, un grupo di(alquil de C_{1-4})amino, un grupo 1-pirrolidinilo, un grupo 1-piperidilo, un grupo morfolino, un grupo alcoxicarbonilo de C_{1-4}, un grupo alquiltio de C_{1-6}, un grupo anular heteroaromático sustituido opcionalmente por un átomo de halógeno, un grupo aralquilo y lo similar. Los sustituyentes preferidos incluyen átomos de halógeno (por ejemplo, un átomo de flúor, un átomo de cloro, etc.), grupos alquilo de C_{1-6} (por ejemplo, un grupo metilo, un grupo isopropilo, un grupo ter-butilo, un grupo 1-propilbutilo, etc.), grupos haloalquilo de C_{1-4} (por ejemplo, un grupo trifluorometilo, etc.), grupos alquenilo de C_{2-4} (por ejemplo, un grupo alilo, etc.), grupos alquiltio de C_{1-6} (por ejemplo, un grupo metiltio, etc.), un grupo alquilo de C_{1-6} (por ejemplo, un grupo metilo, etc.), sustituido por un grupo di(alquil de C_{1-6})aminocarbonilo (por ejemplo, un grupo dietilaminocarbonilo, etc.), un grupo heteroaromático (por ejemplo, un grupo tienilo, un grupo imidazolilo, etc.) sustituido opcionalmente por un átomo de halógeno (por ejemplo, un átomo de cloro, etc.) y grupos aralquilo (por ejemplo, un grupo bencilo, etc.).

El "grupo anular heteroaromático sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^4, R^5, R^6, R^7, R^8, R^9 o

R^{10}, es el "grupo anular heteroaromático" definido anteriormente, el cual es de manera preferida un grupo oxazolilo, un grupo tiazolilo, un grupo piridilo, un grupo benzotienilo, un grupo bencimidazolilo o un grupo quinolilo.

El "grupo anular heteroaromático sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^4, R^5, R^6, R^7, R^8, R^9 o R^{10}, está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados de lo siguiente. Como tal sustituyente, pueden mencionarse un átomo de halógeno, un grupo alquilo de C_{1-6}, un grupo alquilo de C_{1-6} sustituido por un grupo di(alquil de C_{1-6})aminocarbonilo, un grupo haloalquilo de C_{1-4}, un grupo alcoxi de C_{1-4}, un grupo alquenilo de C_{2-4}, un grupo carboxi, un grupo hidroxilo, un grupo ciano, un grupo nitro, un grupo amino, un grupo alquilamino de C_{1-4}, un grupo di(alquil de C_{1-4})amino, un grupo 1-pirrolidinilo, un grupo 1-piperidilo, un grupo morfolino, un grupo alcoxicarbonilo de C_{1-4}, un grupo alquiltio de C_{1-6}, un grupo arilo sustituido opcionalmente por un átomo de halógeno, un grupo anular heteroaromático sustituido opcionalmente por un átomo de halógeno, un grupo aralquilo y lo similar. Los sustituyentes preferidos incluyen átomos de halógeno (por ejemplo, un átomo de flúor, un átomo de cloro, etc.), grupos alquilo de C_{1-6} (por ejemplo, un grupo metilo, un grupo isopropilo, un grupo terbutilo, un grupo 1-propilbutilo, etc.), grupos haloalquilo de C_{1-4} (por ejemplo, un grupo trifluorometilo, etc.), grupos alquenilo de C_{2-4} (por ejemplo, un grupo alilo, etc.), grupos alquiltio de C_{1-6} (por ejemplo, un grupo metilito, etc.), grupo alquilo de C_{1-6} (por ejemplo, un grupo metilo, etc.) sustituido por un grupo di(alquil de C_{1-6})aminocarbonilo (por ejemplo, un grupo dietilaminocarbonilo,

etc.), un grupo arilo (por ejemplo, un grupo fenilo, etc.) sustituido opcionalmente por un átomo de halógeno (por ejemplo, un átomo de cloro, etc.), un grupo anular heteroaromático (por ejemplo, un grupo tienilo, un grupo imidazolilo, etc.) sustituido opcionalmente por un átomo de halógeno (por ejemplo, un átomo de cloro, etc.), y grupos aralquilo (por ejemplo, un grupo bencilo, etc.).

El "grupo alcoxicarbonilo de C_{1-4}", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^4, R^5, R^6, R^7, R^8, R^9 o R^{10} es el "grupo alcoxicarbonilo de C_{1-4}" definido anteriormente, el cual es, de manera preferida un grupo etoxicarbonilo, un grupo propoxicarbonilo o un grupo isobutoxicarbonilo.

El "grupo cicloalquilo de C_{3-7}", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^4, R^5, R^6, R^7, R^8, R^9 o R^{10} es el "grupo cicloalquilo de C_{3-7}" definido anteriormente, el cual es de manera preferida un grupo ciclohexilo.

El "grupo arilo sustituido opcionalmente" para R^4, R^5, R^6, R^7, R^8, R^9 o R^{10} está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados de lo siguiente. Como tal sustituyente, pueden mencionarse un átomo de halógeno, un grupo alquilo de C_{1-6}, un grupo haloalquilo de C_{1-4}, un grupo alcoxi de C_{1-4}, un grupo carboxi, un grupo hidroxilo, un grupo ciano, un grupo nitro, un grupo amino, un grupo alquilamino de C_{1-4}, un grupo di(alquil de C_{1-4})amino, un grupo 1-pirrolidinilo, un grupo 1-piperidilo, un grupo morfolino, un grupo alcoxicarbonilo de C_{1-4}, un grupo anular heteroaromático sustituido

opcionalmente por un átomo de halógeno, un grupo aralquilo y lo similar. Los sustituyentes preferidos incluyen átomos de halógeno (por ejemplo, un átomo de flúor, un átomo de cloro, etc.), grupos alquilo de C_{1-6} (por ejemplo, un grupo metilo, un grupo isopropilo, un grupo ter-butilo, un grupo 1-propilbutilo, etc.), grupos haloalquilo de C_{1-4} (por ejemplo, un grupo trifluorometilo, etc.), grupos anulares heteroaromáticos (por ejemplo, un grupo tienilo, un grupo imidazolilo, etc.) sustituido opcionalmente por un átomo de halógeno (por ejemplo, un átomo de cloro, etc.), y grupos aralquilo (por ejemplo, un grupo bencilo, etc.).

El "grupo anular heteroaromático sustituido opcionalmente" para R^4, R^5, R^6, R^7, R^8, R^9 o R^{10} está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados de lo siguiente. Como tal sustituyente, pueden mencionarse un átomo de halógeno, un grupo alquilo de C_{1-6}, un grupo haloalquilo de C_{1-4}, un grupo alcoxi de C_{1-4}, un grupo carboxi, un grupo hidroxilo, un grupo ciano, un grupo nitro, un grupo amino, un grupo alquilamino de C_{1-4}, un grupo di(alquil de C_{1-4})amino, un grupo 1-pirrolidinilo, un grupo 1-piperidilo, un grupo morfolino, un grupo alcoxicarbonilo de C_{1-4}, un grupo arilo sustituido opcionalmente por un átomo de halógeno, un grupo anular heteroaromático sustituido opcionalmente por un átomo de halógeno, un grupo aralquilo y lo similar. Los sustituyentes preferidos incluyen átomos de halógeno (por ejemplo, un átomo de flúor, un átomo de cloro, etc.), grupos alquilo de C_{1-6} (por ejemplo, un grupo metilo, un grupo isopropilo, un grupo ter-butilo, un grupo 1-propilbutilo, etc.), grupos haloalquilo de C_{1-4} (por ejemplo, un grupo trifluorometilo, etc.), un grupo arilo (por ejemplo, un grupo fenilo, etc.)

sustituido opcionalmente por un átomo de halógeno (por ejemplo, un átomo de cloro, etc.), un grupo anular heteroaromático (por ejemplo, un grupo tienilo, un grupo imidazolilo, etc.) sustituido opcionalmente por un átomo de halógeno (por ejemplo, un átomo de cloro, etc.), y un grupo aralquilo (por ejemplo, un grupo bencilo, etc.).

El "grupo arilo sustituido opcionalmente" para R^{15}, R^{16} o R^{17} está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados de lo siguiente. Como tales sustituyentes, pueden mencionarse un átomo de halógeno, un grupo alquilo de C_{1-8}, un grupo haloalquilo de C_{1-4}, un grupo alcoxi de C_{1-4}, un grupo carboxi, un grupo hidroxilo, un grupo ciano, un grupo nitro, un grupo amino, un grupo alquilamino de C_{1-4}, un grupo di(alquil de C_{1-4})amino, un grupo 1-pirrolidinilo, un grupo 1-piperidilo, un grupo morfolino, un grupo C_{1-4} alcoxicarbonilo y lo similar. Los sustituyentes preferidos incluyen átomos de halógeno (por ejemplo, un átomo de cloro, etc.), grupos alquilo de C_{1-8} (por ejemplo, un grupo metilo, un grupo isopropilo, etc.), grupos alcoxi de C_{1-4} (por ejemplo, un grupo metoxi, etc.), grupos carboxi y grupos di(alquil de C_{1-4})amino (por ejemplo, un grupo dimetilamino, etc.).

El "grupo anular heteroaromático sustituido opcionalmente" para R^{15}, R^{16} o R^{17} está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados de lo siguiente. Como tales sustituyentes, pueden mencionarse un átomo de halógeno, un grupo alquilo de C_{1-8}, un grupo haloalquilo de C_{1-4}, un grupo alcoxi de C_{1-4}, un grupo carboxi, un grupo hidroxilo, un grupo ciano, un grupo nitro, un grupo amino, un grupo

alquilamino de C_{1-4}, un grupo di(alquil de C_{1-4})amino, un grupo 1-pirrolidinilo, un grupo 1-piperidilo, un grupo morfolino, un grupo C_{1-4} alcoxicarbonilo y lo similar. Los sustituyentes preferidos incluyen átomos de halógeno (por ejemplo, un átomo de cloro, etc.), grupos alquilo de C_{1-6} (por ejemplo, un grupo metilo, un grupo isopropilo, etc.), grupos alcoxi de C_{1-4} (por ejemplo, un grupo metoxi, etc.), un grupo carboxi y grupos di(alquil de C_{1-4})amino (por ejemplo, un grupo dimetilamino, etc.).

El "grupo alquilo de C_{1-6}" para R^{15}, R^{16} o R^{17} está sustituido opcionalmente por un grupo arilo sustituido opcionalmente, un grupo anular heteroaromático sustituido opcionalmente, un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo arilo o sustituido opcionalmente por un grupo ariloxi. Como la porción "grupo alquilo de C_{1-6}" cuando el "grupo alquilo de C_{1-6}" está sustituido, es de manera preferida un grupo metilo.

El "grupo arilo" del "grupo arilo sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{15}, R^{16} o R^{17}, es el "grupo arilo" definido anteriormente, de manera preferida un grupo fenilo o un grupo naftilo.

El "grupo arilo sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{15}, R^{16} o R^{17} está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados de lo siguiente. Como tales sustituyentes, pueden mencionarse un átomo de halógeno, un grupo alquilo de C_{1-6}, un grupo haloalquilo de C_{1-4}, un grupo alcoxi de C_{1-4}, un grupo carboxi, un grupo hidroxilo, un grupo ciano, un grupo nitro, un grupo amino, un

grupo alquilamino de C_{1-4}, un grupo di(alquil de C_{1-4})amino, un grupo 1-pirrolidinilo, un grupo 1-piperidilo, un grupo morfolino, un grupo C_{1-4} alcoxicarbonilo y lo similar. Los sustituyentes preferidos incluyen átomos de halógeno (por ejemplo, un átomo de cloro, etc.), grupos alquilo de C_{1-6} (por ejemplo, un grupo metilo, un grupo isopropilo, etc.), grupos alcoxi de C_{1-4} (por ejemplo, un grupo metoxi, etc.), un grupo carboxi, grupos di(alquil de C_{1-4})amino (por ejemplo, un grupo dimetilamino, etc.), un grupo 1-pirrolidinilo, un grupo 1-piperidilo y un grupo morfolino.

La porción "grupo anular heteroaromático" del "grupo anular heteroaromático sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{15}, R^{16} o R^{17} es el "grupo anular heteroaromático" definido anteriormente, de manera preferida un grupo oxazolilo, un grupo tiazolilo, un grupo piridilo, un grupo benzotienilo, un grupo bencimidazolilo o un grupo quinolilo.

El "grupo anular heteroaromático sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{15}, R^{16} o R^{17} está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados de lo siguiente. Como tales sustituyentes, pueden mencionarse un átomo de halógeno, un grupo alquilo de C_{1-6}, un grupo haloalquilo de C_{1-4}, un grupo alcoxi de C_{1-4}, un grupo carboxi, un grupo hidroxilo, un grupo ciano, un grupo nitro, un grupo amino, un grupo alquilamino de C_{1-4}, un grupo di(alquil de C_{1-4})amino, un grupo 1-pirrolidinilo, un grupo 1-piperidilo, un grupo morfolino, un grupo C_{1-4} alcoxicarbonilo y lo similar. Los sustituyentes preferidos

incluyen átomos de halógeno (por ejemplo, un átomo de cloro, etc.), grupos alquilo de C_{1-6} (por ejemplo, un grupo metilo, un grupo isopropilo, etc.), grupos alcoxi de C_{1-4} (por ejemplo, un grupo metoxi, etc.), un grupo carboxi, grupos di(alquil de C_{1-4})amino (por ejemplo, un grupo dimetilamino, etc.), un grupo 1-pirrolidinilo, un grupo 1-piperidilo y un grupo morfolino.

La porción "grupo alcoxi de C_{1-4}" del "grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo arilo", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{15}, R^{16} o R^{17}, es el "grupo alcoxi de C_{1-4}" definido anteriormente, de manera preferida un grupo metoxi.

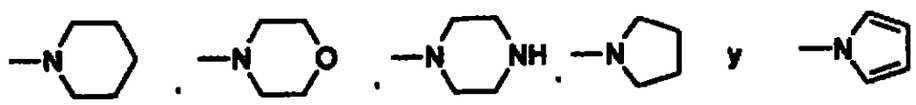
La porción "grupo arilo" del "grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo arilo", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{15}, R^{16} o R^{17} es el "grupo arilo" definido anteriormente, de manera preferida un grupo fenilo.

La porción "grupo ariloxi" del "grupo ariloxi sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{15}, R^{16} o R^{17} es el "grupo ariloxi" definido anteriormente, de manera preferida, un grupo fenoxi.

El "grupo ariloxi sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{15}, R^{16} o R^{17} está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados de lo siguiente. Como tales sustituyentes, pueden mencionarse un átomo de halógeno, un grupo alquilo de C_{1-6}, un grupo haloalquilo de C_{1-4}, un grupo alcoxi de C_{1-4}, un grupo carboxi, un grupo hidroxilo, un grupo ciano, un grupo nitro, un grupo amino, un

grupo alquilamino de C_{1-4}, un grupo di(alquil de C_{1-4})amino, un grupo 1-pirrolidinilo, un grupo 1-piperidilo, un grupo morfolino, un grupo C_{1-4} alcoxicarbonilo y lo similar. Los sustituyentes preferidos incluyen un átomo de halógeno (por ejemplo, un átomo de cloro, etc.), un grupo alquilo de C_{1-6} (por ejemplo, un grupo metilo, un grupo isopropilo, etc.), un grupo alcoxi de C_{1-4} (por ejemplo, un grupo metoxi, etc.), un grupo carboxi, un grupo di(alquil de C_{1-4})amino (por ejemplo, un grupo dimetilamino, etc.), un grupo 1-pirrolidinilo, un grupo 1-piperidilo y un grupo morfolino.

El "heteroanillo de 5 a 7 miembros que contiene opcionalmente al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre", que está formado por R^{15} y R^{18} junto con el átomo de nitrógeno unido al mismo es, de manera preferida un "heteroanillo de 5 a 7 miembros saturado o no saturado que contiene 1 a 3 heteroátomos seleccionados del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre", el cual se ejemplifica específicamente por un heteroanillo seleccionado del grupo que consiste de



El "grupo alquilo de C_{1-6}" para R^{21} está sustituido opcionalmente por grupo arilo sustituido opcionalmente o un grupo anular heteroaromático sustituido opcionalmente.

La porción "grupo arilo" del "grupo arilo sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{21} es el "grupo arilo" definido anteriormente, de manera preferida, un grupo fenilo.

El "grupo arilo sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{21} está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados de lo siguiente. Como tales sustituyentes, pueden mencionarse un átomo de halógeno, un grupo alquilo de C_{1-6}, un grupo haloalquilo de C_{1-4}, un grupo alcoxi de C_{1-4}, un grupo carboxi, un grupo hidroxilo, un grupo ciano, un grupo nitro, un grupo amino, un grupo alquilamino de C_{1-4}, un grupo di(alquil de C_{1-4})amino, un grupo 1-pirrolidinilo, un grupo 1-piperidilo, un grupo morfolino, un grupo alcoxicarbonilo de C_{1-4} y lo similar. Los sustituyentes preferidos incluyen átomos de halógeno (por ejemplo, un átomo de cloro, un átomo de flúor, etc.), grupos alquilo de C_{1-6} (por ejemplo, un grupo metilo, etc.), y grupos haloalquilo de C_{1-4} (por ejemplo, un grupo trifluorometilo, etc.).

La porción "grupo anular heteroaromático" del "grupo anular heteroaromático sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{21} es el "grupo anular heteroaromático" definido anteriormente, de manera preferida un grupo oxazolilo, un grupo tiazolilo, un grupo piridilo, un grupo benzotienilo, un grupo bencimidazolilo o un grupo quinolilo.

El "grupo anular heteroaromático sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{21} está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados de lo siguiente. Como tales sustituyentes, pueden mencionarse un átomo de halógeno, un grupo alquilo de C_{1-6}, un grupo haloalquilo de C_{1-4}, un grupo alcoxi de C_{1-4}, un grupo carboxi, un grupo hidroxilo, un grupo ciano, un grupo nitro, un grupo amino, un grupo alquilamino de C_{1-4}, un grupo di(alquil de C_{1-4})amino, un grupo 1-pirrolidinilo, un grupo 1-piperidilo, un grupo morfolino, un grupo alcoxicarbonilo de C_{1-4} y lo similar. Los sustituyentes preferidos incluyen un átomo de halógeno (por ejemplo, un átomo de cloro, un átomo de flúor, etc.), un grupo alquilo de C_{1-6} (por ejemplo, un grupo metilo, etc.), y un grupo haloalquilo de C_{1-4} (por ejemplo, un grupo trifluorometilo, etc.).

El "grupo arilo sustituido opcionalmente" para R^{21} está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados de lo siguiente. Como tales sustituyentes, pueden mencionarse un átomo de halógeno, un grupo alquilo de C_{1-6}, un grupo haloalquilo de C_{1-4}, un grupo alcoxi de C_{1-4}, un grupo carboxi, un grupo hidroxilo, un grupo ciano, un grupo nitro, un grupo amino, un grupo alquilamino de C_{1-4}, un grupo di(alquil de C_{1-4})amino, un grupo 1-pirrolidinilo, un grupo 1-piperidilo, un grupo morfolino, un grupo alcoxicarbonilo de C_{1-4} y lo similar. Los sustituyentes preferidos incluyen un átomo de halógeno (por ejemplo, un átomo de cloro, un átomo de flúor, etc.), un grupo alquilo de C_{1-6} (por ejemplo, un grupo metilo, etc.) y un grupo haloalquilo de C_{1-4} (por ejemplo, un grupo trifluorometilo, etc.).

El "grupo anular heteroaromático sustituido opcionalmente" para R^{21} está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados de lo siguiente. Como tales sustituyentes, pueden mencionarse un átomo de halógeno, un grupo alquilo de C_{1-6}, un grupo haloalquilo de C_{1-4}, un grupo alcoxi de C_{1-4}, un grupo carboxi, un grupo hidroxilo, un grupo ciano, un grupo nitro, un grupo amino, un grupo alquilamino de C_{1-4}, un grupo di(alquil de C_{1-4})amino, un grupo 1-pirrolidinilo, un grupo 1-piperidilo, un grupo morfolino, un grupo alcoxicarbonilo de C_{1-4} y lo similar. Los sustituyentes preferidos incluyen un átomo de halógeno (por ejemplo, un átomo de cloro, un átomo de flúor, etc.), un grupo alquilo de C_{1-6} (por ejemplo, un grupo metilo, etc.) y un grupo haloalquilo de C_{1-4} (por ejemplo, un grupo trifluorometilo, etc.).

El "grupo alquilcarbonilo de C_{1-4}" para R^{23} o R^{24} está sustituido opcionalmente por un grupo amino, un grupo alquilamino de C_{1-4} o di(alquil de C_{1-4})amino.

El "grupo alquilamino de C_{1-4}", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{23} o R^{24} es el "grupo alquilamino de C_{1-4}" definido anteriormente, de manera preferida, un grupo metilamino.

El "grupo di(alquil de C_{1-4})amino", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{23} o R^{24} es el "grupo di(alquil de C_{1-4})amino" definido anteriormente, de manera preferida, un grupo dimetilamino.

El "grupo alquilo de C_{1-6}" para R^{11} o R^{12} está sustituido opcionalmente por un sustituyente seleccionado del grupo que consiste de un grupo cicloalquilo de C_{3-7}, un grupo arilo sustituido opcionalmente, un grupo

heteroanular sustituido opcionalmente, un grupo hidroxilo, un grupo alquilamino de C_{1-4} y un grupo di(alquil de C_{1-4})amino.

La porción "grupo arilo" del "arilo sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{11} o R^{12}, es el "grupo arilo" definido anteriormente, de manera preferida, un grupo fenilo.

El "grupo arilo sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{11} o R^{12} está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados de lo siguiente. Como tales sustituyentes, pueden mencionarse un átomo de halógeno, un grupo alquilo de C_{1-4}, un grupo haloalquilo de C_{1-4}, un grupo alcoxi de C_{1-4}, un grupo carboxi, un grupo hidroxilo, un grupo ciano, un grupo nitro, un grupo amino, un grupo alcoxicarbonilo de C_{1-4} y lo similar. Los sustituyentes preferidos incluyen un átomo de halógeno y un grupo haloalquilo de C_{1-4}.

La porción "grupo heterocíclico" del "grupo heterocíclico sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-6}" para R^{11} o R^{12} es "un grupo heterocíclico de 5 a 7 miembros, saturado o no saturado, que contiene de 1 a 3 heteroátomos seleccionados del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre", el cual se ejemplifica específicamente por un grupo furilo, un grupo tienilo, un grupo pirrolilo, un grupo oxazolilo, un grupo isoxazolilo, un grupo tiazolilo, un grupo isotiazolilo, un grupo imidazolilo, un grupo pirazolilo, un grupo piridilo, un grupo piridacinilo, un grupo pirimidinilo, un grupo piracinilo, un grupo tetrahidrofurilo, un grupo tetrahidrotienilo, un grupo pirrolidinilo, un

grupo pirazolidinilo, un grupo imidazolidinilo, un grupo oxazolidinilo, un grupo tiazolidinilo, un grupo tetrahidropiranilo, un grupo dioxanilo, un grupo piperidinilo, un grupo piperacinilo, un grupo morfolinilo y lo similar, de manera preferida un grupo tetrahidropiranilo.

El "grupo heterocíclico sustituido opcionalmente", que es un sustituyente en el "grupo alquilo de C_{1-8}" para R^{11} o R^{12} está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados de lo siguiente. Como tales sustituyentes, pueden mencionarse un átomo de halógeno, un grupo alquilo de C_{1-4}, grupo haloalquilo de C_{1-4}, un grupo alcoxi de C_{1-4}, un grupo carboxi, un grupo hidroxilo, un grupo ciano, un grupo nitro, un grupo amino, un grupo alcoxicarbonilo de C_{1-4} y lo similar.

El "grupo alquilamino de C_{1-4}", que es un sustituyente en el "grupo alquilo de C_{1-8}" para R^{11} o R^{12} es el "grupo alquilamino de C_{1-4}" definido anteriormente, de manera preferida, un grupo metilamino.

El "grupo di(alquil de C_{1-4})amino", que es un sustituyente en el "grupo alquilo de C_{1-8}" para R^{11} o R^{12} es el "grupo di(alquil de C_{1-4})amino" definido anteriormente, de manera preferida, un grupo dimetilamino.

El "grupo alquilcarbonilo de C_{1-4}" para R^{11} o R^{12} está sustituido opcionalmente por un grupo hidroxilo o un grupo alcoxi de C_{1-4}.

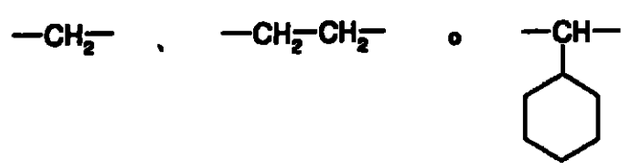
El "grupo alcoxi de C_{1-4}", que es un sustituyente en el "grupo alquilcarbonilo de C_{1-4}" para R^{11} o R^{12} es el "grupo alcoxi de C_{1-4}" definido anteriormente.

El "cicloalcano de C_{3-7}" formado por R^{13} y R^{14} junto con el átomo de carbono unido al mismo, es un cicloalcano que tiene de 3 a 7 átomos de carbono, el cual se ejemplifica específicamente por ciclopropano, ciclobutano, ciclopentano, ciclohexano y cicloheptano. El preferido es el cicloalcano que tiene de 5 a 7 átomos de carbono, particularmente de manera preferida, ciclopentano o ciclohexano.

El "heteroanillo de 5 a 7 miembros que tiene al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre", que está formado por R^{13} y R^{14} junto con el átomo de carbono unido al mismo es, de manera preferida, un "heteroanillo de 5 a 7 miembros que contiene opcionalmente al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre", el cual se ejemplifica específicamente por tetrahidropirano, tiano y lo similar, particularmente de manera preferida, tetrahidropirano.

El grupo alquileno de C_{1-4} para A está sustituido opcionalmente por un grupo cicloalquilo de C_{3-7}. Como tal grupo cicloalquilo de C_{3-7}, puede mencionarse el "grupo cicloalquilo de C_{3-7}" definido anteriormente.

El "grupo alquileno de C_{1-4} sustituido opcionalmente por un grupo cicloalquilo de C_{3-7}" para A es de manera preferida



de manera más preferida -CH_2-.

El "grupo cicloalquilo de C_{3-7}" para Z es de manera preferida un grupo ciclopentilo o un grupo ciclohexilo, de manera más preferida, un grupo ciclohexilo.

El "grupo cicloalquilo de C_{3-7}" para Z está sustituido opcionalmente por un grupo arilo (este grupo arilo está sustituido opcionalmente por 1 a 5 (de manera preferida, 1 a 3) átomos de halógeno o un grupo alquilo de C_{1-6}) o un grupo anular heteroaromático (este grupo anular heteroaromático está sustituido opcionalmente por 1 a 5 (de manera preferida, 1 a 3) átomos de halógeno o un grupo alquilo de C_{1-6}). Tal sustituyente del "grupo cicloalquilo de C_{3-7}" es de manera preferida, un grupo fenilo sustituido opcionalmente por 1 a 3 átomos de halógeno o un grupo alquilo de C_{1-6}.

El "grupo arilo" para Z es, de manera preferida, un grupo fenilo o un grupo bifenililo (por ejemplo, un grupo 2-bifenililo, un grupo 3-bifenililo, un grupo 4-bifenililo), de manera más preferida, un grupo fenilo.

El "grupo arilo" para Z está sustituido opcionalmente por 1 a 5 (de manera preferida, 1 a 3) sustituyentes seleccionados de lo siguiente.

(a) un grupo heterocíclico sustituido opcionalmente por un grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4},

(b) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por un grupo hidroxilo, un grupo oxo, un átomo de halógeno o un grupo alquilo de C_{1-6},

(c) un grupo carboxi,

(d) un átomo de halógeno,

(e) un grupo alquilo de C_{1-6},

(f) un grupo haloalquilo de C_{1-4},

(g) un grupo alquilamino de C_{1-4},

(h) un grupo di(alquil de C_{1-4})amino,

(i) un grupo alquiltio de C_{1-6},

(j) un grupo alcoxi de C_{1-4},

(k) un grupo alquilcarbonilo de C_{1-4} y

(l) un grupo nitro.

Como tales sustituyentes, el preferido es un grupo alquilo de C_{1-6}.

El "grupo heterocíclico" del "grupo heterocíclico sustituido opcionalmente por un grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4}", que es un sustituyente en el "grupo arilo" para Z es, de manera preferida, un "grupo heterocíclico de 5 a 7 miembros, saturado o no saturado que contiene opcionalmente de 1 a 3 heteroátomos seleccionados del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre", el cual se ejemplifica específicamente por un grupo furilo, un grupo tienilo, un grupo pirrolilo, un grupo oxazolilo, un grupo isoxazolilo, un grupo tiazolilo, un grupo isotiazolilo, un grupo imidazolilo, un grupo pirazolilo, un grupo piridilo, un grupo piridacinilo, un grupo pirimidinilo, un grupo piracinilo, un grupo tetrahidrofurilo, un grupo tetrahidrotienilo, un grupo pirrolidinilo, un grupo pirazolidinilo, un grupo imidazolidinilo, un grupo oxazolidinilo, un grupo

tiazolidinilo, un grupo tetrahidropiranilo, un grupo dioxanilo, un grupo piperidinilo, un grupo piperacinilo, un grupo morfolinilo y lo similar. Los preferidos son un grupo piperidinilo, un grupo morfolinilo, un grupo piperacinilo, un grupo pirrolidinilo, un grupo pirrolilo y un grupo tetrahidropiranilo.

El sustituyente en el "grupo heterocíclico" es, de manera preferida un grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4}.

El "cicloalquilo de C_{3-7}" del "grupo cicloalquilo de C_{3-7} sustituido opcionalmente por un grupo hidroxilo, un grupo oxo, un átomo de halógeno o un grupo alquilo de C_{1-6}", que es un sustituyente en el "grupo arilo" para Z, es de manera preferida un grupo ciclopentilo o un grupo ciclohexilo, de manera más preferida, un grupo ciclohexilo. El "grupo cicloalquilo de C_{3-7}" está sustituido opcionalmente por 1 a 5 (de manera preferida, 1 a 3) sustituyentes seleccionados del grupo que consiste de un grupo hidroxilo, un grupo oxo, un átomo de halógeno y un grupo alquilo de C_{1-6}. Como el sustituyente en el "grupo cicloalquilo de C_{3-7}" es, de manera preferida, un átomo de halógeno o grupo alquilo de C_{1-4}.

Como el "átomo de halógeno", que es un sustituyente en el "grupo arilo" para Z, puede mencionarse el "átomo de halógeno" definido anteriormente, el cual es, de manera preferida, un átomo de flúor, un átomo de cloro o un átomo de bromo, particularmente de manera preferida, un átomo de cloro.

Como el "grupo alquilo de C_{1-6}", que es el sustituyente en el "grupo arilo" para Z, puede mencionarse el "grupo alquilo de C_{1-6}" definido anteriormente. De manera preferida, es un grupo isopropilo, un grupo isobutilo, un grupo sec-butilo, un grupo ter-butilo, un grupo isopentilo, neopentilo, un grupo ter-pentilo, un grupo 1-etilpropilo o un grupo 1-propilbutilo, de manera más preferida, un grupo isopentilo, un grupo neopentilo, un grupo ter-pentilo, un grupo 1-etilpropilo o un grupo 1-propilbutilo, particularmente de manera preferida, un grupo neopentilo, un grupo 1-etilpropilo o un grupo 1-propilbutilo.

Como el "grupo haloalquilo de C_{1-4}", que es el sustituyente en el "grupo arilo" para Z, puede mencionarse el "grupo haloalquilo de C_{1-4}" definido anteriormente, se le da preferencia a un grupo trifluorometilo.

Como el "grupo alquilamino de C_{1-4}", que es el sustituyente en el "grupo arilo" para Z, puede mencionarse el "grupo alquilamino de C_{1-4}" definido anteriormente, se le da preferencia a un grupo metilamino, un grupo etilamino y un grupo isopropilamino.

Como el "grupo di(alquil de C_{1-4})amino", que es el sustituyente en el "grupo arilo" para Z, puede mencionarse el "grupo di(alquil de C_{1-4})amino" definido anteriormente, se le da preferencia a un grupo dimetilamino, un grupo dietilamino y un grupo dipropilamino.

Como el "grupo alquiltio de C_{1-6}", que es el sustituyente en el "grupo arilo" para Z, puede mencionarse el "grupo alquiltio de C_{1-6}" definido anteriormente, se le da preferencia a un grupo isopentiltio.

Como el "grupo alcoxi de C_{1-4}", que es el sustituyente en el "grupo arilo" para Z, puede mencionarse el "grupo alcoxi de C_{1-4}" definido anteriormente.

Como el "grupo alquilcarbonilo de C_{1-4}", que es el sustituyente en el "grupo arilo" para Z, puede mencionarse el "grupo alquilcarbonilo de C_{1-4}" definido anteriormente, se le da preferencia a un grupo acetilo.

El "grupo anular heteroaromático" para Z es, de manera preferida, un "grupo anular heteroaromático de 5 a 10 miembros mono o fusionado que contiene de 1 a 3 heteroátomos seleccionados del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre", el cual se ejemplifica específicamente por un grupo furilo, un grupo tienilo, un grupo pirrolilo, un grupo oxazolilo, un grupo isoxazolilo, un grupo tiazolilo, un grupo isotiazolilo, un grupo imidazolilo, un grupo pirazolilo, un grupo piridilo, un grupo piridacinilo, un grupo pirimidinilo, un grupo piracinilo, un grupo indolilo, un grupo isoindolilo, un grupo benzofuranilo, un grupo benzotienilo, un grupo benzoimidazolilo, un grupo benzotiazolilo, un grupo benzoxazolilo y lo similar. Particularmente preferidos son un grupo tiazolilo y un grupo piridilo.

El "grupo anular heteroaromático" para Z está sustituido opcionalmente por 1 a 5 (de manera preferida, de 1 a 3) sustituyentes seleccionados de lo siguiente.

(a) un grupo heterocíclico sustituido opcionalmente por grupo alquilo de C_{1-4} o un grupo C_{1-4} alquilcarbonilo,

(b) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por un grupo hidroxilo, un grupo oxo, un átomo de halógeno o un grupo alquilo de C_{1-6},

(c) un grupo carboxi,

(d) un átomo de halógeno,

(e) un grupo alquilo de C_{1-6},

(f) un grupo haloalquilo de C_{1-4},

(g) un grupo alquilamino de C_{1-4},

(h) un grupo di(C_{1-4} alquil)amino,

(i) un grupo alquiltio de C_{1-6},

(j) un grupo alcoxi de C_{1-4},

(k) un grupo alquilcarbonilo de C_{1-4} y

(l) un grupo arilo sustituido opcionalmente por un átomo de halógeno o un grupo haloalquilo de C_{1-4}.

Como tales sustituyentes, los preferidos son (a) un grupo heterocíclico, (b) un grupo alquilo de C_{1-6} y (c) un grupo arilo sustituido opcionalmente por un átomo de halógeno o un grupo haloalquilo de C_{1-4}.

El "grupo heterocíclico" del "grupo heterocíclico sustituido opcionalmente por grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4}", que es un sustituyente en el "grupo anular heteroaromático" para Z es, de manera preferida, un "grupo heterocíclico de 5 a 7 miembros, saturado o no saturado que contiene opcionalmente de 1 a 3 heteroátomos seleccionados del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un

átomo de azufre", el cual se ejemplifica específicamente por un grupo furilo, un grupo tienilo, un grupo pirrolilo, un grupo oxazolilo, un grupo isoxazolilo, un grupo tiazolilo, un grupo isotiazolilo, un grupo imidazolilo, un grupo pirazolilo, un grupo piridilo, un grupo piridacinilo, un grupo pirimidinilo, un grupo piracinilo, un grupo tetrahidrofurilo, un grupo tetrahidrotienilo, un grupo pirrolidinilo, un grupo pirazolidinilo, un grupo imidazolidinilo, un grupo oxazolidinilo, un grupo tiazolidinilo, un grupo tetrahidropiranilo, un grupo dioxanilo, un grupo piperidinilo, un grupo piperacinilo, un grupo morfolinilo y lo similar. Los preferidos son un grupo piperidinilo, un grupo morfolinilo, un grupo piperacinilo, un grupo pirrolidinilo, un grupo pirrolilo y un grupo tetrahidropiranilo.

El sustituyente en el "grupo heterocíclico" es, de manera preferida, un grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4}.

El "cicloalquilo de C_{3-7}" del "grupo cicloalquilo de C_{3-7} sustituido opcionalmente por un grupo hidroxilo, un grupo oxo, un átomo de halógeno o grupo alquilo de C_{1-6}", que es un sustituyente en el "grupo anular heteroaromático" para Z es, de manera preferida, un grupo ciclopentilo o un grupo ciclohexilo, de manera más preferida, un grupo ciclohexilo. El "grupo cicloalquilo de C_{3-7}" está sustituido opcionalmente por 1 a 5 (de manera preferida 1 a 3) sustituyentes seleccionados del grupo que consiste de un grupo hidroxilo, un grupo oxo, un átomo de halógeno y un grupo alquilo de C_{1-6}. El sustituyente en el "grupo cicloalquilo de C_{3-7}" es, de manera preferida, un átomo de halógeno o grupo alquilo de C_{1-4}.

Como el "átomo de halógeno", que es el sustituyente en el "grupo anular heteroaromático" para Z, puede mencionarse un "átomo de halógeno" definido anteriormente, se le da preferencia a un átomo de flúor, un átomo de cloro y un átomo de bromo, particularmente de manera preferida, un átomo de cloro.

Como el "grupo alquilo de C_{1-8}", que es el sustituyente en el "grupo anular heteroaromático" para Z, puede mencionarse el "grupo alquilo de C_{1-8}" definido anteriormente. Los preferidos son un grupo isopropilo, un grupo isobutilo, un grupo sec-butilo, un grupo ter-butilo, un grupo isopentilo, neopentilo, un grupo ter-pentilo, un grupo 1-etilpropilo y un grupo 1-propilbutilo, los más preferidos son un grupo isopentilo, un grupo neopentilo, un grupo ter-pentilo, un grupo 1-etilpropilo y un grupo 1-propilbutilo, los particularmente preferidos son un grupo neopentilo, un grupo 1-etilpropilo y un grupo 1-propilbutilo.

Como el "grupo haloalquilo de C_{1-4}", que es el sustituyente en el "grupo anular heteroaromático" para Z, puede mencionarse el "grupo haloalquilo de C_{1-4}" definido anteriormente, se le da preferencia a un grupo trifluorometilo.

Como el "grupo alquilamino de C_{1-4}", que es el sustituyente en el "grupo anular heteroaromático" para Z, puede mencionarse el "grupo alquilamino de C_{1-4}" definido anteriormente, se le da preferencia a un grupo metilamino, un grupo etilamino y un grupo isopropilamino.

Como el "grupo di(alquil de C_{1-4})amino", que es el sustituyente en el "grupo anular heteroaromático" para Z, puede mencionarse el "grupo di(alquil de C_{1-4})amino" definido anteriormente, se le da preferencia a un grupo dimetilamino, un grupo dietilamino y un grupo dipropilamino.

Como el "grupo alquiltio de C_{1-6}", que es el sustituyente en el "grupo anular heteroaromático" para Z, puede mencionarse el "grupo alquiltio de C_{1-6}" definido anteriormente, , se le da preferencia a un grupo isopentiltio.

Como el "grupo alcoxi de C_{1-4}", que es el sustituyente en el "grupo anular heteroaromático" para Z, puede mencionarse el "grupo alcoxi de C_{1-4}" definido anteriormente.

Como el "grupo alquilcarbonilo de C_{1-4}", que es el sustituyente en el "grupo anular heteroaromático" para Z, puede mencionarse el "grupo alquilcarbonilo de C_{1-4}" definido anteriormente, se le da preferencia a un grupo acetilo.

Como el "grupo arilo sustituido opcionalmente por un átomo de halógeno o un grupo haloalquilo de C_{1-4}", que es el sustituyente en el "grupo anular heteroaromático" para Z, puede mencionarse de manera preferida el "grupo fenilo sustituido opcionalmente por un átomo de halógeno o un grupo haloalquilo de C_{1-4}".

El "grupo piperacinilo" para Z está sustituido opcionalmente por 1 a 5 (de manera preferida 1 a 3) sustituyentes seleccionados de lo siguiente.

(a) un grupo fenilo,

(b) un grupo fenilalquilo de C_{1-4},

(c) un grupo benzoilo sustituido opcionalmente por un átomo de halógeno y

(d) un grupo fenilalcoxicarbonilo de C_{1-4}.

El "grupo fenilalquilo de C_{1-4}", que es un sustituyente en el "grupo piperacinilo" para Z, es un grupo fenilalquilo que tiene el "grupo alquilo de C_{1-4}" definido anteriormente como la "porción alquilo", el cual se ejemplifica específicamente por un grupo bencilo, un grupo fenetilo, un grupo 1-feniletilo, un grupo 3-fenilpropilo y lo similar. De manera preferida, es un grupo bencilo.

El "grupo benzoilo sustituido opcionalmente por un átomo de halógeno", que es un sustituyente en el "grupo piperacinilo" para Z, es de manera preferida un grupo benzoilo sustituido opcionalmente por 1 a 5 del "átomo de halógeno" definido anteriormente, el cual se ejemplifica específicamente por un grupo clorobenzoilo, un grupo bromobenzoilo y lo similar.

El "grupo fenilalcoxicarbonilo de C_{1-4}", que es un sustituyente en el "grupo piperacinilo" para Z, es un "grupo fenilalcoxicarbonilo que tiene el grupo alcoxi de C_{1-4} definido anteriormente como la porción alcoxi, el cual se ejemplifica específicamente por un grupo benciloxicarbonilo y lo similar. El preferido es un grupo benciloxicarbonilo.

En la fórmula [I], las modalidades preferidas incluyen lo siguiente.

V es, de manera preferida =N- o =CH-.

W es, de manera preferida -S-.

m es, de manera preferida 1 ó 2.

R^1 y R^2 son, de manera preferida, cada uno un átomo de hidrógeno.

X es, de manera preferida, los siguientes (1) a (4).

(1)

$-N(R^4)-$, $-SO_2-N(R^5)-$, $-CO-N(R^7)-$ o $-O-$

en donde R^4 es un átomo de hidrógeno o un grupo alquilo de C_{1-6}, R^5 es un átomo de hidrógeno o un grupo alquilo de C_{1-6} y R^7 es un átomo de hidrógeno o un grupo alquilo de C_{1-6},

(2)

$-N(R^4)-$

en donde R^4 es un grupo alquilo de C_{1-6} sustituido por

(a) un grupo arilo sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un átomo de halógeno, un grupo alquilo de C_{1-6} y un grupo haloalquilo de C_{1-4},

(b) un grupo anular heteroaromático sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-6},

(c) un grupo carboxi,

(d) un grupo alcoxicarbonilo de C_{1-4},

(e) $-CO-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son cada uno, de manera independiente, un átomo de hidrógeno, un grupo arilo (este grupo arilo está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste

de un grupo alquilo de C_{1-6}, un grupo alcoxi de C_{1-4}, un grupo carboxi y un grupo di(alquil de C_{1-4})amino), un grupo anular heteroaromático, un grupo alquilo de C_{1-6} (este grupo alquilo de C_{1-6} está sustituido opcionalmente por un grupo arilo), o, junto con el átomo de nitrógeno unido al mismo, puede formar un heteroanillo de 5 a 7 miembros que contiene además, opcionalmente, al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre,

(f) $-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son cada uno de manera independiente un átomo de hidrógeno o un grupo arilo,

(g) $-O-R^{17}$

en donde R^{17} es un grupo arilo o

(h) un grupo cicloalquilo de C_{3-7},

(3) $-N(R^4)-$

en donde R^4 es

(a) $-CO-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son cada uno de manera independiente un átomo de hidrógeno, un grupo arilo (este grupo arilo está sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-6}), un grupo alquilo de C_{1-6}, o, junto con el átomo de nitrógeno unido al mismo, puede formar un anillo de indolina o puede formar un heteroanillo de 5 a 7 miembros que contiene opcionalmente además, al menos un heteroátomo seleccionado del grupo que

consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre,

(b) $-SO_2-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son cada uno de manera independiente un grupo arilo o un grupo alquilo de C_{1-6},

(c) $-CO-R^{17}$

en donde R^{17} es un grupo arilo (este grupo arilo está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un grupo alquilo de C_{1-6} y un grupo alcoxi de C_{1-4}), un grupo anular heteroaromático o un grupo alquilo de C_{1-6} (este grupo alquilo de C_{1-6} está sustituido opcionalmente por un grupo arilo sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un átomo de halógeno y un grupo alquilo de C_{1-6}, un grupo anular heteroaromático, un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo arilo o un grupo ariloxi sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-6}),

(d) $-SO_2-R^{17}$

en donde R^{17} es un grupo arilo o

(e) un grupo arilo

o

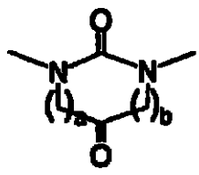
(4) $-N(R^6)-CO-$, $-N(R^6)-CO-N(R^5)-$ o $-N(R^{10})-(CH_2)_k-N(R^5)-$

en donde

R^5 es un grupo alquilo de C_{1-6} sustituido opcionalmente por un átomo de hidrógeno o un grupo arilo,

R^8 es un átomo de hidrógeno o un grupo alquilo de C_{1-6},

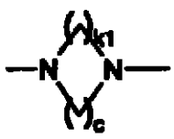
R^9 está enlazado con R^5 para formar



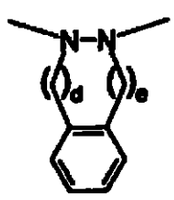
en donde a y b son cada uno de manera independiente 0, 1 ó 2,

k es 0 o un entero de 1 a 4,

R^{10} está enlazado con R^5 para formar



en donde k1 y c son cada uno de manera independiente 0 o un entero de 1 a 4 o



en donde d y e son cada uno de manera independiente 0, 1 ó 2.

n es de manera preferida 0 o un entero de 1 a 3.

P es de manera preferida 0 ó 1.

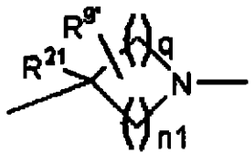
L es de manera preferida, los siguientes (1) a (4).

(1)

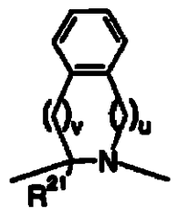
$-C(R^{20})(R^{21})-$

en donde

R^{20} está enlazado con R^4 para formar



en donde n1 y q son cada uno de manera independiente 0 o un entero de 1 a 4 y $R^{9'}$ es un átomo de hidrógeno, un grupo hidroxilo, un grupo alquilo de C_{1-6}, un grupo carboxi o un grupo alcoxi de C_{1-6} o



en donde u y v son cada uno de manera independiente 0, 1 ó 2,

R^{21} es un átomo de hidrógeno,

(2)



en donde E es un grupo fenilo, un grupo furilo, un grupo isoxazolilo o un grupo piridilo y R^{22} es un átomo de hidrógeno,

(3)

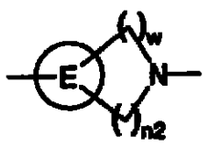


en donde

E es un grupo fenilo,

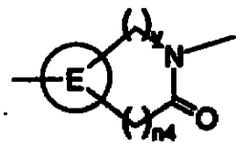
R^{22} es

(a) unido con R^4 para formar



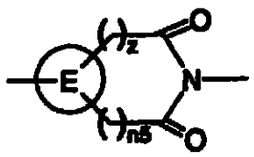
en donde n2 y w son cada uno de manera independiente 0 o un entero de 1 a 3,

(b) unido con R^7 para formar



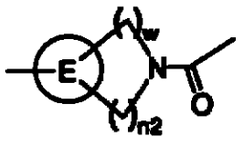
en donde n4 y y son cada uno de manera independiente 0, 1 ó 2,

(c) unido con R^7 para formar



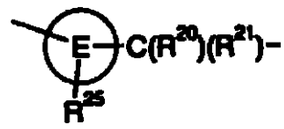
en donde n5 y z son cada uno de manera independiente 0 ó 1 o

(d) unido con R^8 para formar



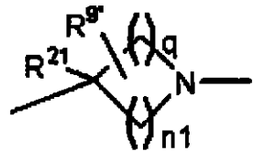
en donde n2 y w son cada uno de manera independiente 0 o un entero de 1 a 3 o

(4)



en donde

R^{20} está enlazado con R^4 para formar



en donde n1 y q son cada uno de manera independiente 0 o un entero de 1 a 4 y $R^{9'}$ es un átomo de hidrógeno, un grupo hidroxilo, un grupo alquilo de C_{1-6}, un grupo carboxi o un grupo alcoxi de C_{1-6},

R^{21} es un átomo de hidrógeno,

E es un grupo fenilo, un grupo furilo, un grupo isoxazolilo o un grupo piridilo, y

R^{25} es un átomo de hidrógeno.

R es, de manera preferida $-COO(R^{19})$, $-A^1-COO(R^{19})$ o $-O-A^1-COO(R^{19})$

en donde A^1 es un grupo alquileno de C_{1-4} y R^{19} es un átomo de hidrógeno o un grupo alquilo de C_{1-4}.

B es, de manera preferida, un grupo fenilo o un grupo anular heteroaromático (este grupo anular heteroaromático se selecciona de manera preferida del grupo que consiste de un grupo tienilo, un grupo tiazolilo, un grupo pirazolilo, un grupo 1,3,4-tiadiazolilo, un grupo piridilo, un grupo piridacinilo, un grupo pirimidinilo, un grupo indolilo, un grupo bencimidazolilo, un grupo benzotiazolilo y un grupo benzoxazolilo).

Cuando V es =CH-, la posición de la sustitución de B en el anillo de tiofeno o de furano formado por V junto con W es, de manera preferida, en la posición 4 o la posición 5, y cuando V es =N-, la posición de la sustitución de B en el anillo de tiazol u oxazol formado por V junto con W es, de manera preferida, en la posición 4.

R^3 es de manera preferida un átomo de hidrógeno.

Y es de manera preferida $-C(R^{13})(R^{14})-N(R^{12})-$, $-C(R^{13})(R^{14})-O-$, $-N(R^{11})-$ u $-O-$

en donde R^{11} es un átomo de hidrógeno o un grupo alquilo de C_{1-6}, R^{12} es un átomo de hidrógeno o un grupo alquilo de C_{1-6}, y R^{13} y R^{14} son cada uno un átomo de hidrógeno.

s es de manera preferida 0 ó 1.

A es de manera preferida un grupo metileno.

Y, s y A son, de manera preferida los siguientes (1) o (2).

(1) Y es $-C(R^{13})(R^{14})-N(R^{12})-$ o $-C(R^{13})(R^{14})-O-$

en donde R^{12} es un átomo de hidrógeno o un grupo alquilo de C_{1-6} y R^{13} y R^{14} son cada uno un átomo de hidrógeno,

y

s es 0.

(2) Y es -N(R^{11})- u -O-

en donde R^{11} es un átomo de hidrógeno o un grupo alquilo de C_{1-6},

y

s es 1 y A es un grupo metileno.

Z es de manera preferida un grupo arilo sustituido por sustituyentes seleccionados del grupo que consiste de,

(a) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de átomo de halógeno y un grupo alquilo de C_{1-6},

(b) un átomo de halógeno,

(c) un grupo alquilo de C_{1-6},

(d) un grupo haloalquilo de C_{1-4},

(e) un grupo di(C_{1-4} alquil)amino,

(f) un grupo alquiltio de C_{1-6} y

(g) un grupo alquilcarbonilo C_{1-4}.

Z es, de manera más preferida, un grupo fenilo sustituido por un grupo alquilo de C_{1-6} (este grupo alquilo de C_{1-6} se selecciona del grupo que consiste de un grupo isopropilo, un grupo isobutilo, un grupo sec-butilo, un grupo ter-butilo, un grupo isopentilo, un grupo neopentilo, un grupo ter-pentilo, un grupo 1-etilpropilo y un grupo 1-propilbutilo).

Z es particularmente, de manera preferida, un grupo fenilo sustituido por un grupo 1-etilpropilo o un grupo 1-propilbutilo.

En la fórmula [I], las modalidades particularmente preferidas incluyen lo siguiente.

V es particularmente de manera preferida =N- o =CH-.

W es particularmente de manera preferida -S-.

m es particularmente de manera preferida 1.

R^1 y R^2 son cada uno de manera preferida, un átomo de hidrógeno.

X, n, p y L son particularmente de manera preferida los siguientes (1) a (7).

(1)

X es $-N(R^4)-$

en donde R^4 es un grupo alquilo de C_{1-6} sustituido por un grupo anular heteroaromático sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-6}

y

n es 1 y p es 0.

(2)

X es $-N(R^4)-$

en donde R^4 es un grupo alquilo de C_{1-6} sustituido por $-CO-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son cada uno de manera independiente un átomo de hidrógeno, un grupo arilo (este grupo arilo está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un grupo alquilo de C_{1-8}, un grupo alcoxi de C_{1-4}, un grupo carboxi y un grupo di(alquil de C_{1-4})amino), un grupo anular heteroaromático, un grupo alquilo de C_{1-6} (este grupo alquilo de C_{1-6} es sustituido opcionalmente por un grupo arilo), o, junto con el átomo de nitrógeno unido al mismo, puede formar un heteroanillo de 5 a 7 miembros que contiene además, opcionalmente al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre

y

n es 1 y p es 0.

(3)

X es $-N(R^4)-$

en donde R^4 es $-CO-N(R^{15})(R^{16})$

en donde R^{15} y R^{16} son cada uno de manera independiente un átomo de hidrógeno, un grupo arilo (este grupo arilo está sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-8}), o un grupo alquilo de C_{1-6}, o, junto con el átomo de nitrógeno unido al mismo, puede formar un anillo de indolina o puede formar un heteroanillo de 5 a 7 miembros que contiene opcionalmente además al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre

y

n es 1 y p es 0.

(4)

X es $-N(R^4)-$, $-SO_2-N(R^5)-$, $-CO-N(R^7)-$ u -O-

en donde R^4 es un átomo de hidrógeno o un grupo alquilo de C_{1-6}, R^5 es un átomo de hidrógeno o un grupo alquilo de C_{1-6}, y R^7 es un átomo de hidrógeno o un grupo alquilo de C_{1-6},

y

n es 0, p es 1 y L es



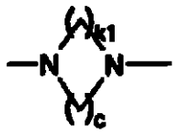
en donde E es un grupo piridilo y R^{22} es un átomo de hidrógeno.

(5)

X es $-N(R^{10})-(CH_2)_k-N(R^5)-$

en donde k es 0 o un entero de 1 a 4, y

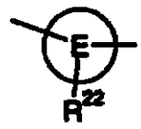
R^{10} está enlazado con R^5 para formar



en donde k1 y c son cada uno de manera independiente 0 o un entero de 1 a 4,

y

n es 0 o un entero de 1 a 4, p es 1 y L es



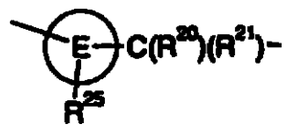
en donde E es un grupo fenilo, un grupo furilo, un grupo isoxazolilo o un grupo piridilo y R^{22} es un átomo de hidrógeno.

(6)

X es $-N(R^4)-$

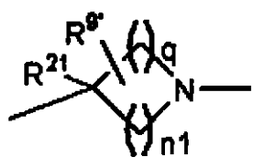
y

n es 0 o un entero de 1 a 4, p es 1 y L es



en donde

R^{20} está enlazado con R^4 para formar



en donde n1 y q son cada uno de manera independiente 0 o un entero de 1 a 4 y $R^{9'}$ es un átomo de hidrógeno, un grupo hidroxilo, un grupo alquilo de C_{1-6}, un grupo carboxi o un grupo alcoxi de C_{1-6},

R^{21} es un átomo de hidrógeno,

E es un grupo fenilo, un grupo furilo, un grupo isoxazolilo o un grupo piridilo, y

R^{25} es un átomo de hidrógeno.

(7)

X es $-N(R^4)-$

y

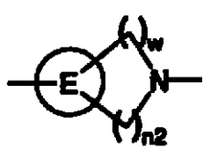
n es 0 o un entero de 1 a 3, p es 1 y L es



en donde

E es un grupo fenilo,

R^{22} está enlazado con R^4 para formar



en donde n2 y w son cada uno de manera independiente 0 o un entero de 1 a 3.

R es particularmente de manera preferida $-COO(R^{19})$

en donde R^{19} es un átomo de hidrógeno o un grupo alquilo de C_{1-4}.

B es particularmente de manera preferida un grupo fenilo.

Cuando V es =CH-, la posición de la sustitución de B en el anillo de tiofeno o furano formado por V junto con W es, de manera preferida, en la posición 4 o en la posición 5, y cuando V es =N-, la posición de la sustitución de B en el anillo de tiazol u oxazol formado por V junto con W es particularmente de manera preferida, en la posición 4.

R^3 es particularmente de manera preferida, un átomo de hidrógeno.

Y, s y A son cada uno particularmente de manera preferida, los siguientes (1) o (2).

(1)

Y es $-C(R^{13})(R^{14})-N(R^{12})-$ o $-C(R^{13})(R^{14})-O-$

en donde R^{12} es un átomo de hidrógeno o un grupo alquilo de C_{1-6} y R^{13} y R^{14} son cada uno un átomo de hidrógeno,

y

s es 0.

(2)

Y es $-N(R^{11})-$ u $-O-$

en donde R^{11} es un átomo de hidrógeno o un grupo alquilo de C_{1-6},

y

s es 1 y A es un grupo metileno.

Z es particularmente de manera preferida, un grupo fenilo sustituido por un grupo 1-etilpropilo o un grupo 1-propilbutilo.

En la fórmula [II], las modalidades preferidas incluyen lo siguiente.

V es de manera preferida =CH-.

W es de manera preferida -S-.

Y^{100} es de manera preferida $-CH_2-$.

R^{100} es de manera preferida, un grupo hidroxilo o un átomo de cloro.

B es de manera preferida un grupo fenilo.

La posición de la sustitución de B en el anillo de tiofeno formado por V junto con W es de manera preferida la posición 4.

R^3 es de manera preferida un átomo de hidrógeno.

La "sal farmacéuticamente aceptable" puede ser cualquiera, siempre que forme una sal no tóxica con un compuesto de la fórmula [I] mencionada anteriormente, y puede obtenerse mediante la reacción con ácidos inorgánicos tales como ácido clorhídrico, ácido sulfúrico, ácido fosfórico, ácido bromhídrico y lo similar; ácidos orgánicos tales como ácido oxálico, ácido malónico, ácido cítrico, ácido fumárico, ácido láctico, ácido málico, ácido succínico, ácido tartárico, ácido acético, ácido trifluoroacético, ácido glucónico, ácido ascórbico, ácido metilsulfónico, ácido bencilsulfónico y lo similar; bases inorgánicas tales como hidróxido de sodio, hidróxido de potasio, hidróxido de calcio, hidróxido de magnesio, hidróxido de amonio y lo similar; bases orgánicas tales como metilamina, dietilamina, trietilamina, trietanolamina, etilendiamina, tris(hidroximetil)metilamina, guanidina, colina,

cinconina, N-metil-D-glucamina y lo similar; o aminoácidos tales como lisina, histidina, arginina, alanina y lo similar. La presente invención también abarca productos que contienen agua, hidratos y solvatos de cada compuesto.

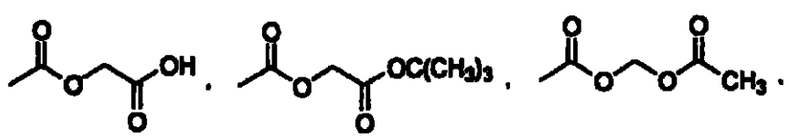
Existen varios isómeros del compuesto representados por la fórmula [I] mencionada anteriormente. Por ejemplo, la forma E y la forma Z están presentes como isómeros geométricos, y cuando existe un átomo de carbono asimétrico, están presentes un enantiómero y un diastereómero como estereoisómeros basados en el mismo. En algunos casos, puede estar presente un tautómero. En consecuencia, la presente invención abarca todos estos isómeros y mezclas de los mismos.

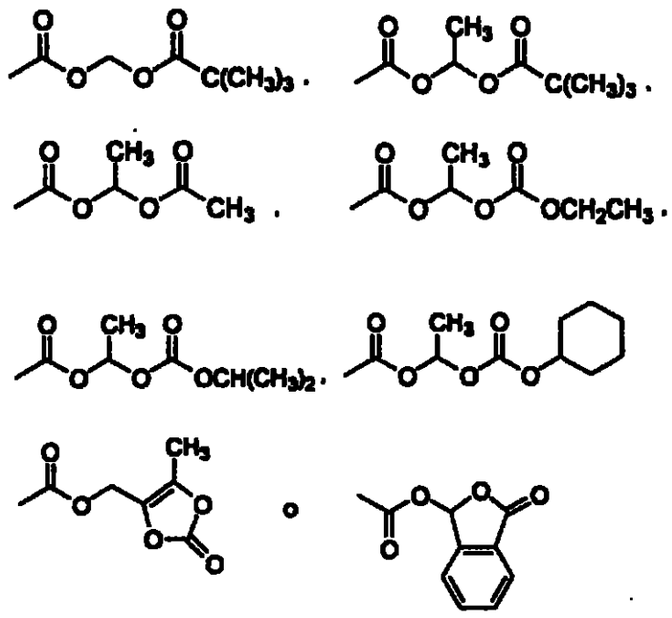
La presente invención también abarca un profármaco y un metabolito del compuesto representado por la fórmula [I].

Un "profármaco" es un derivado del compuesto de la presente invención, el cual tiene un grupo capaz de la descomposición química o metabólica, y muestra la eficacia inherente tras la restauración al compuesto original después de la administración a un organismo viviente. Este incluye complejos y sales libres de un enlace covalente.

Por ejemplo, puede utilizarse un derivado de éster conocido como un profármaco en el campo de los agentes farmacéuticos, el cual es, específicamente un derivado de éster, en donde la porción $-COOR^7$ para R está representada por las siguientes fórmulas.

$-CO_2CH_3$, $-CO_2CH_2CH_3$,





Cuando el compuesto de la presente invención se utiliza como una preparación farmacéutica, se mezcla generalmente con un portador, excipiente, diluyente, agente de extensión, desintegrantes, estabilizante, conservador, amortiguador, emulsificante, agente aromático, colorante, edulcorante, espesante, corrector, adyuvantes de la disolución, farmacéuticamente aceptables, y otros aditivos conocidos generalmente *per se*, que son específicamente agua, aceite vegetal, alcohol tal como etanol, alcohol bencílico etc., polietilen glicol, triacetato de glicerol, gelatina, lactosa, carbohidratos tales como almidón y lo similar, estearato de magnesio, talco, lanolina, vaselina y lo similar, y se administran sistémica o tópicamente, oral o parenteralmente en la forma de una tableta, píldora, polvo, gránulo, supositorio, inyección, gotas para los ojos, líquido, cápsula, trocisco, aerosol,

elíxir, suspensión, emulsión, jarabe y lo similar, mediante métodos convencionales.

Aunque la dosis del compuesto de la presente invención varía dependiendo de la edad, el peso corporal, los síntomas, la enfermedad a ser tratada, el método de administración y lo similar, es de generalmente 1 mg a 1,000 mg para una dosis a un adulto, que se administra una vez al día a varias veces al día.

El compuesto [I] de la presente invención puede administrarse como un inhibidor de la PTP1B o un inhibidor del regulador negativo del receptor de la tirosina cinasa, un fármaco para la profilaxis o tratamiento de la diabetes, un fármaco para la profilaxis o el tratamiento de las complicaciones diabéticas (retinopatía, nefropatía, neuropatía, síndrome X o síndrome metabólico, enfermedades cardiacas isquémicas (infarto al miocardio, angina de pecho, etc.) y apoplejías (infarto cerebral, hemorragia cerebral, hemorragia subaracoidea, etc.), un fármaco para la profilaxis o el tratamiento de la hiperlipidemia, un fármaco para la profilaxis o el tratamiento de la obesidad, un fármaco para la profilaxis o el tratamiento de enfermedades neurodegenerativa (edema de la mácula, degeneración macular, etc.), un fármaco para la profilaxis o el tratamiento de enfermedades mediadas por la PTP1B y lo similar en mamíferos (humano, ratón, rata, conejo, perro, gato, bovino, porcino, simio, etc).

El compuesto [I] de la presente invención tiene una actividad inhibidora selectiva superior de la PTP1B. Por la "actividad inhibidora

selectiva superior de la PTP1B" se quiere decir que la actividad inhibidora de la PTP1B es mayor que en comparación con las otras proteínas tirosina fosfatasas (por ejemplo, actividad inhibidora de la proteína tirosina fosfatasa de los linfocitos T (TCPTP)), lo cual significa, específicamente, por ejemplo, que la CI_{50} para la PTP1B es tan baja como 1/10 o por debajo de aquélla para la TCPTP, de manera más preferida 1/60 o menor, particularmente, de manera preferida, 1/300 o menor. Así, el compuesto [I] de la presente invención puede utilizarse como un inhibidor de la PTP1B, un inhibidor del regulador negativo del receptor de la tirosina cinasa, un fármaco para la profilaxis o el tratamiento de la diabetes, un fármaco para la profilaxis o el tratamiento de las complicaciones diabéticas, un fármaco para la profilaxis o el tratamiento de la hiperlipidemia, un fármaco para la profilaxis o el tratamiento de la obesidad, enfermedad neurodegenerativa y lo similar o un fármaco para la profilaxis o el tratamiento de enfermedades mediadas por la PTP1B, que cause menos efectos laterales.

El "inhibidor del regulador negativo del receptor de la tirosina cinasa" se refiere a un agente farmacéutico que inhibe un factor que regula la señalización intracelular hacia una dirección negativa, señalización la cual surge de la activación de un receptor de tirosina cinasa tras la unión con un ligando, mejorando por lo tanto la señal. En el caso de un receptor de la insulina, por ejemplo, que es uno de los receptores de las tirosina cinasas, en donde, como resultado de la activación del receptor unido con la insulina, la región intracelular del receptor mismo, el IRS (sustrato del receptor de la

insulina) y lo similar, se fosforilan y ocurre la señalización intracelular que causa la captación de la glucosa, un agente farmacéutico que inhiba un factor que regula tal señalización hacia la dirección negativa, es un inhibidor del regulador negativo del receptor de la tirosina cinasa, en donde un ejemplo representativo es un inhibidor de la PTP1B. El inhibidor del regulador negativo del receptor de la tirosina cinasa es diferente de los mejoradores existentes de la sensibilidad a la insulina (agonistas del PPAR, tales como un derivado de tiazolidindiona, etc.). Para ser precisos, debido a que un inhibidor del regulador negativo del receptor de la tirosina cinasa, representado por un inhibidor de la PTP1B, actúa directamente en una señal intracelular inducida por la insulina, se espera una alta eficacia en los mamíferos (pacientes diabéticos del tipo sin obesidad, etc.), que exhiba una eficacia insuficiente con la administración de los mejoradores existentes de la sensibilidad a la insulina, y pueden evitarse los efectos laterales que tienen los mejoradores existentes de la sensibilidad a la insulina.

El compuesto [I] de la presente invención puede utilizarse en combinación con otros agentes terapéuticos para la diabetes, para el propósito de la profilaxis o tratamiento de la diabetes o las complicaciones diabéticas (particularmente, complicaciones microangiogénicas, en otras palabras, retinopatía, nefropatía, neuropatía, etc.) y administrarse concurrentemente a los mamíferos. En la presente invención, los "agentes terapéuticos para la diabetes" abarcan los agentes terapéuticos para las complicaciones diabéticas (particularmente, complicaciones

microangiogénicas). Además, el compuesto [I] de la presente invención puede utilizarse en combinación con otros agentes terapéuticos para la hiperlipidemia, con el propósito ce la profilaxis o el tratamiento de la hiperlipidemia y administrase concurrentemente con los mamíferos. Además, el compuesto [I] de la presente invención puede utilizarse en combinación con otros agentes terapéuticos para la obesidad, con el propósito de la profilaxis o el tratamiento de la obesidad y administrase concurrentemente con los mamíferos.

Además, el compuesto [I] de la presente invención puede utilizarse en combinación con agentes terapéuticos para la diabetes, agentes terapéuticos para la hiperlipidemia, agentes terapéuticos para la obesidad, agentes terapéuticos para la hipertensión y/o agentes terapéuticos para la trombosis, con el propósito de la profilaxis o el tratamiento de las complicaciones diabéticas (particularmente, complicaciones de las grandes arterias, en otras palabras, síndrome X o síndrome metabólico, enfermedades cardiacas isquémicas (infarto al miocardio, angina de pecho, etc.), apoplejías (infarto cerebral, hemorragia cerebral, hemorragia subaracnoidea, etc.) etc.) y administrase concurrentemente con los mamíferos.

Cuando el compuesto se utiliza en combinación con agentes terapéuticos para la diabetes, agentes terapéuticos para la hiperlipidemia, agentes terapéuticos para la obesidad, agentes terapéuticos para la hipertensión o agentes terapéuticos para la trombosis (referidos de aquí en adelante como un agente farmacéutico concomitante), el compuesto de la

presente invención puede administrarse simultáneamente junto con un agente farmacéutico concomitante, o puede administrarse con intervalos de tiempo. Cuando el compuesto se utiliza en combinación con un agente farmacéutico concomitante, el compuesto de la presente invención y un agente farmacéutico concomitante pueden administrarse como una composición farmacéutica que los contiene. De manera alterna, una composición farmacéutica que contiene el compuesto de la presente invención y una composición farmacéutica que contiene un agente farmacéutico concomitante puede administrarse de manera separada. La ruta de administración de cada composición farmacéutica puede ser la misma o diferente.

Cuando el compuesto se utiliza en combinación con un agente farmacéutico concomitante y cuando el agente farmacéutico concomitante tiene un mecanismo de acción diferente del compuesto de la presente invención (por ejemplo, secretagogo de insulina, agente de biguanida, inhibidor de la α-glucosidasa, preparación de insulina, mejorador de la sensibilidad de la insulina, inhibidor del regulador negativo del receptor de la tirosina cinasa diferente del inhibidor de la PTP1B, etc.), se espera un efecto aditivo de la profilaxis o el tratamiento, basado en las acciones respectivas del compuesto de la presente invención y el agente farmacéutico concomitante, así como un efecto amplificado de la profilaxis o el tratamiento que combine ambas acciones. Así, en cada caso del compuesto de la presente invención y el agente farmacéutico concomitante, se espera que tengan una alta eficacia

por la administración de una dosis menor, en comparación con aquélla administrada sola y, como resultado, solucionen los efectos laterales que no pueden evitarse en caso de administrarse solos. Por lo tanto, el compuesto de la presente invención puede administrarse a una sola dosis de 1 mg a 1,000 mg, o incluso en una dosis menor, una vez al día a varias veces al día. El agente farmacéutico concomitante puede administrarse a una dosis empleada generalmente para la profilaxis o tratamiento de la diabetes o las complicaciones diabéticas, hiperlipidemia u obesidad, o incluso a una dosis menor.

Como agentes terapéuticos para la diabetes que son utilizados como agentes farmacéuticos concomitantes, pueden mencionarse secretagogos de la insulina (bloqueadores del canal de potasio dependiente de ATP (K(ATP)) (sulfonilureas, sulfonamidas, derivados de fenilalanina, etc.)), biguanidas, inhibidores de la α-glucosidasa, formulaciones de insulina, análogos de la insulina, mejoradores de la sensibilidad a la insulina (agonistas del receptor activado de los proliferadores de peroxisoma (PPAR)-gamma tales como derivados de tiazolidindiona (glitazonas)), IL-11, agentes anti-CD25 (Receptor IL-2) (tales como anticuerpos monoclonales), antagonistas de la angiotensina (AT1), inhibidores de la enzima que convierten la angiotensina (ACE), inhibidores de la aldosa reductasa, antioxidantes (activadores de la proteína cinasa/inhibidores de la transcriptasa inversa), estimulante de la carnitina acetiltransferasa, antidepresivos, glucocorticoides, retilina, agonistas de la formación de radicales y activadores de la transcetolasa. También

pueden mencionarse los agonistas del adrenoceptor beta3, mejoradores de la sensibilidad a la insulina, moduladores del receptor nuclear, receptores activados del proliferador de la peroxisoma, antagonistas de PPAR-alfa, antagonistas de PPAR-gamma, ligandos de PPAR-delta (agonistas o antagonistas), fibratos, fármacos que actúan en los receptores retinoides (retinoides, etc.), inhibidores de la proteína tirosina fosfatasa (PTP) (diferentes a los compuestos de la invención), inhibidores de la proteína tirosina fosfatasa-1B (PTP1B) (diferentes a los compuestos de la invención), inhibidores de la proteína tirosina fosfatasa de los linfocitos T (TCPTP) (diferentes a los compuestos de la invención), inhibidores de la proteína relacionada con el antígeno común del leucocito (LAR), inhibidores de la inositol fosfatasa 2 que contiene SH2 (SHIP2), inhibidores de la cinasa NH2 terminal c-Jun (JNK), agonistas del receptor de la insulina, estimulantes del receptor de la cinasa, antagonistas del factor de crecimiento similar a la insulina (IGF)-1, inhibidores de la dipeptidil-peptidasa IV, agonistas del péptido 1 similar al glucagon (GLP1), GLP1, leptina, activadores del canal de potasio dependiente de ATP; agonistas de VPAC2 (receptor para el péptido intestinal vasoactivo (VIP)), agonistas de P2Y; antagonistas de la proteína beta amiloide, inhibidores de la apoptosis, agonistas de TGR79, agonistas de GPR40, inhibidores del cotransportador de sodio-glucosa (inhibidores de SGLT-2, etc.), inhibidores de la glucógeno fosforilasa, inhibidores de fructosa-bifosfatasa, inhibidores de la fosfoenolpiruvato carboxicinasa (PEPCK), inhibidores de la piruvato deshidrogenasa cinasa, inhibidores de la glucosa-6-

fosfatasa, inhibidores de la glucógeno sintasa (GSK)-3, activadores de la glucocinasa, antagonistas del glucagon, moduladores del transductor de la señal y el activador de la transcripción (STAT)-3, inhibidores del factor de transcripción con cabeza de horquilla (FOXO-1), agonistas de la interleucina (IL) tales como agonistas de la IL-10 y agonistas de la IL-4, inhibidores de la producción de la IL-6, inhibidores de la producción del factor de necrosis del tumor (TNF)-alfa, inhibidores de la expresión de la proteína quimioatrayente del monocito (MCP)-1, moduladores de la adipocitocina, inhibidores de la producción del tipo 1 del inhibidor del activador del plasminógeno (PAI-1), mejoradores de la producción de adiponectina, agonistas del receptor de la adiponectina, adiponectina, inhibidores de la producción de resistina, antagonistas del receptor de la resistina, antagonistas del adrenorreceptor alfa-2, antagonistas del adrenoceptor beta-2, antagonistas de 5-HT6, inhibidor de la serina carboxipeptidasa, mejoradores de la expresión del casete A1 que se une a ATP (ABCA1), agonistas del receptor retinoide X (RXR), ligandos del receptor X del hígado (LXR) (agonistas o antagonistas), inhibidores de la proteína de unión al ácido graso de los adipocitos (FABP) (aP2), antagonistas del colesterol, antagonistas de la adenosina A2B, agonistas del adrenorreceptor alfa1, adrenorreceptores alfa2, inhibidores de la carnitina O-palmitoiltransferasa, activadores de la proteína cinasa activada por AMP (AMPK), activadores de la traslocación del transportador de la glucosa (GLUT)-4, antagonistas del receptor del glucocorticoide, moduladores del receptor del glucocorticoide, inhibidores de la 11beta-hidroxiesteroide

deshidrogenasa, inhibidores de la liberación de la hormona de crecimiento, análogos de somatostatina, agonistas de la somatostatina sst5, agonistas de la somatostatina sst2, factores que liberan la hormona del crecimiento (GHRF), inhibidores de la producción de grelina, antagonistas del receptor de la grelina, inhibidores de la cinasa, oligonucleótidos inhibidores de la expresión de PTPN1, antioxidantes, depuradores del ácido nítrico, depuradores de radicales libres, inductores de la heme oxigenasa (HO)-1, inhibidores de EGFR (erbB1), inhibidores de la fosfodiesterasa III, inhibidores de la fosfodiesterasa IV, inhibidores de la acetil-CoA carboxilasa (ACC), inhibidores de la carnitina palmitoiltransferasa (CPT) 1, activadores del sensor de la glucosa, inhibidores de la proteína de transferencia de triglicéridos microsomales (MTP), inhibidores de la diacilglicerol aciltransferasa (DGAT), estatinas, inhibidores de la proteína colesteril éster transferasa (CETP), cualquier otros agentes que disminuyan la glucosa, agentes anti-CD3 (tales como anticuerpos monoclonales), estimulantes de la glutamato descarboxilasa, combinación de gastrina y factor de crecimiento epidérmico (EGF), inhibidores de la calcineurina, antioxidantes (metaloporfirinas, etc.), NAD+ ADP-ribosiltransferasa (poli(ADP-ribosa)polimerasa; inhibidores de PARP), inmunoestimulantes, agonista del receptor de la quimiocina, antagonista del receptor de la quimiocina, complejos de vanadio, inhibidores de la proteína cinasa p38, inhibidores del producto final de la glucación avanzada (AGE) (inhibidores de la reacción de Maillard), heparinas de bajo peso molecular (LMW), inhibidores de la óxido nítrico sintasa inducible,

agentes del factor de crecimiento derivado de las antiplaquetas (PDGF) (tales como anticuerpos monoclonales), inhibidores de la angiogénesis (inductores de la apoptosis, antagonistas de la endotelina (ETA), etc.), antagonistas de la somatostatina sst2, moduladores del factor de crecimiento, inhibidores de la adhesión celular, inhibidores de la amadorasa, antagonistas del receptor del factor de crecimiento transformante (TGF)-beta, inhibidores de la señal del receptor TGF-beta, inhibidores de la producción de TGF-beta, anticuerpos anti-TGF-beta, anticuerpos del receptor anti-TGF-beta, agentes del receptor de la lipotroteína de baja densidad oxidada, similar a la anti-lectina (tales como anticuerpos monoclonales), antagonistas del receptor Edge, inhibidores de la señal del receptor Edge, mejoradores del factor neurotrófico, agentes neurotróficos, factor del crecimiento nervioso (NGF), agonistas del NGF, factor del crecimiento endotelial vascular (VEGF), neurotrofina (NT)-3, inductores de NT-3, inhibidores de la proteína cinasa (PK) C beta, fármacos que actúan en la transmisión mediada por el ácido gamma-aminobutírico (GABA), inhibidores de la recaptación de 5-HT; antagonistas de 5-HT2A, inhibidores de la recaptación de la norepinefrina, fármacos que actúan en los receptores vainilloides, agonistas del receptor cannabinoide, IL-6, antagonistas del D-aspartato de N-metilo (NMDA), prostaglandina E1, análogos de prostaciclina, activadores de la piruvato deshidrogenasa, mejoradores de la expresión de la óxido nítrico sintasa (NOS) 3, agonistas generales de la proteína para el choque por calor, bloqueadores del canal de sodio, inhibidores de la NAALADasa, inhibidores de la bomba general, erizo sónico-IgG, antagonistas

del receptor de VEGF, inhibidores de la señal de VEGF, factor derivado del pigmento epitelial (PEDF), anticuerpos monoclonales anti-VEGF, inhibidores de la matriz de la metaloproteinasa, inhibidores de la metionina aminopeptidasa-2, agonistas de la somatostatina sst1, inhibidores de la tirosina cinasa, antagonistas del factor de crecimiento endotelial, antagonistas de la vitronectina (alfavbeta3, alfavbeta5, etc.), inhibidores del factor inducible por hipoxia (HIF), antagonistas del receptor de la neuropilina-1, antagonistas del receptor de la angiopoyetina-2, inhibidores de la producción de la angiopoyetina-2, agonistas del receptor de la angiopoyetina-1, inductores de la angiopoyetina-1, y lo similar. Por ejemplo, nateglinida, glimepirida, glibenclamida, gliclazida, acetohexamida, tolbutamida, gliclopiramida, tolazamida, glibuzol, glipizida, glibornurida, gliquidona, repaglinida, clorhidrato de metformina, clorhidrato de buformina, voglibosa, acarbosa, epalrestat, miglitol, insulina, clorhidrato de pioglitazona, maleato de rosiglitazona, picolinato de cromo/biotina, V-411, interleucina-11 humana recombinante, daclixirnab (daclizumab), losartan de potasio, captopril, clorhidrato de imidapril, ácido alfa-lipoico, clorhidrato de levacecarnina (acetil-L-carnitina, levocarnitin acetilo), captopril, retilina, verteporfin, benfotiamina y fluocinolon acetónido se utilizan en combinación como agentes farmacéuticos concomitantes para el compuesto de la presente invención. También utilizados como agentes farmacéuticos concomitantes están la balaglitazona, rivoglitazona, isaglitazona (netoglitazona), clorhidrato de criptolepina, acetato de triproamilina (pramlintida), hidrato de mitiglinida cálcica, muraglitazar,

tesaglitazar, oxeglitazar, insulina glulisina, insulina detemir, monoconjugado 2 de hexil-insulina, inhalador de insulina AeroDose, AIR-insulina, Technosphere/insulina, insulina ADNr, cualquier otra insulina humana inhalada, pulmonar u oral humana, exendin-4, sulfostin, liraglítido, amida del péptido 1 similar al glucagon, recombinante (7-36) (AC-2592), dexlipotam, ciclipostin R, ramipril, ácido deshidrotrametenólico, famoxin, metoxima-3,4-defostatina, demetilasterriquinona B-1, adiponectina (humana), salacinol, leporin B, TAK-654, MBX-102, ADD-9918, ADD-9922, NN-304, NN-344, BIM-51077, LABI (NN-1215), SNAC/Insulina, LAF-237, 823093, 825964, 815541, P93/01, SSR-162329, LY-510929 (LY-929), LBL-752 (DRF-MDX8, DRF-4158), GW-677954, LY-307161 SR, CJC-1131, SUN-E7001, ZP-10A (AVE-0010), MB-6322 (CS-917), BVT-2498, péptido INGAP, LY-818, TH-9507, ISIS-113715, SR-58611, YM-178, SB-418790 (AZ-40140, GW-427353), N-5984, NN-2501, RF-1051, HMR-1426, NOX-700, ATL-962, 869682, R-1439, R-765, GW-501516, GI-181771, ST-1326, VDO-52, A-348441, BLX-1002, TLK-19781, ZYH-2, BLX-2001, NC-1567, R-1440, (FMS)3-insulina, péptido de la cadena B de la insulina (9-23), insulina estabilizada con Genapol, insulina transdérmica, metreleptina (leptina humana de metionil recombinante), terapia con islotes de neogénesis, NBI-6024, NN-344, O-346, DiaPep227 (AVE-0277), TRX-4, rhGAD65, rhIGF-I (rhIGFBP-3), R-1524 (ISA-247, ISAtx-247), TRX-4-TolerMab, MnTE-2-Pyp5+ (AEOL-10113), CTCM-226, irbesartan, telmisartan, candesartan cilexetil (hexetil), pratosartan, piridoxamina (piridoxilamina), litoespermato B de magnesio (sal se magnesio del ácido litoespérmico B),

sulodexida, aminoguanidina (pimagedina), pirfenidona, 1D11, CR-002, T-8, (+)-A-127722 (A-147627, ABT-627), ED-4914, fidarestat, clorhidrato de nefazodona, clorhidrato de venlafaxina, pregabalina, hidrato de mesilato de ruboxistaurina, factor de crecimiento nervioso humano recombinante, capsavanil, dronabinol/cannabidiol, atexacina alfa (interleucina-6), clorhidrato de memantina, dexlipotam, beraprost sódico, maleato de arimoclomol, SX-3201 (AS-3201, SX-3030), TAK-428, QR-333, clorhidrato de ruboxistaurina, acetato de octreótido, aminoguanidina (pimagedina), pegaptanib octasódico, hialuronidasa, sescandelina, batimastat, angiopoyetina-1 recombinante, LY-338522, BIM-23190, AdPEDF.11 (Ad(GV)PEDF.11D), VEGF Trap (VEG Trap(R1R2), CVT-3634, y lo similar. De manera preferida, otros agentes terapéuticos para la diabetes incluyen preparaciones de insulina, secretagogos de insulina, biguanida, inhibidores de la α-glucosidasa y mejoradores de la sensibilidad a la insulina, tales como insulina, glibenclamida, tolbutamida, nateglinida, clorhidrato de metformina, voglibosa y clorhidrato de pioglitazona.

Como agentes terapéuticos para la hiperlipidemia, que se utilizan como agentes farmacéuticos concomitantes, pueden mencionarse los inhibidores de la HMG-CoA reductasa (estatinas), fibratos, inhibidores de la expresión de TNFSF6, agentes que incrementan el colesterol de HDL, mejoradores de la expresión de ApoA1, inhibidores de la expresión de SPP1 (osteopontina), fármacos que actúan sobre los receptores activados por el proliferador de la peroxisoma (PPAR), antagonistas del PPAR-alfa,

estimulantes del factor de eliminación de la lipasa, antagonistas del colesterol, antagonistas de agregación de las plaquetas, antioxidantes, inhibidores de la biosíntesis del colesterol, sobrerreguladores del receptor de LDL, secuestrantes del ácido biliar, inhibidores de la absorción del colesterol y ácidos nicotínicos. También pueden mencionarse los inhibidores de ACAT, agonistas de la adenosina A1, inhibidores de la expression de ApoB, inhibidores de la secreción de ApoB, inhibidores de la proteína de transferencia de los triglicéridos microsomales (MTP), agentes que incrementan el colesterol de HDL, inhibidores de la proteína de transferencia del éster de colesterilo (CETP), inhibidores del transportador del ácido biliar ileal, mejoradores de la sensibilidad a la insulina, antagonistas del PPAR-alfa, agonistas del PPAR-gamma, agonistas del PPAR-delta, inhibidores de la escualeno sintasa, agonistas de testosterona, inhibidores de la 11beta-hidroxiesteroide deshidrogenasa, inhibidores de la 15-lipoxigenasa, antagonistas de 5-HT2, mejoradores de la expresión de ABCA1, inhibidores de la ACAT, agonistas RXR retinoides, agonistas del receptor X del hígado (LXR), inhibidores de la acetil-CoA carboxilasa, inhibidores de la acetil-CoA tiolasa, agonistas de la adenosina A2A, activadores de la adenylato ciclasa, inhibidores del adiposito FABP (aP2), inhibidores del queratinocito FABP (k-FABP), inhibidores de la aldosa reductasa, inhibidores de la angiogénesis, agentes anti-ICAM-1, antioxidantes, antagonistas de VCAM-1, antiestrógenos, agonistas de estrógenos, inhibidores de la peroxidación de lípidos, inhibidores de la secreción de ApoB, agentes que disminuyen el ApoB-100, inductores de

la apoptosis, inhibidores de la apoptosis, inhibidores de la ATP citrato liasa, agonistas del adrenoceptor beta-3, bloqueadores del canal de calcio, inhibidores de la carnitina O-palmitoiltransferasa, inhibidores de la colesterol esterasa, fármacos que actúan en los receptores X farnesoides (FXR), agonistas del receptor X farnesoide (FXR), fármacos que actúan en los receptores de la hormona tiroides, fármacos que actúna en las hormonas de la tiroides, hormonas de la tiroides, hormonas de la paratiroides, inhibidores de la farnesil transferasa, inhibidores de la glucógeno fosforilasa a, inhibidores de la lanosterol 14alfa-desmetilasa, inhibidores de la lanosterol sintasa, antagonistas de la histamina H1, inhibidores de la óxido nítrico sintasa, antagonistas del tromboxano A2, inhibidores de la triacilglicerol lipasa, inhibidores de la alfa-glucosidasa, sobrerreguladores del receptor de LDL, inhibidores de la expresión de LYPLA1, fármacos antiinflamatorios no esteroidales, inhibidores de PDGFR, inhibidores de la fosfolipasa A2, antagonistas del factor de activación de las plaquetas (PAF), activadores del canal de potasio, prostaglandinas, ligandos SCAP, inhibidores de la escualeno epoxidasa, moduladores selectivos del receptor de estrógenos (SERM), inhibidores de la esterol DELTA14-reductasa, antagonistas de la vasopresina V1a, y lo similar. Por ejemplo, la lovastatina, pravastatina (eptastatina) sódica, fluvastatina (fluindostainina) sódica, rosuvastatina de calcio, atorvastatina de calcio, simvastatina (sinvinolina), pitavastatina (itavastatina, nisvastatina) de calcio, ronifibrato (ronifibrato), binifibrato (binifibrato), clinofibrato, ciprofibrato, clofibrato, etofibrato, fenofibrato, bezafibrato, gemfibrozil, acipimox, éster

etílico del ácido eicosapentaenoico (icosapent, icopenato, icosapentato), probucol, policosanol, clorhidrato de colesevelam, colestiramina (resina de colestiramina), clorhidrato de colestipol, colestimida (colestilan), ezetimibe y niacina (ácido nicotínico) se utilizan en combinación como los agentes farmacéuticos concomitantes para el compuesto de la presente invención. También utilizados como agentes farmacéuticos concomitantes son el pactimibe, eflucimibe, implitapide, vesículas unilaminares grandes, fosfato de campestanol ascorbilo, fosfato de sitostanol ascorbilo, besilato de amlodipino, GW-493838, RPR-749, BAY-13-9952, CP-346086, BTG-511, JTT-705, LY-518674 (LY-674), ESP-31015 (ETC-1001), ETC-642 (ESP-24228, RLT), DRF-4832, S-8921, LY-510929 (LY-929), GW-501516 (GW-516), FM-VP4, JTT-130, GW-590735, 641597, KRP-101, TAK-475, HE-2200 (3beta,7beta,17beta-androstenetriol), D-003, PLT-732, NS-220, KS-01-019, AZD-7806, AZD-4619, AZD-6610, AZD-8294, ZYH-1, DRF-10945, SMP-797, y lo similar.

Como el agente terapéutico para la obesidad, que se utilizan como los agentes farmacéuticos concomitantes, pueden mencionarse el mazindol, inhibidores de la lipasa, inhibidores dobles de la recaptación de 5-HT/norepinefrina, inhibidores de la recaptación de 5-HT, suplementos herbales que contienen efedrina y cafeína, gonadotropinas coriónicas humanas, agonistas adrenoceptores, metamfetamina, fentermina y amfepramona. También pueden mencionarse los fármacos que actúan en los receptores cannabinoides, los antagonsitas del receptor CB1 cannabinoide, agonistas inversos sel receptor CB1 cannabinoide, factor neurotrófico ciliar

(CNTF), hormonas de crecimiento, secretagogos de la hormona de crecimiento, inhibidores de la triacilglicerol lipasa, mejoradores de la expresión de ABCA1, inhibidores de la acetil-CoA carboxilasa, inhibidores del adiposito FABP (aP2), inhibidores de la aldosa reductasa, inhibidores de la alfa-glucosidasa, inhibidores de la alfa-manosidasa, inhibidores de la citrato liasa del ATP, agonistas del receptor de la adenosina A1, inhibidores de la serina carboxipeptidasa, inhibidores de la 11beta-hidroxiesteroide deshidrogenasa, receptores que actúan en el neuropéptido Y (NPY), agonistas del receptor del neuropéptido Y2 (NPY Y2), antagonistas del receptor del neuropéptido Y1 (NPY Y1), antagonistas del receptor del neuropéptido Y5 (NPY Y5), antagonistas de CCK, agonistas de CCK1 (CCKA), antagonistas de CCK2 (CCKB/gastrina), antagonistas de CRF1, agonistas de CRF2, fármacos que actúan en los receptores de la hormona que concentra lal melamina (MCH), antagonistas del receptor de la MCH, fármacos que actúan en los receptores de melanocortina, agonistas de la melanocortina MC1, agonistas de la melanocortina MC3, agonistas de la melanocortina MC4, agonistas de la melanocortina MC5, antagonistas del receptor de la orexina, antagonistas de la orexina OX-1, antagonistas de la orexina OX-2, agonistas de la neurotensina, antagonistas de la taquicinina NK2, fármacos que actúan en las hormonas de la tiroides, agonistas del receptor beta de las hormonas de la tiroides, antagonistas de la galanina GAL1, agonistas inversos del receptor de GHS (Grelina), moduladores del receptor glucocorticoide, agonistas del adrenoceptor beta-2, antagonistas del adrenoceptor beta-2, agonistas del

adrenoceptor beta-3, antagonistas del adrenoceptor-alfa-2, inhibidores de MAO, antagonistas de dopamina D1, antagonistas de dopamina D5, inhibidores de la recaptación de la dopamina, fármacos que liberan dopamina, inhibidores de la recaptación de norepinefrina, fármacos que actúan en los receptores de 5-hidroxitriptamina, estimulantes que liberan 5-HT, antagonistas de 5-HT1A, agonistas de 5-HT1B, fármacos que se unen a los receptores de 5-HT2, antagonistas de 5-HT2A, agonistas de 5-HT2B, agonistas de 5-HT2C (5-HT1C), fármacos que se unen a los receptores de 5-HT6, antagonistas de 5-HT6, fármacos que se unen a los receptores de la histamina H3, antagonistas de la histamina H3, antagonistas opiodes, antagonistas kappa-opioides, agonistas de estrógenos, moduladores selectivos del receptor de estrógeno (SERM), inhibidores de la secreción de apoB, inhibidores de la proteína de transferencia de los triglicéridos microsomales (MTP), benzodiacepinas, agonistas del receptor del sitio GABA(A) BZ, oligonucleótidos inhibidores de la expresión de EBPA, inhibidores de la SAPK1 (JNK), inhibidores de DAT, inhibidores de NET, inhibidores de SERT, inhibidores de la dipeptidil-peptidasa IV, fármacos que actúan en los receptores del péptido 1 similar al glucagon (GLP-1), inhibidores de la tripeptidilo peptidasa II, fármacos que actúan sobre los receptores activados por el proliferador de la peroxisoma (PPAR), antagonistas del PPAR-alfa, agonistas del PPAR-gamma, antagonistas del PPAR-gamma, agonistas parciales del PPAR-gamma, agonistas del PPAR-delta, agonistas del retinoide RXR, antagonistas del retinoide RXR, inhibidores de la ácido graso sintasa,

inhibidores de la glucógeno fosforilasa, inhibidores de la HMG-CoA reductasa, inhibidores de la proteína tirosina fosfatasa (PTP)-1B (diferentes a los compuestos de la invención), metaloporfirinas, inhibidores de la óxido nítrico sintasa, fármacos antiinflamatorios no esteroidales, inhibidores de la fosfodiesterasa III, inhibidores de la fosfodiesterasa PDE3B, inhibidores de SGLT-1, inhibidores de SGLT-2, ligandos del receptor sigma, y lo similar. Por ejemplo, el mazindol, orlistat, monohidrato del clorhidrato de sibutramina, clorhidrato de fluoxetina, gonadotropina coriónica (humana), terapia VNS utilizando el Sistema NCP, metaraminol, clorhidrato de d-metamfetamina, fentermina, clorhidrato de amfepramona (dietilpropion), clorhidrato de benzfetamina y tartrato de fendimetracina se utilizan en combinación como agentes farmacéuticos concomitantes para el compuesto de la presente invención. También se utilizan como agentes farmacéuticos concomitantes el clorhidrato de rimonabant, SR-147778, CNTF (Ax15) (RG-228, RPN-228), axocina pegilada, GI-181771, SR-146131, SR-125180, AOD-9604, ATL-962, PYY3-36 (AC-162352), N-5984, L-796568, ácido garciniánico (ácido (-)-hidroxicítarico), HMR-1426, P-57, 1954, picolinato de cromo/ácido linoleico conjugado, S-2367, APD-356, BVT-5182, Ucn II, C-75, gAcrp30, KB-141, NLC-002, BLX-2002, P-64, T-71 y lo similar.

Como agentes terapéuticos para la hipertensión que son utilizados como agentes farmacéuticos concomitantes, pueden mencionarse las tiazidas, antagonistas de la aldosterona, bloqueadores adrenérgicos de las neuronas, bloqueadores del canal del calcio; antagonistas de la dopamina D2,

antagonistas del adrenoceptor beta, agonistas del adrenoceptor alfa2, activadores de la guanilato ciclasa, antagonistas del adrenoceptor beta1, antagonistas del adrenoceptor alfa1, antioxidantes, inhibidores de la enzima que convierten la angiotensina-I (ACE), inhibidores de intercambio de Na+/H+, antagonistas del adrenoceptor alfa, donadores de óxido nítrico, antagonistas de 5-HT2, activadores del canal de K(ATP), estimulantes de la prostaglandina sintasa diurética del potasio sobrante, agonistas del receptor de la imidazolina I1, antagonistas de la angiotensina AT1, agonistas de la dopamina D1, estimulantes de la guanilato ciclasa, antagonistas del receptor de la endotelina ETA, antagonistas del receptor de la endotelina ETB, mejoradores de la expresión de NOS3, análogos de la prostaciclina, prostaglandinas, antagonistas de la angiotensina II, agonistas de la absorción del electrolito, antagonistas nicotínicos, agonistas de la dopamina D2, inhibidores de la prolactina, antagonistas del factor de activación de las plaquetas (PAF), antagonistas de agregación de las plaquetas, antagonistas del factor de necrosis del tumor, inhibidores de la cinasa Rho, antagonistas PPAR-alfa, moduladores del receptor AMPA; antagonistas del receptor GABA(A) e inhibidores de la fosfodiesterasa V (PDE5A). También pueden mencionarse los agonistas del receptor de 5-HT1A, antagonistas de 5-HT1B, {antagonistas de 5-HT2}, antagonistas de 5-HT2A, inhibidores de ACAT, agonistas de la adenosina A1, antagonistas de la adenosina A1, agonistas de la adenosina A2A, antagonistas de la adenosina A2A, activadores de la adenilato ciclasa, bloqueadores adrenérgicos de las neuronas, inhibidores de AGE (inhibidores

de la reacción de Maillard), inhibidores de la aldosa reductasa, {antagonistas de la aldosterona}, alcaloides, ligandos del adrenoceptor alfa, {antagonistas del adrenoceptor alfa, antagonistas del adrenoceptor alfa1}, antagonistas del adrenoceptor alfa1A, {agonistas del adrenoceptor alfa2}, antagonistas del adrenoceptor alfa2, antagonistas del adrenoceptor beta2, {antagonistas del adrenocetor beta, antagonistas del adrenoceptor beta1}, agonistas del adrenoceptor beta2, péptidos natriuréticos alfa atriales, {moduladores del receptor AMPA}, inhibidores de la angiogénesis, inhibidores de la apoptosis, {inhibidores de la enzima que convierte la angiotensina-I (ACE), antagonistas de la angiotensina AT1 }, antagonistas de la angiotensina AT2, antagonistas del receptor de la angiotensina, fármacos antiinflamatorios, depuradores de radicales libres, {antioxidantes,} activadores del canal de calcio, {bloqueadores del canal de calcio}, bloqueadores del canal del calcio del tipo L, {antagonistas del factor de activación de las plaquetas (PAF)}, inhibidores de la fosfodiesterasa cAMP, agonistas del cannabinoide CB2, agonistas del receptor cannabinoide, agonistas del receptor vanilloide VR1, inhibidores de la quimasa, inhibidores de la ciclooxigenasa-2, agonistas del autorreceptor de la dopamina, agonistas del receptor de la dopamina, agonistas de la dopamina D1, {agonistas de la dopamina D2}, antagonistas de la dopamina D1, {antagonistas de la dopamina D2}, inhibidores de la dopamina-beta-monooxigenasa, antagonistas del receptor de la endotelina, {antagonistas del receptor de la endotelina ETA, antagonistas del receptor de la endotelina ETB}, agonistas del receptor de la endotelina, inhibidores de la enzima que

convierte la endotelina, inhibidores de la encefalinasa, {antagonistas del receptor GABA(A)}, inhibidores de la glicógeno fosforilasa a, inhibidores de la liberación de la hormona del crecimiento, análogos de la somatostatina, {activadores de la guanilato clicasa}, agonistas de la histamina H1, antagonistas de la histamina H1, inhibidores del factor 1-alfa que induce hipoxia (HIF-1alfa), fármacos que actúna en los receptores de imidazolina, {agonistas del receptor de la imidazolina I1}, análogos de la insulina (complejos de zinc), mejoradores de la sensibilidad a la insulina, {antagonistas de PPAR-alfa}, agonistas de PPAR-gamma, agentes reductores de la insulina, {activadores del canal K(ATP)}, bloqueadores del canal K(ATP), inhibidores de la lipoxigenasa, activadores del canal BK(Ca) de conductancia amplia, {inhibidores de intercambio de Na+/H+}, inhibidores de Na+/K+-ATPasa, inhibidores de NADPH oxidasa, inhibidores de neprilisina, antagonistas del neuropéptido Y1 (NPY Y1), agonistas del neuropéptido Y4 (NPY Y4), {antagonistas nicotínicos}, nitratos, {donadores de óxido nítrico}, fármacos antiinflamatorios no esteroidales, inhibidores de la proteína cinasa C (PKC), {mejoradores de la expresión de NOS3}, oligonucleótidos, inhibidores de PDGFR, inhibidores de la fosfodiesterasa, inhibidores de la fosfodiesterasa I, inhibidores de la fosfodiesterasa III, inhibidores de la fosfodiesterasa IV, {inhibidores de la fosfodiesterasa V (PDE5A)}, activadores del canal de potasio, {análogos de la prostaciclina, prostaglandinas}, agonistas prostanoides IP, antagonistas prostanoides TP (tromboxano A2), inhibidores de la tromboxano sintasa, inhibidores de la proteasa, inhibidores de la

proteasoma, inhibidores de la proteína cinasa C (PKC), inhibidores de la renina, {inhibidores de la cinasa Rho}, antagonistas del receptor sigma, bloqueadores del canal del sodio, tiazidas, agentes reductores de triglicéridos, antagonistas de la vasopressina, antagonistas de la vasopressina V1a, antagonistas de la vasopressina V2, y lo similar. Por ejemplo, se utilizan la clorotiazida, hidroclorotiazida, hidroflumetiazida, meticlotiazida, politiazida, xipamida, ciclopentiazida, bendroflumetiazida (bendrofluazida), espironolactona, epoximexrenona (eplerenona), monosulfato de guanetidina, sulfato de guanadrel, verapamil, clorhidrato de propranolol, clorhidrato alprenolol, pindolol, clorhidrato de oxprenolol, maleato de timolol, clorhidrato de sotalol, clorhidrato de acebutolol, clorhidrato de carteolol, sulfato de mepindolol, clorhidrato de arotinolol, clorhidrato de indenolol, clorhidrato de tertatolol, clorhidrato de celiprolol, clorhidrato de tilisolol, nebivolol, sulfato de penbutolol, nadolol, clorhidrato de cloranolol, clorhidrato de bevantol (bevantolol), clonidina, clorhidrato de guanfacina, clorhidrato de diltiazem, clorhidrato de nicardipina, nitrendipina, felodipina, nilvadipina; nivadipina, nisoldipina, clorhidrato de benidipina, besilato de amlodipina, clorhidrato de franidipina (manidipina), lacidipina, isradipina, clorhidrato de barnidipina (mepirodipina), clorhidrato etanólico de efonidipina, cinaldipina (cilnidipina), aranidipina, clorhidrato de lercanidipina (masnidipina), azelnidipina, amlodipina, manidipina (franidipina), nitroprussida sódica, atenolol, tartrato de metoprolol, clorhidrato de betaxolol, bopindolol, fumarato de bisoprolol, clorhidrato de esmolol, carvedilol, succionato de metoprolol, talinolol,

clorhidrato de prazosina, urapidil, clorhidrato de indoramina, clorhidrato de bunazosina, clorhidrato de terazosina, mesilato de doxazosina, urapidil, nifedipina, captopril, maleato de enalapril, lisinopril, perindopril, alacepril, ramipril, clorhidrato de quinapril, clorhidrato de delapril, clorhidrato de benazepril, cilazapril, fosinoprilat, fosinopril sódico, trandolapril, espirapril, clorhidrato de temocapril, clorhidrato de moexipril, clorhidrato de imidapril, zofenopril de calcio, enalaprilat, zofenoprilat, clorhidrato de amilorida, clorhidrato de labetalol, nipradilol (nipradolol), linsidomina, quetanserina, pinacidil, cicletanina (cicletanida), clorhidrato de amosulalol, hidrato del clorhidrato de moxonidina, losartan potásico, valsartan, mesilato de eprosartan, candesartan cilexetilo (hexetilo), irbesartan, telmisartan, olmesartan medoxomilo, mesilato de fenoldopam, cadralacina, fosfato diácido de rilmenidina, bosentan, beraprost sódico, limaprost alfadex (alfa-ciclodextrina), uniprost (treprostinilo sódico), iloprost (ciloprost), clorhidrato de mecamilamina, metergolina, acetato de guanabenz, cloricromeno, fasudilo, doconexent (ácido docosahexaenoico), ciclotiazida, citrato de sildenafil, clortalidona (clortalidona), quinetazona, indapamida, metolazona, clorhidrato de fenoxibenzamina, metirosina (metirosina), diazóxido, torasemida (torsemida), clopamida, clorhidrato de hidralacina, reserpina y metildopa en combinación como agentes farmacéuticos concomitantes para el compuesto de la presente invención. También pueden utilizarse como agentes farmacéuticos concomitantes el omapatrilat, aladotril (alatriopril, fasidotril), AVE-7688 (MDL-107688), 796406, lemildipina, pranidipina, clevidipina,

levamlodipina ((S)-amlodipino), ambrisentan, sitaxsentan sódico, SPP-301 (R-639, RO-67-0565), TBC-3711, PMD-2850 (vacuna de angiotensina), PMD-3117, Binodenoson, cloruro de alagebrio, SLV-306, fumarato de aliskiren, NV-04, MC-4232, ENO, MDL-72832, BP-554, (+)-OSU-191 (OSU-191-(+), U-86192A), WAY-100339, QF-303B (QF-0303B), QF-307B (QF-0307B), QF-311B (QF-0311B), lidanserina (ZK-33839), AP-1067, AHR-16303B, QF-313B (QF-0313B), S-14280, S-35031, S-35120, PR-1173, RG-14718, CCPA, S-ENBA, Sch-59761, FR-166124, GU-285, MDL-101483, CVT-2995, CVT-3032, CVT-3033, 2HE-NECA (HENECA), CGS-21680, CGS-22492, CGS-22989, SHA-40, APEC, KF-17837, OPB-9195, sal de magnesio del ácido litoespérmico B (litoespermato de magnesio B), 6-yodoamilorida, 6-protoberberina (PTB-6), CR-2991, HSR-175, CDRI-93/478, DC-015 (DC-028, DL-028A), BAM-2202, GB-67, YM-11133, Abbott-65265, SK&F-104856, MG-1, L-765314, KMUP-880602, A-68828, YC-1, AB-47, C-112, utibaprilat, FPL-63674 (FPL-63674XX, FPL-63547-diácido), FPL-66564, MDL-100173, MDL-27467A, glicopril, ROO 911, SQ-31440, DU-1777, S-nitrosocaptopril (SNOCAP), Y-23785, nitrato de enalapril, moexiprilat (RS-10029), temocaprilat (RS-5139), CV-5975, imidaprilat (6366 A), REV-6134, BW-B385C, CGS-26582, SA-6817, SA-7060, Sch-54470, S-alilmercaptocaptopril (CPSSA), RB-106, MDL-101628, mixanpril, fasidotrilat (alatrioprilat), BMS-182657, ER-32897, ER-32935, ER-40121, ER-40133 (E-4030), CGS-28106, CGS-30440, Sch-50690, A-81282 (Abbott-81282), A-81988, GA-0050, GA-0113, ZD-7155, RU-63455, RU-64276, RU-65868, embusartan (Bay-10-6734), BIBS-39, BMS-

180560, BMS-181688, BMS-184698, EXP-063, EXP6155, EXP-7711 (IMI), EXP-9270, S-8308, XD-937, XH-148, UP-221-78, UP-275-22, FI-6828K, FR-130739, FR-143187, FR-149581, LR-B/087, RWJ-38970, RWJ-46458, WK-1492 (WK-1492.2K), KR-31080 (SK-1080), KT3-579, KT3-866, KW-3433, LY-285434, LY-301875, LY-302289, L-158338, L-158659, L-158978, L-159093, L-159689, L-161177, L-162154, L-162223, L-162234, L-162393, L-162474, L-163313, L-163579, EMD-69943, EMD-90423, tisartan (CGP-48369), abitesartan (CGP-49870), CP-161418, CP-191166, PD-123177 (EXP-655), PD-123319, PD-150304, SC-50560, SC-51316, SC-51757, SC-51895, SC-54628, SC-54629, U-97018, RWJ-47639, TH-142177, CV-11194, 606A, TA-606, LCY-018, CR-3210, UP-275-13, UR-7198, UR-7280, WK-1260, CL-190133 (CL-332877, CL-190733, CL-190734), WAY-126227, YM-31472, EXP-408, XR-510, L-161021, L-162389, L-162441, L-162537, L-163007, L-163017, L-163958, BMS-248360, DMP-811 (DuP-811, L-708404), SB-203220, LR-B/057, L-159913, L-161816, sesamina, ferulinolol, PF-9104, TZC-1370, O-palmitoil tilisolol, BG6, TZC-8159, Y-22516, clorhidrato de olradipina (S-11568), PCA-50938, H-324/38, ZM-224832, HP-406, BMY-43011, SQ-32321, SQ-32547, SQ-33351, elnadipina, rincofillina, SUN-5647, VULM-999, DCDDP, sagandipina, GR-60139, Goe-5584-A, bromhidrato de siratiazem LR-A/113), GS-386, sornidipina, MCF-1084, MCF-1113, dibudipina, nifedipina deuterada (ISA-1058), McN-6497 (RWJ-26902), CRL-41695, (4S)-(+)-AE0047, Y-24149, s-petasina, NIP-101, UK-52831, UK-55444, UK-56593, UK-51656, P-1268, BBR-2160, RS-88007, RS-5773, SL-85.1097, 83-0256, 83-0327, S-312 (83-

0312), MR-14134, AHR-12742, AHR-16462B, AHR-5360C (AHR-5360), BMY-20014, BMY-20064, BMY-42803, veroxan, labedipinadilol B, labedipinadilol A, FR-172516, vanidipinadilol, xantonolol, Z-6568, F-1850, Wy-27569, M-54033, HU-308, arvanil, BL-3875, BL-4027, TEI-E00548, rutaecarpina (rutecarpina), PD-139899, FPL-65447AA, Z-12571, Z-7760, (S)-Z-11410, FR-138104, MDL-43925, SK&F-102698, A-292438, A-306552, RPR-117820A, RPR-118031A, J-105510, J-105859, J-112287, BMS-182874, TBC-11040, TBC-11192, TBC-2576, TBC-3214, SB-247083, EMD-122946, EMD-94246, fandosentan de potasio (CI-1034, PD-180988), PABSA, YM-62899, YM-91746, LU-302872 (BSF-420627, LU-420627), BMS-187308, IRL-3630, L-747844, RPR-111844, PD-163070, PD-166309, PD-142893, A-192621, CGS-31398, IRL-1620, BQ-485, FR-901366 (WS-009A), KET-011, RES-701-1 (KF-20704), L-744453, L-749329, L-749805, IRL-1737, PD-155080, PD-156252, T-0115 (TA-0115), S-17162, WS-79089B (WS-79089-3, FR-901533), SM-19712, CGS-26303, CGS-26393, CGS-30084, CGS-34043, CGS-34225, CGS-34226, CGS-34753, CGS-35066, KC-12792, SQ-28603, CP-91149, BAY-41-2272, BAY-41-8543, BAY-58-2667, KMUP-1, metilhistaprodifen, suprahistaprodifen, S-23515, S-23757, LNP-509, LNP-911, Zn(car)2Cl2, DRF-4158 (DRF-MDX8, LBL-752), DY-9804, MJ-355, BPDZ-79, BPDZ-83, YM-099, sarakalim (RS-91309), PNU-96293, NS-1608, CPU-23, PST-2107, apocinina, CGS-24128, CGS-24592, CGS-25155, H-394/84, BIBO-3304, 1229U91 (GR-231118, BW-1229U91, GW-1229), RS-7897, C92-4609 (CAS-1609), CHF-2363 (SN011), PROLI/NO, FR-144420, GEA-3175, DS1, NOC-7, MAHMA MONOato, PF-9404, EDTA

(ácido edético), AS-AT1R-ODN mRNA, NX-1975, 5E3623, Sch-51866, Sch-59498, LAS-31180, SK&F-94120, SK&F-95654, Win-63291, DMPPO, DF-100 (A80a), E-4010, zaprinast (M&B-22948), T-1032, clorhidrato de iptakalim, ZM-260384, RP-66784, S-0121, BMS-182264, KC-399, KC-515, SG-209, DY-9708, ER-001533, RWJ-26629, U-94968, KI-4032, KRN-4884, KR-30818 (SKP-818), P-1060, LM-3339, MCC-134, AL-0671, AL-0670, Y-26763, PC-286, TAK-636, diocleína, UR-8081, UR-8218, UR-8225, UR-8267, CL-188294, LP-805, KMUP-880708, cromakalim, BW-68C, FR-181157, FR-181877, ER-017996, PSI, MDL-29152, A-62198, A-65317, A-68064, A-82110, A-70461, ICI-219623, MDL-73323, MDL-74147, S-2864, BW-175, BILA-2157, SQ-30774, SQ-31844, SQ-33800, JTP-2438, JTP-2724, JTP-3072, JTP-4129, JTV-505 (JTP-4761), KRI-1177, KRI-1314, CGP-44099A, CGP-54061, CGP-55128A, CGP-56346A, CGP-56962A, CGP-62198A, CP-108671, CP-71362, PD-132002, SC-46944, SC-56525, U-77436, Ro-44-9375, Ro-66-1132 (RO-0661132, RO-X1), RO-X2, SPP-600, CL-331049, WAY-121604, YM-21095, YM-26365, hidroxifasudilo, Y-30141, H-1152 (HMN-1152), CNS-1307, Ono-1505, JTV-605, YM-176770, JNJ-17079166, FR-161282, y lo similar.

Como agentes terapéuticos para la trombosis que se utilizan como agentes farmacéuticos concomitantes, pueden mencionarse las preparaciones de heparina, heparinas de bajo peso molecular, análogos de heparina, anticoagulantes, inhibidores de la trombina, preparaciones antitrombina, agentes antiplaquetarios, agentes trombolíticos y lo similar. Por ejemplo, se utilizan la heparina cálcica, heparina sódica, dalteparina sódica,

parnaparina sódica, reviparina sódica, danaparoid sódico, warfarina potásica, argatroban, mesilato de gabexato, mesilato de nafamostat, antitrombina III humana, aspirina, dipiridamol, clorhidrato de ticlopidina, cilostazol, limaprost alfadex, ozagrel sódico, clorhidrato de sarpogrelato, icosapentato de etilo, beraprost sódico, urocinasa, tisocinasa, alteplasa, nasaruplasa, nateplasa, monteplasa, pamiteplasa, batroxobina, citrato de sodio, proteína C y lo similar en combinación como agentes farmacéuticos concomitantes para el compuesto de la presente invención.

En lo siguiente, se proporcionan los ejemplos de los métodos de producción del compuesto de la presente invención, utilizados para practicar la presente invención. Sin embargo, los métodos de producción del compuesto de la presente invención no están limitados a aquéllos ejemplificados a continuación.

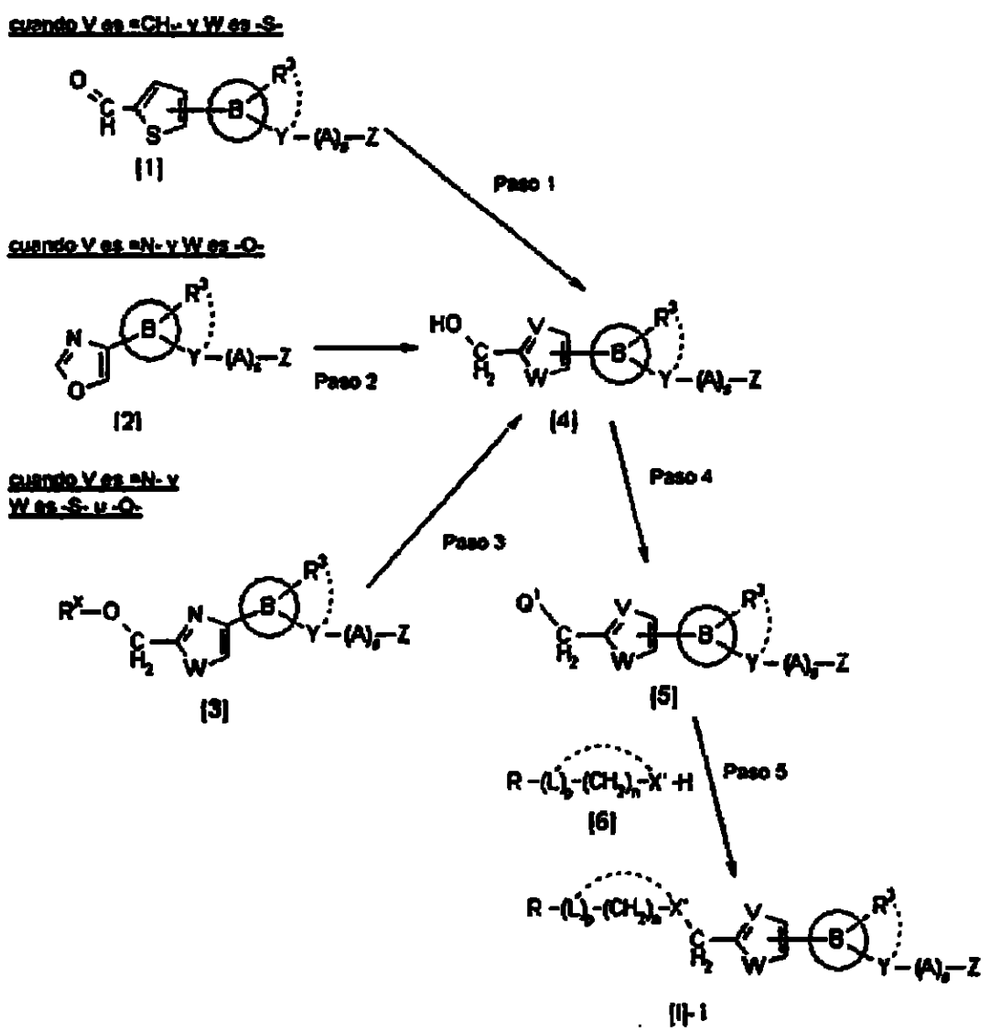
Incluso en la ausencia de una descripción específica en los presentes métodos de producción, puede realizarse la producción eficiente incorporando una modificación en donde sea necesario, tal como introduciendo un grupo protector en un grupo funcional, seguido por la desprotección en un paso posterior, intercambiar el orden del método y los pasos de producción y lo similar.

El tratamiento en cada paso puede realizarse de acuerdo con los métodos empleados generalmente, tales como extracción, lavado, concentración, filtración, ajuste del pH y lo similar, en donde el aislamiento y la purificación pueden realizarse empleando métodos convencionales

adecuados, tales como cristalización, recristalización, cromatografía sobre gel de sílice, HPLC preparativa y lo similar, que puede ser un solo método o dos o más métodos en combinación.

Método de Producción 1

En este Método de Producción, se produce el compuesto [I] en donde m es 1, R^1 y R^2 son cada uno un átomo de hidrógeno y X es $-N(R^4)-$, $-N(R^5)-CO-O-$, -O- o -S-.



en donde Q^1 es un grupo saliente general (por ejemplo, un átomo de halógeno (un átomo de bromo, un átomo de yodo, un átomo de cloro, etc.), un grupo mesiloxi, un grupo tosiloxi, un grupo trifluorometansulfoniloxi, etc.), R^X es un grupo protector de hidroxilo general (por ejemplo, un grupo ter-butildimetilsililo, un grupo benzoilo etc.), X' es $-N(R^4)-$, $-N(R^5)-CO-O-$, -O- o -S-, en donde cada símbolo es como se definió anteriormente y los otros símbolos son como se definió anteriormente.

Paso 1

El compuesto [4] puede obtenerse por la reducción del compuesto [1] en un solvente, utilizando un agente reductor convencional. Como el solvente, pueden mencionarse los alcoholes (metanol, etanol, etc.), solventes de éter (tetrahidrofurano, dioxano, etc.), tolueno y lo similar, y un solvente mezclado de los mismos. Como el agente reductor, puede mencionarse el borohidruro de sodio, borohidruro de litio, diborano, hidruro de litio y aluminio y lo similar. La reacción puede llevarse a cabo de enfriamiento a calentamiento.

Paso 2

El compuesto [4] puede obtenerse haciendo reaccionar el compuesto [2] con paraformaldehído en un solvente, en la presencia de una base para la hidroximetilación. Como el solvente, puede mencionarse el

tolueno, solventes de éter (tetrahidrofurano, éter dietílico etc.) y lo similar y un solvente mezclado de los mismos. Como la base, puede mencionarse una base obtenida utilizando alquillitio (n-butillitio, sec- butillitio, ter-butillitio etc.) y 2,2,6,6-tetrametilpiperidina, diisopropilamina de litio y lo similar. La reacción puede llevarse a cabo con enfriamiento.

Paso 3

El compuesto [4] puede obtenerse mediante la desprotección de R^X del compuesto [3], de acuerdo con métodos convencionales. Cuando R^X es un grupo benzoilo, por ejemplo, el producto objeto puede obtenerse mediante una reacción similar al método ejemplificado en el Paso 30 del Método de Producción 19.

Paso 4

El compuesto [5] puede obtenerse sustituyendo un grupo hidroxilo del compuesto [4] con un grupo saliente convencional, de una manera similar como en el Paso 18 del Método de Producción 10.

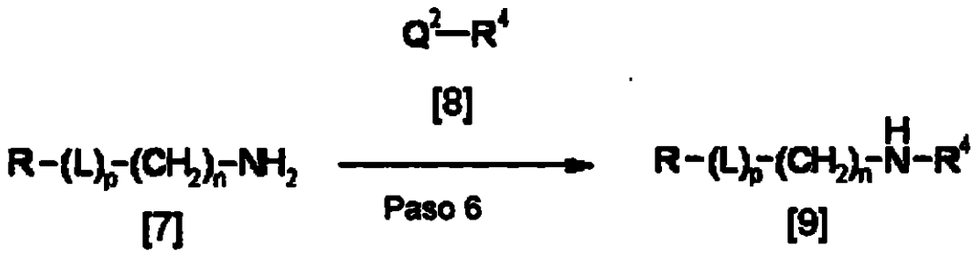
Paso 5

El compuesto [I]-1 puede obtenerse haciendo reaccionar el compuesto [5] con el compuesto [6] en un solvente en la presencia de una base y en la presencia o ausencia de un catalizador. Como el solvente, puede mencionarse la N,N-dimetilacetamida, N,N-dimetilformamida, acetonitrilo,

acetato de etilo, tolueno, solventes de alcohol (metanol, etanol, etc.), solventes de éter (tetrahidrofurano, dioxano, etc.), solventes halogenados (cloroformo, diclorometano, etc.) y lo similar, y un solvente mezclado de los mismos. Como la base, pueden mencionarse las bases inorgánicas, tales como carbonato de potasio, carbonato de sodio y lo similar, y bases orgánicas tales como trietilamina, diisopropiletilamina y lo similar. Como el catalizador, puede mencionarse el yoduro de potasio, sal de amonio cuaternario (yoduro de tetrabutilamonio, bromuro de tetrabutilamonio, etc.) y lo similar. La reacción puede llevarse a cabo de enfriamiento a calentamiento.

Método de Producción 2

En este Método de Producción, de los compuestos [6] utilizados en el Paso 5 del Método de Producción 1, se produce un compuesto en donde X' es -N(R^4)-.



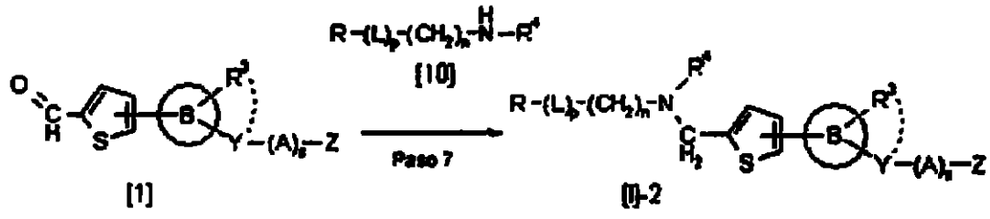
en donde Q^2 es un grupo saliente general, como se describió en el Método de Producción 1 y los otros símbolos son como se definió anteriormente.

Paso 6

El compuesto [9] puede obtenerse haciendo reaccionar el compuesto [7] con el compuesto [8] en un solvente, en la presencia de una base y en la presencia o ausencia de un catalizador. Como el solvente, puede mencionarse la N,N-dimetilacetamida, N,N-dimetilformamida, acetonitrilo, acetato de etilo, tolueno, solventes de alcohol (metanol, etanol, etc.), solventes de éter (tetrahidrofurano, dioxano, etc.), solventes halogenados (cloroformo, diclorometano, etc.) y lo similar y un solvente mezclado de los mismos. Como la base, pueden mencionarse las bases inorgánicas tales como carbonato de potasio, carbonato de sodio y lo similar, y las bases orgánicas tales como trietilamina, diisopropiletilamina y lo similar. Como el catalizador, puede mencionarse el yoduro de potasio, sal de amonio cuaternario (yoduro de tetrabutilamonio, bromuro de tetrabutilamonio, etc.) y lo similar. La reacción puede llevarse a cabo de enfriamiento a calentamiento.

Método de Producción 3

En este Método de Producción, se produce el compuesto [I], en donde V es =CH-, W es -S-, m es 1, R^1 y R^2 son cada uno un átomo de hidrógeno y X es -N(R^4)-.



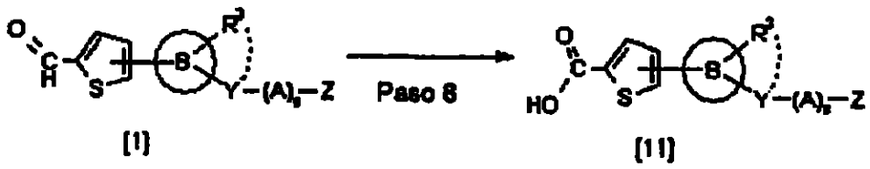
en donde cada símbolo es como se definió anteriormente.

Paso 7

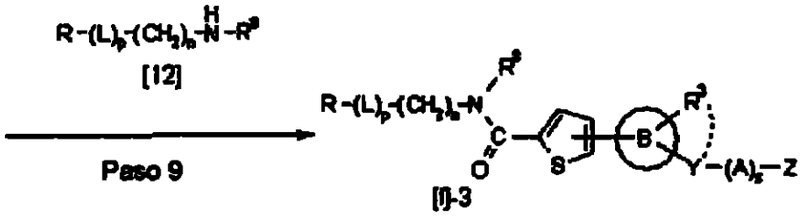
El compuesto [I]-2 puede obtenerse haciendo reaccionar el compuesto [1] con el compuesto [10] en un solvente, en la presencia de un agente reductor y en la presencia o ausencia de una base. Como el solvente, se puede mencionar la N,N-dimetilacetamida, N,N-dimetilformamida, acetonitrilo, acetato de etilo, tolueno, solventes de éter (tetrahidrofurano, dioxano, etc.), solventes halogenados (cloroformo, diclorometano, 1,2-dicloroetano, etc.), solventes de alcohol (metanol, etanol, etc.), ácido acético y lo similar y un solvente mezclado de los mismos. Como el agente reductor, puede mencionarse el borohidruro de sodio, triacetoxiborohidruro de sodio, cianoborohidruro de sodio y lo similar. Como la base, pueden mencionarse las bases orgánicas tales como la piridina y lo similar. La temperatura de reacción es de manera preferida de 0°C - 80°C.

Método de Producción 4

En este Método de Producción, se produce el compuesto [I], en donde V es =CH-, W es -S-, m es 0 y X es -N(R^8)-CO-.



[1] [11]



en donde cada símbolo es como se definió anteriormente.

Paso 8

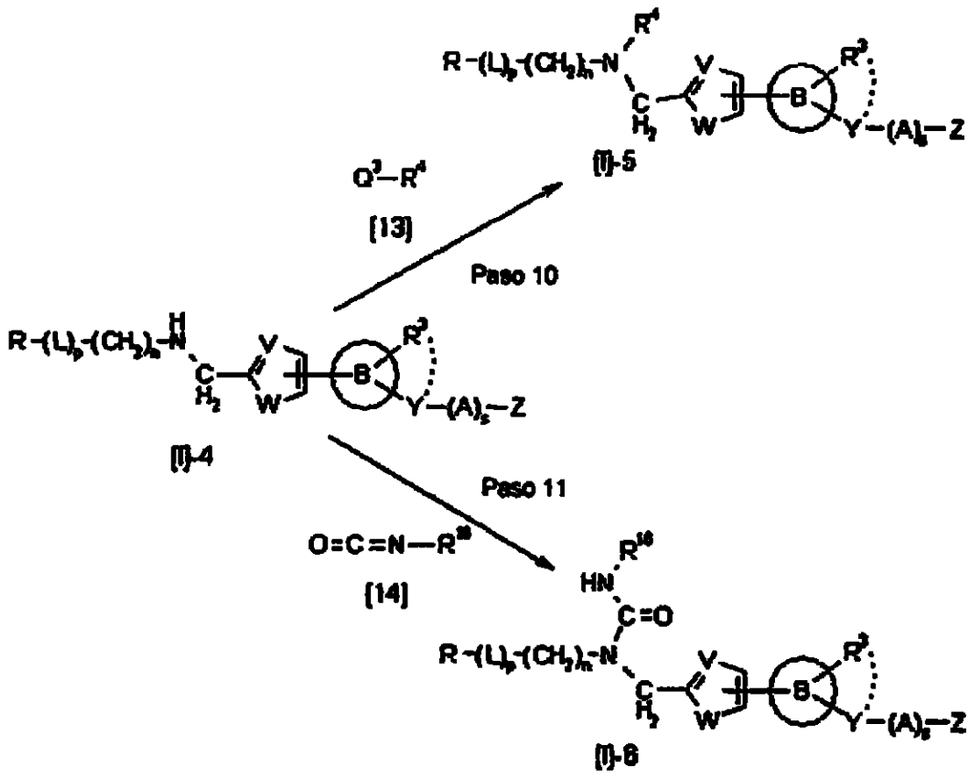
El compuesto [11] puede obtenerse mediante la oxidación del aldehído del compuesto [1], utilizando un agente oxidante convencional en un solvente. Como el solvente, pueden mencionarse los alcoholes (metanol, etanol, etc.), solventes de éter (tetrahidrofurano, dioxano, etc.), acetona, ácido acético, agua y lo similar, y un solvente mezclado de los mismos. Como el agente oxidante, puede mencionarse el clorito de sodio (en donde sea necesario, se agrega un depurador de cloro (ácido sulfámico, etc.)), hipoclorito de sodio, permanganato de potasio, cromato de sodio, nitrato de plata, óxido de plata, 2,2,6,6-tetrametilpiperidin-N-óxido y lo similar. La reacción puede llevarse a cabo de enfriamiento a calentamiento.

Paso 9

El compuesto [I]-3 puede obtenerse mediante la condensación de la amida del compuesto [11] con el compuesto [12] obtenido mediante un método similar a aquél dado en el compuesto [9] en el Método de Producción 2. La condensación de la amida puede realizarse de acuerdo con métodos convencionales. Por ejemplo, puede mencionarse un método que comprende la condensación en un solvente tal como N,N-dimetilformamida, acetonitrilo, tetrahidrofurano, cloroformo, acetato de etilo, cloruro de metileno, tolueno y lo similar, en la presencia de un agente de condensación, tal como diciclohexilcarbodiimida, clorhidrato de la 1-etil-3-(3-dimetilaminopropil)carbodiimida, difenilfosforilazida y lo similar, y en la presencia o ausencia de N-hidroxisuccinimida, 1-hidroxibenzotriazol y lo similar. La temperatura de reacción es de manera preferida de 0°C - 100°C.

Método de Producción 5

En este Método de Producción, se produce el compuesto [I], en donde m es 1, R^1 y R^2 son cada uno un átomo de hidrógeno y X es -N(R^4)-.



en donde Q^3 es un grupo saliente general como se describió en el Método de Producción 1 y los otros símbolos son como se definió anteriormente.

Paso 10

El compuesto [I]-5 puede obtenerse mediante la reacción del compuesto [I]-4 obtenido mediante un método similar a aquél para proporcionar el compuesto [I]-1 en el Método de Producción 1 con el compuesto [13], en un solvente en la presencia o ausencia de una base. Como el solvente, se puede mencionar la N,N-dimetilacetamida, N,N-

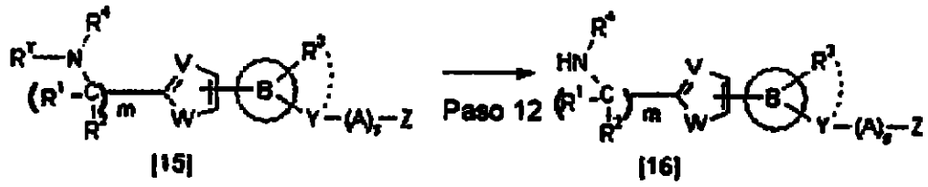
dimetilformamida, acetonitrilo, acetato de etilo, tolueno, solventes de éter (tetrahidrofurano, dioxano, etc.), solventes halogenados (cloroformo, diclorometano, etc.) y lo similar y un solvente mezclado de los mismos. Como la base, se pueden mencionar las bases inorgánicas tales como carbonato de potasio, carbonato de sodio y lo similar y las bases orgánicas tales como trietilamina, diisopropiletilamina y lo similar. La reacción puede llevarse a cabo de enfriamiento a calentamiento.

Paso 11

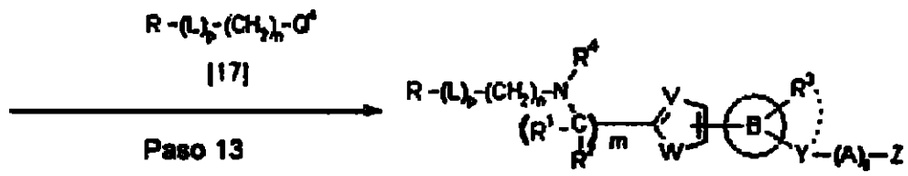
El compuesto [I]-6 puede obtenerse haciendo reaccionar el compuesto [I]-4 con el compuesto [14] en un solvente en la presencia o ausencia de una base. Como el solvente, se puede mencionar la N,N-dimetilacetamida, N,N-dimetilformamida, acetonitrilo, acetato de etilo, tolueno, solventes de éter (tetrahidrofurano, dioxano, etc.), solventes halogenados (cloroformo, diclorometano, etc.) y lo similar y un solvente mezclado de los mismos. Como la base, se pueden mencionar las bases inorgánicas tales como carbonato de potasio, carbonato de sodio y lo similar y las bases orgánicas tales como trietilamina, diisopropiletilamina y lo similar. La reacción puede llevarse a cabo de enfriamiento a calentamiento.

Método de Producción 6

En este Método de Producción, se produce el compuesto [I], en donde m es 1 ó 2 y X es -N(R^4)-.



[15] Paso 12 [16]



Paso 13

[17]

[I-7]

en donde m' es 1 ó 2, Q^4 es un grupo saliente general como se describió en el Método de Producción 1, R^Y es un grupo protector de amina tal como un grupo ter-butoxicarbonilo, un grupo benciloxicarbonilo y lo similar, y los otros símbolos son como se definió anteriormente.

Paso 12

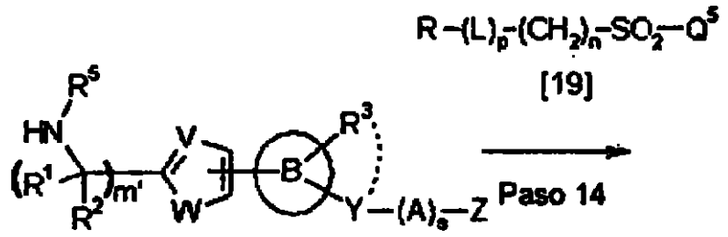
El compuesto [16] puede obtenerse mediante la desprotección de R^Y del compuesto [15]. La desprotección puede realizarse de acuerdo con los métodos convencionales. Por ejemplo, cuando R^Y es un grupo ter-butoxicarbonilo, puede mencionarse un método que comprende la reacción con cloruro de hidrógeno en un solvente tal como dioxano y lo similar. La temperatura de reacción es de manera preferida de 0°C - temperatura ambiente.

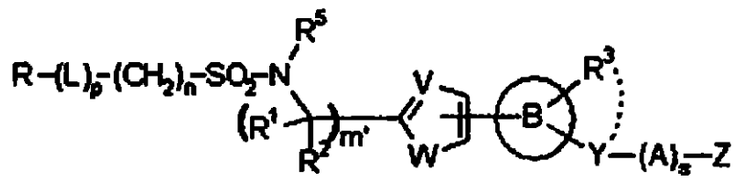
Paso 13

El compuesto [I]-7 puede obtenerse haciendo reaccionar el compuesto [16] con el compuesto [17] en un solvente en la presencia de una base. Como el solvente, se puede mencionar la N,N-dimetilacetamida, N,N-dimetilformamida, acetonitrilo, acetato de etilo, tolueno, solventes de éter (tetrahidrofurano, dioxano, etc.), solventes halogenados (cloroformo, diclorometano, etc.) y lo similar y un solvente mezclado de los mismos. Como la base, pueden mencionarse las bases inorgánicas tales como carbonato de potasio, carbonato de sodio y lo similar y las bases orgánicas tales como trietilamina, diisopropiletilamina y lo similar. La reacción puede llevarse a cabo de enfriamiento a calentamiento.

Método de Producción 7

En este Método de Producción, se produce el compuesto [I], en donde m es 1 ó 2 y X es $-SO_2-N(R^5)-$.





[I]-8

en donde Q^5 es un átomo de halógeno (átomo de bromo, átomo de yodo, átomo de flúor, átomo de cloro, etc.) y los otros símbolos son como se definió anteriormente.

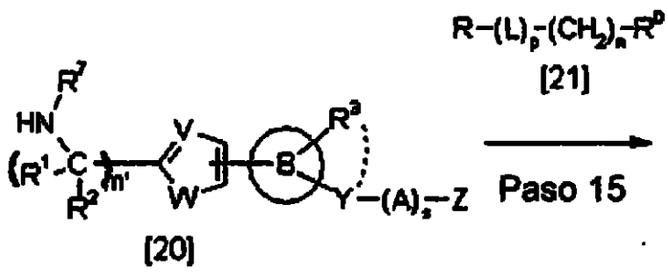
Paso 14

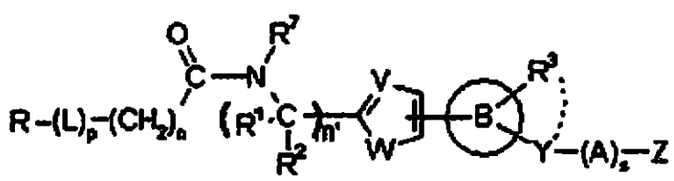
El compuesto [I]-8 puede obtenerse haciendo reaccionar el compuesto [18] obtenido mediante un método similar a aquél para dar el compuesto [16] en el Método de Producción 6 con el compuesto [19], en un solvente en la presencia de una base. Como el solvente, se puede mencionar la N,N-dimetilacetamida, N,N-dimetilformamida, acetonitrilo, acetato de etilo, tolueno, solventes de éter (tetrahidrofurano, dioxano, etc.), solventes halogenados (cloroformo, diclorometano, etc.) y lo similar, y un solvente mezclado de los mismos. Como la base, se pueden mencionar las bases inorgánicas tales como carbonato de potasio, carbonato de sodio y lo similar y

las bases orgánicas tales como trietilamina, diisopropiletilamina y lo similar. La reacción puede llevarse a cabo de temperatura ambiente a calentamiento.

Método de Producción 8

En este Método de Producción, se produce el compuesto [I] en donde m es 1 ó 2 y X es -CO-N(R^7)-.





[I]-9

en donde R^D es un grupo carboxi o un grupo formilo sustituido por un átomo de halógeno (átomo de bromo, átomo de yodo, átomo de flúor, átomo de cloro, etc.), y los otros símbolos son como se definió anteriormente.

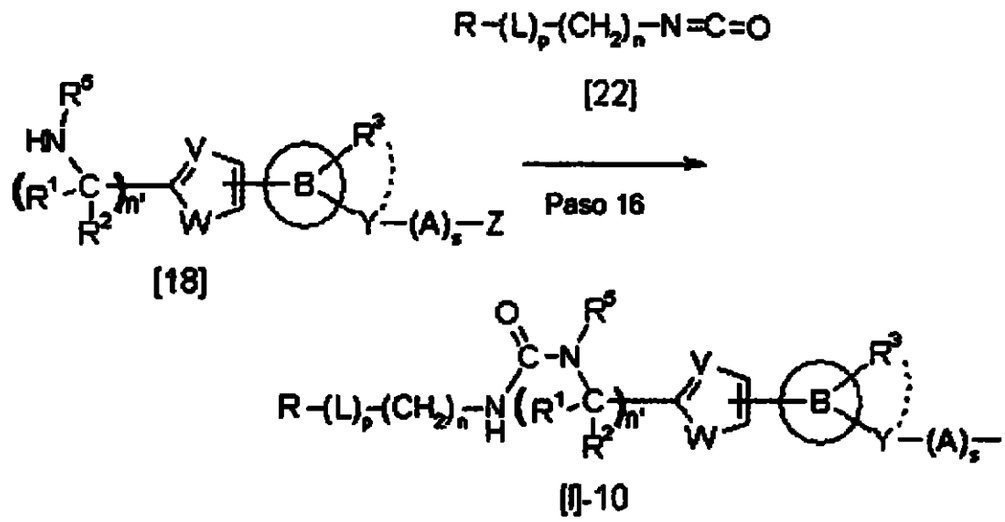
Paso 15

El compuesto [I]-9 puede obtenerse mediante la condensación de la amida del compuesto [20] obtenido por un método similar a aquél para dar el compuesto [16] en el Método de Producción 6 con el compuesto [21].

La condensación de la amida puede realizarse de acuerdo con métodos convencionales. Por ejemplo, en el caso en que R^D sea un grupo carboxi, puede mencionarse un método que comprende la condensación en un solvente tal como N,N-dimetilformamida, acetonitrilo, tetrahidrofurano, cloroformo, acetato de etilo, cloruro de metileno, tolueno y lo similar, en la presencia de un agente de condensación, tal como diciclohexilcarbodiimida, clorhidrato de 1-etil-3-(3-dimetilaminopropil)carbodiimida, difenilfosforilazida y lo similar, y en la presencia o ausencia de N-hidroxisuccinimida, 1-hidroxibenzotriazol y lo similar. La reacción puede llevarse a cabo de enfriamiento a calentamiento. Además, en el caso en que R^D sea un grupo formilo sustituido por un átomo de halógeno, puede mencionarse un método que comprende la condensación en un solvente tal como N,N-dimetilformamida, acetonitrilo, tetrahidrofurano, cloroformo, acetato de etilo, cloruro de metileno, tolueno, agua y lo similar y un solvente mezclado de los mismos, y en la presencia de una base, tal como bases inorgánicas (carbonato ácido de sodio, carbonato de potasio, carbonato ácido de potasio, hidróxido de sodio, etc.) y bases orgánicas (trietilamina, diisopropiletilamina, piridina, etc.), como un ejemplo. La reacción puede llevarse a cabo de enfriamiento a calentamiento.

Método de Producción 9

En este Método de Producción, se produce el compuesto [I], en donde m es 1 ó 2 y X es -NH-CO-N(R^5)-.



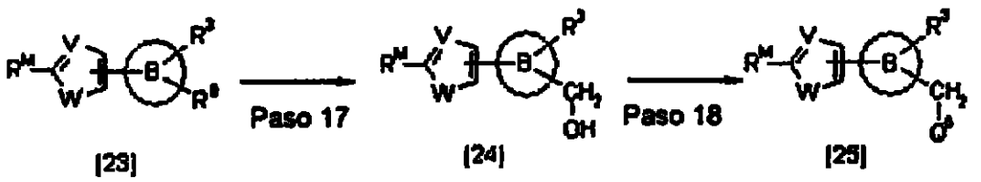
en donde cada símbolo es como se definió anteriormente.

Paso 16

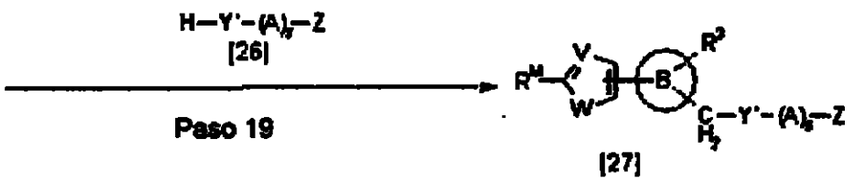
El compuesto [I]-10 puede obtenerse haciendo reaccionar el compuesto [18] con el compuesto [22] en un solvente en la presencia o ausencia de una base. Como el solvente, se puede mencionar la N,N-dimetilacetamida, N,N-dimetilformamida, acetonitrilo, acetato de etilo, tolueno, solventes de éter (tetrahidrofurano, dioxano, etc.), solventes halogenados (cloroformo, diclorometano, etc.) y lo similar y un solvente mezclado de los mismos. Como la base, se pueden mencionar las bases inorgánicas tales como carbonato de potasio, carbonato de sodio y lo similar y las bases orgánicas tales como trietilamina, diisopropiletilamina y lo similar. La reacción puede llevarse a cabo de enfriamiento a calentamiento.

Método de Producción 10

En este Método de Producción, de los compuestos [I], los compuestos [1] utilizado en los Métodos de Producción 1, 3 y 4, los compuestos [2] utilizados en el Método de Producción 1, los compuestos [3] utilizados en el Método de Producción 1 y los compuestos [15] utilizados en el Método de Producción 6, se produce un compuesto en donde Y es $-CH_2-N(R^{12})-$, $-CH_2-O-$ o $-CH_2-S-$.

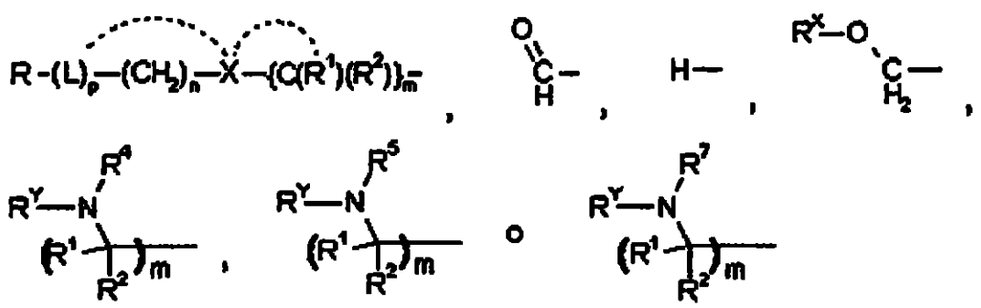


[23] [24] [25]



[27]

en donde R^M es



en donde cada símbolo es como se definió anteriormente, R^B es un grupo carboxi, un grupo carboxi sustituido por un grupo alquilo (grupo metilo, grupo etilo, etc.) o un grupo formilo, Q^6 es un grupo saliente

convencional como se describió en el Método de Producción 1, Y' es -N(R^{12})-, -O- o -S-, en donde cada símbolo es como se definió anteriormente, y los otros símbolos son como se definió anteriormente.

Paso 17

El compuesto [24] puede obtenerse por la activación del compuesto [23] en un solvente, utilizando un agente de activación en donde sea necesario, y la reducción del mismo utilizando un agente reductor convencional. Como el solvente, se pueden mencionar los alcoholes (metanol, etanol, etc.), solventes de éter (tetrahidrofurano, dioxano, etc.), tolueno y lo similar, y un solvente mezclado de los mismos. Como el agente reductor, se puede mencionar el borohidruro de sodio, borohidruro de litio, diborano, hidruro de litio y aluminio y lo similar. Como el agente de activación, por ejemplo, cuando R^8 es un grupo carboxi, puede mencionarse el carbonildiimidazol y lo similar. La reacción puede llevarse a cabo de enfriamiento a calentamiento.

Paso 18

El compuesto [25] puede obtenerse sustituyendo un grupo hidroxilo del compuesto [24] con un grupo saliente convencional de acuerdo con métodos convencionales. Por ejemplo, puede realizarse la conversión a un grupo mesiloxi, un grupo tosiloxi y lo similar, utilizando tal cloruro de sulfonilo en un solvente, en la presencia de una base orgánica. Como el

solvente, puede mencionarse el tolueno, acetato de etilo, solventes halogenados (cloroformo, diclorometano, etc.), solventes de éter (tetrahidrofurano, dioxano, etc.), acetonitrilo, N,N-dimetilformamida y un solvente mezclado de los mismos, y como la base orgánica, puede mencionarse la piridina, trietilamina, diisopropiletilamina y lo similar. La reacción puede llevarse a cabo de enfriamiento a calentamiento. Además, puede realizarse la conversión a un átomo de cloro, utilizando cloruro de tionilo sin solvente o en un solvente. Como el solvente, puede mencionarse el tolueno, acetato de etilo, solventes halogenados (cloroformo, diclorometano, etc.), solventes de éter (tetrahidrofurano, dioxano, etc.) y un solvente mezclado de los mismos. Como un catalizador, puede agregarse N,N-dimetilformamida. La reacción puede llevarse a cabo de enfriamiento a calentamiento. Además, la conversión a un átomo de cloro también puede realizarse convirtiendo a un grupo mesiloxi, un grupo tosiloxi y lo similar, y haciendo reaccionar además, con un cloruro de metal alcalino (cloruro de litio, etc.) o cloruro de amonio cuaternario. Como el solvente, puede mencionarse el acetonitrilo, N,N-dimetilformamida y lo similar. La reacción puede llevarse a cabo de enfriamiento a calentamiento.

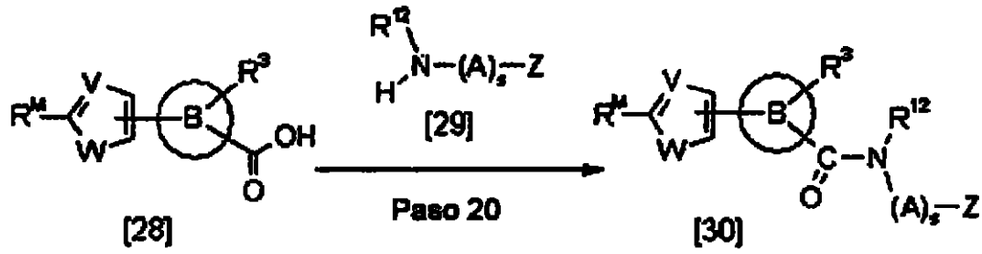
Paso 19

El compuesto [27] puede obtenerse haciendo reaccionar el compuesto [25] con el compuesto [26] en un solvente, en la presencia de una base y en la presencia o ausencia de un catalizador. Como el solvente, puede

mencionarse la N,N-dimetilacetamida, N,N-dimetilformamida, acetonitrilo, acetato de etilo, tolueno, solventes de alcohol (metanol, etanol, etc.), solventes de éter (tetrahidrofurano, dioxano, etc.), solventes halogenados (cloroformo, diclorometano, etc.) y lo similar y un solvente mezclado de los mismos. Como la base, pueden mencionarse las bases inorgánicas tales como carbonato de potasio, carbonato de sodio y lo similar y las bases orgánicas tales como trietilamina, diisopropiletilamina, ter-butóxido de potasio y lo similar. Como el catalizador, puede mencionarse el yoduro de potasio, sales de amonio cuaternario (yoduro de tetrabutilamonio, bromuro de tetrabutilamonio, etc.) y lo similar. La reacción puede llevarse a cabo de temperatura ambiente a calentamiento.

Método de Producción 11

En este Método de Producción, de los compuestos [I], los compuestos [1] utilizados en los Métodos de Producción 1, 3 y 4, los compuestos [2] utilizados en el Método de Producción 1, los compuestos [3] utilizados en el Método de Producción 1 y los compuestos [15] utilizados en el Método de Producción 6, se produce un compuesto en donde Y es -CO-N(R^{12})-.



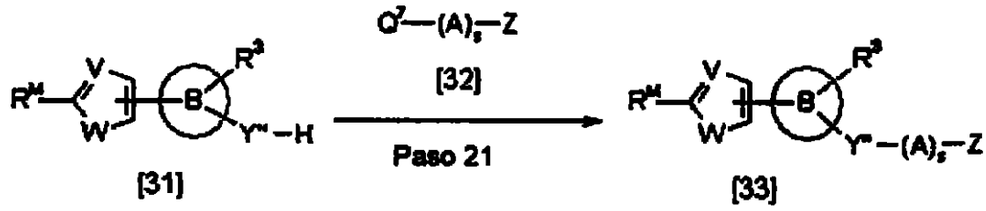
en donde cada símbolo es como se definió anteriormente.

Paso 20

El compuesto [30] puede obtenerse mediante la condensación de la amida del compuesto [28] con el compuesto [29]. La condensación de la amida puede realizarse de acuerdo con métodos convencionales. Por ejemplo, puede mencionarse un método que comprende la condensación en un solvente tal como N,N-dimetilformamida, acetonitrilo, tetrahidrofurano, cloroformo, acetato de etilo, cloruro de metileno, tolueno y lo similar, en la presencia de un agente de condensación tal como diciclohexilcarbodiimida, clorhidrato de 1-etil-3-(3-dimetilaminopropil)carbodiimida, difenilfosforilazida y lo similar, y en la presencia o ausencia de N-hidroxisuccinimida, 1-hidroxibenzotriazol y lo similar. La temperatura de reacción es de manera preferida de 0°C - 100°C

Método de Producción 12

En este Método de Producción, de los compuestos [I], los compuestos [1] utilizados en los Métodos de Producción 1, 3 y 4, los compuestos [2] utilizados en el Método de Producción 1, los compuestos [3] utilizados en el Método de Producción 1 y los compuestos [15] utilizados en el Método de Producción 6, se produce un compuesto en donde Y es -N(R^{11})-, -O- o -S-.



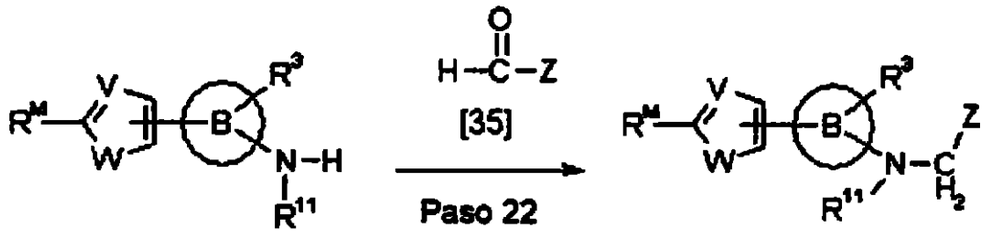
en donde Q^7 es un grupo saliente general como se describió en el Método de Producción 1, Y^a es $-N(R^{11})-$, -O- o -S- y los otros símbolos son como se definió anteriormente.

Paso 21

El compuesto [33] puede obtenerse haciendo reaccionar el compuesto [31] con el compuesto [32] en un solvente en la presencia de una base y en la presencia o ausencia de un catalizador. Como el solvente, puede mencionarse la N,N-dimetilacetamida, N,N-dimetilformamida, acetonitrilo, acetato de etilo, tolueno, solventes de alcohol (metanol, etanol, etc.), solventes de éter (tetrahidrofurano, dioxano, etc.), solventes halogenados (cloroformo, diclorometano, etc.) y lo similar y un solvente mezclado de los mismos. Como la base, pueden mencionarse las bases inorgánicas tales como carbonato de potasio, carbonato de sodio y lo similar y las bases orgánicas tales como trietilamina, diisopropiletilamina y lo similar. Como el catalizador, puede mencionarse el yoduro de potasio, sales de amonio cuaternario (yoduro de tetrabutilamonio, bromuro de tetrabutilamonio, etc.) y lo similar. La reacción puede llevarse a cabo de temperatura ambiente a calentamiento.

Método de Producción 13

En este Método de Producción, de los compuestos [I], los compuestos [1] utilizados en los Métodos de Producción 1, 3 y 4, los compuestos [2] utilizados en el Método de Producción 1, los compuestos [3] utilizados en el Método de Producción 1 y los compuestos [15] utilizados en el Método de Producción 6, se produce un compuesto en donde Y es -N(R^{11})-, s es 1 y A es un grupo metileno.



[34] [36]

en donde cada símbolo es como se definió anteriormente.

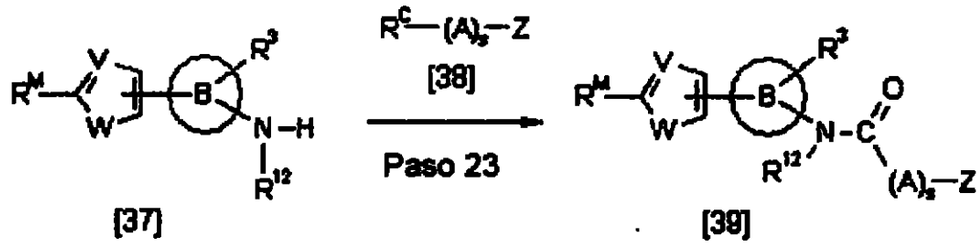
Paso 22

El compuesto [36] puede obtenerse haciendo reaccionar el compuesto [34] con el compuesto [35] en un solvente en la presencia de un agente reductor. Como el solvente, puede mencionarse la N,N-dimetilacetamida, N,N-dimetilformamida, acetonitrilo, acetato de etilo, tolueno, solventes de éter (tetrahidrofurano, dioxano, etc.), solventes halogenados (cloroformo, diclorometano, etc.), ácido acético y lo similar y un solvente mezclado de los mismos. Como el agente reductor, puede mencionarse el

triacetoxiborohidruro de sodio, cianoborohidruro de sodio y lo similar. La temperatura de reacción es de manera preferida de 0°C - 80°C.

Método de Producción 14

En este Método de Producción, de los compuestos [I], los compuestos [1] utilizados en los Métodos de Producción 1, 3 y 4, los compuestos [2] utilizados en el Método de Producción 1, los compuestos [3] utilizados en el Método de Producción 1 y los compuestos [15] utilizados en el Método de Producción 6, se produce un compuesto en donde Y es -N(R^{12})-CO-.



[37] [39]

en donde R^C es un grupo carboxi o un grupo formilo sustituido por un átomo de halógeno (átomo de bromo, átomo de yodo, átomo de flúor, átomo de cloro, etc.), y los otros símbolos son como se definió anteriormente.

Paso 23

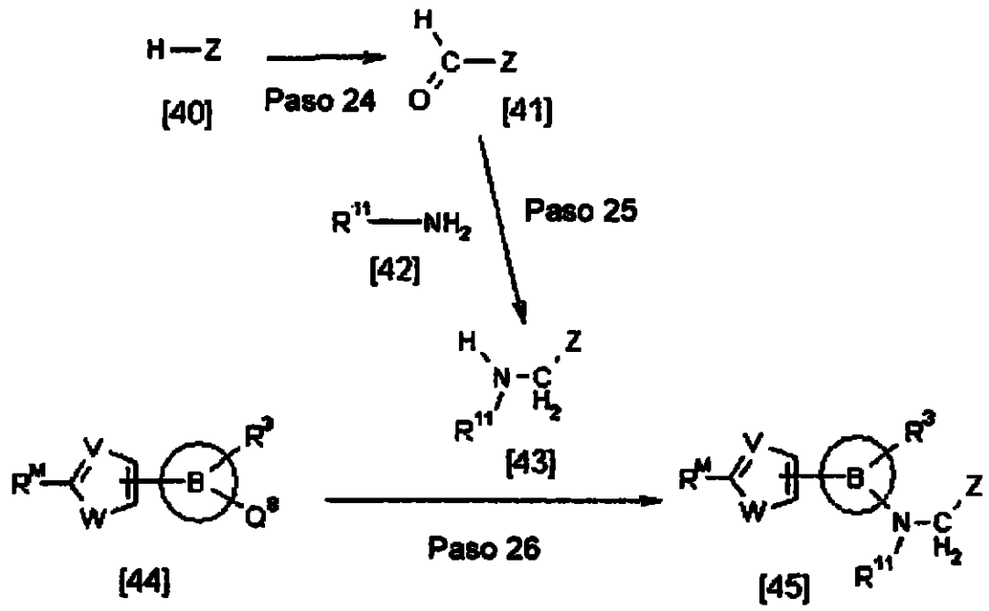
El compuesto [39] puede obtenerse mediante la condensación de la amida del compuesto [37] con el compuesto [38]. La condensación de la amida puede realizarse de acuerdo con métodos convencionales. Por

ejemplo, en el caso de que R^C sea un grupo carboxi, puede mencionarse un método que comprende la condensación en un solvente tal como N,N-dimetilformamida, acetonitrilo, tetrahidrofurano, cloroformo, acetato de etilo, cloruro de metileno, tolueno y lo similar, en la presencia de un agente de condensación tal como diciclohexilcarbodiimida, clorhidrato de 1-etil-3-(3-dimetilaminopropil)carbodiimida, difenilfosforilazida y lo similar, y en la presencia o ausencia de N-hidroxisuccinimida, 1-hidroxibenzotriazol y lo similar. Además, en el caso de que R^C sea un grupo formilo sustituido por un átomo de halógeno, puede mencionarse un método que comprende la condensación en un solvente tal como N,N-dimetilformamida, acetonitrilo, tetrahidrofurano, cloroformo, acetato de etilo, cloruro de metileno, tolueno, agua y lo similar y un solvente mezclado de los mismos, y en la presencia de una base tal como bases inorgánicas (carbonato ácido de sodio, carbonato de potasio, carbonato ácido de potasio, hidróxido de sodio, etc.) y bases orgánicas (trietilamina, diisopropiletilamina, piridina, etc.), como un ejemplo. La reacción puede llevarse a cabo de enfriamiento a calentamiento.

Método de Producción 15

En este Método de Producción, del compuesto [I], el compuesto [1] utilizado en los Métodos de Producción 1, 3 y 4, el compuesto [2] utilizado en el Método de Producción 1, el compuesto [3] utilizado en el Método de Producción 1 y el compuesto [15] utilizado en el Método de Producción 6, se

produce un compuesto en donde Y es -N(R^{11})-, s es 1, y A es un grupo metileno.



en donde Q^8 es un grupo saliente general como se describió en el Método de Producción 1 y los otros símbolos son como se definió anteriormente.

Paso 24

El compuesto [41] puede obtenerse introduciendo un grupo formilo en el compuesto [40], de acuerdo con métodos convencionales. Por ejemplo, cuando Z es un grupo arilo o un grupo anular heteroaromático (el grupo arilo o el grupo anular heteroaromático está sustituido opcionalmente como se describió anteriormente), el compuesto [41] puede sintetizarse haciendo reaccionar el compuesto [40] con éter metílico de diclorometilo en un

solvente, en la presencia de un ácido de Lewis e hidrolizando el compuesto de metoxiclorometilo obtenido. Como el solvente, pueden mencionarse los solventes halogenados (cloroformo, diclorometano, etc.) y lo similar. Como el ácido de Lewis, puede mencionarse el cloruro de aluminio, tetracloruro de titanio, tetracloruro de estaño y lo similar. La reacción puede llevarse a cabo de enfriamiento a temperatura ambiente.

Paso 25

El compuesto [43] puede obtenerse haciendo reaccionar el compuesto [41] con el compuesto [42] en un solvente en la presencia de un agente reductor. Como el solvente, puede mencionarse la N,N-dimetilacetamida, N,N-dimetilformamida, acetonitrilo, acetato de etilo, tolueno, solventes de éter (tetrahidrofurano, dioxano, etc.), solventes halogenados (cloroformo, diclorometano, 1,2-dicloroetano, etc.), solventes de alcohol (metanol, etanol, etc.), ácido acético y lo similar y un solvente mezclado de los mismos. Como el agente reductor, puede mencionarse el borohidruro de sodio, triacetoxiborohidruro de sodio, cianoborohidruro de sodio y lo similar. La temperatura de reacción es de manera preferida de 0°C - 80°C.

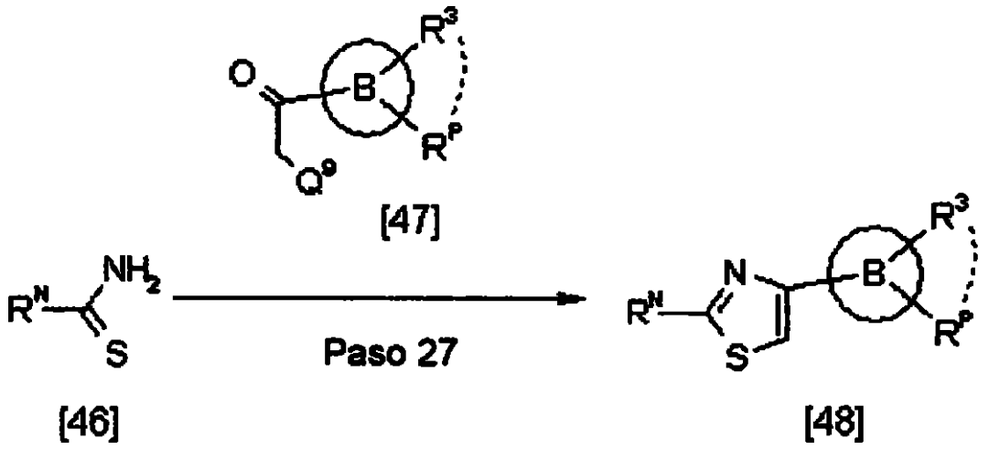
Paso 26

El compuesto [45] puede obtenerse haciendo reaccionar el compuesto [43] con el compuesto [44] en un solvente en la presencia de una base y en la presencia de un catalizador. Como el solvente, puede

mencionarse el tolueno, xileno, solventes de éter (tetrahidrofurano, dioxano, 1,2-dimetoxietano, etc.) y lo similar y un solvente mezclado de los mismos. Como la base, puede mencionarse el carbonato de cesio, ter-butóxido de sodio, fosfato de tripotasio y lo similar. Como el catalizador, puede mencionarse un complejo de paladio (por ejemplo, un complejo formado utilizando acetato de paladio y (R)-(+)-2,2'-bis(difenilfosfino)-1,1'-binaftilo) y lo similar. La reacción puede llevarse a cabo de temperatura ambiente a calentamiento.

Método de Producción 16

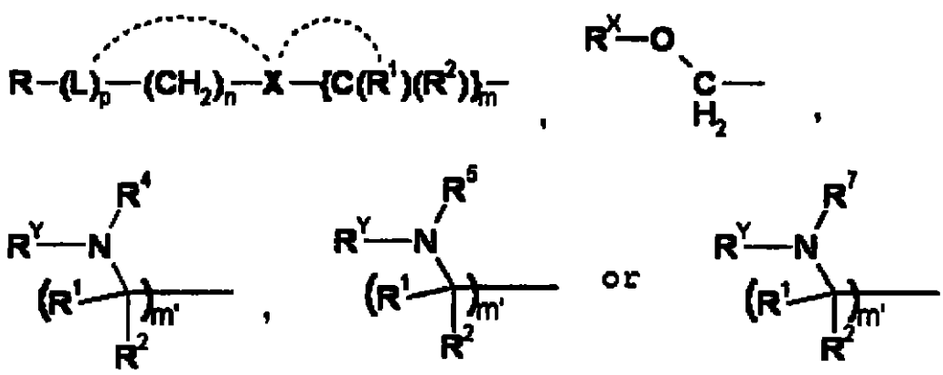
En este Método de Producción, del compuesto [I], el compuesto [3] utilizado en el Método de Producción 1, el compuesto [15] utilizado en el Método de Producción 6, el compuesto [23] utilizado en el Método de Producción 10, el compuesto [28] utilizado en el Método de Producción 11, el compuesto [31] utilizado en el Método de Producción 12, el compuesto [34] utilizado en el Método de Producción 13, el compuesto [37] utilizado en el Método de Producción 14, y el compuesto [44] utilizado en el Método de Producción 15, se produce un compuesto en donde V es =N-, W es -S- y la posición de la sustitución de B en el anillo de tiazol formado por V y W mencionados anteriormente, es la posición 4.



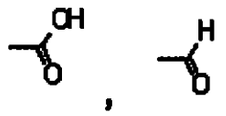
[47]

[46] Paso 27 [48]

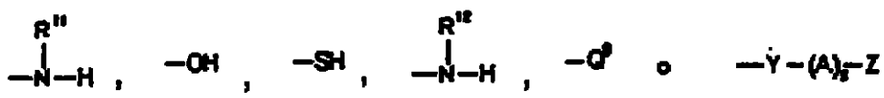
en donde R^N es



en donde cada símbolo es como se definió anteriormente, R^P es



sustituidos por un átomo de halógeno, (átomo de bromo, átomo de yodo, átomo de cloro, etc.),



en donde cada símbolo es como se definió anteriormente, Q^9 es un grupo saliente general como se describió en el Método de Producción 1 y los otros símbolos son como se definió anteriormente.

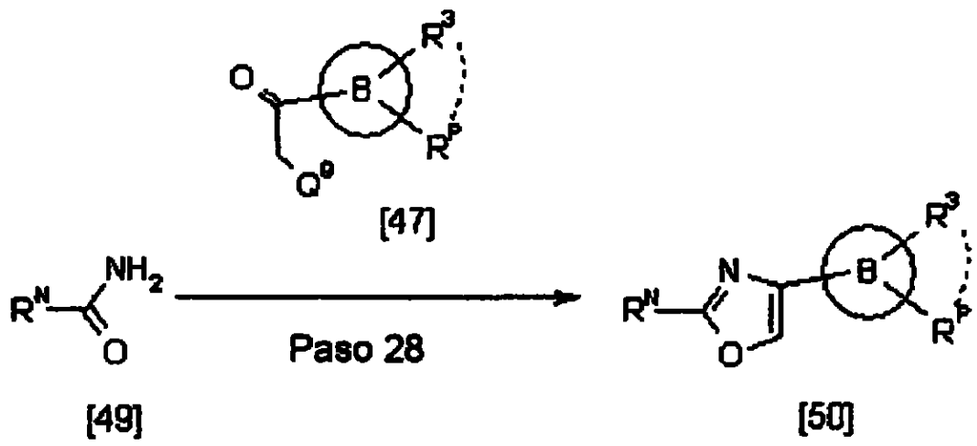
Paso 27

El compuesto [48] puede obtenerse haciendo reaccionar el compuesto [46] con el compuesto [47] en un solvente en la presencia o ausencia de una base. Como el solvente, puede mencionarse la N,N-dimetilacetamida, N,N-dimetilformamida, acetonitrilo, acetato de etilo, solventes de alcohol (metanol, etanol, etc.), solventes de éter (tetrahidrofurano, dioxano, etc.), solventes halogenados (cloroformo, diclorometano, etc.) y lo similar y un solvente mezclado de los mismos. Como la base, pueden mencionarse las bases inorgánicas tales como carbonato ácido de sodio y lo similar y las bases orgánicas tales como diisopropiletilamina y lo similar. La reacción puede llevarse a cabo de enfriamiento a calentamiento.

Método de Producción 17

En este Método de Producción, de los compuestos [I], los compuestos [3] utilizados en el Método de Producción 1, los compuestos [15] utilizados en el Método de Producción 6, los compuestos [23] utilizados en el Método de Producción 10, los compuestos [28] utilizados en el Método de Producción 11, los compuestos [31] utilizados en el Método de Producción 12,

los compuestos [34] utilizados en el Método de Producción 13, los compuestos [37] utilizados en el Método de Producción 14 y los compuestos [44] utilizados en el Método de Producción 15, se produce un compuesto en donde V es =N-, W es -O- y la posición de la sustitución de B en el anillo de oxazol formado por V y W mencionados anteriormente, es la posición 4.



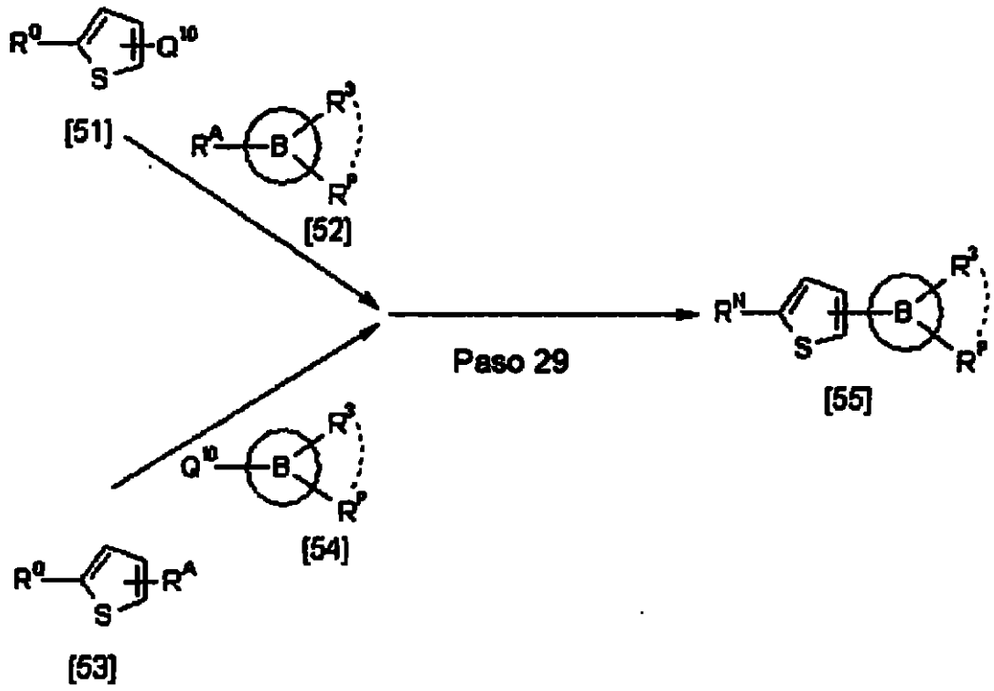
en donde cada símbolo es como se definió anteriormente.

Paso 28

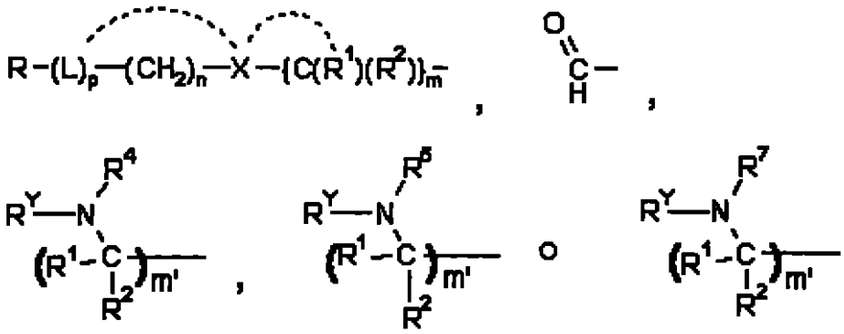
El compuesto [50] puede obtenerse haciendo reaccionar el compuesto [49] con el compuesto [47] sin solvente o en un solvente. Como el solvente, puede mencionarse el acetonitrilo, alcoholes (metanol, etanol, isopropil alcohol etc.), xileno, tolueno y lo similar y un solvente mezclado de los mismos. La reacción puede llevarse a cabo con calentamiento.

Método de Producción 18

En este Método de Producción, de los compuestos [I], los compuestos [1] utilizados en el Método de Producción 1, 3 y 4, los compuestos [15] utilizados en el Método de Producción 6, los compuestos [23] utilizados en el Método de Producción 10, los compuestos [28] utilizados en el Método de Producción 11, los compuestos [31] utilizados en el Método de Producción 12, los compuestos [34] utilizados en el Método de Producción 13, los compuestos [37] utilizados en el Método de Producción 14 y los compuestos [44] utilizados en el Método de Producción 15, se produce el compuesto [I] en donde V es =CH- y W es -S-.



en donde R^Q es



en donde cada símbolo es como se definió anteriormente, Q^{10} es un grupo saliente general como se describió en el Método de Producción 1, R^A es un grupo de ácido borónico (-$B(OH)_2$), y los otros símbolos son como se definió anteriormente.

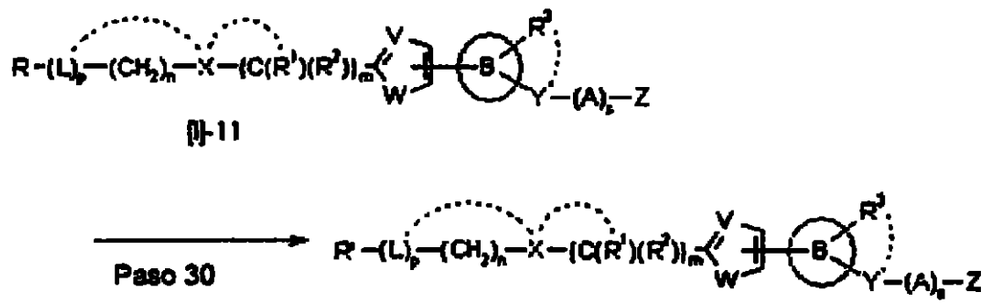
Paso 29

El compuesto [55] puede obtenerse haciendo reaccionar el compuesto [51] con el compuesto [52] o haciendo reaccionar el compuesto [53] con el compuesto [54] en un solvente en la presencia de una base y en la presencia de a catalizador. Como el solvente, se puede mencionar la N,N-dimetilformamida, acetonitrilo, solventes de alcohol (metanol, etanol, etc.), solventes de éter (tetrahidrofurano, 1,2-dimetoxietano, etc.), tolueno, agua y lo similar y un solvente mezclado de los mismos. Como la base, se pueden mencionar las bases inorgánicas tales como el carbonato de potasio, carbonato ácido de potasio, carbonato ácido de sodio, fosfato de potasio y lo similar y las bases orgánicas tales como trietilamina y lo similar. Como el

catalizador, pueden mencionarse los catalizadores de paladio (tetracis(trifenilfosfina)paladio, dicloruro de bis(trifenilfosfina)paladio(II), acetato de paladio-trifenilfosfina, etc.) y lo similar. La reacción puede llevarse a cabo de temperatura ambiente a calentamiento.

Método de Producción 19

En este Método de Producción, se produce el compuesto [I] en donde R es -COOH, -A^1-COOH o -O-A^1-COOH.



[I]-11

[I]-12

en donde R' es -COOH, -A^1-COOH o -O-A^1-COOH y los otros símbolos son como se definió anteriormente.

Paso 30

Cuando R^{19} para R en el compuesto [I]-11 es un grupo alquilo de C_{1-4}, el compuesto [I]-12 puede obtenerse mediante desprotección, de acuerdo con métodos convencionales para dar el ácido carboxílico. Por ejemplo, puede mencionarse un método que comprende la hidrólisis en un

solvente en la presencia de una base. Como el solvente, pueden mencionarse los alcoholes (metanol, etanol, alcohol isopropílico, etc.), tetrahidrofurano, 1,2-dimetoxietano, N,N-dimetilformamida, sulfóxido de dimetilo, agua y lo similar y un solvente mezclado de los mismos. Como la base, pueden mencionarse los hidróxidos de metales alcalinos tales como hidróxido de sodio y lo similar, carbonato de potasio, carbonato de sodio y lo similar. La reacción puede llevarse a cabo de enfriamiento a calentamiento.

Además, al agitar el compuesto [I] obtenido en los Métodos de Producción mencionados anteriormente, en un solvente, tras la adición de un ácido o una base, puede obtenerse una sal farmacéuticamente aceptable del compuesto [I]. Como el solvente, puede mencionarse la 2-butanona, acetona, tetrahidrofurano, acetato de etilo, metanol, etanol, agua, hexano y un solvente mezclado de los mismos. Como el ácido, pueden mencionarse ácidos inorgánicos tales como ácido clorhídrico, ácido sulfúrico, ácido fosfórico y lo similar, y ácidos orgánicos tales como ácido oxálico, ácido malónico, ácido trifluoroacético, ácido metansulfónico, ácido p-toluensulfónico, ácido bencensulfónico y lo similar. Como la base, pueden mencionarse las bases inorgánicas tales como hidróxido de sodio, hidróxido de potasio, hidróxido de calcio y lo similar y las bases orgánicas tales como trietilamina, etilendiamina, tris(hidroximetil)aminometano, N-metil-D-glucamina y lo similar. La reacción puede llevarse a cabo a temperatura ambiente.

El compuesto [I] obtenido anteriormente o una sal farmacéuticamente aceptable del mismo se disuelve o suspende en un

solvente de temperatura ambiente a calentamiento y se agita o deja a 0°C-150°C para permitir la precipitación de los cristales, los cuales se agregan a uń solvente deficiente del compuesto o una sal del mismo, en donde sea necesario, de enfriamiento a temperatura ambiente, y se filtra para dar los cristales del compuesto [I] o una sal farmacéuticamente aceptable del mismo. Como el solvente, puede mencionarse la 2-butanona, acetona, tetrahidrofurano, acetato de etilo, metanol, etanol, agua, hexano y un solvente mezclado de los mismos.

Los Métodos de Producción descritos en la presente especificación son ejemplos de los Métodos de Producción del compuesto de la presente invención, y también pueden producirse compuestos diferentes a aquéllos explicados anteriormente, combinando los métodos convencionales conocidos den el campo de la química orgánica sintética.

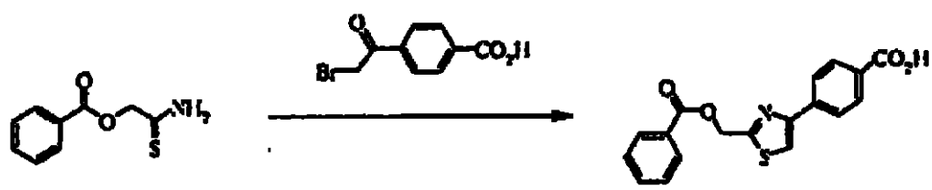
EJEMPLOS

El compuesto representado por la fórmula [I] de la presente invención y un método de producción del mismo se explican con detalle refiriéndose a los Ejemplos, los cuales no deben considerarse como limitantes.

EJEMPLO 1-1

Acido 5-[4-[4-({[4-(1-Etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetoxi}nicotínico

(1) Acido 4-(2-(Benzoiloximetil)tiazol-4-il)benzoico



A una solución del ácido 4-(bromoacetil)benzoico (10 g, 41.14 mmoles) en N,N-dimetilformamida (40 ml). se le agregó 2-(benzoiloxi)etantioamida (8.03 g, 41.14 mmoles) bajo enfriamiento con hielo, y la mezcla se agitó a temperatura ambiente durante 1.5 horas. Después de la terminación de la reacción, se agregaron carbonato ácido de sodio (3.46 g, 41.14 mmoles) y agua enfriamiento con hielo y la mezcla se agitó a temperatura ambiente durante 0.5 horas. Los precipitados se recolectaron mediante filtración. El sólido obtenido se secó bajo presión reducida para proporcionar el compuesto del título (13.089 g, 93.3%).

(2) Benzoato de (4-(4-Hidroximetilfenil)tiazol-2-il)metilo



A una suspensión del ácido 4-(2-(benzoiloximetil)tiazol-4-il)benzoico (0.5 g, 1.47 mmoles) obtenido en el Ejemplo 1-1(1) en tetrahidrofurano (5 ml), se le agregó 1,1'-carbonildiimidazol (0.358 g, 2.21 mmoles) a temperatura ambiente y la mezcla se agitó a 65°C durante 2 horas. A continuación se agregó gota a gota una solución acuosa de borohidruro de sodio (0.056 g, 1.47 mmoles) a temperatura ambiente y la mezcla se agitó a la misma temperatura durante 20 minutos. Después de la terminación de la reacción, se agregaron acetato de etilo y una solución acuosa de carbonato ácido de sodio para la extracción, y la capa orgánica se lavó con agua y salmuera saturada y se secó sobre sulfato de sodio. El solvente se evaporó y el residuo se lavó con un solvente mezclado de hexano-acetato de etilo y se recolectó mediante filtración. El sólido obtenido se secó bajo presión reducida para proporcionar el compuesto del título (370.7 mg, 77.5%).

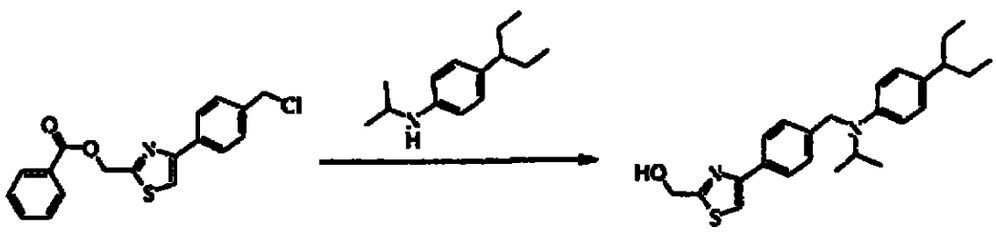
(3) Benzoato de (4-(4-Clorometilfenil)tiazol-2-il)metilo



A una solución del benzoato de (4-(4-hidroximetilfenil)tiazol-2-il)metilo (5.55 g, 17.06 mmoles) obtenido en el Ejemplo 1-1(2) en cloroformo (100 ml), se le agregaron cloruro de tionilo (1.49 ml, 20.67 mmoles) y N,N-

dimetilformamida (cantidad catalítica) bajo enfriamiento con hielo. La mezcla se agitó a temperatura ambiente durante 1 hora. Después de la terminación de la reacción, el solvente se evaporó y el residuo se concentró agregando cloroformo. Se agregó hexano y los precipitados se recolectaron mediante filtración. El sólido obtenido se secó bajo presión reducida para proporcionar el compuesto del título (5.804 g, 98.9%).

(4)(4-(4-(N-Isopropil-4-(1-etilpropil)fenilamino)metilfenil)tiazol-2-il)metanol



A una solución de N-isopropil-4-(1-etilpropil)anilina (7.34 g, 35.78 mmoles) en N,N-dimetilacetamida (35 ml) se le agregaron sucesivamente benzoato de (4-(4-clorometilfenil)tiazol-2-il)metilo (11.18 g, 32.52 mmoles), obtenido en el Ejemplo 1-1(3), carbonato de potasio (4.95 g, 35.78 mmoles) y yoduro de potasio (0.54 g, 3.25 mmoles) y la mezcla se agitó a 80°C durante 3 horas. A continuación, se agregó carbonato de potasio (0.449 g, 3.252 mmoles) y la mezcla se agitó a 70°C durante 12 horas. Después de la terminación de la reacción, se agregaron una mezcla de 50% de acetato de etilo-hexano y agua para la extracción, y la capa orgánica se lavó

sucesivamente con agua y salmuera saturada y se secó sobre sulfato de sodio. El solvente se evaporó y se le agregaron sucesivamente tetrahidrofurano (60 ml), metanol (60 ml) y una solución acuosa 1N de hidróxido de sodio (48.8 ml) al residuo obtenido, a temperatura ambiente. La mezcla se agitó a 75°C durante 1.5 horas. Después de la terminación de la reacción, el solvente se evaporó se agregaron acetato de etilo y agua para la extracción, y la capa orgánica se lavó sucesivamente con agua y salmuera saturada y se secó sobre sulfato de sodio y el solvente se evaporó. El residuo obtenido se purificó mediante cromatografía en columna sobre gel de sílice (hexano:acetato de etilo=4:1→2:1) para proporcionar el compuesto del título (10.664 g, 80.3%).

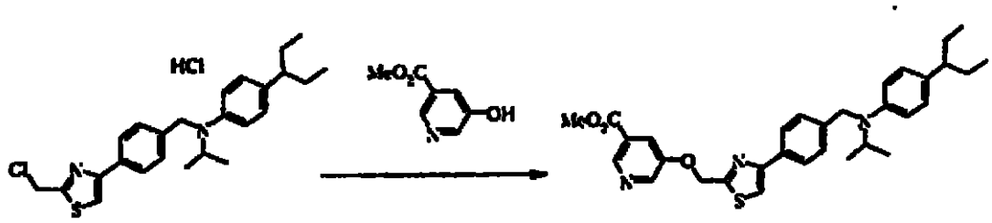
(5) Clorhidrato del cloruro de (4-(4-(N-isopropil-4-(1-etilpropil)fenilamino)metilfenil)tiazol-2-il)metilo



Se agregaron cloruro de tionilo (2.7 ml, 37.1 mmoles) y N,N-dimetilformamida (cantidad catalítica) a cloroformo (30 ml) a temperatura ambiente y se agregó gota a gota una solución de (4-(4-(N-isopropil-4-(1-etilpropil)fenilamino)metilfenil)tiazol-2-il)metanol (10.1 g, 24.7 mmoles)

obtenido en el Ejemplo 1-1(4) en cloroformo (30 ml) bajo enfriamiento con hielo. La mezcla se agitó a temperatura ambiente durante 1 hora. Después de la terminación de la reacción, el solvente se evaporó y el residuo se concentró agregando cloroformo. Se agregó acetato de etilo y la mezcla se agitó durante 0.5 horas. Los precipitados se recolectaron mediante filtración y el sólido obtenido se secó bajo presión reducida para proporcionar el compuesto del título (10.23 g, 89.4%).

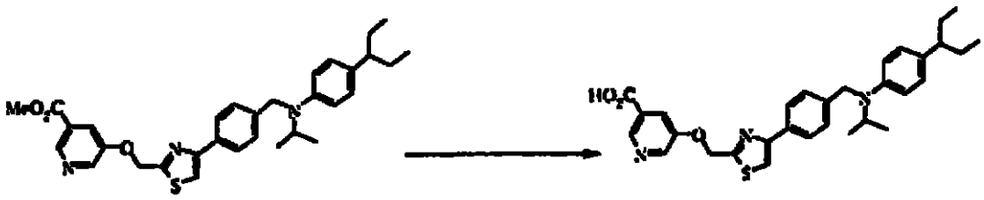
(6) Ester metílico del ácido 5-[4-[4-({[4-(1-Etil-propil)fenil]isopropil-amino}-metil)fenil]tiazol-2-ilmetoxi}nicotínico



A una solución del clorhidrato del cloruro de (4-(4-(N-isopropil-4-(1-etilpropil)fenilamino)metilfenil)tiazol-2-il)metilo (9.92 g, 21.4 mmoles) obtenido en el Ejemplo 1-1(5) y 5-hidroxinicotinato de metilo (3.61 g, 23.5 mmoles) en N,N-dimetilformamida, se le agregaron carbonato de potasio (6.8 g, 49.2 mmoles) y yoduro de potasio (0.355 g, 2.14 mmoles) bajo enfriamiento con hielo, y la mezcla se agitó a 60°C durante 12 horas. Después de la terminación de la reacción, se agregaron acetato de etilo y agua para la extracción y la capa orgánica se lavó sucesivamente con agua y salmuera

saturada y se secó sobre sulfato de sodio y el solvente se evaporó. El residuo obtenido se purificó mediante cromatografía en columna sobre gel de sílice (hexano:acetato de etilo=8:1) y a continuación (cloroformo:acetato de etilo=20:1) para proporcionar el compuesto del título (5.32 g, 45.7%).

(7) Acido 5-{4-[4-({[4-(1-Etilpropil)fenil]isopropilamino}-metil)fenil]tiazol-2-ilmetoxi}nicotínico



A una solución del éster metílico del ácido 5-{4-[4-({[4-(1-etilpropil)-fenil]isopropilamino}metil)fenil]tiazol-2-ilmetoxi}-nicotínico (5.32 g, 9.78 mmoles) obtenido en el Ejemplo 1-1(6) en 50% de tetrahidrofurano-metanol (32 ml), se le agregó una solución acuosa 2N de hidróxido de sodio (9.78 ml) a temperatura ambiente y la mezcla se agitó a 75°C durante 2 horas. Después de la terminación de la reacción, se agregó ácido clorhídrico 2N (9.78 ml) bajo enfriamiento con hielo y los precipitados se recolectaron mediante filtración. El sólido obtenido se secó bajo presión reducida para proporcionar el compuesto del título (5.00 g, 96.5%).

^{1}H RMN (DMSO-d_6, 300 MHz) δ 0.69 (t, J=7.3 Hz, 6H), 1.16 (d, J=6.5 Hz, 6H), 1.48-1.31 (m, 2H), 1.64-1.48 (m, 2H), 2.19-2.06 (m, 1H), 4.23 (quint, J=6.6 Hz, 1H), 5.67 (s, 2H), 6.62 (d, J=8.7 Hz, 2H), 6.89 (d, J=8.6 Hz,

2H), 7.36 (d, J=8.2 Hz, 2H), 7.90 (d, J=8.2 Hz, 2H), 7.99 (dd, J=3.0, 1.5 Hz, 1H), 8.11 (s, 1H), 8.64 (d, J=2.9 Hz, 1H), 8.72 (d, J=1.5 Hz, 1H), 13.43 (s amplio, 1H)

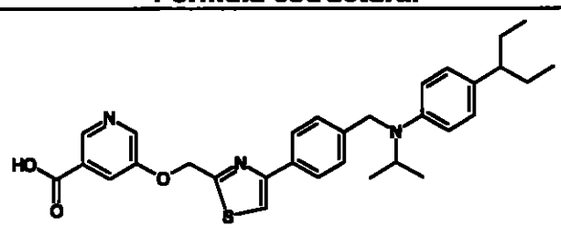
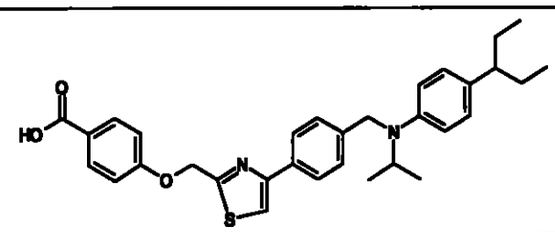
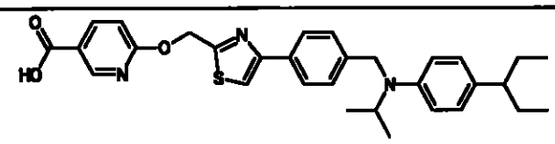
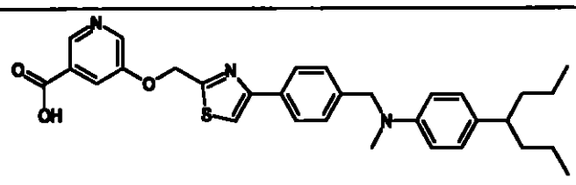
Punto de fusión: 201.5°C

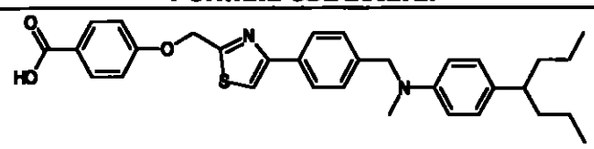
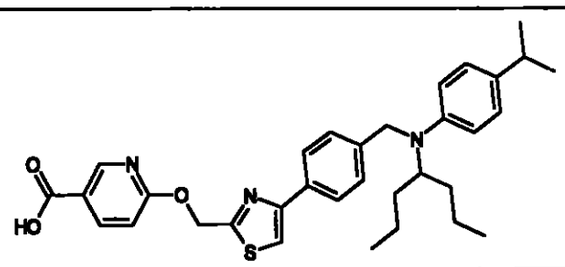
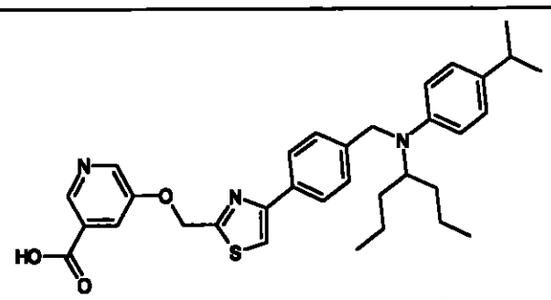
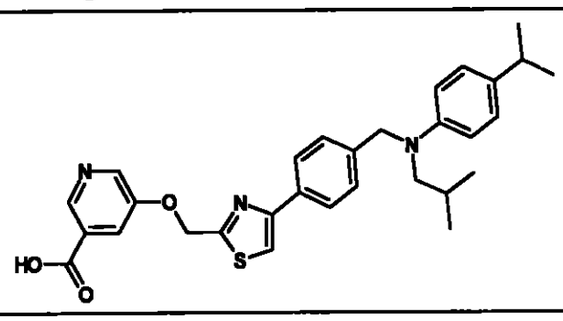
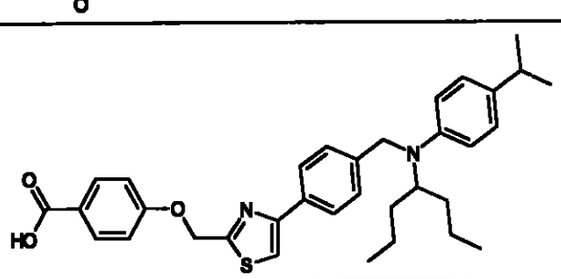
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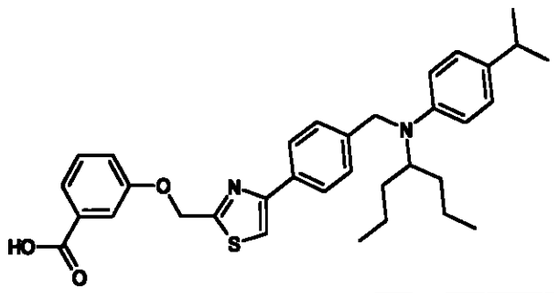
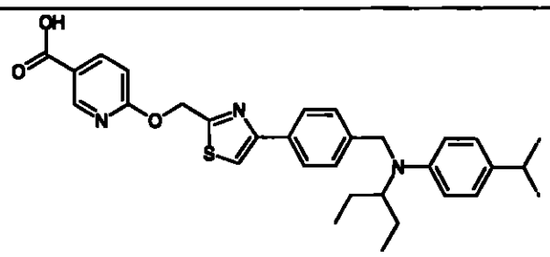
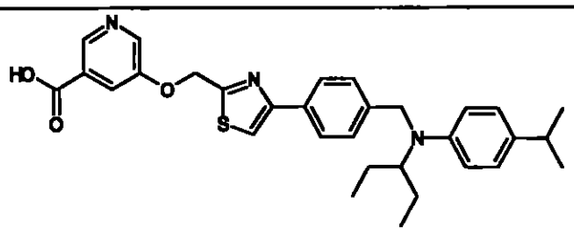
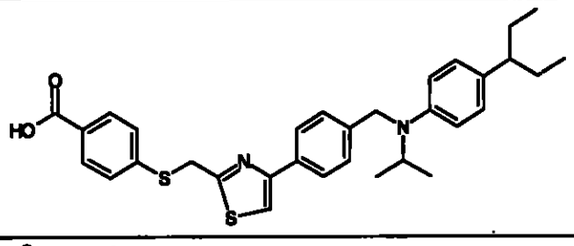
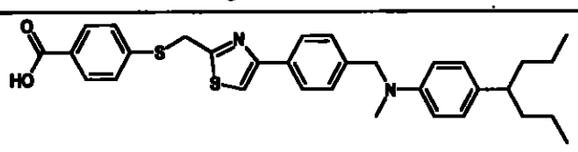
EJEMPLOS 1-2 A 1-186

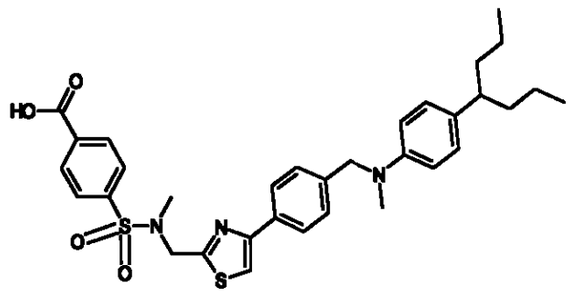
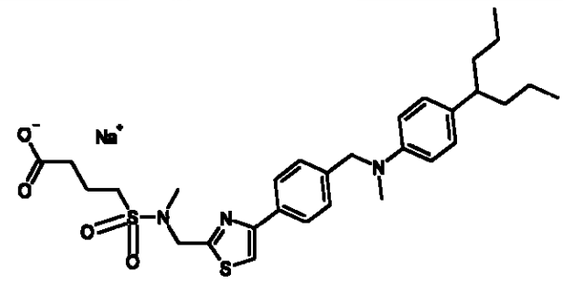
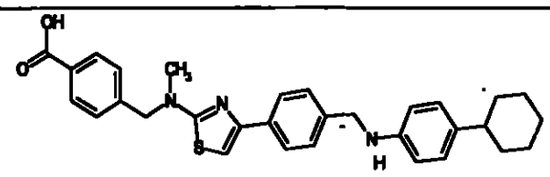
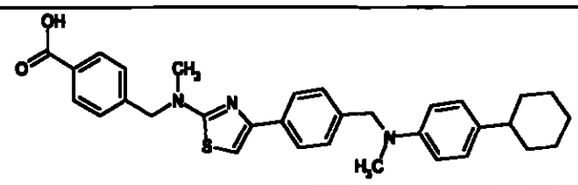
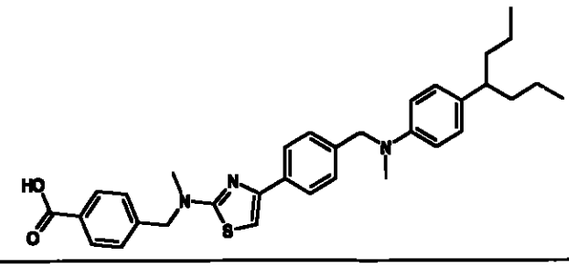
De la misma manera que en el Ejemplo 1-1 y utilizando otros métodos convencionales en donde sea necesario, se producen los compuestos de los Ejemplos 1-2 a 1-186. Las fórmulas estructurales y los valores de las propiedades de los compuestos obtenidos, así como aquéllis del Ejemplo 1-1, se muestran en los siguientes Cuadros.

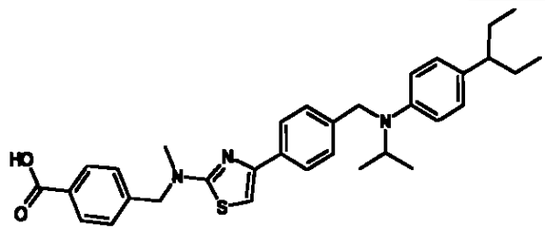
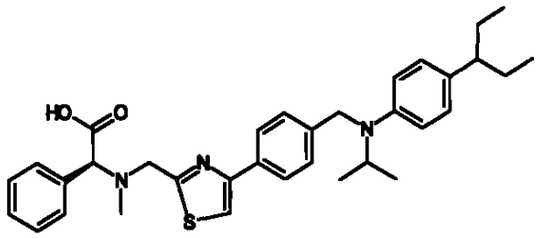
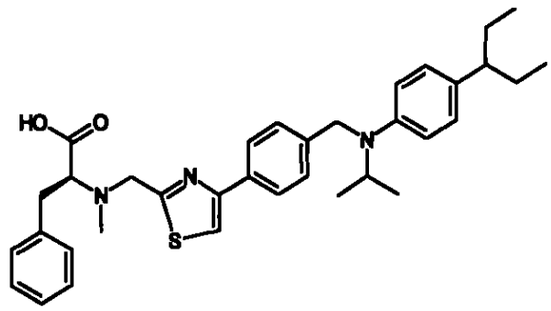
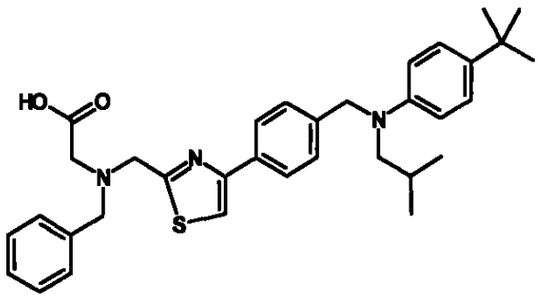
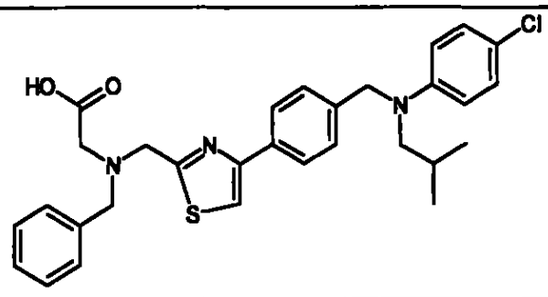
CUADRO 1

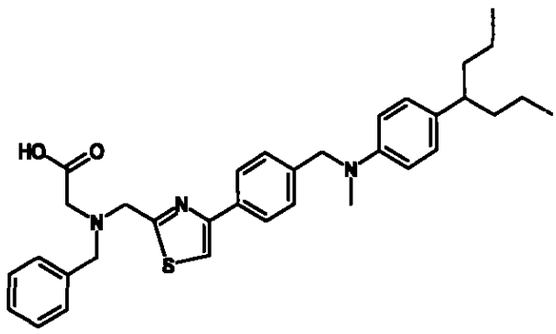
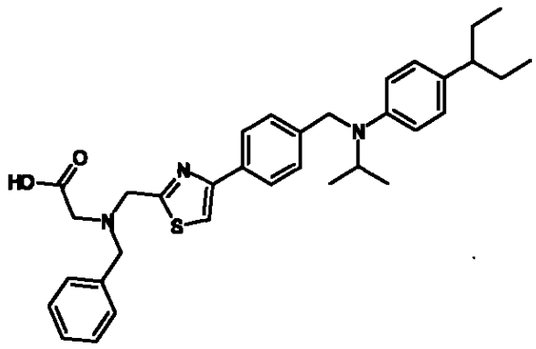
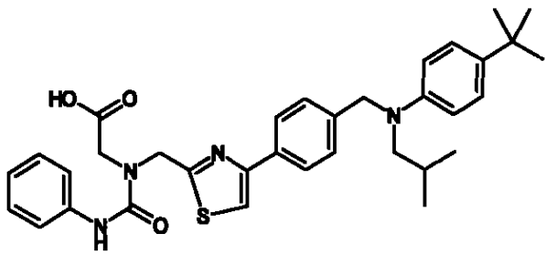
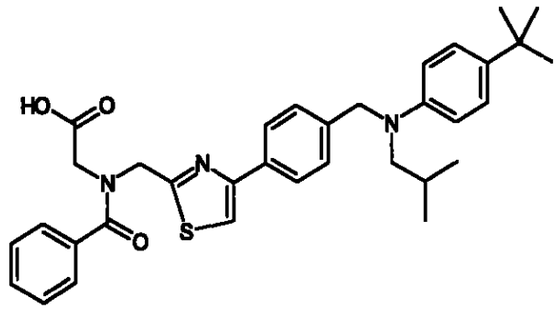
Ejemplo	Fórmula estructural	p.f. (°C)
1-1		201.5
1-2		219
1-3		177-181
1-4		135-138

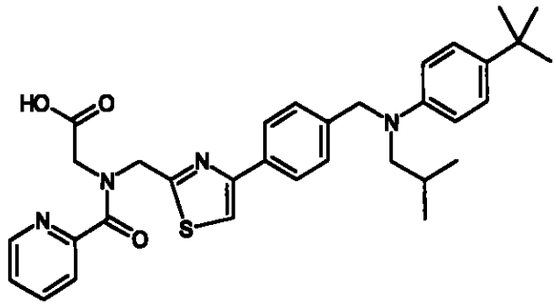
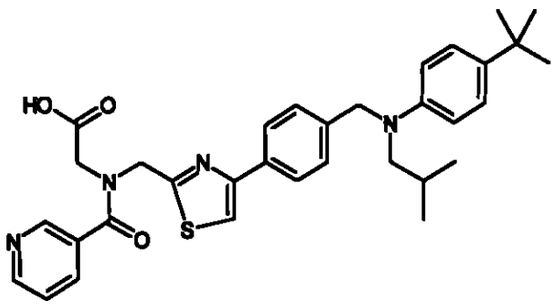
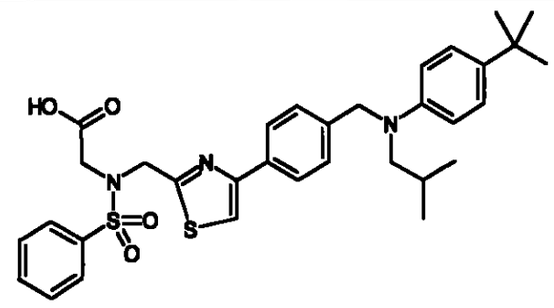
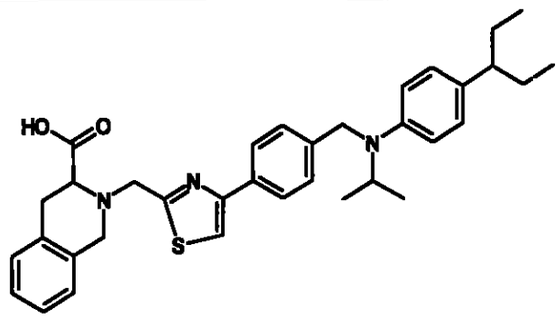
Ejemplo	Fórmula estructural	p.f. (°C)
1-5		161-163
1-6		141-143
1-7		184-185
1-8		196-197
1-9		166-168

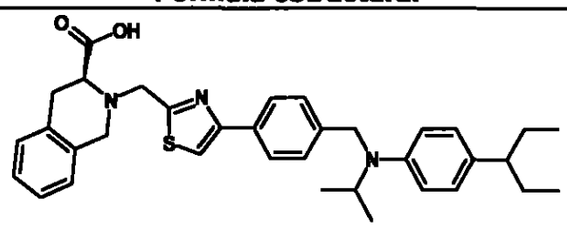
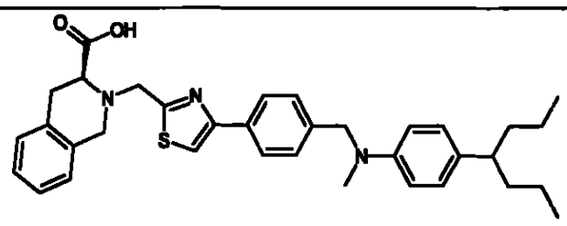
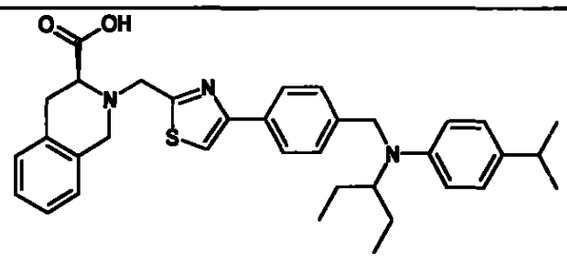
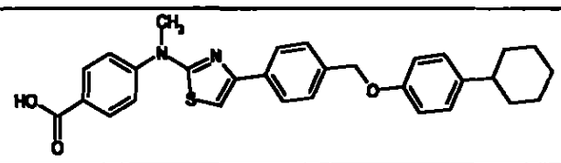
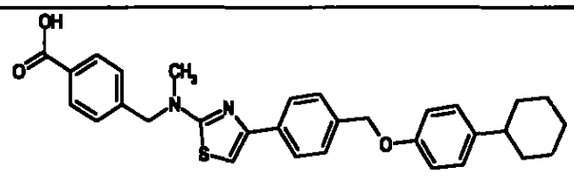
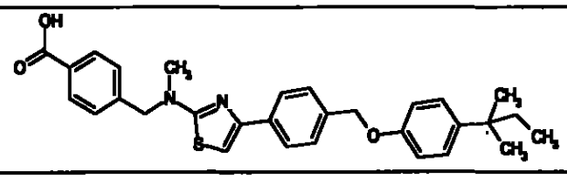
Ejemplo	Fórmula estructural	p.f. (°C)
1-10		127-129
1-11		155-157
1-12		110-114
1-13		132.5
1-14		122-124

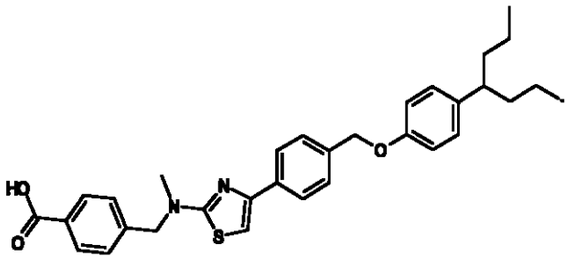
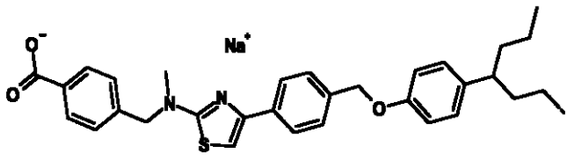
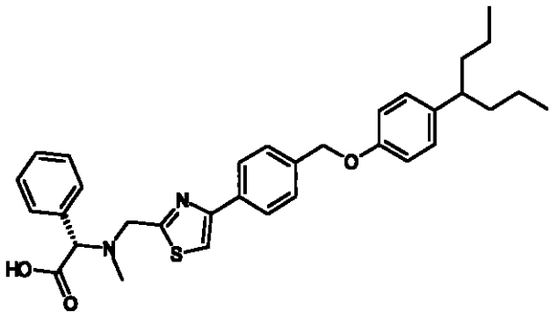
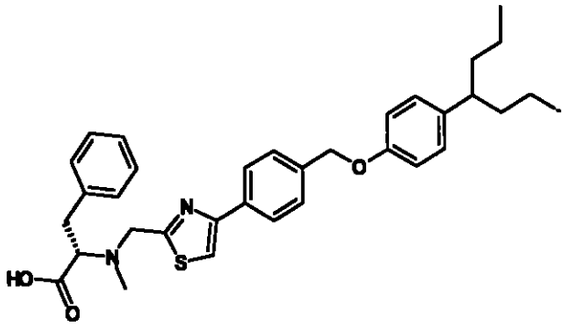
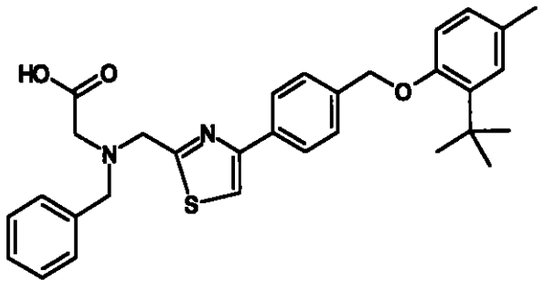
Ejemplo	Fórmula estructural	p.f. (°C)
1-15		amorfo
1-16		217-220
1-17		206-210
1-18		190-192
1-19		110-113

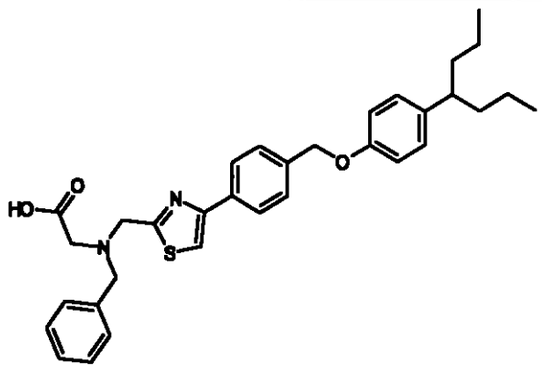
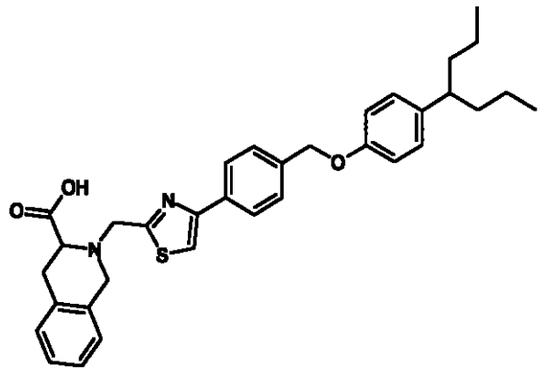
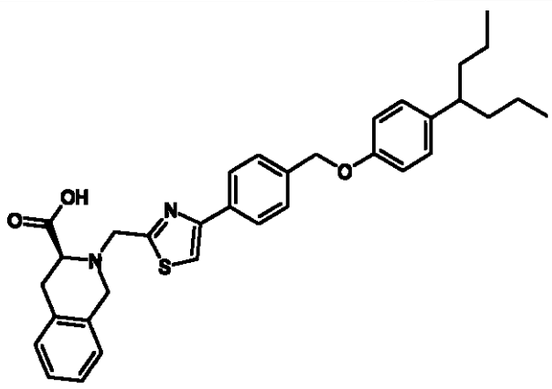
Ejemplo	Fórmula estructural	p.f. (°C)
1-20		150-153
1-21		amorfo
1-22		80
1-23		133
1-24		152

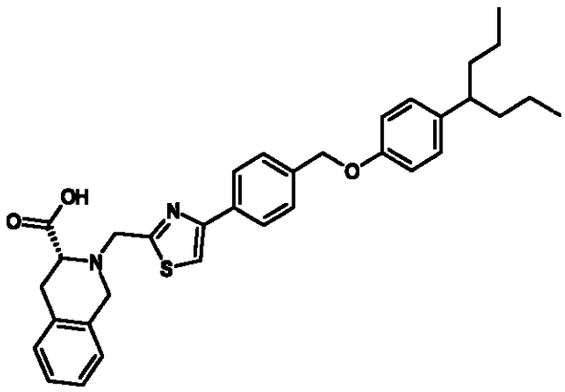
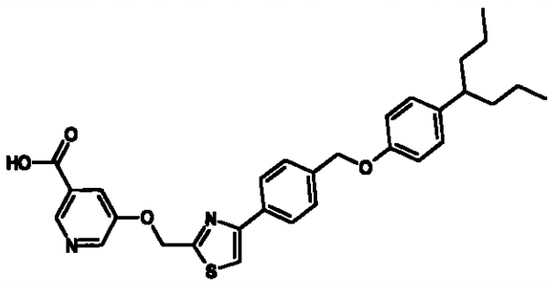
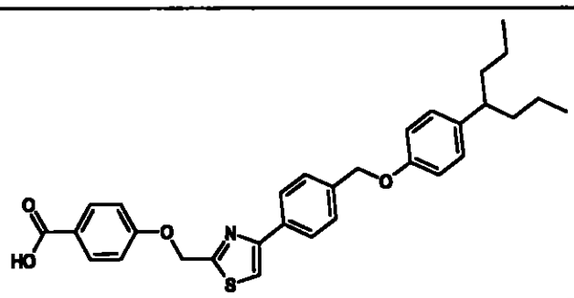
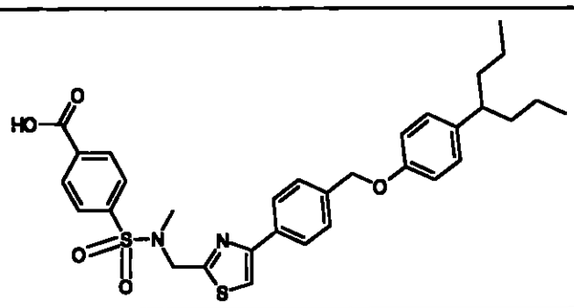
Ejemplo	Fórmula estructural	p.f. (°C)
1-25		138
1-26		amorfo
1-27		119
1-28		147

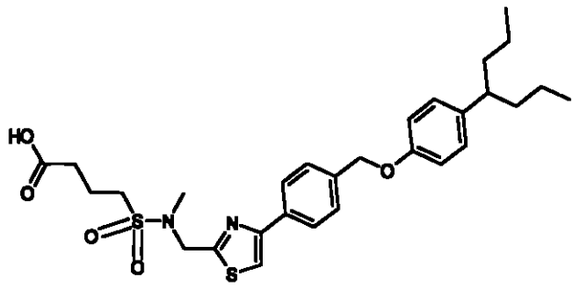
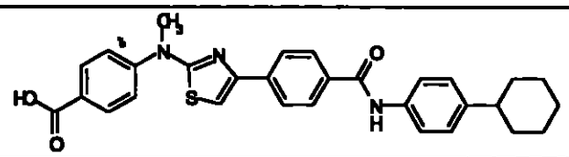
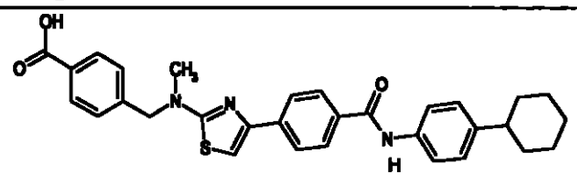
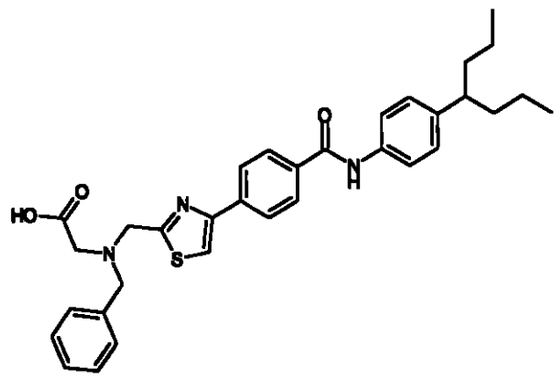
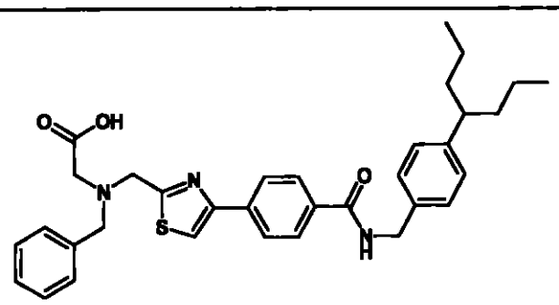
Ejemplo	Fórmula estructural	p.f. (°C)
1-29		160
1-30		193
1-31		168.5
1-32		127.5

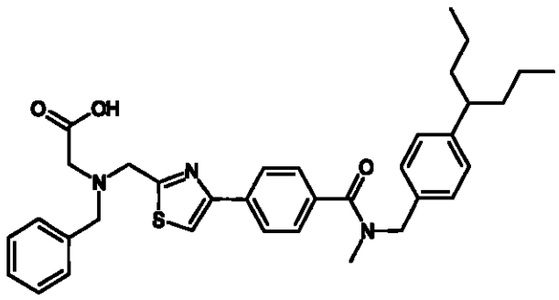
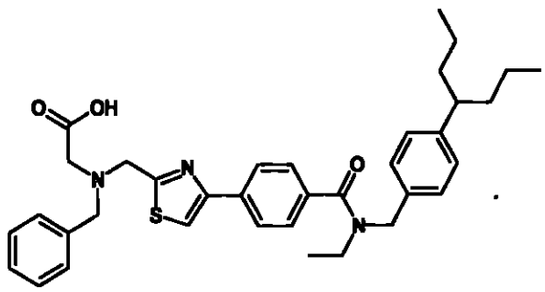
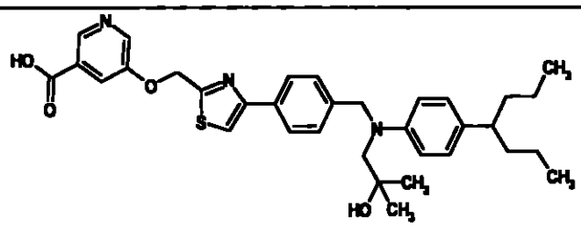
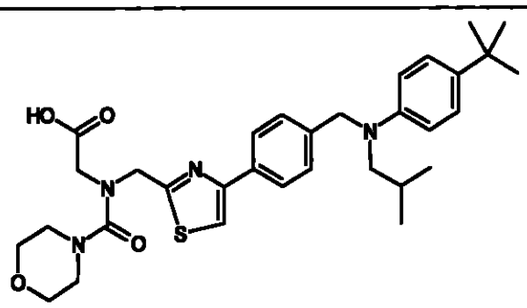
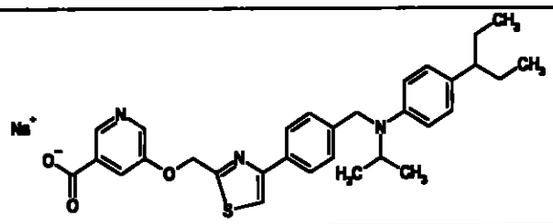
Ejemplo	Fórmula estructural	p.f. (°C)
1-33		amorfo
1-34		amorfo
1-35		110-113
1-36		230-
1-37		209-211
1-38		155-157

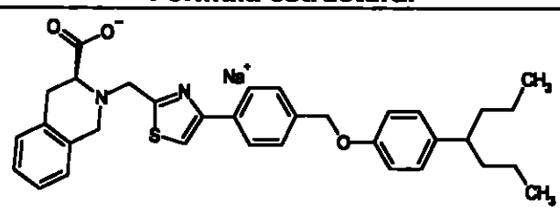
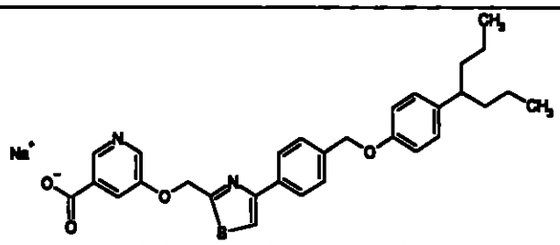
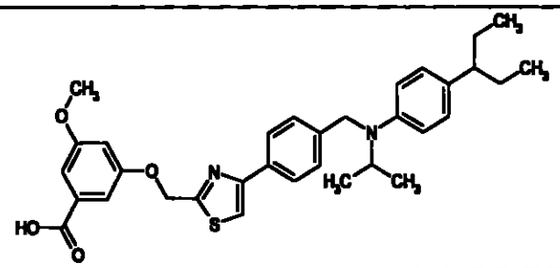
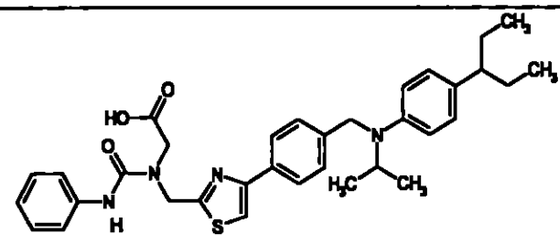
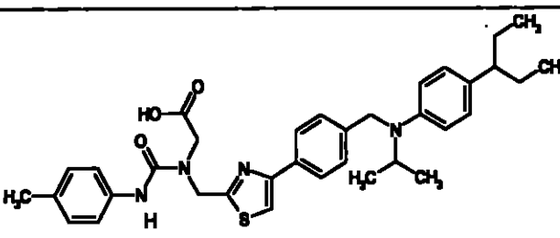
Ejemplo	Fórmula estructural	p.f. (°C)
1-39		156-158
1-40		250-
1-41		amorfo
1-42		114-118
1-43		146

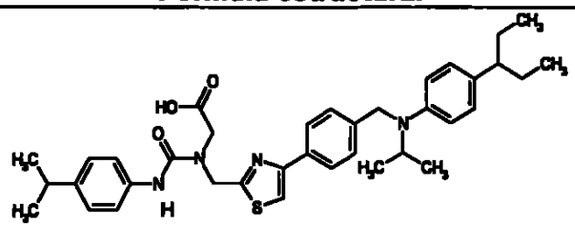
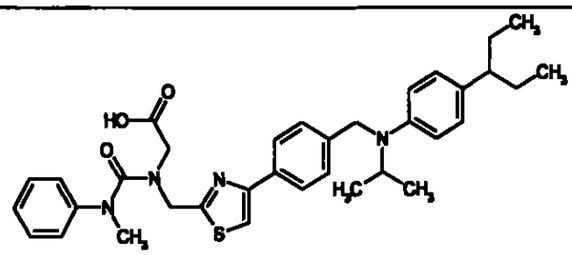
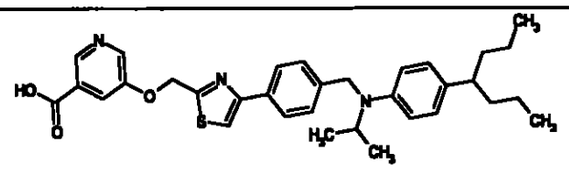
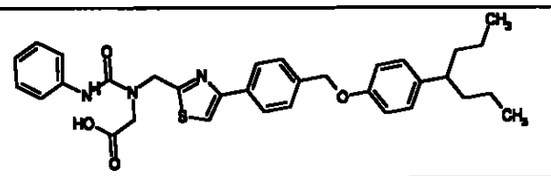
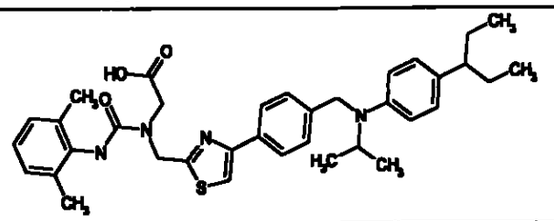
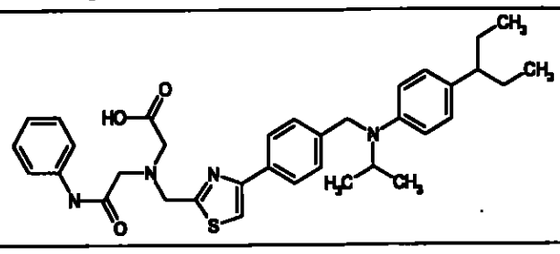
Ejemplo	Fórmula estructural	p.f. (°C)
1-44		138-142
1-45		117-126
1-46		77-82

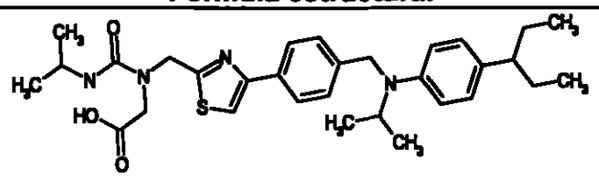
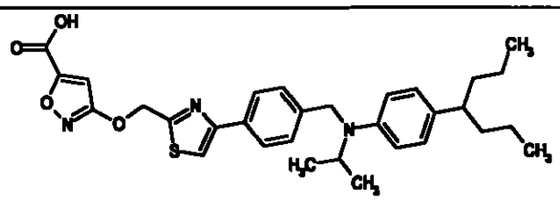
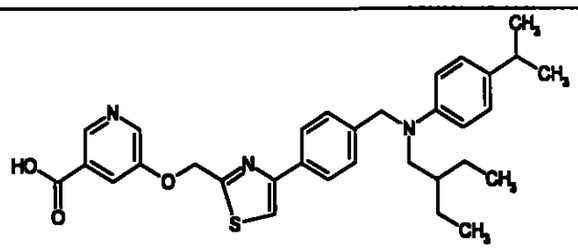
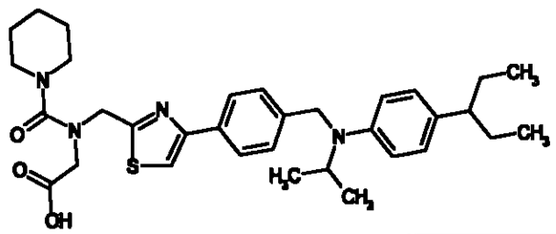
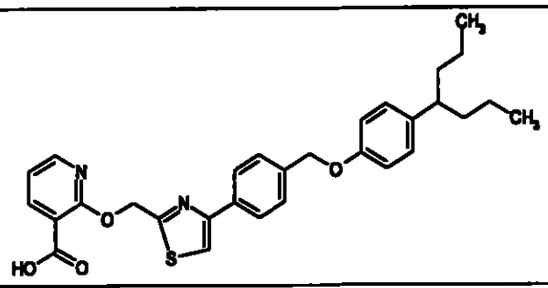
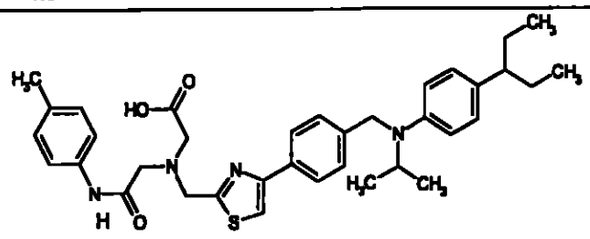
Ejemplo	Fórmula estructural	p.f. (°C)
1-47		77-82
1-48		165-171
1-49		199-202
1-50		amorfo

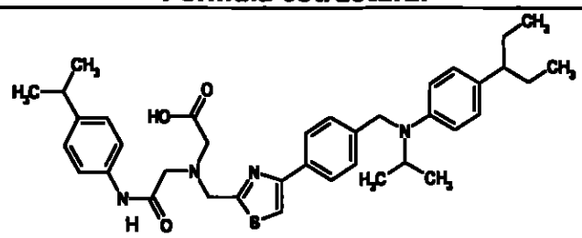
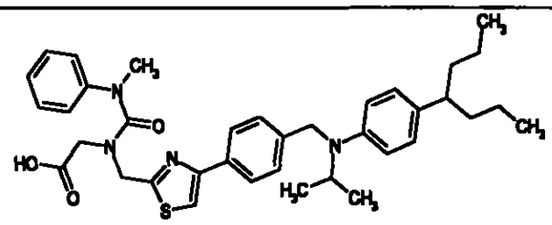
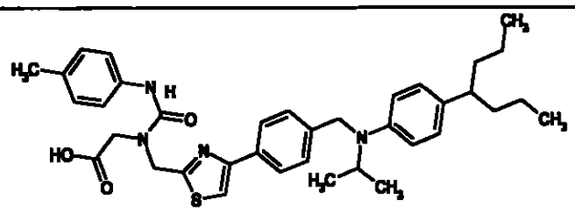
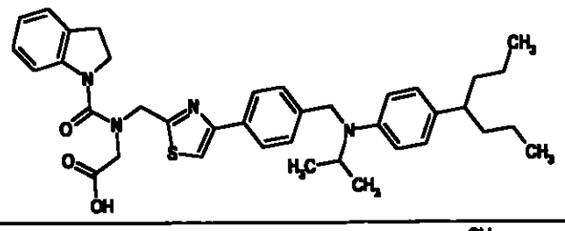
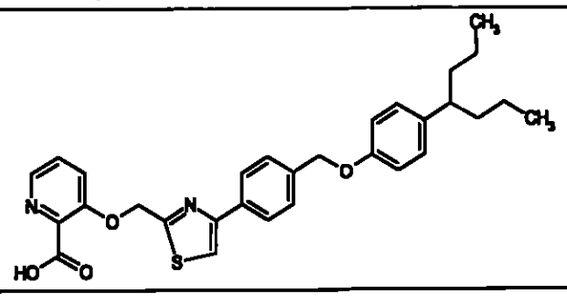
Ejemplo	Fórmula estructural	p.f. (°C)
1-51		103.3-106.3
1-52		250 descomposición
1-53		250-
1-54		201-202
1-55		141-143

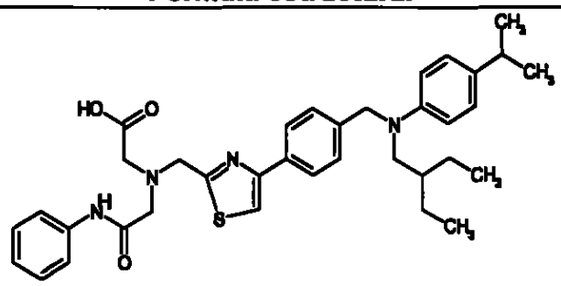
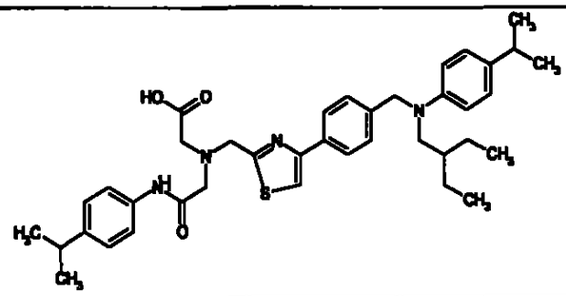
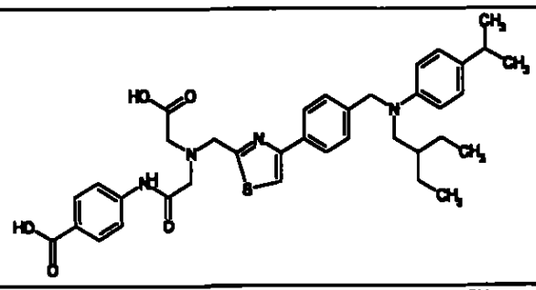
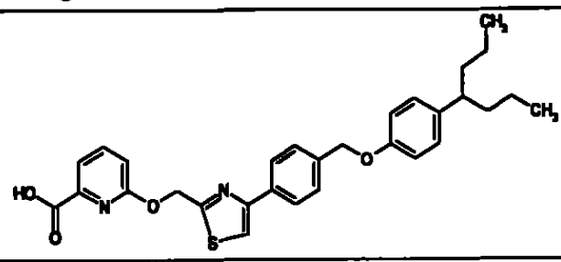
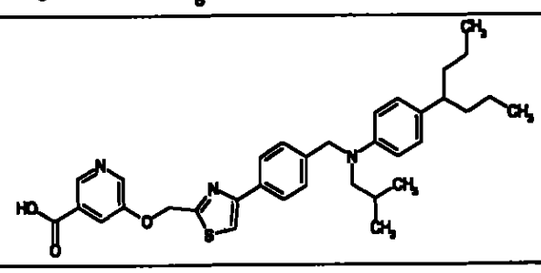
Ejemplo	Fórmula estructural	p.f. (°C)
1-56		65-71
1-57		59-65
1-58		amorfo
1-59		138
1-60		amorfo

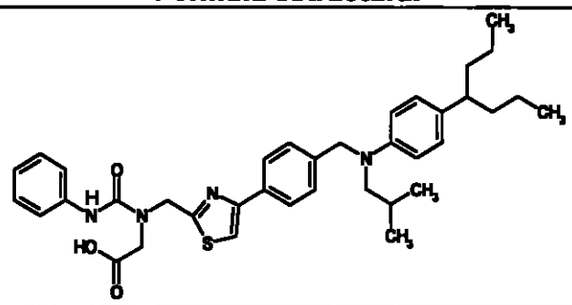
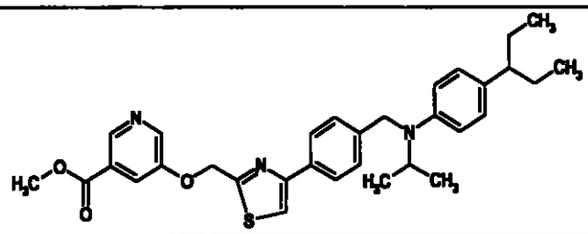
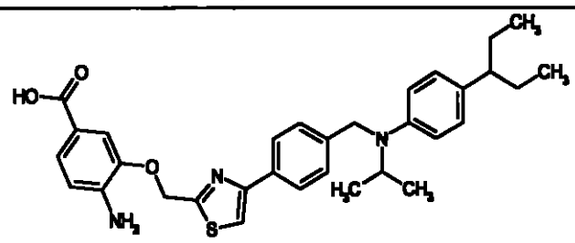
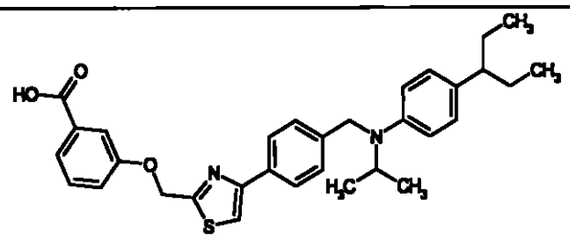
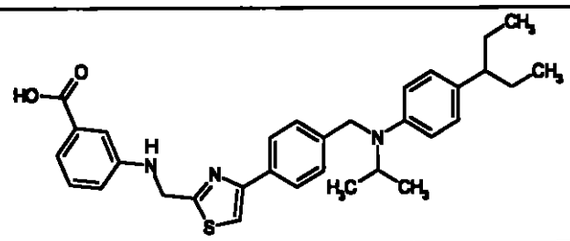
Ejemplo	Fórmula estructural	p.f. (°C)
1-61		250-
1-62		250-
1-63		131
1-64		amorfo
1-65		amorfo

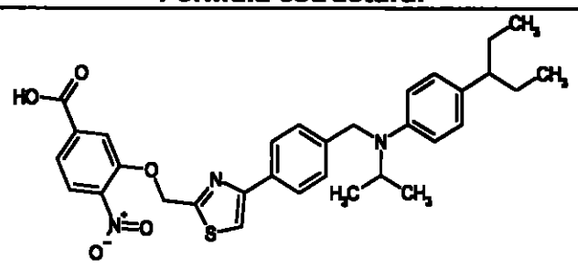
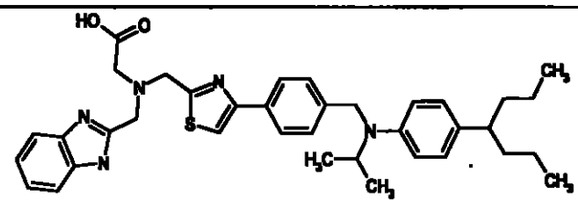
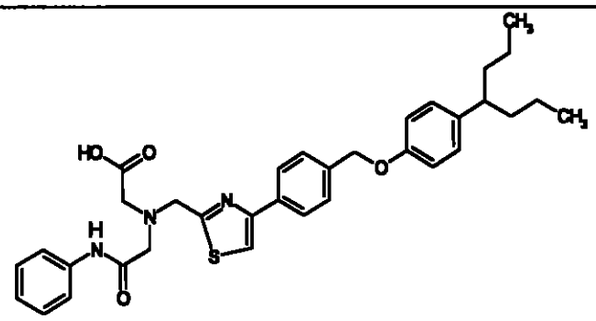
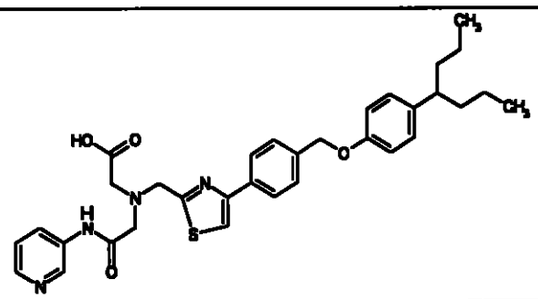
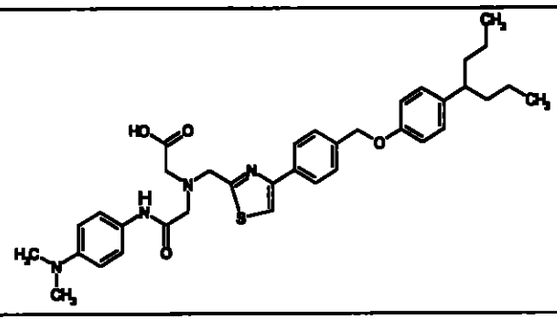
Ejemplo	Fórmula estructural	p.f. (°C)
1-66		amorfo
1-67		amorfo
.1-68		185 descomposición
1-69		amorfo
1-70		amorfo
1-71		amorfo

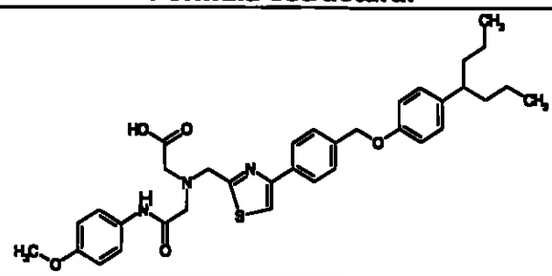
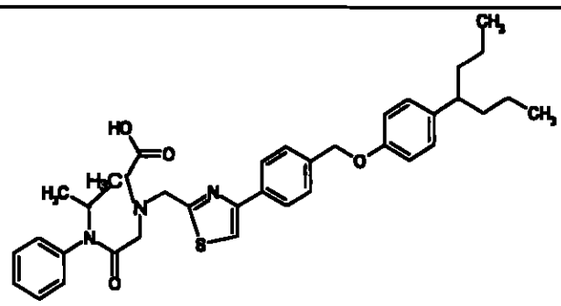
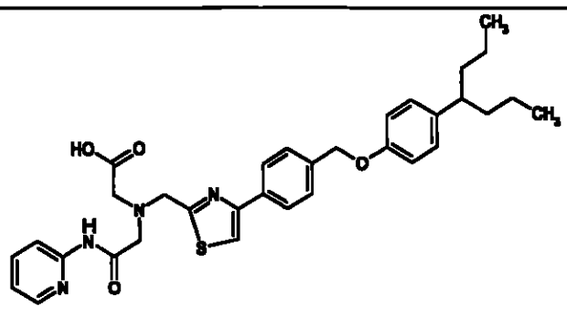
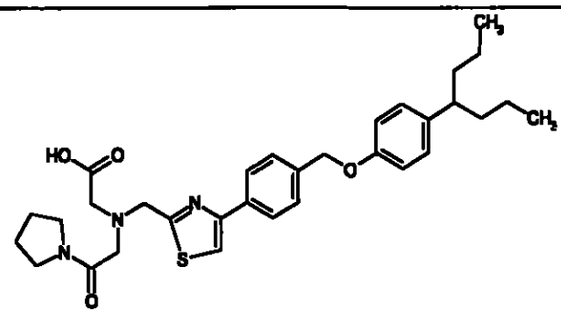
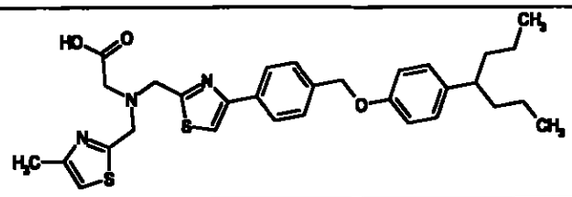
Ejemplo	Fórmula estructural	p.f. (°C)
1-72		amorfo
1-73		amorfo
1-74		181
1-75		amorfo
1-76		154.5
1-77		amorfo

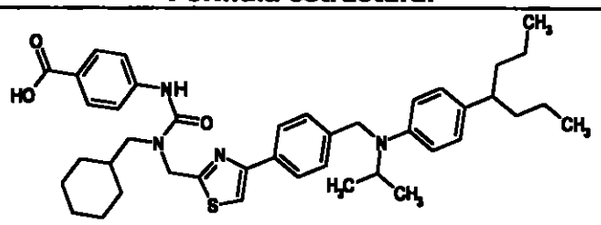
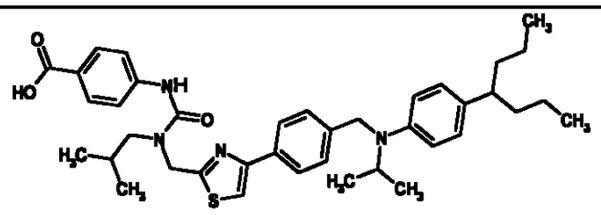
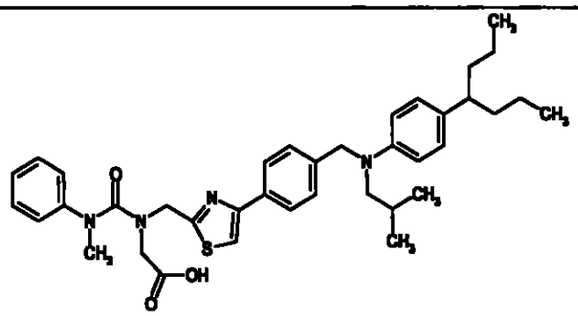
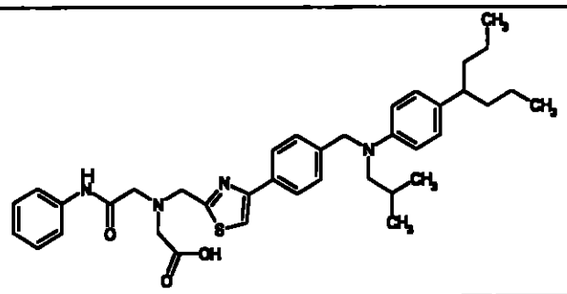
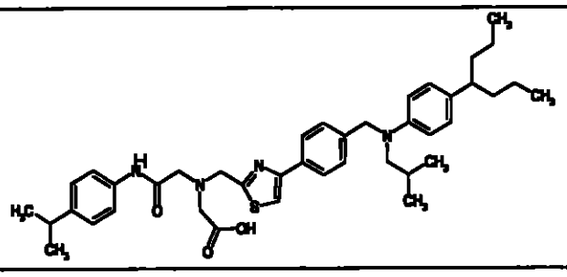
Ejemplo	Fórmula estructural	p.f. (°C)
1-78		amorfo
1-79		amorfo
1-80		amorfo
1-81		amorfo
1-82		138.5 descomposición

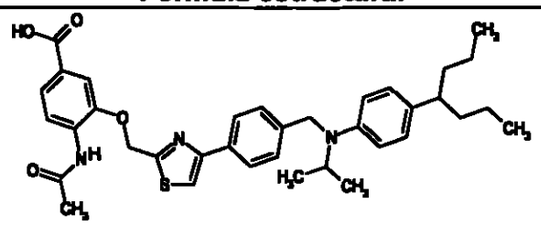
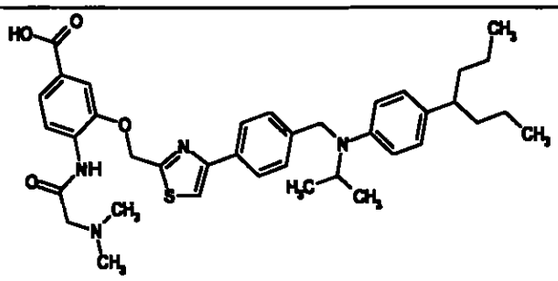
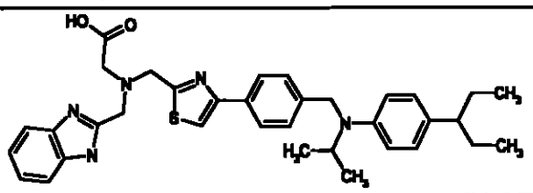
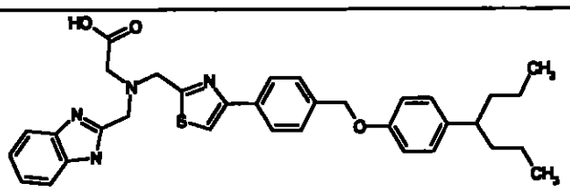
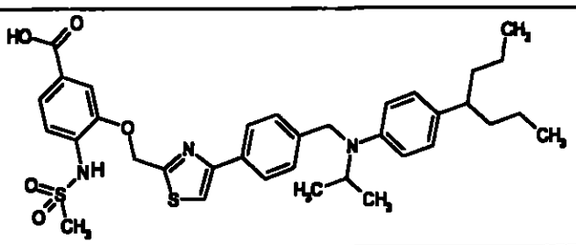
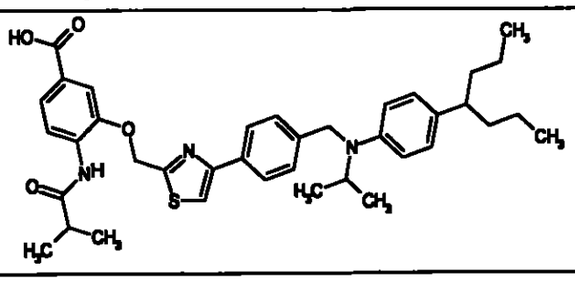
Ejemplo	Fórmula estructural	p.f. (°C)
1-83		amorfo
1-84		amorfo
1-85		amorfo
1-86		amorfo
1-87		amorfo

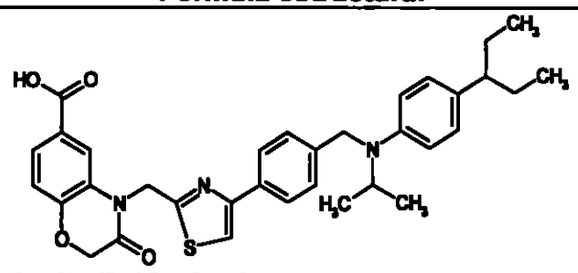
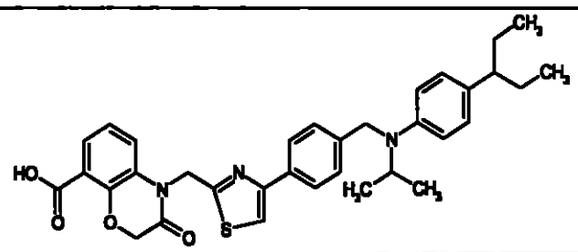
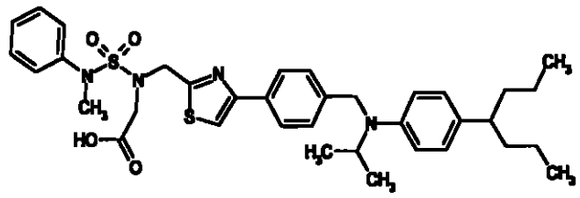
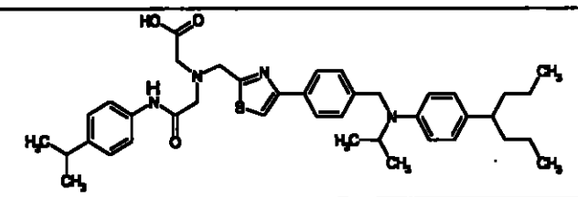
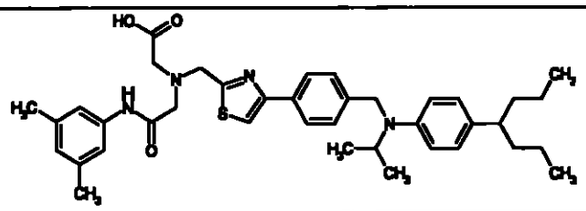
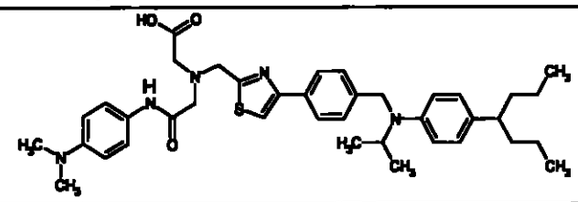
Ejemplo	Fórmula estructural	p.f. (°C)
1-88		amorfo
1-89		111-113
1-90		179-181
1-91		165-167
1-92		159-160

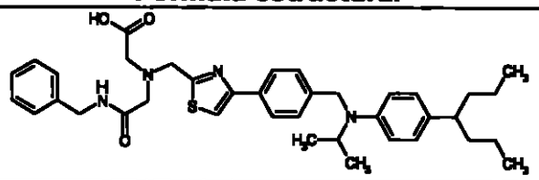
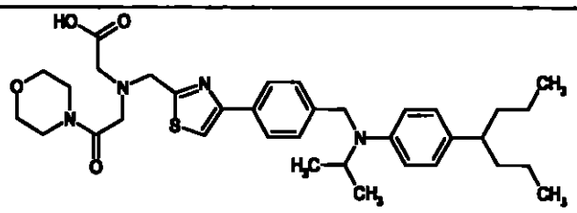
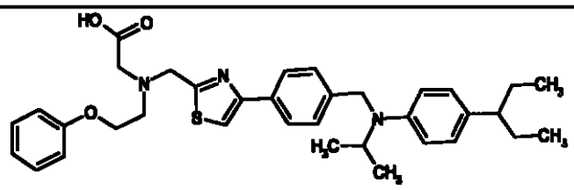
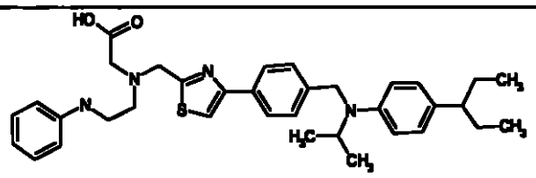
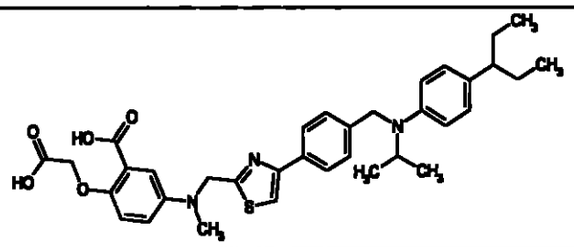
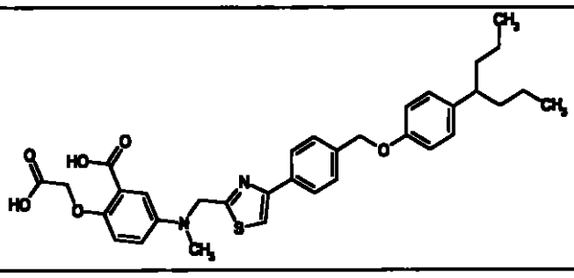
Ejemplo	Fórmula estructural	p.f. (°C)
1-93		198-200
1-94		amorfo
1-95		149.5
1-96		162.5
1-97		192.5

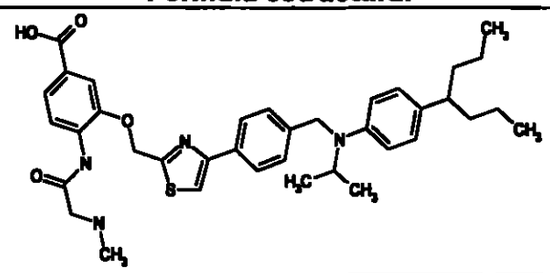
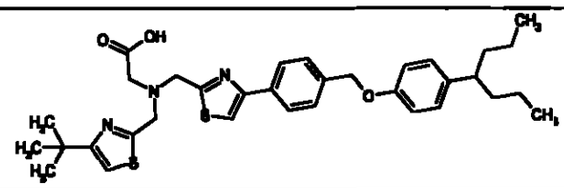
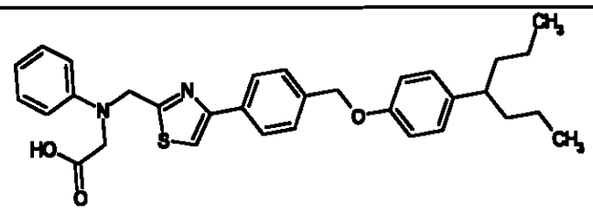
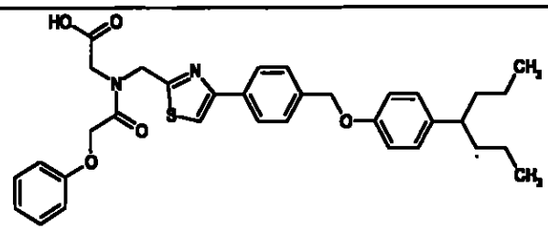
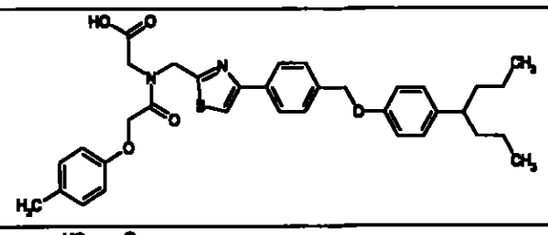
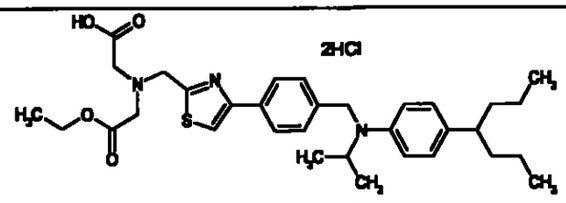
Ejemplo	Fórmula estructural	p.f. (°C)
1-98		176.5
1-99		115.5
1-100		133.5
1-101		amorfo
1-102		amorfo

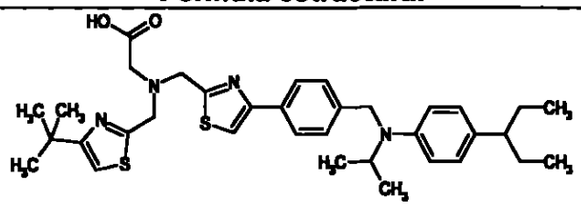
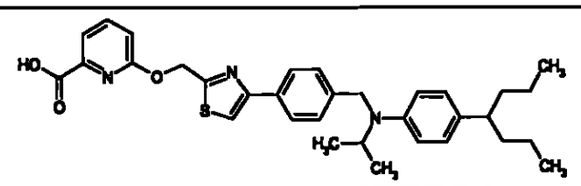
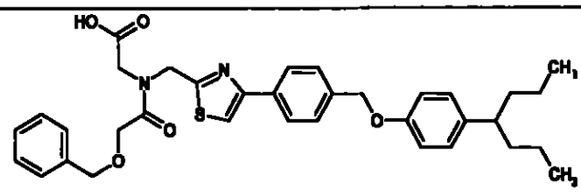
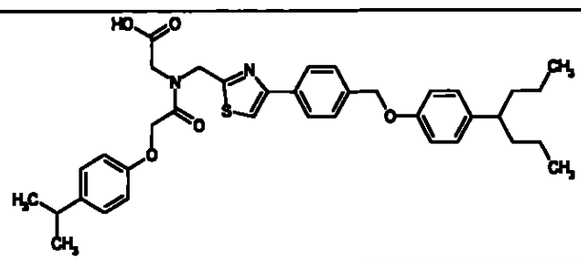
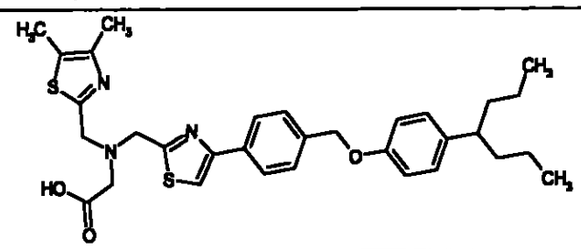
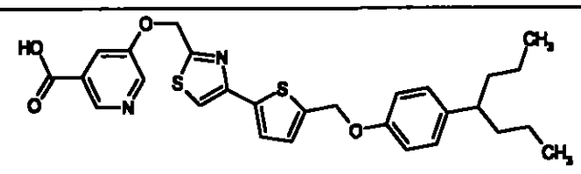
Ejemplo	Fórmula estructural	p.f. (°C)
1-103		amorfo
1-104		amorfo
1-105		amorfo
1-106		amorfo
1-107		amorfo

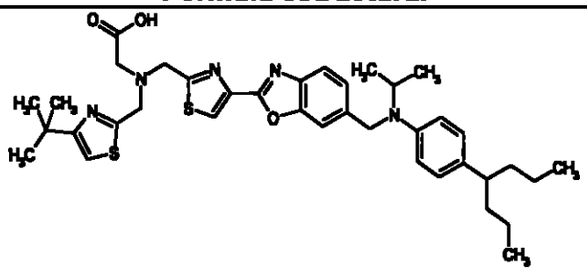
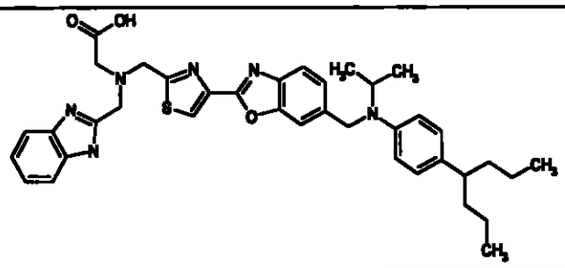
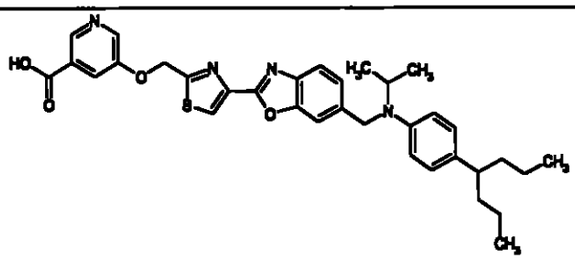
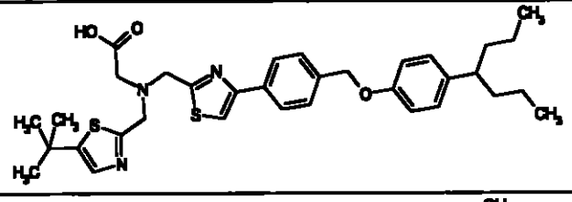
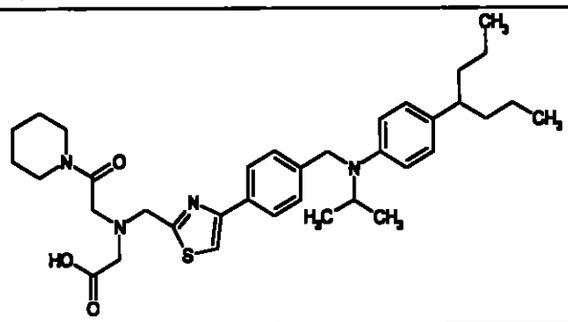
Ejemplo	Fórmula estructural	p.f. (°C)
1-108		129-131
1-109		amorfo
1-110		amorfo
1-111		amorfo
1-112		amorfo
1-113		166-168

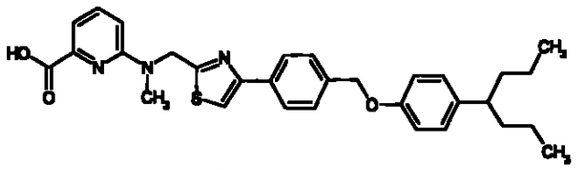
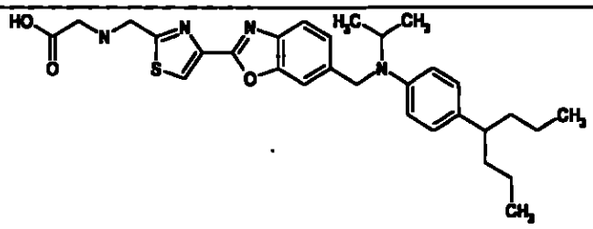
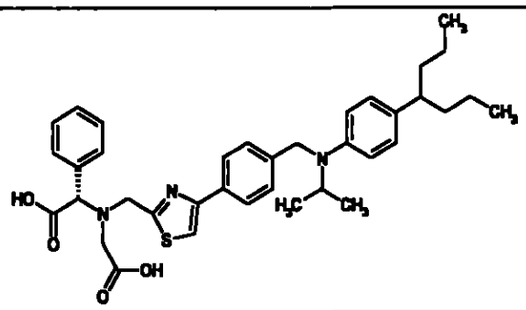
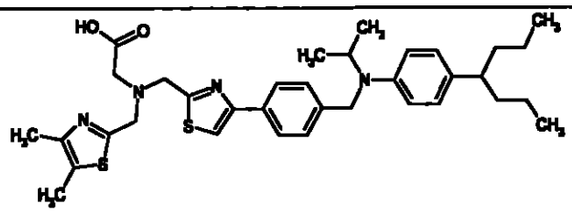
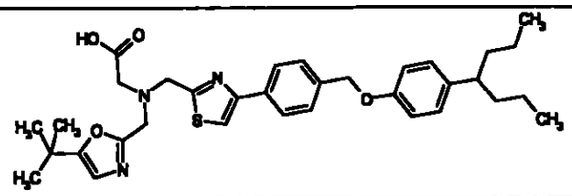
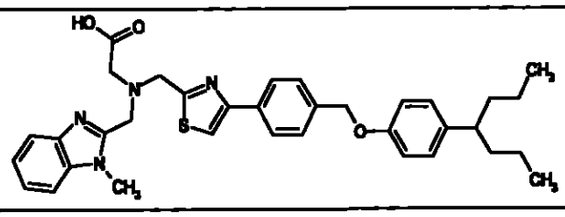
Ejemplo	Fórmula estructural	p.f. (°C)
1-114		amorfo
1-115		amorfo
1-116		146-148
1-117		amorfo
1-118		amorfo
1-119		amorfo

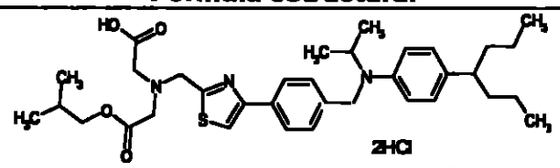
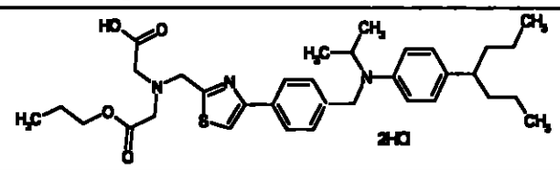
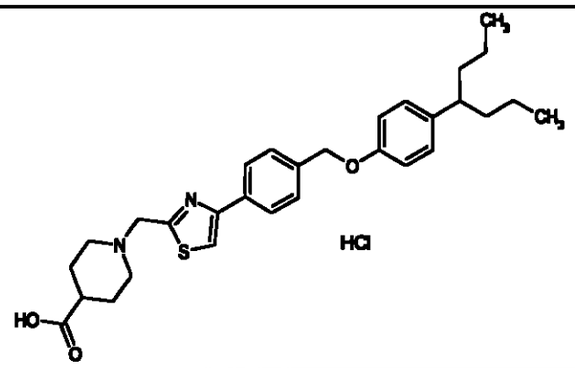
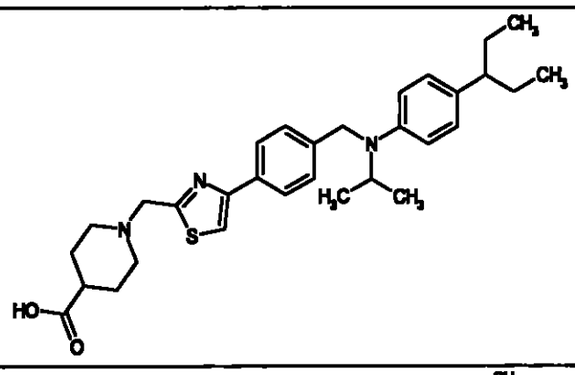
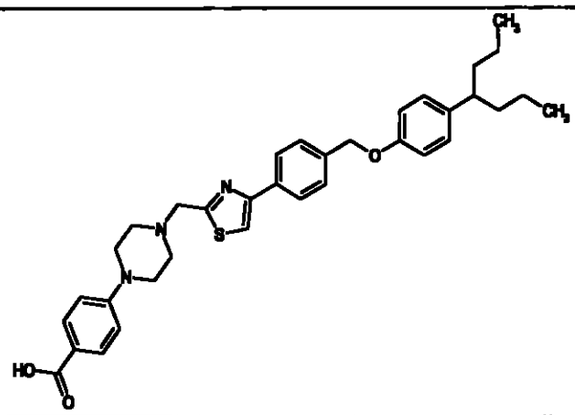
Ejemplo	Fórmula estructural	p.f. (°C)
1-120		amorfo
1-121		amorfo
1-122		amorfo
1-123		amorfo
1-124		124
1-125		122

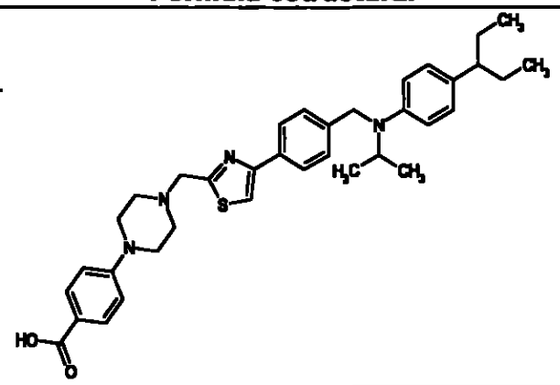
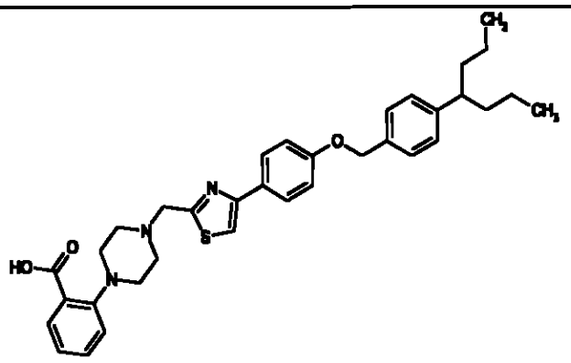
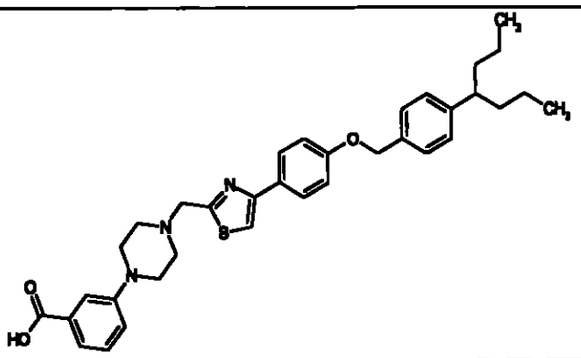
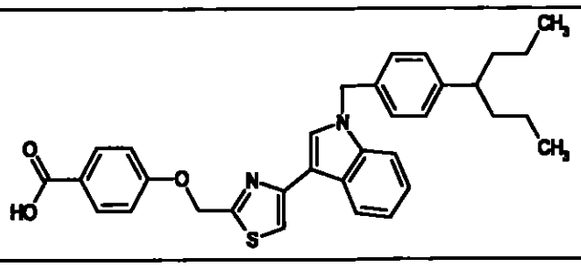
Ejemplo	Fórmula estructural	p.f. (°C)
1-126		210-212
1-127		amorfo
1-128		amorfo
1-129		143-145
1-130		170-172
1-131		amorfo

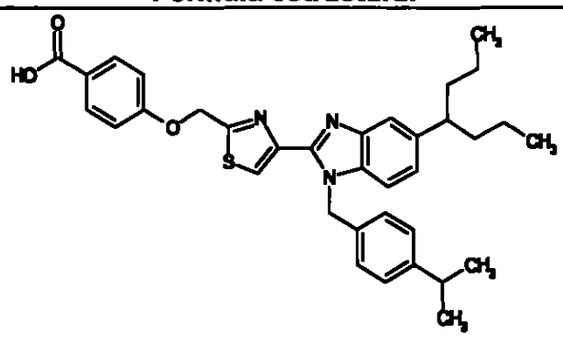
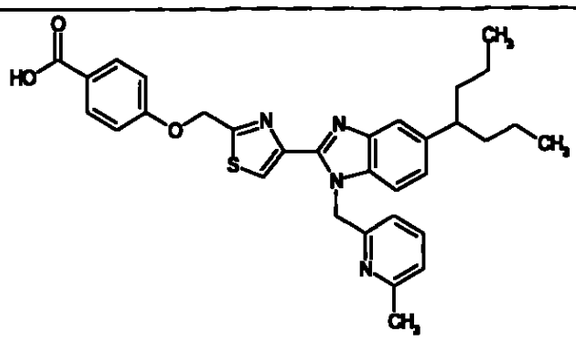
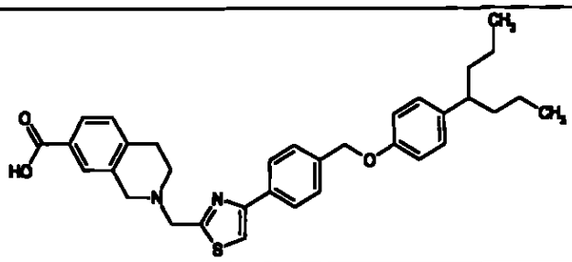
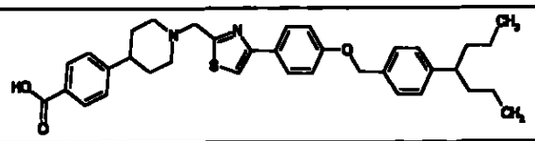
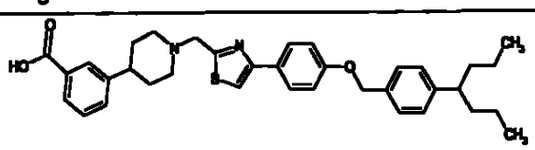
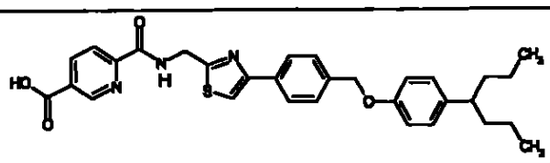
Ejemplo	Fórmula estructural	p.f. (°C)
1-132		amorfo
1-133		amorfo
1-134		158-160
1-135		192-194
1-136		amorfo
1-137		amorfo

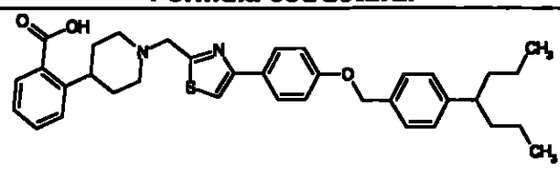
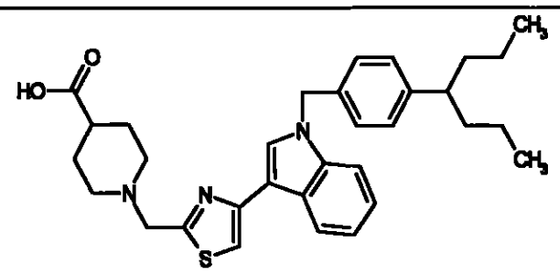
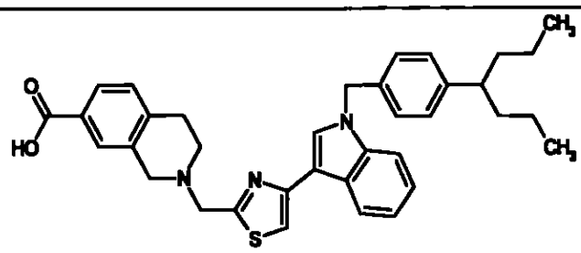
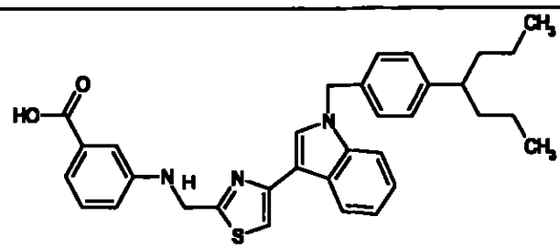
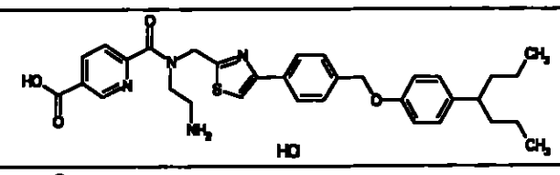
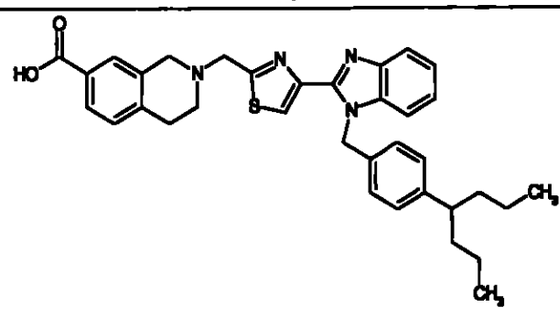
Ejemplo	Fórmula estructural	p.f. (°C)
1-138		98-100
1-139		127-133
1-140		135-138
1-141		amorfo
1-142		amorfo

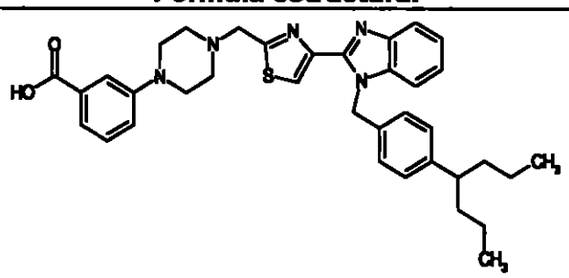
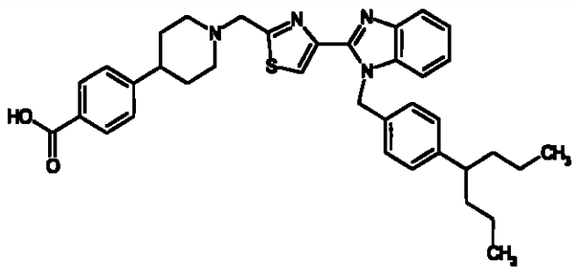
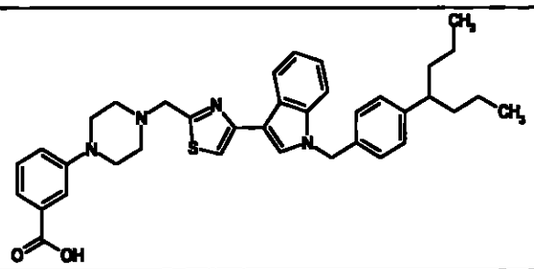
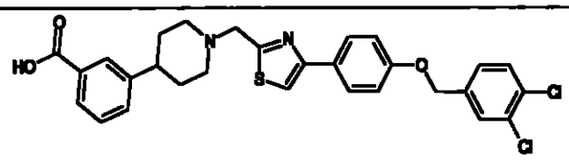
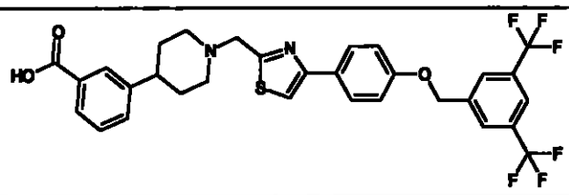
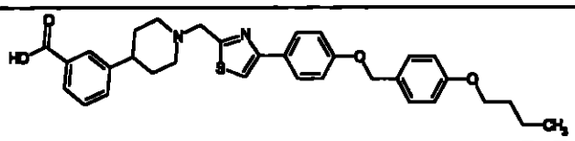
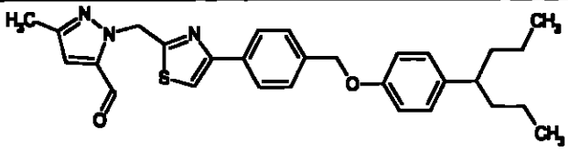
Ejemplo	Fórmula estructural	p.f. (°C)
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1-144		200-
1-145		amorfo
1-146		156-157
1-147		amorfo
1-148		amorfo

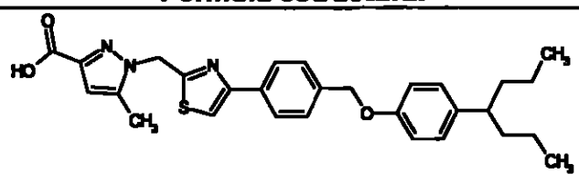
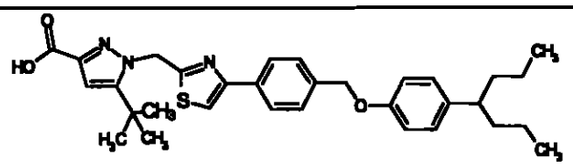
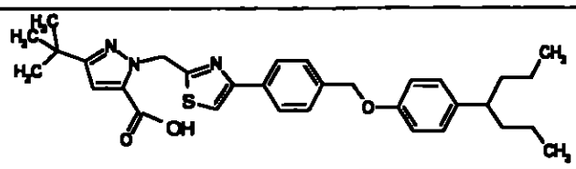
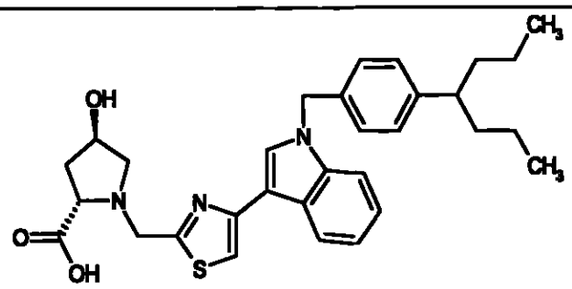
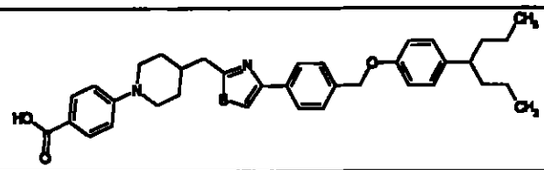
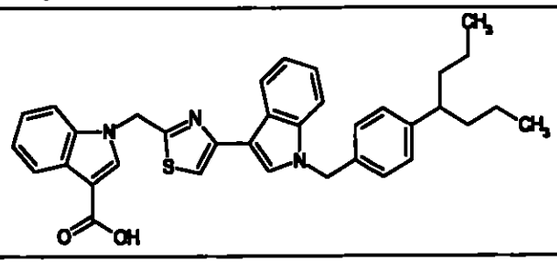
Ejemplo	Fórmula estructural	p.f. (°C)
1-149		amorfo
1-150		amorfo
1-151		amorfo
1-152		149-151
1-153		amorfo

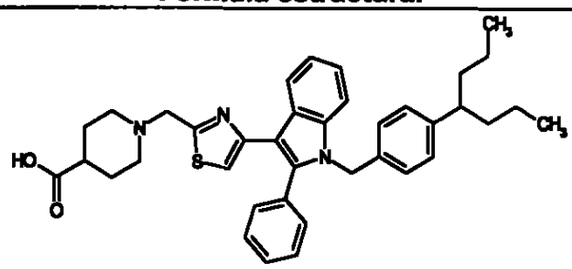
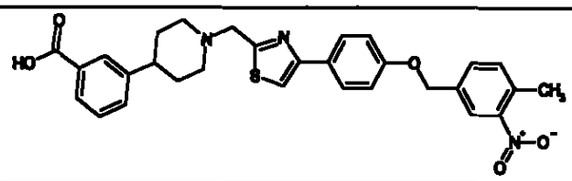
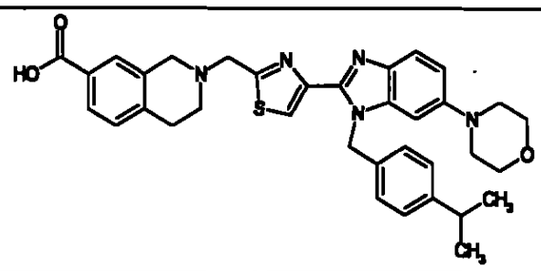
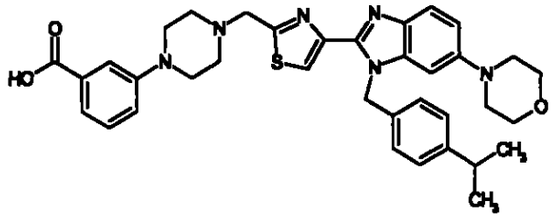
Ejemplo	Fórmula estructural	p.f. (°C)
1-154		232-234
1-155		137-138
1-156		153-154
1-157		199-200

Ejemplo	Fórmula estructural	p.f. (°C)
1-158		147-152
1-159		113-116
1-160		148.5-149.5
1-161		191-193
1-162		187-189
1-163		164-166

Ejemplo	Fórmula estructural	p.f. (°C)
1-164		170-172
1-165		111-115
1-166		124-128
1-167		83-85
1-168		227-229
1-169		189.2-190.3

Ejemplo	Fórmula estructural	p.f. (°C)
1-170		179.8-181.2
1-171		208.5-209.8
1-172		107-110
1-173		197-199
1-174		222-228
1-175		222-225
1-176		141-143

Ejemplo	Fórmula estructural	p.f. (°C)
1-177		185-194
1-178		195-196.5
1-179		123-125
1-180		105-107
1-181		174-175
1-182		148-152

Ejemplo	Fórmula estructural	p.f. (°C)
1-183		101-103
1-184		205-210
1-185		141-143.2
1-186		128.5-131.5

EJEMPLO 2-1

Acido {benzyl-[4-(4-{metil[4-(1-propilbutil)bencil]amino}-fenil)oxazol-2-ilmetil]amino}acético

(1) 4-(1-Propilbutil)benzaldehído



A una solución de tetracloruro de titanio (18.7 ml, 170 mmoles) en cloroformo (50 ml), se le agregó gota a gota una solución de (1-propilbutil)benceno (10.0 g, 56.7 mmoles) y éter metílico de diclorometilo (7.70 ml, 85.1 mmoles) en cloroformo (40 ml) bajo enfriamiento con hielo, y la mezcla se agitó a la misma temperatura durante 1 hora. La mezcla de reacción se vertió en hielo (100 g) y la mezcla se agitó a temperatura ambiente durante 1 hora. La capa orgánica se lavó sucesivamente con agua, una solución acuosa 0.5N de hidróxido de sodio, agua y salmuera saturada y se secó sobre sulfato de magnesio. Después de la filtración, el solvente se eliminó y el residuo se purificó mediante cromatografía en columna sobre gel de sílice (eluyente; acetato de etilo-hexano 1:50) para proporcionar el compuesto del título (10.0 g, rendimiento 87%).

(2) Clorhidrato de N-Metil-4-(1-propilbutil)bencilamina



A una solución de 4-(1-propilbutil)benzaldehído (1.00 g, 4.89 mmoles) obtenida en el Ejemplo 2-1(1) en etanol, se le agregó una solución (2 mol/l, 2.94 ml) de metilamina en metanol bajo enfriamiento con hielo, y la mezcla se agitó a temperatura ambiente durante 30 minutos. El solvente se eliminó y el residuo se disolvió en tetrahidrofurano (10 ml). Se agregó borohidruro de sodio (285 mg, 7.53 mmoles) bajo enfriamiento con hielo, y la

mezcla se agitó a temperatura ambiente durante 1 hora. Se agregó etanol y la mezcla se agitó durante 6 horas. El solvente se eliminó y se agregó cloroformo (10 ml) al residuo. Se agregaron agua y ácido clorhídrico 2N bajo enfriamiento con hielo y la mezcla se agitó a temperatura ambiente durante 3 horas. A la capa orgánica, se le agregó una solución saturada acuosa de carbonato ácido de sodio y dicarbonato de di-ter-butilo (1.28 g, 5.87 mmoles). La mezcla se agitó durante 3 horas. Después de dividirse, la capa orgánica se lavó con salmuera saturada y se secó sobre sulfato de sodio. El solvente se eliminó y el residuo se purificó mediante cromatografía en columna sobre gel de sílice (eluyente; acetato de etilo-hexano 5:95) para dar un aceite.

El aceite obtenido se disolvió en acetato de etilo (2 ml) y se le agregó una solución 4N de cloruro de hidrógeno - acetato de etilo (10 ml) y la mezcla se agitó durante 3 horas. Se agregó hexano (10 ml) y los precipitados se recolectaron mediante filtración y se secaron para proporcionar el compuesto del título (650 mg, rendimiento 52%).

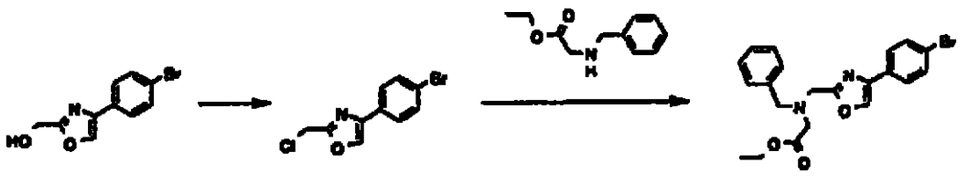
(3) (4-(4-Bromofenil)oxazol-2-il)metanol



Bajo una atmósfera de argón, a una solución de 2,2,6,6-tetrametilpiperidina (227 mg, 1.61 moles) en tetrahidrofurano (3.0 ml, 13 volumen/peso) se le agregó n-butillitio (solución de hexano 1.56M, 0.944 ml,

1.47 mmoles) a 0°C y la mezcla se agitó durante 30 minutos. Después de enfriar a -78°C, se agregó 4-(4-bromofenil)oxazol (300 mg, 1.34 mmoles) y la mezcla se agitó durante 45 minutos. Se agregó una suspensión de paraformaldehído (100 mg, 3.35 mmoles) en tetrahidrofurano (1.5 ml, 15 volumen/peso) y la mezcla se agitó durante 20 minutos. Después de calentar a temperatura ambiente, se agregbó una solución saturada acuosa de cloruro de amonio (5.0 ml). El solvente se eliminó y la mezcla se extrajo con acetato de etilo (15 ml), se lavó con salmuera saturada (10 ml) y se secó sobre sulfato de sodio (1.0 g). El solvente se eliminó y el residuo se purificó mediante cromatografía en columna sobre gel de sílice (solvente de revelado, cloroformo-cloroformo:acetato de etilo=8:2) para proporcionar el compuesto del título (210 mg, rendimiento 62%).

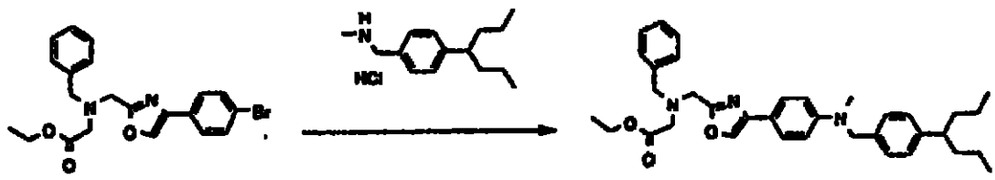
(4) Ester etílico de N-Bencil-N-((4-(4-bromofenil)oxazol-2-il)metil)glicina



Bajo una atmósfera de argón, a una suspensión de (4-(4-bromofenil)oxazol-2-il)metanol (200 mg, 0.787 mmoles) obtenido en el Ejemplo 2-1(3) en cloroformo (4.0 ml, 20 volumen/peso), se le agregó cloruro de tionilo (103 mg, 0.866 mmoles) a 0°C. La mezcla se agitó a temperatura ambiente durante 1 hora y a 60°C durante 1 hora. Se agregó cloruro de tionilo

(103 mg, 0.866 mmoles) a temperatura ambiente y la mezcla se agitó durante 12 horas. Después de eliminar el solvente, se le agregaron sucesivamente acetonitrilo (2.0 ml), éster etílico de N-bencilglicina (0.221 ml, 1.18 mmoles), carbonato de potasio (326 mg, 2.36 mmoles) y yoduro de potasio (13 mg, 0.0787 mmoles). La mezcla se agitó a 60°C durante 1 hora. Se agregó agua destilada (5.0 ml) a temperatura ambiente, y la mezcla se extrajo con un solvente mezclado de hexano:acetato de etilo=1:1, se lavó con salmuera saturada (5.0 ml) y se secó sobre sulfato de sodio (1.0 g). El solvente se eliminó y el residuo se purificó mediante cromatografía en columna sobre gel de sílice (solvente de revelado; hexano:acetato de etilo=9:1) para proporcionar el compuesto del título (220 mg, rendimiento 65%).

(5) Ester metílico del ácido {bencil-[4-(4-{metil-[4-(1-propil-butil)bencil]amino}fenil)oxazol-2-ilmetil]amino}acético



Bajo una atmósfera de argón, a una solución del éster etílico de N-bencil-N-((4-(4-bromofenil)oxazol-2-il)metil)glicina (200 mg, 0.466 mmoles) obtenido en el Ejemplo 2-1(4) en dioxano (2.0 ml) se le agregaron sucesivamente clorhidrato de la N-metil-4-(1-propilbutil)bencilamina (131 mg, 0.512 mmoles) obtenido en el Ejemplo 2-1(2), (R)-(+)-2,2'-bis(difenilfosfino)-

1,1'-binaftilo (29.0 mg, 0.0466 mmoles), carbonato de cesio (334 mg, 1.03 mmoles) y acetato de paladio (5.20 mg, 0.0233 mmoles). La mezcla se agitó a 90°C durante 18 horas y se agregaron (R)-(+)-2,2'-bis(difenilfosfino)-1,1'-binaftilo (70.0 mg, 0.112 mmoles) y acetato de paladio (10.0 mg, 0.0445 mmoles). La mezcla se agitó a 100°C durante 3 horas y se agregó carbonato de cesio (200 mg, 0.614 mmoles). La mezcla se agitó durante 12 horas. Se agregó 4-Morfolinoanilina (83.0 mg, 0.466 mmoles) y la mezcla se agitó durante 4 horas y se pasó a través de Celite a temperatura ambiente. El solvente se eliminó y el residuo se purificó mediante cromatografía en columna sobre gel de sílice (solvente de revelado; hexano:acetato de etilo=9:1) para proporcionar el compuesto del título (35.0 mg, rendimiento 13%).

(6) Acido {benzyl-[4-(4-{metil-[4-(1-propilbutil)bencil]amino}-fenil)oxazol-2-ilmetil]amino}acético



Bajo una atmósfera de argón, a una solución del éster metílico del ácio {bencil[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)oxazol-2-ilmetil]amino}acético (30.0 mg, 0.0528 mmoles), obtenido en el Ejemplo 2-1(5) en tetrahidrofurano (0.50 ml), se le agregaron metanol (0.50 ml) y una solución

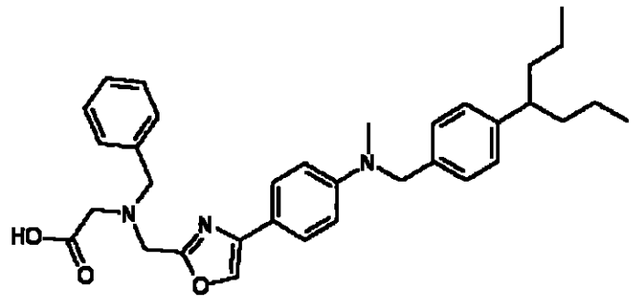
acuosa 2N de hidróxido de sodio (0.0528 ml, 0.106 mmoles). La mezcla se agitó a 70°C durante 1.5 horas y se le agregaron sucesivamente ácido clorhídrico 1N (0.106 ml, 0.106 mmoles) y agua destilada (2.0 ml) a temperatura ambiente. El solvente se eliminó, y se le agregaron sucesivamente hexano (0.2 ml) y agua destilada (2.0 ml). Los precipitados se recolectaron mediante filtración, y se secaron para proporcionar el compuesto del título (16.0 mg, rendimiento 56%).

^{1}H RMN (DMSO-d_6, 300 MHz) δ 0.79 (t, J=7.3 Hz, 6H), 0.95-1.20 (m, 4H), 1.40-1.65 (m, 4H), 2.40-2.60 (m, 1H), 3.02 (s, 3H), 3.81 (s, 2H), 3.93 (s, 2H), 4.57 (s, 2H), 6.78 (d, J=8.8 Hz, 2H), 7.00-7.40 (m, 9H), 7.55 (d, J=8.8 Hz, 2H), 8.30 (s, 1H), 12.30 (s amplio, 1H).

Punto de fusión: 129°C-131°C

La fórmula estrucural y el valor de las propiedades del Ejemplo 2-1 se muestra en el siguiente Cuadro 2.

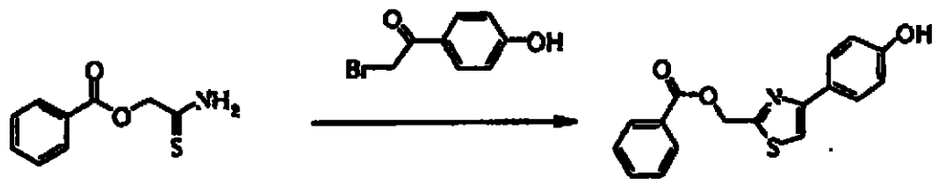
CUADRO 2

Ejemplo	Fórmula Estructural	p.f.(°C)
2-1		129 - 131

EJEMPLO 3-1

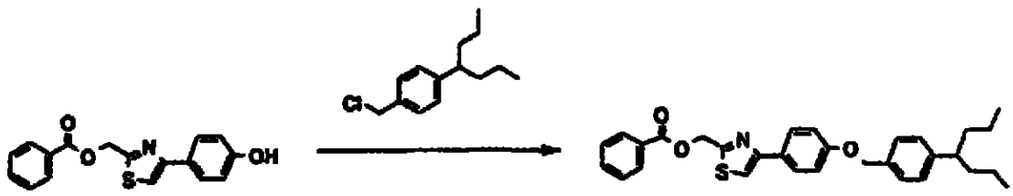
Acido 5-(4-{4-[4-(1-Propilbutil)benciloxi]fenil}tiazol-2-ilmetoxi)nicotínico

(1) Benzoato de (4-(4-Hidroxifenil)tiazol-2-il)metilo



A una solución de 2-(benzoiloxi)etantioamida (4 g, 20.488 mmoles) y carbonato ácido de sodio (1.72 g, 20.488 mmoles) in N,N-dimetilacetamida (4 ml), se le agregó gota a gota una solución de 2-bromo-4'-hidroxiacetofenona (5 g, pureza 88%, 20.488 mmoles) en N,N-dimetilacetamida (8 ml) a temperatura ambiente, y la mezcla se agitó a la misma temperatura durante 2 horas. Después de la terminación de la reacción, se le agregaron etanol y agua y los precipitados se recolectaron mediante filtración y se lavaron con 50% de etanol. El sólido obtenido se secó bajo presión reducida para proporcionar el compuesto del título (5.336 g, 84.1%).

(2) Benzoato de (4-(4-(4-(1-propilbutil)benciloxi)fenil)tiazol-2-il)metilo



A una solución del benzoato de (4-(4-hidroxifenil)tiazol-2-il)metilo (14.0 g, 44.9 mmoles) obtenido en el Ejemplo 3-1(1) en N,N-dimetilacetamida (70 ml), se le agregó cloruro de 4-(1-propilbutil)bencilo (10.1 g, 44.9 mmoles), carbonato de potasio (12.4 g, 89.9 mmoles) y yoduro de potasio (75 mg, 0.45 mmoles) y la mezcla se agitó a 80°C durante 3 horas. Después de dejar enfriar, se agregó acetato de etilo y la mezcla se lavó sucesivamente con agua y salmuera saturada y se secó sobre sulfato de magnesio. Después de la filtración, el solvente se eliminó y se agregó etanol (120 ml). La mezcla se calentó a 50°C. Después de dejar enfriar, los cristales precipitados se recolectaron mediante filtración y se secaron para proporcionar el compuesto del título (19.5 g, rendimiento 87%).

(3) (4-(4-(4-(1-Propilbutil)benciloxi)fenil)tiazol-2-il)metanol



Al benzoato de (4-(4-(4-(1-propilbutil)benciloxi)fenil)tiazol-2-il)metilo (26.5 g, 53.1 mmoles) obtenido en el Ejemplo 3-1(2), se le agregaron metanol (159 ml), tetrahidrofurano (27 ml) y una solución acuosa 2N de

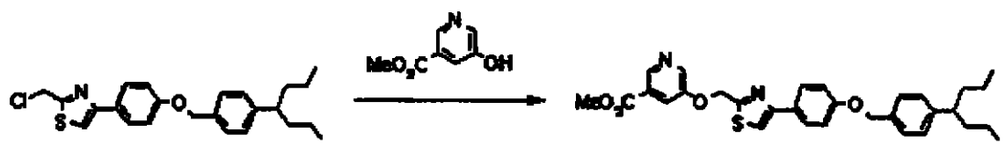
hidróxido de sodio (39.8 ml, 79.6 mmoles) y la mezcla se agitó a 80°C durante 1 hora. El solvente se eliminó y se agregó agua (265 ml). La mezcla se agitó a temperatura ambiente durante 1 hora. Los cristales se recolectaron mediante filtración, se disolvieron en tolueno (100 ml) y acetato de etilo (10 ml). La mezcla se lavó con salmuera saturada y se secó sobre sulfato de magnesio y se filtró, y el solvente se eliminó para proporcionar el compuesto del título (20.5 g, rendimiento 98%).

(4) Cloruro de (4-(4-(4-(1-propilbutil)benciloxi)fenil)tiazol-2-il)metilo



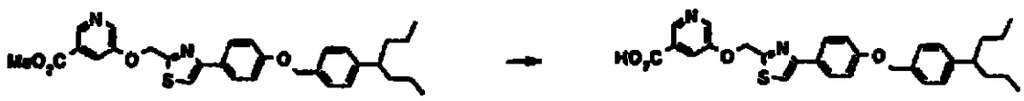
A una solución de (4-(4-(4-(1-propilbutil)benciloxi)fenil)tiazol-2-il)metanol (20.5 g, 51.8 mmoles) obtenido en el Ejemplo 3-1(3) en cloroformo (103 ml), se le agregó cloruro de tionilo (9.17 g, 77.7 mmoles) y la mezcla se agitó a temperatura ambiente durante 1 hora. El solvente se eliminó para proporcionar el compuesto del título (21.9 g, cuantitativo).

(5) Ester metílico del ácido 5-(4-[4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetoxi)nicotínico



Se agregaron N,N-dimetilacetamida (104 ml), 5-hidroxinicotinato de metilo (5.25 g, 40.8 mmoles), carbonato de potasio (13.0 g, 94.2 mmoles) y yoduro de potasio (520 mg, 3.1 mmoles) al cloruro de (4-(4-(4-(1-propilbutil)benciloxi)fenil)tiazol-2-il)metilo (13.0 g, 31.4 mmoles), obtenido en el Ejemplo 3-1(4) y la mezcla se agitó a 75°C durante 2 horas. Después de dejar enfriar, se agregó acetato de etilo y la mezcla se lavó sucesivamente con agua, una solución saturada acuosa de carbonato ácido de sodio, agua y salmuera saturada, y se secó sobre sulfato de magnesio. Después de la filtración, el solvente se eliminó y el residuo se purificó mediante cromatografía en columna sobre gel de sílice (eluyente; tolueno-acetato de etilo, 5:1). Los cristales crudos obtenidos se suspendieron para el lavado con éter, para proporcionar el compuesto del título (9.91 g, rendimiento 59%).

(6) Acido 5-(4-[4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetoxi)nicotínico



Al éster metílico del ácido 5-(4-[4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetoxi)nicotínico (9.50 g, 17.9 mmoles), obtenido en el Ejemplo 3-1(5), se le agregaron tetrahidrofurano (62.5 ml),

etanol (62.5 ml) y una solución acuosa 2N de hidróxido de sodio (17.9 ml, 35.8 mmoles), y la mezcla se agitó a 70°C durante 2.5 horas. Se agregó ácido clorhídrico 2N (17.9 ml, 35.8 mmoles) bajo enfriamiento con hielo y la mezcla se concentró bajo presión reducida. Se agregaron etanol (19 ml) y agua (9.5 ml), y después de la agitación, los cristales se recolectaron mediante filtración y se secaron para proporcionar el compuesto del título (9.15 g, rendimiento 99%).

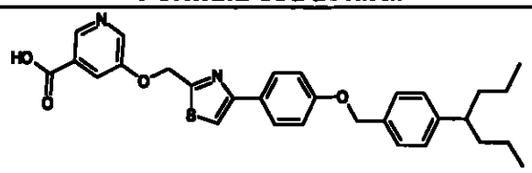
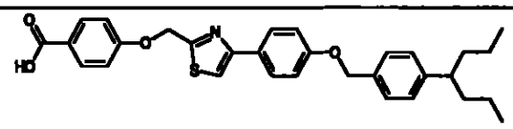
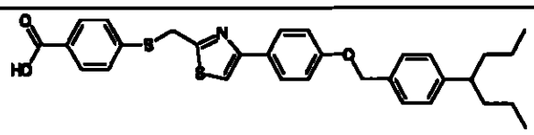
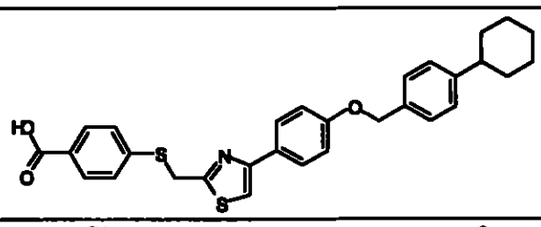
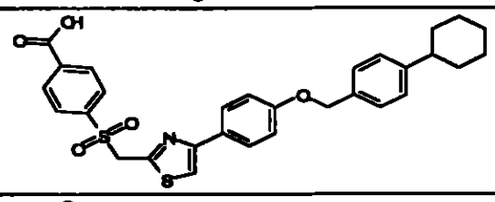
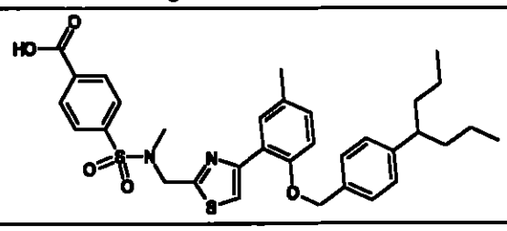
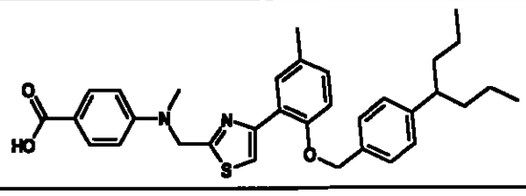
^{1}H RMN (DMSO-d_6, 400 MHz) δ 0.81 (t, J=7.3 Hz, 6H), 1.05-1.13 (m, 4H), 1.48-1.57 (m, 4H), 2.5-2.56 (m, 1H), 5.09 (s, 2H), 5.66 (s, 2H), 7.09 (d, J=9.04 Hz, 2H), 7.19 (d, J=8.32 Hz, 2H), 7.38 (d, J=8.12 Hz, 2H), 7.91 (d, J=9.04 Hz, 2H), 7.98-7.99 (m, 1H), 8.03 (s, 1H), 8.64 (d, J=3 Hz, 1H), 8.72 (d, J=1.4 Hz, 1H), 13.52 (s, 1H)

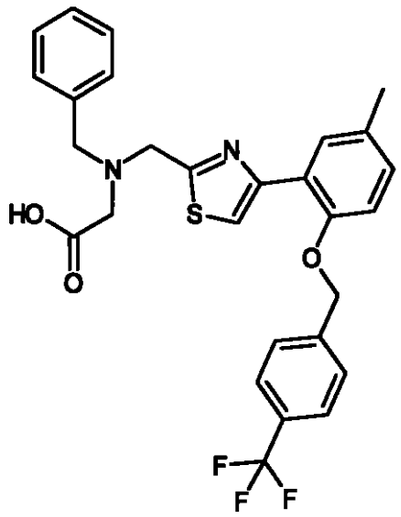
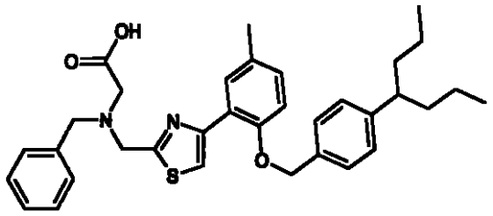
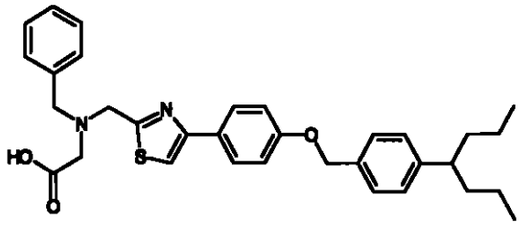
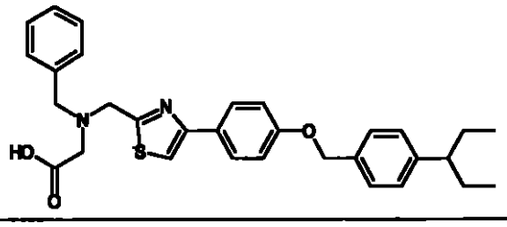
Punto de fusión: 172-174°C

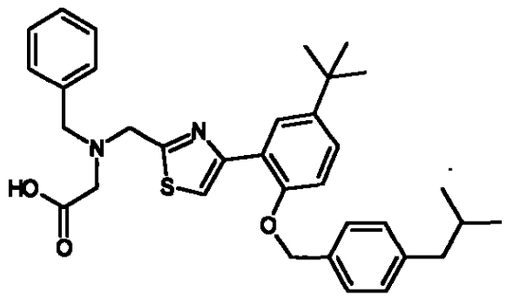
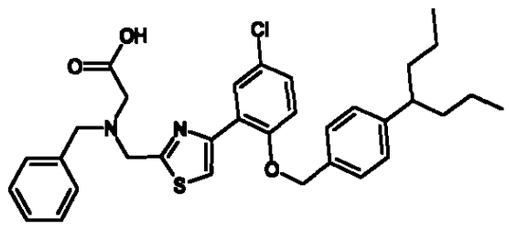
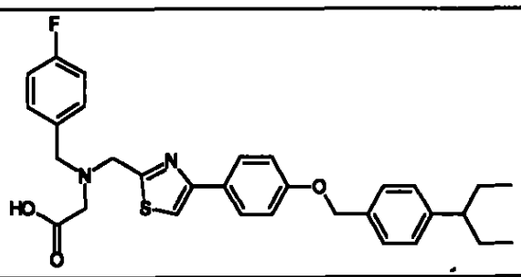
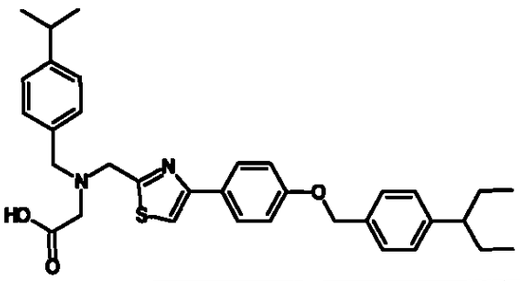
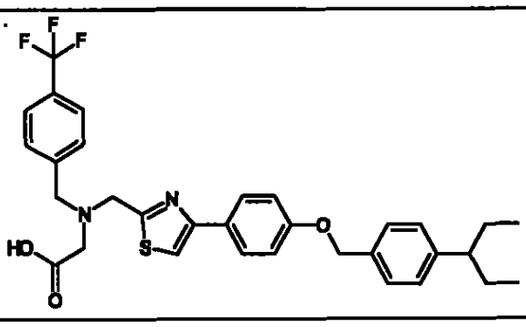
EJEMPLOS 3-2 to 3-132

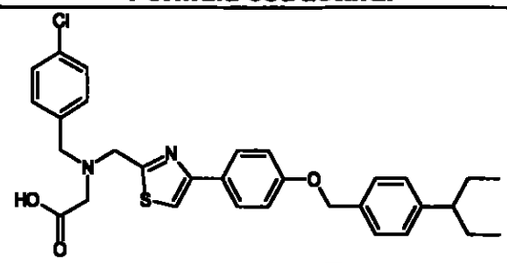
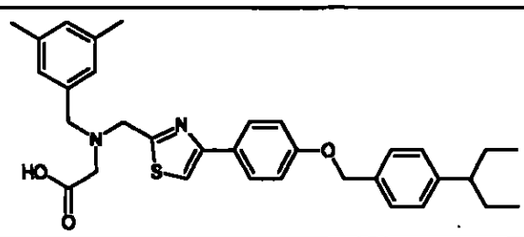
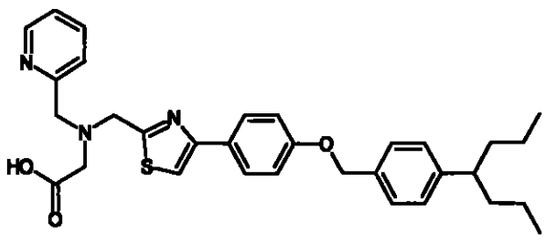
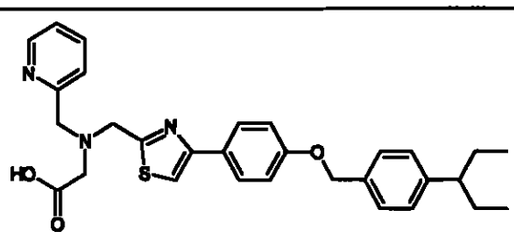
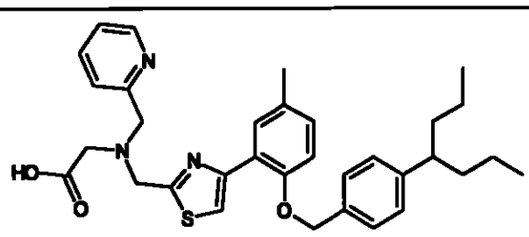
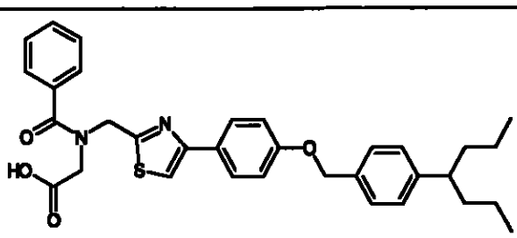
De la misma manera que en el Ejemplo 3-1 y utilizando otros métodos convencionales en donde sea necesario, se producen los compuestos de los Ejemplos 3-2 a 3-132. Las fórmulas estructurales y los valores de las propiedades de los compuestos obtenidos, así como aquéllos del Ejemplo 3-1, se muestran en los siguientes Cuadros.

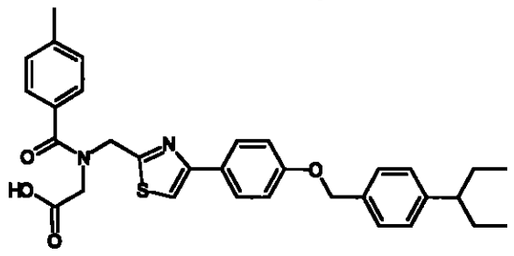
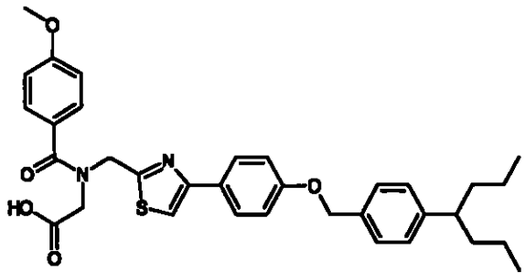
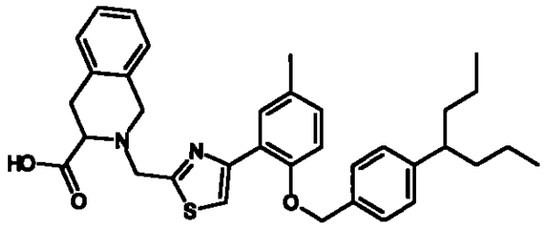
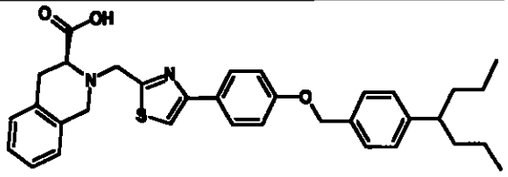
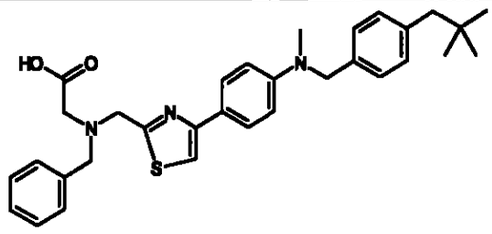
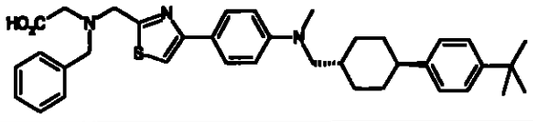
CUADRO 3

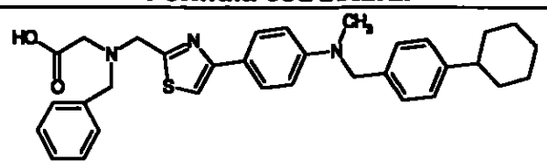
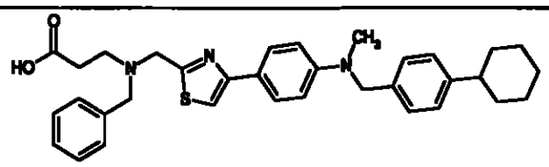
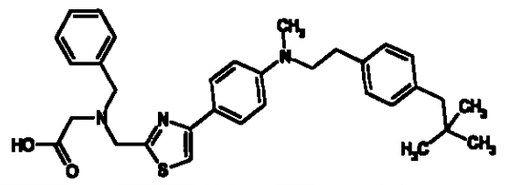
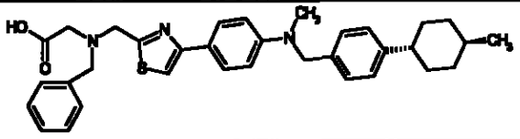
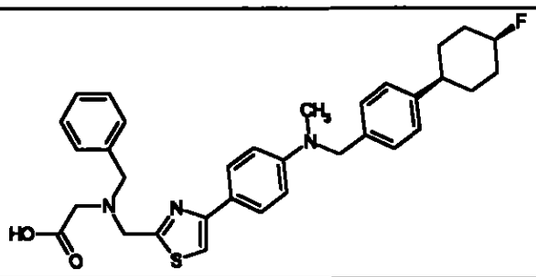
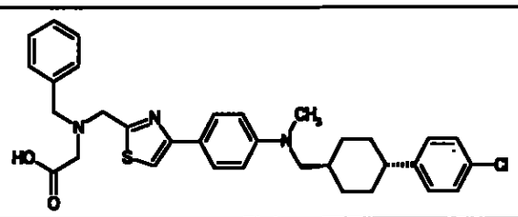
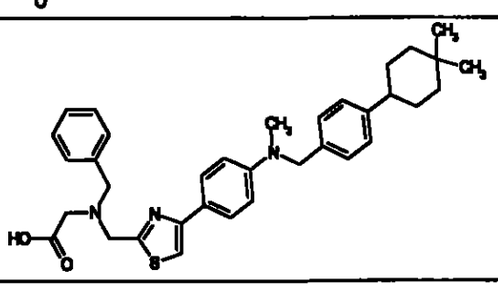
Ejemplo	Fórmula estructural	p. f. (°C)
3-1		172-174
3-2		204-207
3-3		117-118
3-4		amorfo
3-5		amorfo
3-6		130-132
3-7		184-187

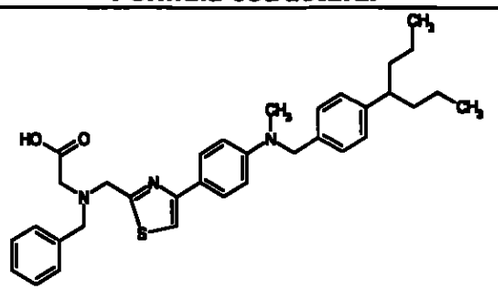
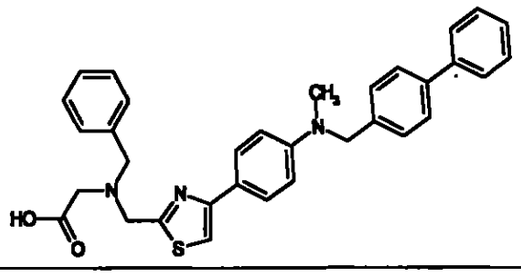
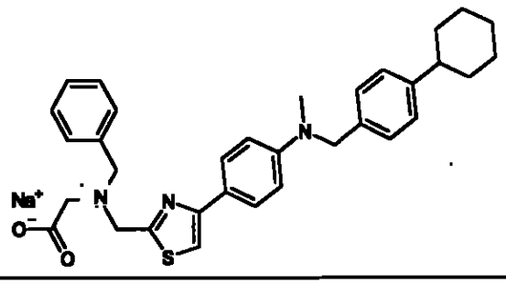
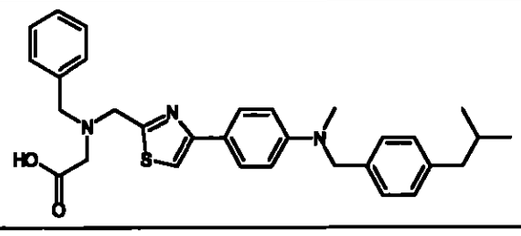
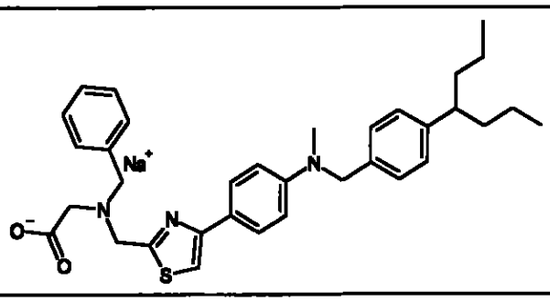
Ejemplo	Fórmula estructural	p. f. (°C)
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3-9		126-128
3-10		145-148
3-11		144-146

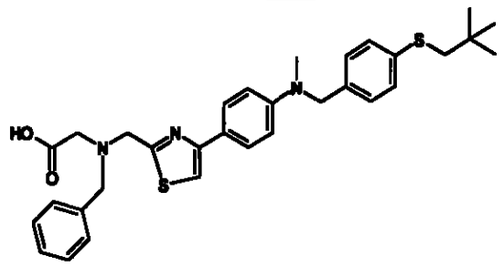
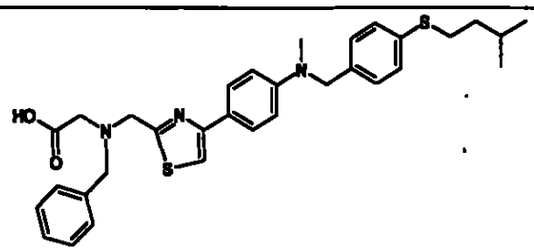
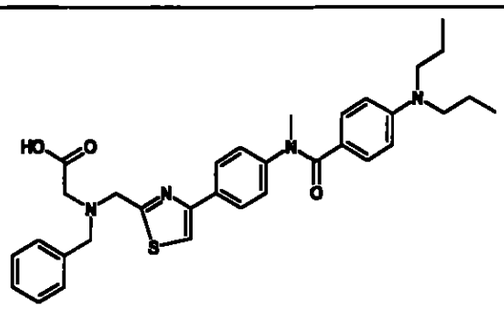
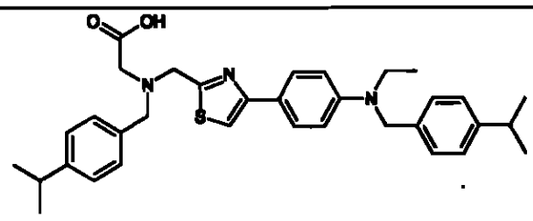
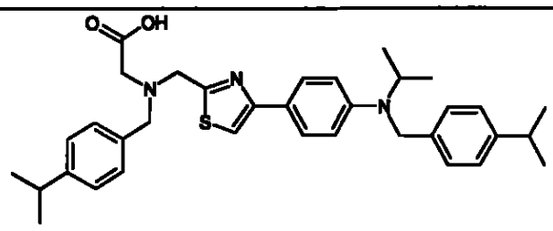
Ejemplo	Fórmula estructural	p. f. (°C)
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3-13		130-131
3-14		153-155
3-15		138-140
3-16		136-138

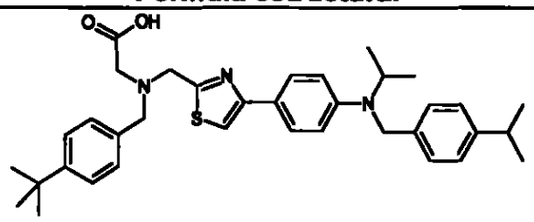
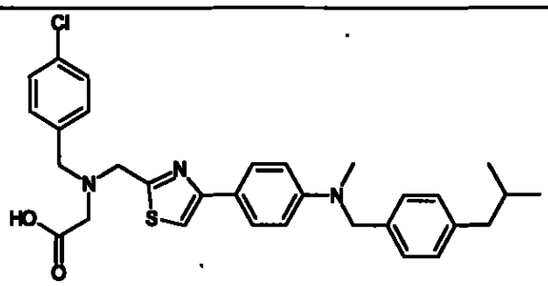
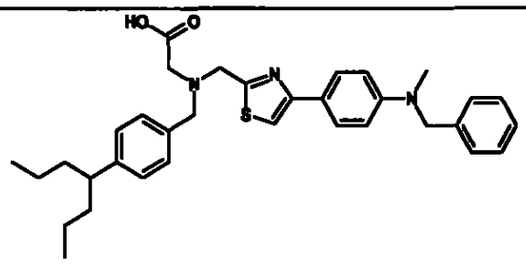
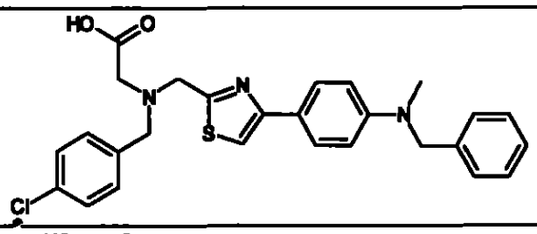
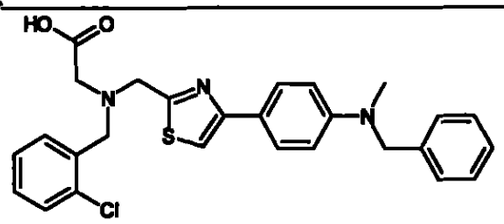
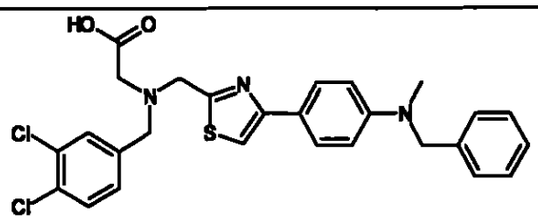
Ejemplo	Fórmula estructural	p. f. (°C)
3-17		154-157
3-18		114-119
3-19		155-156
3-20		156-157
3-21		118-120
3-22		141-144

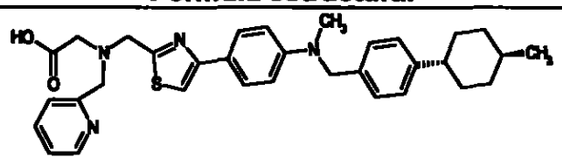
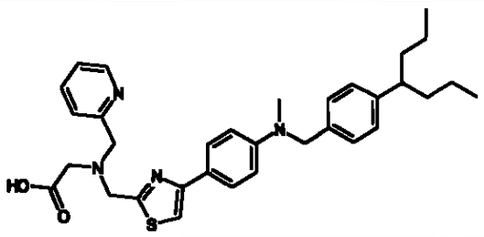
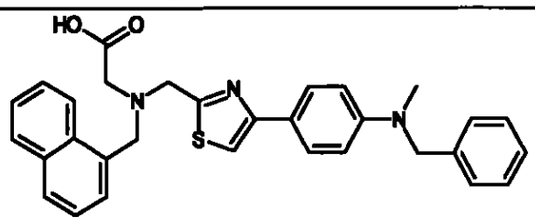
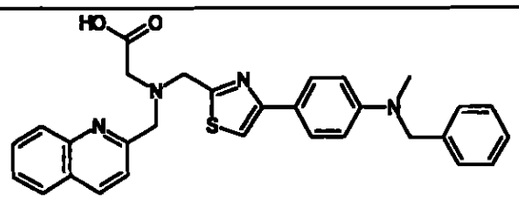
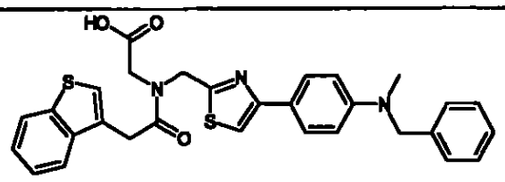
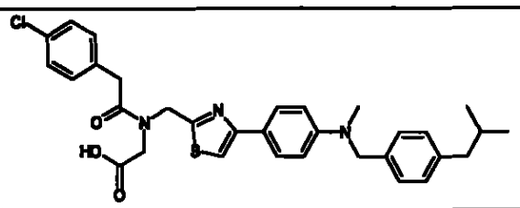
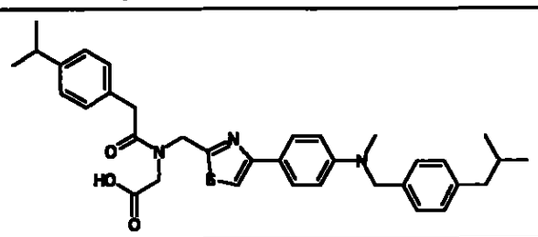
Ejemplo	Fórmula estructural	p. f. (°C)
3-23		142-144
3-24		99-101
3-25		149-152
3-26		90-93
3-27		159-160
3-28		192-195

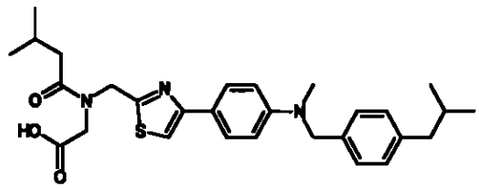
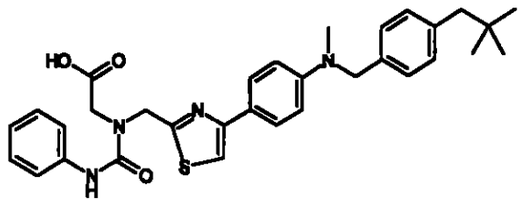
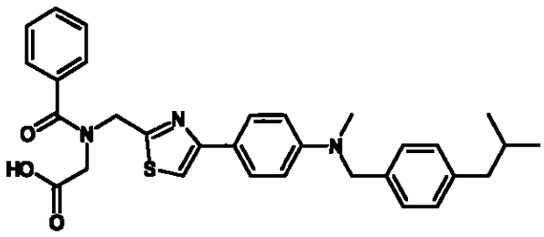
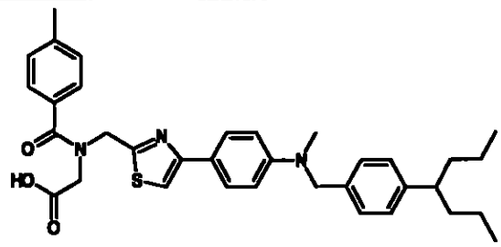
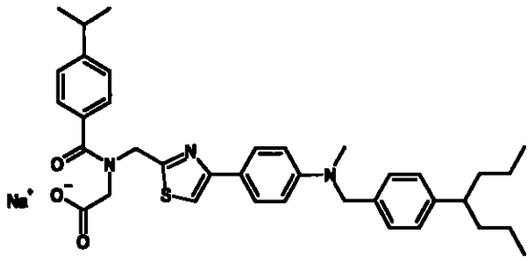
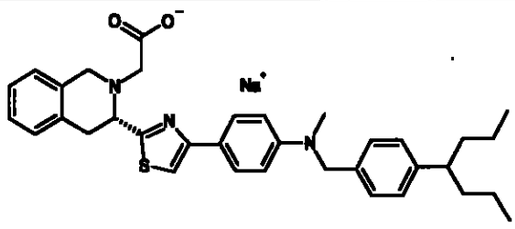
Ejemplo	Fórmula estructural	p. f. (°C)
3-29		148-150
3-30		amorfo
3-31		133-134
3-32		157-159
3-33		146-147
3-34		180-182
3-35		amorfo

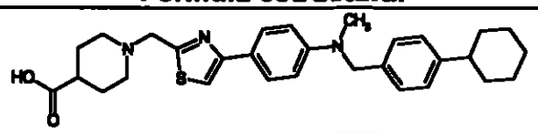
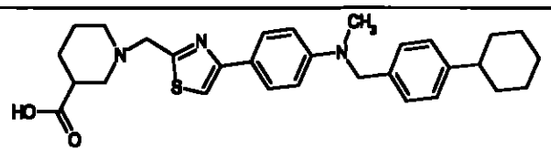
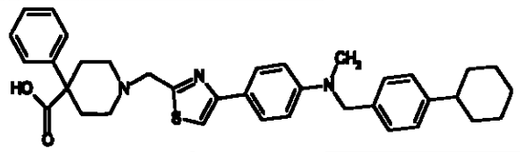
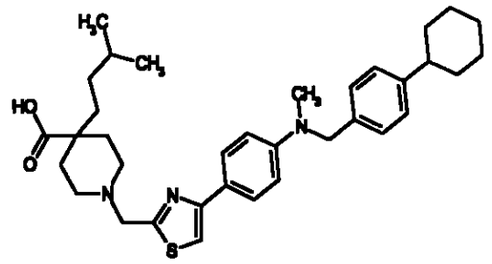
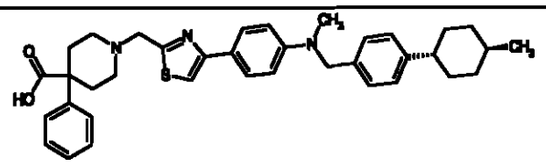
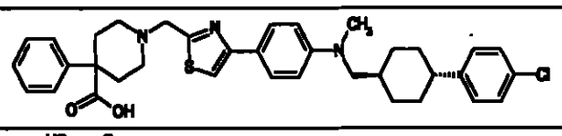
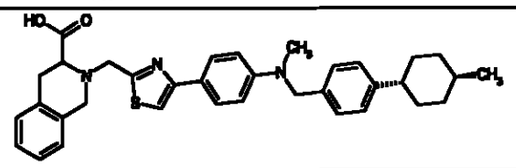
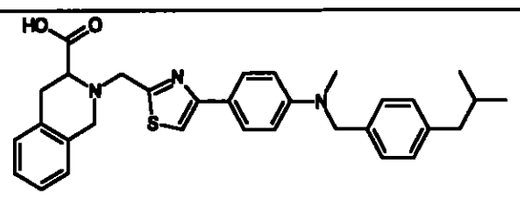
Ejemplo	Fórmula estructural	p. f. (°C)
3-36		amorfo
3-37		167-170
3-38		250-
3-39		149-151
3-40		amorfo

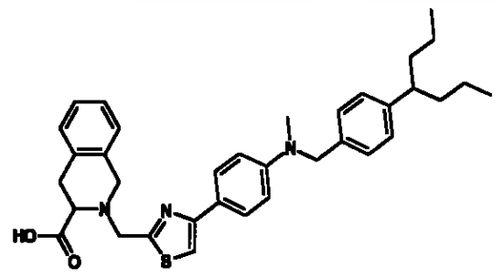
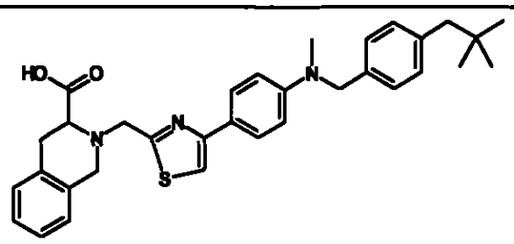
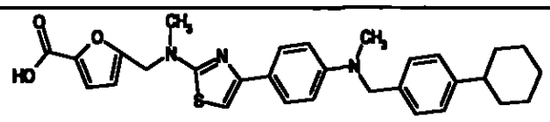
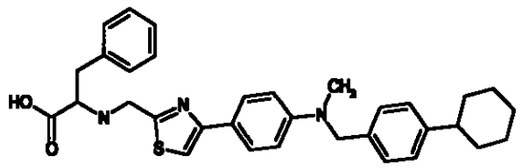
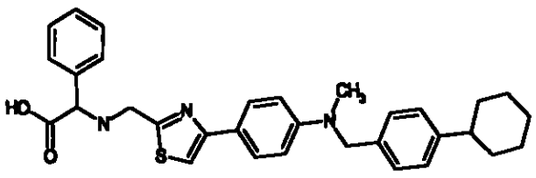
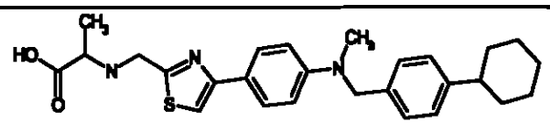
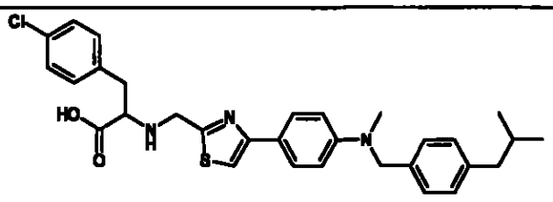
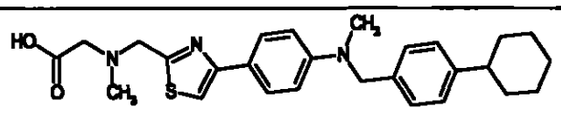
Ejemplo	Fórmula estructural	p. f. (ºC)
3-41		143
3-42		122
3-43		amorfo
3-44		74-78
3-45		77-82

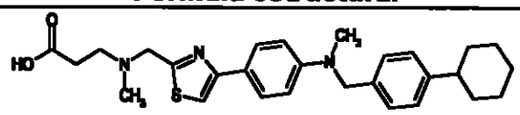
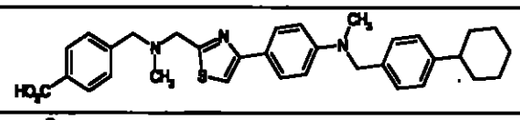
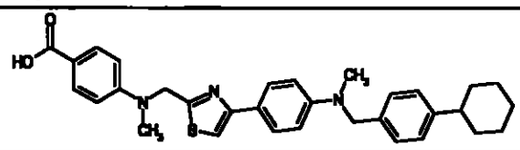
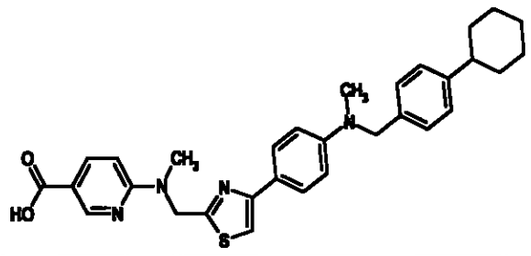
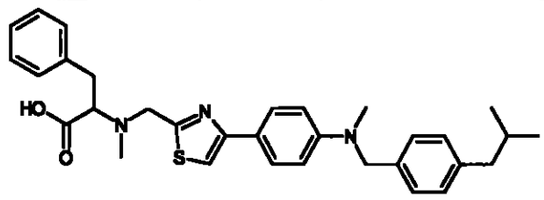
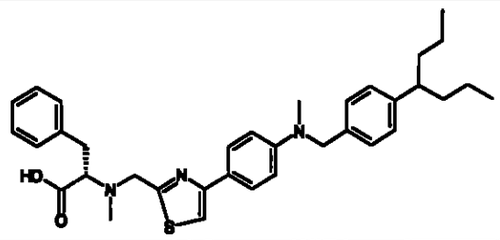
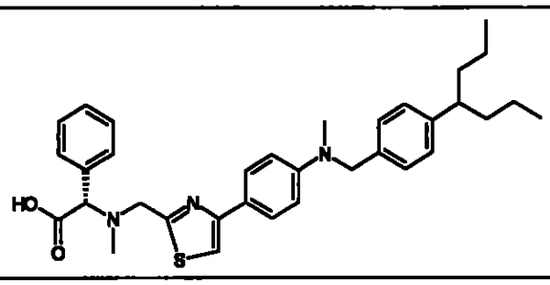
Ejemplo	Fórmula estructural	p. f. (°C)
3-46		82-87
3-47		153-157
3-48		137-140
3-49		140-142
3-50		132-134
3-51		69-72

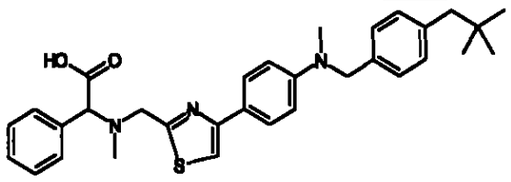
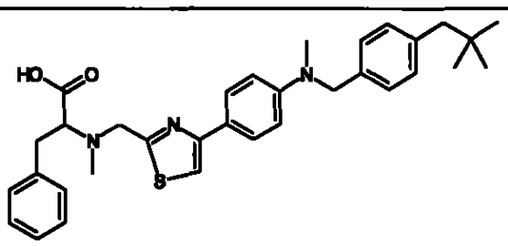
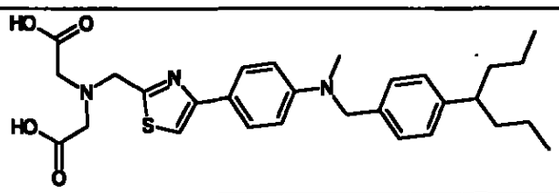
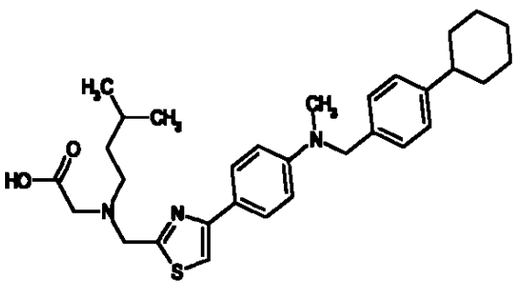
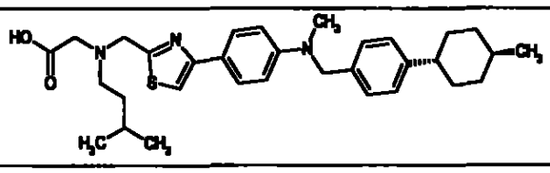
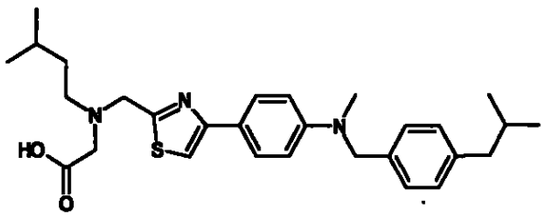
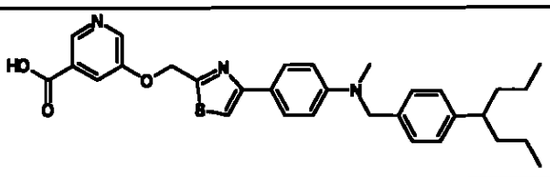
Ejemplo	Fórmula estructural	p. f. (°C)
3-52		230-
3-53		117-120
3-54		78-83
3-55		144-147
3-56		186-188
3-57		150-152
3-58		124-126

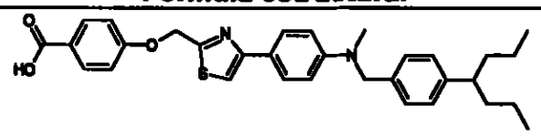
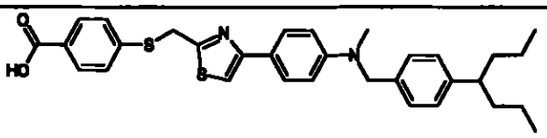
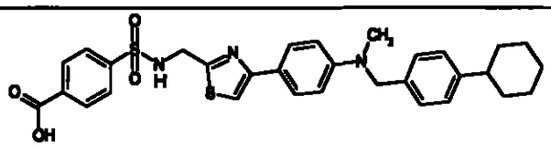
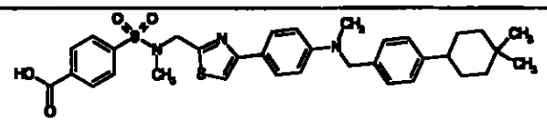
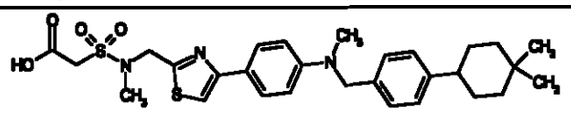
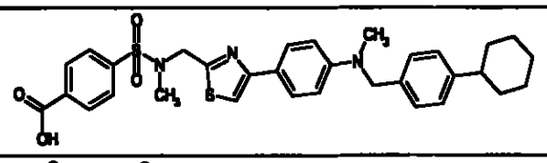
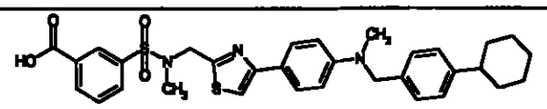
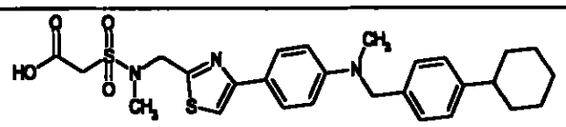
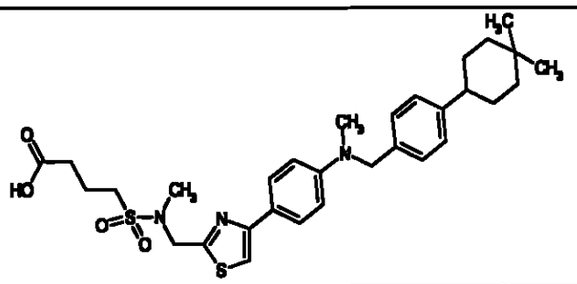
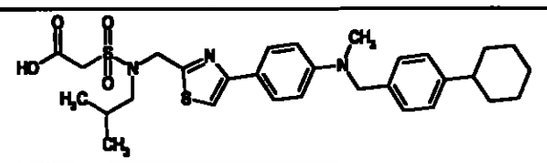
Ejemplo	Fórmula estructural	p. f. (°C)
3-59		117-118
3-60		152-153
3-61		143-145
3-62		114-117
3-63		183-188
3-64		186-187

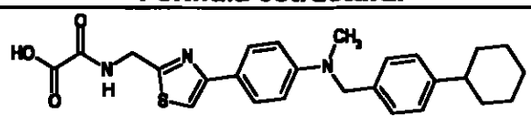
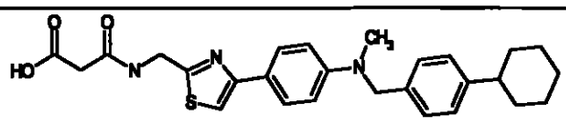
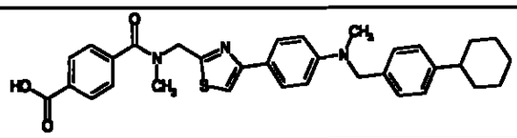
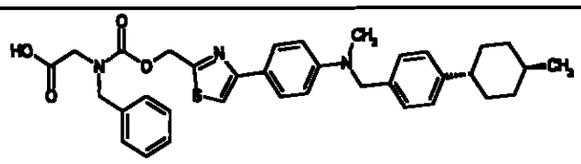
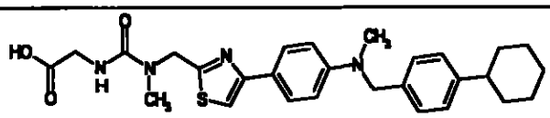
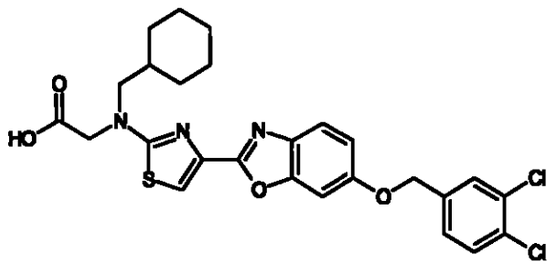
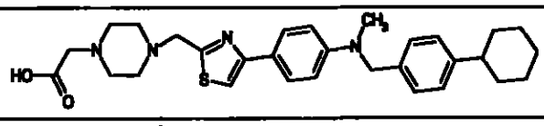
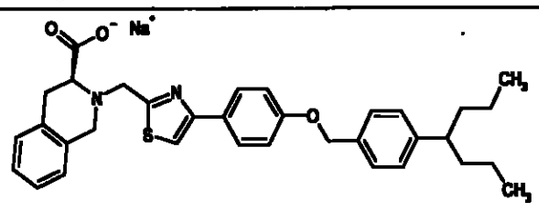
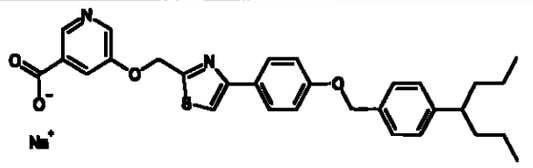
Ejemplo	Fórmula estructural	p. f. (°C)
3-65		amorfo
3-66		176-180
3-67		220-222
3-68		233-235
3-69		229-231
3-70		167-170 descomposición
3-71		202-205
3-72		168-170

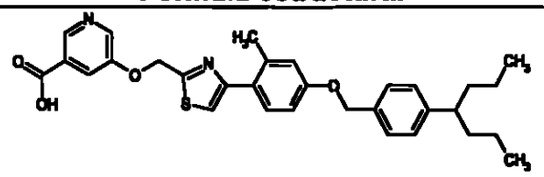
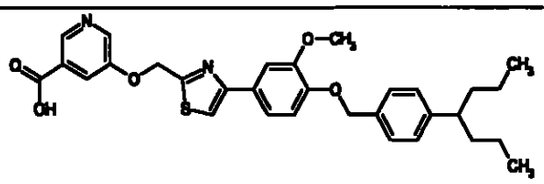
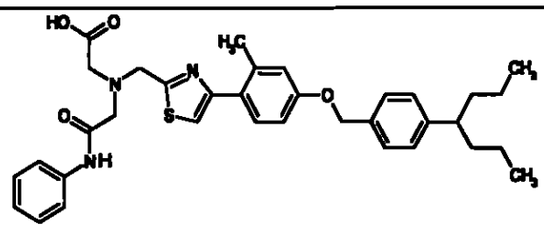
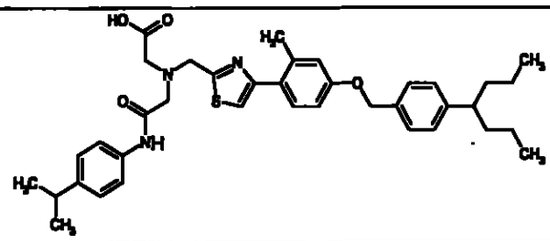
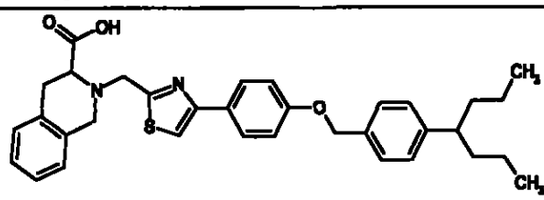
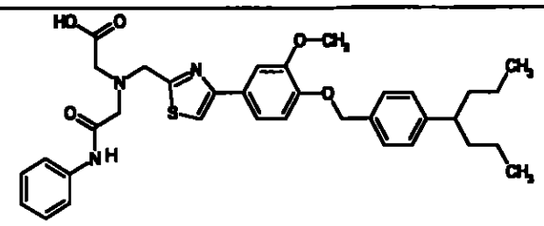
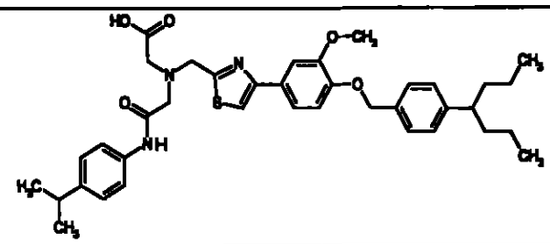
Ejemplo	Fórmula estructural	p. f. (°C)
3-73		176-179
3-74		175-177
3-75		158-161
3-76		185-190
3-77		183-186
3-78		135-138
3-79		199-204
3-80		152-155

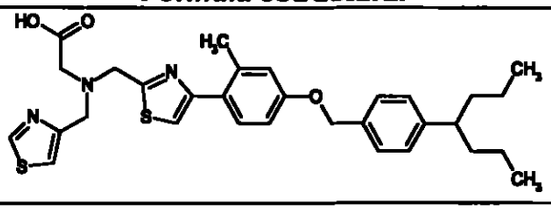
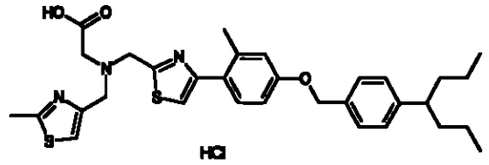
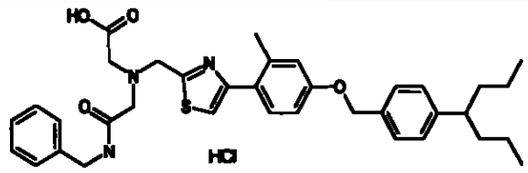
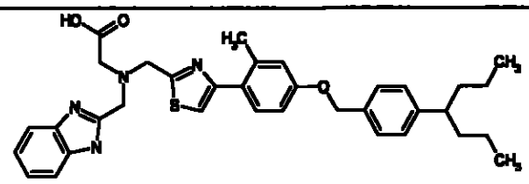
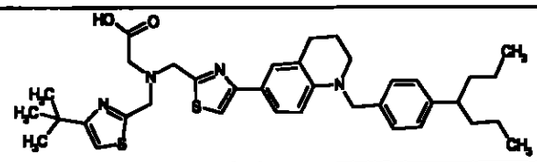
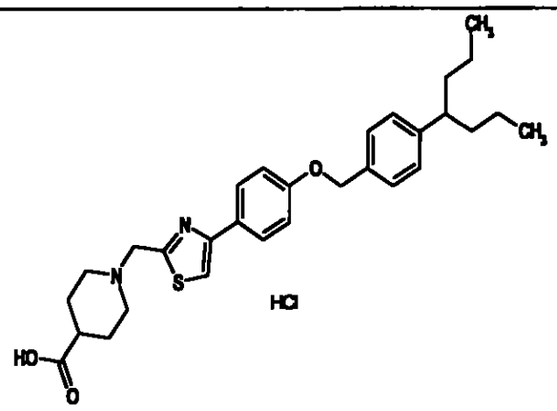
Ejemplo	Fórmula estructural	p. f. (°C)
3-81		amorfo
3-82		amorfo
3-83		amorfo
3-84		226-228
3-85		138-139
3-86		143
3-87		146

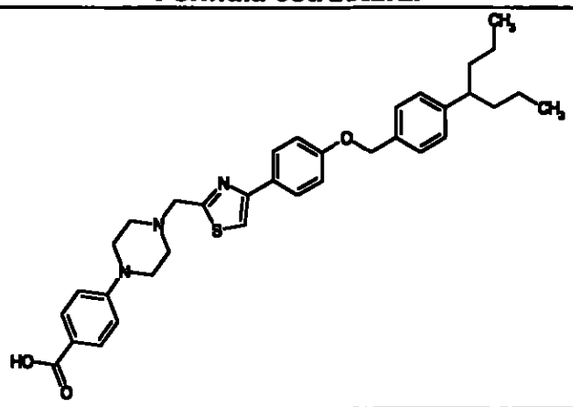
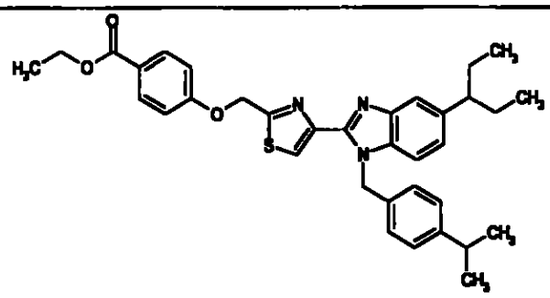
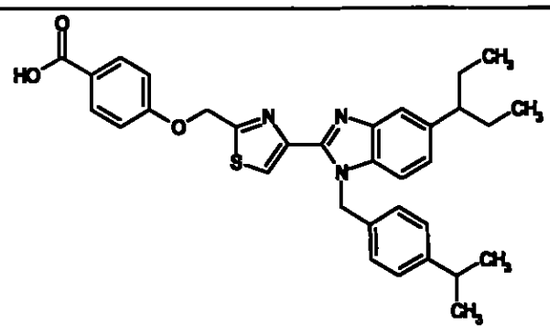
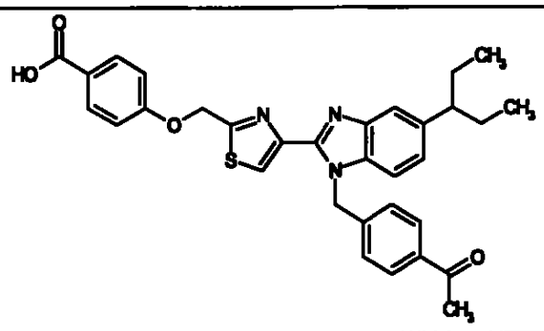
Ejemplo	Fórmula estructural	p. f. (°C)
3-88		171-173
3-89		160-161
3-90		amorfo
3-91		153-154
3-92		166-167
3-93		155 -156
3-94		178-181

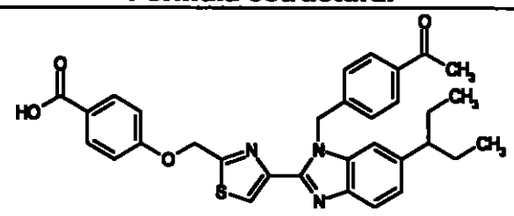
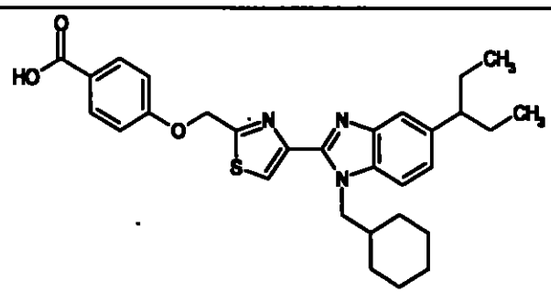
Ejemplo	Fórmula estructural	p. f. (°C)
3-95		175-177
3-96		126-127
3-97		202-203
3-98		218-221
3-99		184-190
3-100		193-196
3-101		164-166
3-102		178-183
3-103		amorfo
3-104		104-110

Ejemplo	Fórmula estructural	p. f. (°C)
3-105		amorfo
3-106		amorfo
3-107		162-164
3-108		amorfo
3-109		149-150
3-110		198-200
3-111		190-191
3-112		254-255
3-113		amorfo

Ejemplo	Fórmula estructural	p. f. (°C)
3-114		148-150
3-115		156-158
3-116		amorfo
3-117		amorfo
3-118		127-130
3-119		amorfo
3-120		amorfo

Ejemplo	Fórmula estructural	p. f. (°C)
3-121		103-104
3-122		98-103
3-123		amorfo
3-124		amorfo
3-125		132-135
3-126		amorfo

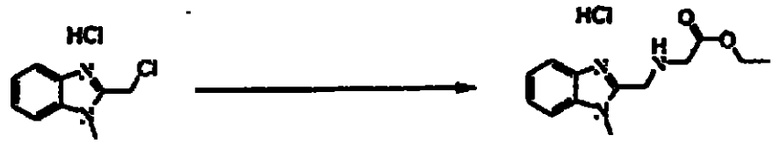
Ejemplo	Fórmula estructural	p. f. (°C)
3-127		241-243
3-128		106-107
3-129		139-142
3-130		127-132

Ejemplo	Fórmula estructural	p. f. (°C)
3-131		138-139
3-132		176-183

EJEMPLO 4-1

Acido [(1-metil-1H-bencimidazol-2-ilmetil)-5-(4-[4-(1-propil-butil)fenoximetil]fenil}tiofen-2-ilmetil]amino]acético

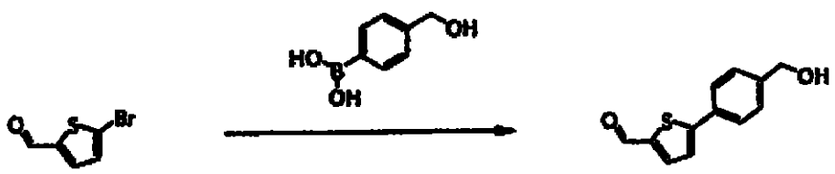
(1) Clorhidrato del éster etílico de la N-(1-metil-1H-bencimidazol-2-ilmetil)glicina



A una suspensión del clorhidrato del 2-clorometil-1-metil-1H-bencimidazol (81.135 g, 0.374 mmoles) en acetonitrilo (800 ml), se le agregaron el clorhidrato del éster etílico de glicina (156.5 g, 1.12 moles), carbonato de potasio (284.1 g, 2.06 moles) y yoduro de potasio (6.2 g, 0.037

moles) y la mezcla se agitó a 75°C durante 1.5 horas. Después de la terminación de la reacción, se agregaron acetato de etilo y agua para la extracción, y la capa orgánica se lavó con agua y salmuera saturada y se secó sobre sulfato de sodio. El solvente se evaporó, y el residuo obtenido se disolvió en acetato de etilo. Se le agregó una solución 4N de ácido clorhídrico/acetato de etilo (93 ml) y el solvente se evaporó. Se agregó acetato de etilo al residuo obtenido y los sólidos resultantes se recolectaron mediante filtración para proporcionar el compuesto del título (74.4 g, 70%).

(2) 5-(4-Hidroximetilfenil)tiofen-2-carbaldehído



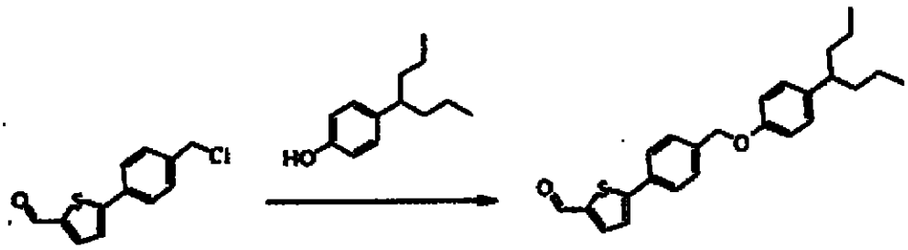
A una suspensión de 5-bromotiofen-2-carbaldehído (125.7 g, 0.658 moles), ácido 4-hidroximetilfenilborónico (100 g, 0.658 moles) y carbonato de potasio (136.43 g, 0.987 moles) en metanol al 50% (880 ml) se le agregó dicloruro de bis(trifenilfosfina)paladio(II) (4.62 g, 6.58 mmoles) y la mezcla se agitó a 80°C durante 1.5 horas. Después de la terminación de la reacción, los sólidos resultantes se recolectaron mediante filtración. El sólido obtenido se secó bajo presión reducida para proporcionar el compuesto del título (137.2 g, 96%).

(3) 5-(4-Clorometilfenil)tiofen-2-carbaldehído



A una solución del 5-(4-hidroximetilfenil)tiofen-2-carbaldehído (20 g, 91.6 mmoles) obtenido en el Ejemplo 4-1(2) y trietilamina (15.3 ml, 110 mmoles) en acetonitrilo, se le agregó gota a gota cloruro de metansulfonilo (8.51 ml, 110 mmoles) bajo enfriamiento con hielo y la mezcla se agitó a temperatura ambiente durante 1 hora. Se agregó cloruro de litio (7.77 g, 183.3 mmoles) a la mezcla de reacción y la mezcla se agitó a 55°C durante 1 hora. Después de la terminación de la reacción, se agregó agua a temperatura ambiente y los sólidos resultantes se recolectaron mediante filtración. El sólido obtenido se secó bajo presión reducida para proporcionar el compuesto del título (19.3 g, 89%).

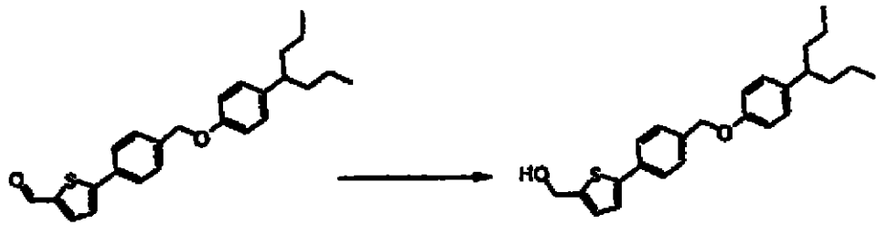
(4) 5-(4-(4-(1-propilbutil)fenoximetil)fenil)tiofen-2-carbaldehído



A una solución del 4-(1-propilbutil)fenol (15.6 g, 81.1 mmoles) en N,N-dimetilacetamida (192 ml) se le agregaron sucesivamente 5-(4-

clorometilfenil)tiofen-2-carbaldehído (19.2 g, 81.1 mmoles) obtenido en el Ejemplo 4-1(3), carbonato de potasio (22.4 g, 162.2 mmoles) y yoduro de potasio (2.69 g, 16.2 mmoles) y la mezcla se agitó a 90°C durante 1.5 horas. Después de la terminación de la reacción, se agregaron acetato de etilo y agua a temperatura ambiente y la mezcla se extrajo. La capa orgánica se lavó sucesivamente con agua y salmuera saturada y se secó sobre sulfato de magnesio. El solvente se evaporó y el residuo obtenido residue se agitó en hexano/éter diisopropílico=3/1. Los sólidos resultantes se recolectaron mediante filtración y el sólido obtenido se secó bajo presión reducida para proporcionar el compuesto del título (25.9 g, 81%).

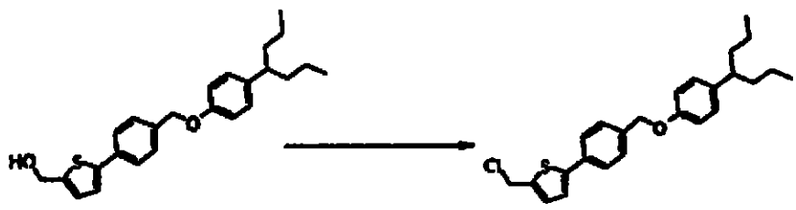
(5) (5-(4-(4-(1-propilbutil)fenoximetil)fenil)tiofen-2-il)metanol



A una solución del 5-(4-(4-(1-propilbutil)fenoximetil)fenil)tiofen-2-carbaldehído (25.9 g, 66 mmoles) obtenido en el Ejemplo 4-1(4) en tetrahidrofurano (260 ml) y etanol (260 ml), se le agregó borohidruro de sodio (2.5 g, 66 mmoles) bajo enfriamiento con hielo y la mezcla se agitó a temperatura ambiente durante 0.5 horas. Después de la terminación de la reacción, el solvente se concentró parcialmente. Al residuo obtenido, se le agregó acetato de etilo, una solución saturada acuosa de carbonato ácido de

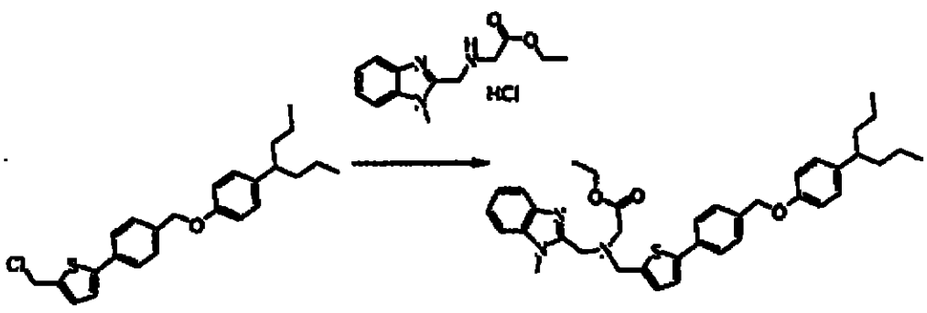
sodio y agua y la mezcla se agitó durante 0.5 horas. La mezcla se extrajo y la capa orgánica se lavó con salmuera saturada, y se secó sobre sulfato de magnesio. El solvente se evaporó y el residuo obtenido se purificó mediante cromatografía en columna sobre gel de sílice (cloroformo:metanol=50:1→10:1) para proporcionar el compuesto del título (23.6 g, 91%).

(6) Cloruro de (5-(4-(4-(1-propilbutil)fenoximetil)fenil)tiofen-2-il)metilo



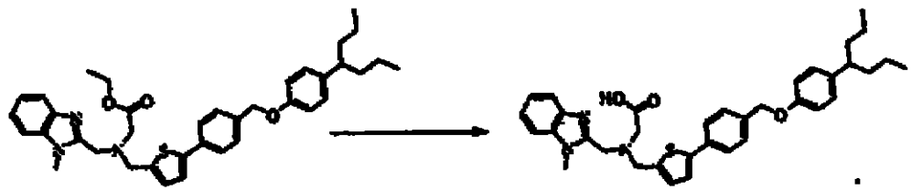
A una solución del (5-(4-(4-(1-propilbutil)fenoximetil)fenil)tiofen-2-il)metanol (23.6 g, 59.8 mmoles) obtenido en el Ejemplo 4-1(5) en cloroformo (354 ml), se le agregó cloruro de tionilo (8.73 ml, 119.6 mmoles) a temperatura ambiente y la mezcla se agitó a la misma temperatura durante 1 hora. Después de la terminación de la reacción, el solvente se evaporó y el residuo obtenido se concentró agregando cloroformo y se secó bajo presión reducida para proporcionar el compuesto del título (24.6 g, 100%).

(7) Ester metílico del ácido [(1-metil-1H-bencimidazol-2-ilmetil)-5-[4-[4-(1-propil-butil)fenoximetil]fenil]tiofen-2-ilmetil]amino]acético



A una solución del cloruro de (5-(4-(4-(1-propilbutil)fenoximetil)fenil)tiofen-2-il)metilo (0.687 g, 1.66 mmoles) obtenido en el Ejemplo 4-1(6) en acetonitrilo, se le agregaron el clorhidrato del éster etílico de la N-(1-metil-1H-bencimidazol-2-ilmetil)glicina (0.674 g, 1.83 mmoles), obtenido en el Ejemplo 4-1(1), carbonato de potasio (0.69 g, 5.0 mmoles) y yoduro de potasio (0.055 g, 0.33 mmoles) y la mezcla se agitó a 80°C durante 1.5 horas. Después de la terminación de la reacción, se agregaron acetato de etilo y agua. La mezcla se extrajo y la capa orgánica se lavó con salmuera saturada y se secó sobre sulfato de magnesio. El solvente se evaporó, y el residuo obtenido se purificó mediante cromatografía en columna sobre gel de sílice (cloroformo:metanol=100:1→20:1) para proporcionar el compuesto del título (0.633 g, 61%).

(8) Acido [(1-Metil-1H-bencimidazol-2-ilmetil)-5-[4-[4-(1-propil-butil)fenoximetil]fenil]tiofen-2-ilmetil]amino]acético

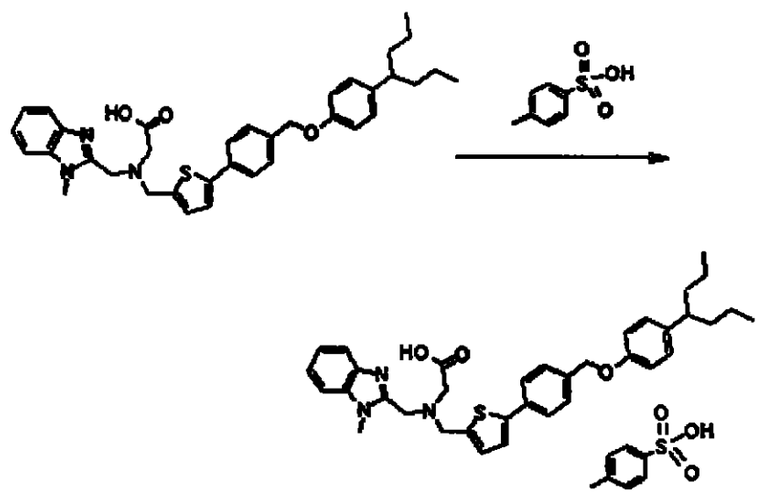


A una solución del éster etílico del ácido [(1-metil-1H-bencimidazol-2-ilmetil)-5-[4-[4-(1-propilbutil)fenoximetil]fenil]tiofen-2-ilmetil]amino]acético (5 g, 8.01 mmoles) obtenido en el Ejemplo 4-1(7) en 50% de tetrahidrofurano-etanol (100 ml), se le agregó una solución acuosa 1N de hidróxido de sodio (16 ml) a temperatura ambiente, y la mezcla se agitó a 80°C durante 1 hora. Después de la terminación de la reacción, se agregó ácido clorhídrico 1N (16 ml) bajo enfriamiento con hielo, y la mezcla se agitó a temperatura ambiente. Los sólidos resultantes se recolectaron mediante filtración. El sólido obtenido se secó bajo presión reducida para proporcionar el compuesto del título (4.63 g, 97%).

^{1}H RMN (DMSO-d_6, 300 MHz) δ 0.79 (t, J=7.3 Hz, 6H), 0.96-1.18 (m, 4H), 1.34-1.60 (m, 4H), 3.36 (s, 2H), 3.88 (s, 3H), 4.04 (s, 2H), 4.16 (s, 2H), 5.06 (s, 2H), 6.92 (d, J=8.7 Hz, 2H), 7.01 (d, J=3.4 Hz, 1H), 7.07 (d, J=8.7 Hz, 2H), 7.14-7.26 (m, 2H), 7.35 (d, J=3.4 Hz, 1H), 7.46 (d, J=8.3 Hz, 2H), 7.53 (d, J=7.5 Hz, 1H), 7.58-7.65 (m, 3H), 12.52 (s amplio, 1H)

EJEMPLO 4-40

p-toluensulfonato del ácido [(1-metil-1H-bencimidazol-2-ilmetil)-5-{4-[4-(1-propil-butil)fenoximetil]fenil}tiofen-2-ilmetil]amino]acético



A una suspensión del ácido [(1-metil-1H-bencimidazol-2-ilmetil)-5-{4-[4-(1-propil-butil)fenoximetil]fenil}-tiofen-2-ilmetil]amino]acético (200 mg, 0.336 mmoles) obtenido en el Ejemplo 4-1 en 2-butanona (5 ml), se le agregó monohidrato del ácido p-toluensulfónico (64 mg, 0.37 mmoles) y la mezcla se agitó a temperatura ambiente durante 30 minutos. Los cristales se recolectaron mediante filtración y se secaron para proporcionar el compuesto del título (231 mg, 90%).

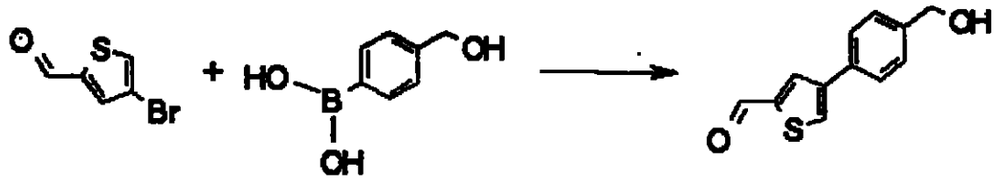
^{1}H RMN (DMSO-d_6, 300 MHz) δ 0.79 (t, J=7.3 Hz, 6H), 0.95-1.20 (m, 4H), 1.32-1.60 (m, 4H), 2.28 (s, 3H), 2.40-2.54 (m, 1H), 3.62 (s, 2H), 4.00 (s, 3H), 4.19 (s, 2H), 4.46 (s, 2H), 5.05 (s, 2H), 6.92 (d, J=8.6 Hz, 2H), 6.98-7.14 (m, 5H), 7.25 (d, J=3.6 Hz, 1H), 7.36-7.58 (m, 8H), 7.76 (d, J=9.0 Hz, 1H), 7.89 (d, J=9.0 Hz, 1H)

Punto de fusión: 100°C-135°C

EJEMPLO 4-2

Acido 5-(4-[4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi)nicotínico

(1) 4-(4-Hidroximetilfenil)tiofen-2-carbaldehído



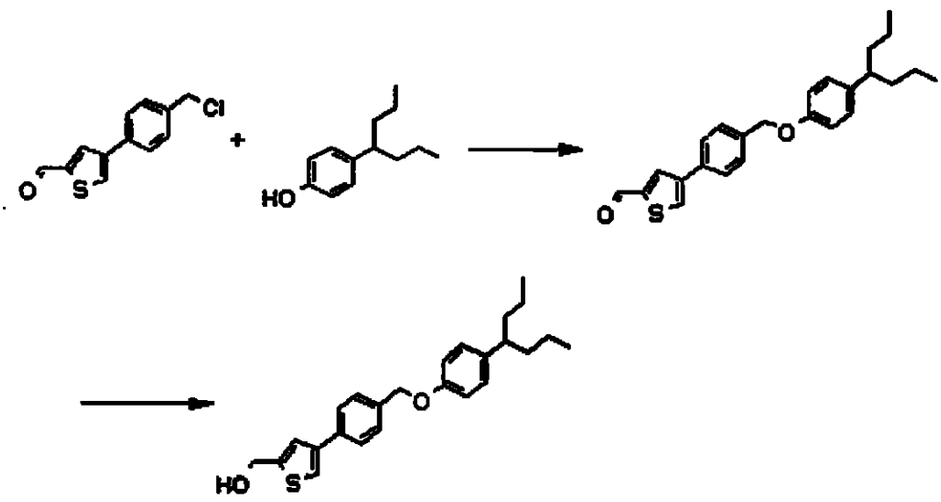
A una solución del 4-bromotiofen-2-carbaldehído (100 g, 0.523 moles) en tetrahidrofurano (500 ml), se le agregaron el dicloruro de bis(trifenilfosfina)paladio(II) (3.67 g, 52.3 mmoles), ácido 4-hidroximetilfenilborónico (79.5 g, 0.523 moles), carbonato ácido de sodio (66.0 g, 0.786 moles) y agua (1000 ml) y la mezcla se agitó a una temperatura interna de 62-63°C durante 3 horas. Después de dejar enfriar, se agregó acetato de etilo a la mezcla de reacción. La capa orgánica se lavó con salmuera saturada y se concentró para dar un producto crudo (140 g). Al producto crudo obtenido, se le agregó tolueno (400 ml) y hexano (100 ml) y la mezcla se agitó. Los sólidos se recolectaron mediante filtración y se secaron para proporcionar el compuesto del título (95.4 g, 83%).

(2) 4-(4-clorometilfenil)tiofen-2-carbaldehído



A una solución del 4-(4-hidroximetilfenil)tiofen-2-carbaldehído (95.4 g, 0.437 moles) y trietilamina (73.1 ml, 0.524 moles) en N,N-dimetilformamida (763 ml), se le agregó gota a gora cloruro de metansulfonilo (40.6 ml, 0.524 moles) bajo enfriamiento con hielo y la mezcla se agitó a temperatura ambiente durante 2 horas. Se agregó cloruro de litio (37.1 g, 0.874 moles) a la mezcla de reacción y la mezcla se agitó a 60°C durante 1 hora. Después de dejar enfriar, se agregó agua y los sólidos resultantes se recolectaron mediante filtración. El sólido obtenido se suspendió en éter diisopropílico (465 ml) y la mezcla se agitó a una temperatura interna de 60-65°C durante 1.5 horas. Después de dejar enfriar, los sólidos se recolectaron mediante filtración y se secaron para proporcionar el compuesto del título (83.2 g, 80%).

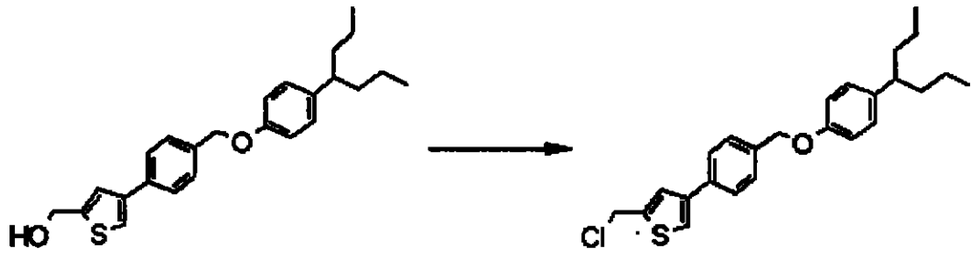
(3) (4-(4-(4-(1-propilbutil)fenoximetil)fenil)tiofen-2-il)metanol



A una solución del 4-(4-clorometilfenil)tiofen-2-carbaldehído (21.1 g, 88.9 mmoles) en N,N-dimetilacetamida (105 ml) se le agregaron sucesivamente 4-(1-propilbutil)fenol (18.7 g, 97.8 mmoles), carbonato de potasio (36.8 g, 267 mmoles) y yoduro de potasio (1.47 g, 8.89 mmoles) y la mezcla se agitó a 90°C durante 1.5 horas. Después de la terminación de la reacción, se agregaron acetato de etilo y agua a temperatura ambiente. La mezcla se extrajo y la capa orgánica se lavó sucesivamente con agua y salmuera saturada y se secó sobre sulfato de magnesio. El solvente se evaporó y el residuo obtenido (68 g) se disolvió en etanol (100 ml). Se agregó borohidruro de sodio (37.8 g, 88.9 mmoles) bajo enfriamiento con hielo y la mezcla se agitó a temperatura ambiente durante 1 hora. Se agregaron agua y acetato de etilo a la mezcla de reacción y la capa orgánica se lavó sucesivamente con una solución acuosa 1N de hidróxido de sodio, agua y salmuera saturada y se secó sobre sulfato de magnesio. El solvente se

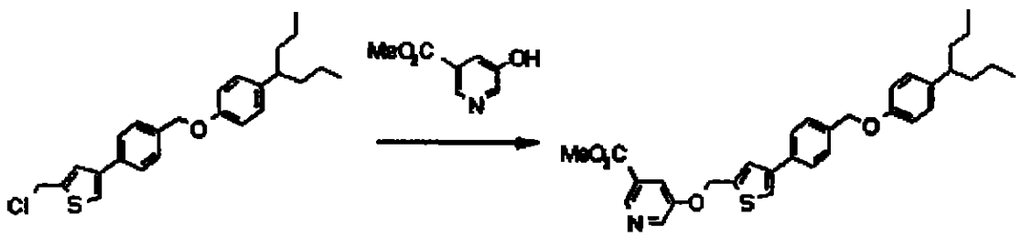
evaporó y el residuo obtenido se purificó mediante cromatografía en columna sobre gel de sílice (cloroformo:metanol=100:1→50:1) para dar un producto crudo (29.9 g). El producto crudo (14.5 g) se purificó mediante cromatografía en columna sobre gel de sílice (acetato de etilo:hexano=1:5→1:4) para proporcionar el compuesto del título (11.9 g).

(4) Cloruro de (4-(4-(4-(1-propilbutil)fenoximetil)fenil)tiofen-2-il)metilo



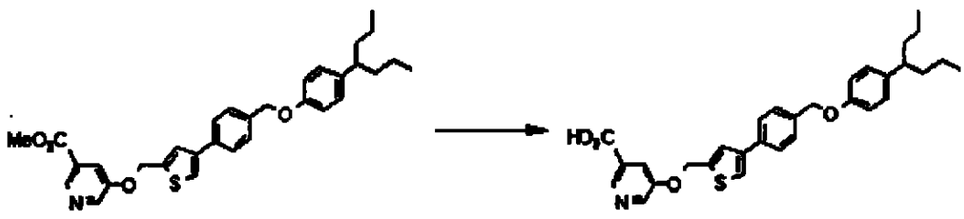
A una solución del (4-(4-(4-(1-propilbutil)fenoximetil)-fenil)tiofen-2-il)metanol (11.9 g, 30.2 mmoles) en cloroformo (60 ml), se le agregó cloruro de tionilo (4.40 ml, 60.4 mmoles) y la mezcla se agitó a temperatura ambiente durante 30 minutos. El solvente se evaporó y se agrego cloruro de tionilo (10.0 ml, 137 mmoles). La mezcla se agitó a temperatura ambiente durante 20 minutos. La mezcla de reacción se concentró bajo presión y el residuo obtenido se concentró agregando cloroformo para proporcionar el compuesto del título (12.5 g, 100%).

(5) Ester metílico del ácido 5-(4-[4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi)nicotínico



Al cloruro de (4-(4-(4-(1-propilbutil)fenoximetil)fenil)tiofen-2-il)metilo (5.00 g, 12.1 mmoles) se le agregaron N,N-dimetilacetamida (25 ml), éster metílico del ácido 5-hidroxinicotínico (2.04 g, 13.3 mmoles), carbonato de cesio (11.8 g, 36.3 mmoles), yoduro de potasio (201 mg, 1.21 mmoles) y bromuro de tetra-n-butilamonio (390 mg, 1.21 mmoles) y la mezcla se agitó a 60°C durante 1.5 horas. Después de dejar enfriar, se agregó acetato de etilo y la mezcla se lavó sucesivamente con agua y salmuera saturada. Después de la concentración, el concentrado se purificó mediante cromatografía en columna sobre gel de sílice (acetato de etilo:hexano=2:5→1:2) para proporcionar el compuesto del título (5.19 g, 81%).

(6) Acido 5-(4-[4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi)nicotínico



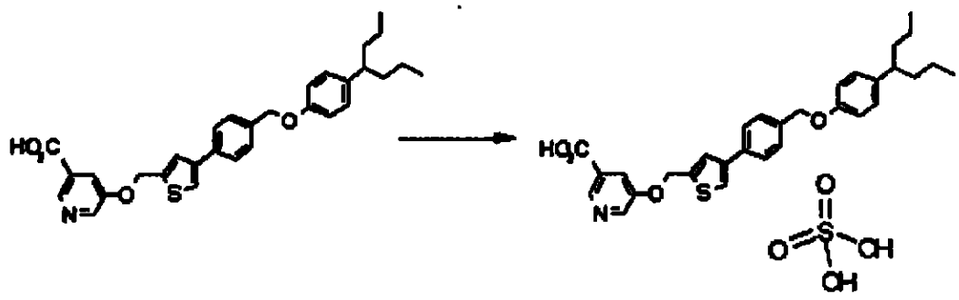
Al éster metílico del ácido 5-(4-[4-[4-(1-propilbutil)fenoximetil]fenil}-tiofen-2-ilmetoxi)nicotínico (5.04 g, 9.52 mmoles) se le agregaron tetrahidrofurano (25 ml), etanol (25 ml) y una solución acuosa 2N de hidróxido de sodio (5.00 ml, 10 mmoles) y la mezcla se agitó a 60°C durante 1.5 horas. Después de dejar enfriar, se agregaron ácido clorhídrico 2N (5.00 ml, 10 mmoles) y agua (30 ml). Los sólidos precipitados se recolectaron mediante filtración y se secaron para proporcionar el compuesto del título (4.77 g, rendimiento 97%).

^{1}H RMN (DMSO-d_6, 300 MHz) δ 0.80 (t, J=7.3 Hz, 6H), 1.00-1.12 (m, 4H), 1.38-1.57 (m, 4H), 2.40-2.50 (m, 1H), 5.07 (s, 2H), 5.48 (s, 2H), 6.93 (d, J=8.6 Hz, 2H), 7.07 (d, J=8.6 Hz, 2H), 7.49 (d, J=7.9 Hz, 2H), 7.70-7.70 (m, 1H), 7.72 (d, J=8.3 Hz, 2H), 7.88-7.89 (m, 1H), 7.91 (d, J=1.5 Hz, 1H), 8.56 (d, J=2.6 Hz, 1H), 8.69 (d, J=1.5 Hz, 1H), 13.41 (s amplio, 1H)

Punto de fusión: 157-159°C

EJEMPLO 4-41

Sulfato del ácido 5-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi)nicotínico



A una suspensión del ácido 5-(4-[4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetoxi)nicotínico (200 mg, 0.388 mmoles) obtenido en el Ejemplo 4-2 en 2-butanona (2 ml), se le agregó ácido sulfúrico concentrado (0.0207 ml, 0.388 mmoles) y la mezcla se agitó a temperatura ambiente durante 1 hora. Los sólidos se recolectaron mediante filtración y se secaron para proporcionar el compuesto del título (224 mg, rendimiento 94%).

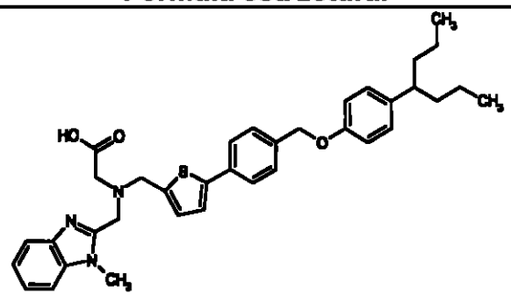
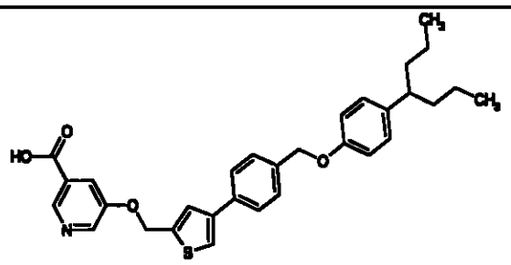
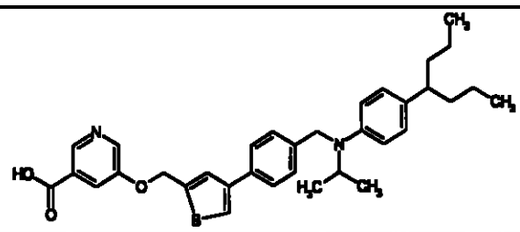
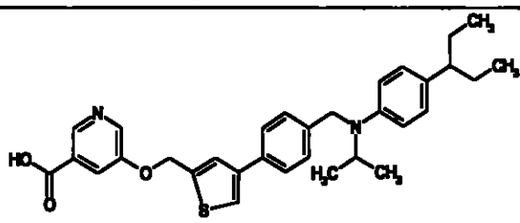
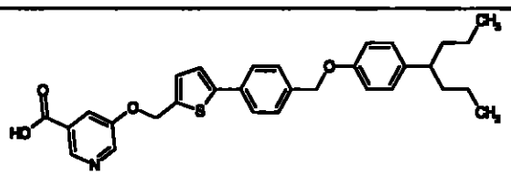
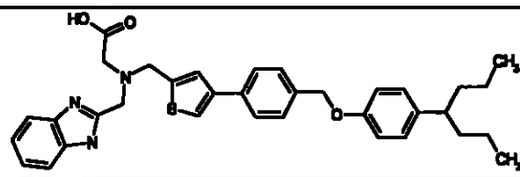
^{1}H RMN (DMSO-d_6, 300 MHz) 0.80 (t, J=7.3 Hz, 6H), 0.98-1.15 (m, 4H), 1.38-1.59 (m, 4H), 2.39-2.54 (m, 1H), 5.07 (s, 2H), 5.52 (s, 2H), 6.93 (d, J=8.6 Hz, 2H), 7.07 (d, J=8.7 Hz, 2H), 7.49 (d, J=8.3 Hz, 2H), 7.71 (s, 1H), 7.72 (d, J=6.4 Hz, 2H), 7.93 (d, J=1.5 Hz, 1H), 8.00 (s amplio, 1H), 8.65-8.67 (m, 1H), 8.73-8.76 (m, 1H)

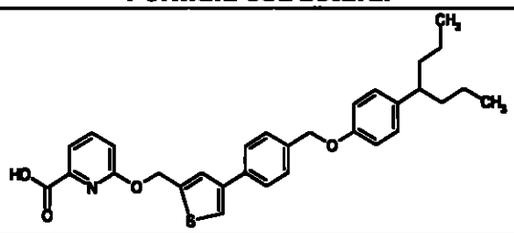
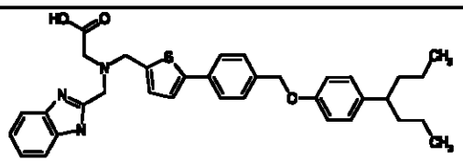
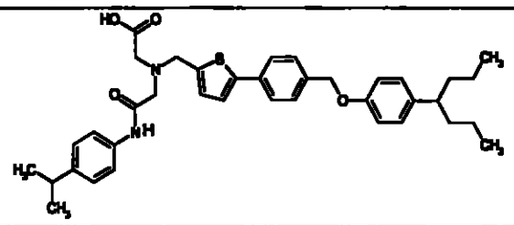
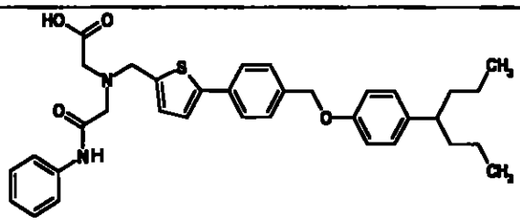
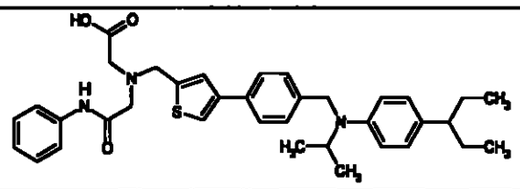
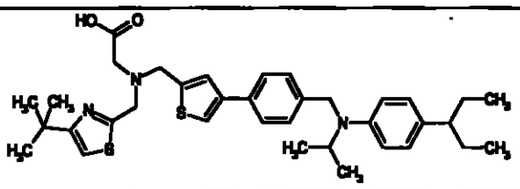
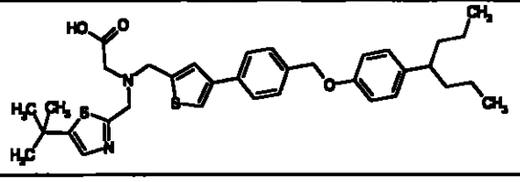
Punto de fusión: 125°C (dec.)

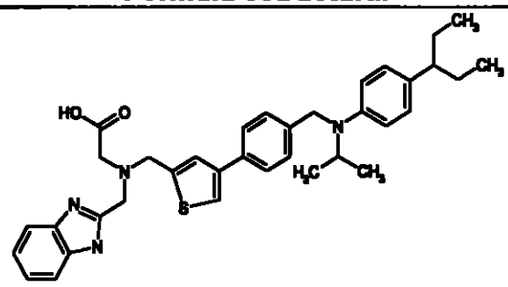
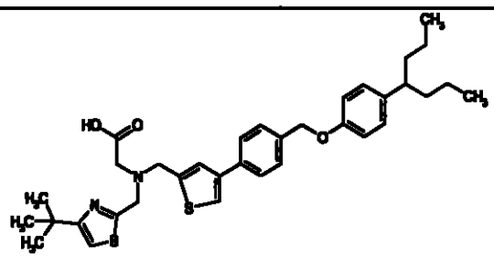
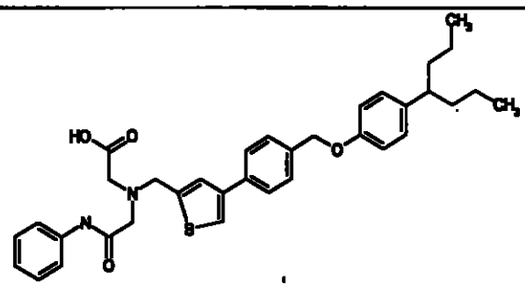
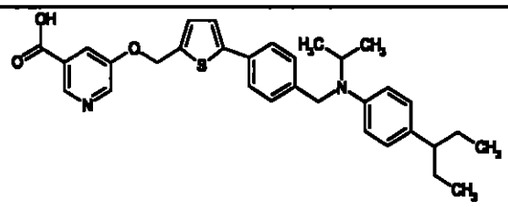
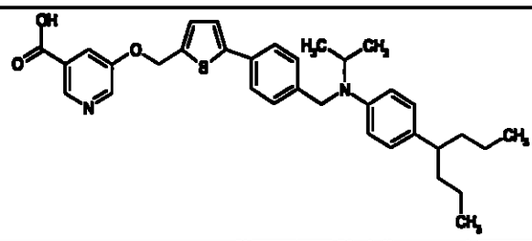
EJEMPLOS 4-3 A 4-39 Y 4-42 A 4-107

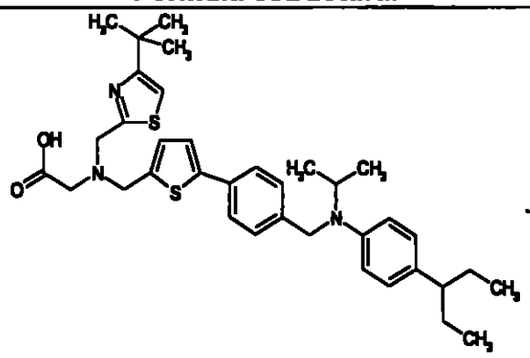
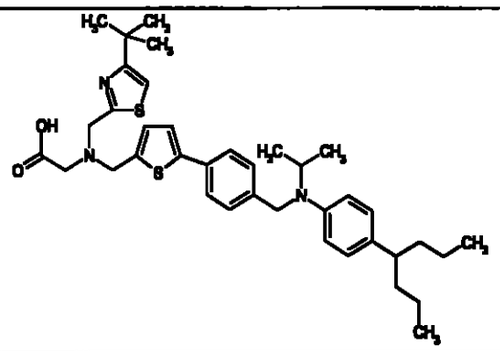
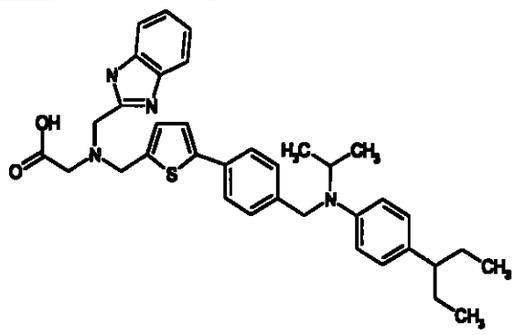
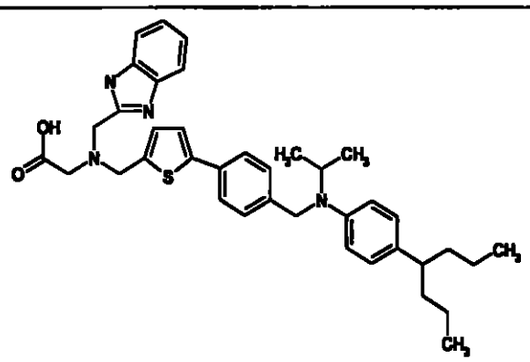
De la misma manera que en los Ejemplos 4-1, 4-2, 4-40 y 4-41 y utilizando otros métodos convencionales en donde sea necesario, se producen los compuestos de los Ejemplos 4-3 a 4-39 y los Ejemplos 4-42 a 4-107. Las fórmulas estructurales y los valores de las propiedades de los compuestos obtenidso, así como aquéllos de los Ejemplos 4-1, 4-2, 4-40 y 4-41, se muestran en los siguientes Cuadros.

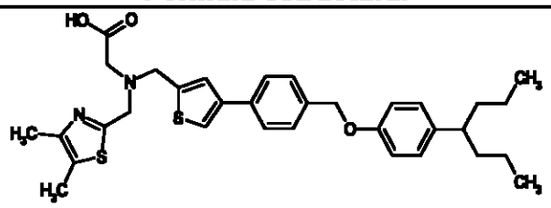
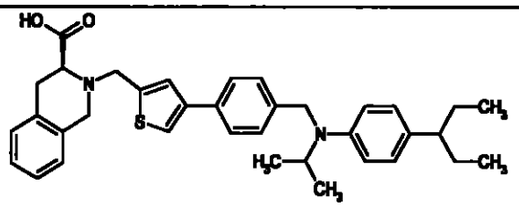
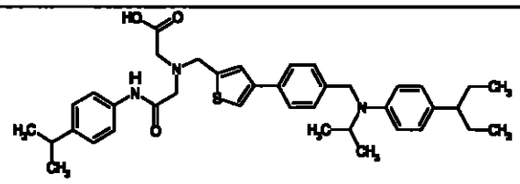
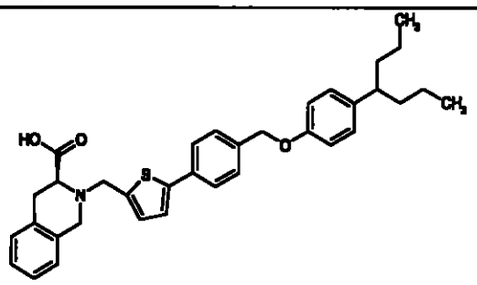
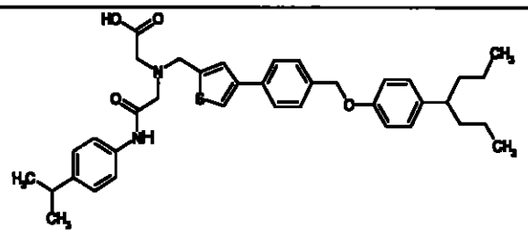
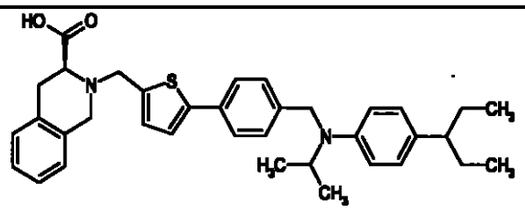
CUADRO 4

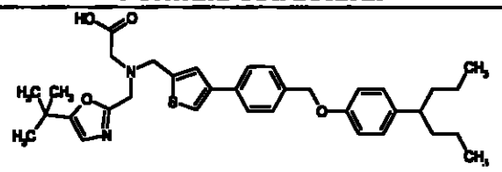
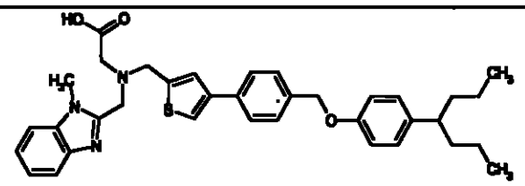
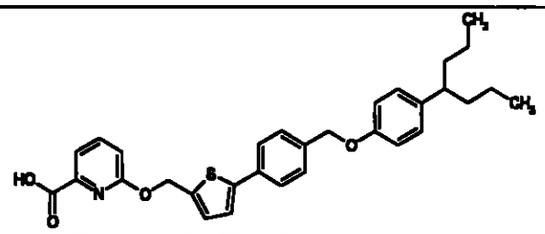
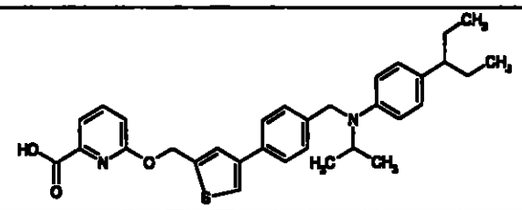
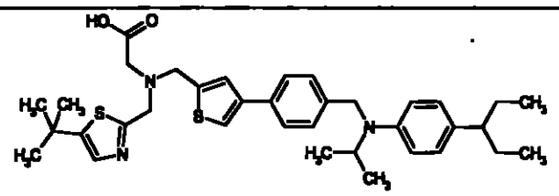
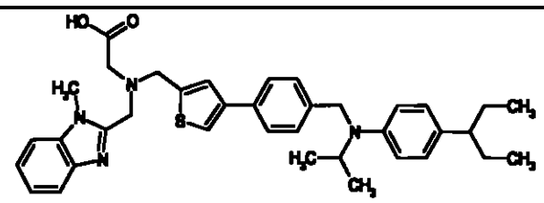
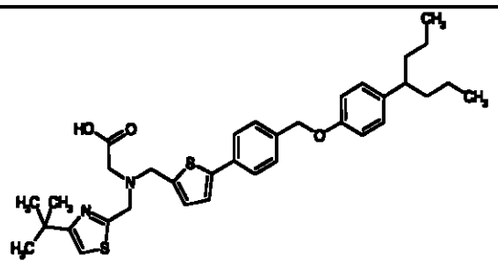
Ejemplo	Formula estructural	p. f. (°C)
4-1		amorfo
4-2		157-159
4-3		156
4-4		160
4-5		153-155
4-6		153-155

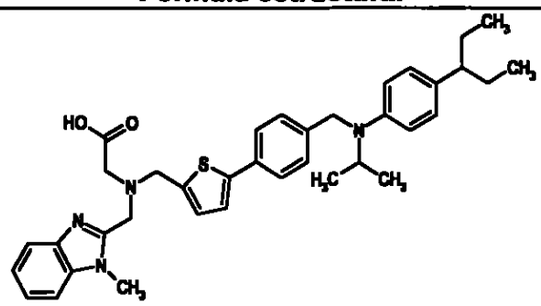
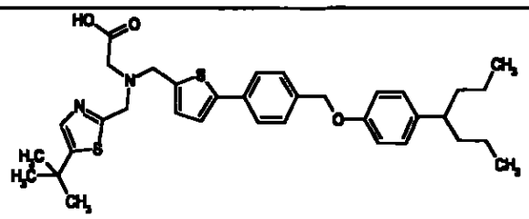
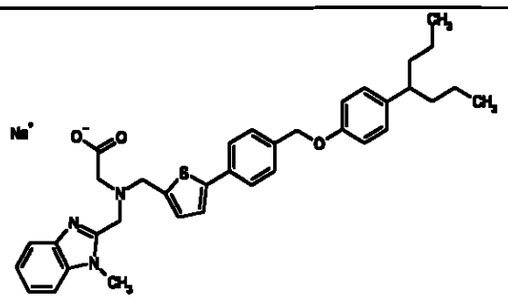
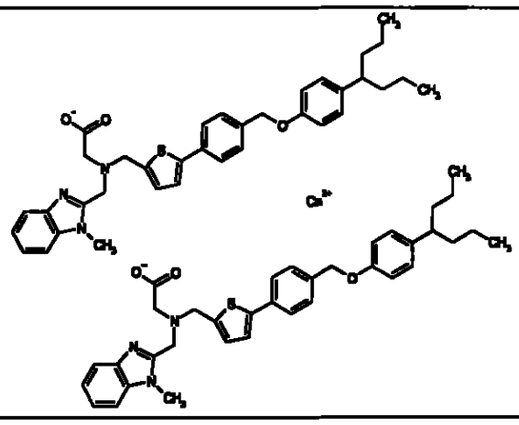
Ejemplo	Formula estructural	p. f. (°C)
4-7		amorfo
4-8		173-175
4-9		172-174
4-10		122-124
4-11		amorfo
4-12		amorfo
4-13		amorfo

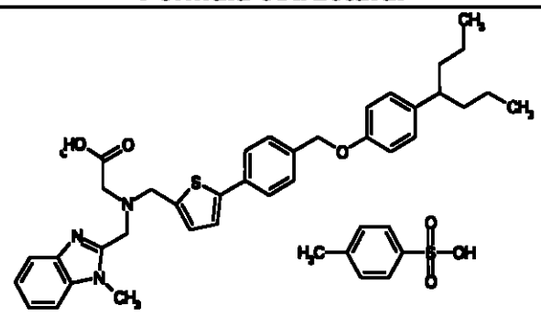
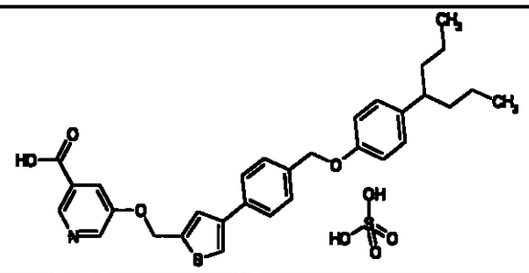
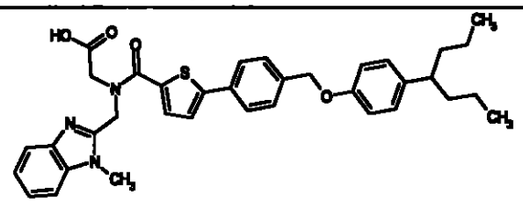
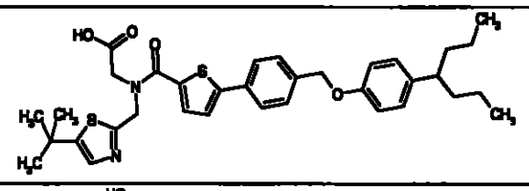
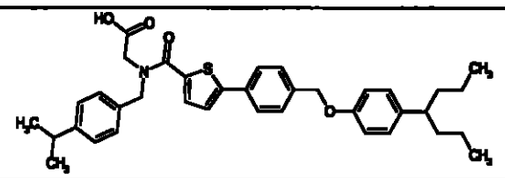
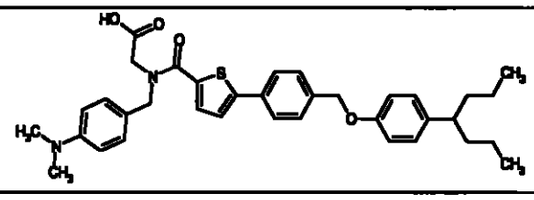
Ejemplo	Formula estructural	p. f. (°C)
4-14		amorfo
4-15		166
4-16		155
4-17		160-164
4-18		93-98

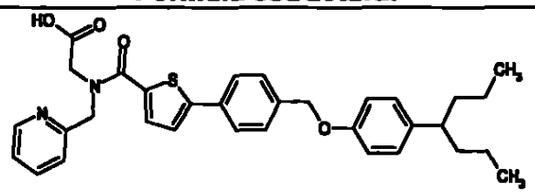
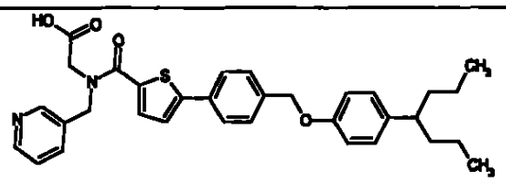
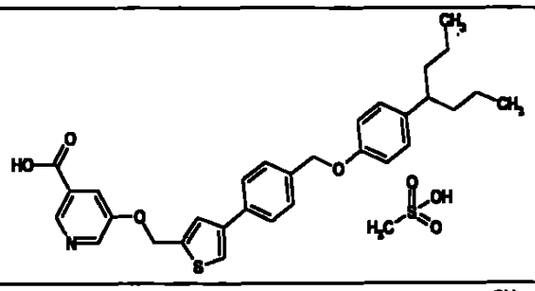
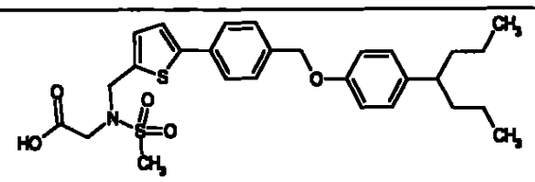
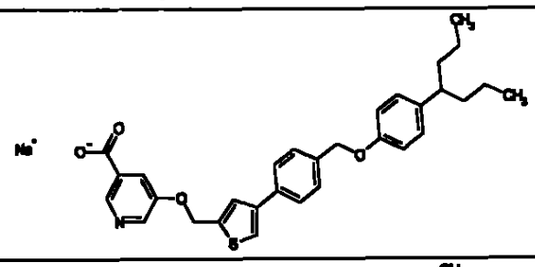
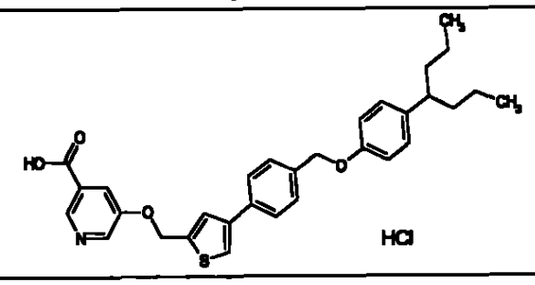
Ejemplo	Formula estructural	p. f. (°C)
4-19		92-98
4-20		78-82
4-21		142-146
4-22		144-150

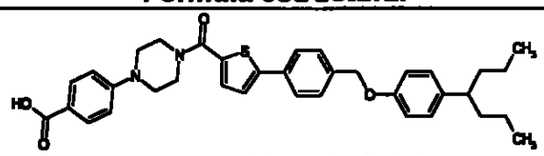
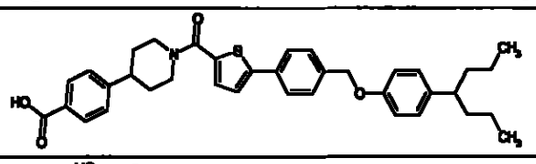
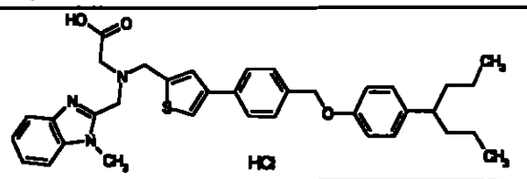
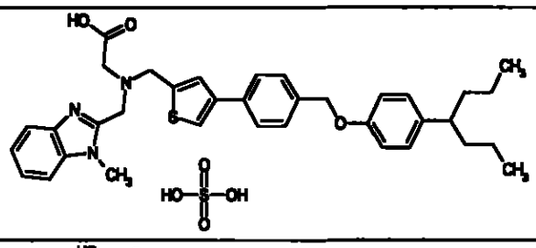
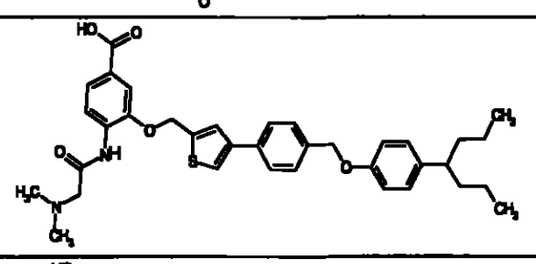
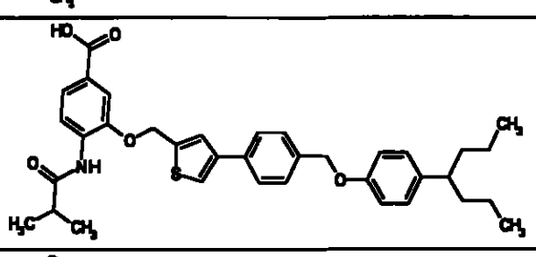
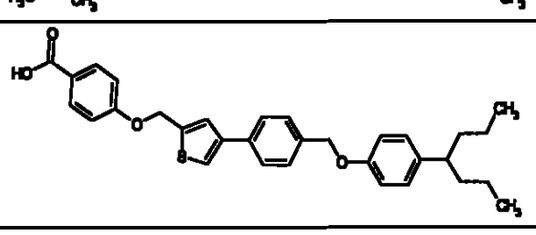
Ejemplo	Formula estructural	p. f. (°C)
4-23		amorfo
4-24		amorfo
4-25		amorfo
4-26		amorfo
4-27		164-166
4-28		152

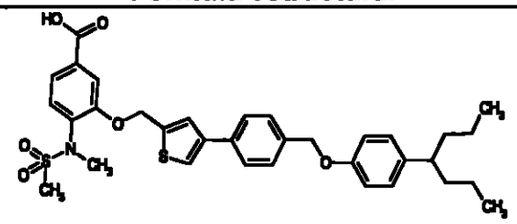
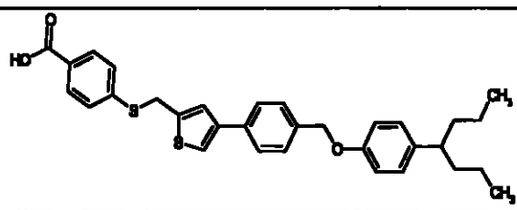
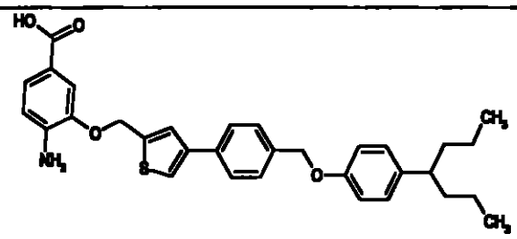
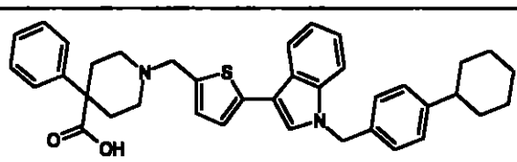
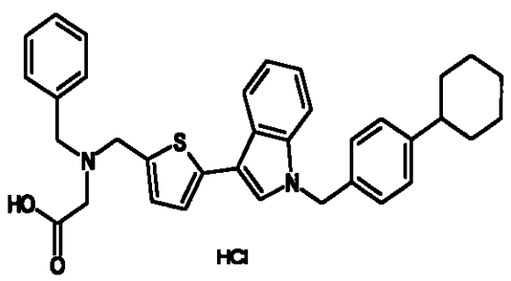
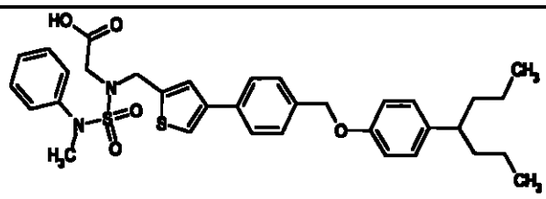
Ejemplo	Formula estructural	p. f. (°C)
4-29		120.5
4-30		amorfo
4-31		amorfo
4-32		amorfo
4-33		amorfo
4-34		amorfo
4-35		amorfo

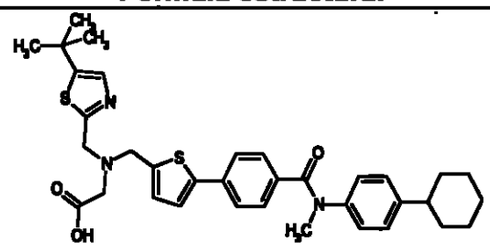
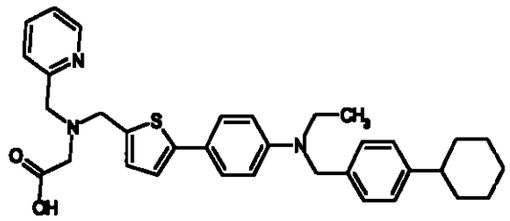
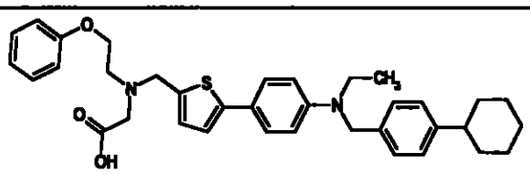
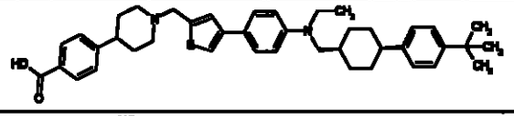
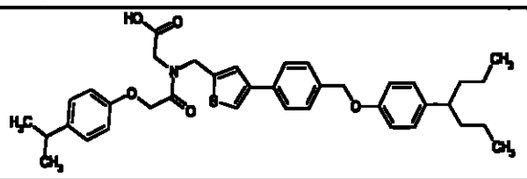
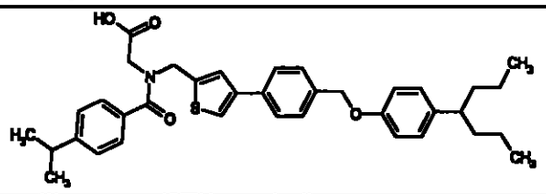
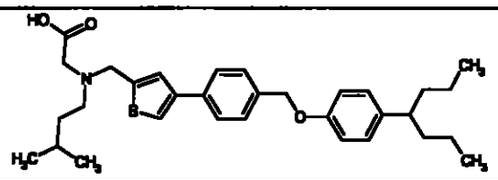
Ejemplo	Formula estructural	p. f. (°C)
4-36		amorfo
4-37		amorfo
4-38		200-203
4-39		amorfo

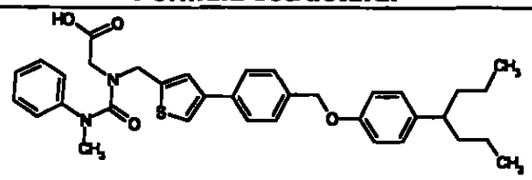
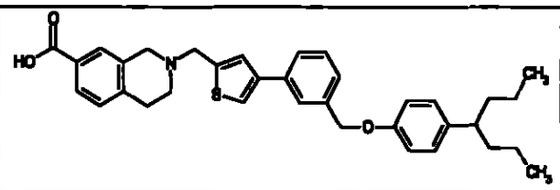
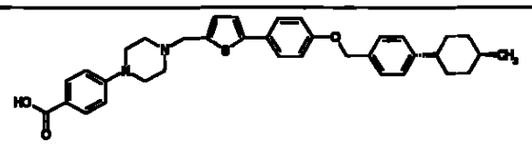
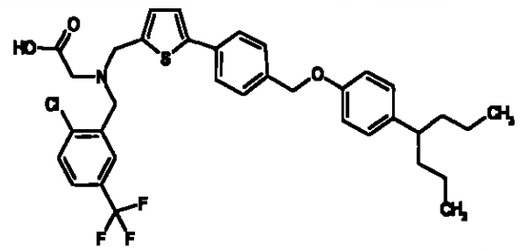
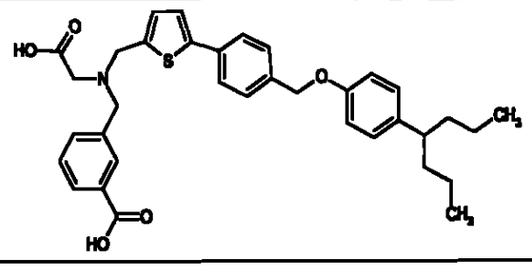
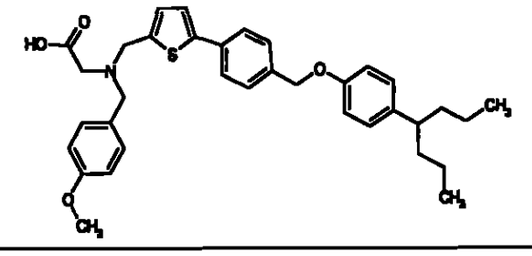
Ejemplo	Formula estructural	p. f. (°C)
4-40		100-135
4-41		125 descomposición
4-42		185-188
4-43		amorfo
4-44		134-136
4-45		137-139

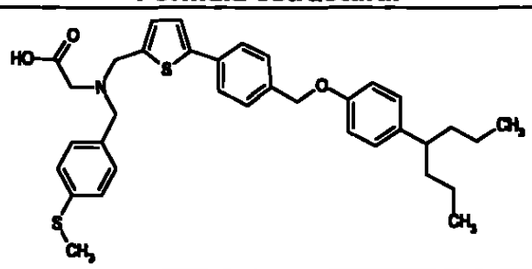
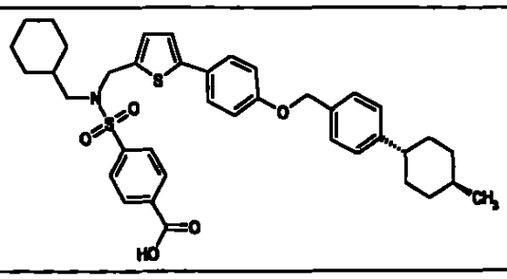
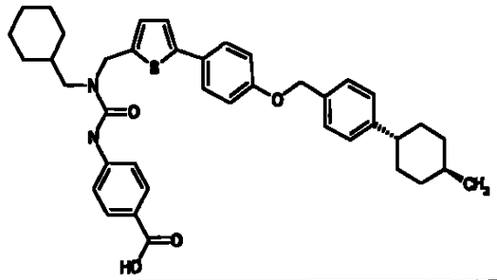
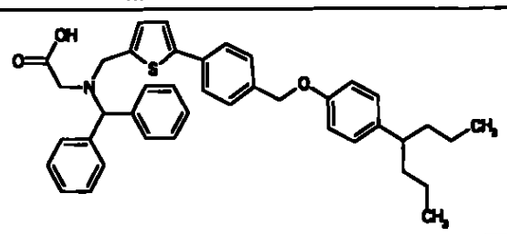
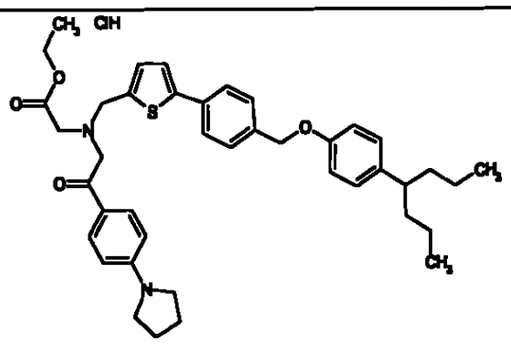
Ejemplo	Formula estructural	p. f. (°C)
4-46		147-150
4-47		153-156
4-48		151-155 descomposición
4-49		133.1-136.5
4-50		250 ~
4-51		170-173

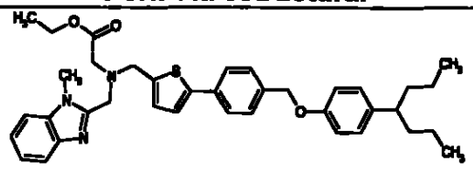
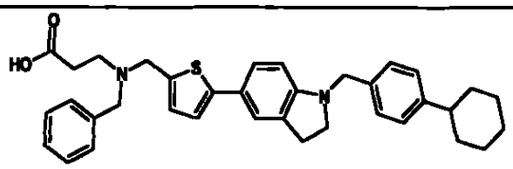
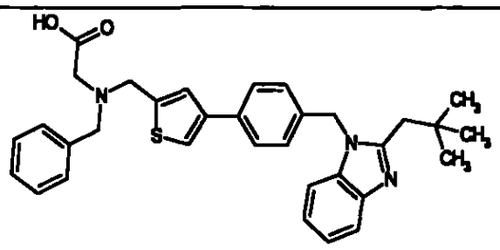
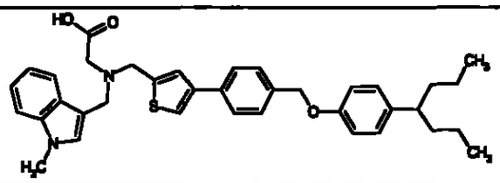
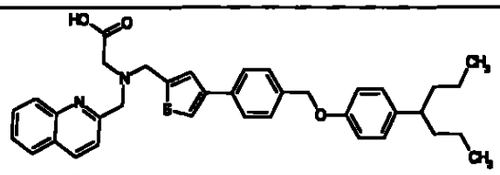
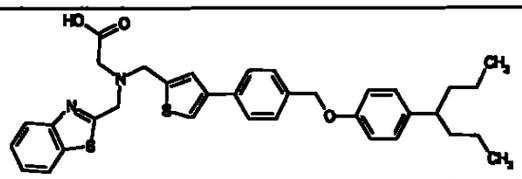
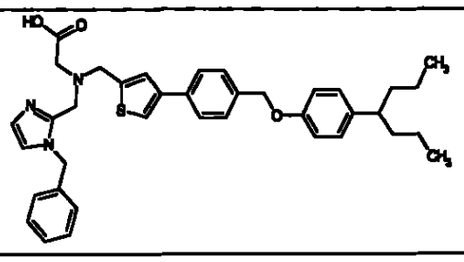
Ejemplo	Formula estructural	p. f. (°C)
4-52		amorfo
4-53		176-178
4-54		165.7-166.8
4-55		137.5-141.5
4-56		amorfo
4-57		153.7-154.9
4-58		194.2-195.5

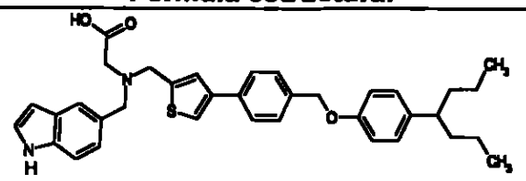
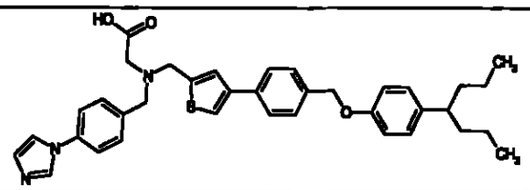
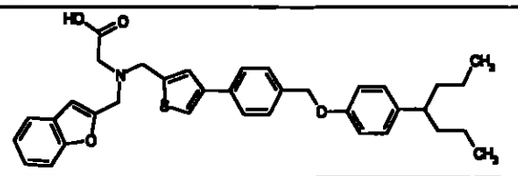
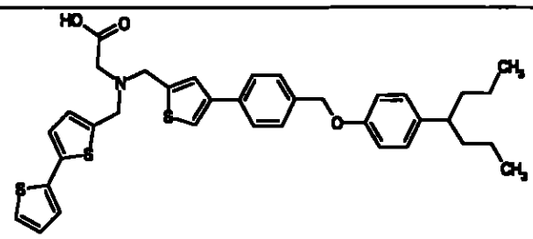
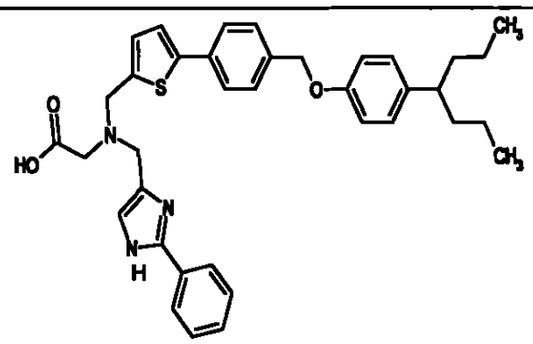
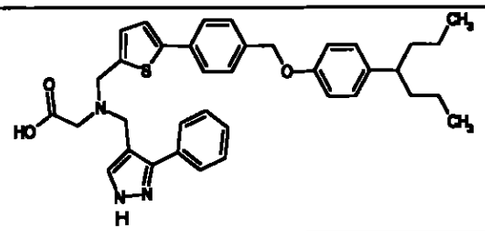
Ejemplo	Formula estructural	p. f. (°C)
4-59		amorfo
4-60		133.9-135.1
4-61		156.5-165.5
4-62	 HCl	227.3-233.6
4-63	 HCl	161-164.3
4-64		139-140.2

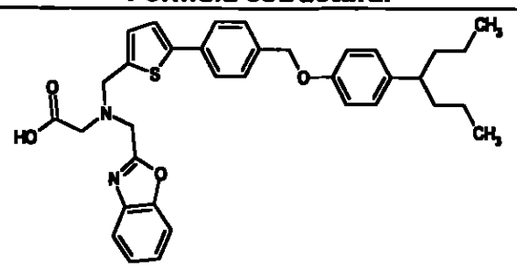
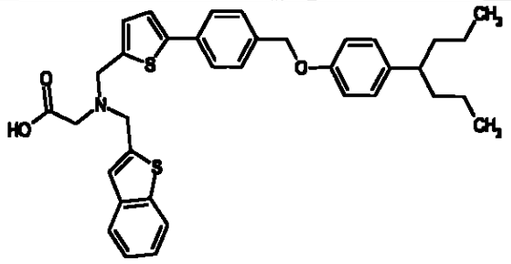
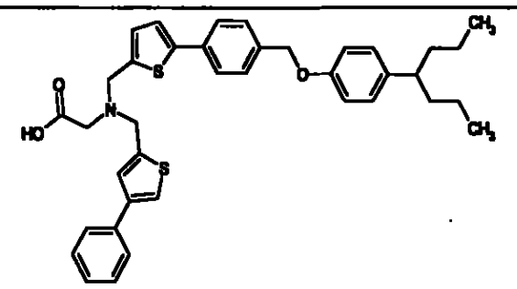
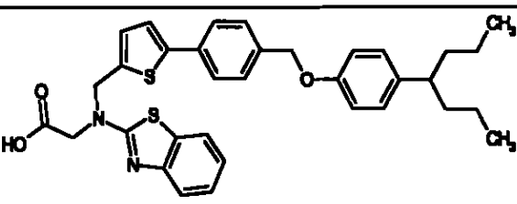
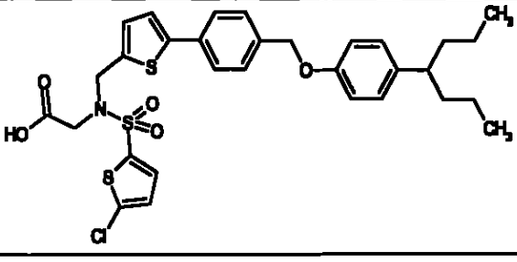
Ejemplo	Formula estructural	p. f. (°C)
4-65		amorfo
4-66		128-131
4-67		141-144
4-68		225-229 descomposición
4-69		146-152
4-70		109-111
4-71		176-182

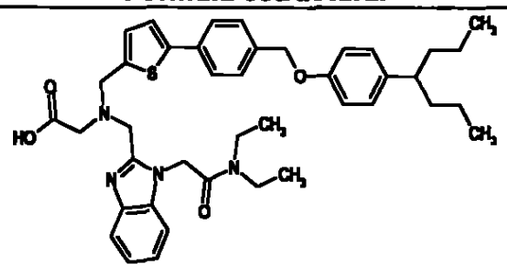
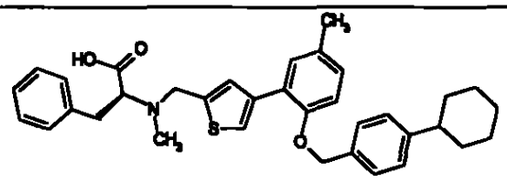
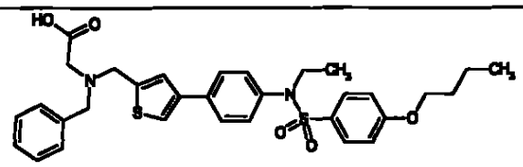
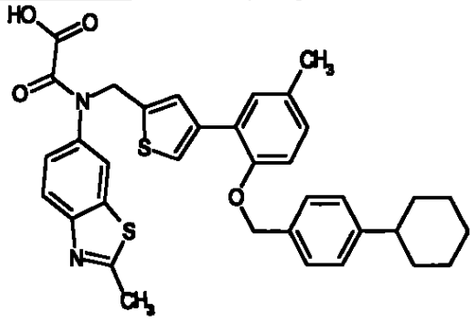
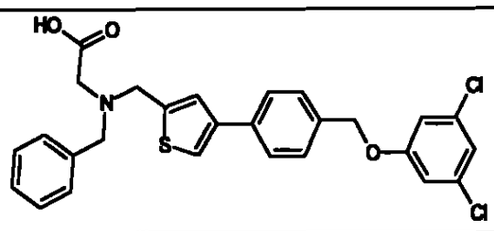
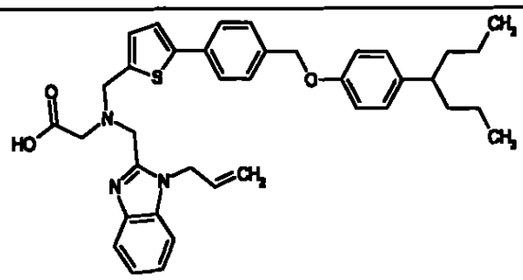
Ejemplo	Formula estructural	p. f. (°C)
4-72		amorfo
4-73		69.4-78.3
4-74		242.4-265.9
4-75		92.6-94.7
4-76		202.8-206.4
4-77		195.7-196.8

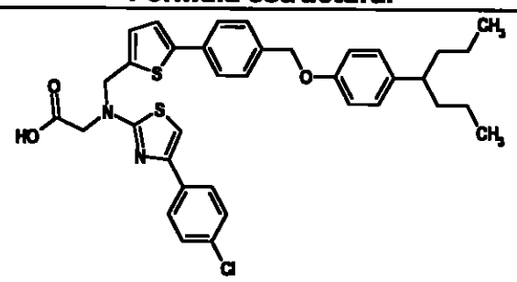
Ejemplo	Formula estructural	p. f. (ºC)
4-78		202.7-204.3
4-79		234-241.8
4-80		168-169.9
4-81		amorfo
4-82		75.3-79.3

Ejemplo	Formula estructural	p. f. (°C)
4-83		82-84
4-84		121-128
4-85		161-166
4-86		170.5-171.9
4-87		137.3-138.7
4-88		150.9-152.8
4-89		135.2-136

Ejemplo	Formula estructural	p. f. (°C)
4-90		203.4-205.3
4-91		167.5-169.9
4-92		146.7-148.9
4-93		203.8-206.2
4-94		131.8-137.6
4-95		145.9-149.3

Ejemplo	Formula estructural	p. f. (°C)
4-96		127.4-130
4-97		202.3-204.4
4-98		181.4-184.5
4-99		104.4-107.2
4-100		151.2-154.4

Ejemplo	Formula estructural	p. f. (°C)
4-101		194.8-197
4-102		117-123.1
4-103		120.7-123.3
4-104		115.9-121.1
4-105		202.3-204.2
4-106		141.2-144.1

Ejemplo	Formula estructural	p. f. (°C)
4-107		116-117.6

Los Ejemplos de Formulación se muestran en lo siguiente, lo cual no debe considerarse como limitante de la presente invención.

Ejemplos de Formulación

(a) compuesto del Ejemplo 1	10	g
(b) lactosa	50	g
(c) almidón de maíz	15	g
(d) carboximetilcelulosa sódica	44	g
(e) estearato de magnesio	1	g

La cantidad total de (a), (b) y (c) y 30 g de (d) se amasó con agua, se secó in vacuo y se granuló. Los gránulos obtenidos se mezclaron con 14 g de (d) y 1 g de (e) y se tabletearon con una máquina tableteadota para proporcionar 1000 tabletas que contienen 10 mg de (a) por tableta.

Los resultados de prueba de la actividad inhibidora de la proteína tirosina fosfatasa 1B de la presente invención se muestra en lo siguiente.

EJEMPLO EXPERIMENTAL 1

(Actividad inhibidorea de la proteína tirosina fosfatasa 1B)

Preparación del amortiguador de ensayo:

Se preparó un amortiguador de Tris-HCl 50 mM (pH 7.5), NaCl 50 mM y ditiotreitol 3 mM (DTT).

Preparación de la muestra:

Se prepararon soluciones de DMSO 10 mM de 0.1, 0.3, 1, 3 y 10 μM del compuesto de prueba, y se diluyeron con el amortiguador de ensayo mencionado anteriormente a la concentración final de sulfóxido de dimetilo (DMSO) de no más que el 1%. Se utilizó el amortiguador de ensayo como el control.

Preparación del sustrato:

Un péptido sintético, en donde tres tirosinas en 12 aminoácidos, del 1142avo al 1153avo de la secuencia del receptor de la insulina se habían fosforilado, se diluyó con el amortiguador de ensayo mencionado anteriormente a 80 μM.

Preparación de la enzima:

La proteína tirosina fosfatasa 1B recombinante humana (fabricada por UBI) se diluyó con el amortiguador de ensayo mencionado anteriormente (1.2 ng/25 μl).

(Método de Evaluación)

La muestra (10 μl) preparada como se mencionó anteriormente y un sustrato (25 μl), se agregaron sucesivamente a una placa de 96 pozos, y se agregó la enzima (25 μl) preparada como se mencionó anteriormente y se mezclaron. La mezcla se incubó a temperatura ambiente durante 60 minutos y se agregó verde de malaquita (120 μl, Biomoles), el cual es un reactivo coloreado. La mezcla se incubó además a temperatura ambiente durante 20 minutos, para dejar que el color se desarrollara. Se midió una absorbancia a 650 nm en un lector de placas, basándose en lo cual, se evaluó la actividad inhibidora de la proteína tirosina fosfatasa 1B del compuesto de prueba. Los resultados se muestran en los Cuadros 5 y 6.

La actividad inhibidora de la proteína tirosina fosfatasa de los linfocitos T, de los compuestos de los Ejemplos 1-1, 1-27, 1-48, 1-65, 1-66, 1-68, 1-71, 1-77, 1-78, 1-80, 1-86, 1-88, 1-89, 1-94, 1-97, 1-105, 1-109, 1-110, 1-111, 1-119, 1-120, 1-126, 1-130, 1-132, 1-138, 1-139, 1-140, 1-141, 1-146, 1-149, 1-153, 1-155, 1-156, 1-160, 1-161, 1-162, 3-1, 3-117, 3-120, 3-124, 4-1, 4-2, 4-6, 4-8, 4-9, 4-17, 4-18, 4-19, 4-21, 4-27, 4-30, 4-31, 4-34, 4-36 y 4-37 se evaluó y comparó con la actividad inhibidora de la proteína tirosina fosfatasa 1B mencionada anteriormente. Como resultdo, la CI_{50} de la proteína tirosina

fosfatasa 1B fue tan baja como 1/60 o por debajo de la CI_{50} de la proteína tirosina fosfatasa de los linfocitos T.

EJEMPLO EXPERIMENTAL 2

(Actividad hipoglucémica)

Una suspensión de metil celulosa al 0.5% del compuesto de prueba se administró oralmente a ratones ob/ob machos de 6 a 9 semanas de edad, agrupados de acuerdo con el nivel de glucosa. Sólo se administró una solución de metil celulosa al 0.5% al grupo de control.

Se extrajo la sangre bajo condiciones de ayuno, condición la cual inició simultáneamente con la administración, al retirar el alimento. La sangre se extrajo bajo anestesia de la vena orbital, 3 horas después de la administración. La sangre así tomada se centrifugó y se midió el nivel de glucosa en sangre del plasma obtenido mediante el método de la hexocinasa (equipo de medición de glucosa). Para la evaluación, se muestra el porcentaje (%) de disminución del nivel de glucosa del compuesto de prueba-grupo administrado, con relación al grupo de control. Los resultados se muestran en los Cuadros 5 a 9.

CUADRO 5

Ejemplo	Actividad inhibidora PTP1B (CI50; μM)	Velocidad de disminución de la glucosa en sangre (%)	
		Dosis (mg/kg)	3 horas después
1-1	0.28	1	45
1-15	0.13	1	35
1-19	0.10	1	35
1-25	0.13	1	25
1-37	0.14	3	26
1-39	0.19	1	32
1-44	0.22	1	20
1-45	0.066	1	32
1-48	0.23	1	46
1-50	0.14	—	
1-53	0.24	—	
1-78	0.18	3	24
1-141	0.35	—	
3-9	0.17	1	18
3-10	0.20	1	18
3-14	0.38	—	
3-15	0.27	1	25
3-21	0.45	1	27
3-25	0.14	1	20
3-26	0.11	—	
3-29	0.41	3	41
3-32	0.18	1	14
3-34	0.16	—	

CUADRO 6

Ejemplo	Actividad inhibidora de la PTP1B (IC50; μM)	Velocidad de disminución de la glucosa en sangre (%)	
		Dosis (mg/kg)	3 horas después
3-35	0.073	—	
3-36	0.10	3	52
3-52	0.54	1	28
3-53	0.28	1	20
3-58	0.39	1	23
3-64	0.21	1	13
3-67	0.23	3	20
3-69	0.16	—	
3-70	0.16	—	
3-71	0.095	—	
3-73	0.20	1	14
3-76	0.48	1	33
3-86	0.20	1	16
3-87	0.21	—	
3-92	0.18	1	26
3-98	0.16	3	31
3-100	0.15	3	20
3-108	0.16	1	29
4-1	0.15	—	
4-6	0.092	—	
4-9	0.12	—	
4-30	0.17	—	
4-35	0.087	—	

CUADRO 7

Ejemplo	Actividad inhibidora de la PTP1B (IC50; μM)	Velocidad de disminución de la glucosa en sangre (%)	
		Dosis (mg/kg)	3 horas después
1-155	0.37	—	
1-156	0.19	—	
1-157	0.17	—	
1-158	0.29	—	
1-160	0.31	—	
1-161	0.18	—	
1-162	0.21	—	
1-166	0.31	—	
1-167	0.41	—	
1-172	0.28	—	
1-178	0.44	—	
1-181	0.20	—	
1-182	0.19	—	
4-42	0.17	—	
4-43	0.16	—	
4-44	0.12	—	
4-45	0.27	—	
4-52	0.15	—	
4-53	0.07	—	
4-54	0.14	—	
4-55	0.17	—	
4-56	0.20	—	
4-57	0.17	—	

CUADRO 8

Ejemplo	Actividad inhibidora de la PTP1B (IC50; μM)	Velocidad de disminución de la glucosa en sangre (%)	
		Dosis (mg/kg)	3 horas después
4-58	0.19	—	
4-59	0.18	—	
4-60	<0.1	—	
4-61	0.25	—	
4-62	0.45	—	
4-63	0.42	—	
4-64	0.24	—	
4-66	0.45	—	
4-67	0.23	—	
4-68	<0.1	—	
4-69	0.15	—	
4-70	0.17	—	
4-72	0.29	—	
4-73	0.19	—	
4-74	0.11	—	
4-75	<0.1	—	
4-77	0.40	—	
4-78	0.38	—	
4-79	<0.1	—	
4-80	<0.1	—	
4-81	<0.1	—	
4-82	0.48	—	
4-84	0.27	—	

CUADRO 9

Ejemplo	Actividad inhibidora de la PTP1B (IC50; μM)	Velocidad de disminución de la glucosa en sangre (%)	
		Dosis (mg/kg)	3 horas después
4-87	0.12	—	
4-88	<0.1	—	
4-89	0.49	—	
4-90	0.16	—	
4-91	0.17	—	
4-92	<0.1	—	
4-93	<0.1	—	
4-94	0.12	—	
4-95	0.28	—	
4-96	0.12	—	
4-97	0.11	—	
4-98	<0.1	—	
4-99	<0.1	—	
4-100	<0.1	—	
4-101	0.10	—	
4-102	0.37	—	
4-104	0.20	—	
4-106	0.16	—	
4-107	<0.1	—	

EJEMPLO EXPERIMENTAL 3

(Efecto del uso concomitante con insulina en la actividad hipoglucémica)

Una suspensión de metil celulosa al 0.5% del compuesto de prueba {nota: Ejemplo 3-40 (30 mg/kg)} (grupo de uso concomitante del compuesto de prueba e insulina) o una solución de metil celulosa al 0.5% sola (grupo de administración de insulina) se administró oralmente a ratas SD

macho de 7 semanas de edad, una vez al día durante 8 días, y 3 horas después, se administró insulina (0.6 U/kg) subcutáneamente.

Se extrajo la sangre en el día del inicio de la administración, antes de la administración de la insulina en el día 8 y 1 hora a partir de la misma de la vena de la cola. Para extraer la sangre, los animales ayunaron después de la administración de la insulina. La sangre así tomada se centrifugó y se midió el nivel de glucosa en sangre del plasma obtenido mediante el método de la hexocinasa (equipo de medición de glucosa). Para la evaluación, se muestra el porcentaje (%) de disminución del nivel de glucosa del compuesto de prueba y el grupo del uso concomitante de insulina, una hora después, con relación a antes de la administración de la insulina. Los resultados se muestran en el Cuadro 10.

CUADRO 10

	Dosis del compuesto de prueba (mg/kg)	Velocidad de disminución de la glucosa en sangre (%)	
		Día de inicio de la administración	Día 8
Grupo de administración de la insulina	——	29	17
Grupo de uso concomitante del compuesto de prueba e insulina (Ejemplo 3-40)	30	43	36

EJEMPLO EXPERIMENTAL 4

(Efecto del uso concomitante con glibenclamida en la actividad hipoglicémica)

A ratones ob/ob hembra de 10 semanas de edad, agrupados de acuerdo con el nivel de glucosa, se les administró oralmente una suspensión de metil celulosa al 0.5% del compuesto de prueba {nota: Ejemplo 4-2 (1 mg/kg)} (grupo al que se le administró el compuesto de prueba), una suspensión de metil celulosa al 0.5% de glibenclamida (3 mg/kg) (grupo al que se le administró glibenclamida), simultáneamente tanto una suspensión de metil celulosa al 0.5% del compuesto de prueba como una suspensión de metil celulosa al 0.5% (glibenclamida 3 mg/kg) (grupo de uso concomitante del compuesto de prueba y glibenclamida) o una solución de metil celulosa al 0.5% sola (grupo de control).

La sangre se extrajo bajo condiciones de ayuno, condición la cual inició simultáneamente con la administración, retirando el alimento. La sangre se extrajo bajo anestesia de la vena orbital 3 y 5 horas después de la administración. La sangre así tomada se centrifugó y se midió el nivel de glucosa en sangre del plasma obtenido mediante el método de la hexocinasa (equipo de medición de glucosa). Para la evaluación, se muestra el porcentaje (%) de disminución del nivel de glucosa de cada grupo diferente al grupo de control, con relación al grupo de control. Los resultados se muestran en el Cuadro 11.

CUADRO 11

	Dosis del compuesto de prueba (mg/kg)	Velocidad de disminución de la glucosa en sangre (%)	
		3 horas después	5 horas después
Grupo al que se le administro la glibenclamida	—	44	40
Grupo al que se le administró el compuesto de prueba (Ejemplo 4-2)	1	48	20
Grupo de uso concomitante del compuesto de prueba y glibenclamida (Ejemplo 4-2)	1	64	60

EJEMPLO EXPERIMENTAL 5

(Efecto del uso concomitante con tolbutamida en la actividad hipoglicémica)

A ratones db/db machos de 10 semanas de edad, agrupados de acuerdo con el nivel de glucosa, se les administró oralmente una suspensión de metil celulosa al 0.5% del compuesto de prueba {nota: Ejemplo 4-5 (5 mg/kg)} (grupo al que se le administró el compuesto de prueba), una suspensión de metil celulosa al 0.5% de tolbutamida (30 mg/kg) (grupo al que se le administró la tolbutamida), simultáneamente tanto una suspensión de metil celulosa al 0.5% del compuesto de prueba como una suspensión de metil celulosa al 0.5% (tolbutamida 30 mg/kg) (grupo de uso concomitante del

compuesto de prueba y tolbutamida) o una solución de metil celulosa al 0.5% sola (grupo de control).

La sangre se extrajo bajo condiciones de ayuno, condición la cual inició simultáneamente con la administración, retirando el alimento. La sangre se extrajo bajo anestesia de la vena orbital 5 horas después de la administración. La sangre así tomada se centrifugó y se midió el nivel de glucosa en sangre del plasma obtenido mediante el método de la hexocinasa (equipo de medición de glucosa). Para la evaluación, se muestra el porcentaje (%) de disminución del nivel de glucosa de cada grupo diferente al grupo de control, con relación al grupo de control. Los resultados se muestran en el Cuadro 12.

CUADRO 12

	Dosis del compuesto de prueba (mg/kg)	Velocidad de disminución de la glucosa en sangre (%) 5 horas después
Grupo al que se le administró la tolbutamida	—	26
Grupo al que se le administró el compuesto de prueba (Ejemplo 4-5)	5	26
Grupo de uso concomitante del compuesto de prueba y tolbutamida (Ejemplo 4-5)	5	30

EJEMPLO EXPERIMENTAL 6

(Efecto del uso concomitante con nateglinida en la actividad hipoglucémica)

A ratones db/db machos de 10 semanas de edad agrupados de acuerdo con el nivel de glucosa se les administró oralmente una suspensión de metil celulosa al 0.5% del compuesto de prueba {nota: Ejemplo 4-5 (5 mg/kg)} (grupo al que se le administró el compuesto de prueba), una suspensión de metil celulosa al 0.5% de nateglinida (30 mg/kg) (grupo al que se le administró la nateglinida), simultáneamente tanto una suspensión de metil celulosa al 0.5% del compuesto de prueba como una suspensión de metil celulosa al 0.5% (nateglinida 30 mg/kg) (grupo de uso concomitante del compuesto de prueba y nateglinida) o una solución de metil celulosa al 0.5% sola (grupo de control).

La sangre se extrajo bajo condiciones de ayuno, condición la cual inició simultáneamente con la administración, retirando el alimento. La sangre se extrajo bajo anestesia de la vena orbital 2 horas después de la administración. La sangre así tomada se centrifugó y se midió el nivel de glucosa en sangre del plasma obtenido mediante el método de la hexocinasa (equipo de medición de glucosa). Para la evaluación, se muestra el porcentaje (%) de disminución del nivel de glucosa de cada grupo diferente al grupo de control, con relación al grupo de control. Los resultados se muestran en el Cuadro 13.

CUADRO 13

	Dosis del compuesto de prueba (mg/kg)	Velocidad de disminución de la glucosa en sangre (%) 2 horas después
Grupo al que se le administró la nateglinida	—	5
Grupo al que se le administró el compuesto de prueba (Ejemplo 4-5)	5	11
Grupo de uso concomitante del compuesto de prueba y nateglinida (Ejemplo 4-5)	5	19

EJEMPLO EXPERIMENTAL 7

(Efecto del uso concomitante con metformina en el clorhidrato hipoglucémico) (sic)

A ratones ob/ob hembras de 10 semanas de edad agrupados de acuerdo con el nivel de glucosa, se les administró oralmente una suspensión de metil celulosa al 0.5% del compuesto de prueba {nota: Ejemplo 4-2 (1 mg/kg)} (grupo al que se le administró el compuesto de prueba), una suspensión de metil celulosa al 0.5% de cloruro de metformina (30 mg/kg) (grupo al que se le administró la metformina), simultáneamente tanto una suspensión de metil celulosa al 0.5% del compuesto de prueba como una suspensión de metil celulosa al 0.5% (cloruro de metformina 30 mg/kg) (grupo

de uso concomitante del compuesto de prueba y metformina) o una solución de metil celulosa al 0.5% sola (grupo de control). Los ratones ob/ob ayunaron durante 3 horas antes de la administración.

La sangre se extrajo bajo condiciones de ayuno, condición la cual inició simultáneamente con la administración, retirando el alimento. La sangre se extrajo bajo anestesia de la vena orbital 3 y 5 horas después de la administración. La sangre así tomada se centrifugó y se midió el nivel de glucosa en sangre del plasma obtenido mediante el método de la hexocinasa (equipo de medición de glucosa). Para la evaluación, se muestra el porcentaje (%) de disminución del nivel de glucosa de cada grupo diferente al grupo de control, con relación al grupo de control. Los resultados se muestran en el Cuadro 14.

CUADRO 14

	Dosis del compuesto de prueba (mg/kg)	Velocidad de disminución de la glucosa en sangre (%)	
		3 horas después	5 horas después
Grupo al que se le administró la metformina	—	17	39
Grupo al que se le administró el compuesto de prueba (Ejemplo 4-2)	1	19	20
Grupo de uso concomitante del compuesto de prueba y metformina (Ejemplo 4-2)	1	40	51

EJEMPLO EXPERIMENTAL 8

(Efecto del uso concomitante con voglibosa en la actividad hipoglucémica)

A ratones ob/ob hembras de 9 semanas de edad agrupados de acuerdo al nivel de glucosa, se les administró oralmente una suspensión de metil celulosa al 0.5% del compuesto de prueba {nota: Ejemplo 4-2 (1 mg/kg)} (grupo al que se le administró el compuesto de prueba), una suspensión de metil celulosa al 0.5% de voglibosa (0.3 mg/kg) (grupo al que se le administró la voglibosa), simultáneamente tanto una suspensión de metil celulosa al 0.5% del compuesto de prueba como una suspensión de metil celulosa al 0.5% (voglibosa 0.3 mg/kg) (grupo de uso concomitante del compuesto de prueba y voglibosa) o una solución de metil celulosa al 0.5% sola (grupo de control). Una hora más tarde, se cargó la sucrosa (2 g/5 mL/kg).

La sangre se extrajo bajo condiciones de ayuno, condición la cual se inició simultáneamente con la carga, retirando el alimento. La sangre se extrajo bajo anestesia de la vena orbital 1 y 2 horas después de la carga de sucrosa. La sangre así tomada se centrifugó y se midió el nivel de glucosa en sangre del plasma obtenido mediante el método de la hexocinasa (equipo de medición de glucosa). Para la evaluación, se muestra el porcentaje (%) de disminución del nivel de glucosa de cada grupo diferente al grupo de control, con relación al grupo de control. Los resultados se muestran en el Cuadro 15.

CUADRO 15

	Dosis del compuesto de prueba (mg/kg)	Velocidad de disminución de la glucosa en sangre (%)	
		1 hora después	2 horas después
Grupo al que se le adminstró la voglibosa	—	35	38
Grupo al que se le administró el compuesto de prueba (Ejemplo 4-2)	1	32	40
Grupo de uso concomitante del compuesto de prueba y voglibosa (Ejemplo 4-2)	1	49	54

EJEMPLO EXPERIMENTAL 9

(Efecto del uso concomitante con clorhidrato de Pioglitazona en la actividad hipoglucémica)

A ratones db/db machos de 8 semanas, agrupados de acuerdo con el nivel de glucosa con alimentación completa, se les administró oralmente una suspensión de metil celulosa al 0.5% del compuesto de prueba {nota: Ejemplo 4-5 (10 mg/kg)} (grupo al que se le administró el compuesto de prueba), una suspensión de metil celulosa al 0.5% de clorhidrato de Pioglitazona (3 mg/kg) (grupo al que se le administró la Pioglitazona), simultáneamente tanto una suspensión de metil celulosa al 0.5% del compuesto de prueba como una suspensión de metil celulosa al 0.5%

(clorhidrato de Pioglitazona 3 mg/kg) (grupo de uso concomitante del compuesto de prueba y Pioglitazona) o una solución de metil celulosa al 0.5% sola (grupo de control), una vez al día, durante 3 días.

La sangre se extrajo bajo condiciones de ayuno, condición la cual inició simultáneamente con la administración, retirando el alimento. La sangre se extrajo bajo anestesia de la vena orbital en el día 1 de la administración y 3 horas después de la administración en el día 3. La sangre así tomada se centrifugó y se midió el nivel de glucosa en sangre del plasma obtenido mediante el método de la hexocinasa (equipo de medición de glucosa). Para la evaluación, se muestra el porcentaje (%) de disminución del nivel de glucosa de cada grupo diferente al grupo de control, con relación al grupo de control. Los resultados se muestran en el Cuadro 16.

CUADRO 16

	Dosis del compuesto de prueba (mg/kg)	Velocidad de disminución de la glucosa en sangre (%)	
		Día de inicio de la administración	Día 3
Grupo al que se le administró la Pioglitazona	—	11	44
Grupo al que se le administró el compuesto de prueba (Ejemplo 4-5)	10	24	32
Grupo de uso concomitante del compuesto de prueba y Pioglitazona (Ejemplo 4-5)	10	30	48

Los datos de la RMN de los compuestos de los Ejemplos se muestran en los siguientes Cuadros.

CUADRO 17

Ejemplo	solvente, Hz	RMN (δ)
1-1	DMSO-d6, 300MHz	0.69 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.5 Hz, 6H), 1.48-1.31 (m, 2H), 1.64-1.48 (m, 2H), 2.19-2.06 (m, 1H), 4.23 (quint, J = 6.6 Hz, 1H), 5.67 (s, 2H), 6.62 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 7.36 (d, J = 8.2 Hz, 2H), 7.90 (d, J = 8.2 Hz, 2H), 7.99 (dd, J = 3.0, 1.5 Hz, 1H), 8.11 (s, 1H), 8.64 (d, J = 2.9 Hz, 1H), 8.72 (d, J = 1.5 Hz, 1H), 13.43 (s amplio, 1H).
1-2	DMSO-d6, 400MHz	0.68 (t, J = 7.4 Hz, 6H), 1.14 (d, J = 8.0 Hz, 6H), 1.32-1.46 (m, 2H), 1.50-1.62 (m, 2H), 2.08-2.17 (m, 1H), 4.23 (quint, J = 6.6 Hz, 1H), 4.37 (s, 2H), 5.57 (s, 2H), 6.62 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.17 (d, J = 9.2 Hz, 2H), 7.36 (d, J = 8.3 Hz, 2H), 7.89 (d, J = 8.8 Hz, 2H), 7.91 (d, J = 9.0 Hz, 2H), 8.09 (s, 1H), 12.64 (s amplio, 1H).
1-3	DMSO-d6, 400MHz	0.68 (t, J = 7.2 Hz, 6H), 1.16 (d, J = 6.4 Hz, 2H), 1.35-1.45 (m, 2H), 1.50-1.60 (m, 2H), 2.10-2.15 (m, 1H), 4.20-4.25 (m, 1H), 4.37 (s, 2H), 5.75 (s, 2H), 6.61 (d, J = 10.2 Hz, 2H), 6.87 (d, J = 11.6 Hz, 2H), 6.99 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 10.8 Hz, 2H), 7.88 (d, J = 8.1 Hz, 2H), 8.04 (s, 1H), 8.18 (d, J = 8.0 Hz, 1H), 8.70 (s, 1H)
1-4	DMSO-d6, 400MHz	0.79 (t, J = 7.2 Hz, 6H), 1.05-1.11 (m, 4H), 1.39-1.50 (m, 4H), 2.34-2.39 (m, 1H), 2.97 (s, 3H), 4.52 (s, 2H), 5.65 (s, 2H), 6.67 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.0 Hz, 2H), 7.30 (d, J = 8.0 Hz, 2H), 7.91 (d, J = 8.7 Hz, 2H), 7.96-7.97 (m, 1H), 8.12 (s, 1H), 8.62 (d, J = 2.8 Hz, 1H), 8.71 (d, J = 1.4 Hz, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-5	DMSO-d6, 400MHz	0.79 (t, J = 7.2 Hz, 6H), 1.03-1.11 (m, 4H), 1.39-1.50 (m, 4H), 2.34-2.39 (m, 1H), 2.97 (s, 3H), 4.52 (s, 2H), 5.56 (s, 2H), , 6.67 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 7.15 (d, J = 8.8 Hz, 2H), 7.30 (d, J = 8.8 Hz, 2H), 7.91-7.93 (m, 4H), 8.11 (s, 1H)
1-6	DMSO-d6, 300MHz	0.85 (t, J = 7.3 Hz, 6H), 1.10 (d, J = 6.8 Hz, 6H), 1.25-1.64 (m, 8H), 2.65-2.74 (m, 1H), 3.84-3.91 (m, 1H), 4.37 (s, 2H), 5.77 (s, 2H), 6.66 (d, J = 9.1 Hz, 2H), 6.94 (d, J = 8.7 Hz, 2H), 7.06 (d, J = 9.4 Hz, 1H), 7.31 (d, J = 8.6 Hz, 2H), 7.84 (d, J = 8.3 Hz, 2H), 8.04 (s, 1H), 8.22 (dd, J = 2.3, 8.7 Hz, 1H), 8.75 (dd, J = 0.7, 2.6 Hz, 1H), 13.05 (s amplio, 1H)
1-7	DMSO-d6, 300MHz	0.85 (t, J = 7.2 Hz, 6H), 1.11 (d, J = 6.8 Hz, 6H), 1.25-1.64 (m, 8H), 2.65-2.74 (m, 1H), 3.83-3.92 (m, 1H), 4.37 (s, 2H), 5.65 (s, 2H), 6.66 (d, J = 8.6 Hz, 2H), 6.94 (d, J = 8.7 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 7.86 (d, J = 8.3 Hz, 2H), 7.98-7.98 (s amplio, 1H), 8.09 (s, 1H), 8.63-8.63 (s amplio, 1H), 8.72 (s, 1H), 13.38 (s amplio, 1H)
1-8	DMSO-d6, 300MHz	0.92 (d, J = 6.8 Hz, 6H), 1.12 (d, J = 7.2 Hz, 6H), 2.00-2.13 (m, 1H), 2.67-2.78 (m, 1H), 3.24 (d, J = 7.1 Hz, 2H), 4.58 (s, 2H), 5.66 (s, 2H), 6.59 (d, J = 9.0 Hz, 2H), 6.97 (d, J = 8.6 Hz, 2H), 7.26 (d, J = 8.3 Hz, 2H), 7.88 (d, J = 8.3 Hz, 2H), 7.99-7.99 (m, 1H), 8.10 (s, 1H), 8.64 (d, J = 3.0 Hz, 1H), 8.72 (d, J = 1.5 Hz, 1H), 13.46 (s amplio, 1H)
1-9	DMSO-d6, 300MHz	0.85 (t, J = 7.2 Hz, 6H), 1.11 (d, J = 7.2 Hz, 6H), 1.29-1.62 (m, 8H), 2.65-2.74 (m, 1H), 3.83-3.95 (m, 1H), 4.37 (s, 2H), 5.56 (s, 2H), 6.66 (d, J = 8.6 Hz, 2H), 6.94 (d, J = 8.7 Hz, 2H), 7.17 (d, J = 9.1 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 7.85 (d, J = 8.3 Hz, 2H), 7.92 (d, J = 9.0 Hz, 2H), 8.07 (s, 1H), 12.58 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-10	DMSO-d6, 300MHz	0.85 (t, J = 7.2 Hz, 6H), 1.11 (d, J = 6.8 Hz, 6H), 1.25-1.68 (m, 8H), 2.65-2.75 (m, 1H), 3.84-3.93 (m, 1H), 4.37 (s, 2H), 5.55 (s, 2H), 6.66 (d, J = 8.7 Hz, 2H), 6.94 (d, J = 8.7 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 7.35-7.36 (m, 1H), 7.45 (t, J = 7.9 Hz, 1H), 7.57-7.62 (m, 2H), 7.86 (d, J = 8.3 Hz, 2H), 8.06 (s, 1H), 12.91 (s amplio, 1H)
1-11	DMSO-d6, 300MHz	0.87 (t, J = 6.0 Hz, 6H), 1.09 (d,J = 9.0 Hz, 6H), 1.37-1.70 (m, 4H), 2.65-2.72 (m, 1H), 3.55-3.82 (m, 1H), 4.35 (s, 2H), 5.74 (s, 2H), 6.67 (d,J = 9.0 Hz, 2H), 6.92 (d,J = 9.0 Hz, 2H), 7.04 (d,J = 9.0 Hz, 1H), 7.31 (d,J = 9.0 Hz, 2H), 7.82 (d,J = 9.0 Hz, 2H), 8.01 (s, 1H), 8.20 (d,J = 6.0 Hz, 1H), 8.73 (d,J = 3.0 Hz, 1H)
1-12	DMSO-d6, 300MHz	0.88 (t, J = 6.0 Hz, 6H), 1.10 (t, J = 6.0 Hz, 6H), 1.37-1.72 (m, 4H), 2.53-2.76 (m, 1H), 3.57-3.84 (m, 1H), 4.36 (s, 2H), 5.63 (s, 2H), 6.45-6.76 (m, 2H), 6.83-7.07 (m, 2H), 7.19-7.42 (m, 2H), 7.80-7.86 (m, 2H), 7.92-7.95 (m, 1H), 8.04-8.08 (m, 1H), 8.59 (m, 1H), 8.7 (m, 1H)
1-13	DMSO-d6, 400MHz	0.68 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.7 Hz, 6H), 1.33-1.46 (m, 2H), 1.49-1.62 (m, 2H), 2.07-2.17 (m, 1H), 4.22 (quit, J = 6.5 Hz, 1H), 4.36 (s, 2H), 4.78 (s, 2H), 6.61 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 7.33 (d, J = 8.3 Hz, 2H), 7.50 (d, J = 8.8 Hz, 2H), 7.84 (d, J = 8.6 Hz, 4H), 7.92 (s, 1H), 12.80 (s amplio, 1H).
1-14	DMSO-d6, 400MHz	0.79 (t, J = 7.2 Hz, 6H), 1.03-1.11 (m, 4H), 1.39-1.50 (m, 4H), 2.34-2.39 (m, 1H), 2.97 (s, 3H), 4.50 (s, 2H), 4.78 (s, 2H), , 6.66 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 8.0 Hz, 2H), 7.82-7.85 (m, 4H), 7.94 (s, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-15	DMSO-d6, 300MHz	0.79 (t, J = 7.1 Hz, 6H), 1.02-1.16 (m, 4H), 1.35-1.52 (m, 4H), 2.32-2.42 (m, 1H), 2.87 (s, 3H), 2.96 (s, 3H), 4.51 (s, 2H), 4.68 (s, 2H), 6.67 (d, J = 8.8 Hz, 2H), 6.94 (d, J = 8.8 Hz, 2H), 7.27 (d, J = 8.1 Hz, 2H), 7.79 (d, J = 8.4 Hz, 2H), 7.97 (d, J = 8.8 Hz, 2H), 8.02 (s, 1H), 8.13 (d, J = 8.8 Hz, 2H), 13.20 (s amplio, 1H)
1-16	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 1.02-1.15 (m, 4H), 1.37-1.53 (m, 4H), 1.78-1.88 (m, 2H), 1.99 (t, J = 7.0 Hz, 2H), 2.32-2.42 (m, 1H), 2.89 (s, 3H), 2.97 (s, 3H), 3.21-3.26 (m, 2H), 4.52 (s, 2H), 4.67 (s, 2H), 6.68 (d, J = 8.8 Hz, 2H), 6.94 (d, J = 8.8 Hz, 2H), 7.30 (d, J = 8.1 Hz, 2H), 7.89 (d, J = 8.1 Hz, 2H), 8.04 (s, 1H)
1-17	DMSO-d6, 400MHz	1.11-1.37 (m, 5H), 1.61-1.78 (m, 5H), 2.23-2.33 (m, 1H), 3.09 (s, 3H), 4.22 (s, 2H), 4.83 (s, 2H), 5.97 (s amplio, 1H), 6.48 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 8.4 Hz, 2H), 7.12 (s, 1H), 7.34 (d, J = 8.6 Hz, 2H), 7.44 (d, J = 8.1 Hz, 2H), 7.78 (d, J = 8.2 Hz, 2H), 7.92 (d, J = 8.6 Hz, 2H), 12.78 (s amplio, 1H)
1-18	DMSO-d6, 400MHz	1.12-1.40 (m, 5H), 1.63-1.82 (m, 5H), 2.29-2.38 (m, 1H), 2.96 (s, 3H), 3.09 (s, 3H), 4.49 (s, 2H), 4.82 (s, 2H), 6.65 (d, J = 8.6 Hz, 2H), 6.99 (d, J = 8.6 Hz, 2H), 7.12 (s, 1H), 7.21 (d, J = 8.1 Hz, 2H), 7.43 (d, J = 8.1 Hz, 2H), 7.77 (d, J = 8.1 Hz, 2H), 7.92 (d, J = 8.1 Hz, 2H)
1-19	DMSO-d6, 300MHz	0.78 (t, J = 7.4 Hz, 6H), 0.98-1.17 (m, 4H), 1.32-1.54 (m, 4H), 2.29-2.42 (m, 1H), 2.95 (s, 3H), 3.09 (s, 3H), 4.49 (s, 2H), 4.83 (s, 2H), 6.66 (d, J = 8.7 Hz, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.14 (s, 1H), 7.23 (d, J = 8.3 Hz, 2H), 7.43 (d, J = 8.3 Hz, 2H), 7.78 (d, J = 8.3 Hz, 2H), 7.92 (d, J = 8.3 Hz, 2H), 12.82 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-20	DMSO-d6, 300MHz	0.68 (t, J = 7.2 Hz, 6H), 1.15 (d, J = 6.4 Hz, 6H), 1.32-1.47 (m, 2H), 1.49-1.64 (m, 2H), 2.05-2.19 (m, 1H), 3.09 (s, 3H), 4.15-4.28 (m, 1H), 4.34 (s, 2H), 4.83 (s, 2H), 6.61 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 7.12 (s, 1H), 7.28 (d, J = 8.3 Hz, 2H), 7.43 (d, J = 7.9 Hz, 2H), 7.77 (d, J = 8.3 Hz, 2H), 7.92 (d, J = 7.9 Hz, 2H), 12.82 (s amplio, 1H)
1-21	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6H), 1.15 (d, J = 6.6 Hz, 6H), 1.33-1.46 (m, 2H), 1.48-1.61 (m, 2H), 2.06-2.18 (m, 1H), 2.34 (s, 3H), 3.85 (d, J = 15.0 Hz, 1H), 4.02 (d, J = 15.4 Hz, 1H), 4.22 (quint, J = 6.6 Hz, 1H), 4.36 (s, 2H), 4.50 (s, 2H), 6.62 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 7.34 (t, J = 7.1 Hz, 1H), 7.40 (t, J = 7.0 Hz, 2H), 7.47 (d, J = 7.0 Hz, 2H), 7.84 (d, J = 8.1 Hz, 2H), 7.93 (s, 1H), 12.66 (s amplio, 1H).
1-22	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.6 Hz, 6H), 1.30-1.47 (m, 2H), 1.48-1.61 (m, 2H), 2.07-2.19 (m, 1H), 2.37 (s, 3H), 2.94 (dd, J = 14.1, 8.2 Hz, 1H), 3.08 (dd, J = 13.9, 7.0 Hz, 1H), 3.70 (t, J = 7.7 Hz, 1H), 4.02 (d, J = 15.8 Hz, 1H), 4.17 (d, J = 15.8 Hz, 1H), 4.22 (t, J = 6.0 Hz, 1H), 4.36 (s, 2H), 6.62 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.16-7.30 (m, 5H), 7.32 (d, J = 8.4 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H), 7.86 (s, 1H), 12.53 (s amplio, 1H).
1-23	DMSO-d6, 300MHz	0.92 (d, J = 6.6 Hz, 6H), 1.19 (s, 9H), 2.05 (sept, J = 7.2 Hz, 1H), 3.24 (d, J = 7.5 Hz, 2H), 3.35 (s, 2H), 3.86 (s, 2H), 4.17 (s, 2H), 4.57 (s, 2H), 6.58 (d, J = 8.7 Hz, 2H), 7.11 (d, J = 9.0 Hz, 2H), 7.20-7.45 (m, 5H), 7.84 (d, J = 8.1 Hz, 2H), 7.94 (s, 1H), 13.38 (s amplio, 1H).

Ejemplo	solvente, Hz	RMN (δ)
1-24	DMSO-d6, 300MHz	0.92 (d, J = 6.6 Hz, 6H), 2.05 (sept, J = 6.8 Hz, 1H), 3.28 (d, J = 6.8 Hz, 2H), 3.36 (s, 2H), 3.86 (s, 2H), 4.17 (s, 2H), 4.61 (s, 2H), 6.65 (d, J = 9.0 Hz, 2H), 7.10 (d, J = 9.0 Hz, 2H), 7.21 (d, J = 7.8 Hz, 2H), 7.07-7.43 (m, 5H), 7.85 (d, J = 8.4 Hz, 2H), 7.95 (s, 1H), 12.37 (s amplio, 1H).
1-25	DMSO-d6, 300MHz	0.79 (t, J = 7.1 Hz, 6H), 1.00-1.28 (m, 4H), 1.34-1.58 (m, 4H), 2.30-2.42 (m, 3H), 2.97 (s, 3H), 3.36 (s, 2H), 3.87 (s, 2H), 4.18 (s, 2H), 4.51 (s, 2H), 6.67 (d, J = 8.7 Hz, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.28 (d, J = 8.3 Hz, 2H), 7.22-7.43 (m, 5H), 7.87 (d, J = 8.4 Hz, 2H), 7.97 (s, 1H), 12.38 (s amplio, 1H).
1-26	MeOH-d4, 300MHz	0.70 (t, J = 7.3 Hz, 6H), 1.26 (d, J = 6.4 Hz, 6H), 1.36-1.53 (m, 2H), 1.53-1.70 (m, 2H), 2.11-2.24 (m, 1H), 3.45 (s, 2H), 3.97 (s, 2H), 4.16-4.30 (m, 3H), 4.50 (s, 2H), 6.81 (d, J = 8.6 Hz, 2H), 6.97 (d, J = 8.7 Hz, 2H), 7.21-7.38 (m, 5H), 7.44 (d, J = 6.7 Hz, 2H), 7.68 (s, 1H), 7.78 (d, J = 8.3 Hz, 2H)
1-27	DMSO-d6, 300MHz	0.92 (d, J = 6.8 Hz, 6H), 1.19 (s, 9H), 2.05 (sept, J = 6.8 Hz, 1H), 3.25 (d, J = 7.1 Hz, 2H), 4.01 (s, 2H), 4.58 (s, 2H), 4.85 (s, 2H), 6.60 (d, J = 8.7 Hz, 2H), 6.93 (t, J = 7.3 Hz, 1H), 7.11 (d, J = 9.1 Hz, 2H), 7.23 (t, J = 7.9 Hz, 2H), 7.24 (d, J = 8.7 Hz, 2H), 7.43 (d, J = 7.5 Hz, 2H), 7.85 (d, J = 8.3 Hz, 2H), 7.94 (s, 1H), 9.47 (s amplio, 1H).
1-28	DMSO-d6, 300MHz	0.92 (d, J = 6.4 Hz, 6H), 1.19 (s, 9H), 2.05 (sept, J = 7.0 Hz, 1H), 3.25 (d, J = 7.2 Hz, 2H), 4.05-4.25 (m, 2H), 4.58 (s, 2H), 4.76-5.01 (m, 2H), 6.59 (d, J = 8.7 Hz, 2H), 7.11 (d, J = 8.7 Hz, 2H), 7.26 (d, J = 7.9 Hz, 2H), 7.33-7.53 (m, 5H), 7.81-7.90 (m, 2H), 7.97-7.03 (m, 1H), 12.84 (s amplio, 1H).

Ejemplo	solvente, Hz	RMN (δ)
1-29	DMSO-d6, 300MHz	0.91 (d, J = 6.6 Hz, 6H), 1.22 (s, 9H), 2.04 (sept, J = 6.8 Hz, 1H), 3.19 (d, J = 7.0 Hz, 2H), 4.36 (s amplio, 2H), 4.54 (s, 2H), 5.07 (s, 2H), 6.67 (d, J = 8.8 Hz, 2H), 7.13 (d, J = 8.8 Hz, 2H), 7.26 (d, J = 8.4 Hz, 2H), 7.47 (ddd, J = 7.6, 4.8, 1.2 Hz, 1H), 7.70 (dt, J = 7.7, 1.1 Hz, 1H), 7.81 (d, J = 8.1 Hz, 2H), 7.82 (s, 1H), 7.91 (td, J = 7.7, 1.8 Hz, 1H), 8.56 (d, J = 4.8 Hz, 1H).
1-30	DMSO-d6, 300MHz	0.92 (d, J = 6.6 Hz, 6H), 1.22 (s, 9H), 2.04 (sept, J = 6.8 Hz, 1H), 3.20 (d, J = 7.0 Hz, 2H), 4.18 (s, 2H), 4.54 (s, 2H), 4.93 (s, 2H), 6.67 (d, J = 9.1 Hz, 2H), 7.13 (d, J = 8.8 Hz, 2H), 7.44 (ddd, J = 7.9, 5.0, 0.9 Hz, 1H), 7.78-7.86 (m, 4H), 8.60-8.65 (m, 2H).
1-31	DMSO-d6, 300MHz	0.92 (d, J = 6.8 Hz, 6H), 1.19 (s, 9H), 2.05 (sept, J = 6.6 Hz, 1H), 3.24 (d, J = 7.2 Hz, 2H), 4.11 (s, 2H), 4.58 (s, 2H), 4.83 (s, 2H), 6.58 (d, J = 9.0 Hz, 2H), 7.11 (d, J = 8.7 Hz, 2H), 7.23 (d, J = 8.3 Hz, 2H), 7.55 (t, J = 7.5 Hz, 2H), 7.63 (t, J = 7.3 Hz, 1H), 7.76 (d, J = 8.3 Hz, 2H), 7.86 (d, J = 7.5 Hz, 2H), 7.95 (s, 1H), 12.82 (s amplio, 1H).
1-32	DMSO-d6, 300MHz	0.69 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.6 Hz, 6H), 1.33-1.46 (m, 2H), 1.47-1.64 (m, 2H), 2.07-2.18 (m, 1H), 3.09 (dd, J = 16.5, 3.3 Hz, 1H), 3.18 (dd, J = 16.1, 6.2 Hz, 1H), 3.94 (d, J = 16.1 Hz, 1H), 3.97 (dd, J = 5.9, 3.6 Hz, 1H), 4.09 (d, J = 15.8 Hz, 1H), 4.21 (d, J = 6.2 Hz, 1H), 4.26 (d, J = 8.4 Hz, 1H), 4.37 (s, 2H), 4.39 (d, J = 15.8 Hz, 1H), 6.62 (d, J = 8.8 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 7.01-7.17 (m, 4H), 7.34 (d, J = 8.1 Hz, 2H), 7.87 (d, J = 8.0 Hz, 2H), 7.94 (s, 1H), 12.51 (s amplio, 1H).

Ejemplo	solvente, Hz	RMN (δ)
1-33	DMSO-d6, 300MHz	0.69 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.4 Hz, 6H), 1.32-1.48 (m, 2H), 1.48-1.65 (m, 2H), 2.06-2.20 (m, 1H), 3.09 (dd, J = 3.4, 16.2 Hz, 1H), 3.18 (dd, J = 6.0, 16.2 Hz, 1H), 3.86-4.00 (m, 2H), 4.09 (d, J = 15.4 Hz, 1H), 4.16-4.45 (m, 5H), 6.62 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 6.99-7.19 (m, 4H), 7.34 (d, J = 8.3 Hz, 2H), 7.87 (d, J = 8.3 Hz, 2H), 7.94 (s, 1H), 12.55 (s amplio, 1H)
1-34	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.98-1.17 (m, 4H), 1.33-1.58 (m, 4H), 2.30-2.44 (m, 1H), 2.98 (s, 3H), 3.10 (dd, J = 2.6, 15.8 Hz, 1H), 3.19 (dd, J = 6.0, 15.8 Hz, 1H), 3.87-4.03 (m, 2H), 4.10 (d, J = 15.5 Hz, 1H), 4.26 (d, J = 15.8 Hz, 1H), 4.41 (d, J = 15.8 Hz, 1H), 4.52 (s, 2H), 6.68 (d, J = 7.9 Hz, 2H), 6.94 (d, J = 8.3 Hz, 2H), 6.99-7.20 (m, 4H), 7.29 (d, J = 8.3 Hz, 2H), 7.88 (d, J = 7.9 Hz, 2H), 7.97 (s, 1H)
1-35	DMSO-d6, 300MHz	0.89 (t, J = 9.0 Hz, 6H), 1.09 (t, J = 9.0 Hz, 6H), 1.32-1.73 (m, 4H), 2.61-2.75 (m, 1H), 3.09 (s, 2H), 3.65-3.74 (m, 1H), 3.84-.89 (m, 2H), 4.06-4.19 (m, 1H), 4.24-4.25 (m, 1H), 4.33-4.40 (m, 3H), 6.68 (d,J = 9.0 Hz, 2H), 6.91-6.94 (m, 2H), 6.98-7.04 (m, 1H), 7.10-7.13 (m, 3H), 7.30 (d,J = 6.0 Hz, 2H), 7.81 (d,J = 6.0 Hz, 2H), 7.90 (s, 1H)
1-36	DMSO-d6, 400MHz	1.14-1.42 (m, 5H), 1.64-1.82 (m, 5H), 2.38-2.45 (m, 1H), 3.60 (s, 3H), 5.08 (s, 2H), 6.92 (d, J = 8.6 Hz, 2H), 7.12 (d, J = 8.6 Hz, 2H), 7.41 (s, 1H), 7.47 (d, J = 8.2 Hz, 2H), 7.70 (d, J = 8.6 Hz, 2H), 7.89 (d, J = 8.2 Hz, 2H), 7.99 (d, J = 8.6 Hz, 2H), 12.81 (s amplio, 1H)
1-37	DMSO-d6, 400MHz	1.14-1.42 (m, 5H), 1.64-1.81 (m, 5H), 2.37-2.46 (m, 1H), 3.10 (s, 3H), 4.84 (s, 2H), 5.06 (s, 2H), 6.91 (d, J = 8.6 Hz, 2H), 7.12 (d, J = 8.6 Hz, 2H), 7.20 (s, 1H), 7.43 (d, J = 5.4 Hz, 2H), 7.45 (d, J = 5.4 Hz, 2H), 7.86 (d, J = 8.1 Hz, 2H), 7.93 (d, J = 8.1 Hz, 2H)

Ejemplo	solvente, Hz	RMN (δ)
1-38	DMSO-d6, 400MHz	0.61 (t, J = 7.4 Hz, 3H), 1.20 (s, 6H), 1.57 (c, J = 7.3 Hz, 2H), 3.10 (s, 3H), 4.83 (s, 2H), 5.06 (s, 2H), 6.92 (d, J = 8.8 Hz, 2H), 7.20-7.22 (m, 3H), 7.43 (d, J = 8.8 Hz, 4H), 7.85 (d, J = 8.0 Hz, 2H), 7.91 (d, J = 8.0 Hz, 2H)
1-39	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.93-1.18 (m, 4H), 1.32-1.59 (m, 4H), 2.38-2.55 (m, 1H), 3.11 (s, 3H), 4.84 (s, 2H), 5.06 (s, 2H), 6.92 (d, J = 8.6 Hz, 2H), 7.06 (d, J = 8.6 Hz, 2H), 7.22 (s, 1H), 7.45 (d, J = 8.2 Hz, 4H), 7.87 (d, J = 8.2 Hz, 2H), 7.93 (d, J = 8.2 Hz, 2H), 12.83 (s amplio, 1H)
1-40	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.99-1.17 (m, 4H), 1.38-1.60 (m, 4H), 2.40-2.52 (m, 1H), 3.07 (s, 3H), 4.73 (s, 2H), 5.06 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.06 (d, J = 8.7 Hz, 2H), 7.19-7.23 (m, 3H), 7.45 (d, J = 8.3 Hz, 2H), 7.82 (d, J = 7.9 Hz, 2H), 7.89 (d, J = 8.3 Hz, 2H)
1-41	MeOH-d4, 300MHz	0.83 (t, J = 7.3 Hz, 6H), 1.05-1.22 (m, 4H), 1.40-1.64 (m, 4H), 2.40-2.53 (m, 1H), 2.61 (s, 3H), 4.21 (d, J = 15.1 Hz, 1H), 4.34 (d, J = 15.1 Hz, 1H), 4.66 (s, 1H), 5.08 (s, 2H), 6.91 (d, J = 8.7 Hz, 2H), 7.04 (d, J = 8.7 Hz, 2H), 7.35-7.45 (m, 3H), 7.46-7.59 (m, 4H), 7.83 (s, 1H), 7.93 (d, J = 8.3 Hz, 2H)
1-42	DMSO-d6, 300MHz	0.79 (t, J = 7.4 Hz, 6H), 0.99-1.17 (m, 4H), 1.36-1.61 (m, 4H), 2.40 (s, 3H), 2.40-2.52 (m, 1H), 2.95 (dd, J = 8.3, 13.9 Hz, 1H), 3.08 (dd, J = 7.1, 13.9 Hz, 1H), 3.73 (t, J = 7.5 Hz, 1H), 4.05 (d, J = 15.8 Hz, 1H), 4.21 (d, J = 15.8 Hz, 1H), 5.07 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.16-7.33 (m, 5H), 7.49 (d, J = 8.3 Hz, 2H), 7.81-8.05 (m, 3H)
1-43	DMSO-d6, 300MHz	1.34 (s, 9H), 2.23 (s, 3H), 3.37 (s, 2H), 3.88 (s, 2H), 4.20 (s, 2H), 5.12 (s, 2H), 6.96 (s, 2H), 7.04 (s, 1H), 7.22-7.45 (m, 5H), 7.53 (d, J = 8.4 Hz, 2H), 7.97 (d, J = 8.1 Hz, 2H), 8.05 (s, 1H), 12.38 (s amplio, 1H).

Ejemplo	solvente, Hz	RMN (δ)
1-44	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.95-1.18 (m, 4H), 1.33-1.60 (m, 4H), 2.40-2.54 (m, 1H), 3.38 (s, 2H), 3.88 (s, 2H), 4.20 (s, 2H), 5.08 (s, 2H), 6.93 (d, J = 8.6 Hz, 2H), 7.07 (d, J = 8.6 Hz, 2H), 7.22-7.45 (m, 5H), 7.50 (d, J = 8.2 Hz, 2H), 7.96 (d, J = 8.2 Hz, 2H), 8.05 (s, 1H)
1-45	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 0.99-1.18 (m, 4H), 1.37-1.61 (m, 4H), 2.39-2.51 (m, 1H), 3.10 (dd, J = 3.4, 16.2 Hz, 1H), 3.19 (dd, J = 5.6, 15.8 Hz, 1H), 3.88-4.03 (m, 2H), 4.10 (d, J = 15.8 Hz, 1H), 4.27 (d, J = 15.8 Hz, 1H), 4.42 (d, J = 15.8 Hz, 1H), 5.09 (s, 2H), 6.94 (d, J = 8.6 Hz, 2H), 7.01-7.20 (m, 6H), 7.51 (d, J = 8.3 Hz, 2H), 7.97 (d, J = 8.3 Hz, 2H), 8.04 (s, 1H), 12.56 (s amplio, 1H)
1-46	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 0.99-1.18 (m, 4H), 1.37-1.61 (m, 4H), 2.39-2.51 (m, 1H), 3.10 (dd, J = 3.4, 16.2 Hz, 1H), 3.19 (dd, J = 5.6, 15.8 Hz, 1H), 3.88-4.03 (m, 2H), 4.10 (d, J = 15.8 Hz, 1H), 4.27 (d, J = 15.8 Hz, 1H), 4.42 (d, J = 15.8 Hz, 1H), 5.09 (s, 2H), 6.94 (d, J = 8.6 Hz, 2H), 7.01-7.20 (m, 6H), 7.51 (d, J = 8.3 Hz, 2H), 7.97 (d, J = 8.3 Hz, 2H), 8.04 (s, 1H), 12.56 (s amplio, 1H)
1-47	DMSO-d6, 300MHz	0.80 (t, J = 7.4 Hz, 6H), 0.98-1.17 (m, 4H), 1.36-1.60 (m, 4H), 2.39-2.53 (m, 1H), 3.10 (dd, J = 2.6, 15.8 Hz, 1H), 3.19 (dd, J = 5.6, 16.2 Hz, 1H), 3.88-4.02 (m, 2H), 4.10 (d, J = 16.2 Hz, 1H), 4.27 (d, J = 15.5 Hz, 2H), 4.42 (d, J = 15.8 Hz, 2H), 5.08 (s, 2H), 6.94 (d, J = 8.3 Hz, 2H), 7.01-7.21 (m, 6H), 7.51 (d, J = 7.9 Hz, 2H), 7.97 (d, J = 7.9 Hz, 2H), 8.05 (s, 1H), 12.59 (s amplio, 1H)
1-48	DMSO-d6, 300MHz	0.80 (t, J = 7.2 Hz, 6H), 1.02-1.15 (m, 4H), 1.38-1.57 (m, 4H), 2.41-2.48 (m, 1H), 5.10 (s, 2H), 5.69 (s, 2H), 6.94 (d, J = 8.6 Hz, 2H), 7.08 (d, J = 8.7 Hz, 2H), 7.53 (d, J = 8.3 Hz, 2H), 7.99-8.02 (m, 3H), 8.21 (s, 1H), 8.66 (d, J = 3.0 Hz, 1H), 8.74 (d, J = 1.5 Hz, 1H), 13.48 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-49	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 1.02-1.15 (m, 4H), 1.38-1.58 (m, 4H), 2.41-2.50 (m, 1H), 5.10 (s, 2H), 5.60 (s, 2H), 6.94 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 9.0 Hz, 2H), 7.19 (d, J = 9.1 Hz, 2H), 7.53 (d, J = 8.3 Hz, 2H), 7.93 (d, J = 9.1 Hz, 2H), 8.00 (d, J = 8.3 Hz, 2H), 8.19 (s, 1H), 12.66 (s amplio, 1H)
1-50	DMSO-d6, 300MHz	0.80 (t, J = 7.2 Hz, 6H), 1.02-1.17 (m, 4H), 1.38-1.56 (m, 4H), 2.41-2.49 (m, 1H), 2.88 (s, 3H), 4.70 (s, 2H), 5.08 (s, 2H), 6.94 (d, J = 8.8 Hz, 2H), 7.08 (d, J = 8.8 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.87 (d, J = 8.4 Hz, 2H), 7.98 (d, J = 8.8 Hz, 2H), 8.10 (s, 1H), 8.14 (d, J = 8.8 Hz, 2H), 13.38 (s amplio, 1H)
1-51	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 1.02-1.15 (m, 4H), 1.38-1.56 (m, 4H), 1.88-1.98 (m, 2H), 2.41 (t, J = 7.3 Hz, 2H), 2.45-2.49 (m, 1H), 2.92 (s, 3H), 3.25-3.28 (m, 2H), 4.72 (s, 2H), 5.09 (s, 2H), 6.94 (d, J = 8.8 Hz, 2H), 7.08 (d, J = 8.8 Hz, 2H), 7.52 (d, J = 8.4 Hz, 2H), 7.97 (d, J = 8.1 Hz, 2H), 8.13 (s, 1H), 12.17 (s amplio, 1H)
1-52	DMSO-d6, 400MHz	1.16-1.46 (m, 5H), 1.67-1.85 (m, 5H), 2.40-2.56 (m, 1H), 3.62 (s, 3H), 7.20 (d, J = 8.6 Hz, 2H), 7.58 (s, 1H), 7.68 (d, J = 8.6 Hz, 2H), 7.71 (d, J = 9.2 Hz, 2H), 7.95-8.05 (m, 6H), 10.14 (s, 1H), 12.75 (s amplio, 1H)
1-53	DMSO-d6, 400MHz	1.17-1.45 (m, 5H), 1.67-1.83 (m, 5H), 2.43-2.52 (m, 1H), 3.13 (s, 3H), 4.86 (s, 2H), 7.19 (d, J = 8.6 Hz, 2H), 7.39 (s, 1H), 7.46 (d, J = 8.6 Hz, 2H), 7.67 (d, J = 8.6 Hz, 2H), 7.94 (d, J = 8.6 Hz, 2H), 7.96 (d, J = 9.2 Hz, 2H), 7.99 (d, J = 9.2 Hz, 2H), 10.11 (s, 1H), 12.69 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-54	DMSO-d6, 300MHz	0.82 (t, J = 7.2 Hz, 6H), 1.01-1.21 (m, 4H), 1.41-1.63 (m, 4H), 3.39 (s, 2H), 3.89 (s, 2H), 4.22 (s, 2H), 7.14 (d, J = 8.6 Hz, 2H), 7.24-7.46 (m, 5H), 7.68 (d, J = 8.3 Hz, 2H), 8.02 (d, J = 8.7 Hz, 2H), 8.09 (d, J = 8.7 Hz, 2H), 8.23 (s, 1H), 10.19 (s, 1H), 12.42 (s amplio, 1H)
1-55	DMSO-d6, 300MHz	0.79 (t, J = 6.0 Hz, 6H), 1.04-1.12 (m, 4H), 1.45-1.56 (m, 4H), 2.43-2.48 (m, 1H), 3.38 (s, 2H), 3.88 (s, 2H), 4.21 (s, 2H), 4.47 (d,J = 6.0 Hz, 2H), 7.12 (d,J = 9.0 Hz, 2H), 7.23-7.45 (m, 8H), 7.97 (d,J = 9.0 Hz, 2H), 8.04 (d,J = 9.0 Hz, 2H), 8.19 (s, 1H), 9.03 (t, J = 6.0 Hz, 1H)
1-56	DMSO-d6, 300MHz	0.80 (t, J = 6.0 Hz, 6H), 1.06-1.18 (m, 4H), 1.47-1.54 (m, 4H), 2.88 (s, 3H), 3.37 (s, 2H), 3.88 (s, 2H), 4.20 (s, 2H), 4.50-4.64 (m, 2H), 7.17 (d,J = 9.0 Hz, 2H), 7.25-7.42 (m, 10H), 7.51 (d,J = 6.0 Hz, 2H), 8.00 (d,J = 6.0 Hz, 2H), 8.14 (s, 1H)
1-57	DMSO-d6, 300MHz	0.80 (t, J = 6.0 Hz, 6H), 0.93-1.24 (m, 10H), 1.40-1.67 (m, 4H), 3.37 (s, 2H), 3.88 (s, 2H), 4.20 (s, 2H), 4.48-4.65 (m, 1H), 7.15-7.49 (m, 12H), 8.00 (d,J = 6.0 Hz, 2H), 8.13 (s, 1H)
1-58	DMSO-d6, 300MHz	0.77 (t, J = 7.3 Hz, 6H), 1.00-1.10 (m, 4H), 1.19 (s, 6H), 1.33-1.48 (m, 4H), 2.27-2.37 (m, 1H), 3.40 (s, 2H), 4.45 (s amplio, 1H), 4.72 (s, 2H), 5.66 (s, 2H), 6.66 (d, J = 8.6 Hz, 2H), 6.84 (d, J = 8.8 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 7.87 (d, J = 8.3 Hz, 2H), 7.98-7.99 (m, 1H), 8.10 (s, 1H), 8.64 (d, J = 2.9 Hz, 1H), 8.73 (d, J = 1.4 Hz, 1H)
1-59	DMSO-d6, 400MHz	0.92 (d, J = 6.5 Hz, 6H), 1.19 (s, 9H), 2.05 (sept, J = 6.7 Hz, 1H), 3.19 (t, J = 4.5 Hz, 4H), 3.24 (d, J = 7.2 Hz, 2H), 3.57 (t, J = 4.5 Hz, 4H), 3.92 (s, 2H), 4.58 (s, 2H), 4.68 (s, 2H), 6.58 (d, J = 8.8 Hz, 2H), 7.10 (d, J = 9.0 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 7.84 (d, J = 8.1 Hz, 2H), 7.95 (s, 1H), 12.69 (s amplio, 1H).

Ejemplo	solvente, Hz	RMN (δ)
1-60	DMSO-d6, 300MHz	0.69 (t, J = 7.4 Hz, 6H), 1.16 (d, J = 6.8 Hz, 6H), 1.31-1.48 (m, 2H), 1.48-1.64 (m, 2H), 2.06-2.19 (m, 1H), 4.23 (sept, J = 6.6 Hz, 1H), 4.38 (s, 2H), 5.56 (s, 2H), 6.62 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 7.36 (d, J = 8.3 Hz, 2H), 7.80 (dd, J = 3.0, 1.5 Hz, 1H), 7.90 (d, J = 8.3 Hz, 2H), 8.08 (s, 1H), 8.31 (d, J = 3.0 Hz, 1H), 8.61 (d, J = 1.1 Hz, 1H).
1-61	DMSO-d6, 300MHz	0.79 (t, J = 9.0 Hz, 6H), 1.02-1.11 (m, 4H), 1.40-1.56 (m, 4H), 2.40-2.51 (m, 1H), 2.95-3.00 (m, 1H), 3.14-3.22 (m, 1H), 3.31-3.36 (m, 2H), 3.69 (d,J = 15.0 Hz, 1H), 4.28-4.42 (m, 3H), 5.07 (s, 2H), 6.91-7.08 (m, 8H), 7.49 (d,J = 9.0 Hz, 2H), 7.96 (d,J = 9.0 Hz, 2H), 7.97 (s, 1H)
1-62	DMSO-d6, 300MHz	0.80 (t, J = 7.2 Hz, 6H), 1.00-1.17 (m, 4H), 1.35-1.62 (m, 4H), 2.40-2.53 (m, 1H), 5.09 (s, 2H), 5.58 (s, 2H), 6.94 (d, J = 8.6 Hz, 2H), 7.08 (d, J = 9.0 Hz, 2H), 7.53 (d, J = 8.3 Hz, 2H), 7.80 (dd, J = 3.0, 1.5 Hz, 1H), 8.00 (d, J = 8.3 Hz, 2H), 8.18 (s, 1H), 8.32 (d, J = 3.0 Hz, 1H), 8.61 (d, J = 1.1 Hz, 1H).
1-63	DMSO-d6, 400MHz	0.68 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.5 Hz, 6H), 1.34-1.45 (m, 2H), 1.50-1.61 (m, 2H), 2.09-2.16 (m, 1H), 3.79 (s, 3H), 4.23 (sep, J = 6.5 Hz, 1H), 4.37 (s, 2H), 5.54 (s, 2H), 6.62 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 6.92 (t, J = 2.4 Hz, 1H), 7.10 (dd, J = 2.4, 1.2 Hz, 1H), 7.22 (dd, J = 2.4, 1.2 Hz, 1H), 7.35 (d, J = 8.6 Hz, 2H), 7.89 (d, J = 8.6 Hz, 2H), 8.08 (s, 1H), 13.03 (s amplio, 1H)
1-64	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.6 Hz, 6H), 1.32-1.47 (m, 2H), 1.49-1.63 (m, 2H), 2.08-2.17 (m, 1H), 4.05 (s, 2H), 4.22 (sep, J = 6.6 Hz, 1H), 4.37 (s, 2H), 4.87 (s, 2H), 6.62 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 6.93 (t,J = 7.3 Hz, 1H), 6.94 (t, J = 7.3 Hz, 2H), 7.34 (d,J = 8.4 Hz, 2H), 7.44 (d, J = 7.3 Hz, 2H), 7.87 (d, J = 8.4 Hz, 2H), 7.94 (s, 1H), 9.49 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-65	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.6 Hz, 6H), 1.32-1.47 (m, 2H), 1.49-1.63 (m, 2H), 2.08-2.18 (m, 1H), 2.22 (s, 3H), 4.19-4.28 (m, 3H), 4.37 (s, 2H), 4.89 (s, 2H), 6.62 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 7.04 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 7.87 (d, J = 8.4 Hz, 2H), 7.95 (s, 1H), 8.80 (s amplio, 1H), 12.70 (s amplio, 1H)
1-66	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 7.0 Hz, 12H), 1.33-1.47 (m, 2H), 1.49-1.63 (m, 2H), 2.06-2.17 (m, 1H), 2.80 (sep, J = 7.0 Hz, 1H), 4.04 (s, 2H), 4.22 (sep, J = 7.0 Hz, 1H), 4.37 (s, 2H), 4.86 (s, 2H), 6.62 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 7.09 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 4H), 7.87 (d, J = 8.4 Hz, 2H), 7.93 (s, 1H), 9.32 (s amplio, 1H)
1-67	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.6 Hz, 6H), 1.32-1.47 (m, 2H), 1.49-1.63 (m, 2H), 2.08-2.18 (m, 1H), 3.08 (s, 3H), 3.81 (s, 2H), 4.22 (sep, J = 6.6 Hz, 1H), 4.37 (s, 2H), 4.63 (s, 2H), 6.62 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.10-7.15 (m, 1H), 7.26-7.36 (m, 6H), 7.84 (d, J = 8.1 Hz, 2H), 7.93 (s, 1H), 12.42 (s amplio, 1H)
1-68	DMSO-d6, 400MHz	0.77 (t, J = 7.3 Hz, 6H), 1.02-1.11 (m, 4H), 1.16 (d, J = 6.5 Hz, 6H), 1.33-1.51 (m, 4H), 2.29-2.37 (m, 1H), 4.22 (sep,J = 6.5 Hz, 1H), 4.36 (s, 2H), 5.66 (s, 2H), 6.59 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 7.89 (d, J = 8.4 Hz, 4H), 7.98 (dd, J = 3.0, 1.6 Hz, 1H), 8.10 (s, 1H), 8.63 (d, J = 3.0 Hz, 1H), 8.71 (d, J = 1.6 Hz, 1H), 13.44 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-69	DMSO-d6, 300MHz	0.80 (t, J = 7.0 Hz, 6H), 0.98-1.18 (m, 4H), 1.36-1.60 (m, 4H), 2.39-2.54 (m, 1H), 4.18 (s, 2H), 4.91 (s, 2H), 5.09 (s, 2H), 6.94 (d, J = 8.7 Hz, 2H), 6.95 (t, J = 8.6 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.24 (t, J = 7.8 Hz, 2H), 7.46 (d, J = 7.5 Hz, 2H), 7.51 (d, J = 8.1 Hz, 2H), 7.97 (d, J = 8.1 Hz, 2H), 8.05 (s, 1H), 9.11 (s amplio, 1H)
1-70	DMSO-d6, 400MHz	0.68 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.6 Hz, 6H), 1.33-1.47 (m, 2H), 1.49-1.60 (m, 2H), 2.08-2.17 (m, 7H), 4.18-4.25 (m, 3H), 4.37 (s, 2H), 4.90 (s, 2H), 6.62 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.02 (s, 2H), 7.34 (d, J = 8.4 Hz, 2H), 7.86 (d, J = 8.4 Hz, 2H), 7.96 (s, 1H), 8.16 (s amplio, 1H), 12.70 (s amplio, 1H)
1-71	DMSO-d6, 400MHz	0.68 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.6 Hz, 6H), 1.33-1.47 (m, 2H), 1.49-1.63 (m, 2H), 2.08-2.18 (m, 1H), 3.44 (s amplio, 2H), 3.56 (s amplio, 2H), 4.21 (sep, J = 6.6 Hz, 1H), 4.22 (s, 2H), 4.36 (s, 2H), 6.61 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.01-7.04 (m, 1H), 7.23-7.31 (m, 4H), 7.61 (d, J = 8.4 Hz, 2H), 7.84 (d, J = 8.4 Hz, 2H), 7.94 (s, 1H), 10.94 (s amplio, 1H)
1-72	DMSO-d6, 300MHz	0.68 (t, J = 7.2 Hz, 6H), 1.16 (d, J = 6.3 Hz, 6H), 1.33 (d, J = 6.6 Hz, 6H), 1.37-1.65 (m, 4H), 2.06-2.21 (m, 1H), 3.50-3.70 (m, 1H), 4.06 (s, 2H), 4.14-4.29 (m, 1H), 4.37 (s, 2H), 4.84 (s, 2H), 6.62 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 7.8 Hz, 2H), 7.86 (d, J = 8.1 Hz, 2H), 8.01 (s, 1H), 12.22 (s amplio, 1H)
1-73	DMSO-d6, 400MHz	14.43 (s amplio, 1H), 8.12 (s, 1H), 7.88 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 7.07 (s, 1H), 6.87 (d, J = 8.8 Hz, 2H), 6.60 (d, J = 8.8 Hz, 2H), 5.66 (s, 2H), 4.37 (s, 2H), 4.17-4.27 (m, 1H), 2.27-2.39 (m, 1H), 1.32-1.52 (m, 4H), 1.16 (d, J = 6.4 Hz, 6H), 0.99-1.12 (m, 4H), 0.78 (t, J = 7.2 Hz, 6H)

Ejemplo	solvente, Hz	RMN (δ)
1-74	DMSO-d6, 300MHz	0.86 (t, J = 7.5 Hz, 6H), 1.12 (d, J = 6.8 Hz, 6H), 1.22-1.45 (m, 4H), 1.70 (sept, J = 6.0 Hz, 1H), 2.71 (sept, J = 6.8 Hz, 1H), 3.33 (s, 2H), 4.57 (s, 2H), 5.66 (s, 2H), 6.97 (d, J = 8.7 Hz, 2H), 7.26 (d, J = 8.3 Hz, 2H), 7.88 (d, J = 8.3 Hz, 2H), 7.98 (dd, J = 3.0, 1.5 Hz, 1H), 8.11 (s, 1H), 8.64 (d, J = 3.0 Hz, 1H), 8.72 (d, J = 1.9 Hz, 1H), 13.44 (s amplio, 1H).
1-75	DMSO-d6, 400MHz	0.68 (t, J = 7.4 Hz, 6H), 1.15 (d, J = 6.4 Hz, 6H), 1.32-1.66 (m, 10H), 2.06-2.16 (m, 1H), 2.92-2.98 (m, 2H), 3.07-3.18 (m, 2H), 3.31-3.48 (m, 1H), 3.72 (s, 1H), 4.01-4.09 (m, 1H), 4.16-4.27 (m, 1H), 4.36 (s, 2H), 4.62 (s, 1H), 6.60 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 7.6 Hz, 2H), 7.84 (d, J = 8.0 Hz, 2H), 7.91 (s, 1H)
1-76	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 0.99-1.18 (m, 4H), 1.35-1.61 (m, 4H), 2.40-2.55 (m, 1H), 5.09 (s, 2H), 5.79 (s, 2H), 6.94 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.18 (dd, J = 7.4, 5.1 Hz, 1H), 7.52 (d, J = 8.3 Hz, 2H), 7.99 (d, J = 8.3 Hz, 2H), 8.20 (dd, J = 7.3, 2.1 Hz, 1H), 8.40 (dd, J = 4.9, 1.9 Hz, 1H), 13.08 (s amplio, 1H).
1-77	DMSO-d6, 400MHz	0.68 (t, J = 7.4 Hz, 6H), 1.15 (d, J = 6.6 Hz, 6H), 1.34-1.45 (m, 2H), 1.49-1.63 (m, 2H), 2.08-2.15 (m, 1H), 2.22 (s, 3H), 3.41 (s amplio, 2H), 3.53 (s amplio, 2H), 4.18-4.23 (m, 3H), 4.35 (s, 2H), 6.60 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 7.06 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.4 Hz, 2H), 7.84 (d, J = 8.4 Hz, 2H), 7.93 (s, 1H), 10.91 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-78	DMSO-d6, 400MHz	0.68 (t, J = 7.3 Hz, 6H), 1.15 (d, J = 6.5 Hz, 6H), 1.16 (d, J = 6.5 Hz, 6H), 1.34-1.45 (m, 2H), 1.50-1.60 (m, 2H), 2.08-2.16 (m, 1H), 2.82 (sep, J = 6.5 Hz, 1H), 3.55 (s, 2H), 3.61 (s, 2H), 4.22 (sep, J = 6.5 Hz, 1H), 4.26 (s, 2H), 4.36 (s, 2H), 6.60 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 7.14 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 8.3 Hz, 2H), 7.49 (d, J = 8.3 Hz, 2H), 7.84 (d, J = 8.3 Hz, 2H), 7.95 (s, 1H), 10.01 (s amplio, 1H), 12.67 (s amplio, 1H)
1-79	DMSO-d6, 300MHz	0.77 (t, J = 7.3 Hz, 6H), 1.01-1.10 (m, 4H), 1.15 (d, J = 6.6 Hz, 6H), 1.34-1.50 (m, 4H), 2.28-2.38 (m, 1H), 3.08 (s, 3H), 3.67 (s, 2H), 4.22 (sep, J = 6.6 Hz, 1H), 4.36 (s, 2H), 4.66 (s, 2H), 6.61 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 7.06-7.11 (m, 1H), 7.25-7.35 (m, 6H), 7.84 (d, J = 8.1 Hz, 2H), 7.92 (s, 1H)
1-80	DMSO-d6, 300MHz	0.78 (t, J = 7.3 Hz, 6H), 1.01-1.11 (m, 4H), 1.16 (d, J = 6.6 Hz, 6H), 1.35-1.48 (m, 4H), 2.23 (s, 3H), 2.31-2.39 (m, 1H), 4.19-4.26 (m, 3H), 4.37 (s, 2H), 4.89 (s, 2H), 6.61 (d, J = 8.4 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 7.05 (d, J = 8.4 Hz, 2H), 7.33 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 7.87 (d, J = 8.1 Hz, 2H), 7.96 (s, 1H), 8.76 (s amplio, 1H), 12.71 (s amplio, 1H)
1-81	DMSO-d6, 400MHz	0.77 (t, J = 7.4 Hz, 6H), 0.99-1.11 (m, 4H), 1.15 (d, J = 6.4 Hz, 6H), 1.31-1.52 (m, 4H), 2.27-2.37 (m, 1H), 3.01 (t, J = 8.4 Hz, 2H), 3.86 (t, J = 8.2 Hz, 2H), 4.02 (s, 2H), 4.16-4.26 (m, 1H), 4.36 (s, 2H), 4.82 (s, 2H), 6.59 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 6.83-6.92 (m, 1H), 7.11 (t, J = 8.2 Hz, 1H), 7.19 (d, J = 7.6 Hz, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 8.4 Hz, 2H), 7.86 (d, J = 8.4 Hz, 2H), 7.97 (s, 1H), 13.03 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-82	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 0.99-1.19 (m, 4H), 1.37-1.60 (m, 4H), 2.40-2.53 (m, 1H), 5.09 (s, 2H), 5.63 (s, 2H), 6.94 (d, J = 8.7 Hz, 2H), 7.08 (d, J = 8.7 Hz, 2H), 7.53 (d, J = 8.3 Hz, 2H), 7.54 (dd, J = 8.5, 4.7 Hz, 1H), 7.80 (dd, J = 8.7, 1.1 Hz, 1H), 7.99 (d, J = 8.3 Hz, 2H), 8.19 (s, 1H), 8.23 (dd, J = 4.5, 1.1 Hz, 1H), 13.22 (s amplio, 1H).
1-83	DMSO-d6, 300MHz	0.86 (t, J = 7.3 Hz, 6H), 1.12 (d, J = 6.8 Hz, 6H), 1.23-1.44 (m, 4H), 1.70 (sept, J = 6.4 Hz, 1H), 2.71 (sept, J = 7.0 Hz, 1H), 3.30 (d, J = 7.0 Hz, 2H), 3.52-3.69 (m, 4H), 4.28 (s, 2H), 4.53 (s, 2H), 6.59 (d, J = 8.7 Hz, 2H), 6.97 (d, J = 8.7 Hz, 2H), 7.04 (t, J = 7.4 Hz, 1H), 7.22 (d, J = 8.3 Hz, 2H), 7.29 (t, J = 7.9 Hz, 2H), 7.59 (d, J = 7.5 Hz, 2H), 7.84 (d, J = 7.9 Hz, 2H), 7.96 (s, 1H), 10.05 (s amplio, 1H), 12.54 (s amplio, 1H).
1-84	DMSO-d6, 300MHz	0.86 (t, J = 7.4 Hz, 6H), 1.12 (d, J = 6.8 Hz, 6H), 1.17 (d, J = 6.8 Hz, 6H), 1.26-1.44 (m, 4H), 1.63-1.75 (m, 1H), 2.71 (sept, J = 7.0 Hz, 1H), 2.83 (sept, J = 7.0 Hz, 1H), 3.30 (d, J = 7.0 Hz, 2H), 3.50-3.70 (m, 4H), 4.27 (s, 2H), 4.55 (s, 2H), 6.59 (d, J = 8.7 Hz, 2H), 6.97 (d, J = 8.6 Hz, 2H), 7.15 (d, J = 8.3 Hz, 2H), 7.22 (d, J = 8.3 Hz, 2H), 7.49 (d, J = 8.7 Hz, 2H), 7.84 (d, J = 7.9 Hz, 2H), 7.97 (s, 1H), 9.93 (s amplio, 1H), 12.55 (s amplio, 1H).
1-85	DMSO-d6, 300MHz	0.86 (t, J = 7.4 Hz, 6H), 1.12 (d, J = 6.8 Hz, 6H), 1.22-1.45 (m, 4H), 1.69 (sept, J = 6.6 Hz, 1H), 2.71 (sept, J = 7.0 Hz, 1H), 3.30 (d, J = 6.8 Hz, 2H), 3.60-3.69 (m, 4H), 4.28 (s, 2H), 6.59 (d, J = 8.7 Hz, 2H), 6.97 (d, J = 8.6 Hz, 2H), 7.22 (d, J = 8.3 Hz, 2H), 7.70 (d, J = 9.0 Hz, 2H), 7.83 (d, J = 8.3 Hz, 2H), 7.88 (d, J = 8.7 Hz, 2H), 7.95 (s, 1H), 10.33 (s, 1H), 12.66 (s amplio, 2H).

Ejemplo	solvente, Hz	RMN (δ)
1-86	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 0.98-1.18 (m, 4H), 1.36-1.61 (m, 4H), 2.40-2.53 (m, 1H), 5.09 (s, 2H), 5.81 (s, 2H), 6.94 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.22 (d, J = 7.5 Hz, 1H), 7.52 (d, J = 8.3 Hz, 2H), 7.75 (d, J = 7.5 Hz, 1H), 7.96 (dd, J = 8.1, 7.3 Hz, 1H), 7.99 (d, J = 8.3 Hz, 2H), 8.15 (s, 1H), 13.17 (s amplio, 1H).
1-87	DMSO-d6, 300MHz	0.78 (t, J = 7.2 Hz, 6H), 0.92 (d, J = 6.6 Hz, 6H), 1.01-1.14 (m, 4H), 1.33-1.56 (m, 4H), 1.98-2.10 (m, 1H), 2.27-2.40 (m, 1H), 3.24 (d, J = 7.2 Hz, 2H), 4.58 (s, 2H), 5.55 (s, 2H), 6.60 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 7.78 (dd, J = 3.0, 1.5 Hz, 1H), 7.89 (d, J = 8.1 Hz, 2H), 8.09 (s, 1H), 8.30 (d, J = 3.3 Hz, 1H), 8.60 (d, J = 0.9 Hz, 1H)
1-88	DMSO-d6, 300MHz	0.78 (t, J = 7.2 Hz, 6H), 0.92 (d, J = 6.9 Hz, 6H), 1.00-1.16 (m, 4H), 1.32-1.50 (m, 4H), 1.97-2.11 (m, 1H), 2.25-2.39 (m, 1H), 3.23 (d, J = 7.2 Hz, 2H), 3.97 (s amplio, 2H), 4.57 (s, 2H), 4.84 (s, 2H), 6.59 (d, J = 9.3 Hz, 2H), 6.86-6.97 (m, 3H), 7.20-7.28 (m, 4H), 7.42 (d, J = 8.4 Hz, 2H), 7.86 (d, J = 7.8 Hz, 2H), 7.95 (s, 1H)
1-89	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.8 Hz, 6H), 1.35-1.63 (m, 4H), 2.08-2.18 (m, 1H), 3.89 (s, 3H), 4.19-4.28 (m, 1H), 4.38 (s, 2H), 5.68 (s, 2H), 6.62 (d, J = 9.0 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 7.36 (d, J = 8.3 Hz, 2H), 7.90 (d, J = 8.3 Hz, 2H), 8.02-8.04 (m, 1H), 8.11 (s, 1H), 8.68 (d, J = 2.6 Hz, 1H), 8.74 (d, J = 1.9 Hz, 1H)
1-90	DMSO-d6, 300MHz	0.69 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.5 Hz, 6H), 1.25-1.65 (m, 4H), 2.05-2.20 (m, 1H), 4.15-4.30 (m, 1H), 4.38 (s, 2H), 5.49 (s, 2H), 5.62 (s, 2H), 6.62 (d, J = 8.7 Hz, 2H), 6.68 (d, J = 8.2 Hz, 1H), 6.89 (d, J = 8.7 Hz, 2H), 7.35-7.45 (m, 3H), 7.51 (s amplio, 1H), 7.90 (d, J = 8.2 Hz, 2H), 8.08 (s, 1H).

Ejemplo	solvente, Hz	RMN (δ)
1-91	DMSO-d6, 300MHz	0.69 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.6 Hz, 6H), 1.30-1.65 (m, 4H), 2.05-2.20 (m, 1H), 4.15-4.30 (m, 1H), 4.38 (s, 2H), 5.56 (s, 2H), 6.62 (d, J = 8.3 Hz, 2H), 6.68 (d, J = 8.3 Hz, 2H), 7.30-7.40 (m, 3H), 7.45 (t, J = 7.7 Hz, 1H), 7.58 (d, J = 7.7 Hz, 1H), 7.62 (s amplio, 1H), 7.90 (d, J = 8.7 Hz, 2H), 8.08 (s, 1H).
1-92	DMSO-d6, 300MHz	0.69 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.6 Hz, 6H), 1.30-1.65 (m, 4H), 2.05-2.20 (m, 1H), 4.15-4.30 (m, 1H), 4.37 (s, 2H), 4.65 (d, J = 6.0 Hz, 2H), 6.62 (d, J = 8.7 Hz, 2H), 6.70-7.00 (m, 4H), 7.20-7.30 (m, 3H), 7.34 (d, J = 8.4 Hz, 2H), 7.80-7.90 (m, 3H), 12.66 (s amplio, 1H).
1-93	DMSO-d6, 400MHz	0.68 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.5 Hz, 6H), 1.35-1.65 (m, 4H), 2.10-2.20 (m, 1H), 4.20-4.30 (m, 1H), 4.37 (s, 2H), 5.78 (s, 2H), 6.61 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 7.69 (dd, J = 8.3, 1.5 Hz, 1H), 7.89 (d, J = 8.4 Hz, 2H), 8.01 (d, J = 8.3 Hz, 1H), 8.05 (d, J = 1.5 Hz, 1H), 8.10 (s, 1H).
1-94	DMSO-d6, 300MHz	0.77 (t, J = 7.3 Hz, 6H), 0.98-1.21 (m, 10H), 1.31-1.54 (m, 4H), 2.25-2.41 (m, 1H), 3.61 (s, 2H), 4.14-4.43 (m, 7H), 6.60 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 7.17-7.26 (m, 2H), 7.32 (d, J = 8.3 Hz, 2H), 7.52-7.61 (m, 2H), 7.83 (d, J = 8.3 Hz, 2H), 7.94 (s, 1H)
1-95	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.99-1.18 (m, 4H), 1.35-1.61 (m, 4H), 2.40-2.54 (m, 1H), 3.60 (s, 2H), 3.66 (s, 2H), 4.30 (s, 2H), 5.08 (s, 2H), 6.93 (d, J = 9.0 Hz, 2H), 7.05 (t, J = 7.3 Hz, 1H), 7.07 (d, J = 8.7 Hz, 2H), 7.30 (t, J = 7.9 Hz, 2H), 7.49 (d, J = 8.3 Hz, 2H), 7.60 (d, J = 7.6 Hz, 2H), 7.95 (d, J = 8.7 Hz, 2H), 8.06 (s, 1H), 10.01 (s, 1H), 12.65 (s amplio, 1H).

Ejemplo	solvente, Hz	RMN (δ)
1-96	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 0.96-1.16 (m, 4H), 1.36-1.59 (m, 4H), 2.38-2.54 (m, 1H), 3.66 (s, 2H), 3.67 (s, 2H), 4.31 (s, 2H), 5.08 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.34 (dd, J = 8.3, 4.5 Hz, 1H), 7.49 (d, J = 8.3 Hz, 2H), 7.95 (d, J = 8.3 Hz, 2H), 8.05 (ddd, J = 8.5, 2.4, 1.5 Hz, 1H), 8.05 (s, 1H), 8.26 (dd, J = 4.9, 1.5 Hz, 1H), 8.73 (d, J = 2.6 Hz, 1H), 10.20 (s, 1H), 12.63 (s amplio, 1H).
1-97	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.99-1.17 (m, 4H), 1.37-1.60 (m, 4H), 2.39-2.52 (m, 1H), 2.84 (s, 6H), 3.54 (s, 2H), 3.64 (s, 2H), 4.28 (s, 2H), 5.08 (s, 2H), 6.69 (d, J = 9.1 Hz, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.6 Hz, 2H), 7.41 (d, J = 9.0 Hz, 2H), 7.49 (d, J = 8.3 Hz, 2H), 7.95 (d, J = 8.3 Hz, 2H), 8.06 (s, 1H), 9.70 (s, 1H), 12.63 (s amplio, 1H).
1-98	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.99-1.16 (m, 4H), 1.36-1.60 (m, 4H), 2.39-2.52 (m, 1H), 3.57 (s, 2H), 3.65 (s, 2H), 3.72 (s, 3H), 4.29 (s, 2H), 5.08 (s, 2H), 6.88 (d, J = 9.0 Hz, 2H), 6.93 (d, J = 8.6 Hz, 2H), 7.07 (d, J = 8.6 Hz, 2H), 7.49 (d, J = 8.3 Hz, 2H), 7.51 (d, J = 9.1 Hz, 2H), 7.95 (d, J = 8.3 Hz, 2H), 8.06 (s, 1H), 9.86 (s, 1H), 12.63 (s amplio, 1H).
1-99	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.96 (d, J = 6.8 Hz, 6H), 1.00-1.14 (m, 4H), 1.36-1.58 (m, 4H), 2.38-2.53 (m, 1H), 3.16 (s, 2H), 3.53 (s, 2H), 4.17 (s, 2H), 4.83 (t, J = 6.4 Hz, 1H), 5.09 (s, 2H), 6.94 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.10-7.16 (m, 2H), 7.33-7.40 (m, 3H), 7.51 (d, J = 8.3 Hz, 2H), 7.93 (d, J = 8.3 Hz, 2H), 8.01 (s, 1H), 12.44 (s amplio, 1H).

Ejemplo	solvente, Hz	RMN (δ)
1-100	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.98-1.16 (m, 4H), 1.36-1.61 (m, 4H), 2.40-2.54 (m, 1H), 3.64 (s, 4H), 4.30 (s, 2H), 5.08 (s, 2H), 6.93 (d, J = 8.3 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.11 (ddd, J = 7.2, 4.8, 1.0 Hz, 1H), 7.49 (d, J = 8.3 Hz, 2H), 7.78 (ddd, J = 8.4, 7.2, 1.0 Hz, 1H), 7.97 (d, J = 7.9 Hz, 2H), 8.06 (s, 1H), 8.09 (d, J = 8.3 Hz, 1H), 8.31 (ddd, J = 4.9, 1.9, 0.7 Hz, 1H), 10.22 (s, 1H), 12.61 (s amplio, 1H).
1-101	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.99-1.17 (m, 4H), 1.35-1.60 (m, 4H), 1.71-1.93 (m, 4H), 2.40-2.54 (m, 1H), 3.11-3.51 (m, 6H), 3.78 (s amplio, 2H), 4.28 (s amplio, 2H), 5.09 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.53 (d, J = 7.9 Hz, 2H), 8.01 (d, J = 7.9 Hz, 2H), 8.19 (s, 1H).
1-102	DMSO-d6, 400MHz	0.79 (t, J = 7.4 Hz, 6H), 0.99-1.14 (m, 4H), 1.37-1.59 (m, 4H), 2.32 (s, 3H), 2.40-2.49 (m, 1H), 3.50 (s, 2H), 4.21 (s, 2H), 4.28 (s, 2H), 5.07 (s, 2H), 6.92 (d, J = 8.8 Hz, 2H), 7.06 (d, J = 8.4 Hz, 2H), 7.20 (s amplio, 1H), 7.49 (d, J = 8.4 Hz, 2H), 7.94 (d, J = 8.4 Hz, 2H), 8.06 (s, 1H), 12.57 (s amplio, 1H),
1-103	DMSO-d6, 300MHz	0.77 (t, J = 7.3 Hz, 6H), 0.88-1.17 (m, 15H), 1.32-1.51 (m, 4H), 1.56-1.72 (m, 5H), 2.28-2.39 (m, 1H), 3.38 (d, J = 7.3 Hz, 2H), 4.22 (sep, J = 6.6 Hz, 1H), 4.36 (s, 2H), 4.90 (s, 2H), 6.61 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 7.60 (d, J = 8.4 Hz, 2H), 7.82-7.87 (m, 4H), 7.94 (s, 1H), 8.88 (s amplio, 1H), 12.54 (s amplio, 1H)
1-104	DMSO(NaOD)-d6, 400MHz	0.77 (t, J = 7.3 Hz, 6H), 0.77 (d, J = 6.7 Hz, 6H), 1.02-1.11 (m, 4H), 1.14 (d, J = 6.5 Hz, 6H), 1.34-1.50 (m, 4H), 1.94-2.01 (m, 1H), 2.29-2.37 (m, 1H), 3.31-3.38 (m, 2H), 4.21 (sep, J = 6.5 Hz, 1H), 4.36 (s, 2H), 4.88 (s, 2H), 6.59 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H), 7.75 (d, J = 8.4 Hz, 2H), 7.86 (d, J = 8.4 Hz, 2H), 7.93 (s, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-105	DMSO-d6, 300MHz	0.78 (t, J = 7.1 Hz, 6H), 0.92 (d, J = 6.3 Hz, 6H), 1.00-1.13 (m, 4H), 1.31-1.55 (m, 4H), 1.96-2.10 (m, 1H), 2.26-2.39 (m, 1H), 3.08 (s, 3H), 3.23 (d, J = 7.5 Hz, 2H), 3.78 (s, 2H), 4.57 (s, 2H), 4.63 (s, 2H), 6.59 (d, J = 9.0 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 7.09-7.14 (m, 1H), 7.24-7.36 (m, 6H), 7.83 (d, J = 8.1 Hz, 2H), 7.93 (s, 1H)
1-106	DMSO-d6, 400MHz	0.78 (t, J = 7.4 Hz, 6H), 0.92 (d, J = 6.4 Hz, 6H), 1.02-1.12 (m, 4H), 1.34-1.51 (m, 4H), 2.00-2.07 (m, 1H), 2.30-2.36 (m, 1H), 3.22 (d, J = 6.4 Hz, 2H), 3.42 (s amplio, 2H), 3.51 (s, 2H), 4.22 (s, 2H), 4.56 (s, 2H), 6.57 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 8.4 Hz, 2H), 6.99-7.04 (m, 1H), 7.22 (d, J = 8.0 Hz, 2H), 7.26 (dd, J = 8.8, 7.2 Hz, 2H), 7.65 (d, J = 8.8 Hz, 2H), 7.82 (d, J = 8.8 Hz, 2H), 7.93 (s, 1H)
1-107	DMSO-d6, 400MHz	0.78 (t, J = 7.2 Hz, 6H), 0.92 (d, J = 6.4 Hz, 6H), 1.01-1.12 (m, 4H), 1.17 (d, J = 6.8 Hz, 6H), 1.33-1.51 (m, 4H), 1.98-2.09 (m, 1H), 2.28-2.37 (m, 1H), 2.82 (c, J = 9.2 Hz, 1H), 3.22 (d, J = 7.6 Hz, 2H), 3.54 (s, 2H), 3.59 (s, 2H), 4.25 (s, 2H), 4.56 (s, 2H), 6.57 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 8.4 Hz, 2H), 7.14 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.49 (d, J = 8.8 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H), 7.95 (s, 1H)
1-108	DMSO-d6, 300MHz	0.78 (t, J = 7.4 Hz, 6H), 0.98-1.14 (m, 4H), 1.16 (d, J = 6.4 Hz, 6H), 1.30-1.55 (m, 4H), 2.15 (s, 3H), 2.25-2.40 (m, 1H), 4.15-4.30 (m, 1H), 4.37 (s, 2H), 5.64 (s, 2H), 6.61 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H), 7.57 (dd, J = 8.6, 1.9 Hz, 1H), 7.78 (d, J = 1.9 Hz, 1H), 7.91 (d, J = 8.1 Hz, 2H), 8.09 (s, 1H), 8.14 (d, J = 8.6 Hz, 1H), 9.43 (s, 1H), 12.72 (s amplio, 1H).

Ejemplo	solvente, Hz	RMN (δ)
1-109	DMSO-d6, 300MHz	0.78 (t, J = 7.3 Hz, 6H), 1.00-1.15 (m, 4H), 1.16 (d, J = 6.4 Hz, 6H), 1.30-1.53 (m, 4H), 2.30 (s, 6H), 2.25-2.40 (m, 1H), 3.14 (s, 2H), 4.15-4.30 (m, 1H), 4.37 (s, 2H), 5.67 (s, 2H), 6.61 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 7.36 (d, J = 8.5 Hz, 2H), 7.65 (dd, J = 8.5, 1.5 Hz, 1H), 7.78 (d, J = 1.5 Hz, 1H), 7.91 (d, J = 8.5 Hz, 2H), 8.14 (s, 1H), 8.41 (d, J = 8.5 Hz, 1H), 10.00 (s, 1H), 12.81 (s amplio, 1H).
1-110	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.4 Hz, 6H), 1.31-1.48 (m, 2H), 1.49-1.64 (m, 2H), 2.06-2.19 (m, 1H), 3.58 (s, 2H), 4.15-4.40 (m, 7H), 6.62 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 7.14-7.22 (m, 2H), 7.33 (d, J = 8.3 Hz, 2H), 7.50-7.58 (m, 2H), 7.84 (d, J = 8.3 Hz, 2H), 7.95 (s, 1H)
1-111	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.97-1.18 (m, 4H), 1.36-1.61 (m, 4H), 2.39-2.54 (m, 1H), 3.59 (s, 2H), 4.20 (s, 2H), 4.33 (s, 2H), 5.08 (s, 2H), 6.93 (d, J = 8.6 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.12-7.21 (m, 2H), 7.44-7.58 (m, 4H), 7.95 (d, J = 8.3 Hz, 2H), 8.05 (s, 1H)
1-112	DMSO-d6, 300MHz	0.78 (t, J = 7.4 Hz, 6H), 1.00-1.15 (m, 4H), 1.16 (d, J = 6.4 Hz, 6H), 1.30-1.55 (m, 4H), 2.25-2.40 (m, 1H), 3.08 (s, 3H), 4.15-4.30 (m, 1H), 4.37 (s, 2H), 5.62 (s, 2H), 6.61 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 7.36 (d, J = 8.3 Hz, 2H), 7.45 (d, J = 8.3 Hz, 1H), 7.60 (dd, J = 8.3, 1.9 Hz, 1H), 7.81 (d, J = 1.9 Hz, 1H), 7.91 (d, J = 8.3 Hz, 2H)8.10 (s, 1H), 9.33 (s amplio, 1H), 12.91 (s amplio, 1H).

Ejemplo	solvente, Hz	RMN (δ)
1-113	DMSO-d6, 300MHz	0.78 (t, J = 7.4 Hz, 6H), 0.98-1.15 (m, 1H), 1.11 (d, J = 6.8 Hz, 6H), 1.16 (d, J = 6.4 Hz, 6H), 1.30-1.55 (m, 1H), 2.25-2.40 (m, 1H), 2.75-2.90 (m, 1H), 4.15-4.30 (m, 1H), 4.37 (s, 2H), 5.63 (s, 2H), 6.61 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.7 Hz, 2H), 7.36 (d, J = 8.3 Hz, 2H), 7.59 (dd, J = 8.4, 1.5 Hz, 1H), 7.78 (d, J = 1.5 Hz, 1H), 7.90 (d, J = 8.3 Hz, 2H), 8.09 (s, 1H), 8.13 (d, J = 8.4 Hz, 1H), 9.24 (s, 1H), 12.77 (s amplio, 1H).
1-114	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.4 Hz, 6H), 1.32-1.46 (m, 2H), 1.48-1.63 (m, 2H), 2.05-2.21 (m, 1H), 4.23 (sept, J = 6.8 Hz, 1H), 4.37 (s, 2H), 4.88 (s, 2H), 5.47 (s, 2H), 6.61 (d, J = 9.1 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 7.12 (d, J = 8.3 Hz, 1H), 7.34 (d, J = 8.3 Hz, 2H), 7.62 (dd, J = 8.3, 1.9 Hz, 1H), 7.92 (d, J = 8.3 Hz, 2H), 8.01 (s, 1H), 8.18 (d, J = 1.9 Hz, 1H), 12.84 (s amplio, 1H).
1-115	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6H), 1.15 (d, J = 6.4 Hz, 6H), 1.32-1.47 (m, 2H), 1.48-1.64 (m, 2H), 2.07-2.18 (m, 1H), 4.22 (sept, J = 6.6 Hz, 1H), 4.37 (s, 2H), 4.84 (s, 2H), 5.49 (s, 2H), 6.61 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 7.10 (t, J = 8.1 Hz, 1H), 7.34 (d, J = 8.3 Hz, 2H), 7.38 (dd, J = 7.9, 1.5 Hz, 1H), 7.52 (dd, J = 8.1, 1.3 Hz, 1H), 7.85 (d, J = 8.3 Hz, 2H), 7.99 (s, 1H), 12.91 (s amplio, 1H).
1-116	DMSO-d6, 300MHz	0.77 (t, J = 7.3 Hz, 6H), 1.01-1.10 (m, 4H), 1.16 (d, J = 6.6 Hz, 6H), 1.32-1.50 (m, 4H), 2.29-2.38 (m, 1H), 3.17 (s, 3H), 4.02 (s, 2H), 4.18-4.26 (m, 1H), 4.37 (s, 2H), 4.80 (s, 2H), 6.61 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.25-7.43 (m, 7H), 7.87 (d, J = 8.4 Hz, 2H), 8.02 (s, 1H), 12.96 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-117	DMSO-d6, 300MHz	0.77 (t, J = 7.3 Hz, 6H), 1.00-1.14 (m, 4H), 1.15 (d, J = 6.6 Hz, 6H), 1.16 (d, J = 6.6 Hz, 6H), 1.32-1.52 (m, 4H), 2.27-2.39 (m, 1H), 2.82 (sep, J = 6.6 Hz, 1H), 3.51 (s amplio, 2H), 3.55 (s amplio, 2H), 4.17-4.28 (m, 3H), 4.36 (s, 2H), 6.60 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.15 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.52 (d, J = 8.4 Hz, 2H), 7.85 (d, J = 8.4 Hz, 2H), 7.95 (s, 1H)
1-118	DMSO-d6, 400MHz	0.78 (t, J = 7.3 Hz, 6H), 1.02-1.12 (m, 4H), 1.15 (d, J = 6.5 Hz, 6H), 1.34-1.51 (m, 4H), 2.18 (s, 6H), 2.30-2.37 (m, 1H), 3.54 (s, 2H), 3.60 (s, 2H), 4.21 (sep, J = 6.5 Hz, 1H), 4.25 (s, 2H), 4.35 (s, 2H), 6.59 (d, J = 8.6 Hz, 2H), 6.66 (s, 1H), 6.87 (d, J = 8.6 Hz, 2H), 7.20 (s, 2H), 7.31 (d, J = 8.1 Hz, 2H), 7.84 (d, J = 8.1 Hz, 2H), 7.95 (s, 1H), 9.97 (s amplio, 1H), 12.70 (s amplio, 1H)
1-119	DMSO-d6, 400MHz	0.77 (t, J = 7.3 Hz, 6H), 1.02-1.11 (m, 4H), 1.15 (d, J = 6.5 Hz, 6H), 1.30-1.50 (m, 4H), 2.29-2.37 (m, 1H), 2.83 (s, 6H), 3.44 (s, 2H), 3.52 (s, 2H), 3.62 (s, 2H), 4.21 (sep, J = 6.5 Hz, 1H), 4.25 (s, 2H), 4.35 (s, 2H), 6.59 (d, J = 8.6 Hz, 2H), 6.66 (d, J = 9.0 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 9.0 Hz, 2H), 7.84 (d, J = 8.4 Hz, 2H), 7.95 (s, 1H), 9.68 (s, 1H), 12.61 (s amplio, 1H)
1-120	DMSO-d6, 400MHz	0.77 (t, J = 7.3 Hz, 6H), 1.02-1.11 (m, 4H), 1.15 (d, J = 6.5 Hz, 6H), 1.34-1.51 (m, 4H), 2.29-2.37 (m, 1H), 3.44 (s, 2H), 3.54 (s, 2H), 4.18-4.25 (m, 3H), 4.31 (d, J = 6.0 Hz, 2H), 4.35 (s, 2H), 6.59 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 7.17-7.28 (m, 5H), 7.31 (d, J = 8.4 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H), 7.94 (s, 1H), 8.40 (t, J = 6.0 Hz, 1H), 12.59 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-121	DMSO-d6, 400MHz	0.77 (t, J = 7.3 Hz, 6H), 1.02-1.11 (m, 4H), 1.15 (d, J = 6.5 Hz, 6H), 1.34-1.50 (m, 4H), 2.29-2.37 (m, 1H), 3.29-3.58 (m, 10H), 3.67 (s, 2H), 4.19 (s, 2H), 4.21 (sep, J = 6.5 Hz, 1H), 4.35 (s, 2H), 6.59 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.84 (d, J = 8.4 Hz, 2H), 7.94 (s, 1H), 12.54 (s amplio, 1H)
1-122	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.4 Hz, 6H), 1.32-1.61 (m, 4H), 2.05-2.17 (m, 1H), 3.13 (t, J = 5.8 Hz, 2H), 3.55 (s, 2H), 4.09 (t, J = 5.8 Hz, 2H), 4.17-4.30 (m, 3H), 4.36 (s, 2H), 6.62 (d, J = 8.6 Hz, 2H), 6.87-6.93 (m, 5H), 7.25 (t, J = 7.9 Hz, 2H), 7.33 (d, J = 8.6 Hz, 2H), 7.85 (d, J = 8.3 Hz, 2H), 7.92 (s, 1H)
1-123	DMSO-d6, 300MHz	0.67 (t, J = 7.4 Hz, 6H), 1.14 (d, J = 6.4 Hz, 6H), 1.31-1.62 (m, 4H), 2.05-2.18 (m, 1H), 2.90 (t, J = 6.4 Hz, 2H), 3.13 (t, J = 6.4 Hz, 2H), 3.32 (s, 2H), 4.15-4.28 (m, 3H), 4.34 (s, 2H), 6.47-6.73 (m, 5H), 6.87 (d, J = 8.6 Hz, 2H), 7.05 (t, J = 7.9 Hz, 2H), 7.31 (d, J = 8.3 Hz, 2H), 7.83 (d, J = 7.9 Hz, 2H), 7.91 (s, 1H)
1-124	DMSO-d6, 300MHz	0.69 (t, J = 7.17 Hz, 6H), 1.16 (d, J = 6.39 Hz, 6H), 1.33-1.45 (m, 2H), 1.48-1.62 (m, 2H), 2.08-2.18 (m, 1H), 3.04 (s, 3H), 4.23 (quint, J = 6.39 Hz, 1H), 4.37 (s, 2H), 4.63 (s, 2H), 4.84 (s, 2H), 6.63 (d, J = 8.67 Hz, 2H), 6.89 (d, J = 8.67 Hz, 2H), 6.94 (d, J = 9.78 Hz, 1H), 6.99 (dd, J = 9.78, 2.64 Hz, 1H), 7.12 (d, J = 2.64 Hz, 1H), 7.34 (d, J = 8.28 Hz, 2H), 7.87 (d, J = 8.28 Hz, 2H), 7.90 (s, 1H)
1-125	DMSO-d6, 300MHz	0.80 (t, J = 7.15 Hz, 3H), 0.98-1.14 (m, 4H), 1.41-1.57 (m, 4H), 2.31-2.41 (m, 1H), 3.05 (s, 3H), 4.64 (s, 2H), 4.86 (s, 2H), 5.08 (s, 2H), 6.92-6.97 (m, 4H), 7.06-7.12 (m, 2H), 7.51 (d, J = 8.24 Hz, 2H), 7.97 (d, J = 8.24 Hz, 2H), 7.99 (s, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-126	DMSO-d6, 300MHz	1HRMN(DMSO-d6, 300MHz)δ.78 (t, J = 7.2 Hz, 6H).95-1.15 (m, 4H), 1.16 (d, J = 6.8 Hz, 6H), 1.30-1.55 (m, 4H), 2.30-2.40 (m, 1H), 2.34 (s, 3H), 3.27 (s, 2H), 4.15-4.30 (m, 1H), 4.37 (s, 2H), 5.67 (s, 2H), 6.61 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 8.5 Hz, 2H), 7.36 (d, J = 8.3 Hz, 2H), 7.63 (dd, J = 8.5, 1.5 Hz, 1H), 7.78 (d, J = 1.5 Hz, 1H), 7.91 (d, J = 8.3 Hz, 2H), 8.12 (s, 1H), 8.43 (d, J = 8.5 Hz, 1H).
1-127	DMSO-d6, 400MHz	0.79 (t, J = 7.2 Hz, 6H), 1.01-1.14 (m, 4H), 1.26 (s, 9H), 1.37-1.57 (m, 4H), 2.41-2.49 (m, 1H), 3.42 (s, 2H), 4.22 (s, 2H), 4.28 (s, 2H), 5.07 (s, 2H), 6.92 (d, J = 8.8 Hz, 2H), 7.06 (d, J = 8.8 Hz, 2H), 7.16 (s, 1H), 7.48 (d, J = 8.0 Hz, 2H), 7.94 (d, J = 8.4 Hz, 2H), 8.04 (s, 1H)
1-128	DMSO-d6, 400MHz	0.80 (t, J = 7.4 Hz, 6H), 1.00-1.17 (m, 4H), 1.38-1.57 (m, 4H), 2.41-2.52 (m, 1H), 4.28 (s, 2H), 4.92 (s, 2H), 5.08 (s, 2H), 6.65-6.72 (m, 1H), 6.68 (d, J = 8.0 Hz, 2H), 6.93 (d, J = 8.8 Hz, 2H), 7.06 (d, J = 8.4 Hz, 2H), 7.16 (dd, J = 7.2, 7.2 Hz, 2H), 7.51 (d, J = 8.4 Hz, 2H), 7.97 (d, J = 8.0 Hz, 2H), 7.99 (s, 1H), 12.74 (s amplio, 1H)
1-129	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.95-1.20 (m, 4H), 1.35-1.60 (m, 4H), 2.40-2.53 (m, 1H), 4.10 (s, 2 Hx0.4), 4.37 (s, 2Hx0.6), 4.80-5.12 (m, 6H), 6.85-6.98 (m, 5H), 7.07 (d, J = 8.6 Hz, 2Hx0.6), 7.04-7.31 (m, 2H), 7.15-7.31 (m, 2H), 7.51 (d, J = 7.9 Hz, 2Hx0.4), 7.96 (d, J = 8.3 Hz, 2Hx0.6), 7.97 (d, J = 7.9 Hz, 2Hx0.4), 8.06 (s, 1Hx0.6), 8.13 (s, 1Hx0.4), 12.73 (s amplio, 1Hx0.4), 13.07 (s amplio, 1Hx0.6).

Ejemplo	solvente, Hz	RMN (δ)
1-130	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.95-1.20 (m, 4H), 1.35-1.60 (m, 4H), 2.19 (s, 3 Hx0.4), 2.22 (s, 3 Hx0.6), 2.40-2.53 (m, 1H), 4.10 (s, 2 Hx0.4), 4.36 (s, 2 Hx0.6), 4.78 (s, 2 Hx0.6), 4.84 (s, 2 Hx0.6), 5.03 (s, 2 Hx0.4), 5.05 (s, 2 Hx0.4), 5.09 (s, 2H), 6.75-7.10 (m, 8H), 7.51 (d, J = 8.3 Hz, 2H), 7.96 (d, J = 8.3 Hz, 2H), 8.06 (s, 1Hx0.6), 8.12 (s, 1Hx0.4), 12.73 (s amplio, 1Hx0.4), 13.05 (s amplio, 1Hx0.6).
1-131	DMSO-d6, 400MHz	0.61-0.69 (m, 6H), 0.74-0.97 (m, 4H), 1.18 (d, J = 6.3 Hz, 3H), 1.30-1.50 (m, 4H), 1.63 (d, J = 6.0 Hz, 3H), 2.39-2.48 (m, 1H), 3.56 (s, 2H), 3.65 (s, 2H), 4.03-4.14 (m, 3H), 4.21 (s, 2H), 4.60-4.68 (m, 1H), 4.96-5.02 (m, 1H), 7.14 (d, J = 8.1 Hz, 2H), 7.39 (d, J = 8.1 Hz, 2H), 7.55 (d, J = 8.1 Hz, 2H), 7.67 (d, J = 8.1 Hz, 2H), 7.99 (s, 1H), 12.63 (s amplio, 1H)
1-132	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.6 Hz, 6H), 1.26 (s, 9H), 1.32-1.47 (m, 2H), 1.49-1.63 (m, 2H), 2.08-2.17 (m, 1H), 3.45 (s, 2H), 4.19-4.29 (m, 5H), 4.36 (s, 2H), 6.62 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.17 (s, 1H), 7.33 (d, J = 8.1 Hz, 2H), 7.85 (d, J = 8.1 Hz, 2H), 7.96 (s, 1H)
1-133	DMSO-d6, 300MHz	0.77 (t, J = 7.3 Hz, 6H), 1.01-1.13 (m, 4H), 1.16 (d, J = 6.2 Hz, 6H), 1.35-1.51 (m, 4H), 2.29-2.38 (m, 1H), 4.22 (sep, J = 6.2 Hz, 1H), 4.37 (s, 2H), 5.79 (s, 2H), 6.61 (d, J = 8.8 Hz, 2H), 6.89 (d, J = 8.8 Hz, 2H), 7.19 (d, J = 8.1 Hz, 2H), 7.35 (d, J = 8.1 Hz, 2H), 7.74 (d, J = 7.3 Hz, 2H), 7.89 (d, J = 8.4 Hz, 2H), 7.92-7.97 (m, 1H), 8.05 (s, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-134	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.95-1.20 (m, 4H), 1.35-1.60 (m, 4H), 2.40-2.53 (m, 1H), 4.10 (s, 2 Hx0.4), 4.23 (s, 2 Hx0.6), 4.29 (s, 2 Hx0.6), 4.41 (s, 2 Hx0.4), 4.52 (s, 2 Hx0.6), 4.54 (s, 2 Hx0.4), 4.84 (s, 2 Hx0.6), 4.97 (s, 2x0.4H), 5.09 (s, 2H), 6.94 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.25-7.40 (m, 5H), 7.45-7.55 (m, 2H), 7.92-7.98 (m, 2H), 8.06 (s, 1Hx0.6), 8.08 (s, 1Hx0.4), 12.80 (s amplio, 1H).
1-135	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.96-1.21 (m, 4H), 1.13 (d, J = 6.8 Hz, 6 Hx0.4), 1.16 (d, J = 7.1 Hz, 6 Hx0.6), 1.34-1.62 (m, 4H), 2.39-2.54 (m, 1H), 2.70-2.89 (m, 1H), 4.10 (s, 2 Hx0.4), 4.36 (s, 2 Hx0.6), 4.79 (s, 2 Hx0.6), 4.84 (s, 2 Hx0.6), 5.04 (s, 2 Hx0.4), 5.05 (s, 2 Hx0.4), 5.09 (s, 2H), 6.77-6.87 (m, 2H), 6.90-6.98 (m, 2H), 7.02-7.15 (m, 4H), 7.51 (d, J = 8.1 Hz, 2H), 7.97 (d, J = 8.1 Hz, 2 Hx0.6), 7.98 (d, J = 8.1 Hz, 2 Hx04), 8.06 (s, 1Hx0.6), 8.13 (s, 1Hx0.4), 12.75 (br.s, 1Hx0.4), 13.01 (br.s, 1Hx0.6).
1-136	DMSO-d6, 400MHz	0.80 (t, J = 8.2 Hz, 6H), 0.99-1.16 (m, 4H), 1.37-1.58 (m, 4H), 2.20 (s, 3H), 2.30 (s, 3H), 2.41-2.52 (m, 1H), 3.46 (s, 2H), 4.12 (s, 2H), 4.26 (s, 2H), 5.07 (s, 2H), 6.93 (d, J = 6.8 Hz, 2H), 7.06 (d, J = 8.8 Hz, 2H), 7.49 (d, J = 8.4 Hz, 2H), 7.94 (d, J = 8.0 Hz, 2H), 8.05 (s, 1H), 12.65 (s amplio, 1H),
1-137	DMSO-d6, 400MHz	0.79 (t, J = 7.2 Hz, 6H), 0.99-1.15 (m, 4H), 1.38-1.58 (m, 4H), 2.40-2.52 (m, 1H), 5.24 (s, 2H), 5.56 (s, 2H), 5.56 (s, 2H), 6.94 (d, J = 7.6 Hz, 2H), 7.07 (d, J = 8.0 Hz, 2H), 7.17 (s amplio, 1H), 7.48 (s amplio, 1H), 7.80 (s, 1H), 8.01 (s, 1H), 8.37 (s, 1H), 8.63 (s, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-138	DMSO-d6, 300MHz	0.77 (t, J = 6.0 Hz, 6H), 1.03-1.09 (m, 4H), 1.18 (d,J = 9.0 Hz, 6H), 1.26 (s, 9H), 1.38-1.45 (m, 4H), 2.30-2.42 (m, 1H), 3.54 (s, 2H), 4.24 (s, 2H), 4.25-4.30 (m, 1H), 4.32 (s, 2H), 4.50 (s, 2H), 6.65 (d,J = 9.0 Hz, 2H), 6.90 (d,J = 9.0 Hz, 2H), 7.20 (s, 1H), 7.38 (d,J = 9.0 Hz, 1H), 7.62 (s, 1H), 7.73 (d,J = 9.0 Hz, 1H), 8.57 (s, 1H)
1-139	DMSO-d6, 300MHz	0.77 (t, J = 6.0 Hz, 6H), 1.02-1.10 (m, 4H), 1.18 (d,J = 9.0 Hz, 6H), 1.38-1.44 (m, 4H), 2.30-2.36 (m, 1H), 3.61 (s, 2H), 4.19 (s, 2H), 4.20-4.25 (m, 1H), 4.36 (s, 2H), 4.50 (s, 2H), 6.65 (d,J = 9.0 Hz, 2H), 6.90 (d,J = 9.0 Hz, 2H), 7.13 (m, 2H), 7.38 (d,J = 9.0 Hz, 1H), 7.53-7.56 (m, 2H), 7.62 (s, 1H), 7.73 (d,J = 9.0 Hz, 1H), 8.55 (s, 1H)
1-140	DMSO-d6, 300MHz	0.78 (t, J = 6.0 Hz, 6H), 1.02 (m, 4H), 1.19 (d,J = 6.0 Hz, 6H), 1.34-1.52 (m, 4H), 2.30-2.38 (m, 1H), 4.20 (s, 2H), 4.25-4.27 (m, 1H), 4.37 (s, 2H), 6.66 (d,J = 9.0 Hz, 2H), 7.03 (d,J = 66.0 Hz, 2H), 7.16-7.20 (m, 2H), 7.40-7.42 (m, 1H), 7.56-7.59 (m, 2H), 7.63 (s, 1H), 7.74 (d,J = 9.0 Hz, 1H), 8.56 (s, 1H)
1-141	DMSO-d6, 400MHz	0.79 (t, J = 7.2 Hz, 6H), 0.99-1.14 (m, 4H), 1.33 (s, 9H), 1.37-1.57 (m, 4H), 2.41-2.53 (m, 1H), 3.43 (s, 2H), 4.17 (s, 2H), 4.27 (s, 2H), 5.07 (s, 2H), 6.92 (d, J = 8.4 Hz, 2H), 7.06 (d, J = 8.4 Hz, 2H), 7.41 (s, 1H), 7.49 (d, J = 8.4 Hz, 2H), 7.94 (d, J = 8.4 Hz, 2H), 8.05 (s, 1H)
1-142	DMSO-d6, 300MHz	0.76 (t, J = 7.2 Hz, 6H), 0.99-1.09 (m, 4H), 1.14 (d, J = 6.0 Hz, 6H), 1.30-1.56 (m, 10H), 2.25-2.38 (m, 1H), 3.14 (s amplio, 2H), 3.41 (s amplio, 4H), 3.62 (s, 2H), 4.12 (s, 2H), 4.17-4.25 (m, 1H), 4.34 (s, 2H), 6.59 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 7.5 Hz, 2H), 7.84 (d, J = 6.9 Hz, 2H), 7.92 (s, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-143	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 0.98-1.18 (m, 4H), 1.35-1.61 (m, 4H), 2.35-2.53 (m, 1H), 3.18 (s, 3H), 5.08 (s, 2H), 5.22 (s, 2H), 6.94 (d, J = 8.7 Hz, 2H), 7.01 (d, J = 8.4 Hz, 1H), 7.07 (d, J = 8.7 Hz, 2H), 7.35 (d, J = 6.8 Hz, 1H), 7.51 (d, J = 7.9 Hz, 2H), 7.74 (dd, J = 8.4, 6.8 Hz, 1H), 7.96 (d, J = 7.9 Hz, 2H), 7.99 (s, 1H), 12.60 (s amplio, 1H).
1-144	DMSO-d6, 300MHz	0.77 (t, J = 6.0 Hz, 6H), 1.02-1.10 (m, 4H), 1.18 (d,J = 9.0 Hz, 6H), 1.38-1.48 (m, 4H), 2.30-2.35 (m, 1H), 3.40 (s, 2H), 4.14 (s, 2H), 4.22-4.28 (m, 1H), 4.50 (s, 1H), 6.65 (d,J = 9.0 Hz, 2H), 6.90 (d,J = 9.0 Hz, 2H), 7.38 (d,J = 9.0 Hz, 1H), 7.62 (s, 1H), 7.73 (d,J = 9.0 Hz, 1H), 7.89 (m, 1H), 8.52 (s, 1H)
1-145	DMSO-d6, 300MHz	0.61-0.83 (m, 6H), 1.00-1.24 (m, 6H), 1.35-1.65 (m, 8H), 2.27-2.39 (m, 1H), 3.19-3.34 (m, 2H), 4.03-4.26 (m, 2H), 4.36 (s amplio, 1H), 4.61-4.72 (m, 1H), 4.83 (s amplio, 1H), 4.96-5.06 (m, 1H), 6.62 (s amplio, 2H), 6.88 (s amplio, 2H), 7.17 (brd, J = 8.4 Hz, 2H), 7.28-7.53 (m, 3H), 7.69 (brd, J = 7.2 Hz, 2H), 7.79-7.87 (m, 1H), 7.91-7.99 (m, 2H)
1-146	DMSO-d6, 300MHz	0.78 (t, J = 7.3 Hz, 6H), 1.01-1.22 (m, 4H), 1.16 (d, J = 6.6 Hz, 6H), 1.32-1.52 (m, 4H), 2.20 (s, 3H), 2.28-2.38 (m, 1H), 2.30 (s, 3H), 3.48 (s, 2H), 4.11 (s, 2H), 4.18-4.28 (m, 1H), 4.25 (s, 2H), 4.36 (s, 2H), 6.61 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 7.86 (d, J = 8.0 Hz, 2H), 7.97 (s, 1H), 12.57 (s amplio, 1H)
1-147	DMSO-d6, 400MHz	0.79 (t, J = 7.4 Hz, 6H), 0.99-1.14 (m, 4H), 1.23 (s, 9H), 1.37-1.56 (m, 4H), 2.39-2.49 (m, 1H), 3.48 (s, 2H), 4.03 (s, 2H), 4.23 (s, 2H), 5.07 (s, 2H), 6.72 (s, 1H), 6.92 (d, J = 8.8 Hz, 2H), 7.06 (d, J = 8.8 Hz, 2H), 7.48 (d, J = 8.4 Hz, 2H), 7.93 (d, J = 8.0 Hz, 2H), 8.02 (s, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-148	DMSO-d6, 300MHz	0.79 (t, J = 7.4 Hz, 6H), 0.98-1.16 (m, 4H), 1.35-1.60 (m, 4H), 2.40-2.54 (m, 1H), 3.65 (s, 2H), 3.96 (s, 3H), 4.36 (s, 2H), 4.45 (s, 2H), 5.07 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.31-7.44 (m, 2H), 7.47 (d, J = 8.3 Hz, 2H), 7.64-7.77 (m, 2H), 7.88 (d, J = 8.3 Hz, 2H), 7.98 (s, 1H)
1-149	DMSO-d6 +D2O+NaHCO3, 300MH z	0.78 (t, J = 7.4 Hz, 6H), 0.87 (d, J = 6.4 Hz, 6H), 0.99-1.13 (m, 4H), 1.16 (d, J = 6.4 Hz, 6H), 1.32-1.50 (m, 4H), 1.78-1.90 (m, 1H), 2.26-2.39 (m, 1H), 3.08 (s, 2H), 3.72 (s, 2H), 3.82 (d, J = 6.4 Hz, 2H), 4.16-4.26 (m, 3H), 4.36 (s, 2H), 6.60 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 7.84 (d, J = 8.3 Hz, 2H), 7.89 (s, 1H)
1-150	DMSO-d6 +D2O+NaHCO3, 300MH z	0.78 (t, J = 7.2 Hz, 6H), 0.86 (t, J = 7.4 Hz, 3H), 0.98-1.12 (m, 4H), 1.16 (d, J = 6.4 Hz, 6H), 1.30-1.63 (m, 6H), 2.27-2.40 (m, 1H), 3.98 (t, J = 6.6 Hz, 2H), 4.17-4.25 (m, 3H), 4.35 (s, 2H), 6.60 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 7.33 (d, J = 8.3 Hz, 2H), 7.84 (d, J = 8.3 Hz, 2H), 7.88 (s, 1H)
1-151	DMSO-d6, 300MHz	0.80 (t, J = 7.2 Hz, 6H), 1.01-1.15 (m, 4H), 1.37-1.58 (m, 4H), 1.75-2.16 (m, 5H), 2.43-2.46 (m, 1H), 3.11 (s amplio, 2H), 3.55 (s amplio, 2H), 3.86 (s amplio, 1H), 5.10 (s, 2H), 6.94 (d, J = 8.7 Hz, 2H), 7.08 (d, J = 8.7 Hz, 2H), 7.54 (d, J = 9.0 Hz, 2H), 8.01 (d, J = 9.0 Hz, 2H), 8.32 (s amplio, 1H), 11.54 (s amplio, 1H), 12.45 (s amplio, 1H)
1-152	DMSO-d6, 300MHz	0.69 (t, J = 7.3 Hz, 6H), 1.16 (d, J = 6.8 Hz, 6H), 1.33-1.65 (m, 6H), 1.76-1.87 (m, 2H), 2.08-2.30 (m, 4H), 2.83-2.92 (m, 2H), 3.84 (s, 2H), 4.18-4.27 (m, 1H), 4.36 (s, 2H), 6.62 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 7.34 (d, J = 8.3 Hz, 2H), 7.86 (d, J = 7.9 Hz, 2H), 7.95 (s, 1H), 12.15 (s, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-153	DMSO-d6, 300MHz	0.80 (t, J = 7.2 Hz, 6H), 1.01-1.18 (m, 4H), 1.38-1.58 (m, 4H), 2.42-2.48 (m, 1H), 2.70 (s amplio, 4H), 3.35 (s amplio, 4H), 3.96 (s, 2H), 5.09 (s, 2H), 6.94 (d, J = 9.1 Hz, 2H), 6.98 (d, J = 9.4 Hz, 2H), 7.08 (d, J = 8.7 Hz, 2H), 7.51 (d, J = 8.3 Hz, 2H), 7.78 (d, J = 9.0 Hz, 2H), 7.98 (d, J = 8.3 Hz, 2H), 8.08 (s, 1H), 12.29 (s amplio, 1H)
1-154	DMSO-d6, 300MHz	0.69 (t, J = 7.4 Hz, 6H), 1.16 (d, J = 6.4 Hz, 6H), 1.34-1.62 (m, 4H), 2.08-2.18 (m, 1H), 2.68 (s amplio, 4H), 3.36 (s amplio, 4H), 3.94 (s, 2H), 4.18-4.27 (m, 1H), 4.37 (s, 2H), 6.62 (d, J = 8.6 Hz, 2H), 6.89 (d, J = 8.6 Hz, 2H), 6.97 (d, J = 9.0 Hz, 2H), 7.34 (d, J = 7.9 Hz, 2H), 7.77 (d, J = 9.0 Hz, 2H), 7.87 (d, J = 8.3 Hz, 2H), 7.98 (s, 1H), 12.29 (s amplio, 1H)
1-155	DMSO-d6, 300MHz	0.81 (t, J = 7.3 Hz, 6H), 1.00-1.19 (m, 4H), 1.43-1.59 (m, 4H), 2.53-2.61 (m, 1H), 2.81 (s amplio, 4H), 3.13 (s amplio, 4H), 4.01 (s, 2H), 5.09 (s, 2H), 7.07 (d, J = 12.7 Hz, 2H), 7.19 (d, J = 8.3 Hz, 2H), 7.35-7.42 (m, 3H), 7.62-7.74 (m, 2H), 7.89 (d, J = 9.0 Hz, 2H), 7.92 (s, 1H), 7.98-8.01 (m, 1H), 12.81 (s amplio, 1H)
1-156	DMSO-d6, 300MHz	0.81 (t, J = 7.2 Hz, 6H), 1.02-1.18 (m, 4H), 1.45-1.61 (m, 4H), 2.55-2.60 (m, 1H), 2.72 (s amplio, 4H), 3.23 (s amplio, 4H), 3.95 (s, 2H), 5.09 (s, 2H), 7.08 (d, J = 9.1 Hz, 2H), 7.16-7.23 (m, 3H), 7.31 (d, J = 7.5 Hz, 2H), 7.34-7.42 (m, 2H), 7.47 (s amplio, 1H), 7.89 (d, J = 9.0 Hz, 2H), 7.90 (s amplio, 1H), 12.84 (s amplio, 1H)
1-157	DMSO-d6, 300MHz	0.76 (t, J = 7.3 Hz, 6H), 0.93 (m, 4H), 1.36 (m, 4H), 5.45 (s, 2H), 5.60 (s, 2H), 7.09 (m, 9H), 7.57 (d,J = 7.3 Hz, 1H), 7.85 (s, 1H), 7.93 (d,J = 8.4 Hz, 2H), 8.06 (s, 1H), 8.11 (d,J = 8.1 Hz, 1H)
1-158	DMSO-d6, 300MHz	0.74 (t, J = 7.5 Hz, 6H), 0.98 (m, 4H), 1.06 (d,J = 7.2 Hz, 6H), 1.48 (m, 4H), 2.7 (m, 1H), 5.59 (s, 2H), 5.92 (s, 2H), 6.99 (m, 6H), 7.37 (s, 1H), 7.42 (d,J = 8.3 Hz, 1H), 7.80 (d,J = 8.7 Hz, 2H), 8.41 (s, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-159	CDCl3, 300MHz	0.82 (t, J = 7.2 Hz, 6H), 1.09 (m, 4H), 1.53 (s, 3H), 1.54 (m, 4H), 2.53 (m, 1H), 0.82 (s, 1H), 6.99 (d,J = 6.8 Hz, 1H), 7.14 (m, 1H), 7.25 (s, 3H), 7.30 (d,J = 8.3 Hz, 1H), 7.38 (s, 1H), 8.04 (s amplio, 1H)
1-160	DMSO-d6, 300MHz	0.80 (t, J = 7.1 Hz, 6H), 0.99-1.16 (m, 4H), 1.38-1.59 (m, 4H), 2.40-2.50 (m, 1H), 2.82-2.98 (m, 4H), 3.84 (s, 2H), 4.09 (s, 2H), 5.09 (s, 2H), 6.94 (d, J = 8.8 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 8.1 Hz, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.66 (s, 1H), 7.72 (d, J = 8.1 Hz, 1H), 7.99 (d, J = 8.1 Hz, 2H), 8.08 (s, 1H), 12.79 (s, 1H)
1-161	DMSO-d6, 300MHz	0.81 (t, J = 7.3 Hz, 6H), 1.00-1.18 (m, 4H), 1.43-1.60 (m, 4H), 1.64-1.83 (m, 4H), 2.29 (t, J = 11.1 Hz, 3H), 2.55-2.67 (m, 1H), 3.06 (d, J = 11.3 Hz, 2H), 3.90 (s, 2H), 5.08 (s, 2H), 7.07 (d, J = 8.6 Hz, 2H), 7.19 (d, J = 8.3 Hz, 2H), 7.37-7.41 (m, 4H), 7.86-7.89 (m, 5H)
1-162	DMSO-d6, 300MHz	0.81 (t, J = 7.3 Hz, 6H), 1.02-1.19 (m, 4H), 1.43-1.60 (m, 4H), 1.66-1.86 (m, 4H), 2.30 (t, J = 10.5 Hz, 2H), 2.53-2.68 (m, 2H), 3.06 (d, J = 11.7 Hz, 2H), 3.91 (s, 2H), 5.09 (s, 2H), 7.07 (d, J = 8.6 Hz, 2H), 7.19 (d, J = 7.9 Hz, 2H), 7.37-7.46 (m, 3H), 7.54 (d, J = 7.9 Hz, 1H), 7.78 (d, J = 7.5 Hz, 1H), 7.83 (s, 1H), 7.87-7.90 (m, 3H), 12.93 (s amplio, 1H)
1-163	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 0.98-1.18 (m, 4H), 1.36-1.60 (m, 4H), 2.39-2.53 (m, 1H), 4.85 (d, J = 6.3 Hz, 2H), 5.09 (s, 2H), 6.94 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.51 (d, J = 8.3 Hz, 2H), 7.97 (d, J = 8.3 Hz, 2H), 8.01 (s, 1H), 8.20 (dd, J = 8.1, .9 Hz, 1H), 8.48 (dd, J = 8.1, 2.1 Hz, 1H), 9.14 (dd, J = 2.1, .9 Hz, 1H), 9.88 (t, J = 6.3 Hz, 1H), 13.74 (s amplio, 1H).

Ejemplo	solvente, Hz	RMN (δ)
1-164	DMSO-d6, 300MHz	0.81 (t, J = 7.2 Hz, 6H), 1.03-1.17 (m, 4H), 1.48-1.59 (m, 4H), 1.70-1.80 (m, 4H), 2.19-2.30 (m, 2H), 2.48-2.59 (m, 2H), 3.06 (d, J = 10.9 Hz, 2H), 3.90 (s, 2H), 5.08 (s, 2H), 7.07 (d, J = 9.0 Hz, 2H), 7.19 (d, J = 8.3 Hz, 2H), 7.24-7.31 (m, 1H), 7.38 (d, J = 8.3 Hz, 2H), 7.45-7.53 (m, 2H), 7.66 (d, J = 8.3 Hz, 1H), 7.87-7.89 (m, 3H)
1-165	CDCl3, 300MHz	0.80 (t, J = 7.2 Hz, 6H), 1.06 (m, 4H), 1.43 (m, 4H), 2 (m, 4H), 2.42 (m, 2H), 2.64 (m, 1H), 3.17 (m, 2H), 4.17 (s, 2H), 5.31 (s, 2H), 7.02 (m, 4H), 7.21 (m, 5H), 7.33 (m, 2H), 7.69 (s, 1H), 7.99 (m, 1H)
1-166	CDCl3, 300MHz	0.80 (t, J = 7.5 Hz, 6H), 1.03 (m, 4H), 1.43 (m, 4H), 2.41 (m, 1H), 3.10-3.25 (m, 4H), 4.12 (m, 2H), 4.32 (m, 2H), 5.32 (s, 2H), 7.02-7.09 (m, 4H), 7.21 (m, 6H), 7.34 (m, 2H), 7.72 (s, 1H), 7.77 (s, 1H), 7.85 (d,J = 6.4 Hz, 1H), 8.01 (t, J = 3.0 Hz, 1H)
1-167	DMSO-d6, 300MHz	0.77 (t, J = 7.3 Hz, 6H), 1 (m, 4H), 1.42 (m, 4H), 4.68 (s, 2H), 5.44 (s, 2H), 6.86 (m, 1H), 7.1 (m, 9H), 7.56 (d,J = 7.7 Hz, 1H), 7.65 (s, 1H), 8.04 (s, 1H), 8.10 (d,J = 7.3 Hz, 1H)
1-168	DMSO-d6, 300MHz	0.80 (t, J = 7.2 Hz, 6H), 0.98-1.19 (m, 4H), 1.36-1.62 (m, 4H), 2.39-2.53 (m, 1H), 3.07-3.32 (m, 2H), 3.66-4.10 (m, 2H), 5.02-5.12 (m, 4H), 6.94 (d, J = 8.5 Hz, 2H), 7.08 (d, J = 8.5 Hz, 2H), 7.48-7.58 (m, 2H), 7.84 (d, J = 7.9 Hz, 1Hx0.5), 7.89 (d, J = 8.3 Hz, 1Hx0.5), 7.92-8.14 (m, 5H), 8.12 (s, 1Hx0.5), 8.13 (s, 1Hx0.5), 8.39-8.48 (m, 1H), 9.04 (d, J = 1.5 Hz, 1Hx0.5), 9.15 (d, J = 1.5 Hz, 1Hx0.5), 13.67 (s amplio, 1H).
1-169	DMSO-d6, 300MHz	0.72 (t, J = 7.4 Hz, 6H), 0.87-1.08 (m, 4H), 1.30-1.53 (m, 4H), 2.36-2.47 (m, 1H), 2.78-2.92 (m, 4H), 3.80 (s, 2H), 4.12 (s, 2H), 6.05 (s, 2H), 6.98-7.09 (m, 4H), 7.20-7.30 (m, 3H), 7.56-7.75 (m, 4H), 8.40 (s, 1H), 12.77 (s, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-170	DMSO-d6, 300MHz	0.73 (t, J = 7.2 Hz, 6H), 0.89-1.09 (m, 4H), 1.31-1.54 (m, 4H), 2.37-2.50 (m, 1H), 2.69 (s amplio, 4H), 3.19 (s amplio, 4H), 4.00 (s, 2H), 6.04 (s, 2H), 7.05 (s, 4H), 7.16-7.41 (m, 5H), 7.46 (s amplio, 1H), 7.57-7.74 (m, 2H), 8.42 (s, 1H), 12.71 (s amplio, 1H)
1-171	DMSO-d6, 300MHz	0.70 (t, J = 6.8 Hz, 6H), 0.85-1.07 (m, 4H), 1.30-1.51 (m, 4H), 1.57-1.79 (m, 4H), 2.20-2.63 (m, 4H), 2.94-3.05 (m, 2H), 3.96 (s, 2H), 6.04 (s, 2H), 7.03 (s, 4H), 7.24 (s amplio, 2H), 7.35 (d, J = 7.5 Hz, 2H), 7.56-7.73 (m, 2H), 7.87 (d, J = 7.5 Hz, 2H), 8.39 (s, 1H)
1-172	DMSO-d6, 300MHz	0.75 (t, J = 7.5 Hz, 6H), 0.96 (m, 4H), 1.4 (m, 4H), 2.72 (m, 4H), 3.22 (m, 4H), 3.95 (s, 2H), 5.42 (s, 2H), 7.07-7.20 (m, 7H), 7.31 (m, 1H), 7.45 (s, 1H), 7.54 (d,J = 7.2 Hz, 1H), 7.73 (s, 1H), 8.09 (d,J = 6.0 Hz, 1H)
1-173	DMSO-d6, 300MHz	1.64-1.85 (m, 4H), 2.30 (t, J = 10.4 Hz, 2H), 2.58-2.68 (m, 1H), 3.06 (d, J = 11.7 Hz, 2H), 3.90 (s, 2H), 5.17 (s, 2H), 7.08 (d, J = 9.0 Hz, 2H), 7.40-7.54 (m, 3H), 7.67 (d, J = 8.3 Hz, 1H), 7.75 (d, J = 2.3 Hz, 1H), 7.76-7.80 (m, 1H), 7.81-7.84 (m, 1H), 7.86-7.91 (m, 3H)
1-174	DMSO-d6, 300MHz	1.72-2.12 (m, 4H), 2.26-2.46 (m, 2H), 2.80-3.03 (m, 1H), 3.54-3.80 (m, 2H), 4.82 (s, 2H), 5.38 (s, 2H), 7.16 (d, J = 8.3 Hz, 2H), 7.42-7.53 (m, 2H), 7.77-7.86 (m, 2H), 7.96 (d, J = 7.9 Hz, 2H), 8.11-8.19 (m, 3H), 12.94 (s amplio, 1H)
1-175	DMSO-d6, 300MHz	0.93 (t, J = 7.4 Hz, 3H), 1.37-1.49 (m, 2H), 1.65-1.85 (m, 6H), 2.25-2.35 (m, 2H), 3.02-3.10 (m, 3H), 3.90 (s, 2H), 3.97 (t, J = 6.4 Hz, 2H), 5.05 (s, 2H), 6.94 (d, J = 8.7 Hz, 2H), 7.05 (d, J = 9.0 Hz, 2H), 7.36-7.44 (m, 3H), 7.49-7.54 (m, 1H), 7.75-7.88 (m, 5H)

Ejemplo	solvente, Hz	RMN (δ)
1-176	DMSO-d6, 400MHz	0.80 (t, J = 7.3 Hz, 6H), 1.02-1.13 (m, 4H), 1.40-1.57 (m, 4H), 2.21 (s, 3H), 2.42-2.51 (m, 1H), 5.08 (s, 2H), 6.00 (s, 2H), 6.72 (s, 1H), 6.93 (d, J = 8.6 Hz, 2H), 7.06 (d, J = 8.6 Hz, 2H), 7.50 (d, J = 8.3 Hz, 2H), 7.93 (d, J = 8.3 Hz, 2H), 8.03 (s, 1H), 13.52 (s amplio, 1H)
1-177	DMSO-d6, 400MHz	0.79 (t, J = 7.3 Hz, 6H), 1.02-1.13 (m, 4H), 1.39-1.56 (m, 4H), 2.39 (s, 3H), 2.42-2.52 (m, 1H), 5.08 (s, 2H), 5.77 (s, 2H), 6.56 (s, 1H), 6.92 (d, J = 8.6 Hz, 2H), 7.06 (d, J = 8.6 Hz, 2H), 7.51 (d, J = 8.1 Hz, 2H), 7.94 (d, J = 8.1 Hz, 2H), 8.10 (s, 1H), 12.67 (s amplio, 1H)
1-178	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 1.01-1.15 (m, 4H), 1.36 (s, 9H), 1.40-1.59 (m, 4H), 2.41-2.53 (m, 1H), 5.09 (s, 2H), 5.90 (s, 2H), 6.54 (s, 1H), 6.94 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.4 Hz, 2H), 7.52 (d, J = 8.1 Hz, 2H), 7.96 (d, J = 8.1 Hz, 2H), 8.09 (s, 1H), 12.74 (s amplio, 1H)
1-179	DMSO-d6, 300MHz	0.80 (t, J = 7.1 Hz, 6H), 1.02-1.15 (m, 4H), 1.28 (s, 9H), 1.38-1.56 (m, 4H), 2.42-2.55 (m, 1H), 5.09 (s, 2H), 6.04 (s, 2H), 6.81 (s, 1H), 6.94 (d, J = 8.8 Hz, 2H), 7.08 (d, J = 8.8 Hz, 2H), 7.51 (d, J = 8.4 Hz, 2H), 7.95 (d, J = 8.4 Hz, 2H), 8.03 (s, 1H)
1-180	DMSO-d6, 300MHz	0.76 (t, J = 7.3 Hz, 6H), 0.99 (m, 4H), 1.42 (m, 4H), 1.9 (m, 2H), 2.44 (m, 1H), 3.27 (m, 3H), 3.60 (t, J = 8.1 Hz, 1H), 4.04 (d,J = 15.4 Hz, 1H), 4.26 (m, 2H), 5.43 (s, 2H), 7.09 (m, 7H), 7.54 (d,J = 7.0 Hz, 1H), 7.70 (s, 1H), 8.01 (s, 1H), 8.11 (d,J = 7.3 Hz, 1H)
1-181	DMSO-d6 , 400MHz	0.77 (t, J = 7.3 Hz, 6H), 1.00-1.11 (m, 4H), 1.26-1.54 (m, 6H), 1.77 (brd, J = 14.8 Hz, 2H), 1.96-2.04 (m, 1H), 2.39-2.45 (m, 1H), 2.80 (brt, J = 12.3 Hz, 2H), 2.98 (d, J = 6.9 Hz, 2H), 3.87 (brd, J = 13.0 Hz, 2H), 5.05 (s, 2H), 6.90 (d, J = 8.6 Hz, 4H), 7.04 (d, J = 8.6 Hz, 2H), 7.47 (d, J = 8.1 Hz, 2H), 7.70 (d, J = 9.0 Hz, 2H), 7.93 (d, J = 8.1 Hz, 2H), 7.95 (s, 1H), 12.16 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
1-182	DMSO-d6, 300MHz	0.76 (t, J = 7.3 Hz, 6H), 0.97-1.09 (m, 4H), 1.39-1.52 (m, 4H), 2.44-2.50 (m, 1H), 5.44 (s, 2H), 5.95 (s, 2H), 7.10 (d,J = 8.4 Hz, 2H), 7.17 (d,J = 8.4 Hz, 2H), 7.21-7.28 (m, 3H), 7.54 (d,J = 7.0 Hz, 1H), 7.68 (d,J = 7.0 Hz, 1H), 7.70 (s, 1H), 8.03 (s, 1H), 8.04-8.10 (m, 2H), 8.29 (s, 1H)
1-183	DMSO-d6, 300MHz	0.74 (t, J = 7.1 Hz, 6H), 0.95-1.10 (m, 4H), 1.36-1.57 (m, 6H), 1.77-1.80 (m, 2H), 2.11-2.18 (m, 3H), 2.40-2.43 (m, 1H), 2.80-2.84 (m, 2H), 3.80 (s, 2H), 5.24 (s, 2H), 6.63 (s, 1H), 6.77 (d,J = 7.9 Hz, 2H), 6.97 (d,J = 7.9 Hz, 2H), 7.10-7.20 (m, 2H), 7.32-7.44 (m, 6H), 8.16 (dd, J = 1.9, 9.0 Hz, 1H)
1-184	DMSO-d6, 300MHz	1.63-1.85 (m, 4H), 2.25-2.35 (m, 2H), 2.52 (s, 3H), 2.59-2.74 (m, 1H), 3.06 (d, J = 12.8 Hz, 2H), 3.90 (s, 2H), 5.24 (s, 2H), 7.09 (d, J = 9.0 Hz, 2H), 7.42 (t, J = 7.7 Hz, 1H), 7.51-7.58 (m, 2H), 7.70-7.83 (m, 3H), 7.86-7.92 (m, 3H), 8.09 (d, J = 1.9 Hz, 1H)
1-185	DMSO-d6, 300MHz	1.10 (d, J = 6.8 Hz, 6H), 2.71-2.92 (m, 5H), 3.11 (s amplio, 4H), 3.71-3.82 (m, 6H), 4.11 (s, 2H), 6.00 (s, 2H), 6.96-7.12 (m, 6H), 7.24 (d, J = 7.9 Hz, 1H), 7.53 (d, J = 9.1 Hz, 1H), 7.61 (s, 1H), 7.71 (d, J = 8.3 Hz, 1H), 8.29 (s, 1H), 12.78 (s amplio, 1H)
1-186	DMSO-d6, 300MHz	1.11 (d, J = 6.4 Hz, 6H), 2.66 (s amplio, 4H), 2.72-2.83 (m, 1H), 3.07-3.22 (m, 8H), 3.75 (s amplio, 4H), 3.98 (s, 2H), 6.00 (s, 2H), 6.95-7.23 (m, 6H), 7.28-7.41 (m, 3H), 7.45 (s, 1H), 7.53 (d, J = 9.1 Hz, 1H), 8.30 (s, 1H), 12.82 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
2-1	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.95-1.20 (m, 4H), 1.40-1.65 (m, 4H), 2.40-2.60 (m, 1H), 3.02 (s, 3H), 3.81 (s, 2H), 3.93 (s, 2H), 4.57 (s, 2H), 6.78 (d, J = 8.8 Hz, 2H), 7.00-7.40 (m, 9H), 7.55 (d, J = 8.8 Hz, 2H), 8.30 (s, 1H), 12.30 (s amplio, 1H).
3-1	DMSO-d6, 400MHz	0.81 (t, J = 7.3 Hz, 6H), 1.05-1.13 (m, 4H), 1.48-1.57 (m, 4H), 2.5-2.56 (m, 1H), 5.09 (s, 2H), 5.66 (s, 2H), 7.09 (d, J = 9.04 Hz, 2H), 7.19 (d, J = 8.32 Hz, 2H), 7.38 (d, J = 8.12 Hz, 2H), 7.91 (d, J = 9.04 Hz, 2H), 7.98-7.99 (m, 1H), 8.03 (s, 1H), 8.64 (d, J = 3 Hz, 1H), 8.72 (d, J = 1.4 Hz, 1H), 13.52 (s, 1H)
3-2	DMSO-d6, 400MHz	0.81 (t.J = 7.3 Hz, 6H), 1.05-1.13 (m, 4H), 1.48-1.57 (m, 4H), 2.50-2.56 (m, 1H), 5.09 (s, 2H), 5.57 (s, 2H), 7.09 (d, J = 9.2 Hz, 2H), 7.17-7.19 (m, 4H), 7.38 (d, J = 12.0 Hz, 2H), 7.89-7.91 (m, 4H), 8.01 (s, 1H)
3-3	DMSO-d6, 400MHz	0.81 (t.J = 7.3 Hz, 6H), 1.05-1.13 (m, 4H), 1.48-1.57 (m, 4H), 2.50-2.56 (m, 1H), 4.78 (s, 2H), 5.08 (s, 2H), 7.07 (d, J = 8.8 Hz, 2H), 7.18 (d, J = 8.1 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 8.0 Hz, 2H), 7.82-7.86 (m, 5H)
3-4	DMSO-d6, 300MHz	1.14-1.49 (m, 5H), 1.64-1.84 (m, 5H), 2.44-2.54 (m, 1H), 4.77 (s, 2H), 5.09 (s, 2H), 7.06 (d, J = 9.0 Hz, 2H), 7.24 (d, J = 8.3 Hz, 2H), 7.37 (d, J = 8.3 Hz, 2H), 7.50 (d, J = 8.7 Hz, 2H), 7.82-7.86 (m, 5H)
3-5	DMSO-d6, 400MHz	1.16-1.45 (m, 5H), 1.67-1.83 (m, 5H), 2.45-2.56 (m, 1H), 5.07 (s, 2H), 5.37 (s, 2H), 7.00 (d, J = 9.0 Hz, 2H), 7.24 (d, J = 8.1 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H), 7.65 (d, J = 9.0 Hz, 2H), 7.94-7.96 (m, 3H), 8.13 (d, J = 8.8 Hz, 2H)

Ejemplo	solvente, Hz	RMN (δ)
3-6	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 1.02-1.16 (m, 4H), 1.46-1.60 (m, 4H), 2.27 (s, 3H), 2.54-2.58 (m, 1H), 2.86 (s, 3H), 4.68 (s, 2H), 5.19 (s, 2H), 7.10 (d, J = 0.8 Hz, 2H), 7.18 (d, J = 8.3 Hz, 2H), 7.39 (d, J = 8.3 Hz, 2H), 7.78 (s, 1H), 7.95-7.98 (m, 3H), 8.13 (d, J = 8.3 Hz, 2H), 13.39 (s amplio, 1H)
3-7	DMSO-d6, 300MHz	0.78 (t, J = 7.4 Hz, 6H), 0.97-1.16 (m, 4H), 1.40-1.60 (m, 4H), 2.30 (s, 3H), 2.51-2.56 (m, 1H), 3.17 (s, 3H), 5.00 (s, 2H), 5.19 (s, 2H), 6.85 (d, J = 9.0 Hz, 2H), 7.10 (s, 1H), 7.11 (s, 1H), 7.16 (d, J = 7.9 Hz, 2H), 7.37 (d, J = 8.3 Hz, 2H), 7.77 (d, J = 8.7 Hz, 2H), 7.86 (s, 1H), 7.96 (s, 1H), 12.16 (s amplio, 1H)
3-8	DMSO-d6, 300MHz	2.28 (s, 3H), 3.36 (s, 2H), 3.84 (s, 2H), 4.19 (s, 2H), 5.36 (s, 2H), 7.07-7.08 (m, 2H), 7.27-7.42 (m, 5H), 7.67-7.77 (m, 4H), 7.94-7.98 (m, 2H)
3-9	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 1.02-1.14 (m, 4H), 1.43-1.60 (m, 4H), 2.29 (s, 3H), 2.51-2.57 (m, 1H), 3.35 (s, 2H), 3.86 (s, 2H), 4.19 (s, 2H), 5.19 (s, 2H), 7.10-7.10 (m, 2H), 7.18 (d, J = 8.1 Hz, 2H), 7.25-7.30 (m, 1H), 7.33-7.42 (m, 6H), 7.91 (s, 1H), 7.94 (amplio, 1H)
3-10	DMSO-d6, 400MHz	0.81 (t.J = 7.3 Hz, 6H), 1.05-1.13 (m, 4H), 1.48-1.57 (m, 4H), 2.50-2.56 (m, 1H), 3.40 (s, 2H), 3.86 (s, 2H), 4.17 (s, 2H), 5.07 (s, 2H), 7.06 (d, J = 9.2 Hz, 2H), 7.19 (d, J = 6.0 Hz, 2H), 7.26-7.68 (m, 5H), 7.86-7.90 (m, 3H)
3-11	DMSO-d6, 400MHz	0.72 (t, J = 7.4 Hz, 6H), 1.48-1.55 (m, 2H), 1.61-1.68 (m, 2H), 2.30-2.33 (m, 1H), 3.35 (s, 2H), 3.86 (s, 2H), 4.17 (s, 2H), 5.08 (s, 2H), 7.06 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 7.2 Hz, 2H), 7.26-7.38 (m, 7H), 7.86-7.87 (m, 3H)
3-12	DMSO-d6, 300MHz	0.86 (d, J = 6.6 Hz, 6H), 1.29 (s, 9H), 1.79-1.88 (m, 1H), 2.45 (d, J = 7.4 Hz, 2H), 3.37 (s; 2H), 3.87 (s, 2H), 4.20 (s, 2H), 5.21 (s, 2H), 7.11-7.19 (m, 3H), 7.25-7.44 (m, 8H), 7.93 (s, 1H), 8.18 (d, J = 2.6 Hz, 1H), 12.41 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
3-6	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 1.02-1.16 (m, 4H), 1.46-1.60 (m, 4H), 2.27 (s, 3H), 2.54-2.58 (m, 1H), 2.86 (s, 3H), 4.68 (s, 2H), 5.19 (s, 2H), 7.10 (d, J = 0.8 Hz, 2H), 7.18 (d, J = 8.3 Hz, 2H), 7.39 (d, J = 8.3 Hz, 2H), 7.78 (s, 1H), 7.95-7.98 (m, 3H), 8.13 (d, J = 8.3 Hz, 2H), 13.39 (s amplio, 1H)
3-7	DMSO-d6, 300MHz	0.78 (t, J = 7.4 Hz, 6H), 0.97-1.16 (m, 4H), 1.40-1.60 (m, 4H), 2.30 (s, 3H), 2.51-2.56 (m, 1H), 3.17 (s, 3H), 5.00 (s, 2H), 5.19 (s, 2H), 6.85 (d, J = 9.0 Hz, 2H), 7.10 (s, 1H), 7.11 (s, 1H), 7.16 (d, J = 7.9 Hz, 2H), 7.37 (d, J = 8.3 Hz, 2H), 7.77 (d, J = 8.7 Hz, 2H), 7.86 (s, 1H), 7.96 (s, 1H), 12.16 (s amplio, 1H)
3-8	DMSO-d6, 300MHz	2.28 (s, 3H), 3.36 (s, 2H), 3.84 (s, 2H), 4.19 (s, 2H), 5.36 (s, 2H), 7.07-7.08 (m, 2H), 7.27-7.42 (m, 5H), 7.67-7.77 (m, 4H), 7.94-7.98 (m, 2H)
3-9	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 1.02-1.14 (m, 4H), 1.43-1.60 (m, 4H), 2.29 (s, 3H), 2.51-2.57 (m, 1H), 3.35 (s, 2H), 3.86 (s, 2H), 4.19 (s, 2H), 5.19 (s, 2H), 7.10-7.10 (m, 2H), 7.18 (d, J = 8.1 Hz, 2H), 7.25-7.30 (m, 1H), 7.33-7.42 (m, 6H), 7.91 (s, 1H), 7.94 (amplio, 1H)
3-10	DMSO-d6, 400MHz	0.81 (t.J = 7.3 Hz, 6H), 1.05-1.13 (m, 4H), 1.48-1.57 (m, 4H), 2.50-2.56 (m, 1H), 3.40 (s, 2H), 3.86 (s, 2H), 4.17 (s, 2H), 5.07 (s, 2H), 7.06 (d, J = 9.2 Hz, 2H), 7.19 (d, J = 6.0 Hz, 2H), 7.26-7.68 (m, 5H), 7.86-7.90 (m, 3H)
3-11	DMSO-d6, 400MHz	0.72 (t, J = 7.4 Hz, 6H), 1.48-1.55 (m, 2H), 1.61-1.68 (m, 2H), 2.30-2.33 (m, 1H), 3.35 (s, 2H), 3.86 (s, 2H), 4.17 (s, 2H), 5.08 (s, 2H), 7.06 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 7.2 Hz, 2H), 7.26-7.38 (m, 7H), 7.86-7.87 (m, 3H)
3-12	DMSO-d6, 300MHz	0.86 (d, J = 6.6 Hz, 6H), 1.29 (s, 9H), 1.79-1.88 (m, 1H), 2.45 (d, J = 7.4 Hz, 2H), 3.37 (s, 2H), 3.87 (s, 2H), 4.20 (s, 2H), 5.21 (s, 2H), 7.11-7.19 (m, 3H), 7.25-7.44 (m, 8H), 7.93 (s, 1H), 8.18 (d, J = 2.6 Hz, 1H), 12.41 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
3-13	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 1.02-1.16 (m, 4H), 1.41-1.62 (m, 4H), 2.52-2.59 (m, 1H), 3.36 (s, 2H), 3.86 (s, 2H), 4.19 (s, 2H), 5.26 (s, 2H), 7.18-7.42 (m, 11H), 8.00 (s, 1H), 8.11 (d, J = 2.9 Hz, 1H), 12.41 (s amplio, 1H)
3-14	DMSO-d6, 400MHz	0.72 (t, J = 7.4 Hz, 6H), 1.48-1.55 (m, 2H), 1.61-1.68 (m, 2H), 2.30-2.33 (m, 1H), 3.37 (s, 2H), 3.85 (s, 2H), 4.16 (s, 2H), 5.08 (s, 2H), 7.06 (d, J = 8.8 Hz, 2H), 7.18-7.28 (m, 4H), 7.36-7.42 (m, 4H), 7.86-7.89 (m, 3H)
3-15	DMSO-d6, 300MHz	0.72 (t, J = 7.4 Hz, 6H), 1.19 (d, J = 6.9 Hz, 6H), 1.45-1.53 (m, 2H), 1.63-1.66 (m, 2H), 2.33-2.36 (m, 1H), 2.85-2.88 (m, 1H), 3.35 (s, 2H), 3.83 (s, 2H), 4.16 (s, 2H), 5.09 (s, 2H), 7.07 (d, J = 11.2 Hz, 2H), 7.17-7.23 (m, 4H), 7.31 (d, J = 8.1 Hz, 2H), 7.39 (d, J = 8.1 Hz, 2H), 7.85-7.87 (m, 3H)
3-16	DMSO-d6, 400MHz	0.72 (t, J = 7.4 Hz, 6H), 1.45-1.53 (m, 2H), 1.63-1.66 (m, 2H), 2.30-2.34 (m, 1H),, 3.40 (s, 2H), 3.97 (s, 2H), 4.30 (s, 2H), 5.09 (s, 2H), 7.07 (d, J = 8.1 Hz, 2H) , 7.08 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.65 (d, J = 8.0 Hz, 2H), 7.72 (d, J = 8.0 Hz, 2H), 7.84-7.87 (m, 3H)
3-17	DMSO-d6, 400MHz	0.72 (t, J = 7.4 Hz, 6H), 1.45-1.53 (m, 2H), 1.63-1.66 (m, 2H), 2.30-2.34 (m, 1H), 3.37 (s, 2H), 3.85 (s, 2H), 4.30 (s, 2H) , 5.09 (s, 2H), 7.08 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H), 7.37-7.44 (m, 6H), 7.86-7.90 (m, 3H)
3-18	DMSO-d6, 400MHz	0.72 (t, J = 7.4 Hz, 6H), 1.45-1.53 (m, 2H), 1.63-1.66 (m, 2H), , 2.26 (s, 6H), 2.30-2.40 (m, 1H), 3.48 (s, 2H), 3.89 (s, 2H), 4.25 (s, 2H), 5.09 (s, 2H), 6.92 (s, 1H), 7.03-7.08 (m, 4H), 7.20 (d, J = 8.0 Hz, 2H), 7.38 (d, J = 8.0 Hz, 2H), 7.86-7.91 (m, 3H)

Ejemplo	solvente, Hz	RMN (δ)
3-19	DMSO-d6, 400MHz	0.81 (t.J = 7.3 Hz, 6H), 1.05-1.13 (m, 4H), 1.48-1.57 (m, 4H), 2.50-2.56 (m, 1H), 3.45 (s, 2H), 4.00 (s, 2H), 4.23 (s, 2H), 5.07 (s, 2H), 7.06 (d, J = 9.2 Hz, 2H), 7.19 (d, J = 5.6 Hz, 2H), 7.36-7.37 (m, 1H), 7.35-7.37 (m, 2H), 7.57-7.60 (m, 1H), 7.81-7.85 (m, 4H), 8.48-8.49 (m, 1H)
3-20	DMSO-d6, 300MHz	0.72 (t, J = 7.4 Hz, 6H), 1.48-1.55 (m, 2H), 1.61-1.68 (m, 2H), 2.30-2.33 (m, 1H), 3.46 (s, 2H), 4.02 (s, 2H), 4.23 (s, 2H), 5.09 (s, 2H), 7.07 (d, J = 11.6 Hz, 2H), 7.18 (d, J = 8.1 Hz, 2H), 7.26-7.29 (m, 1H), 7.39 (d, J = 9.0 Hz, 2H), 7.57 (d, J = 9.0 Hz, 1H), 7.80-7.87 (m, 4H), 8.50 (d, J = 3.9 Hz, 1H)
3-21	DMSO-d6, 300MHz	0.80 (t, J = 7.2 Hz, 6H), 0.99-1.19 (m, 4H), 1.42-1.62 (m, 4H), 2.29 (s, 3H), 2.46-2.58 (m, 1H), 3.45 (s, 2H), 4.01 (s, 2H), 4.24 (s, 2H), 5.19 (s, 2H), 7.10 (s, 2H), 7.18 (d, J = 8.1 Hz, 2H), 7.25-7.30 (m, 1H), 7.39 (d, J = 8.1 Hz, 2H), 7.57 (d, J = 7.8 Hz, 1H), 7.80 (dt, J = 1.9, 7.8 Hz, 1H), 7.90 (s, 1H), 7.93 (s, 1H), 8.49-8.51 (m, 1H)
3-22	DMSO-d6, 400MHz	0.81 (t.J = 7.3 Hz, 6H), 1.05-1.13 (m, 4H), 1.48-1.57 (m, 4H), 2.50-2.56 (m, 1H), 4.09 (s, 2HX0.55), 4.21 (s, 2HX0.45), 4.80 (s, 2HX0.45), 4.97 (s, 2HX0.55), 5.09 (s, 2H), 7.08 (d, J = 9.2 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 7.36-7.38 (m, 3H), 7.46-7.48 (m, 4H), 7.87-7.89 (m, 3H)
3-23	DMSO-d6, 300MHz	0.72 (t, J = 7.4 Hz, 6H), 1.45-1.53 (m, 2H), 1.63-1.66 (m, 2H), 2.33-2.36 (m, 4H), 4.10 (s, 1H), 4.20 (s, 1H), 4.82 (s, 1H), 4.94 (s, 1H), 5.10 (s, 2H), 7.09 (d, J = 9.0 Hz, 2H), 7.18 (d, J = 8.1 Hz, 2H), 7.26-7.28 (m, 3H), 7.37-7.40 (m, 3H), 7.86-7.91 (m, 3H)

Ejemplo	solvente, Hz	RMN (δ)
3-24	DMSO-d6, 400MHz	0.81 (t,J = 7.3 Hz, 6H), 1.05-1.13 (m, 4H), 1.48-1.57 (m, 4H), 2.50-2.56 (m, 1H), 3.78 (s, 3H), 4.11 (s, 2H), 4.86-4.92 (m, 2H), 5.08 (s, 2H), 7.02 (d, J = 8.0 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 4.0 Hz, 2H), 7.36-7.41 (m, 4H), 7.86-7.96 (m, 3H)
3-25	DMSO-d6, 300MHz	0.79 (t, J = 7.4 Hz, 6H), 0.96-1.17 (m, 4H), 1.41-1.62 (m, 4H), 2.29 (s, 3H), 2.46-2.57 (m, 1H), 3.05-3.22 (m, 2H), 3.91 (d, J = 15.5 Hz, 1H), 3.95-3.99 (m, 1H), 4.09 (d, J = 15.5 Hz, 1H), 4.26 (d, J = 15.5 Hz, 1H), 4.40 (d, J = 15.5 Hz, 1H), 5.20 (s, 2H), 7.02-7.19 (m, 8H), 7.39 (d, J = 8.3 Hz, 2H), 7.92 (s, 1H)
3-26	DMSO-d6, 400MHz	0.81 (t, J = 7.3 Hz, 6H), 1.04-1.15 (m, 4H), 1.46-1.59 (m, 4H), 2.52-2.57 (m, 1H), 3.10 (dd, J = 3.5, 16.2 Hz, 1H), 3.17 (dd, J = 6.0, 16.4 Hz, 1H), 3.92 (d, J = 15.8 Hz, 1H), 3.94-3.97 (m, 1H), 4.09 (d, J = 15.8 Hz, 1H), 4.25 (d, J = 15.8 Hz, 1H), 4.39 (d, J = 15.8 Hz, 1H), 5.08 (s, 2H), 7.02-7.16 (m, 6H), 7.18 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H), 7.86 (s, 1H), 7.87 (d, J = 8.8 Hz, 2H)
3-27	DMSO-d6, 400MHz	0.84 (s, 9H), 2.42 (s, 3H), 3.03 (s, 3H), 3.35 (s, 2H), 3.85 (s, 2H), 4.15 (s, 2H), 4.58 (s, 2H), 6.76 (d, J = 8.8 Hz, 2H), 7.05 (d, J = 7.9 Hz, 2H), 7.11 (d, J = 8.1 Hz, 2H), 7.26 (t, J = 6.9 Hz, 1H), 7.34 (t, J = 7.4 Hz, 2H), 7.39 (d, J = 7.0 Hz, 2H), 7.65 (s, 1H), 7.70 (d, J = 8.8 Hz, 2H), 12.37 (s amplio, 1H).
3-28	DMSO-d6, 300MHz	1.18-1.20 (m, 2H), 1.24 (s, 9H), 1.55-1.76 (m, 2H), 2.28-2.47 (m, 1H), 2.98 (s, 3H), 3.25 (d,J = 6.0 Hz, 2H), 3.36 (s, 2H), 3.87 (s, 2H), 4.16 (s, 2H), 6.72 (d,J = 9.0 Hz, 2H), 7.12 (d,J = 9.0 Hz, 2H), 7.23-7.28 (m, 3H), 7.31-7.44 (m, 4H), 7.65 (s, 1H), 7.73 (d,J = 9.0 Hz, 2H)

Ejemplo	solvente, Hz	RMN (δ)
3-29	DMSO-d6, 300MHz	1.20-1.45 (m, 5H), 1.65-1.80 (m, 5H), 1.40-1.45 (m, 1H), 3.03 (s, 3H), 3.35 (s, 2H), 3.86 (s, 2H), 4.15 (s, 2H), 4.56 (s, 2H), 6.76 (d, J = 12.0 Hz, 2H), 7.09-7.16 (m, 4H), 7.26-7.39 (m, 5H), 7.66-7.72 (m, 3H)
3-30	DMSO-d6, 300MHz	1.20-1.40 (m, 5H), 1.60-1.80 (m, 5H), 2.45-2.50 (m, 1H), 2.51 (t, J = 6.0 Hz, 2H), 2.77 (t, J = 6.0 Hz, 2H), 3.02 (s, 3H), 3.69 (s, 2H), 3.92 (s, 2H), 4.56 (s, 2H), 6.75 (d, J = 9.0 Hz, 2H), 7.09-7.16 (m, 4H), 7.31-7.41 (m, 5H), 7.64 (s, 1H), 7.71 (d, J = 9.0 Hz, 2H)
3-31	DMSO-d6, 400MHz	0.84 (s, 9H), 2.42 (s, 2H), 2.87 (s, 3H), 3.31 (s, 2H), 3.35 (s, 2H), 3.86 (s, 2H), 4.15 (s, 2H), 6.72 (d, J = 9.0 Hz, 2H), 7.03 (d, J = 7.9 Hz, 2H), 7.14 (d, J = 7.9 Hz, 2H), 7.23-7.29 (m, 1H), 7.32-7.44 (m, 4H), 7.65 (s, 1H), 7.72 (d, J = 9.0 Hz, 2H), 12.40 (s amplio, 1H).
3-32	DMSO-d6, 300MHz	0.89 (d, J = 6.5 Hz, 3H), 1.01-1.05 (m, 2H), 1.30-1.45 (m, 3H), 1.70-1.75 (m, 4H), 3.35 (s, 2H), 3.86 (s, 2H), 4.15 (s, 2H), 4.55 (s, 2H), 6.76 (d, J = 9.0 Hz, 2H), 7.09-7.16 (m, 4H), 7.26-7.29 (m, 1H), 7.35-7.41 (m, 4H), 7.65 (s, 1H), 7.71 (d, J = 8.9 Hz, 2H)
3-33	DMSO-d6, 300MHz	1.55-1.64 (m, 6H), 1.92-2.03 (m, 2H), 2.50-2.55 (m, 1H), 3.35 (s, 2H), 3.86 (s, 2H), 4.15 (s, 2H), 4.57 (s, 2H), 4.83 (d,J = 15.0 Hz, 1H), 6.77 (d,J = 9.0 Hz, 2H), 7.13-7.16 (m, 4H), 7.32-7.39 (m, 4H), 7.65 (s, 1H), 7.71 (d,J = 8.8 Hz, 2H)
3-34	DMSO-d6, 400MHz	1.12-1.21 (m, 2H), 1.32-1.43 (m, 2H), 1.78 (d,J = 12.0 Hz, 4H), 2.40-2.50 (m, 2H), 2.96 (s, 3H), 3.24 (d,J = 4.0 Hz, 2H), 3.35 (s, 2H), 3.85 (s, 2H), 4.14 (s, 2H), 6.69 (d,J = 8.0 Hz, 2H), 7.63 (s, 1H), 7.70 (d,J = 8.0 Hz, 2H)

Ejemplo	solvente, Hz	RMN (δ)
3-35	DMSO-d6, 300MHz	0.92 (s, 3H), 0.94 (s, 3H), 1.23-1.63 (m, 8H), 2.33-2.40 (m, 1H), 3.02 (s, 3H), 3.35 (s, 2H), 3.85 (s, 2H), 4.14 (s, 2H), 4.55 (s, 2H), 6.75 (d, J = 6.7 Hz, 2H), 7.10 (d, J = 6.2 Hz, 2H), 7.17 (d, J = 6.0 Hz, 2H), 7.26 (t, J = 5.3 Hz, 1H), 7.32-7.40 (m, 4H), 7.64 (s, 1H), 7.70 (d, J = 6.7 Hz, 2H), 12.39 (s amplio, 1H)
3-36	DMSO-d6, 300MHz	0.78 (t, J = 7.3 Hz, 6H), 1.00-1.18 (m, 4H), 1.38-1.59 (m, 4H), 2.40-2.58 (m, 1H), 3.03 (s, 3H), 3.32 (s, 2H), 3.86 (s, 2H), 4.15 (s, 2H), 4.57 (s, 2H), 6.77 (d, J = 8.9 Hz, 2H), 7.06-7.15 (m, 4H), 7.21-7.44 (m, 5H), 7.66 (s, 1H), 7.72 (d, J = 8.8 Hz, 2H).
3-37	DMSO-d6, 300MHz	3.08 (s, 3H), 3.35 (s, 2H), 3.86 (s, 2H), 4.15 (s, 2H), 4.66 (s, 2H), 6.79 (d, J = 8.6 Hz, 2H), 7.22-7.46 (m, 10H), 7.60-7.65 (m, 4H), 7.67 (s, 1H), 7.73 (d, J = 9.0 Hz, 2H)
3-38	DMSO-d6, 300MHz	1.14-1.43 (m, 5H), 1.63-1.82 (m, 5H), 2.38-2.49 (m, 1H), 2.94 (s, 2H), 3.02 (s, 3H), 3.90 (s, 2H), 4.19 (s, 2H), 4.55 (s, 2H), 6.75 (d, J = 9.0 Hz, 2H), 7.11 (d, J = 8.3 Hz, 2H), 7.15 (d, J = 8.3 Hz, 2H), 7.21 (t, J = 7.2 Hz, 1H), 7.31 (t, J = 7.3 Hz, 2H), 7.39 (d, J = 7.2 Hz, 2H), 7.58 (s, 1H), 7.70 (d, J = 9.0 Hz, 2H)
3-39	DMSO-d6, 400MHz	0.85 (d, J = 6.8 Hz, 6H), 1.75-1.81 (m, 1H), 2.39 (d, J = 6.8 Hz, 2H), 3.02 (s, 3H), 3.34 (s, 2H), 3.85 (s, 2H), 4.14 (s, 2H), 4.56 (s, 2H), 6.76 (d, J = 8.0 Hz, 2H), 7.08-7.10 (m, 4H), 7.20-7.25 (m, 1H), 7.33-7.40 (m, 4H), 7.64 (s, 1H), 7.69 (d, J = 8.0 Hz, 2H)
3-40	DMSO-d6, 400MHz	0.78 (t, J = 7.3 Hz, 6H), 0.99-1.15 (m, 4H), 1.40-1.56 (m, 4H), 2.43-2.52 (m, 1H), 2.93 (s, 2H), 3.02 (s, 3H), 3.90 (s, 2H), 4.19 (s, 2H), 4.56 (s, 2H), 6.75 (d, J = 9.1 Hz, 2H), 7.08 (d, J = 8.3 Hz, 2H), 7.11 (d, J = 8.3 Hz, 2H), 7.20 (t, J = 7.3 Hz, 1H), 7.30 (t, J = 7.3 Hz, 2H), 7.38 (d, J = 7.3 Hz, 2H), 7.58 (s, 1H), 7.69 (d, J = 9.1 Hz, 2H)

Ejemplo	solvente, Hz	RMN (δ)
3-41	DMSO-d6, 300MHz	0.97 (s, 9H), 2.89 (s, 2H), 3.02 (s, 3H), 3.86 (s, 2H), 4.15 (s, 2H), 4.56 (s, 2H), 6.75 (d, J = 8.87 Hz, 2H), 7.13 (d, J = 8.25 Hz, 2H), 7.25-7.40 (m, 7H), 7.67 (s, 1H), 7.71 (d, J = 8.87, 2H)
3-42	DMSO-d6, 400MHz	0.86 (d, J = 6.72, 6H), 1.40-1.46 (m, 2H), 1.61-1.71 (m, 1H), 2.90 (d, J = 7.64 Hz, 1H), 2.92 (d, J = 7.64 Hz, 1H), 3.03 (s, 3H), 3.85 (s, 2H), 4.15 (s, 2H), 4.57 (s, 2H), 6.74 (d, J = 9.04 Hz, 2H), 7.14 (d, J = 8.36 Hz, 2H), 7.24-7.28 (m, 3H), 7.32-7.40 (m, 4H), 7.66 (s, 1H), 7.70 (d, J = 9.04, 2H)
3-43	DMSO-d6, 300MHz	0.81 (t, J = 7.2 Hz, 6H), 1.44 (tc, J = 7.8, 7.2 Hz, 4H), 3.19 (dd, J = 7.8, 7.8 Hz, 4H), 3.34 (s, 3H), 3.36 (s, 2H), 3.86 (s, 2H), 4.17 (s, 2H), 6.40 (d, J = 8.7 Hz, 2H), 7.12 (d, J = 9.0 Hz, 2H), 7.17 (d, J = 8.7 Hz, 2H), 7.21-7.43 (m, 5H), 7.84 (d, J = 9.0 Hz, 2H), 8.00 (s, 1H), 12.38 (s amplio, 1H).
3-44	DMSO-d6, 300MHz	1.12-1.20 (m, 15H), 2.80-2.89 (m, 2H), 3.24 (s, 2H), 3.15-3.52 (m, 2H), 3.82 (s, 2H), 4.15 (s, 2H), 4.52 (s, 2H), 6.70 (d,J = 9.0 Hz, 2H), 7.13-7.22 (m, 8H), 7.31 (d,J = 9.0 Hz, 2H), 7.61 (s, 1H), 7.68 (d,J = 9.0 Hz, 2H)
3-45	DMSO-d6, 300MHz	1.15-1.19 (m, 18H), 2.76-2.89 (m, 1H), 3.79 (s, 2H), 4.11 (s, 2H), 4.27-4.33 (m, 1H), 4.38 (s, 2H), 6.69 (d,J = 9.0 Hz, 2H), 7.15-7.32 (m, 8H), 7.60-7.66 (m, 3H)
3-46	DMSO-d6, 300MHz	1.14 (d,J = 6.0 Hz, 6H), 1.17 (s, 9H), 1.24 (d,J = 6.0 Hz, 6H), 2.74-2.90 (m, 1H), 3.79 (s, 2H), 4.12 (s, 2H), 4.23-4.36 (m, 1H), 4.38 (s, 2H), 6.68 (d,J = 6.0 Hz, 2H), 7.14-7.17 (m, 3H), 7.27-7.42 (m, 4H), 7.60-7.72 (m, 3H)
3-47	DMSO-d6, 400MHz	0.82 (d, J = 19.6 Hz, 6H), 1.75-1.82 (m, 1H), 2.40 (d, J = 14.4 Hz, 2H), 3.03 (s, 3H), 3.34 (s, 2H), 3.84 (s, 2H), 4.26 (s, 2H), 4.56 (s, 2H), 6.77 (d, J = 8.0 Hz, 2H), 7.08-7.11 (m, 4H), 7.40-7.41 (m, 4H), 7.64 (s, 1H), 7.69 (d, J = 8.0 Hz, 2H)

Ejemplo	solvente, Hz	RMN (δ)
3-48	DMSO-d6, 300MHz	0.79 (t, J = 6.0 Hz, 6H), 1.04-1.13 (m, 4H), 1.48-1.56 (m, 4H), 2.49-2.51 (m, 1H), 3.05 (s, 3H), 3.44 (m, 2H), 3.91 (s, 2H), 4.22 (s, 2H), 4.62 (s, 2H), 6.78 (d,J = 9.0 Hz, 1H), 7.15 (d,J = 9.0 Hz, 2H), 7.20-7.24 (m, 3H), 7.30-7.35 (m, 5H), 7.69-7.74 (m, 2H)
3-49	DMSO-d6, 300MHz	3.05 (s, 3H), 3.36 (s, 2H), 3.85 (s, 2H), 4.14 (s, 2H), 4.61 (s, 2H), 6.74-6.79 (m, 2H), 7.20-7.42 (m, 9H), 7.66 (s, 1H), 7.72 (d,J = 6.0 Hz, 2H)
3-50	DMSO-d6, 300MHz	3.04 (s, 3H), 3.42 (s, 2H), 4.02 (s, 2H), 4.22 (s, 2H), 4.61 (s, 2H), 6.76 (d,J = 6.0 Hz, 2H), 7.20-7.44 (m, 8H), 7.64-7.72 (m, 4H)
3-51	DMSO-d6, 300MHz	3.05 (s, 3H), 3.40 (s, 2H), 3.87 (s, 2H), 4.13 (s, 2H), 4.62 (s, 2H), 6.77 (d,J = 9.0 Hz, 2H), 7.20-7.45 (m, 6H), 7.58-7.74 (m, 6H)
3-52	DMSO-d6, 300MHz	0.89 (d, J = 6.0 Hz, 3H), 1.00-1.80 (m, 2H), 1.33-1.46 (m, 3H), 1.72-1.75 (m, 4H), 2.35-2.43 (m, 1H), 2.95 (s, 2H), 3.02 (s, 3H), 4.10 (s, 2H), 4.22 (s, 2H), 4.55 (s, 2H), 6.74 (d, J = 9.1 Hz, 2H), 7.09-7.11 (m, 4H), 7.16-7.22 (m, 1H), 7.57-7.79 (m, 5H), 8.45 (d, J = 4.1 Hz, 2H)
3-53	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.97-1.16 (m, 4H), 1.36-1.59 (m, 4H), 2.43-2.53 (m, 1H), 3.03 (s, 3H), 3.44 (s, 2H), 4.00 (s, 2H), 4.21 (s, 2H), 4.57 (s, 2H), 6.77 (d, J = 9.1 Hz, 2H), 7.09 (d, J = 8.7 Hz, 2H), 7.12 (d, J = 8.7 Hz, 2H), 7.28 (dd, J = 7.5, 4.5 Hz, 1H), 7.57 (d, J = 7.5 Hz, 1H), 7.65 (s, 1H), 7.71 (d, J = 9.1 Hz, 2H), 7.81 (dt, J = 1.9, 7.5 Hz, 1H), 8.50 (dd, J = 4.5, 1.9 Hz, 1H)
3-54	DMSO-d6, 300MHz	3.04 (s, 3H), 3.39 (s, 2H), 4.21 (s, 2H), 4.36 (s, 2H), 4.61 (s, 2H), 6.76 (d,J = 9.0 Hz, 2H), 7.20-7.35 (m, 5H), 7.44-7.72 (m, 9H), 7.85-7.91 (m, 2H), 8.41-8.444 (m, 1H)

Ejemplo	solvente, Hz	RMN (δ)
3-55	DMSO-d6, 300MHz	3.05 (s, 3H), 3.51 (s, 2H), 4.22 (s, 2H), 4.27 (s, 2H), 4.61 (s, 2H), 6.76 (d,J = 9.0 Hz, 2H), 7.23 (t, J = 9.0 Hz, 3H), 7.32 (t, J = 9.0 Hz, 2H), 7.57-7.82 (m, 7H), 7.98 (t, J = 6.0 Hz, 2H), 8.42 (d,J = 9.0 Hz, 1H)
3-56	DMSO-d6, 300MHz	3.06 (s, 3H), 3.96 (s, 1H), 4.13 (d,J = 12.0 Hz, 2H), 4.44 (s, 1H), 4.63 (s, 2H), 4.82 (s, 1H), 5.10 (s, 1H), 6.78 (d,J = 9.0 Hz, 2H), 7.21-7.37 (m, 7H), 7.52 (d,J = 6.0 Hz, 1H), 7.66-7.76 (m, 4H), 7.96-7.98 (m, 1H)
3-57	DMSO-d6, 400MHz	0.84 (t.J = 7.3 Hz, 6H), 1.73-1.78 (m, 1H), 2.40 (d, J = 7.2 Hz, 2H), 3.03 (s, 3H), 3.70 (s, 1H), 3.90 (s, 1H), 4.07 (s, 1H), 4.34 (s, 1H), 4.57 (s, 2H), 4.78 (s, 1H), 5.02 (s, 1H), 6.75-6.77 (m, 2H), 7.10-7.12 (m, 4H), 7.24-7.27 (m, 2H), 7.33-7.36 (m, 2H), 7.64-7.71 (m, 3H)
3-58	DMSO-d6, 400MHz	0.846 (t, J = 7.4H, 6H), 1.18 (t, J = 8.4 Hz, 6H), 1.76-1.81 (m, 1H), 2.40 (d, J = 6.8 Hz, 2H), 2.82-2.86 (m, 1H), 3.03 (s, 3H), 3.63 (s, 1H), 3.83 (s, 1H), 4.06 (s, 1H), 4.30 (s, 1H), 4.55 (s, 2H), 4.78 (s, 1H), 4.99 (s, 1H), 6.75-6.77 (m, 2H), 7.07-7.16 (m, 8H), 7.64-7.72 (m, 3H)
3-59	DMSO-d6, 400MHz	0.82-0.90 (m, 12H), 1.74-1.81 (m, 1H), 2.02-2.04 (m, 1H), 2.15 (d, J = 8.0 Hz, 1H), 2.33 (d, J = 8.0 Hz, 1H), 2.39 (d, J = 7.0 Hz, 2H), 3.02 (s, 3H), 4.03 (s, 1H), 4.24 (s, 1H), 4.56 (s, 2H), 4.74 (s, 1H), 4.91 (s, 1H), 6.72-6.76 (m, 2H), 7.05-7.11 (m, 4H), 7.61-7.70 (m, 3H)
3-60	DMSO-d6, 300MHz	0.85 (s, 9H), 2.43 (s, 2H), 3.04 (s, 3H), 4.21 (s, 2H), 4.59 (s, 2H), 4.90 (s, 2H), 6.77 (d, J = 8.9 Hz, 2H), 6.96 (d, J = 7.3 Hz, 1H), 7.07 (d, J = 8.2 Hz, 2H), 7.13 (d, J = 8.1 Hz, 2H), 7.24 (dd, J = 7.9, 7.9 Hz, 2H), 7.45 (d, J = 7.6 Hz, 2H), 7.67 (s, 1H), 7.73 (d, J = 8.8 Hz, 2H), 8.79 (s, 1H), 12.58 (s amplio, 1H).

Ejemplo	solvente, Hz	RMN (δ)
3-61	DMSO-d6, 400MHz	0.83 (d, J = 12.0 Hz, 6H), 1.75-1.82 (m, 1H) , 2.40 (d, J = 16.0 Hz, 2H), 3.03 (s, 3H), 4.07 (s, 1H), 4.19 (s, 1H), 4.57 (s, 2H), 4.77 (s, 1H), 4.93 (s, 1H), 6.76 (d, J = 8.0 Hz, 2H), 7.09-7.12 (m, 4H), 7.36-7.37 (m, 1H), 7.45-7.48 (m, 4H), 7.67-7.71 (m, 3H)
3-62	DMSO-d6, 400MHz	0.81 (t.J = 7.3 Hz, 6H), 1.05-1.13 (m, 4H), 1.48-1.57 (m, 4H), 2.31 (s, 3H), 2.50-2.56 (m, 1H), 3.00 (s, 3H), 3.92 (s, 2HX0.58), 4.15 (s, 2HX0.42), 4.57 (s, 2H), 4.78 (s, 2HX0.42), 4.90 (s, 2HX0.58), 6.77 (d, J = 8.0 Hz, 2H), 7.07-7.13 (m, 4H), 7.23-7.39 (m, 4H), 7.69-7.73 (m, 3H)
3-63	DMSO-d6, 400MHz	0.81 (t.J = 7.3 Hz, 6H), 1.05-1.13 (m, 4H), 1.21 (d, J = 8.0 Hz, 6H), 1.42-1.52 (m, 4H), 2.48-2.50 (m, 1H), 2.89-2.93 (m, 1H), 3.20 (s, 3H), 3.45 (s, 2H), 4.57 (s, 2H), 4.88 (s, 2H), 6.77 (d, J = 8.0 Hz, 2H), 7.08-7.13 (m, 4H), 7.26 (d, J = 8.0 Hz, 2H), 7.40 (d, J = 8.0 Hz, 2H), 7.66 (s, 1H), 7.73 (d, J = 8.0 Hz, 2H)
3-64	DMSO-d6, 300MHz	0.79 (t, J = 9.0 Hz, 6H), 1.02-1.12 (m, 4H), 1.43-1.54 (m, 4H), 2.96-2.06 (m, 5H), 3.78 (d,J = 15.0 Hz, 1H), 4.16 (d,J = 15.0 Hz, 1H), 4.56 (s, 2H), 4.72-4.76 (m, 1H), 6.76 (d,J = 9.0 Hz, 2H), 7.05-7.12 (m, 7H), 7.48 (s, 1H), 7.68 (d,J = 9.0 Hz, 2H)
3-65	DMSO-d6, 300MHz	1.15-1.86 (m, 13H), 2.12-2.29 (m, 3H), 2.39-2.48 (m, 1H), 2.82-2.91 (m, 2H), 3.03 (s, 3H), 3.81 (s, 2H), 4.56 (s, 2H), 6.75 (d, J = 9.1 Hz, 2H), 7.11 (d, J = 8.4 Hz, 2H), 7.16 (d, J = 8.4 Hz, 2H), 7.64 (s, 1H), 7.71 (d, J = 8.8 Hz, 2H), 12.11 (s amplio, 1H)
3-66	DMSO-d6, 300MHz	1.20-1.82 (m, 14H), 2.00-2.12 (m, 2H), 2.16-2.20 (m, 1H), 2.45-2.50 (m, 1H), 2.78-2.82 (m, 1H), 2.90-2.95 (m, 1H), 3.02 (s, 3H), 3.78 (s, 2H), 4.55 (s, 2H), 6.75 (d, J = 9.0 Hz, 2H), 7.09-7.16 (m, 4H), 7.62 (s, 1H), 7.70 (d, J = 12.0 Hz, 2H)

Ejemplo	solvente, Hz	RMN (δ)
3-67	DMSO-d6, 300MHz	1.20-1.40 (m, 5H), 1.60-1.80 (m, 7H), 2.20-2.50 (m, 5H), 2.80-2.90 (m, 2H), 3.03 (s, 3H), 3.81 (s, 2H), 4.56 (s, 2H), 6.75 (d, J = 9.0 Hz, 2H), 7.09-7.14 (m, 4H), 7.25-7.28 (m, 1H), 7.35-7.42 (m, 4H), 7.63 (s, 1H), 7.70 (d, J = 8.9 Hz, 2H)
3-68	DMSO-d6, 300MHz	0.84 (d, J = 6.6 Hz, 6H), 1.02-1.50 (m, 12H), 1.65-1.81 (m, 5H), 1.95-2.04 (m, 2H), 2.15-2.26 (m, 2H), 2.39-2.49 (m, 1H), 2.69-2.79 (m, 2H), 3.03 (s, 3H), 3.78 (s, 2H), 4.56 (s, 2H), 6.75 (d, J = 9.1 Hz, 2H), 7.10-7.17 (m, 4H), 7.63 (s, 1H), 7.70 (d, J = 8.8 Hz, 2H)
3-69	DMSO-d6, 300MHz	0.89 (d, J = 6.0 Hz, 3H), 1.00-1.10 (m, 2H), 1.30-1.40 (m, 3H), 1.72-1.95 (m, 6H), 2.30-2.50 (m, 5H), 2.80-2.90 (m, 2H), 3.03 (s, 3H), 3.81 (s, 2H), 4.56 (s, 2H), 6.75 (d, J = 9.0 Hz, 2H), 7.09-7.17 (m, 4H), 7.25-7.30 (m, 1H), 7.32-7.37 (m, 4H), 7.64 (s, 1H), 7.70 (d, J = 11.7 Hz, 2H)
3-70	DMSO-d6, 300MHz	1.08-1.19 (m, 2H), 1.30-1.44 (m, 2H), 1.57-1.67 (m, 2H), 2.35-2.44 (m, 2H), 2.75 (d,J = 8.0 Hz, 2H), 2.96 (s, 3H), 3.25-3.30 (m, 4H), 3.74 (s, 2H), 6.69 (d,J = 8.0 Hz, 2H), 7.08 (t, J = 4.0 Hz, 1H), 7.18-7.23 (m, 5H), 7.28 (d,J = 8.0 Hz, 2H), 7.37 (d,J = 8.0 Hz, 2H), 7.59 (s, 1H), 7.70 (d,J = 12.0 Hz, 2H)
3-71	DMSO-d6, 300MHz	0.89 (d, J = 4.8 Hz, 3H), 1.01-1.10 (m, 2H), 1.30-1.50 (m, 3H), 1.70-1.80 (m, 4H), 3.10-3.20 (m, 1H), 3.10-3.20 (m, 2H), 3.88-4.11 (m, 3H), , 4.30 (dd, J = 37.7, 11.6 Hz, 2H), 4.56 (s, 2H), 6.76 (d, J = 9.0 Hz, 2H), 7.04-7.17 (m, 8H), 7.64 (s, 1H), 7.72 (d, J = 8.8 Hz, 2H)
3-72	DMSO-d6, 300MHz	0.84 (d, J = 6.8 Hz, 6H), 1.70-1.80 (m, 1H), 2.39 (d, J = 4.4 Hz, 2H), 3.03 (s, 3H), 3.10-3.20 (m, 2H), 3.89-4.06 (m, 3H), 4.22 (d, J = 15.6 Hz, 1H), 4.36 (d, J = 15.6 Hz, 1H), 4.57 (s, 2H), 6.75 (d, J = 10.8 Hz, 2H), 7.03-7.15 (m, 8H), 7.64 (s, 1H), 7.71 (d, J = 10.0 Hz, 2H)

Ejemplo	solvente, Hz	RMN (δ)
3-73	DMSO-d6, 300MHz	0.79 (t, J = 7.4 Hz, 6H), 1.01-1.14 (m, 4H), 1.39-1.56 (m, 4H), 2.43-2.48 (m, 1H), 3.03 (s, 3H), 3.11-3.16 (m, 2H), 4.00 (ABc, J = 15.6, 41.6 Hz, 2H), 3.95-3.97 (m, 1H), 4.30 (ABc, J = 15.8, 50.1 Hz, 2H), 4.57 (s, 2H), 6.77 (d, J = 9.1 Hz, 2H), 7.02-7.16 (m, 8H), 7.65 (s, 1H), 7.73 (d, J = 8.6 Hz, 2H), 12.54 (s amplio, 1H)
3-74	DMSO-d6, 300MHz	0.85 (s, 9H), 2.43 (s, 2H), 3.04 (s, 3H), 3.10-3.20 (m, 2H), 3.92 (d, J = 16.1 Hz, 1H), 3.90-4.00 (m, 1H), 4.10 (d, J = 7.7 Hz, 1H), 4.23 (d, J = 15.7 Hz, 1H), 4.37 (d, J = 15.7 Hz, 1H), 4.59 (s, 2H), 6.77 (d, J = 8.9 Hz, 2H), 7.00-7.20 (m, 8H), 7.66 (s, 1H), 7.72 (d, J = 8.8 Hz, 2H), 12.50 (s amplio, 1H).
3-75	DMSO-d6, 400MHz	1.21-1.34 (m, 5H), 1.69-1.74 (m, 5H), 2.44-2.54 (m, 1H), 3.02 (s, 3H), 3.70 (s, 3H), 4.55 (s, 2H), 4.77 (s, 2H), 6.54 (s, 1H), 6.71 (d, J = 8.0 Hz, 2H), 6.87 (s, 1H), 7.11-7.14 (m, 5H), 7.64 (d, J = 8.0 Hz, 2H)
3-76	DMSO-d6, 300MHz	1.20-1.45 (m, 5H), 1.60-1.85 (m, 5H), 2.45-2.50 (m, 1H), 2.80-3.00 (m, 2H), 3.35-3.38 (m, 1H), 3.83 (d, J = 15.0 Hz, 1H), 4.09 (d, J = 15.0 Hz, 1H), 4.55 (s, 2H), 6.74 (d, J = 9.0 Hz, 2H), 7.09-7.25 (m, 9H), 7.53 (s, 1H), 7.67 (d, J = 9.0 Hz, 2H)
3-77	DMSO-d6, 400MHz	1.21-1.40 (m, 5H), 1.69-1.80 (m, 5H), 2.44-2.50 (m, 1H), 3.90-3.96 (m, 2H), 4.34 (s, 1H), 4.55 (s, 2H), 6.75 (d, J = 8.8 Hz, 2H), 7.12-7.14 (m, 4H), 7.28-7.40 (m, 5H), 7.60 (s, 1H), 7.69 (d, J = 8.3 Hz, 2H)
3-78	DMSO-d6, 400MHz	1.14 (d, J = 12.0 Hz, 3H), 1.20-1.40 (m, 5H), 1.65-1.80 (m, 5H), 2.44-2.50 (m, 1H), 3.05-3.08 (m, 1H), 3.85 (d, J = 16.0 Hz, 1H), 4.09 (d, J = 16.0 Hz, 1H), 4.75 (s, 2H), 6.74 (d, J = 8.0 Hz, 2H), 7.09-7.15 (m, 4H), 7.57 (s, 1H), 7.70 (d, J = 8.8 Hz, 2H)

Ejemplo	solvente, Hz	RMN (δ)
3-79	DMSO-d6, 400MHz	0.83 (d, J = 14.0 Hz, 6H), 1.78-1.90 (m, 1H), 2.39 (d, J = 5.6 Hz, 2H), 2.82-3.02 (m, 2H), 3.02 (s, 3H), 3.44-3.45 (m, 1H), 3.87 (d, J = 16.0 Hz, 1H), 4.11 (d, J = 16.0 Hz, 1H), 4.56 (s, 2H), 6.73 (d, J = 8.0 Hz, 2H), 7.08-7.11 (m, 4H), 7.27-7.30 (m, 4H), 7.55 (s, 1H), 7.67 (d, J = 10.8 Hz, 2H)
3-80	DMSO-d6, 300MHz	1.08-1.35 (m, 5H), 1.60-1.77 (m, 5H), 2.44-2.54 (m, 1H), 2.40 (s, 3H), 2.44-2.50 (m, 1H), 3.03 (s, 3H), 3.38 (s, 3H), 4.04 (s, 2H), 4.56 (s, 2H), 6.76 (d, J = 12.0 Hz, 2H), 7.09-7.17 (m, 5H), 7.66-7.72 (m, 2H)
3-81	DMSO-d6, 300MHz	1.14-1.45 (m, 5H), 1.63-1.83 (m, 5H), 2.29 (s, 3H), 2.39-2.49 (m, 1H), 2.43 (t, J = 7.2 Hz, 2H), 2.74 (t, J = 7.1 Hz, 2H), 3.03 (s, 3H), 3.87 (s, 2H), 4.56 (s, 2H), 6.76 (d, J = 8.8 Hz, 2H), 7.10-7.17 (m, 4H), 7.65 (s, 1H), 7.71 (d, J = 8.8 Hz, 2H)
3-82	DMSO-d6, 400MHz	1.19-1.41 (m, 5H), 1.67-1.77 (m, 5H), 2.26 (s, 3H), 2.44-2.47 (m, 1H), 3.03 (s, 3H), 3.66 (s, 2H), 3.88 (s, 2H), 4.56 (s, 2H), 6.76 (d, J = 9.2, 2H), 7.10-7.16 (m, 4H), 7.37 (d, J = 8.1, 2H), 7.66 (s, 1H), 7.71 (d, J = 8.6, 2H), 7.87 (d, J = 9, 2H)
3-83	DMSO-d6, 300MHz	1.16-1.41 (m, 5H), 1.67-1.81 (m, 5H), 2.41-2.48 (m, 1H), 3.03 (s, 3H), 3.07 (s, 3H), 4.56 (s, 2H), 4.84 (s, 2H), 6.68 (d, J = 6.9 Hz, 2H), 6.76 (d, J = 6.5 Hz, 2H), 7.10-7.17 (m, 4H), 7.57 (s, 1H), 7.68-7.73 (m, 4H)
3-84	DMSO-d6, 400MHz	1.13-1.41 (m, 5H), 1.65-1.81 (m, 5H), 2.40-2.48 (m, 1H), 3.03 (s, 3H), 3.20 (s, 3H), 4.56 (s, 2H), 5.14 (s, 2H), 6.75 (d, J = 9.0 Hz, 2H), 6.80 (d, J = 9.0 Hz, 1H), 7.09-7.15 (m, 4H), 7.59 (s, 1H), 7.70 (d, J = 9.0 Hz, 2H), 7.97 (dd, J = 2.3, 9.0 Hz, 1H), 8.64 (dd, J = 0.8, 2.4 Hz, 1H), 12.46 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
3-85	DMSO-d6, 400MHz	0.83 (d, J = 13.6 Hz, 6H), 1.70-1.80 (m, 1H), 2.32-2.37 (m, 5H), 2.90-3.00 (m, 2H), 3.02 (s, 3H), 3.60-3.70 (m, 1H), 3.98 (d, J = 16.0 Hz 1H), 4.14 (d, J = 16.0 Hz, 1H), 4.56 (s, 2H), 6.74 (d, J = 9.2 Hz, 2H), 7.08-7.11 (m, 4H), 7.18-7.20 (m, 1H), 7.25-7.27 (m, 4H), 7.56 (s, 1H), 7.67 (d, J = 8.0 Hz, 2H)
3-86	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.96-1.15 (m, 4H), 1.40-1.57 (m, 4H), 2.37 (s, 3H), 2.41-2.5 (m, 1H), 2.93 (dd, J = 14.1, 7.7, 1H), 3.02 (s, 3H), 3.06 (dd, J = 14.1, 7.7 Hz, 1H), 3.69 (t, J = 7.7 Hz, 1H), 4.00 (d, J = 15.8 Hz, 1H), 4.15 (d, J = 15.8 Hz, 1H), 4.56 (s, 2H), 6.76 (d, J = 8.9 Hz, 2H), 7.09 (d, J = 8.6 Hz, 2H), 7.12 (d, J = 8.6 Hz, 2H), 7.19-7.28 (m, 5H), 7.57 (s, 1H), 7.69 (d, J = 8.9 Hz, 2H)
3-87	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.96-1.15 (m, 4H), 1.40-1.57 (m, 4H), 2.34 (s, 3H), 2.42-2.5 (m, 1H), 3.02 (s, 3H), 3.83 (d, J = 15.3 Hz, 1H), 3.98 (d, J = 15.3 Hz, 1H), 4.50 (s, 1H), 4.56 (s, 2H), 6.76 (d, J = 8.7 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 7.33-7.48 (m, 5H), 7.64 (s, 1H), 7.70 (d, J = 8.7 Hz, 2H)
3-88	DMSO-d6, 400MHz	0.84 (s, 9H), 2.33 (s, 3H), 2.42 (s, 2H), 3.02 (s, 3H), 3.82 (d, J = 15.2 Hz, 1H), 3.96 (d, J = 15.6 Hz, 1H), 4.48 (s, 1H), .00 (s, 2H), 6.74 (d, J = 8.8 Hz, 2H), 7.05 (d, J = 7.6 Hz, 2H), 7.10 (d, J = 7.6 Hz, 2H), 7.32 (t, J = 7.2 Hz, 1H), 7.39 (t, J = 7.4 Hz, 2H), 7.45 (d, J = 8.9 Hz, 2H), 7.63 (s, 1H), 7.65 (d, J = 15.2 Hz, 2H).

Ejemplo	solvente, Hz	RMN (δ)
3-89	DMSO-d6, 400MHz	0.84 (s, 9H), 2.36 (s, 3H), 2.42 (s, 2H), 2.93 (dd, J = 14.2, 8.1 Hz, 1H), 3.02 (s, 3H), 3.05 (dd, J = 14.1, 7.2 Hz, 1H), 3.68 (t, J = 8.0 Hz, 1H), 4.01 (d, J = 12.0 Hz, 1H), 4.14 (d, J = 15.6 Hz, 1H), 4.57 (s, 2H), 6.74 (d, J = 9.0 Hz, 2H), 7.05 (d, J = 8.1 Hz, 2H), 7.10 (d, J = 8.1 Hz, 2H), 7.19 (c, J = 4.4 Hz, 1H), 7.26 (d, J = 4.6 Hz, 2H), 7.56 (s, 1H), 7.67 (d, J = 8.8 Hz, 2H), 12.48 (s amplio, 1H).
3-90	DMSO-d6, 400MHz	0.79 (t, J = 7.3 Hz, 6H), 1.00-1.14 (m, 4H), 1.41-1.57 (m, 4H), 2.44-2.48 (m, 1H), 3.03 (s, 3H), 3.51 (s, 4H), 4.16 (s, 2H), 4.57 (s, 2H), 6.76 (d, J = 9.0 Hz, 2H), 7.09 (d, J = 8.6 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 7.64 (s, 1H), 7.70 (d, J = 9.0 Hz, 2H)
3-91	DMSO-d6, 300MHz	0.83 (d, J = 5.0 Hz, 6H), 1.17-1.41 (m, 7H), 1.54-1.62 (m, 1H), 1.67-1.77 (m, 5H), 2.41-2.49 (m, 1H), 2.66-2.70 (m, 2H), 3.02 (s, 3H), 3.41 (s, 2H), 4.10 (s, 2H), 6.74 (d, J = 6.9 Hz, 2H), 7.09-7.15 (m, 4H), 7.61 (s, 1H), 7.69 (d, J = 6.6 Hz, 2H)
3-92	DMSO-d6, 300MHz	0.84 (d, J = 6.7 Hz, 6H), 0.91 (d, J = 17.6 Hz, 3H), 0.95-1.05 (m, 2H), 1.30-1.42 (m, 5H), 1.50-1.60 (m, 1H), 1.72-1.76 (m, 4H), 2.45-2.50 (m, 1H), 2.60-2.70 (m, 2H), 3.02 (s, 3H), 3.41 (s, 2H), 4.10 (s, 2H), 4.56 (s, 2H), 6.75 (d, J = 9.0 Hz, 2H), 7.09-7.17 (m, 4H), 7.62 (s, 1H), 7.70 (d, J = 8.8 Hz, 2H)
3-93	DMSO-d6, 400MHz	0.87-0.84 (m, 12H), 1.33-1.37 (m, 2H), 1.58-4.61 (m, 1H), 1.75-1.78 (m, 1H), 2.39 (d, J = 7.2 Hz, 2H), 2.65-2.69 (m, 2H), 3.02 (s, 3H), 3.40 (s, 2H), 4.09 (s, 2H), 4.56 (s, 2H), 6.74 (d, J = 9.2 Hz, 2H), 7.06-7.11 (m, 4H), 7.61 (s, 1H), 7.68 (d, J = 11.6 Hz, 2H)

Ejemplo	solvente, Hz	RMN (δ)
3-94	DMSO-d6, 400MHz	0.81 (t.J = 7.3 Hz, 6H), 1.05-1.13 (m, 4H), 1.48-1.57 (m, 4H), 2.50-2.56 (m, 1H), 3.00 (s, 3H), 4.56 (s, 2H), 5.61 (s, 2H), 6.78 (d, J = 8.8 Hz, 2H), 7.10-7.13 (m, 4H), 7.75 (d, J = 8.4 Hz, 2H), 7.81 (s, 1H), 7.97 (s, 1H), 8.63 (s, 1H), 8.71 (s, 1H)
3-95	DMSO-d6, 400MHz	0.81 (t.J = 7.3 Hz, 6H), 1.05-1.13 (m, 4H), 1.48-1.57 (m, 4H), 2.50-2.56 (m, 1H), 3.04 (s, 3H), 4.58 (s, 2H), 5.54 (s, 2H), 6.78 (d, J = 8.8 Hz, 2H), 7.10-7.13 (m, 4H), 7.19 (d, J = 8.0 Hz, 2H), 7.74 (d, J = 8.0 Hz, 2H), 7.80 (s, 1H), 7.91 (d, J = 9.2 Hz, 2H)
3-96	DMSO-d6, 400MHz	0.81 (t.J = 7.3 Hz, 6H), 1.05-1.13 (m, 4H), 1.48-1.57 (m, 4H), 2.50-2.56 (m, 1H), 3.03 (s, 3H), 4.57 (s, 2H), 4.74 (s, 2H), 6.76 (d, J = 9.2 Hz, 2H), 7.10-7.13 (m, 4H), 7.52 (d, J = 8.0 Hz, 2H) , 7.63 (s, 1H), 7.69 (d, J = 9.2 Hz, 2H), 7.83 (d, J = 8.0 Hz, 2H)
3-97	DMSO-d6, 300MHz	1.20-1.40 (m, 5H), 1.60-1.80 (m, 5H), 1.45-1.50 (m, 1H), 3.02 (s, 3H), 4.39 (d, J = 6.3 Hz, 2H), 4.55 (s, 2H), 6.73 (d, J = 9.0 Hz, 2H), 7.10-7.17 (m, 4H), 7.61-7.64 (m, 3H), 7.94 (d, J = 8.4 Hz, 2H), 8.11 (d, J = 8.4 Hz, 2H), 8.80 (t, J = 6.3 Hz, 1H)
3-98	DMSO-d6, 400MHz	0.92 (s, 3H), 0.95 (s, 3H), 1.40-1.61 (m, 8H), 2.31-2.41 (m, 1H), 2.85 (s, 3H), 3.03 (s, 3H), 4.56 (s, 2H), 4.65 (s, 2H), 6.74 (d, J = 8.82 Hz, 2H), 7.12 (d, J = 8.10 Hz, 2H), 7.18 (d, J = 8.10 Hz, 2H), 7.61 (d, J = 8.82 Hz, 2H), 7.69 (s, 1H), 7.97 (d, J = 8.36 Hz, 2H), 8.13 (d, J = 8.36, 2H)
3-99	DMSO-d6, 400MHz	0.92 (s, 3H), 0.95 (s, 3H), 1.40-1.61 (m, 8H), 2.31-2.41 (m, 1H), 2.91 (s, 3H), 3.03 (s, 3H), 4.04 (s, 2H), 4.57 (s, 2H), 4.67 (s, 2H), 6.76 (d, J = 8.84 Hz, 2H), 7.12 (d, J = 8.12 Hz, 2H), 7.18 (d, J = 8.12 Hz, 2H), 7.70 (s, 1H), 7.72 (d, J = 8.84 Hz, 2H)

Ejemplo	solvente, Hz	RMN (δ)
3-100	DMSO-d6, 300MHz	1.20-1.40 (m, 5H), 1.60-1.77 (m, 5H), 2.40-2.50 (m, 1H), 2.84 (s, 3H), 3.03 (s, 3H), 4.55 (s, 2H), 4.65 (s, 2H), 6.73 (d, J = 9.0 Hz, 2H), 7.90-7.16 (m, 4H), 7.61 (d, J = 8.4 Hz, 2H), 7.70 (s, 1H), 7.97 (d, J = 8.1 Hz, 2H), 8.13 (d, J = 8.1 Hz, 2H)
3-101	DMSO-d6, 300MHz	1.20-1.40 (m, 5H), 1.60-1.77 (m, 5H), 2.40-2.50 (m, 1H), 2.85 (s, 3H), 3.03 (s, 3H), 4.56 (s, 2H), 4.65 (s, 2H), 6.74 (d, J = 9.0 Hz, 2H), 7.09-7.17 (m, 4H), 7.62 (d, J = 8.7 Hz, 2H), 7.69 (s, 1H), 7.75 (t, J = 7.8 Hz, 1H), 8.09 (d, J = 8.8 Hz, 1H), 8.20 (d, J = 7.8 Hz, 1H), 8.28 (s, 1H)
3-102	DMSO-d6, 300MHz	1.20-1.40 (m, 5H), 1.60-1.80 (m, 5H), 1.45-1.50 (m, 1H), 2.90 (s, 3H), 3.03 (s, 3H), 3.97 (s, 2H), 4.56 (s, 2H), 4.66 (s, 2H), 6.76 (d, J = 8.7 Hz, 2H), 7.09-7.16 (m, 4H), 7.66-7.74 (m, 3H)
3-103	DMSO-d6, 300MHz	0.92 (s, 3H), 0.95 (s, 3H), 1.24-1.60 (m, 8H), 1.86-1.97 (m, 2H), 2.34-2.42 (m, 3H), 2.89 (s, 3H), 3.04 (s, 3H), 3.23-3.28 (m, 2H), 4.57 (s, 2H), 4.67 (s, 2H), 6.77 (d, J = 8.8 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.1 Hz, 2H), 7.70-7.74 (m, 3H), 12.10 (s amplio, 1H)
3-104	DMSO-d6, 300MHz	0.81 (d, J = 8.5 Hz, 6H), 0.83-0.95 (m, 1H), 1.20-1.45 (m, 5H), 1.60-1.80 (m, 5H), 2.40-2.50 (m, 1H), 3.00-3.07 (m, 5H), 4.22 (s, 2H), 4.56 (s, 2H), 4.73 (s, 2H), 6.76 (d, J = 9.0 Hz, 2H), 7.09-7.17 (m, 4H), 7.70-7.73 (m, 3H)
3-105	DMSO-d6, 300MHz	1.14-1.46 (m, 5H), 1.64-1.85 (m, 5H), 2.38-2.49 (m, 1H), 3.03 (s, 3H), 4.56 (s, 2H), 4.61 (d, J = 6.0 Hz, 2H), 6.76 (d, J = 9.1 Hz, 2H), 7.10-7.17 (m, 4H), 7.64 (s, 1H), 7.71 (d, J = 9.1 Hz, 2H), 9.61 (t, J = 6.2 Hz, 1H)
3-106	DMSO-d6, 300MHz	1.19-1.43 (m, 5H), 1.63-1.81 (m, 5H), 2.40-2.47 (m, 1H), 3.03 (s, 3H), 3.23 (s, 2H), 4.58 (d, J = 6.2 Hz, 2H), 6.76 (d, J = 8.8 Hz, 2H), 7.10-7.18 (m, 4H), 7.63 (s, 1H), 7.72 (d, J = 8.8 Hz, 2H), 8.92 (t, J = 5.8 Hz, 1H), 12.37 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
3-107	DMSO-d6, 300MHz-120□	1.17-1.45 (m, 5H), 1.66-1.85 (m, 5H), 2.44-2.52 (m, 1H), 3.01 (s, 3H), 3.03 (s, 3H), 4.52 (s, 2H), 4.87 (s, 2H), 6.80 (d, J = 8.8 Hz, 2H), 7.14 (s, 4H), 7.54 (d, J = 8.4 Hz, 2H), 7.57 (s, 1H), 7.71 (d, J = 8.8 Hz, 2H), 7.99 (d, J = 8.4 Hz, 2H)
3-108	DMSO-d6, 300MHz	0.89 (d, J = 6.6 Hz, 3H), 1.00-1.50 (m, 2H), 1.35-1.42 (m, 3H), 1.72-1.76 (m, 4H), 2.40-2.50 (m, 1H), 3.04 (s, 3H), 3.92 (d, J = 11.2 Hz, 2H), 4.50-4.56 (m, 4H), 5.40 (d, J = 6.0 Hz, 2H), 6.77 (d, J = 9.0 Hz, 2H), 7.09-7.17 (m, 4H), 7.30-7.40 (m, 5H), 7.70-7.76 (m, 3H)
3-109	DMSO-d6, 400MHz	1.21-1.41 (m, 5H), 1.65-1.80 (m, 5H), 1.45-1.50 (m, 1H), 2.93 (s, 3H), 3.03 (s, 3H), 3.69-3.80 (m, 2H), 4.56 (s, 2H), 4.71 (s, 2H), 6.75 (d, J = 11.6 Hz, 2H), 6.94-7.05 (m, 1H), 7.12-7.16 (m, 4H), 7.64 (s, 1H), 7.71 (d, J = 8.0 Hz, 2H)
3-110	DMSO-d6, 300MHz	1.15-1.25 (m, 4H), 162-1.76 (m, 6H), 3.68 (s, 4H), 4.39 (s, 2H), 5.21 (s, 2H), 7.09 (dd, J = 1.5, 9.0 Hz, 1H), 7.48-7.52 (m, 5H), 7.66-7.69 (m, 6H), 7.77 (s, 1H)
3-111	DMSO-d6, 300MHz	1.20-1.40 (m, 5H), 1.60-1.80 (m, 5H), 2.60-2.75 (m, 4H), 2.80-2.95 (m, 4H), 3.42 (s, 2H), 3.91 (s, 2H), 4.56 (s, 2H), 6.76 (d, J = 9.0 Hz, 2H), 7.09-7.16 (m, 4H), 7.69 (d, J = 4.9 Hz, 2H), 7.73 (s, 1H)
3-112	DMSO-d6, 300MHz	0.81 (t, J = 7.3 Hz, 6H), 0.99-1.21 (m, 4H), 1.41-1.65 (m, 4H), 2.48-2.61 (m, 1H), 2.96 (dd, J = 6.4, 16.2 Hz, 1H), 3.19 (dd, J = 3.8, 16.2 Hz, 1H), 3.68 (d, J = 15.1 Hz, 1H), 4.24-4.44 (m, 3H), 5.08 (s, 2H), 6.95 (d, J = 6.0 Hz, 1H), 6.98-7.11 (m, 6H), 7.19 (d, J = 8.3 Hz, 2H), 7.38 (d, J = 7.9 Hz, 2H), 7.80 (s, 1H), 7.87 (d, J = 8.7 Hz, 2H)

Ejemplo	solvente, Hz	RMN (δ)
3-113	DMSO-d6, 300MHz	0.80 (t, J = 7.2 Hz, 6H), 1.07-1.14 (m, 4H), 1.48-1.58 (m, 4H), 2.5-2.6 (m, 1H), 5.09 (s, 2H), 5.55 (s, 2H), 7.09 (d, J = 9.0 Hz, 2H), 7.19 (d, J = 7.8 Hz, 2H), 7.39 (d, J = 8.1 Hz, 2H), 7.77-7.79 (m, 1H), 7.91 (d, J = 8.7 Hz, 2H), 8.00 (s, 1H), 8.29 (d, J = 3.0 Hz, 1H), 8.60 (d, J = 1.5 Hz, 1H)
3-114	DMSO-d6, 400MHz	0.80 (t, J = 7.2 Hz, 6H), 1.04-1.14 (m, 4H), 1.48-1.58 (m, 4H),, 2.37 (s, 3H), 2.49-2.53 (m, 1H), 5.07 (s, 2H), 5.65 (s, 2H), 6.91 (dd, J = 8.6, 2.8 Hz, 1H), 6.95 (d, J = 2.5 Hz, 1H), 7.18 (d, J = 8.1 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H), 7.54 (d, J = 8.6 Hz, 1H), 7.73 (s, 1H), 7.95-7.96 (m, 1H), 8.63 (d, J = 3.0 Hz, 1H), 8.71 (d, J = 1.6 Hz, 1H)
3-115	DMSO-d6, 400MHz	0.80 (t, J = 7.2 Hz, 6H), 1.07-1.14 (m, 4H), 1.48-1.58 (m, 4H), 2.5-2.6 (m, 1H), 3.83 (s, 3H), 5.05 (s, 2H), 5.66 (s, 2H), 7.12 (d, J = 8.4 Hz, 1H), 7.20 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 7.50-7.54 (m, 2H), 7.99 (s, 1H), 8.08 (s, 1H), 8.63 (s, 1H), 8.71 (s, 1H)
3-116	DMSO-d6, 400MHz	0.80 (t, J = 7.2 Hz, 6H), 1.05-1.14 (m, 4H), 1.48-1.58 (m, 4H) , 2.37 (s, 3H), 3.58 (s, 2H), 3.63 (s, 2H), 4.26 (s, 2H), 5.07 (s, 2H), 6.88 (dd, J = 8.0, 4.0 Hz, 1H), 6.94 (d, J = 4.0 Hz, 1H), 7.04 (t, J = 6.0 Hz, 1H), 7.18 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 8.0 Hz, 1H), 7.28 (d, J = 8.0 Hz, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 8.0 Hz, 1H), 7.56-7.58 (m, 3H)
3-117	DMSO-d6, 400MHz	0.80 (t, J = 7.2 Hz, 6H), 1.05-1.14 (m, 4H), 1.16 (d, t=7.0 Hz, 6H), 1.48-1.58 (m, 4H), 2.37 (s, 3H), 2.50-2.55 (m, 1H), 2.8-2.90 (m, 1H), 3.53 (s, 4H), 4.23 (s, 2H), 5.06 (s, 2H), 6.88 (dd, J = 8.0, 4.0 Hz, 1H), 6.94 (d, J = 4.0 Hz, 1H), 7.05-7.19 (m, 4H), 7.36 (d, J = 8.0 Hz, 2H), 7.50-7.60 (m, 4H)

Ejemplo	solvente, Hz	RMN (δ)
3-118	DMSO-d6, 300MHz	0.81 (t, J = 7.4 Hz, 6H), 0.99-1.20 (m, 4H), 1.41-1.64 (m, 4H), 2.48-2.61 (m, 1H), 3.10 (dd, J = 2.6, 16.2 Hz, 1H), 3.18 (dd, J = 5.7, 16.9 Hz, 1H), 3.87-4.01 (m, 2H), 4.09 (d, J = 15.8 Hz, 1H), 4.25 (d, J = 15.8 Hz, 1H), 4.40 (d, J = 15.5 Hz, 1H), 5.09 (s, 2H), 7.00-7.23 (m, 8H), 7.38 (d, J = 8.3 Hz, 2H), 7.84-7.93 (m, 3H), 12.65 (s amplio, 1H)
3-119	DMSO-d6, 400MHz	0.80 (t, J = 7.2 Hz, 6H), 1.05-1.14 (m, 4H), 1.48-1.58 (m, 4H), 2.50-2.54 (m, 1H), 3.58 (s, 2H), 3.64 (s, 2H), 3.80 (s, 3H), 4.27 (s, 2H), 5.40 (s, 2H), 7.04 (t, J = 8.0 Hz, 1H), 7.08 (d, J = 8.0 Hz, 1H), 7.18 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.36 (d, J = 8.0 Hz, 2H), 7.46 (dd, J = 8.0, 4.0 Hz, 1H), 7.50 (d, J = 4.0 Hz, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.93 (s, 1H)
3-120	DMSO-d6, 400MHz	0.80 (t, J = 7.2 Hz, 6H), 1.05-1.14 (m, 4H), 1.16 (d, t=7.0 Hz, 6H), 1.48-1.58 (m, 4H), 2.50-2.55 (m, 1H), 2.80-2.90 (m, 1H), 3.56 (s, 2H), 3.63 (s, 2H), 3.80 (s, 3H), 4.26 (s, 2H), 5.03 (s, 2H), 7.08 (d, J = 8.0 Hz, 1H), 7.15-7.19 (m, 4H), 7.36 (d, J = 8.0 Hz, 2H), 7.44-7.50 (m, 4H), 7.93 (s, 1H)
3-121	DMSO-d6, 400MHz	0.80 (t, J = 7.2 Hz, 6H), 1.05-1.14 (m, 4H), 1.48-1.58 (m, 4H), 2.38 (s, 3H), 2.50-2.54 (m, 1H), 3.45 (s, 2H), 4.05 (s, 2H), 4.19 (s, 2H), 5.02 (s, 2H), 6.89 (d, J = 8.0 Hz, 1H), 6.94 (d, J = 4.0 Hz, 1H), 7.18 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.51-7.56 (m, 3H), 9.07 (d, J = 4.0 Hz, 2H)
3-122	DMSO-d6, 400MHz	0.81 (t, J = 7.3 Hz, 6H), 1.02-1.05 (m, 4H), 1.40-1.50 (m, 4H), 2.40 (s, 3H), 2.49-2.53 (m, 1H), 2.66 (s, 3H), 3.85 (s, 2H), 4.29 (s, 2H), 4.51 (s, 2H), 5.07 (s, 2H), 6.91 (dd, J = 8.0, 4.0 Hz, 1H), 6.96 (d, J = 4.0 Hz, 1H), 7.18 (d, J = 8.0 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.55 (s, 1H), 7.70 (s, 1H)

Ejemplo	solvente, Hz	RMN (δ)
3-123	DMSO-d6, 400MHz	0.81 (t, J = 7.3 Hz, 6H), 1.05-1.15 (m, 4H), 1.40-1.50 (m, 4H), 2.38 (s, 3H), 2.45-2.55 (m, 1H), 3.58 (s, 2H), 3.68 (s, 2H), 4.30 (s, 2H), 4.31 (s, 2H), 5.07 (s, 2H), 6.88 (dd, J = 12.0, 4.0 Hz, 1H), 6.94 (d, J = 2.0 Hz, 1H), 7.18 (d, J = 8.0 Hz, 2H), 7.22-7.30 (m, 5H), 7.36 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 8.0 Hz, 1H), 7.62 (s, 1H)
3-124	DMSO-d6, 400MHz	0.80 (t, J = 7.2 Hz, 6H), 1.05-1.14 (m, 4H), 1.48-1.58 (m, 4H), 2.38 (s, 3H), 2.50-2.54 (m, 1H), 3.54 (s, 2H), 4.17 (s, 2H), 4.28 (s, 2H), 5.06 (s, 2H), 6.89 (d, J = 8.0 Hz, 1H), 6.94 (d, J = 4.0 Hz, 1H), 7.14-7.18 (m, 4H), 7.35 (d,J = 8 Hz, 2H), 7.49-7.56 (m, 4H)
3-125	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 1.00-1.14 (m, 4H), 1.26 (s, 9H), 1.40-1.58 (m, 4H), 1.89-1.98 (m, 2H), 2.42-2.55 (m, 1H), 2.75-2.82 (m, 2H), 3.35-3.42 (m, 2H), 3.49 (s, 2H), 4.19 (s, 2H), 4.21 (s, 2H), 4.49 (s, 2H), 6.53 (d, J = 9.0 Hz, 1H), 7.09-7.18 (m, 5H), 7.45 (d, J = 9.0 Hz, 1H), 7.49 (s, 1H), 7.61 (s, 1H), 12.58 (s amplio, 1H)
3-126	DMSO-d6, 300MHz	0.81 (t, J = 7.2 Hz, 6H), 1.00-1.19 (m, 4H), 1.43-1.63 (m, 4H), 1.98 (brm, 4H), 2.53-2.59 (m, 1H), 3.13 (s amplio, 2H), 3.61 (s amplio, 2H), 4.73 (s amplio, 2H), 5.10 (s, 2H), 7.12 (d, J = 9.1 Hz, 2H), 7.20 (d, J = 7.9 Hz, 2H), 7.38 (d, J = 8.3 Hz, 2H), 7.93 (d, J = 8.7 Hz, 2H), 8.14 (s amplio, 1H), 10.74 (s amplio, 1H), 12.52 (s amplio, 1H)
3-127	DMSO-d6, 300MHz	0.81 (t, J = 7.3 Hz, 6H), 1.02-1.19 (m, 4H), 1.46-1.61 (m, 4H), 2.52-2.59 (m, 1H), 2.69 (s amplio, 4H), 3.35 (s amplio, 4H), 3.94 (s, 2H), 5.09 (s, 2H), 6.98 (d, J = 9.1 Hz, 2H), 7.08 (d, J = 9.0 Hz, 2H), 7.19 (d, J = 8.3 Hz, 2H), 7.38 (d, J = 7.9 Hz, 2H), 7.77 (d, J = 9.0 Hz, 2H), 7.89 (d, J = 9.0 Hz, 2H), 7.90 (s, 1H), 12.27 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
3-128	DMSO-d6, 300MHz	0.71 (t, J = 9.0 Hz, 6H), 1.11 (d,J = 6.0 Hz, 6H), 1.29 (t, J = 6.0 Hz, 3H), 1.56-1.71 (m, 4H), 2.38-2.42 (m, 1H), 2.76-2.83 (m, 1H), 4.26 (c, J = 6.0, 2H), 5.66 (s, 2H), 5.97 (s, 2H), 7.05-7.20 (m, 5H), 7.43 (s, 1H), 7.49 (d,J = 9.0 Hz, 1H), 7.87 (d,J = 9.0 Hz, 2H), 8.47 (s, 1H)
3-129	DMSO-d6, 300MHz	0.72 (t, J = 6.0 Hz, 6H), 1.11 (d,J = 0.9 Hz, 6H), 1.52-1.74 (m, 4H), 2.42-2.46 (m, 1H), 2.75-2.84 (m, 1H), 5.66 (s, 2H), 5.99 (s, 2H), 7.06-7.18 (m, 9H), 7.44 (s, 1H), 7.50 (d,J = 9.0 Hz, 1H), 7.87 (d,J = 9.0 Hz, 2H), 8.48 (s, 1H)
3-130	DMSO-d6, 300MHz	0.79 (t, J = 6.0 Hz, 6H), 1.15 (s, 3H), 1.57-1.89 (m, 4H), 2.42-2.52 (m, 1H), 5.43 (s, 2H), 6.10 (s, 2H), 6.99-7.09 (m, 3H), 7.24-7.33 (m, 15H), 7.65 (t, J = 9.0 Hz, 1H), 7.90 (d,J = 6.3 Hz, 1H), 7.99-8.03 (m, 3H)
3-131	DMSO-d6, 300MHz	0.68 (t, J = 6.0 Hz, 6H), 1.48-1.76 (m, 4H), 2.35-2.42 (m, 1H), 5.61 (s, 2H), 6.14 (s, 2H), 7.07 (s, 1H), 7.10 (d,J = 9.0 Hz, 2H), 7.20 (d,J = 6.0 Hz, 2H), 7.35 (s, 1H), 7.62 (d,J = 6.0 Hz, 1H), 7.82 (d,J = 6.0 Hz, 2H), 7.83 (d,J = 9.0 Hz, 2H), 8.47 (s, 1H)
3-132	DMSO-d6, 300MHz	0.74 (t, J = 6.0 Hz, 6H), 0.89-1.10 (m, 9H), 1.42-1.778 (m, 13H), 2.38-2.45 (m, 1H), 4.58 (d,J = 6.0 Hz, 2H), 5.65 (s, 2H), 7.08-7.16 (m, 3H), 7.41 (s, 1H), 7.53 (d,J = 9.0 Hz, 1H), 7.91 (d,J = 9.0 Hz, 2H), 8.42 (s, 1H)
4-1	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.96-1.18 (m, 4H), 1.34-1.60 (m, 4H), 3.36 (s, 2H), 3.88 (s, 3H), 4.04 (s, 2H), 4.16 (s, 2H), 5.06 (s, 2H), 6.92 (d, J = 8.7 Hz, 2H), 7.01 (d, J = 3.4 Hz, 1H), 7.07 (d, J = 8.7 Hz, 2H), 7.14-7.26 (m, 2H), 7.35 (d, J = 3.4 Hz, 1H), 7.46 (d, J = 8.3 Hz, 2H), 7.53 (d, J = 7.5 Hz, 1H), 7.58-7.65 (m, 3H), 12.52 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
4-2	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 1.00-1.12 (m, 4H), 1.38-1.57 (m, 4H), 2.40-2.50 (m, 1H), 5.07 (s, 2H), 5.48 (s, 2H), 6.93 (d, J = 8.6 Hz, 2H), 7.07 (d, J = 8.6 Hz, 2H), 7.49 (d, J = 7.9 Hz, 2H), 7.69-7.71 (m, 1H), 7.72 (d, J = 8.3 Hz, 2H), 7.88-7.89 (m, 1H), 7.91 (d, J = 1.5 Hz, 1H), 8.56 (d, J = 2.6 Hz, 1H), 8.69 (d, J = 1.5 Hz, 1H), 13.41 (s amplio, 1H)
4-3	DMSO-d6, 300MHz	0.78 (t, J = 7.4 Hz, 6H), 1.00-1.12 (m, 4H), 1.15 (d, J = 6.4 Hz, 6H), 1.30-1.53 (m, 4H), 2.27-2.41 (m, 1H), 4.22 (sept, J = 6.8 Hz, 1H), 4.35 (s, 2H), 5.48 (s, 2H), 6.60 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 9.0 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 7.62 (d, J = 8.7 Hz, 2H), 7.65 (d, J = 1.5 Hz, 1H), 7.83 (d, J = 1.5 Hz, 1H), 7.89 (dd, J = 3.0, 1.5 Hz, 1H), 8.59 (d, J = 2.6 Hz, 1H), 8.69 (d, J = 1.5 Hz, 1H), 13.48 (s amplio, 1H).
4-4	DMSO-d6, 300MHz	0.69 (t, J = 7.4 Hz, 6H), 1.16 (d, J = 6.4 Hz, 6H), 1.32-1.47 (m, 2H), 1.48-1.64 (m, 2H), 2.06-2.18 (m, 1H), 4.23 (sept, J = 6.6 Hz, 1H), 4.36 (s, 2H), 5.48 (s, 2H), 6.62 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 9.0 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 7.62 (d, J = 8.3 Hz, 2H), 7.65 (d, J = 1.1 Hz, 1H), 7.83 (d, J = 1.5 Hz, 1H), 7.89 (dd, J = 2.8, 1.7 Hz, 1H), 8.59 (d, J = 3.0 Hz, 1H), 8.69 (d, J = 1.5 Hz, 1H), 13.48 (s amplio, 1H).
4-5	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 1.01-1.14 (m, 4H), 1.37-1.58 (m, 4H), 2.41-2.48 (m, 1H), 5.07 (s, 2H), 5.48 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.26 (d, J = 3.8 Hz, 1H), 7.45 (d, J = 3.8 Hz, 1H), 7.49 (d, J = 8.3 Hz, 2H), 7.67 (d, J = 8.3 Hz, 2H), 7.88-7.90 (m, 1H), 8.58 (d, J = 2.6 Hz, 1H), 8.70 (d, J = 1.5 Hz, 1H), 13.53 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
4-6	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.97-1.17 (m, 4H), 1.35-1.60 (m, 4H), 2.38-2.53 (m, 1H), 3.45 (s, 2H), 4.12 (s, 4H), 5.06 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.11-7.20 (m, 2H), 7.41-7.59 (m, 5H), 7.69 (d, J = 8.3 Hz, 2H), 7.75-7.80 (m, 1H)
4-7	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 0.99-1.17 (m, 4H), 1.36-1.59 (m, 4H), 2.38-2.53 (m, 1H), 5.07 (s, 2H), 5.63 (s, 2H), 6.93 (d, J = 8.6 Hz, 2H), 7.07 (d, J = 8.6 Hz, 2H), 7.10 (dd, J = 8.3, 0.7 Hz, 1H), 7.48 (d, J = 8.3 Hz, 2H), 7.71 (d, J = 7.6 Hz, 2H), 7.72 (d, J = 0.8 Hz, 1H), 7.79 (d, J = 1.5 Hz, 1H), 7.87 (d, J = 1.5 Hz, 1H), 7.90 (dd, J = 8.3, 7.2 Hz, 1H), 13.17 (s amplio, 1H).
4-8	DMSO-d6, 400MHz	0.80 (t, J = 7.2 Hz, 6H), 1.05-1.14 (m, 4H), 1.48-1.58 (m, 4H), 2.45-2.50 (m, 1H), 3.42 (s, 2H), 4.07 (s, 4H), 5.06 (s, 2H), 6.89 (d, J = 8.0 Hz, 2H), 7.00-7.05 (m, 3H), 7.11-7.13 (m, 2H), 7.35 (d, J = 4.0 Hz, 1H), 7.44 (d, J = 12.0 Hz, 2H), 7.48-7.50 (m, 2H), 7.60 (d, J = 8.0 Hz, 2H)
4-9	DMSO-d6, 400MHz	0.77 (t, J = 7.3 Hz, 6H), 1.02-1.05 (m, 4H), 1.15 (d, J = 4.0 Hz, 6H), 1.40-1.51 (m, 4H), 2.40-2.45 (m, 1H), 2.79-2.84 (m, 1H), 3.44 (s, 2H), 3.51 (s, 2H), 4.04 (s, 2H), 5.03 (s, 2H), 6.89 (d, J = 8.0 Hz, 2H), 6.99 (d, J = 4.0 Hz, 1H), 7.03 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 4.0 Hz, 1H), 7.43 (d, J = 8.0 Hz, 2H), 7.48 (d, J = 8.0 Hz, 2H), 7.58 (d, J = 8.0 Hz, 2H)
4-10	DMSO-d6, 400MHz	0.77 (t, J = 7.3 Hz, 6H), 1.02-1.05 (m, 4H), 1.40-1.51 (m, 4H), 2.40-2.45 (m, 1H), 3.47 (s, 2H), 3.51 (s, 2H), 4.70 (s, 2H), 5.05 (s, 2H), 6.91 (d, J = 8.0 Hz, 2H), 7.01 (d, J = 2.0 Hz, 1H), 7.03-7.07 (m, 3H), 7.28-7.31 (m, 2H), 7.35 (d, J = 3.0 Hz, 1H), 7.45 (d, J = 8.0 Hz, 2H), 7.59-7.62 (m, 4H)

Ejemplo	solvente, Hz	RMN (δ)
4-11	DMSO-d6, 400MHz	0.68 (t, J = 7.3 Hz, 6H), 1.15 (d, J = 6.5 Hz, 6H), 1.34-1.45 (m, 2H), 1.50-1.60 (m, 2H), 2.08-2.15 (m, 1H), 3.46 (s, 2H), 3.50 (s, 2H), 4.07 (s, 2H), 4.21 (sep, J = 6.5 Hz, 1H), 4.34 (s, 2H), 6.60 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 7.03 (t, J = 7.3 Hz, 1H), 7.26-7.31 (m, 4H), 7.40 (s, 1H), 7.56-7.61 (m, 4H), 7.69 (s, 1H), 10.11 (s amplio, 1H), 12.64 (s amplio, 1H)
4-12	DMSO-d6, 400MHz	0.68 (t, J = 7.3 Hz, 6H), 1.15 (d, J = 6.5 Hz, 6H), 1.34-1.45 (m, 2H), 1.50-1.60 (m, 2H), 2.08-2.15 (m, 1H), 3.41 (s, 2H), 4.07 (s, 2H), 4.11 (s, 2H), 4.21 (sep, J = 6.5 Hz, 1H), 4.34 (s, 2H), 6.60 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.15 (s, 1H), 7.16 (d, J = 8.6 Hz, 2H), 7.28 (d, J = 8.1 Hz, 2H), 7.38 (s, 1H), 7.58 (d, J = 8.1 Hz, 2H), 7.70 (s, 1H), 12.48 (s amplio, 1H)
4-13	DMSO-d6, 400MHz	0.79 (t, J = 7.2 Hz, 6H), 1.01-1.14 (m, 4H), 1.33 (s, 9H), 1.37-1.58 (m, 4H), 2.41-2.51 (m, 1H), 3.37 (s, 2H), 4.09 (s, 4H), 5.05 (s, 2H), 6.91 (d, J = 8.4 Hz, 2H), 7.05 (d, J = 8.4 Hz, 2H), 7.39 (s, 1H), 7.42 (s amplio, 1H), 7.45 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 8.0 Hz, 2H), 7.77 (d, J = 1.2 Hz, 1H)
4-14	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6H), 1.15 (d, J = 6.7 Hz, 6H), 1.32-1.46 (m, 2H), 1.48-1.64 (m, 2H), 2.05-2.18 (m, 1H), 3.43 (s, 2H), 4.10 (s, 4H), 4.22 (sept, J = 6.6 Hz, 1H), 4.35 (s, 2H), 6.61 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.7 Hz, 2H), 7.14 (dd, J = 6.0, 3.0 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H), 7.41 (d, J = 1.1 Hz, 1H), 7.52 (dd, J = 5.8, 3.2 Hz, 1H), 7.59 (d, J = 8.3 Hz, 2H), 7.69 (d, J = 1.5 Hz, 1H), 12.43 (s amplio, 1H).

Ejemplo	solvente, Hz	RMN (δ)
4-15	DMSO-d6, 300MHz	0.76 (t, J = 7.17 Hz, 6H), 0.98-1.16 (m, 4H), 1.23 (s, 9H), 1.34-1.56 (m, 4H), 2.38-2.46 (m, 1H), 3.39 (s, 2H), 4.05 (s, 2H), 4.10 (s, 2H), 5.02 (s, 2H), 6.89 (d, J = 8.60 Hz, 2H), 7.03 (d, J = 8.60 Hz, 2H), 7.14 (s, 1H), 7.41 (s, 1H), 7.43 (d, J = 8.31 Hz, 2H), 7.66 (d, J = 8.31 Hz, 2H), 7.76 (s, 1H)
4-16	DMSO-d6, 300MHz	0.76 (t, J = 7.14 Hz, 6H), 0.97-1.11 (m, 4H), 1.34-1.55 (m, 4H), 2.36-2.46 (m, 1H), 3.45 (s, 2H), 3.52 (s, 2H), 4.07 (s, 2H), 5.02 (s, 2H), 6.89 (d, J = 8.67 Hz, 2H), 7.01 (d, J = 6.39 Hz, 1H), 7.03 (d, J = 8.67 Hz, 2H), 7.28 (dd, J = 8.28, 7.53 Hz, 2H), 7.42 (d, J = 8.28 Hz, 2H), 7.43 (d, J = 1.5 Hz, 1H), 7.57 (d, J = 7.53 Hz, 2H), 7.65 (d, J = 8.31 Hz, 2H), 7.75 (d, J = 1.5 Hz, 1H), 9.93 (s, 1H)
4-17	DMSO-d6, 300MHz	0.67 (t, J = 4.0 Hz, 6H), 1.14 (d,J = 8.0 Hz, 6H), 1.39-1.43 (m, 2H), 1.50-1.60 (m, 2H), 2.08-2.15 (m, 1H), 4.34 (s, 2H), 5.44 (s, 2H), 6.59 (d,J = 8.0 Hz, 2H), 6.87 (d,J = 12.0 Hz, 2H), 7.22 (d,J = 4.0 Hz, 1H), 7.30 (d,J = 8.0 Hz, 2H), 7.36 (d,J = 4.0 Hz, 1H), 7.56 (d,J = 8.0 Hz, 2H), 7.85 (s, 1H), 8.82 (s, 1H), 8.66 (s, 1H)
4-18	DMSO-d6, 400MHz	0.77 (t, J = 8.0 Hz, 6H), 1.02-1.10 (m, 4H), 1.14 (d,J = 4.0 Hz, 6H), 1.31-1.50 (m, 4H), 2.29-2.37 (m, 1H), 4.15-4.26 (m, 1H), 4.33 (s, 2H), 5.43 (s, 2H), 6.58 (d,J = 12.0 Hz, 2H), 6.87 (d,J = 12.0 Hz, 2H), 7.22 (s, 1H), 7.30 (d,J = 8.0 Hz, 1H), 7.36 (d,J = 4.0 Hz, 2H), 7.56 (d,J = 8.0 Hz, 2H), 7.84 (s, 1H), 8.51 (s, 1H), 8.65 (s, 1H)
4-19	DMSO-d6, 400MHz	0.63 (t, J = 8.0 Hz, 6H), 1.10 (d,J = 8.0 Hz, 6H), 1.21 (s, 9H), 1.33-1.38 (m, 2H), 1.45-1.52 (m, 2H), 2.27 (m, 1H), 3.25-3.60 (m, 1H), 3.98 (s, 2H), 4.06 (s, 2H), 4.29 (s, 2H), 6.55 (d,J = 8.0 Hz, 2H), 6.82 (d,J = 8.0 Hz, 2H), 6.92 (d,J = 4.0 Hz, 1H), 7.10 (s, 1H), 7.25 (d,J = 12.0 Hz, 2H), 7.24 (s, 1H), 7.49 (d,J = 8.0 Hz, 2H)

Ejemplo	solvente, Hz	RMN (δ)
4-20	DMSO-d6, 300MHz	0.78 (t, J = 9.0 Hz, 6H), 1.01-1.13 (m, 4H), 1.15 (d,J = 6.0 Hz, 6H), 1.26 (s, 9H), 1.38-1.49 (m, 4H), 2.28-2.35 (m, 1H), 3.33 (s, 2H), 4.06 (s, 2H), 4.13 (s, 2H), 4.14-4.24 (m, 1H), 4.34 (s, 2H), 6.60 (d,J = 9.0 Hz, 2H), 6.89 (d,J = 9.0 Hz, 2H), 6.96 (d,J = 6.0 Hz, 1H), 7.13 (s, 1H), 7.29 (d,J = 12.0 Hz, 2H), 7.29 (s, 1H), 7.54 (d,J = 6.0 Hz, 2H)
4-21	DMSO-d6, 300MHz	0.67 (t, J = 4.0 Hz, 6H), 1.14 (d,J = 8.0 Hz, 6H), 1.30-1.43 (m, 2H), 1.48-1.60 (m, 2H), 2.06-2.14 (m, 1H), 3.40 (s, 2H), 4.06 (s, 2H), 4.07 (s, 2H), 4.18-4.25 (m, 1H), 4.33 (s, 2H), 6.59 (d,J = 8.0 Hz, 2H), 6.86 (d,J = 8.0 Hz, 2H), 7.00 (d,J = 4.0 Hz, 1H), 7.12-7.14 (m, 2H), 7.28 (m, 3H), 7.48-7.54 (m, 3H)
4-22	DMSO-d6, 300MHz	0.78 (t, J = 9.0 Hz, 6H), 1.01-1.14 (m, 4H), 1.15 (d,J = 6.0 Hz, 6H), 1.36-1.48 (m, 4H), 2.24-2.40 (m, 1H), 4.07 (s, 4H), 4.17-4.25 (m, 1H), 4.34 (s, 2H), 6.60 (d,J = 6.0 Hz, 2H), 6.89 (d,J = 9.0 Hz, 2H), 6.97-7.43 (m, 6H), 7.43-7.69 (m, 3H)
4-23	DMSO-d6, 400MHz	0.79 (t, J = 7.3 Hz, 6H), 1.01-1.14 (m, 4H), 1.39-1.56 (m, 4H), 2.20 (s, 3H), 2.29 (s, 3H), 2.41-2.49 (m, 1H), 3.37 (s, 2H), 4.04 (s, 2H), 4.08 (s, 2H), 5.05 (s, 2H), 6.91 (d, J = 8.6 Hz, 2H), 7.05 (d, J = 8.6 Hz, 2H), 7.42 (s, 1H), 7.45 (d, J = 8.1 Hz, 2H), 7.68 (d, J = 8.1 Hz, 2H), 7.77 (s, 1H)
4-24	DMSO-d6, 400MHz	0.68 (t, J = 7.2 Hz, 6H), 1.15 (d, J = 6.3 Hz, 6H), 1.34-1.45 (m, 2H), 1.51-1.61 (m, 2H), 2.09-2.16 (m, 1H), 3.04-3.17 (m, 2H), 3.83-3.96 (m, 2H), 4.00-4.09 (m, 1H), 4.16-4.27 (m, 3H), 4.34 (s, 2H), 6.60 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 7.00-7.16 (m, 4H), 7.29 (d, J = 8.1 Hz, 2H), 7.45 (s amplio, 3H), 7.61 (d, J = 8.1 Hz, 2H), 7.71 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
4-25	DMSO-d6, 400MHz	0.68 (t, J = 7.3 Hz, 6H), 1.15 (d, J = 7.0 Hz, 6H), 1.17 (d, J = 7.0 Hz, 6H), 1.34-1.45 (m, 2H), 1.50-1.60 (m, 2H), 2.08-2.16 (m, 1H), 2.82 (sep, J = 7.0 Hz, 1H), 3.45 (s, 2H), 3.53 (s, 2H), 4.08 (s, 2H), 4.21 (sep, J = 7.0 Hz, 1H), 4.34 (s, 2H), 6.60 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 7.16 (d, J = 8.6 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 7.41 (s, 1H), 7.50 (d, J = 8.6 Hz, 2H), 7.57 (d, J = 8.4 Hz, 2H), 7.69 (s, 1H), 9.85 (s, 1H), 12.58 (s amplio, 1H)
4-26	DMSO-d6, 400MHz	0.79 (t, J = 7.4 Hz, 6H), 1.00-1.14 (m, 4H), 1.39-1.56 (m, 4H), 2.42-2.48 (m, 1H), 3.17-3.43 (m, 2H), 4.15-4.63 (m, 5H), 5.07 (s, 2H), 6.92 (d, J = 8.8 Hz, 2H), 7.06 (d, J = 8.8 Hz, 2H), 7.18-7.28 (m, 5H), 7.48-7.50 (m, 3H), 7.67 (d, J = 8.4 Hz, 2H)
4-27	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.99-1.18 (m, 4H), 1.18 (d, J = 6.8 Hz, 6H), 1.32-1.60 (m, 4H), 2.39-2.55 (m, 1H), 2.75-2.91 (m, 1H), 3.47 (s, 2H), 3.55 (s, 2H), 4.10 (s, 2H), 5.06 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.18 (d, J = 8.7 Hz, 2H), 7.42-7.53 (m, 5H), 7.68 (d, J = 8.3 Hz, 2H), 7.79 (d, J = 1.5 Hz, 1H), 9.87 (s, 1H), 12.50 (s amplio, 1H).
4-28	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6H), 1.14 (d, J = 6.6 Hz, 6H), 1.32-1.47 (m, 2H), 1.49-1.62 (m, 2H), 2.08-2.17 (m, 1H), 3.04 (dd, J = 16.3, 3.5 Hz, 1H), 3.11 (dd, J = 16.3, 6.2 Hz, 1H), 3.81-3.86 (m, 2H), 4.00 (d, J = 15.8 Hz, 1H), 4.14-4.26 (m, 3H), 4.34 (s, 2H), 6.60 (d, J = 8.4 Hz, 2H), 6.88 (d, J = 8.4 Hz, 2H), 7.00-7.14 (m, 5H), 7.28-7.31 (m, 3H), 7.54 (d, J = 8.0 Hz, 2H), 12.47 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
4-29	DMSO-d6, 300MHz	0.79 (t, J = 7.1 Hz, 6H), 1.01-1.14 (m, 4H), 1.25 (s, 9H), 1.38-1.58 (m, 4H), 2.41-2.50 (m, 1H), 3.39 (s, 2H), 3.95 (s, 2H), 4.03 (s, 2H), 5.06 (s, 2H), 6.75 (s, 1H), 6.93 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.4 Hz, 2H), 7.40 (s, 1H), 7.47 (d, J = 8.4 Hz, 2H), 7.69 (d, J = 8.4 Hz, 2H), 7.78 (s, 1H), 12.40 (s amplio, 1H)
4-30	DMSO-d6, 400MHz	0.79 (t, J = 7.3 Hz, 6H), 1.00-1.14 (m, 4H), 1.39-1.56 (m, 4H), 2.41-2.49 (m, 1H), 3.36 (s, 2H), 3.86 (s, 3H), 4.06 (s, 2H), 4.17 (s, 2H), 5.05 (s, 2H), 6.91 (d, J = 8.6 Hz, 2H), 7.05 (d, J = 8.8 Hz, 2H), 7.16 (t, J = 7.4 Hz, 1H), 7.23 (t, J = 7.4 Hz, 1H), 7.41 (s, 1H), 7.44 (d, J = 8.1 Hz, 2H), 7.52 (d, J = 7.4 Hz, 1H), 7.59 (d, J = 7.4 Hz, 1H), 7.65 (d, J = 8.1 Hz, 2H), 7.75 (s, 1H)
4-31	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.99-1.14 (m, 4H), 1.38-1.59 (m, 4H), 2.41-2.46 (m, 1H), 5.06 (s, 2H), 5.62 (s, 2H), 6.92 (d, J = 8.4 Hz, 2H), 7.05-7.11 (m, 3H), 7.30 (d, J = 3.6 Hz, 1H), 7.42 (d, J = 3.3 Hz, 1H), 7.48 (d, J = 8.1 Hz, 2H), 7.65 (d, J = 7.8 Hz, 2H), 7.71 (d, J = 7.2 Hz, 1H), 7.90 (dd, J = 8.1, 7.2 Hz, 1H)
4-32	DMSO-d6, 300MHz	0.69 (t, J = 7.17 Hz, 6H), 1.16 (d, J = 6.59 Hz, 6H), 1.35-1.47 (m, 2H), 1.48-1.63 (m, 2H), 2.07-2.18 (m, 1H), 4.22 (quint, J = 6.59 Hz, 1H), 4.35 (s, 2H), 5.53 (s, 2H), 6.62 (d, J = 8.66 Hz, 2H), 6.68 (dd, J = 8.10, 0.75 Hz, 1H), 6.88 (d, J = 8.66 Hz, 2H), 7.30 (d, J = 8.28 Hz, 2H), 7.41 (dd, J = 7.14, 0.75 Hz, 1H), 7.61 (dd, J = 8.10, 7.14 Hz, 1H), 7.64 (d, J = 8.28 Hz, 2H), 7.76 (d, J = 1.5 Hz, 1H), 7.78 (d, J = 1.5 Hz, 1H)

Ejemplo	solvente, Hz	RMN (δ)
4-33	DMSO-d6, 300MHz	0.68 (t, J = 7.1 Hz, 6H), 1.14 (d, J = 6.8 Hz, 6H), 1.33 (s, 9H), 1.35-1.60 (m, 4H), 2.07-2.18 (m, 1H), 3.41 (s, 2H), 4.08 (s, 4H), 4.22 (sep, J = 6.6 Hz, 1H), 4.35 (s, 2H), 6.61 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 7.39 (s, 1H), 7.41 (s, 1H), 7.60 (d, J = 8.4 Hz, 2H), 7.72 (s, 1H), 12.48 (s amplio, 1H)
4-34	DMSO-d6, 300MHz	0.68 (t, J = 7.3 Hz, 6H), 1.15 (d, J = 6.6 Hz, 6H), 1.32-1.47 (m, 2H), 1.49-1.62 (m, 2H), 2.08-2.17 (m, 1H), 3.37 (s, 2H), 3.86 (s, 3H), 4.06 (s, 2H), 4.17 (s, 2H), 4.22 (sep, J = 6.6 Hz, 1H), 4.34 (s, 2H), 6.61 (d, J = 8.8 Hz, 2H), 6.88 (d, J = 8.8 Hz, 2H), 7.16-7.30 (m, 4H), 7.38 (s amplio, 1H), 7.52-7.61 (m, 4H), 7.67 (s amplio, 1H)
4-35	DMSO-d6, 400MHz	0.79 (t, J = 7.4 Hz, 6H), 1.01-1.14 (m, 4H), 1.27 (s, 9H), 1.39-1.56 (m, 4H), 2.41-2.48 (m, 1H), 3.42 (s, 2H), 4.13 (s, 2H), 5.06 (s, 2H), 6.92 (d, J = 8.8 Hz, 2H), 7.00 (d, J = 3.6 Hz, 1H), 7.06 (d, J = 8.4 Hz, 2H), 7.16 (s, 1H), 7.36 (d, J = 3.6 Hz, 1H), 7.46 (d, J = 8.4 Hz, 2H), 7.63 (d, J = 8.4 Hz, 2H)
4-36	DMSO-d6, 300MHz	0.69 (t, J = 7.2 Hz, 6H), 1.15 (d, J = 6.6 Hz, 6H), 1.32-1.63 (m, 4H), 2.07-2.18 (m, 1H), 3.36 (s, 2H), 3.87 (s, 3H), 4.03 (s, 2H), 4.16 (s, 2H), 4.18-4.26 (m, 1H), 4.34 (s, 2H), 6.61 (d, J = 8.7 Hz, 2H), 6.89 (d, J = 8.4 Hz, 2H), 6.99 (d, J = 3.6 Hz, 1H), 7.16-7.31 (m, 5H), 7.53 (brd, J = 8.4 Hz, 3H), 7.60 (d, J = 7.2 Hz, 1H)
4-37	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 0.98-1.16 (m, 4H), 1.34 (s, 9H), 1.37-1.59 (m, 4H), 2.39-2.53 (m, 1H), 3.41 (s, 2H), 4.06 (s, 2H), 4.10 (s, 2H), 5.07 (s, 2H), 6.93 (d, J = 7.9 Hz, 2H), 7.01 (d, J = 3.0 Hz, 1H), 7.07 (d, J = 8.3 Hz, 2H), 7.37 (d, J = 3.4 Hz, 1H), 7.41-7.43 (m, 1H), 7.48 (d, J = 7.9 Hz, 2H), 7.64 (d, J = 7.9 Hz, 2H), 12.51 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
4-38	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.98-1.17 (m, 4H), 1.36-1.59 (m, 4H), 2.39-2.54 (m, 1H), 2.94 (s, 2H), 3.91 (s, 2H), 4.03 (s, 3H), 4.16 (s, 2H), 5.05 (s, 2H), 6.86-6.98 (m, 3H), 7.06 (d, J = 8.7 Hz, 2H), 7.12-7.26 (m, 2H), 7.30 (d, J = 3.4 Hz, 1H), 7.44 (d, J = 8.3 Hz, 2H), 7.51 (d, J = 7.2 Hz, 1H), 7.55-7.63 (m, 3H)
4-39	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.97-1.17 (m, 4H), 1.34-1.60 (m, 4H), 2.37-2.55 (m, 1H), 3.02 (s amplio, 2H), 3.95 (s amplio, 5H), 4.14 (s amplio, 2H), 5.04 (s amplio, 2H), 6.91 (brd, J = 8.3 Hz, 3H), 7.06 (d, J = 8.6 Hz, 2H), 7.10-7.27 (m, 2H), 7.27-7.35 (m, 1H), 7.35-7.68 (m, 6H)
4-40	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.95-1.20 (m, 4H), 1.32-1.60 (m, 4H), 2.28 (s, 3H), 2.40-2.54 (m, 1H), 3.62 (s, 2H), 4.00 (s, 3H), 4.19 (s, 2H), 4.46 (s, 2H), 5.05 (s, 2H), 6.92 (d, J = 8.6 Hz, 2H), 6.98-7.14 (m, 5H), 7.25 (d, J = 3.6 Hz, 1H), 7.36-7.58 (m, 8H), 7.76 (d, J = 9.0 Hz, 1H), 7.89 (d, J = 9.0 Hz, 1H)
4-41	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 0.98-1.15 (m, 4H), 1.38-1.59 (m, 4H), 2.39-2.54 (m, 1H), 5.07 (s, 2H), 5.52 (s, 2H), 6.93 (d, J = 8.6 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.49 (d, J = 8.3 Hz, 2H), 7.71 (s, 1H), 7.72 (d, J = 6.4 Hz, 2H), 7.93 (d, J = 1.5 Hz, 1H), 8.00 (s amplio, 1H), 8.65-8.67 (m, 1H), 8.73-8.76 (m, 1H)
4-42	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 1.00-1.14 (m, 4H), 1.37-1.60 (m, 4H), 2.40-2.54 (m, 1H), 3.80 (s amplio, 3H), 4.08-4.62 (m, 2H), 4.92-5.36 (m, 4H), 6.92 (d, J = 8.6 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.16-7.80 (m, 10H)
4-43	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.93-1.15 (m, 4H), 1.16-1.60 (m, 13H), 2.36-2.55 (m, 1H), 4.16 (s amplio, 2Hx0.45), 4.43 (s amplio, 2Hx0.55), 4.70-5.25 (m, 4H), 6.93 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.4 Hz, 2H), 7.29-7.62 (m, 5H), 7.72-7.75 (m, 2H)

Ejemplo	solvente, Hz	RMN (δ)
4-44	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.97-1.15 (m, 4H), 1.20 (d, J = 6.8 Hz, 6H), 1.35-1.59 (m, 4H), 2.39-2.54 (m, 1H), 2.81-2.96 (m, 1H), 4.01 (s amplio, 2Hx0.60), 4.23 (s amplio, 2Hx0.40), 4.63 (s amplio, 2Hx0.40), 4.88 (s amplio, 2Hx0.60), 5.08 (s, 2H), 6.92 (d, J = 8.7 Hz, 2H), 7.06 (d, J = 8.7 Hz, 2H), 7.16-7.40 (m, 5H), 7.41-7.56 (m, 3H), 7.71 (d, J = 7.9 Hz, 2H)
4-45	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.97-1.19 (m, 4H), 1.35-1.60 (m, 4H), 2.37-2.56 (m, 1H), 2.89 (s, 6H), 3.84-4.30 (m, 2H), 4.40-4.93 (m, 2H), 5.09 (s, 2H), 6.73 (brd, J = 7.2 Hz, 2H), 6.93 (d, J = 8.6 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.15 (brd, J = 7.9 Hz, 2H), 7.31 (d, J = 3.8 Hz, 1H), 7.44-7.57 (m, 3H), 7.72 (d, J = 8.3 Hz, 2H)
4-46	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.95-1.18 (m, 4H), 1.35-1.61 (m, 4H), 2.39-2.55 (m, 1H), 4.11 (s amplio, 2Hx0.62), 4.46 (s amplio, 2Hx0.38), 4.77 (s amplio, 2Hx0.38), 4.99 (s amplio, 2Hx0.62), 5.08 (s, 2H), 6.92 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.25-7.60 (m, 6H), 7.61-7.92 (m, 3H), 8.42-8.72 (m, 1H)
4-47	DMSO-d6, 300MHz	0.79 (t, J = 7.4 Hz, 6H), 0.97-1.18 (m, 4H), 1.34-1.60 (m, 4H), 2.37-2.55 (m, 1H), 3.94-4.50 (m, 2H), 4.59-5.07 (m, 2H), 5.09 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.19-7.58 (m, 5H), 7.72 (d, J = 7.9 Hz, 2H), 7.79 (d, J = 7.5 Hz, 1H), 8.51 (d, J = 4.5 Hz, 1H), 8.58 (s, 1H)
4-48	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 1.00-1.15 (m, 4H), 1.38-1.58 (m, 4H), 2.40 (s, 3H), 2.42-2.50 (m, 1H), 5.07 (s, 2H), 5.53 (s, 2H), 6.93 (d, J = 8.6 Hz, 2H), 7.07 (d, J = 8.6 Hz, 2H), 7.49 (d, J = 8.3 Hz, 2H), 7.71-7.75 (m, 3H), 7.93 (d, J = 1.5 Hz, 1H), 8.04 (s amplio, 1H), 8.69 (d, J = 2.6 Hz, 1H), 8.76 (d, J = 1.5 Hz, 1H)

Ejemplo	solvente, Hz	RMN (δ)
4-49	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.97-1.18 (m, 4H), 1.35-1.61 (m, 4H), 2.39-2.53 (m, 1H), 3.09 (s, 3H), 3.91 (s, 2H), 4.62 (s, 2H), 5.07 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.03-7.12 (m, 3H), 7.39 (d, J = 3.8 Hz, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.66 (d, J = 8.5 Hz, 2H), 12.95 (s amplio, 1H).
4-50	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 0.99-1.17 (m, 4H), 1.37-1.58 (m, 4H), 2.40-2.54 (m, 1H), 5.07 (s, 2H), 5.39 (s, 2H), 6.93 (d, J = 8.3 Hz, 2H), 7.07 (d, J = 8.6 Hz, 2H), 7.48 (d, J = 8.3 Hz, 2H), 7.67 (s amplio, 1H), 7.72 (d, J = 8.3 Hz, 2H), 7.79 (dd, J = 1.5, 3.0 Hz, 1H), 7.89 (d, J = 1.5 Hz, 1H), 8.26 (d, J = 3.0 Hz, 1H), 8.60 (d, J = 1.1 Hz, 1H)
4-51	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 1.00-1.15 (m, 4H), 1.38-1.58 (m, 4H), 2.39-2.54 (m, 1H), 5.07 (s, 2H), 5.52 (s, 2H), 6.93 (d, J = 8.6 Hz, 2H), 7.07 (d, J = 8.6 Hz, 2H), 7.49 (d, J = 8.3 Hz, 2H), 7.71 (s, 1H), 7.72 (d, J = 6.8 Hz, 2H), 7.93 (d, J = 1.5 Hz, 1H), 7.99 (s amplio, 1H), 8.65-8.67 (m, 1H), 8.73-8.75 (m, 1H)
4-52	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 0.97-1.19 (m, 4H), 1.36-1.62 (m, 4H), 2.40-2.55 (m, 1H), 3.45 (s amplio, 4H), 3.84 (s amplio, 4H), 5.10 (s, 2H), 6.96 (dd, J = 8.7, 12.8 Hz, 4H), 7.08 (d, J = 8.3 Hz, 2H), 7.46-7.59 (m, 4H), 7.78 (dd, J = 8.3, 15.5 Hz, 4H)
4-53	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.98-1.19 (m, 4H), 1.36-1.59 (m, 4H), 1.60-1.80 (m, 2H), 1.88 (brd, J = 11.3 Hz, 2H), 2.40-2.54 (m, 1H), 2.88-3.02 (m, 1H), 3.03-3.22 (m, 2H), 4.46 (brd, J = 13.2 Hz, 2H), 5.09 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.38-7.58 (m, 6H), 7.74 (d, J = 8.3 Hz, 2H), 7.89 (d, J = 8.3 Hz, 2H)

Ejemplo	solvente, Hz	RMN (δ)
4-54	DMSO-d6, 300MHz	0.79 (t, J = 7.4 Hz, 6H), 0.98-1.18 (m, 4H), 1.36-1.60 (m, 4H), 2.39-2.53 (m, 1H), 3.64 (s, 2H), 3.99 (s, 3H), 4.21 (s, 2H), 4.48 (s, 2H), 5.06 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.40-7.68 (m, 8H), 7.71-7.76 (m, 1H), 7.85-7.91 (m, 1H).
4-55	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.98-1.18 (m, 4H), 1.36-1.59 (m, 4H), 2.40-2.50 (m, 1H), 3.64 (s, 2H), 3.99 (s, 3H), 4.22 (s, 2H), 4.48 (s, 2H), 5.06 (s, 2H), 6.93 (d, J = 8.8 Hz, 2H), 7.07 (d, J = 8.8 Hz, 2H), 7.42-7.63 (m, 7H), 7.66 (s, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.89 (d, J = 8.8 Hz, 1H)
4-56	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.96-1.18 (m, 4H), 1.35-1.60 (m, 4H), 2.33 (s, 6H), 2.38-2.54 (m, 1H), 5.07 (s, 2H), 5.51 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.49 (d, J = 7.9 Hz, 2H), 7.60-7.78 (m, 5H), 7.93 (d, J = 1.1 Hz, 1H), 8.35 (d, J = 8.3 Hz, 1H), 9.99 (s, 1H), 12.76 (s amplio, 1H).
4-57	DMSO-d6, 300MHz	0.80 (t, J = 7.2 Hz, 6H), 0.97-1.16 (m, 4H), 1.10 (d, J = 6.8 Hz, 6H), 1.35-1.60 (m, 4H), 2.39-2.53 (m, 1H), 2.71-2.87 (m, 1H), 5.07 (s, 2H), 5.48 (s, 2H), 6.93 (d, J = 8.6 Hz, 2H), 7.07 (d, J = 8.6 Hz, 2H), 7.49 (d, J = 8.3 Hz, 2H), 7.56 (dd, J = 8.6, 1.4 Hz, 1H), 7.66-7.73 (m, 4H), 7.90 (d, J = 1.4 Hz, 1H), 8.11 (d, J = 8.6 Hz, 1H), 9.10 (s, 1H), 12.85 (s amplio, 1H).
4-58	DMSO-d6, 300MHz	0.80 (t, J = 7.2 Hz, 6H), 0.97-1.18 (m, 4H), 1.34-1.61 (m, 4H), 2.38-2.54 (m, 1H), 5.07 (s, 2H), 5.40 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.14 (d, J = 8.7 Hz, 2H), 7.49 (d, J = 7.9 Hz, 2H), 7.68-7.75 (m, 3H), 7.87-7.94 (m, 3H), 12.66 (s amplio, 1H).

Ejemplo	solvente, Hz	RMN (δ)
4-59	DMSO-d6, 300MHz	0.80 (t, J = 7.2 Hz, 6H), 0.98-1.18 (m, 4H), 1.36-1.59 (m, 4H), 2.39-2.54 (m, 1H), 2.99 (s, 3H), 3.18 (s, 3H), 5.07 (s, 2H), 5.51 (s, 2H), 6.93 (d, J = 8.5 Hz, 2H), 7.07 (d, J = 8.5 Hz, 2H), 7.43 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 8.1 Hz, 2H), 7.58 (dd, J = 8.0, 1.5 Hz, 1H), 7.70 (s, 1H), 7.71 (d, J = 8.1 Hz, 2H), 7.78 (d, J = 1.5 Hz, 1H), 7.92 (s, 1H), 13.17 (s amplio, 1H).
4-60	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.98-1.18 (m, 4H), 1.35-1.60 (m, 4H), 2.39-2.54 (m, 1H), 4.63 (s, 2H), 5.06 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.06 (d, J = 8.7 Hz, 2H), 7.42-7.54 (m, 5H), 7.66 (d, J = 8.3 Hz, 2H), 7.73 (d, J = 1.1 Hz, 1H), 7.86 (d, J = 8.3 Hz, 2H), 12.90 (s amplio, 1H).
4-61	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 0.99-1.19 (m, 4H), 1.36-1.60 (m, 4H), 2.40-2.54 (m, 1H), 5.07 (s, 2H), 5.33 (s, 2H), 5.54 (s, 2H), 6.67 (d, J = 8.0 Hz, 1H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.39 (dd, J = 8.0, 1.6 Hz, 1H), 7.45-7.52 (m, 3H), 7.65-7.76 (m, 3H), 7.88 (d, J = 1.6 Hz, 1H), 12.11 (s amplio, 1H).
4-62	DMSO-d6, 400MHz	1.11-1.41 (m, 5H), 1.61-1.81 (m, 5H), 2.00-3.68 (m, 9H), 4.30-4.76 (m, 2H), 5.41 (s, 2H), 7.09-7.44 (m, 13H), 7.57 (d, J = 7.9 Hz, 1H), 7.88 (d, J = 7.9 Hz, 1H), 7.96 (s, 1H)
4-63	DMSO-d6, 300MHz	1.12-1.44 (m, 5H), 1.60-1.83 (m, 5H), 2.37-2.48 (m, 1H), 3.28 (s, 2H), 3.83 (s, 2H), 4.00 (s, 2H), 5.40 (s, 2H), 6.97 (d, J = 3.7 Hz, 1H), 7.11-7.44 (m, 12H), 7.52-7.57 (m, 1H), 7.85-7.90 (m, 1H), 7.88 (s, 1H), 12.35 (s amplio, 1H)
4-64	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.99-1.15 (m, 4H), 1.38-1.59 (m, 4H), 2.39-2.53 (m, 1H), 3.18 (s, 3H), 3.85 (s, 2H), 4.65 (s, 2H), 5.07 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.6 Hz, 2H), 7.25-7.35 (m, 1H), 7.39-7.43 (m, 4H), 7.45-7.51 (m, 3H), 7.68 (d, J = 8.2 Hz, 2H), 7.84 (d, J = 1.6 Hz, 1H)

Ejemplo	solvente, Hz	RMN (δ)
4-65	DMSO-d6, 300MHz	1.08-1.39 (m, 5H), 1.27 (s, 9H), 1.61-1.77 (m, 5H), 2.34-2.47 (m, 1H), 3.16 (s amplio, 2H), 3.35 (s amplio, 3H), 4.01 (s amplio, 2H), 4.08 (s amplio, 2H), 6.97 (brd, J = 2.6 Hz, 1H), 7.06 (brd, J = 8.7 Hz, 2H), 7.10 (brd, J = 8.7 Hz, 2H), 7.24 (brd, J = 8.7 Hz, 2H), 7.32 (brd, J = 3.0 Hz, 1H), 7.37-7.43 (m, 3H)
4-66	DMSO-d6, 300MHz	1.08-1.45 (m, 5H), 1.13 (t, J = 7.0 Hz, 3H), 1.62-1.84 (m, 5H), 2.38-2.54 (m, 1H), 3.32 (s, 2H), 3.48 (c, J = 6.9 Hz, 2H), 3.92 (s, 2H), 3.97 (s, 2H), 4.51 (s, 2H), 6.67 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 3.4 Hz, 2H), 7.04 (d, J = 3.8 Hz, 2H), 7.12 (d, J = 8.7 Hz, 2H), 7.16 (d, J = 8.3 Hz, 2H), 7.24-7.28 (m, 1H), 7.36 (d, J = 8.7 Hz, 2H), 7.54 (d, J = 7.5 Hz, 1H), 7.77-7.83 (m, 1H), 8.48 (d, J = 4.1 Hz, 1H), 12.45 (s amplio, 1H)
4-67	DMSO-d6, 300MHz	1.09-1.44 (m, 5H), 1.13 (t, J = 7.0 Hz, 3H), 1.64-1.82 (m, 5H), 2.38-2.51 (m, 1H), 3.03 (t, J = 5.8 Hz, 2H), 3.47 (c, J = 7.1 Hz, 2H), 3.44 (s, 2H), 4.05 (t, J = 7.2 Hz, 2H), 4.03 (s, 2H), 4.51 (s, 2H), 6.65 (s, 2H), 6.68 (s, 2H), 6.85-6.94 (m, 4H), 7.03 (d, J = 3.4 Hz, 1H), 7.12 (d, J = 8.3 Hz, 2H), 7.16 (d, J = 8.3 Hz, 2H), 7.26 (t, J = 7.9 Hz, 2H), 7.35 (d, J = 8.7 Hz, 2H), 12.31 (s amplio, 1H)
4-68	DMSO-d6, 300MHz	1.02-1.47 (m, 4H), 1.08 (t, J = 6.8 Hz, 3H), 1.24 (s, 9H), 1.61-1.87 (m, 9H), 2.05-2.16 (m, 2H), 2.38-2.47 (m, 1H), 2.53-2.65 (m, 1H), 3.02 (brd, J = 11.3 Hz, 2H), 3.16 (brd, J = 6.4 Hz, 2H), 3.41 (c, J = 6.9 Hz, 2H), 3.72 (s, 2H), 6.68 (d, J = 8.7 Hz, 2H), 7.12 (d, J = 8.3 Hz, 2H), 7.23-7.30 (m, 3H), 7.38 (d, J = 7.9 Hz, 2H), 7.42 (s, 1H), 7.46 (d, J = 8.3 Hz, 2H), 7.87 (d, J = 8.3 Hz, 2H), 12.78 (s amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
4-69	DMSO-d6, 300MHz	0.79 (t, J = 7.4 Hz, 6H), 1.01-1.21 (m, 4H), 1.15 (d, J = 7.2 Hz, 6H), 1.37-1.59 (m, 4H), 2.40-2.51 (m, 1H), 2.72-2.87 (m, 1H), 3.95 (s, 2H), 4.65 (s, 2Hx0.75), 4.74 (s, 2Hx0.75), 4.85 (s, 2Hx0.25), 4.91 (s, 2Hx0.25), 5.05 (s, 2H), 6.79-6.86 (m, 2H), 6.92 (d, J = 8.3 Hz, 2H), 7.03-7.13 (m, 4H), 7.42-7.57 (m, 3H), 7.62-7.85 (m, 3H)
4-70	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.99-1.15 (m, 4H), 1.21 (d, J = 6.8 Hz, 6H), 1.37-1.58 (m, 4H), 2.40-2.51 (m, 1H), 2.86-3.00 (m, 1H), 3.93 (s, 2Hx0.5), 4.08 (s, 2Hx0.5), 4.69 (s, 2Hx0.5), 4.81 (s, 2Hx0.5), 5.07 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.26-7.61 (m, 7H), 7.71 (d, J = 7.9 Hz, 2H), 7.81 (s, 1H)
4-71	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.84 (d, J = 6.8 Hz, 6H), 1.00-1.17 (m, 4H), 1.29-1.65 (m, 7H), 2.41-2.51 (m, 1H), 2.63 (t, J = 7.3 Hz, 2H), 3.30 (s, 2H), 3.99 (s, 2H), 5.06 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.40 (s amplio, 1H), 7.46 (d, J = 8.3 Hz, 2H), 7.69 (d, J = 8.3 Hz, 2H), 7.76 (d, J = 1.1 Hz, 1H), 12.22 (s amplio, 1H)
4-72	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.97-1.16 (m, 4H), 1.37-1.58 (m, 4H), 2.39-2.50 (m, 1H), 3.11 (s, 3H), 3.70 (s, 2H), 4.46 (s, 2H), 5.06 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.06 (d, J = 8.3 Hz, 2H), 7.14 (t, J = 7.2 Hz, 1H), 7.25-7.41 (m, 5H), 7.47 (d, J = 8.3 Hz, 2H), 7.66 (d, J = 8.3 Hz, 2H), 7.75 (d, J = 1.1 Hz, 1H), 11.96 (s amplio, 1H)
4-73	DMSO-d6, 300MHz	0.79 (t, J = 7.4 Hz, 6H), 1.00-1.15 (m, 4H), 1.36-1.58 (m, 4H), 2.41-2.50 (m, 1H), 2.74 (amplio, 2H), 2.85 (amplio, 2H), 3.72 (s, 2H), 3.91 (s, 2H), 5.09 (s, 2H), 6.95 (d, J = 8.3 Hz, 2H), 7.07 (d, J = 8.3 Hz, 2H), 7.23 (d, J = 7.9 Hz, 1H), 7.34-7.46 (m, 3H), 7.48 (s, 1H), 7.61-7.73 (m, 3H), 7.79 (s, 2H), 12.74 (amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
4-74	DMSO-d6, 300MHz	0.91 (d, J = 6.4 Hz, 3H), 0.98-1.13 (m, 2H), 1.34-1.52 (m, 3H), 1.71-1.82 (m, 4H), 2.38-2.49 (m, 1H), 2.51 (amplio, 4H), 3.27 (amplio, 4H), 3.72 (s, 2H), 5.07 (s, 2H), 6.92-6.98 (m, 3H), 7.03 (d, J = 9.0 Hz, 2H), 7.21 (s, 1H), 7.23 (d, J = 8.3 Hz, 2H), 7.35 (d, J = 8.3 Hz, 2H), 7.54 (d, J = 8.7 Hz, 2H), 7.76 (d, J = 8.7 Hz, 2H), 12.25 (s, 1H)
4-75	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 1.01-1.14 (m, 4H), 1.38-1.58 (m, 4H), 2.41-2.49 (m, 1H), 3.41 (s, 2H), 4.04 (s, 2H), 5.06 (s, 2H), 6.92 (d, J = 8.7 Hz, 2H), 6.98 (d, J = 3.8 Hz, 1H), 7.07 (d, J = 8.7 Hz, 2H), 7.34 (d, J = 3.8 Hz, 1H), 7.47 (d, J = 8.3 Hz, 2H), 7.60 (d, J = 8.3 Hz, 2H), 7.63-7.69 (m, 2H), 8.06 (s, 1H), 12.47 (amplio, 1H)
4-76	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 1.00-1.14 (m, 4H), 1.38-1.57 (m, 4H), 2.39-2.50 (m, 1H), 3.29 (s, 2H), 3.88 (s, 2H), 4.00 (s, 2H), 5.07 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.00 (d, J = 3.4 Hz, 1H), 7.07 (d, J = 8.7 Hz, 2H), 7.37 (d, J = 3.4 Hz, 1H), 7.47 (d, J = 8.3 Hz, 2H), 7.51 (d, J = 8.3 Hz, 2H), 7.65 (d, J = 8.3 Hz, 2H), 7.93 (d, J = 8.3 Hz, 2H), 12.52 (amplio, 2H)
4-77	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 1.01-1.16 (m, 4H), 1.38-1.58 (m, 4H), 2.40-2.50 (m, 1H), 3.23 (s, 2H), 3.70 (amplio, 5H), 3.97 (s, 2H), 5.07 (s, 2H), 6.88-6.96 (m, 4H), 6.98 (d, J = 3.8 Hz, 1H), 7.07 (d, J = 8.7 Hz, 2H), 7.28 (d, J = 8.7 Hz, 2H), 7.36 (d, J = 3.4 Hz, 1H), 7.47 (d, J = 8.7 Hz, 2H), 7.65 (d, J = 8.3 Hz, 2H), 12.11 (amplio, 1H)
4-78	DMSO-d6, 300MHz	0.79 (t, J = 7.4 Hz, 6H), 1.01-1.16 (m, 4H), 1.38-1.58 (m, 4H), 2.46 (s, 3H), 3.25 (s, 2H), 3.75 (s, 2H), 3.98 (s, 2H), 5.07 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 6.99 (d, J = 3.4 Hz, 1H), 7.07 (d, J = 8.7 Hz, 2H), 7.24 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.3 Hz, 2H), 7.36 (d, J = 3.4 Hz, 1H), 7.47 (d, J = 8.3 Hz, 2H), 7.65 (d, J = 8.3 Hz, 2H), 12.28 (amplio, 1H)

Ejemplo	solvente, Hz	RMN (δ)
4-79	DMSO-d6, 300MHz-120□	0.73-0.96 (m, 5H), 0.98-1.31 (m, 5H), 1.34-1.89 (m, 13H), 3.20 (d, J = 7.0 Hz, 2H), 4.70 (s, 2H), 5.08 (s, 2H), 6.93 (d, J = 3.7 Hz, 1H), 7.02 (d, J = 8.8 Hz, 2H), 7.13 (d, J = 3.7 Hz, 1H), 7.22 (d, J = 8.1 Hz, 2H), 7.26-7.37 (m, 4H), 7.50 (d, J = 8.8 Hz, 2H), 7.69 (d, J = 8.4 Hz, 2H)
4-80	DMSO-d6, 300MHz	0.87-1.25 (m, 10H), 1.32-1.53 (m, 3H), 1.55-1.82 (m, 10H), 2.38-2.49 (m, 1H), 3.25 (d, J = 6.8 Hz, 2H), 4.71 (s, 2H), 5.06 (s, 2H), 6.98-7.03 (m, 3H), 7.18-7.25 (m, 3H), 7.34 (d, J = 8.3 Hz, 2H), 7.50 (d, J = 8.7 Hz, 2H), 7.61 (d, J = 9.0 Hz, 2H), 7.83 (d, J = 8.7 Hz, 2H), 8.70 (s, 1H), 12.35 (amplio, 1H)
4-81	DMSO-d6, 300MHz	0.80 (t, J = 7.3 Hz, 6H), 1.00-1.17 (m, 4H), 1.37-1.58 (m, 4H), 2.40-2.50 (m, 1H), 3.22 (s, 2H), 3.97 (s, 2H), 5.07 (s, 2H), 5.33 (s, 1H), 6.90-6.98 (m, 3H), 7.07 (d, J = 8.7 Hz, 2H), 7.19-7.27 (m, 2H), 7.30-7.39 (m, 5H), 7.45-7.56 (m, 6H), 7.68 (d, J = 8.3 Hz, 2H), 12.29 (amplio, 1H)
4-82	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 1.00-1.27 (m, 7H), 1.34-1.61 (m, 4H), 1.97 (s amplio, 4H), 3.34 (s amplio, 4H), 4.07-4.19 (m, 2H), 4.60 (s amplio, 2H), 4.76 (s amplio, 2H), 5.08 (s, 2H), 6.59 (d, J = 9.0 Hz, 2H), 6.92 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.30 (s amplio, 1H), 7.41-7.53 (m, 3H), 7.65 (d, J = 7.5 Hz, 2H), 7.76 (d, J = 7.9 Hz, 2H)
4-83	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 1.00-1.20 (m, 4H), 1.15 (t, J = 7.2 Hz, 3H), 1.38-1.58 (m, 4H), 2.40-2.54 (m, 1H), 3.44 (s, 2H), 3.88 (s, 3H), 4.04 (c, J = 7.2 Hz, 2H), 4.02 (s, 2H), 4.14 (s, 2H), 5.06 (s, 2H), 6.92 (d, J = 8.6 Hz, 2H), 7.02 (d, J = 3.8 Hz, 1H), 7.07 (d, J = 9.0 Hz, 2H), 7.17 (t, J = 7.5 Hz, 1H), 7.24 (t, J = 7.7 Hz, 1H), 7.36 (d, J = 3.8 Hz, 1H), 7.46 (d, J = 8.3 Hz, 2H), 7.53 (d, J = 9.1 Hz, 1H), 7.57-7.65 (m, 3H)

Ejemplo	solvente, Hz	RMN (δ)
4-84	DMSO-d6, 300MHz	1.16-1.45 (m, 5H), 1.65-1.83 (m, 5H), 2.39-2.49 (m, 3H), 2.70 (t, J = 7.2 Hz, 2H), 2.93 (t, J = 8.1 Hz, 2H), 3.31 (t, J = 8.5 Hz, 2H), 3.61 (s, 2H), 3.73 (s, 2H), 4.27 (s, 2H), 6.59 (d, J = 8.3 Hz, 1H), 6.88 (d, J = 3.8 Hz, 1H), 7.06 (d, J = 3.8 Hz, 1H), 7.16-7.40 (m, 11H), 12.17 (s amplio, 1H)
4-85	DMSO-d6, 300MHz	1.03 (s, 9H), 2.79 (s, 2H), 3.24 (s, 2H), 3.78 (s, 2H), 4.00 (s, 2H), 5.54 (s, 2H), 7.05-7.18 (m, 4H), 7.21-7.45 (m, 7H), 7.58-7.64 (m, 3H), 7.71 (d, J = 1.5 Hz, 1H), 12.37 (s amplio, 1H)
4-86	DMSO-d6, 300MHz	0.79 (t, J = 7.4 Hz, 6H), 0.97-1.17 (m, 4H), 1.34-1.59 (m, 4H), 2.39-2.55 (m, 1H), 3.26 (s, 2H), 3.76 (s, 3H), 3.96 (s, 2H), 4.03 (s, 2H), 5.06 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 6.99-7.20 (m, 4H), 7.26 (s, 1H), 7.36-7.51 (m, 4H), 7.66-7.80 (m, 4H), 12.22 (s amplio, 1H).
4-87	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.98-1.17 (m, 4H), 1.36-1.58 (m, 4H), 2.38-2.53 (m, 1H), 3.41 (s, 2H), 4.11 (s, 2H), 4.12 (s, 2H), 5.06 (s, 2H), 6.92 (d, J = 8.7 Hz, 2H), 7.07 (d, J = 8.7 Hz, 2H), 7.43-7.48 (m, 3H), 7.54-7.61 (m, 1H), 7.66-7.79 (m, 5H), 7.94-8.00 (m, 2H), 8.37 (d, J = 8.3 Hz, 1H), 12.54 (s amplio, 1H).
4-88	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.97-1.19 (m, 4H), 1.35-1.60 (m, 4H), 2.39-2.54 (m, 1H), 3.51 (s, 2H), 4.18 (s, 2H), 4.33 (s, 2H), 5.06 (s, 2H), 6.93 (d, J = 8.9 Hz, 2H), 7.07 (d, J = 8.9 Hz, 2H), 7.37-7.53 (m, 5H), 7.70 (d, J = 8.3 Hz, 2H), 7.82 (d, J = 1.5 Hz, 1H), 7.90-7.96 (m, 1H), 8.07-8.13 (m, 1H), 12.58 (s amplio, 1H).

Ejemplo	solvente, Hz	RMN (δ)
4-89	DMSO-d6, 300MHz	0.79 (t, J = 7.1 Hz, 6H), 0.98-1.19 (m, 4H), 1.36-1.60 (m, 4H), 2.38-2.55 (m, 1H), 3.28 (s, 2H), 3.84 (s, 2H), 3.98 (s, 2H), 5.07 (s, 2H), 5.29 (s, 2H), 6.86 (d, J = 1.1 Hz, 1H), 6.93 (d, J = 8.4 Hz, 2H), 7.03-7.31 (m, 8H), 7.40-7.43 (m, 1H), 7.47 (d, J = 8.0 Hz, 2H), 7.68 (d, J = 8.0 Hz, 2H), 7.78 (d, J = 1.1 Hz, 1H), 12.62 (s amplio, 1H).
4-90	DMSO-d6, 300MHz	0.79 (t, J = 7.1 Hz, 6H), 0.97-1.17 (m, 4H), 1.36-1.59 (m, 4H), 2.39-2.53 (m, 1H), 3.25 (s, 2H), 3.85 (s, 2H), 4.05 (s, 2H), 5.06 (s, 2H), 6.38-6.41 (m, 1H), 6.93 (d, J = 8.8 Hz, 2H), 7.03-7.15 (m, 3H), 7.29-7.39 (m, 2H), 7.41-7.52 (m, 4H), 7.70 (d, J = 8.1 Hz, 2H), 7.78 (d, J = 1.1 Hz, 1H), 11.04 (s amplio, 1H), 12.30 (s amplio, 1H).
4-91	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.99-1.16 (m, 4H), 1.36-1.58 (m, 4H), 2.38-2.54 (m, 1H), 3.31 (s, 2H), 3.85 (s, 2H), 4.05 (s, 2H), 5.07 (s, 2H), 6.93 (d, J = 8.8 Hz, 2H), 7.04-7.12 (m, 3H), 7.42-7.55 (m, 5H), 7.60-7.75 (m, 5H), 7.79 (d, J = 1.4 Hz, 1H), 8.23-8.26 (m, 1H), 12.42 (s amplio, 1H).
4-92	DMSO-d6, 300MHz	0.79 (t, J = 7.1 Hz, 6H), 0.98-1.18 (m, 4H), 1.36-1.59 (m, 4H), 2.39-2.53 (m, 1H), 3.38 (s, 2H), 4.05 (s, 2H), 4.10 (s, 2H), 5.07 (s, 2H), 6.82 (s, 1H), 6.93 (d, J = 8.6 Hz, 2H), 7.07 (d, J = 8.6 Hz, 2H), 7.19-7.32 (m, 2H), 7.44-7.64 (m, 5H), 7.70 (d, J = 8.4 Hz, 2H), 7.79 (d, J = 1.4 Hz, 1H), 12.44 (s amplio, 1H).
4-93	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.97-1.17 (m, 4H), 1.35-1.59 (m, 4H), 2.39-2.53 (m, 1H), 3.37 (s, 2H), 4.02 (s, 2H), 4.07 (s, 2H), 5.06 (s, 2H), 6.89-6.98 (m, 3H), 7.03-7.10 (m, 3H), 7.14 (d, J = 3.7 Hz, 1H), 7.27 (dd, J = 3.3, 1.1 Hz, 1H), 7.42-7.51 (m, 4H), 7.70 (d, J = 8.1 Hz, 2H), 7.79 (d, J = 1.1 Hz, 1H), 12.46 (s amplio, 1H).

Ejemplo	solvente, Hz	RMN (δ)
4-94	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.97-1.17 (m, 4H), 1.35-1.59 (m, 4H), 2.38-2.54 (m, 1H), 3.34 (s, 2H), 3.83 (s, 2H), 4.01 (s, 2H), 5.06 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 6.99-7.11 (m, 4H), 7.27-7.50 (m, 6H), 7.64 (d, J = 8.3 Hz, 2H), 7.93 (d, J = 7.9 Hz, 2H), 12.42 (s amplio, 1H).
4-95	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.98-1.18 (m, 4H), 1.34-1.59 (m, 4H), 2.38-2.54 (m, 1H), 3.27 (s, 2H), 3.83 (s, 2H), 4.03 (s, 2H), 5.06 (s, 2H), 6.89-6.97 (m, 3H), 7.07 (d, J = 8.7 Hz, 2H), 7.26-7.51 (m, 6H), 7.58-7.66 (m, 3H), 7.79 (d, J = 7.1 Hz, 2H), 12.66 (s amplio, 2H).
4-96	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.97-1.17 (m, 4H), 1.33-1.60 (m, 4H), 2.38-2.53 (m, 1H), 3.51 (s, 2H), 4.15 (s, 2H), 4.21 (s, 2H), 5.06 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 6.98-7.11 (m, 3H), 7.32-7.50 (m, 5H), 7.62 (d, J = 7.9 Hz, 2H), 7.68-7.77 (m, 2H), 12.49 (s amplio, 1H).
4-97	DMSO-d6, 300MHz	0.79 (t, J = 7.3 Hz, 6H), 0.97-1.18 (m, 4H), 1.36-1.61 (m, 4H), 2.40-2.54 (m, 1H), 3.40 (s, 2H), 4.08 (s, 2H), 4.16 (s, 2H), 5.07 (s, 2H), 6.88-7.12 (m, 2H), 7.28-7.41 (m, 3H), 7.48 (d, J = 8.3 Hz, 5H), 7.66 (d, J = 8.3 Hz, 2H), 7.73-7.81 (m, 2H), 7.90-7.97 (m, 1H), 12.48 (s amplio, 1H).
4-98	DMSO-d6, 400MHz	0.80 (t, J = 7.3 Hz, 6H), 0.98-1.16 (m, 4H), 1.37-1.58 (m, 4H), 2.41-2.53 (m, 1H), 3.39 (s, 2H), 4.05 (s, 2H), 4.09 (s, 2H), 5.07 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.02 (d, J = 3.7 Hz, 1H), 7.07 (d, J = 8.7 Hz, 2H), 7.25-7.31 (m, 1H), 7.36-7.50 (m, 6H), 7.63-7.70 (m, 4H), 7.78 (d, J = 1.4 Hz, 1H), 12.46 (s amplio, 1H).

Ejemplo	solvente, Hz	RMN (δ)
4-99	DMSO-d6, 400MHz	0.79 (t, J = 7.3 Hz, 6H), 1.00-1.15 (m, 4H), 1.36-1.57 (m, 4H), 2.40-2.52 (m, 1H), 4.32 (s, 2H), 4.96 (s, 2H), 5.05 (s, 2H), 6.91 (d, J = 8.6 Hz, 2H), 7.02-7.13 (m, 3H), 7.21 (d, J = 3.7 Hz, 1H), 7.28-7.34 (m, 1H), 7.39-7.54 (m, 4H), 7.63 (d, J = 8.3 Hz, 2H), 7.77-7.82 (m, 1H), 12.95 (s amplio, 1H).
4-100	DMSO-d6, 400MHz	0.80 (t, J = 7.3 Hz, 6H), 0.99-1.17 (m, 4H), 1.38-1.58 (m, 4H), 2.40-2.52 (m, 1H), 3.96 (s, 2H), 4.68 (s, 2H), 5.07 (s, 2H), 6.93 (d, J = 8.8 Hz, 2H), 7.03-7.12 (m, 3H), 7.32 (d, J = 4.0 Hz, 1H), 7.37 (d, J = 3.7 Hz, 1H), 7.48 (d, J = 8.5 Hz, 2H), 7.62 (d, J = 8.5 Hz, 2H), 7.67 (d, J = 4.0 Hz, 1H), 12.97 (s amplio, 1H).
4-101	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.96 (t, J = 7.0 Hz, 3H), 1.00-1.17 (m, 4H), 1.23 (t, J = 7.0 Hz, 3H), 1.35-1.61 (m, 4H), 2.37-2.55 (m, 1H), 3.16-3.50 (m, 6H), 3.96 (s, 2H), 4.02 (s, 2H), 5.07 (s, 2H), 5.43 (s, 2H), 6.93 (d, J = 8.7 Hz, 2H), 7.00-7.24 (m, 5H), 7.31-7.41 (m, 2H), 7.48 (d, J = 8.6 Hz, 2H), 7.58-7.68 (m, 3H), 12.08 (s amplio, 1H).
4-102	DMSO-d6, 300MHz	1.14-1.48 (m, 5H), 1.64-1.85 (m, 5H), 2.26 (s, 3H), 2.27 (s, 3H), 2.38-2.54 (m, 1H), 2.87 (dd, J = 7.7, 14.1 Hz, 1H), 3.02 (dd, J = 7.6, 13.9 Hz, 1H), 3.59 (t, J = 7.5 Hz, 1H), 3.81 (d, J = 14.3 Hz, 1H), 3.96 (d, J = 14.3 Hz, 1H), 5.07 (s, 2H), 7.05 (d, J = 1.1 Hz, 2H), 7.14-7.35 (m, 11H), 7.57 (d, J = 1.5 Hz, 1H), 12.48 (s amplio, 1H)
4-103	DMSO-d6, 300MHz	0.93 (t, J = 7.3 Hz, 3H), 0.97 (t, J = 7.0 Hz, 3H), 1.36-1.51 (m, 2H), 1.65-1.77 (m, 2H), 3.26 (s, 2H), 3.57 (c, J = 7.1 Hz, 2H), 3.81 (s, 2H), 4.00-4.08 (m, 4H), 7.07 (t, J = 8.5 Hz, 4H), 7.23-7.44 (m, 6H), 7.48 (d, J = 8.7 Hz, 2H), 7.66 (d, J = 8.4 Hz, 2H), 7.80 (d, J = 1.1 Hz, 1H)

Ejemplo	solvente, Hz	RMN (δ)
4-104	CDCl3-300MHz	1.17-1.51 (m, 5H), 1.67-1.95 (m, 5H), 2.30 (s, 3H), 2.43-2.57 (m, 1H), 2.78 (s, 3H), 4.99 (s, 2H), 5.19 (s, 2H), 6.88 (d, J = 8.3 Hz, 1H), 7.00 (dd, J = 1.8, 8.4 Hz, 1H), 7.14-7.36 (m, 7H), 7.53 (d, J = 1.5 Hz, 1H), 7.70 (d, J = 8.6 Hz, 1H), 7.79 (d, J = 1.9 Hz, 1H)
4-105	DMSO-d6, 400MHz	3.27 (s, 2H), 3.81 (s, 2H), 4.03 (s, 2H), 5.17 (s, 2H), 7.13-7.18 (m, 3H), 7.24-7.29 (m, 1H), 7.32-7.40 (m, 4H), 7.42-7.49 (m, 3H), 7.71 (d, J = 8.3 Hz, 2H), 7.79 (d, J = 1.6 Hz, 1H), 12.40 (s amplio, 1H)
4-106	DMSO-d6,400MHz	0.79 (t, J = 7.3 Hz, 6H), 0.99-1.16 (m, 4H), 1.38-1.58 (m, 4H), 2.40-2.53 (m, 1H), 3.35 (s, 2H), 4.04 (s, 2H), 4.10 (s, 2H), 4.94-5.17 (m, 6H), 5.92-6.04 (m, 1H), 6.92 (d, J = 8.8 Hz, 2H), 7.02-7.10 (m, 3H), 7.16-7.27 (m, 2H), 7.37 (d, J = 3.5 Hz, 1H), 7.44-7.53 (m, 3H), 7.59-7.65 (m, 3H), 12.60 (s amplio, 1H).
4-107	DMSO-d6, 300MHz	0.79 (t, J = 7.2 Hz, 6H), 0.97-1.16 (m, 4H), 1.36-1.60 (m, 4H), 2.39-2.56 (m, 1H), 4.26 (s, 2H), 4.90 (s, 2H), 5.05 (s, 2H), 6.91 (d, J = 8.7 Hz, 2H), 7.06 (d, J = 8.7 Hz, 2H), 7.19 (d, J = 3.6 Hz, 1H), 7.34 (s, 1H), 7.40 (d, J = 3.6 Hz, 1H), 7.42-7.49 (m, 4H), 7.62 (d, J = 8.3 Hz, 2H), 7.86-7.92 (m, 2H), 12.88 (s amplio, 1H).

Aplicabilidad Industrial

Como es claro de los resultados de las pruebas anteriores y lo similar, el compuesto [I] de la presente invención ha demostrado tener una actividad inhibidora de la PTP1B y una actividad hipoglucémica, superiores. Esto es, se espera qe el compuesto [I] de la presente invención proporcione un nuevo tipo de fármaco para la profilaxis o tratamiento de la diabetes, que

mejora directamente la acción de la insulina y aminora el estado hiperglucémico. Además, se espera que el compuesto [I] de la presente invención proporcione un fármaco para la profilaxis o tratamiento de las complicaciones diabéticas (retinopatía, nefropatía, neuropatía, síndrome X o síndrome metabólico, enfermedades cardiacas isquémicas (infarto cardiaco, angina de pecho, etc.), apoplejías (infarto cerebral, hemorragia cerebral, hemorragia subaracnoidea, etc.), hiperlipidemia, obesidad y lo similar, y además, un fármaco para la profilaxis o tratamiento de enfermedades mediadas por la PTP1B.

Además, el compuesto [I] de la presente invención mejora la actividad hipoglucémica, como se muestra en los resultados de las pruebas anteriores, mediante la administración en combinación con cada una de insulina, glibenclamida, tolbutamida, nateglinida, clorhidrato de metformina, voglibosa y clorhidrato de Pioglitazona. Por lo tanto, se espera que el compuesto [I] tenga actividad para mejorar mutuamente y/o complementar la capacidad para disminuir la glucosa en sangre (ayuno, postprandial), que tienen individualmente el compuesto [I] de la presente invención y los agentes terapéuticos para la diabetes, mediante el uso en combinación con otros agentes terapéuticos para la diabetes (particularmente, los agentes terapéuticos correspondientes, diferentes a los agentes terapéuticos para las complicaciones diabéticas), incluyendo una preparación de insulina, secretagogo de insulina, biguanida, inhibidor de la α-glucosidasa y mejorardor de la sensibilidad a la insulina. Además, se espera que el compuesto [I] de la

presente invención logre simultáneamente una mejora de la hiperglicemia y profilaxis o tratamiento de las complicaciones diabéticas (particularmente, complicaciones microangiogénicas), mediante el uso en combinación con otros agentes terapéuticos para la diabetes (particularmente, agentes terapéuticos para las complicaciones diabéticas). Además, se espera que el compuesto [I] de la presente invención aminora la hiperglucemia, los lípidos altos en sangre y la obesidad, y además, que evite la transición a complicaciones diabéticas (particulamente, complicaciones de las grandes arterias) y/o suprima la progresión de las mismas, mediante elsuo en combinación con otros agentes terapéuticos para la hiperlipidemia, agentes terapéuticos para la obesidad, agentes terapéuticos para la hipertensión y/o agentes terapéuticos para la trombosis. En otras palabras, se espera que el compuesto [I] de la presente invención exhiba un alto efecto profiláctico o terapéutico para la diabetes y las complicaciones diabéticas, mediante el uso en combinación con otros agentes terapéuticos para la diabetes, otros agentes terapéuticos para la hiperlipidemia, otros agentes terapéuticos para la obesidad, agentes terapéuticos para la hipertensión o agentes terapéuticos para la trombosis, efecto el cual no está disponible por el uso independiente de cada agente terapéutico.

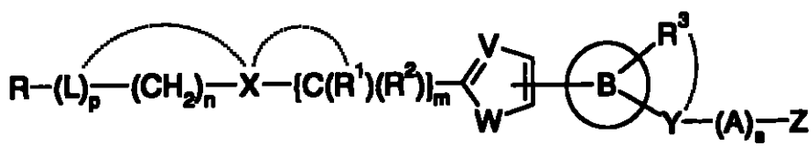
Esta solicitud está basada en las solicitudes de patentes Nos. 2003-105267 y 2003-157590 presentadas en Japón, el contenido de las cuales se incorporan aquí como referencia. Las referencias citadas en la presente, incluyendo las patentes y las solicitudes de patente, se incorporan

en su totalidad como referencia, al grado en que se han descrito en la presente.

NOVEDAD DE LA INVENCION

REIVINDICACIONES

1.- Un compuesto anular heteroaromático de 5 miembros, representado por la fórmula [I]

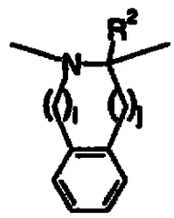


[I]

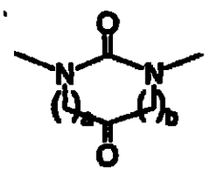
en donde V es =N- o =CH-; W es -S- u -O-; m es 0, 1 ó 2; R^1 y R^2 son cada uno de manera independiente, un átomo de hidrógeno o un grupo alquilo de C_{1-4}; X es $-N(R^4)-$, $-N(R^5)-CO-O-$, $-SO_2-N(R^5)-$, $-N(R^5)-SO_2-$, $-N(R^6)-SO_2-N(R^5)-$, $-CO-N(R^7)-$, $-N(R^8)-CO-$, $-N(R^9)-CO-N(R^5)-$, $-N(R^{10})-(CH_2)_k-N(R^5)-$, $-N(R^{10})-(CH_2)_k-N(R^5)-CO-$, $-C(R^{10})=N-N(R^7)-$, $-N(R^{10})-(CH_2)_k-CH(R^6)-$, -O-, -S- o $-SO_2-$ en donde k es 0 o un entero de 1 a 4, R^4, R^5, R^6, R^7, R^8, R^9 y R^{10} son cada uno de manera independiente (1) un átomo de hidrógeno, (2) un grupo alquilo de C_{1-6} en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por (a) un grupo arilo sustituido opcionalmente, (b) un grupo anular heteroaromático sustituido opcionalmente, (c) un grupo carboxi, (d) un grupo alcoxicarbonilo de C_{1-4}, (e) $-CO-N(R^{15})(R^{16})$ en donde R^{15} y R^{16} son cada uno de manera independiente, un átomo de hidrógeno, un grupo arilo sustituido opcionalmente, un grupo anular heteroaromático sustituido opcionalmente, un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido

opcionalmente por sustituyentes seleccionados del grupo que consiste de un grupo arilo sustituido opcionalmente, un grupo anular heteroaromático sustituido opcionalmente, un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo arilo y un grupo ariloxi sustituido opcionalmente, o, junto con el átomo de nitrógeno unido al mismo, puede formar un anillo de indolina o puede formar un heteroanillo de 5 a 7 miembros que contiene opcionalmente además, al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxigeno y un átomo de azufre, (f) $-N(R^{15})(R^{16})$ en donde R^{15} y R^{16} son como se definió anteriormente, (g) $-O-R^{17}$ en donde R^{17} es un átomo de hidrógeno, un grupo arilo sustituido opcionalmente, un grupo anular heteroaromático sustituido opcionalmente o un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de un grupo arilo sustituido opcionalmente, un grupo anular heteroaromátic sustituido opcionalmente, un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo arilo y un grupo ariloxi sustituido opcionalmente, (h) $-CO-R^{17}$ en donde R^{17} es como se definió anteriormente, (i) $-SO_2-R^{17}$ en donde R^{17} es como se definió anteriormente o (j) un grupo cicloalquilo de C_{3-7}, (3) $-CO-N(R^{15})(R^{16})$ en donde R^{15} y R^{16} son como se definió anteriormente, (4) $-SO_2-N(R^{15})(R^{16})$ en donde R^{15} y R^{16} son como se definió anteriormente, (5) $-CO-R^{17}$ en donde R^{17} es como se definió anteriormente, (6) $-SO_2-R^{17}$ en donde R^{17} es como se definió anteriormente, (7) un grupo arilo sustituido opcionalmente,

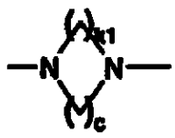
(8) un grupo anular heteroaromático sustituido opcionalmente, o (9) R^4 y R^1 están unidos opcionalmente para formar



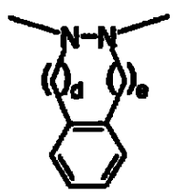
en donde i y j son cada uno de manera independiente 0, 1 ó 2, (10) R^5 y R^9 están unidos opcionalmente para formar



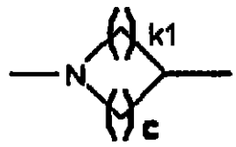
en donde a y b son cada uno de manera independiente 0, 1 ó 2, (11) R^5 y R^{10} están unidos opcionalmente para formar



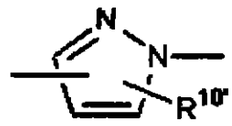
en donde k1 y c son cada uno de manera independiente 0 o un entero de 1 a 4, (12) R^5 y R^{10} están unidos opcionalmente para formar



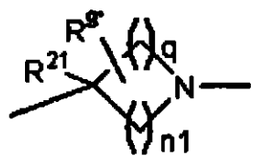
en donde d y e son cada uno de manera independiente 0, 1 ó 2, (13) R^6 y R^{10} están unidos opcionalmente para formar



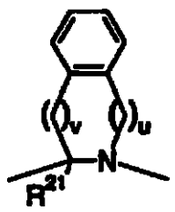
en donde k1 y c son como se definió anteriormente, o (14) R^7 y R^{10} están unidos opcionalmente para formar



en donde $R^{10'}$ es un átomo de hidrógeno o un grupo alquilo de C_{1-6}; n es 0 o un entero de 1 a 4; p es 0 ó 1; L es (1) $-C(R^{20})(R^{21})-$ en donde R^{20} es (a) un átomo de hidrógeno, (b) un grupo alquilo de C_{1-6}, o (c) unido opcionalmente con R^4 o R^6 para formar



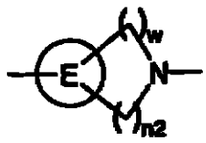
en donde n1 y q son cada uno de manera independiente 0 o un entero de 1 a 4, $R^{9'}$ es un átomo de hidrógeno, un grupo hidroxilo, un grupo alquilo de C_{1-6}, un grupo carboxi o un grupo alcoxi de C_{1-6}, o (d) unido opcionalmente con R^4 para formar



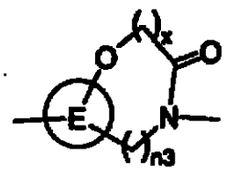
en donde u y v son cada uno de manera independiente 0, 1 ó 2, R^{21} es un átomo de hidrógeno, un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por un grupo arilo sustituido opcionalmente o un grupo anular heteroaromático sustituido opcionalmente, un grupo arilo sustituido opcionalmente o un grupo anular heteroaromático sustituido opcionalmente, (2)



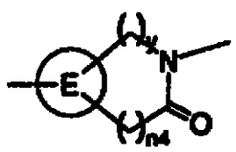
en donde E es un grupo arilo o un grupo anular heteroaromático, R^{22} es (a) un átomo de hidrógeno, (b) un átomo de halógeno, (c) un grupo alquilo de C_{1-4}, (d) un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo carboxi, (e) un grupo alquiltio de C_{1-6}, (f) un grupo nitro, (g) $-N(R^{23})(R^{24})$ en donde R^{23} y R^{24} son cada uno de manera independiente, un átomo de hidrógeno, un grupo alquilo de C_{1-6}, un grupo alquilcarbonilo de C_{1-4} en donde el grupo alquilcarbonilo de C_{1-4} está sustituido opcionalmente por un grupo amino, un grupo alquilamino de C_{1-4} o un grupo di(alquil de C_{1-4})amino, o un grupo alquilsulfonilo de C_{1-4}, o (h) unido opcionalmente con R^4 para formar



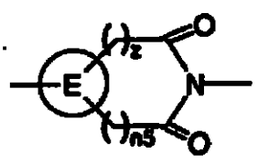
en donde n2 y w son cada uno de manera independiente 0 o un entero de 1 a 3, (i) unido opcionalmente con R^4 para formar



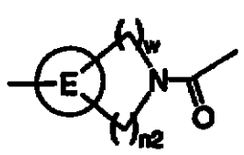
en donde n3 y x son cada uno de manera independiente 0 ó 1, (j) unido opcionalmente con R^7 para formar



en donde n4 y y son cada uno de manera independiente 0, 1 ó 2, (k) unido opcionalmente con R^7 para formar



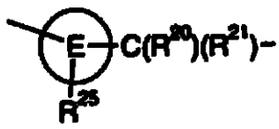
en donde n5 y z son cada uno de manera independiente 0 ó 1, (l) unido opcionalmente con R^8 para formar



en donde n2 y w son cada uno de manera independiente 0 o un entero de 1 a 3, o (m) unido opcionalmente con R^4 para formar



o (3)



en donde R^{20}, R^{21} y E son como se definió anteriormente, R^{25} es (a) un átomo de hidrógeno, (b) un átomo de halógeno, (c) un grupo alquilo de C_{1-4}, (d) un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo carboxi, (e) un grupo alquiltio de C_{1-6}, (f) un grupo nitro o (g) $-N(R^{23})(R^{24})$ en donde R^{23} y R^{24} son como se definió anteriormente; R es $-COO(R^{19})$, $-A^1-COO(R^{19})$ o $-O-A^1-COO(R^{19})$ en donde A^1 es un grupo alquileno de C_{1-4} y R^{19} es un átomo de hidrógeno o un grupo alquilo de C_{1-4}; B es un grupo arilo o un grupo anular heteroaromático; R^3 es (1)un átomo de hidrógeno, (2) un átomo de halógeno, (3) un grupo alquilo de C_{1-6}, (4) un grupo alcoxi de C_{1-6}, (5) un grupo alquilamino de C_{1-6}, (6) un grupo di(alquil de C_{1-6})amino, (7) un grupo ciano, (8) un grupo nitro, (9) un grupo haloalquilo de C_{1-4}, (10) $-S-R^{18}$ en donde R^{18} es un grupo alquilo de C_{1-6} o un grupo arilo, (11) $-SO-R^{18}$ en donde R^{18} es un grupo alquilo de C_{1-6} o un grupo arilo, (12) $-SO_2-R^{18}$ en donde R^{18} es un grupo alquilo de C_{1-6} o un grupo arilo, (13) un grupo arilo o (14) un grupo heterocíclico; Y es -O-, -S-, -SO-, $-SO_2-$, $-N(R^{11})-$, $-N(R^{12})-CO-$, $-N(R^{12})-SO_2-$,

$-SO_2-N(R^{12})-$, $-C(R^{13})(R^{14})-$, $-CO-$, $-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ o $-C(R^{13})(R^{14})-O-$ en donde R^{11} es (1) un átomo de hidrógeno, (2) un grupo alquilo de C_{1-8} en donde el grupo alquilo de C_{1-8} está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de (a) un grupo cicloalquilo de C_{3-7}, (b) un grupo arilo sustituido opcionalmente, (c) un grupo heterocíclico sustituido opcionalmente, (d) un grupo hidroxilo, (e) un grupo alquilamino de C_{1-4} y (f) un grupo di(alquil de C_{1-4})amino, (3) un grupo alquenilo de C_{2-4}, (4) un grupo alquilsulfonilo de C_{1-4}, (5) un grupo alquilcarbonilo de C_{1-4} en donde el grupo alquilcarbonilo de C_{1-4} está sustituido opcionalmente por un grupo hidroxilo o un grupo alcoxi de C_{1-4}, o (6) unido opcionalmente con R^3 para formar



en donde t es un entero de 1 a 4, R^{12} es (1) un átomo de hidrógeno, (2) un grupo alquilo de C_{1-8} en donde el grupo alquilo de C_{1-8} está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de (a) un grupo cicloalquilo de C_{3-7}, (b) un grupo arilo sustituido opcionalmente, (c) un grupo heterocíclico sustituido opcionalmente, (d) un grupo hidroxilo, (e) un grupo alquilamino de C_{1-4} y (f) un grupo di(alquil de C_{1-4})amino, (3) un grupo alquenilo de C_{2-4}, (4) un grupo alquilsulfonilo de C_{1-4} o (5) un grupo alquilcarbonilo de C_{1-4} en donde el grupo alquilcarbonilo de C_{1-4} está sustituido opcionalmente por un grupo hidroxilo o un grupo alcoxi de C_{1-4}, R^{13} y R^{14} son

cada uno de manera independiente, un átomo de hidrógeno, un grupo alquilo de C_{1-4}, u opcionalmente forman un cicloalcano de C_{3-7} junto con el átomo de carbono unido al mismo, u opcionalmente forman, junto con el átomo de carbono unido al mismo, un heteroanillo de 5 a 7 miembros que tiene opcionalmente al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre, con la condición de que, cuando m es 0, p es 1 y L es

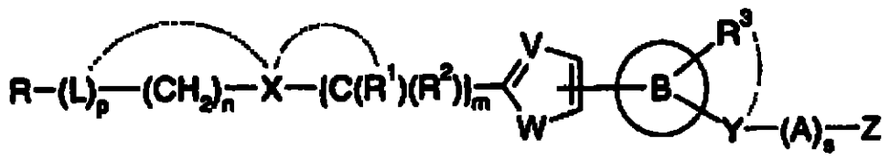


en donde R^{20} y R^{21} son cada uno un átomo de hidrógeno, E es un grupo fenilo, R^{22} es un átomo de hidrógeno, un átomo de halógeno, un grupo alquilo de C_{1-4}, un grupo alcoxi de C_{1-4} o un grupo nitro, R^{25} es un átomo de hidrógeno, un átomo de halógeno, un grupo alquilo de C_{1-4}, un grupo alcoxi de C_{1-4} o un grupo nitro, Y puede ser $-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ o $-C(R^{13})(R^{14})-O-$, en donde R^{12}, R^{13} y R^{14} son como se definió anteriormente; s es 0 ó 1; A es un grupo alquileno de C_{1-4} sustituido opcionalmente por un grupo cicloalquilo de C_{3-7}; Z es (1) un grupo cicloalquilo de C_{3-7} en donde el grupo cicloalquilo de C_{3-7} está sustituido opcionalmente por un grupo arilo, en donde el grupo arilo está sustituido opcionalmente por un átomo de halógeno o un grupo alquilo de C_{1-6}, o un grupo anular heteroaromático, en donde el grupo anular heteroaromático está sustituido opcionalmente por un átomo de

halógeno o un grupo alquilo de C_{1-6}, (2) un grupo arilo en donde el grupo arilo está sustituido por sustituyentes seleccionados del grupo que consiste de (a) un grupo heterocíclico sustituido opcionalmente por un grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4}, (b) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por un grupo hidroxilo, un grupo oxo, un átomo de halógeno o un grupo alquilo de C_{1-6}, (c) un grupo carboxi, (d) un átomo de halógeno, (e) un grupo alquilo de C_{1-6}, (f) un grupo haloalquilo de C_{1-4}, (g) un grupo alquilamino de C_{1-4}, (h) un grupo di(alquil de C_{1-4})amino, (i) un grupo alquiltio de C_{1-6}, (j) un grupo alcoxi de C_{1-4}, (k) un grupo alquilcarbonilo de C_{1-4} y (l) un grupo nitro, (3) un grupo anular heteroaromático en donde el grupo anular heteroaromático está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de (a) un grupo heterocíclico sustituido opcionalmente por un grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4}, (b) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por un grupo hidroxilo, un grupo oxo, un átomo de halógeno o un grupo alquilo de C_{1-6}, (c) un grupo carboxi, (d) un átomo de halógeno, (e) un grupo alquilo de C_{1-6}, (f) un grupo haloalquilo de C_{1-4}, (g) un grupo alquilamino de C_{1-4}, (h) un grupo di(alquil de C_{1-4})amino, (i) un grupo alquiltio de C_{1-6}, (j) un grupo alcoxi de C_{1-4}, (k) un grupo alquilcarbonilo de C_{1-4} y (l) un grupo arilo sustituido opcionalmente por un átomo de halógeno o un grupo haloalquilo de C_{1-4}, (4) un grupo indanilo o (5) un grupo piperacinilo en donde el grupo piperacinilo está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de (a) un grupo fenilo, (b) un grupo fenilalquilo de C_{1-4}, (c) un grupo

benzoilo sustituido opcionalmente por un átomo de halógeno y (d) un grupo fenilalcoxicarbonilo de C_{1-4} o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

2.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 1, caracterizado además porque está representado por la fórmula [I]

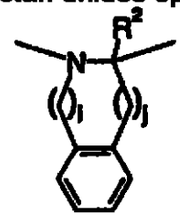


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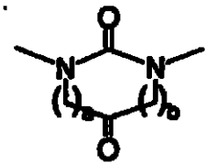
en donde V es =N- o =CH-; W es -S- u -O-; m es 0, 1 ó 2; R^1 y R^2 son cada uno de manera independiente, un átomo de hidrógeno o un grupo alquilo de C_{1-4}; X es $-N(R^4)-$, $-N(R^5)-CO-O-$, $-SO_2-N(R^5)-$, $-N(R^5)-SO_2-$, $-N(R^6)-SO_2-N(R^5)-$, $-CO-N(R^7)-$, $-N(R^8)-CO-$, $-N(R^9)-CO-N(R^5)-$, $-N(R^{10})-(CH_2)_k-N(R^5)-$, -O-, -S- o $-SO_2-$ en donde k es 0 o un entero de 1 a 4, R^4, R^5, R^6, R^7, R^8, R^9 y R^{10} son cada uno de manera independiente (1) un átomo de hidrógeno, (2) un grupo alquilo de C_{1-6} en donde el grupo alquilo de C_{1-6} está sustituido por (a) un grupo arilo sustituido opcionalmente, (b) un grupo anular heteroaromático sustituido opcionalmente, (c) un grupo carboxi, (d) un grupo alcoxicarbonilo de C_{1-4}, (e) $-CO-N(R^{15})(R^{16})$ en donde R^{15} y R^{16} son cada uno de manera independiente, un átomo de hidrógeno, un grupo arilo sustituido opcionalmente, un grupo anular heteroaromático sustituido opcionalmente, un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido

opcionalmente por sustituyentes seleccionados del grupo que consiste de un grupo arilo sustituido opcionalmente, un grupo anular heteroaromático sustituido opcionalmente, un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo arilo y un grupo ariloxi sustituido opcionalmente, o, junto con el átomo de nitrógeno unido al mismo, puede formar un anillo de indolina o puede formar un heteroanillo de 5 a 7 miembros que contiene opcionalmente además al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre, (f) $-N(R^{15})(R^{16})$ en donde R^{15} y R^{16} son como se definió anteriormente, (g) $-O-R^{17}$ en donde R^{17} es un átomo de hidrógeno, un grupo arilo sustituido opcionalmente, un grupo anular heteroaromático sustituido opcionalmente o un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de un grupo arilo sustituido opcionalmente, un grupo anular heteroaromático sustituido opcionalmente, un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo arilo y un grupo ariloxi sustituido opcionalmente, (h) $-CO-R^{17}$ en donde R^{17} es como se definió anteriormente, (i) $-SO_2-R^{17}$ en donde R^{17} es como se definió anteriormente o (j) un grupo cicloalquilo de C_{3-7}, (3) $-CO-N(R^{15})(R^{16})$ en donde R^{15} y R^{16} son como se definió anteriormente, (4) $-SO_2-N(R^{15})(R^{16})$ en donde R^{15} y R^{16} son como se definió anteriormente, (5) $-CO-R^{17}$ en donde R^{17} es como se definió anteriormente, (6) $-SO_2-R^{17}$ en donde R^{17} es como se definió anteriormente, (7) un grupo arilo sustituido opcionalmente,

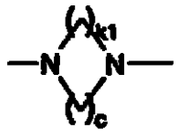
(8) un grupo anular heteroaromático sustituido opcionalmente, o (9) R^4 y R^1 están unidos opcionalmente para formar



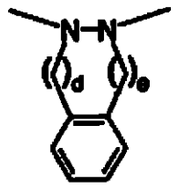
en donde i y j son cada uno de manera independiente 0, 1 ó 2, (10) R^5 y R^9 están unidos opcionalmente para formar



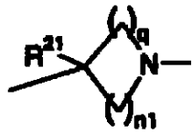
en donde a y b son cada uno de manera independiente 0, 1 ó 2, (11) R^5 y R^{10} están unidos opcionalmente para formar



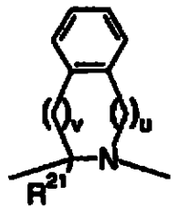
en donde k1 y c son cada uno de manera independiente 0 o un entero de 1 a 4; o (12) R^5 y R^{10} están unidos opcionalmente para formar



en donde d y e son cada uno de manera independiente 0, 1 ó 2; n es 0 o un entero de 1 a 4; p es 0 ó 1; L es (1) $-C(R^{20})(R^{21})-$ en donde R^{20} es (a) un átomo de hidrógeno, (b) un grupo alquilo de C_{1-6}, o (c) unido opcionalmente con R^4 para formar



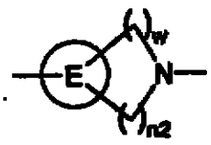
en donde n1 y q son cada uno de manera independiente 0 o un entero de 1 a 4, o (d) unido opcionalmente con R^4 para formar



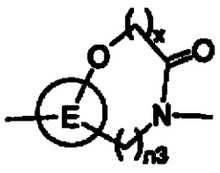
en donde u y v son cada uno de manera independiente 0, 1 ó 2, R^{21} es un átomo de hidrógeno, un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por un grupo arilo sustituido opcionalmente o un grupo anular heteroaromático sustituido opcionalmente, un grupo arilo sustituido opcionalmente o un grupo anular heteroaromático sustituido opcionalmente, (2)



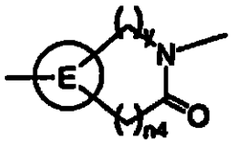
en donde E es un grupo arilo o un grupo anular heteroaromático, R^{22} es (a) un átomo de hidrógeno, (b) un átomo de halógeno, (c) un grupo alquilo de C_{1-4}, (d) un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo carboxi, (e) un grupo alquiltio de C_{1-6}, (f) un grupo nitro, (g) $-N(R^{23})(R^{24})$ en donde R^{23} y R^{24} son cada uno de manera independiente, un átomo de hidrógeno, un grupo alquilo de C_{1-6}, un grupo alquilcarbonilo de C_{1-4} en donde el grupo alquilcarbonilo de C_{1-4} está sustituido opcionalmente por un grupo amino, un grupo alquilamino de C_{1-4} o un grupo di(alquil de C_{1-4})amino, o un grupo alquilsulfonilo de C_{1-4}, o (h) unido opcionalmente con R^4 para formar



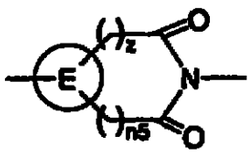
en donde n2 y w son cada uno de manera independiente 0 o un entero de 1 a 3, (i) unido opcionalmente con R^4 para formar



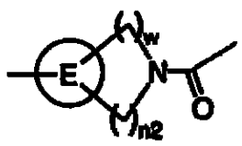
en donde n3 y x son cada uno de manera independiente 0 ó 1, (j) unido opcionalmente con R^7 para formar



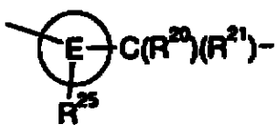
en donde n4 y y son cada uno de manera independiente 0, 1 ó 2, (k) unido opcionalmente con R^7 para formar



en donde n5 y z son cada uno de manera independiente 0 ó 1, o (l) unido opcionalmente con R^8 para formar

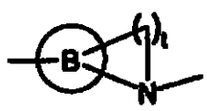


en donde n2 y w son cada uno de manera independiente 0 o un entero de 1 a 3 o (3)



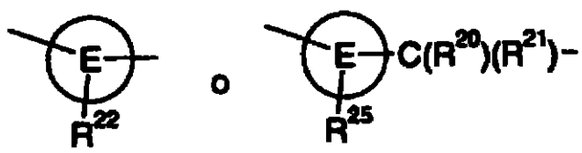
en donde R^{20}, R^{21} y E son como se definió anteriormente, R^{25} es (a) un átomo de hidrógeno, (b) un átomo de halógeno, (c) un grupo alquilo de C_{1-4}, (d) un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo carboxi, (e) un grupo alquiltio de C_{1-6}, (f) un grupo nitro o (g) $-N(R^{23})(R^{24})$ en donde R^{23} y R^{24} son como se definió anteriormente; R es $-COO(R^{19})$, $-A^1-COO(R^{19})$ o $-O-A^1-COO(R^{19})$ en donde A^1 es un grupo alquileno de C_{1-4} y R^{19} es un átomo de hidrógeno o un grupo alquilo de C_{1-4}; B es un grupo arilo o un grupo anular heteroaromático; R^3 es (1)un átomo de hidrógeno, (2) un átomo de halógeno,

(3) un grupo alquilo de C_{1-6}, (4) un grupo alcoxi de C_{1-6}, (5) un grupo alquilamino de C_{1-6}, (6) un grupo di(alquil de C_{1-6})amino, (7) un grupo ciano, (8) un grupo nitro, (9) un grupo haloalquilo de C_{1-4}, (10) $-S-R^{18}$ en donde R^{18} es un grupo alquilo de C_{1-6} o un grupo arilo, (11) $-SO-R^{18}$ en donde R^{18} es un grupo alquilo de C_{1-6} o un grupo arilo, o (12) $-SO_2-R^{18}$ en donde R^{18} es un grupo alquilo de C_{1-6} o un grupo arilo; Y es -O-, -S-, -SO-, $-SO_2-$, $-N(R^{11})-$, $-N(R^{12})-CO-$, $-N(R^{12})-SO_2-$, $-SO_2-N(R^{12})-$, $-C(R^{13})(R^{14})-$, -CO-, $-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ o $-C(R^{13})(R^{14})-O-$ en donde R^{11} es (1) un átomo de hidrógeno, (2) un grupo alquilo de C_{1-6} en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de (a) un grupo cicloalquilo de C_{3-7}, (b) un grupo arilo sustituido opcionalmente, (c) un grupo heterocíclico sustituido opcionalmente, (d) un grupo hidroxilo, (e) un grupo alquilamino de C_{1-4} y (f) un grupo di(alquil de C_{1-4})amino, (3) un grupo alquenilo de C_{2-4}, (4) un grupo alquilsulfonilo de C_{1-4}, (5) un grupo alquilcarbonilo de C_{1-4} en donde el grupo alquilcarbonilo de C_{1-4} está sustituido opcionalmente por un grupo hidroxilo o un grupo alcoxi de C_{1-4}, o (6) unido opcionalmente con R^3 para formar



en donde t es un entero de 1 a 4, R^{12} es (1) un átomo de hidrógeno, (2) un grupo alquilo de C_{1-6} en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de (a)

un grupo cicloalquilo de C_{3-7}, (b) un grupo arilo sustituido opcionalmente, (c) un grupo heterocíclico sustituido opcionalmente, (d) un grupo hidroxilo, (e) un grupo alquilamino de C_{1-4} y (f) un grupo di(alquil de C_{1-4})amino, (3) un grupo alquenilo de C_{2-4}, (4) un grupo alquilsulfonilo de C_{1-4} o (5) un grupo alquilcarbonilo de C_{1-4} en donde el grupo alquilcarbonilo de C_{1-4} está sustituido opcionalmente por un grupo hidroxilo o un grupo alcoxi de C_{1-4}, R^{13} y R^{14} son cada uno de manera independiente, un átomo de hidrógeno, un grupo alquilo de C_{1-4}, u opcionalmente forman un cicloalcano de C_{3-7} junto con el átomo de carbono unido al mismo, u opcionalmente forman, junto con el átomo de carbono unido al mismo, un heteroanillo de 5 a 7 miembros que tiene opcionalmente al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre, con la condición de que, cuando m es 0, p es 1 y L es

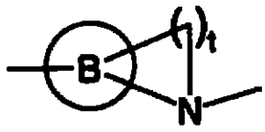


en donde R^{20} y R^{21} son cada uno un átomo de hidrógeno, E es un grupo fenilo, R^{22} es un átomo de hidrógeno, un átomo de halógeno, un grupo alquilo de C_{1-4}, un grupo alcoxi de C_{1-4} o un grupo nitro, y R^{25} es un átomo de hidrógeno, un átomo de halógeno, un grupo alquilo de C_{1-4}, un grupo alcoxi de C_{1-4} o un grupo nitro, Y debe ser $-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ o $-C(R^{13})(R^{14})-O-$, en donde R^{12}, R^{13} y R^{14} son como se definió anteriormente; s

es 0 ó 1; A es un grupo alquileno de C_{1-4} sustituido opcionalmente por un grupo cicloalquilo de C_{3-7}; Z es (1) un grupo cicloalquilo de C_{3-7} en donde el grupo cicloalquilo de C_{3-7} está sustituido opcionalmente por un grupo arilo, en donde el grupo arilo está sustituido opcionalmente por un átomo de halógeno o un grupo alquilo de C_{1-6}, o un grupo anular heteroaromático en donde el grupo anular heteroaromático está sustituido opcionalmente por un átomo de halógeno o un grupo alquilo de C_{1-6}, (2) un grupo arilo en donde el grupo arilo está sustituido por sustituyentes seleccionados del grupo que consiste de (a) un grupo heterocíclico sustituido opcionalmente por un grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4}, (b) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por un grupo hidroxilo, un grupo oxo, un átomo de halógeno o un grupo alquilo de C_{1-6}, (c) un grupo carboxi, (d) un átomo de halógeno, (e) un grupo alquilo de C_{1-6}, (f) un grupo haloalquilo de C_{1-4}, (g) un grupo alquilamino de C_{1-4}, (h) un grupo di(alquil de C_{1-4})amino, (i) un grupo alquiltio de C_{1-6}, (j) un grupo alcoxi de C_{1-4}, y (k) un grupo alquilcarbonilo de C_{1-4}, (3) un grupo anular heteroaromático en donde el grupo anular heteroaromático está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de (a) un grupo heterocíclico sustituido opcionalmente por un grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4}, (b) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por un grupo hidroxilo, un grupo oxo, un átomo de halógeno o un grupo alquilo de C_{1-6}, (c) un grupo carboxi, (d) un átomo de halógeno, (e) un grupo alquilo de C_{1-6}, (f) un grupo haloalquilo de C_{1-4}, (g) un grupo alquilamino de C_{1-4}, (h) un grupo di(alquil de C_{1-4})amino, (i) un grupo

alquiltio de C_{1-6}, (j) un grupo alcoxi de C_{1-4}, (k) un grupo alquilcarbonilo de C_{1-4} y (l) un grupo arilo sustituido opcionalmente por un átomo de halógeno o un grupo haloalquilo de C_{1-4}, (4) un grupo indanilo o (5) un grupo piperacinilo, en donde el grupo piperacinilo está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de (a) un grupo fenilo, (b) un grupo fenilalquilo de C_{1-4}, (c) un grupo benzoilo sustituido opcionalmente por un átomo de halógeno y (d) un grupo fenilalcoxicarbonilo de C_{1-4} o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

3.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 1, caracterizado además porque en la fórmula [I], R^3 es (1) un átomo de hidrógeno, (2) un átomo de halógeno, (3) un grupo alquilo de C_{1-6} o (4) un grupo alcoxi de C_{1-4}; Y es -O-, -N(R^{11})-, -N(R^{12})-CO-, -C(R^{13})(R^{14})-, -C(R^{13})(R^{14})-N(R^{12})-, -CO-N(R^{12})- o -C(R^{13})(R^{14})-O- en donde R^{11} es (1) un átomo de hidrógeno, (2) un grupo alquilo de C_{1-6}, o (3) unido opcionalmente con R^3 para formar



en donde t es 3, R^{12} es un átomo de hidrógeno o un grupo alquilo de C_{1-6}, R^{13} y R^{14} son cada uno un átomo de hidrógeno, con la condición de que cuando m es 0, p es 1, y L es



en donde R^{20} y R^{21} son cada uno un átomo de hidrógeno, E es un grupo fenilo, R^{22} es un átomo de hidrógeno, un grupo alcoxi de C_{1-4} o un grupo nitro, R^{25} es un átomo de hidrógeno, un grupo alcoxi de C_{1-4} o un grupo nitro, Y debe ser $-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ o $-C(R^{13})(R^{14})-O-$, en donde R^{12}, R^{13} y R^{14} son como se definió anteriormente; s es 0 ó 1; A es un grupo alquileno de C_{1-4}; Z es un grupo arilo sustituido por sustituyentes seleccionados del grupo que consiste de (a) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un átomo de halógeno y un grupo alquilo de C_{1-6}, (b) un átomo de halógeno, (c) un grupo alquilo de C_{1-6}, (d) un grupo haloalquilo de C_{1-4}, (e) un grupo di(alquil de C_{1-4})amino, (f) un grupo alquiltio de C_{1-6} y (g) un grupo alquilcarbonilo de C_{1-4}, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

4.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 3, caracterizado además porque V es =N- y W es -S- o -O-, o V es =CH- y W es -S-, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

5.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 4, caracterizado además porque Z es un grupo fenilo sustituido por un grupo alquilo de C_{1-6}, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

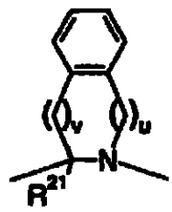
6.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 5, caracterizado además porque Y es

-C(R^{13})(R^{14})-N(R^{12})- o -C(R^{13})(R^{14})-O- en donde R^{12}, R^{13} y R^{14} son como se definen en la reivindicación 3 y s es 0, o Y es -O- o -N(R^{11})- en donde R^{11} es como se define en la reivindicación 3, s es 1, y A es un grupo metileno o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

7.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 6, caracterizado además porque V es =CH-, W es -S-, y la posición de la sustitución de B en el anillo de tiofeno formado por V junto con W está en la posición 4 o la posición 5, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

8.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 7, caracterizado además porque B es un grupo fenilo, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

9.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 8, caracterizado además porque m es 1; R^1 y R^2 son cada uno un átomo de hidrógeno; X es -N(R^4)- u -O- en donde R^4 es un grupo alquilo de C_{1-6} sustituido opcionalmente por (a) un grupo arilo, (b) un grupo anular heteroaromático sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-6} o (c)-CO-N(R^{15})(R^{16}) en donde R^{15} y R^{16} son cada uno de manera independiente, un átomo de hidrógeno o un grupo arilo, en donde el grupo arilo está sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-6}; n es 0 ó 1; p es 0 ó 1; L es (1) -C(R^{20})(R^{21})- en donde R^{20} está enlazado con R^4 para formar



en donde u es 1, v es 1, R^{21} es un átomo de hidrógeno, o (2)



en donde E es un grupo anular heteroaromático y R^{22} es un átomo de hidrógeno; R es -COO(R^{19}) en donde R^{19} es un átomo de hidrógeno, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

10.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 9, caracterizado además porque X es -N(R^4), en donde R^4 es como se define en la reivindicación 9, n es 1 y p es 0, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

11.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 10, caracterizado además porque R^4 es un grupo metilo sustituido por un grupo anular heteroaromático sustituido opcionalmente por un grupo alquilo de C_{1-8}, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

12.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 11, caracterizado además porque el anillo

heteroaromático definido en la reivindicación 11 es un grupo tiazolilo, un grupo oxazolilo o un grupo bencimidazolilo o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

13.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 10, caracterizado además porque R^4 es un grupo metilo sustituido por -CO-N(R^{15})(R^{16}), en donde R^{15} es un átomo de hidrógeno y R^{16} es un grupo arilo sustituido opcionalmente por un grupo alquilo de C_{1-6}, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

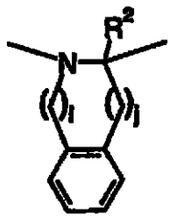
14.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 6, caracterizado además porque V es =N-, W es -S-, y la posición de la sustitución de B en el anillo de tiazol formado por V junto con W está en la posición 4, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

15.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 14, caracterizado además porque B es un grupo fenilo, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

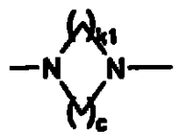
16.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 15, caracterizado además porque m es 0 ó 1; R^1 y R^2 son cada uno de manera independiente, un átomo de hidrógeno o un grupo alquilo de C_{1-4}; X es -N(R^4)-, -N(R^5)-CO-O-, -SO_2-N(R^5)-, -CO-N(R^7)-, -N(R^9)-CO-N(R^5)-, -N(R^{10})-(CH_2)$_k$-N(R^5)-, -O-, -S- o -SO_2- en donde R^4 es (1)

un átomo de hidrógeno, (2) un grupo alquilo de C_{1-6} en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por (a) un grupo arilo sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un átomo de halógeno, un grupo alquilo de C_{1-6} y un grupo haloalquilo de C_{1-4}, (b) un grupo anular heteroaromático sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-6}, (c) un grupo carboxi, (d) un grupo alcoxicarbonilo de C_{1-4}, (e) -CO-N(R^{15})(R^{16}) en donde R^{15} y R^{16} son cada uno de manera independiente, un átomo de hidrógeno, un grupo arilo, en donde el grupo arilo está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un grupo alquilo de C_{1-6}, un grupo alcoxi de C_{1-4}, un grupo carboxi y un grupo di(alquil de C_{1-4})amino, un grupo anular heteroaromático, un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por un grupo arilo, o, junto con el átomo de nitrógeno unido al mismo, puede formar un heteroanillo de 5 a 7 miembros que contiene opcionalmente al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre, (f) -N(R^{15})(R^{16}) en donde R^{15} y R^{16} son cada uno de manera independiente, un átomo de hidrógeno o un grupo arilo, (g) -O-R^{17} en donde R^{17} es un grupo arilo, o (h) un grupo cicloalquilo de C_{3-7}, (3) -CO-N(R^{15})(R^{16}) en donde R^{15} y R^{16} son cada uno de manera independiente, un átomo de hidrógeno, un grupo arilo, en donde el grupo arilo está sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-6}, un grupo alquilo de C_{1-6}, o, junto con el átomo de nitrógeno unido al mismo, puede formar un anillo de indolina o puede formar un

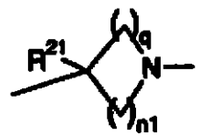
heteroanillo de 5 a 7 miembros que contiene opcionalmente, al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre, (4) $-SO_2-N(R^{15})(R^{16})$ en donde R^{15} y R^{16} son cada uno de manera independiente un grupo arilo o un grupo alquilo de C_{1-6}, (5) $-CO-R^{17}$ en donde R^{17} es un grupo arilo, en donde el grupo arilo está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un grupo alquilo de C_{1-6} y un grupo alcoxi de C_{1-4}, un grupo anular heteroaromático o un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por un grupo arilo sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un átomo de halógeno y un grupo alquilo de C_{1-6}, un grupo anular heteroaromático, un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo arilo o un grupo ariloxi sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-6}, (6) $-SO_2-R^{17}$ en donde R^{17} es un grupo arilo, (7) un grupo arilo, u (8) unido opcionalmente con R^1 para formar



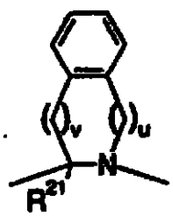
en donde i y j son cada uno 1, R^5 es un átomo de hidrógeno o un grupo arilo o un grupo alquilo de C_{1-6} sustituido opcionalmente por un grupo cicloalquilo de C_{3-7}, R^7 es un átomo de hidrógeno o un grupo alquilo de C_{1-6}, R^9 es un átomo de hidrógeno o un grupo alquilo de C_{1-6}, k es 2, R^{10} es (1) un átomo de hidrógeno, (2) un grupo alquilo de C_{1-6}, o (3) unido opcionalmente con R^5 para formar



en donde k1 y c son cada uno 2; n es 0 o un entero de 1 a 3; p es 0 ó 1; L es (1) $-C(R^{20})(R^{21})-$ en donde R^{20} es (a) un átomo de hidrógeno, (b) un grupo alquilo de C_{1-6}, o (c) unido opcionalmente con R^4 para formar



en donde n1 y q son cada uno de manera independiente un entero de 1 a 3, o (d) unido opcionalmente con R^4 para formar



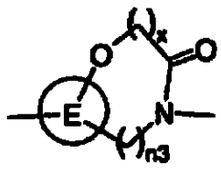
en donde u es 1 y v es 1, R^{21} es un átomo de hidrógeno, un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por un

grupo arilo sustituido opcionalmente por 1 a 3 átomos de halógeno, o un grupo arilo o (2)



en donde E es un grupo arilo o un grupo anular heteroaromático, R^{22} es (a) un átomo de hidrógeno, (b) un grupo alcoxi de C_{1-4} sustituido opcionalmente por un grupo carboxi, (c) un grupo nitro, (d) $-N(R^{23})(R^{24})$ en donde R^{23} y R^{24} son cada uno de manera independiente, un átomo de hidrógeno, un grupo alquilcarbonilo de C_{1-4}, en donde el grupo alquilcarbonilo de C_{1-4} está sustituido opcionalmente por un grupo alquilamino de C_{1-4} o un grupo di(alquil de C_{1-4})amino o un grupo alquilsulfonilo de C_{1-4}, o

(e) unido opcionalmente con R^4 para formar



en donde n3 es 0, x es 1; R es $-COO(R^{19})$ en donde R^{19} es un átomo de hidrógeno o un grupo alquilo de C_{1-4}, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

17.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 16, caracterizado además porque m es 1 y R^1 y R^2 son cada uno un átomo de hidrógeno, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

18.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 17, caracterizado además X es -N(R^4), en donde R^4 es de conformidad con la reivindicación 16, n es 1 y p es 0, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

19.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 18, caracterizado además porque R^4 es un grupo alquilo de C_{1-6} sustituido opcionalmente por (a) un grupo arilo sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un átomo de halógeno, un grupo alquilo de C_{1-6} y un grupo haloalquilo de C_{1-4}, (b) un grupo anular heteroaromático sustituido opcionalmente por 1 a 3 grupos alquilo de C_{1-6}, (c) un grupo carboxi, (d) un grupo alcoxicarbonilo de C_{1-4}, (e) -CO-N(R^{15})(R^{16}) en donde R^{15} y R^{16} son cada uno de manera independiente, un átomo de hidrógeno, un grupo arilo, en donde el grupo arilo está sustituido opcionalmente por 1 a 3 sustituyentes seleccionados del grupo que consiste de un grupo alquilo de C_{1-6}, un grupo alcoxi de C_{1-4}, un grupo carboxi y un grupo di(alquil de C_{1-4})amino, un grupo anular heteroaromático, un grupo alquilo de C_{1-6}, en donde el grupo alquilo de C_{1-6} está sustituido opcionalmente por un grupo arilo, o, junto con el átomo de nitrógeno unido al mismo, puede formar un heteroanillo de 5 a 7 miembros que contiene además, opcionalmente al menos un heteroátomo seleccionado del grupo que consiste de un átomo de nitrógeno, un átomo de oxígeno y un átomo de azufre, (f) -N(R^{15})(R^{16}) en donde R^{15} y R^{16} son cada uno de manera independiente, un átomo de hidrógeno o un grupo arilo, (g) -O-R^{17} en donde

R^{17} es un grupo arilo, o (h) un grupo cicloalquilo de C_{3-7}, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

20.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 19, caracterizado además porque R^4 es un grupo metilo sustituido por un grupo anular heteroaromático sustituido opcionalmente por un grupo alquilo de C_{1-6} o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

21.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 20, caracterizado además porque es un grupo tiazolilo, un grupo oxazolilo, un grupo bencimidazolilo, un grupo piridilo o un grupo quinolilo, o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos.

22.- El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 19, caracterizado además porque donde R^4 es un grupo metilo sustituido por -CO-N(R^{15})(R^{16}), en donde R^{15} es un átomo de hidrógeno y R^{16} es un grupo arilo sustituido opcionalmente por un grupo alquilo de C_{1-6}, o un profármaco del mismo, o una sal farmacéuticamente aceptable del mismo.

23.- El compuesto anular heteroaromático de 5 miembros de conformidad con cualquiera de las reivindicaciones 1 a 22, caracterizado además porque se selecciona del grupo que consiste de los siguientes compuestos, o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos: (1) ácido 5-{4-[4-({[4-(1-etilpropil)fenil]isopropil-

amino}metil)-fenil]tiazol-2-ilmetoxi}nicotínico; (2) ácido 4-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetoxi}benzoico; (3) ácido 6-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetoxi}-nicotínico; (4) ácido 5-{4-[4-({metil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetoxi}nicotínico; (5) ácido 4-{4-[4-({metil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetoxi}benzoico; (6) ácido 6-[4-(4-[[(4-isopropilfenil)(1-propilbutil)amino]metil}-fenil)tiazol-2-ilmetoxi]nicotínico; (7) ácido 5-[4-(4-[[(4-isopropilfenil)(1-propilbutil)amino]metil}-fenil)tiazol-2-ilmetoxi]nicotínico; (8) ácido 5-[4-(4-[[isobutil(4-isopropilfenil)amino]metil}fenil)-tiazol-2-ilmetoxi]-nicotínico; (9) ácido 4-[4-(4-[[(4-isopropilfenil)(1-propilbutil)amino]metil}-fenil)tiazol-2-ilmetoxi]benzoico; (10) ácido 3-[4-(4-[[(4-isopropilfenil)(1-propilbutil)amino]metil}-fenil)tiazol-2-ilmetoxi]benzoico; (11) ácido 6-[4-(4-[[(1-etilpropil)(4-isopropilfenil)amino]metil}-fenil)tiazol-2-ilmetoxi]nicotínico; (12) ácido 5-[4-(4-[[(1-etilpropil)(4-isopropilfenil)amino]metil}-fenil)tiazol-2-ilmetoxi]nicotínico; (13) ácido 4-{4-[4-({[4-(1-etilpropil)fenil]isopropil-amino}metil)-fenil]tiazol-2-ilmetiltio}benzoico; (14) ácido 4-{4-[4-({metil[4-(1-propilbutil)fenil]amino}-metil)-fenil]tiazol-2-ilmetiltio}benzoico; (15) ácido 4-(metil-{4-[4-({metil[4-(1-propilbutil)fenil]amino}-metil)fenil]tiazol-2-ilmetil}sulfamoil)benzoico; (16) 4-(metil{4-[4-({metil[4-(1-propilbutil)fenil]-amino}metil)fenil]-tiazol-2-ilmetil}sulfamoil)butirato de sodio; (17) ácido 4-[[(4-{4-[(4-ciclohexilfenil-amino)metil]fenil}tiazol-2-il)metilamino]metil]benzoico; (18) ácido 4-({[4-(4-[[(4-ciclohexilfenil)metilamino]metil}fenil)-tiazol-2-il]metilamino}-metil)benzoico; (19)ácido 4-[(metil-{4-[4-({metil[4-(1-propilbutil)fenil]amino}-

metil)fenil]tiazol-2-il}amino)metil]benzoico; (20) ácido 4-[({4-[4-({[4-(1-etilpropil)fenil]isopropil-amino}metil)-fenil]tiazol-2-il}metilamino)metil]benzoico; (21) ácido (S)-({4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}metilamino)fenilacético; (22) ácido (S)-2-({4-[4-({[4-(1-etilpropil)fenil]isopropilamino}-metil)fenil]tiazol-2-ilmetil}metilamino)-3-fenilpropiónico; (23) ácido {bencil[4-(4-{[(4-ter-butilfenil)isobutilamino]metil}-fenil)-tiazol-2-ilmetil]amino}acético; (24) ácido {bencil[4-(4-{[(4-cloro-fenil)isobutilamino]metil}fenil)-tiazol-2-ilmetil]amino}acético; (25) ácido (bencil{4-[4-({metil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}amino)acético; (26) ácido (bencil{4-[4-({[4-(1-etilpropil)fenil]isopropil-amino}metil)fenil]tiazol-2-ilmetil}amino)acético; (27) ácido {1-[4-(4-{[(4-ter-butil-fenil)isobutilamino]metil}fenil)-tiazol-2-ilmetil]-3-fenilureido}acético; (28) ácido {benzoil-[4-(4-{[(4-ter-butilfenil)isobutilamino]-metil}-fenil)tiazol-2-ilmetil]amino}acético; (29) ácido [[4-(4-{[(4-ter-butil-fenil)isobutilamino]-metil}fenil)-tiazol-2-ilmetil]-(piridin-2-ilcarbonil)amino]acético; (30) ácido [[4-(4-{[(4-ter-butil-fenil)isobutilamino]metil}fenil)-tiazol-2-ilmetil]-(piridin-3-ilcarbonil)amino]acético; (31) ácido {bencensulfonil-[4-(4-{[(4-ter-butilfenil)isobutilamino]-metil}fenil)tiazol-2-ilmetil]amino}acético; (32) ácido 2-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (33) ácido (S)-2-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}-metil)fenil]tiazol-2-ilmetil}-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (34) ácido (S)-2-{4-[4-({metil[4-(1-propilbutil)fenil]amino}-metil)fenil]tiazol-2-ilmetil}-1,2,3,4-tetrahidroisoquinolin-

3-carboxílico; (35) ácido (S)-2-[4-(4-[[(1-etilpropil)-(4-isopropilfenil)amino]-metil}fenil)tiazol-2-ilmetil]-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (36) ácido 4-({4-[4-(4-ciclohexilfenoximetil)fenil]tiazol-2-il}metilamino)benzoico; (37) ácido 4-[({4-[4-(4-ciclohexilfenoximetil)fenil]tiazol-2-il}metilamino)metil]benzoico; (38) ácido 4-[[(4-{4-[4-(1,1-dimetilpropil)fenoximetil]fenil}tiazol-2-il)metilamino]-metil}benzoico; (39)ácido 4-[[metil-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-il)amino]metil}benzoico; (40) 4-[[metil(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiazol-2-il)amino]metil}-benzoato de sodio; (41) ácido (S)-[metil-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiazol-2-ilmetil)amino]fenilacético; (42) ácido (S)-2-[metil-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiazol-2-ilmetil)amino]-3-fenilpropiónico; (43)ácido (bencil{4-[4-(2-ter-butil-4-metil-fenoximetil)fenil]-tiazol-2-ilmetil}amino)acético; (44) ácido [bencil(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)amino]acético; (45) ácido 2-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (46) ácido (S)-2-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (47) ácido (R)-2-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (48) ácido 5-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetoxi)nicotínico; (49) ácido 4-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetoxi)benzoico; (50) ácido 4-[metil-(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiazol-2-ilmetil)sulfamoil]benzoico; (51) ácido 4-[metil-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)sulfamoil]butírico; (52) ácido 4-({4-[4-(4-ciclohexilfenilcarbamoil)fenil]tiazol-2-il}metilamino)benzoico; (53) ácido

4-[({4-[4-(4-ciclohexilfenilcarbamoil)fenil]tiazol-2-il}metilamino)metil]benzoico; (54) ácido [bencil(4-{4-[4-(1-propilbutil)fenilcarbamoil]fenil}-tiazol-2-ilmetil)amino]acético; (55) ácido [bencil(4-{4-[4-(1-propilbutil)bencilcarbamoil]-fenil}-tiazol-2-ilmetil)amino]acético; (56) ácido {bencil[4-(4-{metil[4-(1-propilbutil)bencil]-carbamoil}-fenil)tiazol-2-ilmetil]amino}acético; (57) ácido {bencil[4-(4-{etil-[4-(1-propilbutil)bencil]-carbamoil}-fenil)tiazol-2-ilmetil]amino}acético; (58) ácido 5-{4-[4-({(2-hidroxi-2-metilpropil)-[4-(1-propilbutil)-fenil]amino}metil)fenil]tiazol-2-ilmetoxi}nicotínico; (59) ácido [[4-(4-{[(4-ter-butil-fenil)isobutilamino]metil}fenil)-tiazol-2-ilmetil]-(morfolin-4-carbonil)amino]acético; (60) 5-{4-[4-({[4-(1-etilpropil)fenil]isopropil-amino}metil)fenil]tiazol-2-ilmetoxi}-nicotinato de sodio; (61) (S)-2-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxilato de sodio; (62) 5-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetoxi)-nicotinato de sodio; (63) ácido 3-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetoxi}-5-metoxi-benzoico; (64) ácido (1-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-3-fenilureido)acético; (65) ácido (1-{4-[4-({[4-(1-etilpropil)fenil]isopropil-amino}metil)-fenil]tiazol-2-ilmetil}-3-p-tolilureido)acético; (66) ácido [1-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-3-(4-isopropilfenil)ureido]acético; (67) ácido (1-{4-[4-({[4-(1-etilpropil)fenil]isopropil-amino}metil)-fenil]tiazol-2-ilmetil}-3-metil-3-fenilureido)acético; (68) ácido 5-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetoxi}nicotínico; (69) ácido [3-fenil-1-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiazol-2-

ilmetil)ureido]acético; (70) ácido (3-(2,6-dimetilfenil)-1-{4-[4-({[4-(1-etilpropil)-fenil]-isopropilamino}metil)fenil]tiazol-2-ilmetil}ureido)acético; (71) ácido ({4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}fenilcarbamoil-metilamino)acético; (72) ácido (1-{4-[4-({[4-(1-etilpropil)fenil]isopropil-amino}metil)-fenil]tiazol-2-ilmetil}-3-isopropil-ureido)acético; (73) ácido 3-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetoxi}-isoxazol-5-carboxílico; (74) ácido 5-[4-(4-{[(2-etilbutil)-(4-isopropilfenil)amino]metil}-fenil)tiazol-2-ilmetoxi]nicotínico; (75) ácido [{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-(piperidin-1-carbonil)amino]acético; (76) ácido 2-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetoxi)nicotínico; (77) ácido [{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-(p-tolilcarbamoilmetil)amino]acético; (78) ácido {{4-[4-({[4-(1-etilpropil)fenil]iso-propilamino}metil)-fenil]tiazol-2-ilmetil}-[(4-isopropilfenilcarbamoil)metil]amino}-acético; (79) ácido (1-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}-3-metil-3-fenilureido)acético; (80)ácido (1-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}-3-p-tolilureido)acético; (81) ácido ((2,3-dihidro-indol-1-carbonil)-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}amino)acético; (82) ácido 3-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetoxi)piridin-2-carboxílico; (83) ácido {[4-(4-{[(2-etilbutil)-(4-isopropilfenil)amino]metil}-fenil)tiazol-2-ilmetil]fenilcarbamoilmetilamino}acético; (84) ácido {[4-(4-{[(2-etilbutil)-(4-isopropilfenil)amino]metil}fenil)-tiazol-2-ilmetil]-[(4-isopropil-

fenilcarbamoil)metil]amino}acético; (85) ácido 4-(2-{carboximetil[4-(4-[[(2-etilbutil)-(4-isopropilfenil)-amino]metil}fenil)tiazol-2-ilmetil]amino}-acetilamino)benzoico; (86)ácido 6-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetoxi)piridin-2-carboxílico; (87) ácido 5-{4-[4-({isobutil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetoxi}nicotínico; (88) ácido (1-{4-[4-({isobutil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}-3-fenilureido)acético; (89) éster metílico del ácido 5-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)fenil]tiazol-2-ilmetoxi}nicotínico; (90) ácido 4-amino-3-{4-[4-({[4-(1-etilpropil)fenil]-isopropilamino}metil)fenil]tiazol-2-ilmetoxi}benzoico; (91) ácido 3-{4-[4-({[4-(1-etilpropil)fenil]isopropil-amino}metil)-fenil]tiazol-2-ilmetoxi}benzoico; (92) ácido 3-({4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}amino)benzoico; (93) ácido 3-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetoxi}-4-nitro-benzoico; (94) ácido ((1H-bencimidazol-2-ilmetil)-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}amino)acético; (95) ácido [fenilcarbamoilmetil(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiazol-2-ilmetil)amino]acético; (96) ácido [(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)-(piridin-3-ilcarbamoilmetil)amino]acético; (97) ácido [[(4-dimetilaminofenilcarbamoil)metil]-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)amino]acético; (98) ácido [[(4-metoxifenilcarbamoil)metil]-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)amino]acético; (99) ácido [[(isopropilfenilcarbamoil)metil]-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)amino]acético; (100) ácido [(4-{4-[4-(1-propilbutil)fenoximetil]-

fenil}tiazol-2-ilmetil)-(piridin-2-ilcarbamoilmetil)amino]acético; (101)ácido [(2-oxo-2-pirrolidin-1-il-etil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético; (102) ácido [(4-metiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético; (103) ácido 4-(3-ciclohexilmetil-3-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}ureido)benzoico; (104) ácido 4-(3-isobutil-3-{4-[4-({isopropil[4-(1-propilbutil)fenil]-amino}metil)fenil]tiazol-2-ilmetil}ureido)benzoico; (105) ácido (1-{4-[4-({isobutil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}-3-metil-3-fenilureido)acético; (106) ácido ({4-[4-({isobutil[4-(1-propilbutil)fenil]-amino}metil)-fenil]tiazol-2-ilmetil}fenilcarbamoilmetilamino)acético; (107) ácido {{4-[4-({isobutil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}-[(4-isopropilfenilcarbamoil)metil]amino}acético; (108) ácido 4-acetilamino-3-{4-[4-({isopropil[4-(1-propilbutil)fenil]-amino}metil)fenil]tiazol-2-ilmetoxi}benzoico; (109) ácido 4-(2-dimetilaminoacetilamino)-3-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetoxi}benzoico; (110) ácido ((1H-bencimidazol-2-ilmetil)-{4-[4-({[4-(1-etilpropil)-fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}amino)acético; (111)ácido [(1H-bencimidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético; (112) ácido 3-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetoxi}-4-metansulfonilaminobenzoico; (113) ácido 4-isobutirilamino-3-{4-[4-({isopropil[4-(1-propilbutil)-fenil]amino}metil)fenil]tiazol-2-ilmetoxi}benzoico; (114) ácido 4-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-3-oxo-3,4-dihidro-2H-benzo[1,4]oxacin-6-carboxílico; (115) ácido 4-{4-

[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-3-oxo-3,4-dihidro-2H-benzo[1,4]oxacin-8-carboxílico; (116) ácido ({4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}-{metilfenilamino-sulfonil}amino)acético; (117) ácido ([(4-isopropilfenilcarbamoil)metil]-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}amino)acético; (118) ácido ([(3,5-dimetilfenilcarbamoil)metil]-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}amino)acético; (119) ácido ([(4-dimetilaminofenilcarbamoil)metil]-{4-[4-({isopropil[4-(1-propilbutil)fenil]-amino}metil)fenil]tiazol-2-ilmetil}amino)acético; (120) ácido ((bencil-carbamoilmetil)-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]tiazol-2-ilmetil}amino)acético; (121) ácido [{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}-[2-(morfolin-4-il)-2-oxo-etil]amino]acético; (122) ácido [{4-[4-({[4-(1-etilpropil)fenil]isopropil-amino}metil)-fenil]tiazol-2-ilmetil}-(2-fenoxietil)amino]acético; (123) ácido [{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-(2-fenilamino-etil)amino]acético; (124) ácido 2-carboximetoxi-5-({4-[4-({[4-(1-etilpropil)-fenil]-isopropilamino}metil)fenil]tiazol-2-ilmetil}metilamino)benzoico; (125) ácido 2-carboximetoxi-5-[metil(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]benzoico; (126) ácido 3-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetoxi}-4-(2-metilamino-acetilamino)benzoico; (127) ácido [(4-ter-butiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético; (128) ácido [fenil(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)amino]acético; (129)

ácido [(2-fenoxiacetil)-(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiazol-2-ilmetil)amino]acético; (130) ácido [(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiazol-2-ilmetil)-(2-p-toliloxi-acetil)amino]acético; (131) diclorhidrato del ácido (etoxicarbonilmetil{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]-tiazol-2-ilmetil}amino)acético; (132) ácido ((4-ter-butiltiazol-2-ilmetil)-{4-[4-({[4-(1-etilpropil)-fenil]isopropilamino}metil)fenil]tiazol-2-ilmetil}amino)acético; (133) ácido 6-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetoxi}-piridin-2-carboxílico; (134) ácido [(2-benciloxi-acetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético; (135) ácido [[2-(4-isopropilfenoxi)acetil]-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético; (136) ácido [(4,5-dimetiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético; (137) ácido 5-(4-{5-[4-(1-propilbutil)fenoximetil]tiofen-2-il}tiazol-2-ilmetoxi)nicotínico; (138) ácido ((4-ter-butiltiazol-2-ilmetil)-{4-[6-({isopropil[4-(1-propilbutil)fenil]amino}metil)-benzoxazol-2-il]tiazol-2-ilmetil}amino)acético; (139) ácido ((1H-bencimidazol-2-ilmetil)-{4-[6-({isopropil[4-(1-propilbutil)fenil]amino}metil)benzoxazol-2-il]tiazol-2-ilmetil}amino)acético; (140) ácido 5-{4-[6-({isopropil[4-(1-propilbutil)fenil]amino}metil)-benzoxazol-2-il]tiazol-2-ilmetoxi}nicotínico; (141) ácido [(5-ter-butiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético; (142) ácido [{4-[4-({isopropil[4-(1-propilbutil)fenil]-amino}metil)-fenil]tiazol-2-ilmetil}-(2-oxo-2-piperidin-1-il-etil)amino]acético; (143) ácido 6-[metil-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)amino]piridin-2-carboxílico; (144) ácido ({4-[6-({isopropil[4-(1-

propilbutil)fenil]amino}metil)-benzoxazol-2-il]tiazol-2-ilmetil}amino)acético; (145) ácido (S)-(carboximetil{4-[4-({isopropil[4-(1-propilbutil)-fenil]-amino}metil)fenil]tiazol-2-ilmetil}amino)fenilacético; (146) ácido ((4,5-dimetiltiazol-2-ilmetil)-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}amino)acético; (147)ácido [(5-ter-butiloxazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético; (148) ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiazol-2-ilmetil)amino]acético; (149)diclorhidrato del ácido (isobutoxicarbonilmetil{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)fenil]-tiazol-2-ilmetil}amino)acético; (150) diclorhidrato del ácido ({4-[4-({isopropil[4-(1-propilbutil)-fenil]amino}metil)fenil]tiazol-2-ilmetil}-propoxicarbonilmetilamino)acético; (151) clorhidrato del ácido 1-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)piperidin-4-carboxílico; (152) ácido 1-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}piperidin-4-carboxílico; (153) ácido 4-[4-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)piperacin-1-il]benzoico; (154) ácido 4-(4-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-piperacin-1-il)benzoico; (155) ácido 2-[4-(4-{4-[4-(1-propilbutil)benciloxi]-fenil}tiazol-2-ilmetil)piperacin-1-il]benzoico; (156) ácido 3-[4-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)piperacin-1-il]benzoico; (157) ácido 4-(4-{1-[4-(1-propilbutil)bencil]-1H-indol-3-il}tiazol-2-ilmetoxi)benzoico; (158) ácido 4-{4-[1-(4-isopropilbencil)-5-(1-propilbutil)-1H-bencimidazol-2-il]tiazol-2-ilmetoxi}benzoico; (159) ácido 4-{4-[1-(6-metilpiridin-2-ilmetil)-5-(1-

propilbutil)-1H-bencimidazol-2-il]tiazol-2-ilmetoxi}benzoico; (160) ácido 2-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-7-carboxílico; (161) ácido 4-[1-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)piperidin-4-il]benzoico; (162) ácido 3-[1-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)piperidin-4-il]benzoico; (163) ácido 6-[(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)carbamoil]nicotínico; (164) ácido 2-[1-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)piperidin-4-il]benzoico; (165) ácido 1-(4-{1-[4-(1-propilbutil)bencil]-1H-indol-3-il}tiazol-2-ilmetil)piperidin-4-carboxílico; (166) ácido 2-(4-{1-[4-(1-propilbutil)bencil]-1H-indol-3-il}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-7-carboxílico; (167) ácido 3-[(4-{1-[4-(1-propilbutil)bencil]-1H-indol-3-il}tiazol-2-ilmetil)amino]-benzoico; (168) clorhidrato del ácido 6-[(2-aminoetil)(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)carbamoil]nicotínico; (169) ácido 2-(4-{1-[4-(1-propilbutil)bencil]-1H-bencimidazol-2-il}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-7-carboxílico; (170) ácido 3-[4-(4-{1-[4-(1-propilbutil)bencil]-1H-bencimidazol-2-il}tiazol-2-ilmetil)piperacin-1-il]benzoico; (171) ácido 4-[1-(4-{1-[4-(1-propilbutil)bencil]-1H-bencimidazol-2-il}tiazol-2-ilmetil)piperidin-4-il]benzoico; (172) ácido 3-[4-(4-{1-[4-(1-propilbutil)bencil]-1H-indol-3-il}tiazol-2-ilmetil)piperacin-1-il]benzoico; (173) ácido 3-(1-{4-[4-(3,4-dicloro-benciloxi)fenil]tiazol-2-ilmetil}-piperidin-4-il)benzoico; (174) ácido 3-(1-{4-[4-(3,5-bis-trifluorometilbenciloxi)fenil]tiazol-2-ilmetil}piperidin-4-il)benzoico; (175) ácido 3-(1-{4-[4-(4-butoxi-benciloxi)-fenil]tiazol-2-ilmetil}-piperidin-4-il)benzoico; (176) ácido 5-metil-2-(4-{4-[4-

(1-propilbutil)fenoximetil]fenil}-tiazol-2-ilmetil)-2H-pirazol-3-carboxílico; (177) ácido 5-metil-1-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiazol-2-ilmetil)-1H-pirazol-3-carboxílico; (178) ácido 5-ter-butil-1-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiazol-2-ilmetil)-1H-pirazol-3-carboxílico; (179)ácido 5-ter-butil-2-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiazol-2-ilmetil)-2H-pirazol-3-carboxílico; (180) ácido (2S,4R)-4-hidroxi-1-(4-{1-[4-(1-propilbutil)bencil]-1H-indol-3-il}tiazol-2-ilmetil)pirrolidine-2-carboxílico; (181) ácido 4-{4-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)piperidin-1-il]benzoico; (182) ácido 1-(4-{1-[4-(1-propilbutil)bencil]-1H-indol-3-il}tiazol-2-ilmetil)-1H-indol-3-carboxílico; (183) ácido 1-(4-{2-fenil-1-[4-(1-propilbutil)bencil]-1H-indol-3-il}tiazol-2-ilmetil)piperidin-4-carboxílico; (184) ácido 3-(1-{4-[4-(4-metil-3-nitrobenciloxi)fenil]tiazol-2-ilmetil}piperidin-4-il)benzoico; (185) ácido 2-{4-[1-(4-isopropilbencil)-6-(morfolin-4-il)-1H-bencimidazol-2-il]tiazol-2-ilmetil}-1,2,3,4-tetrahidroisoquinolin-7-carboxílico; (186) ácido 3-(4-{4-[1-(4-isopropilbencil)-6-(morfolin-4-il)-1H-bencimidazol-2-il]tiazol-2-ilmetil}-piperacin-1-il)benzoico; (187) ácido {bencil[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)-oxazol-2-ilmetil]amino}acético; (188) ácido 5-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetoxi)nicotínico; (189) ácido 4-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetoxi)benzoico; (190) ácido 4-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetiltio)benzoico; (191) ácido 4-{4-[4-(4-ciclohexilbenciloxi)fenil]tiazol-2-ilmetiltio}-benzoico; (192) ácido 4-{4-[4-(4-ciclohexilbenciloxi)fenil]tiazol-2-ilmetansulfonil}benzoico; (193) ácido 4-[metil-(4-{5-metil-2-[4-(1-propilbutil)benciloxi]fenil}-tiazol-2-

ilmetil)sulfamoil]benzoico; (194) ácido 4-[metil-(4-{5-metil-2-[4-(1-propilbutil)benciloxi]fenil}-tiazol-2-ilmetil)amino]benzoico; (195) ácido (bencil{4-[5-metil-2-(4-trifluorometilbenciloxi)fenil]-tiazol-2-ilmetil}amino)acético; (196) ácido [bencil(4-{5-metil-2-[4-(1-propilbutil)benciloxi]fenil}-tiazol-2-ilmetil)amino]acético; (197) ácido [bencil(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)amino]acético; (198) ácido [bencil(4-{4-[4-(1-etilpropil)benciloxi]fenil}tiazol-2-ilmetil)amino]acético; (199) ácido (bencil{4-[5-ter-butil-2-(4-isobutilbenciloxi)fenil]tiazol-2-ilmetil}amino)acético; (200) ácido [bencil(4-{5-cloro-2-[4-(1-propilbutil)benciloxi]fenil}-tiazol-2-ilmetil)amino]acético; (201) ácido [(4-{4-[4-(1-etilpropil)benciloxi]fenil}tiazol-2-ilmetil)-(4-fluoro-bencil)amino]acético; (202) ácido [(4-{4-[4-(1-etilpropil)benciloxi]fenil}tiazol-2-ilmetil)-(4-isopropilbencil)amino]acético; (203) ácido [(4-{4-[4-(1-etilpropil)benciloxi]fenil}tiazol-2-ilmetil)-(4-trifluorometilbencil)amino]acético; (204) ácido [(4-clorobencil)-(4-{4-[4-(1-etilpropil)benciloxi]fenil}-tiazol-2-ilmetil)amino]acético; (205) ácido [(3,5-dimetilbencil)-(4-{4-[4-(1-etilpropil)benciloxi]-fenil}tiazol-2-ilmetil)amino]acético; (206) ácido [(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)-piridin-2-ilmetilamino]acético; (207) ácido [(4-{4-[4-(1-etilpropil)benciloxi]fenil}tiazol-2-ilmetil)-piridin-2-ilmetilamino]acético; (208) ácido [(4-{5-metil-2-[4-(1-propilbutil)benciloxi]-fenil}tiazol-2-ilmetil)-piridin-2-ilmetilamino]acético; (209) ácido [benzoil-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)amino]acético; (210) ácido [(4-{4-[4-(1-etilpropil)benciloxi]fenil}tiazol-2-ilmetil)-(4-metilbenzoil)amino]-

acético; (211) ácido [(4-metoxibenzoil)-(4-{4-[4-(1-propilbutil)benciloxi]-fenil}tiazol-2-ilmetil)amino]acético; (212)ácido 2-(4-{5-metil-2-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (213) ácido (S)-2-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (214) ácido {bencil[4-(4-{[4-(2,2-dimetilpropil)bencil]metilamino}-fenil)tiazol-2-ilmetil]amino}acético; (215) ácido {bencil[4-(4-{[trans-4-(4-ter-butilfenil)-ciclohexilmetil]-metilamino}fenil)tiazol-2-ilmetil]amino}acético; (216) ácido [bencil(4-{4-[(4-ciclohexilbencil)metilamino]fenil}-tiazol-2-ilmetil)amino]acético; (217) ácido 3-[bencil(4-{4-[(4-ciclohexilbencil)metilamino]fenil}-tiazol-2-ilmetil)amino]propiónico; (218) ácido (bencil{4-[4-({2-[4-(2,2-dimetilpropil)fenil]-etil}-metilamino)fenil]tiazol-2-ilmetil}amino)acético; (219) ácido {bencil[4-(4-{metil[4-(trans-4-metil-ciclohexil)bencil]-amino}fenil)tiazol-2-ilmetil]amino}acético; (220) ácido {bencil[4-(4-{[4-(cis-4-fluoro-ciclohexil)bencil]-metilamino}fenil)tiazol-2-ilmetil]amino}acético; (221) ácido {bencil[4-(4-{[trans-4-(4-clorofenil)-ciclohexilmetil]-metilamino}fenil)tiazol-2-ilmetil]amino}acético; (222) ácido {bencil[4-(4-{[4-(4,4-dimetil-ciclohexil)bencil]-metilamino}fenil)tiazol-2-ilmetil]amino}acético; (223) ácido {bencil[4-(4-{metil[4-(1-propilbutil)bencil]amino}-fenil)tiazol-2-ilmetil]amino}acético; (224) ácido (bencil{4-[4-(bifenil-4-ilmetilmetilamino)fenil]tiazol-2-ilmetil}amino)acético; (225) [bencil(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)amino]-acetato de sodio; (226) ácido [bencil(4-{4-[(4-isobutilbencil)metilamino]fenil}tiazol-2-ilmetil)amino]-

acético; (227) {bencil[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)tiazol-2-ilmetil]amino}-acetato de sodio; (228) ácido {bencil[4-(4-{[4-(2,2-dimetilpropiltio)bencil]-metilamino}fenil)tiazol-2-ilmetil]amino}acético; (229) ácido {bencil[4-(4-{metil[4-(3-metilbutiltio)bencil]amino}-fenil)tiazol-2-ilmetil]amino}acético; (230) ácido [bencil(4-{4-[(4-dipropilamino-benzoil)metilamino]-fenil}tiazol-2-ilmetil)amino]acético; (231) ácido [(4-{4-[etil(4-isopropilbencil)amino]fenil}tiazol-2-ilmetil)-(4-isopropilbencil)-amino]acético; (232) ácido [(4-isopropilbencil)-(4-{4-[isopropil-(4-isopropilbencil)amino]fenil}tiazol-2-ilmetil)amino]acético; (233) ácido [(4-ter-butilbencil)-(4-{4-[isopropil-(4-isopropilbencil)-amino]fenil}tiazol-2-ilmetil)amino]acético; (234) ácido [(4-clorobencil)-(4-{4-[(4-isobutilbencil)metilamino]-fenil}tiazol-2-ilmetil)amino]acético; (235) ácido {{4-[4-(bencilmetilamino)fenil]tiazol-2-ilmetil}-[4-(1-propilbutil)bencil]amino}acético; (236) ácido [{4-[4-(bencilmetilamino)fenil]tiazol-2-ilmetil}-(4-cloro-bencil)amino]acético; (237) ácido [{4-[4-(bencilmetilamino)fenil]tiazol-2-ilmetil}-(2-cloro-bencil)amino]acético; (238) ácido [{4-[4-(bencilmetilamino)fenil]tiazol-2-ilmetil}-(3,4-dicloro-bencil)amino]acético; (239) ácido {[4-(4-{metil[4-(trans-4-metil-ciclohexil)bencil]amino}-fenil)tiazol-2-ilmetil]piridin-2-ilmetilamino}acético; (240) ácido {[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)tiazol-2-ilmetil]piridin-2-ilmetilamino}acético; (241) ácido ({4-[4-(bencilmetilamino)fenil]tiazol-2-ilmetil}-naftalen-1-ilmetilamino)acético; (242) ácido ({4-[4-(bencilmetilamino)fenil]tiazol-2-ilmetil}-quinolin-2-ilmetilamino)acético; (243) ácido ((2-benzo[b]tiofen-3-il-acetil)-{4-

[4-(bencilmetilamino)fenil]tiazol-2-ilmetil}amino)acético; (244) ácido [[2-(4-clorofenil)acetil]-(4-{4-[(4-isobutilbencil)-metilamino]fenil}tiazol-2-ilmetil)amino]acético; (245) ácido {(4-{4-[(4-isobutilbencil)metilamino]-fenil}tiazol-2-ilmetil)-[2-(4-isopropilfenil)acetil]amino}acético; (246) ácido [(4-{4-[(4-isobutilbencil)metilamino]fenil}tiazol-2-ilmetil)-(3-metil-butyril)amino]acético; (247) ácido {1-[4-(4-{[4-(2,2-dimetilpropil)bencil]metilamino}fenil)-tiazol-2-ilmetil]-3-fenilureido}acético; (248) ácido [benzoil-(4-{4-[(4-isobutilbencil)metilamino]fenil}-tiazol-2-ilmetil)amino]acético; (249) ácido {(4-metilbenzoil)-[4-(4-{metil[4-(1-propilbutil)bencil]-amino}fenil)tiazol-2-ilmetil]amino}acético; (250) {(4-isopropilbenzoil)-[4-(4-{metil[4-(1-propilbutil)bencil]-amino}fenil)tiazol-2-ilmetil]amino}-acetato de sodio; (251) (S)-{3-[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)tiazol-2-il]-3,4-dihidro-1H-isoquinolin-2-il}-acetato de sodio; (252) ácido 1-(4-{4-[(4-ciclohexilbencil)-metilamino]fenil}tiazol-2-ilmetil)piperidin-4-carboxílico; (253) ácido 1-(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)piperidin-3-carboxílico; (254) ácido 1-(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)-4-fenilpiperidin-4-carboxílico; (255) ácido 1-(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)-4-(3-metilbutil)piperidin-4-carboxílico; (256) ácido 1-[4-(4-{metil[4-(trans-4-metil-ciclohexil)-bencil]-amino}-fenil)tiazol-2-ilmetil]-4-fenilpiperidin-4-carboxílico; (257) ácido 1-[4-(4-{[trans-4-(4-cloro-fenil)-ciclohexilmetil]-metilamino}fenil)tiazol-2-ilmetil]-4-fenilpiperidin-4-carboxílico; (258) ácido 2-[4-(4-{metil[4-(trans-4-metil-ciclohexil)bencil]-amino}fenil)tiazol-2-ilmetil]-1,2,3,4-tetrahidroisoquinolin-3-

carboxílico; (259) ácido 2-(4-{4-[(4-isobutilbencil)metilamino]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (260) ácido 2-[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)-tiazol-2-ilmetil]-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (261) ácido 2-[4-(4-{[4-(2,2-dimetilpropil)bencil]metilamino}fenil)-tiazol-2-ilmetil]-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (262) ácido 5-{[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-il)metilamino]metil}furan-2-carboxílico; (263) ácido 2-[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)amino]-3-fenilpropiónico; (264) ácido [(4-{4-[(4-ciclohexilbencil)metilamino]fenil}-tiazol-2-ilmetil)amino]fenilacético; (265) ácido 2-[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)amino]propiónico; (266) ácido 3-(4-clorofenil)-2-[(4-{4-[(4-isobutilbencil)metilamino]-fenil}tiazol-2-ilmetil)amino]propiónico; (267) ácido [(4-{4-[(4-ciclohexilbencil)metilamino]-fenil}tiazol-2-ilmetil)metilamino]acético; (268) ácido 3-[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)metilamino]propiónico; (269) ácido 4-[[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)metilamino]metil}benzoico; (270) ácido 4-[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)-metilamino]benzoico; (271) ácido 6-[(4-{4-[(4-ciclohexilbencil)-metilamino]fenil}tiazol-2-ilmetil)-metilamino]nicotínico; (272) ácido 2-[(4-{4-[(4-isobutilbencil)-metilamino]fenil}tiazol-2-ilmetil)metilamino]-3-fenilpropiónico; (273)ácido (S)-2-{metil[4-(4-{metil[4-(1-propilbutil)bencil]amino}-fenil)tiazol-2-ilmetil]amino}-3-fenilpropiónico; (274) ácido (S)-{metil[4-(4-{metil[4-(1-propilbutil)bencil]amino}-

fenil)tiazol-2-ilmetil]amino}fenilacético; (275) ácido {[4-(4-[[4-(2,2-dimetilpropil)bencil]metilamino}fenil)-tiazol-2-ilmetil]metilamino}fenilacético; (276) ácido 2-[[4-(4-[[4-(2,2-dimetilpropil)bencil]metilamino}fenil)-tiazol-2-ilmetil]metilamino}-3-fenilpropiónico; (277) ácido {carboximetil[4-(4-{metil[4-(1-propilbutil)bencil]-amino}fenil)tiazol-2-ilmetil]amino}acético; (278) ácido [(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)-(3-metilbutil)amino]acético; (279) ácido {(3-metilbutil)-[4-(4-{metil[4-(trans-4-metil-ciclohexil)-bencil]amino}fenil)tiazol-2-ilmetil]amino}acético; (280) ácido [(4-{4-[(4-isobutilbencil)metilamino]fenil}tiazol-2-ilmetil)-(3-metilbutil)-amino]acético; (281) ácido 5-[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)-tiazol-2-ilmetoxi]nicotínico; (282) ácido 4-[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)-tiazol-2-ilmetoxi]benzoico; (283) ácido 4-[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)-tiazol-2-ilmetiltio]benzoico; (284) ácido 4-[(4-{4-[(4-ciclohexilbencil)metilamino]-fenil}tiazol-2-ilmetil)sulfamoil]benzoico; (285) ácido 4-{[4-(4-[[4-(4,4-dimetil-ciclohexil)bencil]metilamino}-fenil)tiazol-2-ilmetil]metilsulfamoil}benzoico; (286) ácido {[4-(4-[[4-(4,4-dimetil-ciclohexil)bencil]metilamino}-fenil)tiazol-2-ilmetil]metilsulfamoil}acético; (287) ácido 4-[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)metilsulfamoil]benzoico; (288) ácido 3-[(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)-metilsulfamoil]benzoico; (289) ácido [(4-{4-[(4-ciclohexilbencil)-metilamino]fenil}tiazol-2-ilmetil)metilsulfamoil]acético; (290) ácido 4-[[4-(4-[[4-(4,4-dimetil-ciclohexil)bencil]metilamino}-fenil)tiazol-2-ilmetil]metil-

sulfamoil}butírico; (291) ácido [(4-{4-[(4-ciclohexilbencil)metilamino]-fenil}tiazol-2-ilmetil)isobutil-sulfamoil]acético; (292) ácido N-(4-{4-[(4-ciclohexilbencil)metilamino]fenil}tiazol-2-ilmetil)oxámico; (293) ácido {bencil[4-(4-{[4-(1-propilbutil)bencil]metilamino-carbonil}fenil)-tiazol-2-ilmetil]amino}acético; (294) ácido N-(4-{4-[(4-ciclohexilbencil)metilamino]-fenil}tiazol-2-ilmetil)-N-metiltereftalámico; (295) ácido {bencil[4-(4-{metil[4-(trans-4-metil-ciclohexil)bencil]-amino}fenil)tiazol-2-ilmetoxicarbonil]-amino}acético; (296) ácido [3-(4-{4-[(4-ciclohexilbencil)-metilamino]fenil}tiazol-2-ilmetil)-3-metil-ureido]acético; (297) ácido (ciclohexilmetil{4-[6-(3,4-diclorobenciloxi)-benzoxazol-2-il]tiazol-2-il}amino)acético; (298) ácido [4-(4-{4-[(4-ciclohexilbencil)metilamino]-fenil}tiazol-2-ilmetil)piperacin-1-il]acético; (299) (S)-2-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxilato de sodio; (300)5-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetoxi)-nicotinato de sodio; (301) ácido 5-(4-{2-metil-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetoxi)nicotínico; (302) ácido 5-(4-{3-metoxi-4-[4-(1-propilbutil)benciloxi]fenil}-tiazol-2-ilmetoxi)nicotínico; (303) ácido [(4-{2-metil-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)fenilcarbamoil-metilamino]acético; (304) ácido [[(4-isopropilfenilcarbamoil)metil]-(4-{2-metil-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)amino]acético; (305) ácido 2-(4-{4-[4-(1-propilbutil)benciloxi]-fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (306) ácido [(4-{3-metoxi-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)fenilcarbamoilmetilamino]acético; (307)

ácido [[(4-isopropilfenilcarbamoil)metil]-(4-{3-metoxi-4-[4-(1-propilbutil)benciloxi]-fenil}tiazol-2-ilmetil)amino]acético; (308) ácido [(4-{2-metil-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)tiazol-4-ilmetilamino]acético; (309) clorhidrato del ácido [(4-{2-metil-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)-(2-metiltiazol-4-ilmetil)amino]acético; (310) clorhidrato del ácido [(bencilcarbamoilmetil)-(4-{2-metil-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)amino]acético; (311)ácido [(1H-bencimidazol-2-ilmetil)-(4-{2-metil-4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)amino]acético; (312) ácido [(4-ter-butiltiazol-2-ilmetil)-(4-{1-[4-(1-propilbutil)-bencil]-1,2,3,4-tetrahidroquinolin-6-il}tiazol-2-ilmetil)amino]acético; (313) clorhidrato del ácido 1-(4-{4-[4-(1-propilbutil)benciloxi]-fenil}tiazol-2-ilmetil)piperidin-4-carboxílico; (314) ácido 4-[4-(4-{4-[4-(1-propilbutil)benciloxi]fenil}tiazol-2-ilmetil)piperacin-1-il]benzoico; (315) éster etílico del ácido 4-{4-[5-(1-etilpropil)-1-(4-isopropilbencil)-1H-bencimidazol-2-il]tiazol-2-ilmetoxi}benzoico; (316) ácido 4-{4-[5-(1-etilpropil)-1-(4-isopropilbencil)-1H-bencimidazol-2-il]tiazol-2-ilmetoxi}benzoico; (317) ácido 4-{4-[1-(4-acetilbencil)-5-(1-etilpropil)-1H-bencimidazol-2-il]tiazol-2-ilmetoxi}benzoico; (318) ácido 4-{4-[1-(4-acetilbencil)-6-(1-etilpropil)-1H-bencimidazol-2-il]tiazol-2-ilmetoxi}benzoico; (319) ácido 4-{4-[1-ciclohexilmetil-5-(1-etilpropil)-1H-bencimidazol-2-il]tiazol-2-ilmetoxi}benzoico; (320) ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (321) ácido 5-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi)nicotínico; (322) ácido

5-{4-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiofen-2-ilmetoxi}nicotínico; (323) ácido 5-{4-[4-({[4-(1-etilpropil)fenil]isopropil-amino}metil)-fenil]tiofen-2-ilmetoxi}nicotínico; (324) ácido 5-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi)nicotínico; (325) ácido [(1H-bencimidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (326) ácido 6-(4-{4-[4-(1-propilbutil)fenoxi-metil]fenil}tiofen-2-ilmetoxi)piridin-2-carboxílico; (327) ácido [(1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (328) ácido [[(4-isopropilfenilcarbamoil)metil]-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (329) ácido [fenilcarbamoilmetil(5-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]acético; (330) ácido ({4-[4-({[4-(1-etilpropil)fenil]-isopropilamino}metil)-fenil]tiofen-2-ilmetil}fenilcarbamoilmetilamino)acético; (331) ácido ((4-ter-butiltiazol-2-ilmetil)-{4-[4-({[4-(1-etilpropil)-fenil]isopropilamino}metil)fenil]tiofen-2-ilmetil}amino)acético; (332) ácido [(5-ter-butiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)-amino]acético; (333) ácido ((1H-bencimidazol-2-ilmetil)-{4-[4-({[4-(1-etilpropil)-fenil]isopropilamino}metil)fenil]-tiofen-2-ilmetil}amino)acético; (334) ácido [(4-ter-butiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (335) ácido [fenilcarbamoilmetil(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]acético; (336) ácido 5-{5-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiofen-2-ilmetoxi}nicotínico; (337) ácido 5-{5-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiofen-2-

ilmetoxi}nicotínico; (338) ácido ((4-ter-butiltiazol-2-ilmetil)-{5-[4-({[4-(1-etilpropil)-fenil]isopropilamino}metil)fenil]tiofen-2-ilmetil}amino)acético; (339) ácido ((4-ter-butiltiazol-2-ilmetil)-{5-[4-({isopropil[4-(1-propilbutil)-fenil]amino}metil)fenil]tiofen-2-ilmetil}amino)acético; (340) ácido ((1H-bencimidazol-2-ilmetil)-{5-[4-({[4-(1-etilpropil)-fenil]isopropil-amino}metil)fenil]tiofen-2-ilmetil}amino)acético; (341) ácido ((1H-bencimidazol-2-ilmetil)-{5-[4-({isopropil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiofen-2-ilmetil}amino)acético; (342) ácido [(4,5-dimetiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (343) ácido (S)-2-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}-metil)fenil]tiofen-2-ilmetil}-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (344) ácido {{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiofen-2-ilmetil}-[(4-isopropilfenil-carbamoil)metil]amino}acético; (345) ácido (S)-2-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (346) ácido [[(4-isopropilfenilcarbamoil)metil]-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (347) ácido (S)-2-{5-[4-({[4-(1-etilpropil)fenil]isopropilamino}-metil)fenil]tiofen-2-ilmetil}-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (348) ácido [(5-ter-butiloxazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (349) ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (350) ácido 6-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi)piridin-2-carboxílico; (351) ácido 6-{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiofen-2-ilmetoxi}-

piridin-2-carboxílico; (352) ácido ((5-ter-butiltiazol-2-ilmetil)-{4-[4-({[4-(1-etilpropil)-fenil]isopropilamino}metil)fenil]tiofen-2-ilmetil}amino)acético; (353) ácido [{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiofen-2-ilmetil}-(1-metil-1H-bencimidazol-2-ilmetil)amino]acético; (354) ácido [(4-ter-butiltiazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (355) ácido [{5-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiofen-2-ilmetil}-(1-metil-1H-bencimidazol-2-ilmetil)amino]acético; (356) ácido [(5-ter-butiltiazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (357) [(1-metil-1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]-acetato de sodio; (358) bis{[(1-metil-1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]-acetato} de calcio; (359) toluen-4-sulfonato del ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]acético; (360) sulfato del ácido 5-(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetoxi)nicotínico; (361) ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-carbonil)amino]acético; (362) ácido [(5-ter-butiltiazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-carbonil)amino]acético; (363) ácido [(4-isopropilbencil)-(5-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-carbonil)amino]acético; (364) ácido [(4-dimetilaminobencil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-carbonil)amino]acético; (365) ácido [(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-carbonil)-piridin-2-ilmetilamino]acético; (366) ácido [(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-

2-carbonil)-piridin-3-ilmetilamino]acético; (367)metansulfonato del ácido 5-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetoxi)nicotínico; (368) ácido [metansulfonil-(5-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]acético; (369) 5-(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetoxi)-nicotinato de sodio; (370) clorhidrato del ácido 5-(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetoxi)nicotínico; (371) ácido 4-[4-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-carbonil)piperacin-1-il]benzoico; (372) ácido 4-[1-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-carbonil)piperidin-4-il]benzoico; (373) clorhidrato del ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (374) sulfato del ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (375) ácido 4-(2-dimetilaminoacetilamino)-3-(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetoxi)benzoico; (376) ácido 4-isobutirilamino-3-(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetoxi)benzoico; (377)ácido 4-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi)benzoico; (378) ácido 4-(metansulfonilmetilamino)-3-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetoxi)benzoico; (379) ácido 4-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetiltio)benzoico; (380)ácido 4-amino-3-(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}-tiofen-2-ilmetoxi)benzoico; (381) clorhidrato del ácido 1-{5-[1-(4-ciclohexilbencil)-1H-indol-3-il]tiofen-2-ilmetil}-4-fenilpiperidin-4-carboxílico; (382) clorhidrato del ácido (bencil{5-[1-(4-ciclohexilbencil)-1H-indol-3-il]tiofen-2-ilmetil}amino)acético; (383) ácido [(metilfenilsulfamoil)(4-{4-[4-(1-

propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (384) ácido [(5-ter-butiltiazol-2-ilmetil)-(5-{4-[(4-ciclohexil-fenil)metilcarbamoil]fenil}tiofen-2-ilmetil)amino]acético; (385) ácido [(5-{4-[(4-ciclohexilbencil)etilamino]fenil}tiofen-2-ilmetil)piridin-2-ilmetilamino]acético; (386) ácido [(5-{4-[(4-ciclohexilbencil)etilamino]fenil}tiofen-2-ilmetil)-(2-fenoxietil)amino]acético; (387) ácido 4-{1-[4-(4-{[trans-4-(4-ter-butilfenil)-ciclohexilmetil]-etilamino}fenil)tiofen-2-ilmetil]piperidin-4-il}benzoico; (388) ácido [[2-(4-isopropilfenoxi)acetil]-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (389) ácido [(4-isopropilbenzoil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (390) ácido [(3-metilbutil)-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiofen-2-ilmetil)amino]acético; (391) ácido [3-metil-3-fenil-1-(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)ureido]acético; (392) ácido 2-(4-{3-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-7-carboxílico; (393) ácido 4-[4-(5-{4-[4-(trans-4-metil-ciclohexil)benciloxi]fenil}-tiofen-2-ilmetil)piperacin-1-il]benzoico; (394) ácido [(2-cloro-5-trifluorometilbencil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (395) ácido 3-{[carboximetil(5-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]metil}benzoico; (396) ácido [(4-metoxibencil)-(5-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]acético; (397) ácido [(4-metiltiobencil)-(5-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]acético; (398) ácido 4-[ciclohexilmetil(5-{4-[4-(trans-4-metil-ciclohexil)-benciloxi]fenil}tiofen-2-

ilmetil)sulfamoil]benzoico; (399) ácido 4-[3-ciclohexilmetil-3-(5-{4-[4-(trans-4-metil-ciclohexil)benciloxi]fenil}tiofen-2-ilmetil)ureido]benzoico; (400) ácido [benzhidril-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}-tiofen-2-ilmetil)amino]acético; (401) clorhidrato del éster etílico del ácido [[2-oxo-2-(4-pirrolidin-1-il-fenil)etil]-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]-acético; (402)éster etílico del ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (403) ácido 3-(bencil{5-[1-(4-ciclohexilbencil)-2,3-dihidro-1H-indol-5-il]tiofen-2-ilmetil}amino)propiónico; (404) ácido [bencil(4-{4-[2-(2,2-dimetilpropil)bencimidazol-1-ilmetil]fenil}tiofen-2-ilmetil)amino]acético; (405) ácido [(1-metil-1H-indol-3-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (406) ácido [(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)quinolin-2-ilmetilamino]acético; (407) ácido [benzotiazol-2-ilmetil(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (408) ácido [(1-bencil-1H-imidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (409) ácido [(1H-indol-5-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (410) ácido [(4-imidazol-1-ilbencil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (411) ácido [benzofuran-2-ilmetil(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (412) ácido [[2,2']bitiofenil-5-ilmetil(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (413) ácido [(2-fenil-1H-imidazol-4-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-

ilmetil)amino]acético; (414) ácido [(3-fenil-1H-pirazol-4-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (415) ácido [benzoxazol-2-ilmetil(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (416) ácido [benzo[b]tiofen-2-ilmetil(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (417) ácido [(4-feniltiofen-2-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (418) ácido [benzotiazol-2-il-(5-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]acético; (419) ácido [(5-clorotiofen-2-sulfonil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (420) ácido [(1-dietilcarbamoilmetil-1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (421) ácido (S)-({4-[2-(4-ciclohexilbenciloxi)-5-metilfenil]tiofen-2-ilmetil}metilamino)-3-fenilpropiónico; (422)ácido [bencil(4-{4-[(4-butoxi-bencensulfonil)etilamino]-fenil}tiofen-2-ilmetil)amino]acético; (423) ácido N-{4-[2-(4-ciclohexilbenciloxi)-5-metilfenil]tiofen-2-ilmetil}-N-(2-metilbenzotiazol-6-il)oxámico; (424) ácido (bencil{4-[4-(3,5-diclorofenoximetil)fenil]tiofen-2-ilmetil}amino)acético; (425) ácido [(1-alil-1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; y (426) ácido [[4-(4-clorofenil)tiazol-2-il]-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético.

24. El compuesto anular heteroaromático de 5 miembros de conformidad con cualquiera de las reivindicaciones 1 a 23, caracterizado además porque se selecciona del grupo que consiste de los siguientes

compuestos, o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos: (1) ácido (S)-2-(4-[4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (2) ácido {{4-[4-({[4-(1-etilpropil)-fenil]isopropilamino}metil)-fenil]tiazol-2-ilmetil}-[(4-isopropilfenilcarbamoil)-metil]amino}acético; (3) ácido 4-(3-isobutil-3-{4-[4-({isopropil[4-(1-propilbutil)fenil]-amino}metil)fenil]tiazol-2-ilmetil}ureido)benzoico; (4)ácido ({4-[4-({isobutil[4-(1-propilbutil)fenil]amino}metil)-fenil]tiazol-2-ilmetil}fenil-carbamoilmetilamino)acético; (5) ácido ([(4-isopropilfenilcarbamoil)metil]-{4-[4-({isopropil[4-(1-propilbutil)fenil]-amino}metil)fenil]tiazol-2-ilmetil}amino)acético; (6) ácido [(4-ter-butiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]-fenil}tiazol-2-ilmetil)amino]acético; (7) ácido [(4,5-dimetiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético; (8) ácido [(5-ter-butiltiazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)-amino]acético; (9) ácido [[2-(4-isopropilfenoxi)acetil]-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiazol-2-ilmetil)amino]acético; (10) ácido 4-[4-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiazol-2-ilmetil)piperacin-1-il]benzoico; (11) ácido {bencil[4-(4-{metil[4-(1-propilbutil)bencil]amino}fenil)-tiazol-2-ilmetil]amino}-acético; (12) ácido [(1-metil-1H-bencimidazol-2-ilmetil)-5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (13) ácido 5-(4-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetoxi}nicotínico; (14) ácido [(1H-bencimidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (15) ácido [(1H-bencimidazol-2-ilmetil)-(5-{4-[4-(1-

propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (16) ácido [[(4-isopropilfenilcarbamoil)metil]-(5-{4-[4-(1-propilbutil)fenoximetil]fenil}tiofen-2-ilmetil)amino]acético; (17) ácido (S)-2-{4-[4-({[4-(1-etilpropil)fenil]-isopropilamino}-metil)fenil]tiofen-2-ilmetil}-1,2,3,4-tetrahidroisoquinolin-3-carboxílico; (18) ácido {{4-[4-({[4-(1-etilpropil)fenil]isopropilamino}metil)-fenil]tiofen-2-ilmetil}-[(4-isopropilfenilcarbamoil)metil]amino}acético; (19) ácido [(1-metil-1H-bencimidazol-2-ilmetil)-(4-{4-[4-(1-propilbutil)fenoximetil]-fenil}tiofen-2-ilmetil)amino]acético; y (20) ácido [(4-ter-butiltiazol-2-ilmetil)-(5-{4-[4-(1-propilbutil)-fenoximetil]fenil}tiofen-2-ilmetil)amino]acético.

25.- Una composición farmacéutica que comprende el compuesto anular heteroaromático de 5 miembros de cualquiera de las reivindicaciones 1 a 24, o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos y un portador farmacéuticamente aceptable.

26.- Una composición farmacéutica para la inhibición de un regulador negativo del receptor de la tirosina cinasa, que comprende un compuesto anular heteroaromático de 5 miembros de cualquiera de las reivindicaciones 1 a 24, o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos y un portador farmacéuticamente aceptable.

27.- Una composición farmacéutica para la inhibición de la proteína tirosina fosfatasa 1B, que comprende un compuesto anular heteroaromático de 5 miembros de cualquiera de las reivindicaciones 1 a 24, o

un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos y un portador farmacéuticamente aceptable.

28.- Una composición farmacéutica para la profilaxis o el tratamiento de la diabetes, que comprende un compuesto anular heteroaromático de 5 miembros de cualquiera de las reivindicaciones 1 a 24, o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos y un portador farmacéuticamente aceptable.

29.- Una composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia, que comprende un compuesto anular heteroaromático de 5 miembros de cualquiera de las reivindicaciones 1 a 24, o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos y un portador farmacéuticamente aceptable.

30.- Una composición farmacéutica para la profilaxis o el tratamiento de la obesidad, que comprende un compuesto anular heteroaromático de 5 miembros de cualquiera de las reivindicaciones 1 a 24, o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos y un portador farmacéuticamente aceptable.

31.- Una composición farmacéutica para la profilaxis o el tratamiento de las complicaciones diabéticas, que comprende un compuesto anular heteroaromático de 5 miembros de cualquiera de las reivindicaciones 1 a 24, o un profármaco de los mismos, o una sal farmacéuticamente aceptable de los mismos y un portador farmacéuticamente aceptable.

32.- La composición farmacéutica de conformidad con la reivindicación 25, caracterizada además porque se utiliza en combinación con un agente terapéutico para la hiperlipidemia.

33.- La composición farmacéutica de conformidad con la reivindicación 32, caracterizada además porque el agente terapéutico para la hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de inhibidores de la HMG-CoA reductasa (estatinas), fibratos, inhibidores de la expresión de TNFSF6, agentes que incrementan el colesterol de HDL-colesterol, mejoradores de la expresión de ApoA1, inhibidores de la expresión de SPP1 (osteopontina), fármacos que actúan sobre los receptores activados por el proliferador de la peroxisoma (PPAR), antagonistas del PPAR-alfa, estimulantes del factor de eliminación de la lipasa, antagonistas del colesterol, antagonistas de agregación de las plaquetas, antioxidantes, inhibidores de la biosíntesis del colesterol, sobrerreguladores del receptor de LDL, secuestrantes del ácido biliar, inhibidores de la absorción del colesterol y ácidos nicotínicos.

34.- La composición farmacéutica de conformidad con la reivindicación 33, caracterizada además porque el agente terapéutico para hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de lovastatina, pravastatina (eptastatina) sódica, fluvastatina (fluindostainina) sódica, rosuvastatina cálcica, atorvastatina cálcica, simvastatina (sinvinolina), pitavastatina (itavastatina, nisvastatina) cálcica, ronifibrato (ronifibrato), binifibrato (binifibrato), clinofibrato, ciprofibrato,

clofibrato, etofibrato, fenofibrato, bezafibrato, gemfibrozil, acipimox, éster etílico del ácido eicosapentaenoico (icosapent, icopenato, icosapentato), probucol, policosanol, clorhidrato de colesevelam, colestiramina (resina de colestiramina), clorhidrato de colestipol, colestimida (colestilan), ezetimibe y niacina (ácido nicotínico).

35.- La composición farmacéutica de conformidad con la reivindicación 25, caracterizada además porque se utiliza en combinación con un agente terapéutico para la diabetes.

36.- La composición farmacéutica de conformidad con la reivindicación 35, caracterizada además porque el agente terapéutico para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de secretagogos de la insulina, biguanidas, inhibidores de la α-glucosidasa, preparaciones de insulina, análogos de la insulina, mejoradores de la sensibilidad a la insulina, IL-11, agentes anti-CD25 (Receptor IL-2), antagonistas de la angiotensina (AT1), inhibidores de la enzima que convierte la angiotensina (ACE), inhibidores de la aldosa reductasa, antioxidantes, estimulante de la carnitina acetiltransferasa, antidepresivos, glucocorticoides, retilina, agonistas de la formación de radicales y activadores de la transcetolasa.

37.- La composición farmacéutica de conformidad con la reivindicación 36, caracterizada además porque el agente terapéutico para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de nateglinida, glimepirida, glibenclamida, gliclazida, acetohexamida,

tolbutamida, gliclopiramida, tolazamida, glibuzol, glipizida, glibornurida, gliquidona, repaglinida, clorhidrato de metformina, clorhidrato de buformina, voglibosa, acarbosa, epalrestat, miglitol, insulina, clorhidrato de pioglitazona, maleato de rosiglitazona, picolinato de cromo/biotina, V-411, interleucina-11 humana recombinante, daclixímab (daclizumab), losartan potásico, captopril, clorhidrato de imidapril, ácido alfa-lipoico, clorhidrato de levacecarnina (acetil-L-carnitina, levocarnitin acetilo), captopril, retilina, verteporfin, benfotiamina y fluocinolon acetónido.

38.- La composición farmacéutica de conformidad con la reivindicación 25, caracterizada además porque se utiliza en combinación con un agente terapéutico para la obesidad.

39.- La composición farmacéutica de conformidad con la reivindicación 38, caracterizada además porque el agente terapéutico para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, inhibidores de la lipasa, inhibidores dobles de la recaptación de 5-HT/norepinefrina, inhibidores de la recaptación de 5-HT, suplementos herbales que contienen efedrina y cafeína, gonadotropinas coriónicas humanas, agonistas de adrenoceptores, metamfetamina, fentermina y amfepramona.

40.- La composición farmacéutica de conformidad con la reivindicación 39, caracterizada además porque el agente terapéutico para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, orlistat, monohidrato del clorhidrato de sibutramina,

clorhidrato de fluoxetina, gonadotropina coriónica (humana), terapia VNS utilizando el Sistema NCP, metaraminol, clorhidrato de d-metamfetamina, fentermina, clorhidrato de amfepramona (dietilpropion), clorhidrato de benzfetamina y tartrato de fendimetracina.

41.- La composición farmacéutica de conformidad con la reivindicación 25, caracterizada además porque se utiliza en combinación con un agente terapéutico para la hipertensión.

42.- La composición farmacéutica de conformidad con la reivindicación 41, caracterizada además porque el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de tiazidas, antagonistas de la aldosterona, bloqueadores adrenérgicos de las neuronas, bloqueadores del canal del calcio; antagonistas de la dopamina D2, antagonistas del aadrenoceptor beta, agonistas del adrenoceptor alfa2, activadores de la guanilato ciclasa, antagonistas del adrenoceptor beta1, antagonistas del adrenoceptor alfa1, antioxidantes, inhibidores de la enzima que convierten la angiotensina-I (ACE), inhibidores de intercambio de Na+/H+, antagonistas del adrenoceptor alfa, donadores de óxido nítrico, antagonistas de 5-HT2, activadores del canal de K(ATP), estimulantes de la prostaglandina sintasa diurética del potasio sobrante, agonistas del receptor de la imidazolina I1, antagonistas de la angiotensina AT1, agonistas de la dopamina D1, estimulantes de la guanilato ciclasa, antagonistas del receptor de la endotelina ETA, antagonistas del receptor de la endotelina ETB, mejoradores de la expresión de NOS3, análogos de la

prostaciclina, prostaglandinas, antagonistas de la angiotensina II, agonistas de la absorción del electrolito, antagonistas nicotínicos, agonistas de la dopamina D2, inhibidores de la prolactina, antagonistas del factor de activación de las plaquetas (PAF), antagonistas de agregación de las plaquetas, antagonistas del factor de necrosis del tumor, inhibidores de la Rho cinasa, antagonistas del PPAR-alfa, moduladores del receptor AMPA, antagonistas del receptor GABA(A) e inhibidores de la fosfodiesterasa V (PDE5A).

43.- La composición farmacéutica de conformidad con la reivindicación 42, caracterizada además porque el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de clorotiazida, hidroclorotiazida, hidroflumetiazida, meticlotiazida, politiazida, xipamida, ciclopentiazida, bendroflumetiazida (bendrofluazida), espironolactona, epoximexrenona (eplerenona), monosulfato de guanetidina, sulfato de guanadrel, verapamil, clorhidrato de propranolol, clorhidrato alprenolol, pindolol, clorhidrato de oxprenolol, maleato de timolol, clorhidrato de sotalol, clorhidrato de acebutolol, clorhidrato de carteolol, sulfato de mepindolol, clorhidrato de arotinolol, clorhidrato de indenolol, clorhidrato de tertatolol, clorhidrato de celiprolol, clorhidrato de tilisolol, nebivolol, sulfato de penbutolol, nadolol, clorhidrato de cloranolol, clorhidrato de bevantol (bevantolol), clonidina, clorhidrato de guanfacina, clorhidrato de diltiazem, clorhidrato de nicardipina, nitrendipina, felodipina, nilvadipina; nivadipina, nisoldipina, clorhidrato de benidipina, besilato de amlodipina, clorhidrato de franidipina (manidipina), lacidipina, isradipina, clorhidrato de barnidipina

(mepirodipina), clorhidrato etanólico de efonidipina, cinaldipina (cilnidipina), aranidipina, clorhidrato de lercanidipina (masnidipina), azelnidipina, amlodipina, manidipina (franidipina), nitroprussida sódica, atenolol, tartrato de metoprolol, clorhidrato de betaxolol, bopindolol, fumarato de bisoprolol, clorhidrato de esmolol, carvedilol, succinato de metoprolol, talinolol, clorhidrato de prazosina, urapidil, clorhidrato de indoramina; clorhidrato de bunazosina, clorhidrato de terazosina, mesilato de doxazosina, urapidil, nifedipina, captopril, maleato de enalapril, lisinopril, perindopril, alacepril, ramipril, clorhidrato de quinapril, clorhidrato de delapril, clorhidrato de benazepril, cilazapril, fosinoprilat, fosinopril sódico, trandolapril, espirapril, clorhidrato de temocapril, clorhidrato de moexipril, clorhidrato de imidapril, zofenopril cálcico, enalaprilat, zofenoprilat, clorhidrato de amilorida, clorhidrato de labetalol, nipradilol (nipradolol), linsidomina, quetanserina, pinacidil, cicletanina (cicletanida), clorhidrato de amosulalol, hidrato del clorhidrato de moxonidina, losartan potásico, valsartan, mesilato de eprosartan, candesartan cilexetilo (hexetilo), irbesartan, telmisartan, olmesartan medoxomilo, mesilato de fenoldopam, cadralacina, fosfato diácido de rilmenidina, bosentan, beraprost sódico, limaprost alfadex (alfa-ciclodextrina), uniprost (treprostinilo sódico), iloprost (ciloprost), clorhidrato de mecamilamina, metergolina, acetato de guanabenz, cloricromeno, fasudilo, doconexent (ácido docosahexaenoico), ciclotiazida, citrato de sildenafil, clortalidona (clortalidona), quinetazona, indapamida, metolazona, clorhidrato de fenoxibenzamina, metirosina

(metirosina), diazóxido, torasemida (torsemida), clopamida, clorhidrato de hidralacina, reserpina y metildopa.

44.- La composición farmacéutica de conformidad con la reivindicación 25, caracterizada además porque se utiliza en combinación con un agente terapéutico para la trombosis.

45.- La composición farmacéutica de conformidad con la reivindicación 44, caracterizada además porque el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste de preparaciones de heparina, heparinas de bajo peso molecular, análogos de heparina, anticoagulantes, inhibidores de la trombina, preparaciones antitrombina, agentes antiplaquetarios y agentes trombolíticos.

46.- La composición farmacéutica de conformidad con la reivindicación 45, caracterizada además porque el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste de heparina cálcica, heparina sódica, dalteparina sódica, parnaparina sódica, reviparina sódica, danaparoid sódico, warfarina potásica, argatroban, mesilato de gabexato, mesilato de nafamostat, antitrombina III humana, aspirina, dipiridamol, clorhidrato de ticlopidina, cilostazol, limaprost alfadex, ozagrel sódico, clorhidrato de sarpogrelato, icosapentato de etilo, beraprost sódico, urocinasa, tisocinasa, alteplasa, nasaruplasa, nateplasa, monteplasa, pamiteplasa, batroxobina, citrato de sodio y proteína C.

47.- La composición farmacéutica para la profilaxis o el tratamiento de la diabetes, de conformidad con la reivindicación 28,

caracterizada además porque se utiliza en combinación con un agente terapéutico para la hiperlipidemia.

48.- La composición farmacéutica de conformidad con la reivindicación 47, caracterizada además porque el agente terapéutico para la hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de inhibidores de la HMG-CoA reductasa (estatinas), fibratos, inhibidores de la expresión de TNFSF6, agentes que incrementan el colesterol de HDL, mejoradores de la expresión de ApoA1, inhibidores de la expresión de SPP1 (osteopontina), fármacos que actúan sobre los receptores activados por el proliferador de la peroxisoma (PPAR), antagonistas del PPAR-alfa, estimulantes del factor de eliminación de la lipasa, antagonistas del colesterol, antagonistas de agregación de las plaquetas, antioxidantes, inhibidores de la biosíntesis del colesterol, sobrerreguladores del receptor de LDL, secuestrantes del ácido biliar, inhibidores de la absorción del colesterol y ácidos nicotínicos.

49.- La composición farmacéutica de conformidad con la reivindicación 48, caracterizada además porque el agente terapéutico para la hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de lovastatina, pravastatina (eptastatina) sódica, fluvastatina (fluindostainina) sódica, rosuvastatina cálcica, atorvastatina cálcica, simvastatina (sinvinolina), pitavastatina (itavastatina, nisvastatina) cálcica, ronifibrato (ronifibrato), binifibrato (binifibrato), clinofibrato, ciprofibrato, clofibrato, etofibrato, fenofibrato, bezafibrato, gemfibrozil, acipimox, éster

etílico del ácido eicosapentaenoico (icosapent, icopenato, icosapentato), probucol, policosanol, clorhidrato de colesevelam, colestiramina (resina de colestiramina), clorhidrato de colestipol, colestimida (colestilan), ezetimibe y niacina (ácido nicotínico).

50.- La composición farmacéutica para la profilaxis o el tratamiento de la diabetes, de conformidad con la reivindicación 28, caracterizada además porque se utiliza en combinación con un agente terapéutico diferente para la diabetes.

51.- La composición farmacéutica de conformidad con la reivindicación 50, caracterizada además porque el agente terapéutico diferente para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de secretagogos de la insulina, biguanidas, inhibidores de la α-glucosidasa, preparaciones de insulina, análogos de la insulina, mejoradores de la sensibilidad a la insulina, IL-11, agentes anti-CD25 (Receptor IL-2), antagonistas de la angiotensina (AT1), inhibidores de la enzima que convierte la angiotensina (ACE), inhibidores de la aldosa reductasa, antioxidantes, estimulante de la carnitina acetiltransferasa, antidepresivos, glucocorticoides, retilina, agonistas de la formación de radicales y activadores de la transcetolasa.

52.- La composición farmacéutica de conformidad con la reivindicación 51, caracterizada además porque el agente terapéutico diferente para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de nateglinida, glimepirida, glibenclamida, gliclazida,

acetohexamida, tolbutamida, gliclopiramida, tolazamida, glibuzol, glipizida, glibornurida, gliquidona, repaglinida, clorhidrato de metformina, clorhidrato de buformina, voglibosa, acarbosa, epalrestat, miglitol, insulina, clorhidrato de pioglitazona, maleato de rosiglitazona, picolinato de cromo/biotina, V-411, interleucina-11 humana recombinante, daclixímab (daclizumab), losartan potásico, captopril, clorhidrato de imidapril, ácido alfa-lipoico, clorhidrato de levacecarnina (acetil-L-carnitina, levocarnitin acetilo), captopril, retilina, verteporfin, benfotiamina y fluocinolon acetónido.

53.- La composición farmacéutica para la profilaxis o el tratamiento de la diabetes, de conformidad con la reivindicación 28, caracterizada además porque se utiliza en combinación con un agente terapéutico para la obesidad.

54.- La composición farmacéutica de conformidad con la reivindicación 53, caracterizada además porque el agente terapéutico para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, inhibidores de la lipasa, inhibidores dobles de la recaptación de 5-HT/norepinefrina, inhibidores de la recaptación de 5-HT, suplementos herbales que contienen efedrina y cafeína, gonadotropinas coriónicas humanas, agonistas de adrenoceptores, metamfetamina, fentermina y amfepramona.

55.- La composición farmacéutica de conformidad con la reivindicación 54, caracterizada además porque el agente terapéutico para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que

consiste de mazindol, orlistat, monohidrato del clorhidrato de sibutramina, clorhidrato de fluoxetina, gonadotropina coriónica (humana), terapia VNS utilizando el Sistema NCP, metaraminol, clorhidrato de d-metamfetamina, fentermina, clorhidrato de amfepramona (dietilpropion), clorhidrato de benzfetamina y tartrato de fendimetracina.

56.- La composición farmacéutica para la profilaxis o el tratamiento de la diabetes, de conformidad con la reivindicación 28, caracterizada además porque se utiliza en combinación con un agente terapéutico para la hipertensión.

57.- La composición farmacéutica de conformidad con la reivindicación 56, caracterizada además porque el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de tiazidas, antagonistas de la aldosterona, bloqueadores adrenérgicos de las neuronas, bloqueadores del canal del calcio; antagonistas de la dopamina D2, antagonistas del adrenoceptor beta, agonistas del adrenoceptor alfa2, activadores de la guanilato ciclasa, antagonistas del adrenoceptor beta1, antagonistas del adrenoceptor alfa1, antioxidantes, inhibidores de la enzima que convierten la angiotensina-I (ACE), inhibidores de intercambio de Na+/H+, antagonistas del adrenoceptor alfa, donadores de óxido nítrico, antagonistas de 5-HT2, activadores del canal de K(ATP), estimulantes de la prostaglandina sintasa diurética del potasio sobrante, agonistas del receptor de la imidazolina I1, antagonistas de la angiotensina AT1, agonistas de la dopamina D1, estimulantes de la guanilato ciclasa,

antagonistas del receptor de la endotelina ETA, antagonistas del receptor de la endotelina ETB, mejoradores de la expresión de NOS3, análogos de la prostaciclina, prostaglandinas, antagonistas de la angiotensina II, agonistas de la absorción del electrolito, antagonistas nicotínicos, agonistas de la dopamina D2, inhibidores de la prolactina, antagonistas del factor de activación de las plaquetas (PAF), antagonistas de agregación de las plaquetas, antagonistas del factor de necrosis del tumor, inhibidores de la Rho cinasa, antagonistas del PPAR-alfa, moduladores del receptor AMPA, antagonistas del receptor GABA(A) e inhibidores de la fosfodiesterasa V (PDE5A).

58.- La composición farmacéutica de conformidad con la reivindicación 57, caracterizada además porque el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de clorotiazida, hidroclorotiazida, hidroflumetiazida, meticlotiazida, politiazida, xipamida, ciclopentiazida, bendroflumetiazida (bendrofluazida), espironolactona, epoximexrenona (eplerenona), monosulfato de guanetidina, sulfato de guanadrel, verapamil, clorhidrato de propranolol, clorhidrato alprenolol, pindolol, clorhidrato de oxprenolol, maleato de timolol, clorhidrato de sotalol, clorhidrato de acebutolol, clorhidrato de carteolol, sulfato de mepindolol, clorhidrato de arotinolol, clorhidrato de indenolol, clorhidrato de tertatolol, clorhidrato de celiprolol, clorhidrato de tilisolol, nebivolol, sulfato de penbutolol, nadolol, clorhidrato de cloranolol, clorhidrato de bevantol (bevantolol), clonidina, clorhidrato de guanfacina, clorhidrato de diltiazem, clorhidrato de nicardipina, nitrendipina, felodipina, nilvadipina; nivadipina,

nisoldipina, clorhidrato de benidipina, besilato de amlodipina, clorhidrato de franidipina (manidipina), lacidipina, isradipina, clorhidrato de barnidipina (mepirodipina), clorhidrato etanólico de efonidipina, cinaldipina (cilnidipina), aranidipina, clorhidrato de lercanidipina (masnidipina), azelnidipina, amlodipina, manidipina (franidipina), nitroprussida sódica, atenolol, tartrato de metoprolol, clorhidrato de betaxolol, bopindolol, fumarato de bisoprolol, clorhidrato de esmolol, carvedilol, succinato de metoprolol, talinolol, clorhidrato de prazosina, urapidil, clorhidrato de indoramina, clorhidrato de bunazosina, clorhidrato de terazosina, mesilato de doxazosina, urapidil, nifedipina, captopril, maleato de enalapril, lisinopril, perindopril, alacepril, ramipril, clorhidrato de quinapril, clorhidrato de delapril, clorhidrato de benazepril, cilazapril, fosinoprilat, fosinopril sódico, trandolapril, espirapril, clorhidrato de temocapril, clorhidrato de moexipril, clorhidrato de imidapril, zofenopril cálcico, enalaprilat, zofenoprilat, clorhidrato de amilorida, clorhidrato de labetalol, nipradilol (nipradolol), linsidomina, quetanserina, pinacidil, cicletanina (cicletanida), clorhidrato de amosulalol, hidrato del clorhidrato de moxonidina, losartan potásico, valsartan, mesilato de eprosartan, candesartan cilexetilo (hexetilo), irbesartan, telmisartan, olmesartan medoxomilo, mesilato de fenoldopam, cadralacina, fosfato diácido de rilmenidina, bosentan, beraprost sódico, limaprost alfadex (alfa-ciclodextrina), uniprost (treprostinilo sódico), iloprost (ciloprost), clorhidrato de mecamilamina, metergolina, acetato de guanabenz, cloricromeno, fasudilo, doconexent (ácido docosahexaenoico), ciclotiazida, citrato de sildenafil, clortalidona (clortalidona), quinetazona,

indapamida, metolazona, clorhidrato de fenoxibenzamina, metirosina (metirosina), diazóxido, torasemida (torsemida), clopamida, clorhidrato de hidralacina, reserpina y metildopa.

59.- La composición farmacéutica para la profilaxis o el tratamiento de la diabetes de conformidad con la reivindicación 28, caracterizada además porque se utiliza combinación con un agente terapéutico para la trombosis.

60.- La composición farmacéutica de conformidad con la reivindicación 59, caracterizada además porque el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste de preparaciones de heparina, heparinas de bajo peso molecular, análogos de heparina, anticoagulantes, inhibidores de la trombina, preparaciones antitrombina, agentes antiplaquetarios y agentes trombolíticos.

61.- La composición farmacéutica de conformidad con la reivindicación 60, caracterizada además porque el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste de heparina cálcica, heparina sódica, dalteparina sódica, parnaparina sódica, reviparina sódica, danaparoid sódico, warfarina potásica, argatroban, mesilato de gabexato, mesilato de nafamostat, antitrombina III humana, aspirina, dipiridamol, clorhidrato de ticlopidina, cilostazol, limaprost alfadex, ozagrel sódico, clorhidrato de sarpogrelato, icosapentato de etilo, beraprost sódico, urocinasa, tisocinasa, alteplasa, nasaruplasa, nateplasa, monteplasa, pamiteplasa, batroxobina, citrato de sodio y proteína C.

62.- La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia, de conformidad con la reivindicación 29, caracterizada además porque se utiliza en combinación con un agente terapéutico para la hiperlipidemia.

63.- La composición farmacéutica de conformidad con la reivindicación 62, caracterizada además porque el agente terapéutico para hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de inhibidores de la HMG-CoA reductasa (estatinas), fibratos, inhibidores de la expresión de TNFSF6, agentes que incrementan el colesterol de HDL, mejoradores de la expresión de ApoA1, inhibidores de la expresión de SPP1 (osteopontina), fármacos que actúan sobre los receptores activados por el proliferador de la peroxisoma (PPAR), antagonistas del PPAR-alfa, estimulantes del factor de eliminación de la lipasa, antagonistas del colesterol, antagonistas de agregación de las plaquetas, antioxidantes, inhibidores de la biosíntesis del colesterol, sobrerreguladores del receptor de LDL, secuestrantes del ácido biliar, inhibidores de la absorción del colesterol y ácidos nicotínicos.

64.- La composición farmacéutica de conformidad con la reivindicación 63, caracterizada además porque el agente terapéutico para hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de lovastatina, pravastatina (eptastatina) sódica, fluvastatina (fluindostainina) sódica, rosuvastatina cálcica, atorvastatina cálcica, simvastatina (sinvinolina), pitavastatina (itavastatina, nisvastatina) cálcica,

ronifibrato (ronifibrato), binifibrato (binifibrato), clinofibrato, ciprofibrato, clofibrato, etofibrato, fenofibrato, bezafibrato, gemfibrozil, acipimox, éster etílico del ácido eicosapentaenoico (icosapent, icopenato, icosapentato), probucol, policosanol, clorhidrato de colesevelam, colestiramina (resina de colestiramina), clorhidrato de colestipol, colestimida (colestilan), ezetimibe y niacina (ácido nicotínico).

65.- La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia, de conformidad con la reivindicación 29, caracterizada además porque se utiliza en combinación con un agente terapéutico diferente para la diabetes.

66.- La composición farmacéutica de conformidad con la reivindicación 65, caracterizada además porque el agente terapéutico diferente para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de secretagogos de la insulina, biguanidas, inhibidores de la α-glucosidasa, preparaciones de insulina, análogos de la insulina, mejoradores de la sensibilidad a la insulina, IL-11, agentes anti-CD25 (Receptor IL-2), antagonistas de la angiotensina (AT1), inhibidores de la enzima que convierte la angiotensina (ACE), inhibidores de la aldosa reductasa, antioxidantes, estimulante de la carnitina acetiltransferasa, antidepresivos, glucocorticoides, retilina, agonistas de la formación de radicales y activadores de la transcetolasa.

67.- La composición farmacéutica de conformidad con la reivindicación 66, caracterizada además porque el agente terapéutico

diferente para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de nateglinida, glimepirida, glibenclamida, gliclazida, acetohexamida, tolbutamida, gliclopiramida, tolazamida, glibuzol, glipizida, glibornurida, gliquidona, repaglinida, clorhidrato de metformina, clorhidrato de buformina, voglibosa, acarbosa, epalrestat, miglitol, insulina, clorhidrato de pioglitazona, maleato de rosiglitazona, picolinato de cromo/biotina, V-411, interleucina-11 humana recombinante, dacliximab (daclizumab), losartan potásico, captopril, clorhidrato de imidapril, ácido alfa-lipoico, clorhidrato de levacecarnina (acetil-L-carnitina, levocarnitin acetilo), captopril, retilina, verteporfin, benfotiamina y fluocinolon acetónido.

68.- La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia, de conformidad con la reivindicación 29, caracterizada además porque se utiliza en combinación con un agente terapéutico para la obesidad.

69.- La composición farmacéutica de conformidad con la reivindicación 68, caracterizada además porque el agente terapéutico para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, inhibidores de la lipasa, inhibidores dobles de la recaptación de 5-HT/norepinefrina, inhibidores de la recaptación de 5-HT, suplementos herbales que contienen efedrina y cafeína, gonadotropinas coriónicas humanas, agonistas de adrenoceptores, metamfetamina, fentermina y amfepramona.

70.- La composición farmacéutica de conformidad con la reivindicación 69, caracterizada además porque el agente terapéutico para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, orlistat, monohidrato del clorhidrato de sibutramina, clorhidrato de fluoxetina, gonadotropina coriónica (humana), terapia VNS utilizando el Sistema NCP, metaraminol, clorhidrato de d-metamfetamina, fentermina, clorhidrato de amfepramona (dietilpropion), clorhidrato de benzfetamina y tartrato de fendimetracina.

71.- La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia, de conformidad con la reivindicación 29, caracterizada además porque se utiliza en combinación con un agente terapéutico para la hipertensión.

72.- La composición farmacéutica de conformidad con la reivindicación 71, caracterizada además porque el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de tiazidas, antagonistas de la aldosterona, bloqueadores adrenérgicos de las neuronas, bloqueadores del canal del calcio; antagonistas de la dopamina D2, antagonistas del aadrenoceptor beta, agonistas del adrenoceptor alfa2, activadores de la guanilato ciclasa, antagonistas del adrenoceptor beta1, antagonistas del adrenoceptor alfa1, antioxidantes, inhibidores de la enzima que convierten la angiotensina-I (ACE), inhibidores de intercambio de Na+/H+, antagonistas del adrenoceptor alfa, donadores de óxido nítrico, antagonistas de 5-HT2, activadores del canal de K(ATP),

estimulantes de la prostaglandina sintasa diurética del potasio sobrante, agonistas del receptor de la imidazolina I1, antagonistas de la angiotensina AT1, agonistas de la dopamina D1, estimulantes de la guanilato ciclasa, antagonistas del receptor de la endotelina ETA, antagonistas del receptor de la endotelina ETB, mejoradores de la expresión de NOS3, análogos de la prostaciclina, prostaglandinas, antagonistas de la angiotensina II, agonistas de la absorción del electrolito, antagonistas nicotínicos, agonistas de la dopamina D2, inhibidores de la prolactina, antagonistas del factor de activación de las plaquetas (PAF), antagonistas de agregación de las plaquetas, antagonistas del factor de necrosis del tumor, inhibidores de la Rho cinasa, antagonistas del PPAR-alfa, moduladores del receptor AMPA, antagonistas del receptor GABA(A) e inhibidores de la fosfodiesterasa V (PDE5A).

73.- La composición farmacéutica de conformidad con la reivindicación 72, caracterizada ademas porque el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de clorotiazida, hidroclorotiazida, hidroflumetiazida, meticlotiazida, politiazida, xipamida, ciclopentiazida, bendroflumetiazida (bendrofluazida), espironolactona, epoximexrenona (eplerenona), monosulfato de guanetidina, sulfato de guanadrel, verapamil, clorhidrato de propranolol, clorhidrato alprenolol, pindolol, clorhidrato de oxprenolol, maleato de timolol, clorhidrato de sotalol, clorhidrato de acebutolol, clorhidrato de carteolol, sulfato de mepindolol, clorhidrato de arotinolol, clorhidrato de indenolol, clorhidrato de tertatolol, clorhidrato de celiprolol, clorhidrato de tilisolol, nebivolol, sulfato de

penbutolol, nadolol, clorhidrato de cloranolol, clorhidrato de bevantol (bevantolol), clonidina, clorhidrato de guanfacina, clorhidrato de diltiazem, clorhidrato de nicardipina, nitrendipina, felodipina, nilvadipina; nivadipina, nisoldipina, clorhidrato de benidipina, besilato de amlodipina, clorhidrato de franidipina (manidipina), lacidipina, isradipina, clorhidrato de barnidipina (mepirodipina), clorhidrato etanólico de efonidipina, cinaldipina (cilnidipina), aranidipina, clorhidrato de lercanidipina (masnidipina), azelnidipina, amlodipina, manidipina (franidipina), nitroprussida sódica, atenolol, tartrato de metoprolol, clorhidrato de betaxolol, bopindolol, fumarato de bisoprolol, clorhidrato de esmolol, carvedilol, succinato de metoprolol, talinolol, clorhidrato de prazosina, urapidil, clorhidrato de indoramina, clorhidrato de bunazosina, clorhidrato de terazosina, mesilato de doxazosina, urapidil, nifedipina, captopril, maleato de enalapril, lisinopril, perindopril, alacepril, ramipril, clorhidrato de quinapril, clorhidrato de delapril, clorhidrato de benazepril, cilazapril, fosinoprilat, fosinopril sódico, trandolapril, espirapril, clorhidrato de temocapril, clorhidrato de moexipril, clorhidrato de imidapril, zofenopril cálcico, enalaprilat, zofenoprilat, clorhidrato de amilorida, clorhidrato de labetalol, nipradilol (nipradolol), linsidomina, quetanserina, pinacidil, cicletanina (cicletanida), clorhidrato de amosulalol, hidrato del clorhidrato de moxonidina, losartan potásico, valsartan, mesilato de eprosartan, candesartan cilexetilo (hexetilo), irbesartan, telmisartan, olmesartan medoxomilo, mesilato de fenoldopam, cadralacina, fosfato diácido de rilmenidina, bosentan, beraprost sódico, limaprost alfadex (alfa-ciclodextrina), uniprost (treprostinilo sódico),

iloprost (ciloprost), clorhidrato de mecamilamina, metergolina, acetato de guanabenz, cloricromeno, fasudilo, doconexent (ácido docosahexaenoico), ciclotiazida, citrato de sildenafil, clortalidona (clortalidona), quinetazona, indapamida, metolazona, clorhidrato de fenoxibenzamina, metirosina (metirosina), diazóxido, torasemida (torsemida), clopamida, clorhidrato de hidralacina, reserpina y metildopa.

74.- La composición farmacéutica para la profilaxis o el tratamiento de la hiperlipidemia, de conformidad con la reivindicación 29, caracterizada además porque se utiliza en combinación con un agente terapéutico para la trombosis.

75.- La composición farmacéutica de conformidad con la reivindicación 74, caracterizada además porque el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste de preparaciones de heparina, heparinas de bajo peso molecular, análogos de heparina, anticoagulantes, inhibidores de la trombina, preparaciones antitrombina, agentes antiplaquetarios y agentes trombolíticos.

76.- La composición farmacéutica de conformidad con la reivindicación 75, caracterizada además porque el el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste de heparina cálcica, heparina sódica, dalteparina sódica, parnaparina sódica, reviparina sódica, danaparoid sódico, warfarina potásica, argatroban, mesilato de gabexato, mesilato de nafamostat, antitrombina III humana, aspirina, dipiridamol, clorhidrato de ticlopidina, cilostazol, limaprost alfadex,

ozagrel sódico, clorhidrato de sarpogrelato, icosapentato de etilo, beraprost sódico, urocinasa, tisocinasa, alteplasa, nasaruplasa, nateplasa, monteplasa, pamiteplasa, batroxobina, citrato de sodio y proteína C.

77.- La composición farmacéutica para la profilaxis o el tratamiento de la obesidad, de conformidad con la reivindicación 30, caracterizada además porque se utiliza en combinación con un agente terapéutico diferente para la hiperlipidemia.

78.- La composición farmacéutica de conformidad con la reivindicación 77, caracterizada además porque el agente terapéutico diferente para la hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de inhibidores de la HMG-CoA reductasa (estatinas), fibratos, inhibidores de la expresión de TNFSF6, agentes que incrementan el colesterol de HDL, mejoradores de la expresión de ApoA1, inhibidores de la expresión de SPP1 (osteopontina), fármacos que actúan sobre los receptores activados por el proliferador de la peroxisoma (PPAR), antagonistas del PPAR-alfa, estimulantes del factor de eliminación de la lipasa, antagonistas del colesterol, antagonistas de agregación de las plaquetas, antioxidantes, inhibidores de la biosíntesis del colesterol, sobrerreguladores del receptor de LDL, secuestrantes del ácido biliar, inhibidores de la absorción del colesterol y ácidos nicotínicos.

79.- La composición farmacéutica de conformidad con la reivindicación 78, caracterizada además porque el agente terapéutico diferente para la hiperlipidemia es uno o más agentes terapéuticos

seleccionados del grupo que consiste de lovastatina, pravastatina (eptastatina) sódica, fluvastatina (fluindostainina) sódica, rosuvastatina cálcica, atorvastatina cálcica, simvastatina (sinvinolina), pitavastatina (itavastatina, nisvastatina) cálcica, ronifibrato (ronifibrato), binifibrato (binifibrato), clinofibrato, ciprofibrato, clofibrato, etofibrato, fenofibrato, bezafibrato, gemfibrozil, acipimox, éster etílico del ácido eicosapentaenoico (icosapent, icopenato, icosapentato), probucol, policosanol, clorhidrato de colesevelam, colestiramina (resina de colestiramina), clorhidrato de colestipol, colestimida (colestilan), ezetimibe y niacina (ácido nicotínico).

80.- La composición farmacéutica para la profilaxis o el tratamiento de la obesidad, de conformidad con la reivindicación 30, caracterizada además porque se utiliza en combinación con un agente terapéutico para la diabetes.

81.- La composición farmacéutica de conformidad con la reivindicación 80, caracterizada además porque el agente terapéutico para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de secretagogos de la insulina, biguanidas, inhibidores de la α-glucosidasa, preparaciones de insulina, análogos de la insulina, mejoradores de la sensibilidad a la insulina, IL-11, agentes anti-CD25 (Receptor IL-2), antagonistas de la angiotensina (AT1), inhibidores de la enzima que convierte la angiotensina (ACE), inhibidores de la aldosa reductasa, antioxidantes, estimulante de la carnitina acetiltransferasa, antidepresivos, glucocorticoides,

retilina, agonistas de la formación de radicales y activadores de la transcetolasa.

82.- La composición farmacéutica de conformidad con la reivindicación 81, caracterizada además porque el agente terapéutico para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de nateglinida, glimepirida, glibenclamida, gliclazida, acetohexamida, tolbutamida, gliclopiramida, tolazamida, glibuzol, glipizida, glibornurida, gliquidona, repaglinida, clorhidrato de metformina, clorhidrato de buformina, voglibosa, acarbosa, epalrestat, miglitol, insulina, clorhidrato de pioglitazona, maleato de rosiglitazona, picolinato de cromo/biotina, V-411, interleucina-11 humana recombinante, daclixímab (daclizumab), losartan potásico, captopril, clorhidrato de imidapril, ácido alfa-lipoico, clorhidrato de levacecarnina (acetil-L-carnitina, levocarnitin acetilo), captopril, retilina, verteporfin, benfotiamina y fluocinolon acetónido.

83.- La composición farmacéutica para la profilaxis o el tratamiento de la obesidad, de conformidad con la reivindicación 30, caracterizada además porque se utiliza en combinación con un agente terapéutico diferente para la obesidad.

84.- La composición farmacéutica de conformidad con la reivindicación 83, caracterizada además porque el agente terapéutico diferente para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, inhibidores de la lipasa, inhibidores dobles de la recaptación de 5-HT/norepinefrina, inhibidores de la recaptación

de 5-HT, suplementos herbales que contienen efedrina y cafeína, gonadotropinas coriónicas humanas, agonistas de adrenoceptores, metamfetamina, fentermina y amfepramona.

85.- La composición farmacéutica de conformidad con la reivindicación 84, caracterizada además porque el agente terapéutico diferente para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, orlistat, monohidrato del clorhidrato de sibutramina, clorhidrato de fluoxetina, gonadotropina coriónica (humana), terapia VNS utilizando el Sistema NCP, metaraminol, clorhidrato de d-metamfetamina, fentermina, clorhidrato de amfepramona (dietilpropion), clorhidrato de benzfetamina y tartrato de fendimetracina.

86.- La composición farmacéutica para la profilaxis o el tratamiento de la obesidad, de conformidad con la reivindicación 30, caracterizada además porque se utiliza en combinación con un agente terapéutico para la hipertensión.

87.- La composición farmacéutica de conformidad con la reivindicación 86, caracterizada además porque el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de tiazidas, antagonistas de la aldosterona, bloqueadores adrenérgicos de las neuronas, bloqueadores del canal del calcio; antagonistas de la dopamina D2, antagonistas del aadrenoceptor beta, agonistas del adrenoceptor alfa2, activadores de la guanilato ciclasa, antagonistas del adrenoceptor beta1, antagonistas del adrenoceptor alfa1, antioxidantes,

inhibidores de la enzima que convierten la angiotensina-I (ACE), inhibidores de intercambio de Na+/H+, antagonistas del adrenoceptor alfa, donadores de óxido nítrico, antagonistas de 5-HT2, activadores del canal de K(ATP), estimulantes de la prostaglandina sintasa diurética del potasio sobrante, agonistas del receptor de la imidazolina I1, antagonistas de la angiotensina AT1, agonistas de la dopamina D1, estimulantes de la guanilato ciclasa, antagonistas del receptor de la endotelina ETA, antagonistas del receptor de la endotelina ETB, mejoradores de la expresión de NOS3, análogos de la prostaciclina, prostaglandinas, antagonistas de la angiotensina II, agonistas de la absorción del electrolito, antagonistas nicotínicos, agonistas de la dopamina D2, inhibidores de la prolactina, antagonistas del factor de activación de las plaquetas (PAF), antagonistas de agregación de las plaquetas, antagonistas del factor de necrosis del tumor, inhibidores de la Rho cinasa, antagonistas del PPAR-alfa, moduladores del receptor AMPA, antagonistas del receptor GABA(A) e inhibidores de la fosfodiesterasa V (PDE5A).

88.- La composición farmacéutica de conformidad con la reivindicación 87, caracterizada además porque el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de clorotiazida, hidroclorotiazida, hidroflumetiazida, meticlotiazida, politiazida, xipamida, ciclopentiazida, bendroflumetiazida (bendrofluazida), espironolactona, epoximexrenona (eplerenona), monosulfato de guanetidina, sulfato de guanadrel, verapamil, clorhidrato de propranolol, clorhidrato alprenolol, pindolol, clorhidrato de oxprenolol, maleato de timolol, clorhidrato

de sotalol, clorhidrato de acebutolol, clorhidrato de carteolol, sulfato de mepindolol, clorhidrato de arotinolol, clorhidrato de indenolol, clorhidrato de tertatolol, clorhidrato de celiprolol, clorhidrato de tilisolol, nebivolol, sulfato de penbutolol, nadolol, clorhidrato de cloranolol, clorhidrato de bevantol (bevantolol), clonidina, clorhidrato de guanfacina, clorhidrato de diltiazem, clorhidrato de nicardipina, nitrendipina, felodipina, nilvadipina; nivadipina, nisoldipina, clorhidrato de benidipina, besilato de amlodipina, clorhidrato de franidipina (manidipina), lacidipina, isradipina, clorhidrato de barnidipina (mepirodipina), clorhidrato etanólico de efonidipina, cinaldipina (cilnidipina), aranidipina, clorhidrato de lercanidipina (masnidipina), azelnidipina, amlodipina, manidipina (franidipina), nitroprussida sódica, atenolol, tartrato de metoprolol, clorhidrato de betaxolol, bopindolol, fumarato de bisoprolol, clorhidrato de esmolol, carvedilol, succinato de metoprolol, talinolol, clorhidrato de prazosina, urapidil, clorhidrato de indoramina, clorhidrato de bunazosina, clorhidrato de terazosina, mesilato de doxazosina, urapidil, nifedipina, captopril, maleato de enalapril, lisinopril, perindopril, alacepril, ramipril, clorhidrato de quinapril, clorhidrato de delapril, clorhidrato de benazepril, cilazapril, fosinoprilat, fosinopril sódico, trandolapril, espirapril, clorhidrato de temocapril, clorhidrato de moexipril, clorhidrato de imidapril, zofenopril cálcico, enalaprilat, zofenoprilat, clorhidrato de amilorida, clorhidrato de labetalol, nipradilol (nipradolol), linsidomina, quetanserina, pinacidil, cicletanina (cicletanida), clorhidrato de amosulalol, hidrato del clorhidrato de moxonidina, losartan potásico, valsartan, mesilato de eprosartan, candesartan cilexetilo

(hexetilo), irbesartan, telmisartan, olmesartan medoxomilo, mesilato de fenoldopam, cadralacina, fosfato diácido de rilmenidina, bosentan, beraprost sódico, limaprost alfadex (alfa-ciclodextrina), uniprost (treprostinilo sódico), iloprost (ciloprost), clorhidrato de mecamilamina, metergolina, acetato de guanabenz, cloricromeno, fasudilo, doconexent (ácido docosahexaenoico), ciclotiazida, citrato de sildenafil, clortalidona (clortalidona), quinetazona, indapamida, metolazona, clorhidrato de fenoxibenzamina, metirosina (metirosina), diazóxido, torasemida (torsemida), clopamida, clorhidrato de hidralacina, reserpina y metildopa.

89.- La composición farmacéutica para la profilaxis o el tratamiento de la obesidad, de conformidad con la reivindicación 30, caracterizada además porque se utiliza en combinación con un agente terapéutico para la trombosis.

90.- La composición farmacéutica de conformidad con la reivindicación 89, caracterizada además porque el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste de preparaciones de heparina, heparinas de bajo peso molecular, análogos de heparina, anticoagulantes, inhibidores de la trombina, preparaciones antitrombina, agentes antiplaquetarios y agentes trombolíticos.

91.- La composición farmacéutica de conformidad con la reivindicación 90, caracterizada además porque el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste de heparina cálcica, heparina sódica, dalteparina sódica, parnaparina

sódica, reviparina sódica, danaparoid sódico, warfarina potásica, argatroban, mesilato de gabexato, mesilato de nafamostat, antitrombina III humana, aspirina, dipiridamol, clorhidrato de ticlopidina, cilostazol, limaprost alfadex, ozagrel sódico, clorhidrato de sarpogrelato, icosapentato de etilo, beraprost sódico, urocinasa, tisocinasa, alteplasa, nasaruplasa, nateplasa, monteplasa, pamiteplasa, batroxobina, citrato de sodio y proteína C.

92.- La composición farmacéutica para la profilaxis o el tratamiento de las complicaciones diabéticas, de conformidad con la reivindicación 31, caracterizada además porque se utiliza en combinación con un agente terapéutico para la hiperlipidemia.

93.- La composición farmacéutica de conformidad con la reivindicación 92, caracterizada además porque el agente terapéutico para hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de inhibidores de la HMG-CoA reductasa (estatinas), fibratos, inhibidores de la expresión de TNFSF6, agentes que incrementan el colesterol de HDL, mejoradores de la expresión de ApoA1, inhibidores de la expresión de SPP1 (osteopontina), fármacos que actúan sobre los receptores activados por el proliferador de la peroxisoma (PPAR), antagonistas del PPAR-alfa, estimulantes del factor de eliminación de la lipasa, antagonistas del colesterol, antagonistas de agregación de las plaquetas, antioxidantes, inhibidores de la biosíntesis del colesterol, sobrerreguladores del receptor de LDL, secuestrantes del ácido biliar, inhibidores de la absorción del colesterol y ácidos nicotínicos.

94.- La composición farmacéutica de conformidad con la reivindicación 93, caracterizada además porque el agente terapéutico para hiperlipidemia es uno o más agentes terapéuticos seleccionados del grupo que consiste de lovastatina, pravastatina (eptastatina) sódica, fluvastatina (fluindostainina) sódica, rosuvastatina cálcica, atorvastatina cálcica, simvastatina (sinvinolina), pitavastatina (itavastatina, nisvastatina) cálcica, ronifibrato (ronifibrato), binifibrato (binifibrato), clinofibrato, ciprofibrato, clofibrato, etofibrato, fenofibrato, bezafibrato, gemfibrozil, acipimox, éster etílico del ácido eicosapentaenoico (icosapent, icopenato, icosapentato), probucol, policosanol, clorhidrato de colesevelam, colestiramina (resina de colestiramina), clorhidrato de colestipol, colestimida (colestilan), ezetimibe y niacina (ácido nicotínico).

95.- La composición farmacéutica para la profilaxis o el tratamiento de las complicaciones diabéticas, de conformidad con la reivindicación 31, caracterizada además porque se utiliza en combinación con un agente terapéutico para la diabetes.

96.- La composición farmacéutica de conformidad con la reivindicación 95, caracterizada además porque el agente terapéutico para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de secretagogos de la insulina, biguanidas, inhibidores de la α-glucosidasa, preparaciones de insulina, análogos de la insulina, mejoradores de la sensitividad de la insulina, IL-11, agentes anti-CD25 (Receptor IL-2), antagonistas de la angiotensina (AT1), inhibidores de la enzima que convierte

la angiotensina (ACE), inhibidores de la aldosa reductasa, antioxidantes, estimulante de la carnitina acetiltransferasa, antidepresivos, glucocorticoides, retilina, agonistas de la formación de radicales y activadores de la transcetolasa.

97.- La composición farmacéutica de conformidad con la reivindicación 96, caracterizada además porque el agente terapéutico para la diabetes es uno o más agentes terapéuticos seleccionados del grupo que consiste de nateglinida, glimepirida, glibenclamida, gliclazida, acetohexamida, tolbutamida, gliclopiramida, tolazamida, glibuzol, glipizida, glibornurida, gliquidona, repaglinida, clorhidrato de metformina, clorhidrato de buformina, voglibosa, acarbosa, epalrestat, miglitol, insulina, clorhidrato de pioglitazona, maleato de rosiglitazona, picolinato de cromo/biotina, V-411, interleucina-11 humana recombinante, dacliximab (daclizumab), losartan potásico, captopril, clorhidrato de imidapril, ácido alfa-lipoico, clorhidrato de levacecarnina (acetil-L-carnitina, levocarnitin acetilo), captopril, retilina, verteporfin, benfotiamina y fluocinolon acetónido.

98.- La composición farmacéutica para la profilaxis o el tratamiento de las complicaciones diabéticas, de conformidad con la reivindicación 31, caracterizada además porque se utiliza en combinación con un agente terapéutico para la obesidad.

99.- La composición farmacéutica de conformidad con la reivindicación 98, caracterizado además porque el agente terapéutico para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que

consiste de mazindol, inhibidores de la lipasa, inhibidores dobles de la recaptación de 5-HT/norepinefrina, inhibidores de la recaptación de 5-HT, suplementos herbales que contienen efedrina y cafeína, gonadotropinas coriónicas humanas, agonistas de adrenoceptores, metamfetamina, fentermina y amfepramona.

100.- La composición farmacéutica de conformidad con la reivindicación 99, caracterizada además porque el agente terapéutico para la obesidad es uno o más agentes terapéuticos seleccionados del grupo que consiste de mazindol, orlistat, monohidrato del clorhidrato de sibutramina, clorhidrato de fluoxetina, gonadotropina coriónica (humana), terapia VNS utilizando el Sistema NCP, metaraminol, clorhidrato de d-metamfetamina, fentermina, clorhidrato de amfepramona (dietilpropion), clorhidrato de benzfetamina y tartrato de fendimetracina.

101.- La composición farmacéutica para la profilaxis o el tratamiento de las complicaciones diabéticas, de conformidad con la reivindicación 31, caracterizada además porque se utiliza en combinación con un agente terapéutico para la hipertensión.

102.- La composición farmacéutica de conformidad con la reivindicación 101, caracterizada además porque el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de tiazidas, antagonistas de la aldosterona, bloqueadores adrenérgicos de las neuronas, bloqueadores del canal del calcio; antagonistas de la dopamina D2, antagonistas del aadrenoceptor beta, agonistas del

adrenoceptor alfa2, activadores de la guanilato ciclasa, antagonistas del adrenoceptor beta1, antagonistas del adrenoceptor alfa1, antioxidantes, inhibidores de la enzima que convierten la angiotensina-I (ACE), inhibidores de intercambio de Na+/H+, antagonistas del adrenoceptor alfa, donadores de óxido nítrico, antagonistas de 5-HT2, activadores del canal de K(ATP), estimulantes de la prostaglandina sintasa diurética del potasio sobrante, agonistas del receptor de la imidazolina I1, antagonistas de la angiotensina AT1, agonistas de la dopamina D1, estimulantes de la guanilato ciclasa, antagonistas del receptor de la endotelina ETA, antagonistas del receptor de la endotelina ETB, mejoradores de la expresión de NOS3, análogos de la prostaciclina, prostaglandinas, antagonistas de la angiotensina II, agonistas de la absorción del electrolito, antagonistas nicotínicos, agonistas de la dopamina D2, inhibidores de la prolactina, antagonistas del factor de activación de las plaquetas (PAF), antagonistas de agregación de las plaquetas, antagonistas del factor de necrosis del tumor, inhibidores de la Rho cinasa, antagonistas del PPAR-alfa, moduladores del receptor AMPA, antagonistas del receptor GABA(A) e inhibidores de la fosfodiesterasa V (PDE5A).

103.- La composición farmacéutica de conformidad con la reivindicación 102, caracterizada además porque el agente terapéutico para la hipertensión es uno o más agentes terapéuticos seleccionados del grupo que consiste de clorotiazida, hidroclorotiazida, hidroflumetiazida, meticlotiazida, politiazida, xipamida, ciclopentiazida, bendroflumetiazida (bendrofluazida), espironolactona, epoximexrenona (eplerenona), monosulfato de guanetidina,

sulfato de guanadrel, verapamil, clorhidrato de propranolol, clorhidrato alprenolol, pindolol, clorhidrato de oxprenolol, maleato de timolol, clorhidrato de sotalol, clorhidrato de acebutolol, clorhidrato de carteolol, sulfato de mepindolol, clorhidrato de arotinolol, clorhidrato de indenolol, clorhidrato de tertatolol, clorhidrato de celiprolol, clorhidrato de tilisolol, nebivolol, sulfato de penbutolol, nadolol, clorhidrato de cloranolol, clorhidrato de bevantol (bevantolol), clonidina, clorhidrato de guanfacina, clorhidrato de diltiazem, clorhidrato de nicardipina, nitrendipina, felodipina, nilvadipina; nivadipina, nisoldipina, clorhidrato de benidipina, besilato de amlodipina, clorhidrato de franidipina (manidipina), lacidipina, isradipina, clorhidrato de barnidipina (mepirodipina), clorhidrato etanólico de efonidipina, cinaldipina (cilnidipina), aranidipina, clorhidrato de lercanidipina (masnidipina), azelnidipina, amlodipina, manidipina (franidipina), nitroprussida sódica, atenolol, tartrato de metoprolol, clorhidrato de betaxolol, bopindolol, fumarato de bisoprolol, clorhidrato de esmolol, carvedilol, succinato de metoprolol, talinolol, clorhidrato de prazosina, urapidil, clorhidrato de indoramina, clorhidrato de bunazosina, clorhidrato de terazosina, mesilato de doxazosina, urapidil, nifedipina, captopril, maleato de enalapril, lisinopril, perindopril, alacepril, ramipril, clorhidrato de quinapril, clorhidrato de delapril, clorhidrato de benazepril, cilazapril, fosinoprilat, fosinopril sódico, trandolapril, espirapril, clorhidrato de temocapril, clorhidrato de moexipril, clorhidrato de imidapril, zofenopril cálcico, enalaprilat, zofenoprilat, clorhidrato de amilorida, clorhidrato de labetalol, nipradilol (nipradolol), linsidomina, quetanserina, pinacidil, cicletanina

(cicletanida), clorhidrato de amosulalol, hidrato del clorhidrato de moxonidina, losartan potásico, valsartan, mesilato de eprosartan, candesartan cilexetilo (hexetilo), irbesartan, telmisartan, olmesartan medoxomilo, mesilato de fenoldopam, cadralacina, fosfato diácido de rilmenidina, bosentan, beraprost sódico, limaprost alfadex (alfa-ciclodextrina), uniprost (treprostinilo sódico), iloprost (ciloprost), clorhidrato de mecamilamina, metergolina, acetato de guanabenz, cloricromeno, fasudilo, doconexent (ácido docosahexaenoico), ciclotiazida, citrato de sildenafil, clortalidona (clortalidona), quinetazona, indapamida, metolazona, clorhidrato de fenoxibenzamina, metirosina (metirosina), diazóxido, torasemida (torsemida), clopamida, clorhidrato de hidralacina, reserpina y metildopa.

104.- La composición farmacéutica para la profilaxis o el tratamiento de las complicaciones diabéticas, de conformidad con la reivindicación 31, caracterizada además porque se utiliza en combinación con un agente terapéutico para la trombosis.

105.- La composición farmacéutica de conformidad con la reivindicación 104, caracterizada además porque el agente terapéutico para la trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste de preparaciones de heparina, heparinas de bajo peso molecular, análogos de heparina, anticoagulantes, inhibidores de la trombina, preparaciones antitrombina, agentes antiplaquetarios y agentes trombolíticos.

106.- La composición farmacéutica de conformidad con la reivindicación 105, caracterizada además porque el agente terapéutico para la

trombosis es uno o más agentes terapéuticos seleccionados del grupo que consiste de heparina cálcica, heparina sódica, dalteparina sódica, parnaparina sódica, reviparina sódica, danaparoid sódico, warfarina potásica, argatroban, mesilato de gabexato, mesilato de nafamostat, antitrombina III humana, aspirina, dipiridamol, clorhidrato de ticlopidina, cilostazol, limaprost alfadex, ozagrel sódico, clorhidrato de sarpogrelato, icosapentato de etilo, beraprost sódico, urocinasa, tisocinasa, alteplasa, nasaruplasa, nateplasa, monteplasa, pamiteplasa, batroxobina, citrato de sodio y proteína C.

107.- Una composición farmacéutica para la inhibición de un regulador negativo del receptor de la tirosina cinasa, que se utiliza en combinación con un agente terapéutico para la hiperlipidemia.

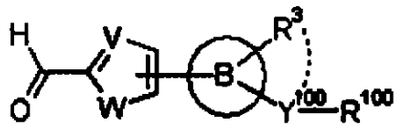
108.- Una composición farmacéutica para la inhibición de un regulador negativo del receptor de la tirosina cinasa, que se utiliza en combinación con un agente terapéutico para la diabetes.

109.- Una composición farmacéutica para la inhibición de un regulador negativo del receptor de la tirosina cinasa, que se utiliza en combinación con un agente terapéutico para la obesidad.

110.- Una composición farmacéutica para la inhibición de un regulador negativo del receptor de la tirosina cinasa, que se utiliza en combinación con un agente terapéutico para la hipertensión.

111.- Una composición farmacéutica para la inhibición de un regulador negativo del receptor de la tirosina cinasa, que se utiliza en combinación con un agente terapéutico para la trombosis.

112.- Un compuesto anular heteroaromático de 5 miembros representado por la fórmula [II]



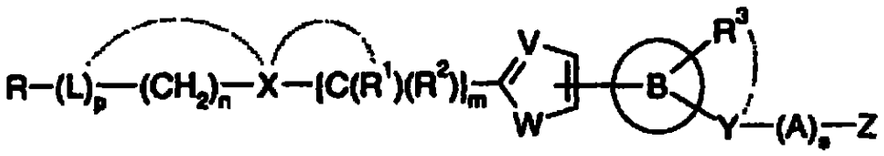
[II]

en donde Y^{100} es $-C(R^{13})(R^{14})-$, R^{13} y R^{14} son como se definen en la reivindicación 1; R^{100} es un grupo hidroxilo o un átomo de halógeno, y V, W y R^3 son cada uno como se definen en la reivindicación 1, o una sal farmacéuticamente aceptable del mismo.

113. El compuesto anular heteroaromático de 5 miembros de conformidad con la reivindicación 112, caracterizado además porque en la fórmula [II], R^{13} y R^{14} son cada uno un átomo de hidrógeno, V es =CH- y W es -S-, o una sal farmacéuticamente aceptable del mismo.

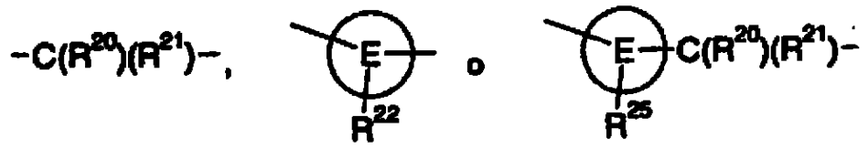
RESUMEN DE LA INVENCION

Un compuesto anular heteroaromático de 5 miembros, representado por la fórmula [I]



[I]

en donde V es CH o N; W es S u O; R^1 y R^2 son cada uno H, etc.; X es $-N(R^4)-$, -O-, -S-, $-SO_2-N(R^5)-$, $-CO-N(R^7)-$ etc.; L es



en donde R^{20}, R^{21}, R^{22} y R^{25} son cada uno H, etc.; E es un grupo arilo o un anillo heteroaromático; R es –COOH etc.; B es arilo, etc.; R^3 es H, etc.; Y es $-C(R^{13})(R^{14})-N(R^{12})-$, $-C(R^{13})(R^{14})-O-$, $-N(R^{11})-$, -O-, etc.; A es alquileno; y Z es arilo, etc., un profármaco del mismo y una sal farmacéuticamente aceptable del mismo; el compuesto [I] tiene una actividad inhibidora superior de la proteína tirosina fosfatasa 1B, y es útil como un agente terapéutico para la diabetes, complicaciones diabéticas, hiperlipidemia, obesidad y lo similar.

DH

P05/1538F

Extracto de publicación
Folios 1159 al 1162

[redacted]

FORMATO DE DIGITALIZACI N
RELACION DE ANEXOS

Royal Technologies S.A.

1153

Item	Expediente No	05110118 No de unidades	No de Folio √
1	CD		
2	DVD		
3	REVISTA		
4	LIBRO		
5	PERIODICO		
6	DISQUETES X	1	✓
7	SOBRE DE MANILA		
8	SOBRE BLANCO TAMAÑO CARTA		
9	SOBRE BLANCO TAMAÑO OFICIO		
10	OTROS:		

Observaciones: GSON DISKETTE 1 EXTRACTO PARA LA PUBLICACION

ALVARO CASTELLANOS M. & CIA.
ABOGADOS
Calle 94 A No. 7 A-09
Apartado 8349
Bogotá, D.C. – COLOMBIA

El solicitante efectúo modificaciones de conformidad con el **Artículo 19 (1)**

En la reivindicación 1, en la parte donde se cita (2) un grupo arilo en donde el grupo arilo está sustituido opcionalmente por sustituyentes seleccionado del grupo que consiste de (a)....(1)

La expresión sustituido opcionalmente se cambió a sustituido.

De conformidad con lo anterior, en la reivindicación 2, se modificó en la parte donde se menciona (2) un grupo arilo en donde el grupo arilo está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste en (a) un grupo heterocíclico...

La expresión sustituido opcionalmente se cambió a sustituido.

Por lo tanto, se anexan las páginas 457 y 467 en inglés y las páginas 488 y 497 en español, que muestran tal cambio.

Dicho cambio se ha efectuado en el capítulo reivindicatorio presentado.

s is 0 or 1;

A is a C_{1-4} alkylene group optionally substituted by a C_{3-7} cycloalkyl group;

Z is

(1) a C_{3-7} cycloalkyl group

wherein said C_{3-7} cycloalkyl group is optionally substituted by an aryl group wherein said aryl group is optionally substituted by a halogen atom or a C_{1-6} alkyl group, or a heteroaromatic ring group wherein said heteroaromatic ring group is optionally substituted by a halogen atom or a C_{1-6} alkyl group,

(2) an aryl group

wherein said aryl group is substituted by substituent(s) selected from the group consisting of

(a) a heterocyclic group optionally substituted by a C_{1-4} alkyl group or a C_{1-4} alkylcarbonyl group,

(b) a C_{3-7} cycloalkyl group optionally substituted by a hydroxyl group, an oxo group, a halogen atom or a C_{1-6} alkyl group,

(c) a carboxy group,

(d) a halogen atom,

(e) a C_{1-8} alkyl group,

(f) a C_{1-4} haloalkyl group,

(g) a C_{1-4} alkylamino group,

(h) a di(C_{1-4} alkyl)amino group,

(i) a C_{1-6} alkylthio group,

(j) a C_{1-4} alkoxy group,

(k) a C_{1-4} alkylcarbonyl group and

(l) a nitro group,

(3) a heteroaromatic ring group

wherein said heteroaromatic ring group is optionally substituted by substituent(s) selected from the group consisting of

(a) a heterocyclic group optionally substituted by a C_{1-4} alkyl

group, R^{22} is a hydrogen atom, a halogen atom, a C_{1-4} alkyl group, a C_{1-4} alkoxy group or a nitro group, and R^{25} is a hydrogen atom, a halogen atom, a C_{1-4} alkyl group, a C_{1-4} alkoxy group or a nitro group,

Y should be

$-C(R^{13})(R^{14})-N(R^{12})-$, $-CO-N(R^{12})-$ or $-C(R^{13})(R^{14})-O-$ wherein R^{12}, R^{13} and R^{14} are as defined above;

s is 0 or 1;

A is a C_{1-4} alkylene group optionally substituted by a C_{3-7} cycloalkyl group;

Z is

(1) a C_{3-7} cycloalkyl group

wherein said C_{3-7} cycloalkyl group is optionally substituted by an aryl group wherein said aryl group is optionally substituted by a halogen atom or a C_{1-6} alkyl group, or a heteroaromatic ring group wherein said heteroaromatic ring group is optionally substituted by a halogen atom or a C_{1-6} alkyl group,

(2) an aryl group

wherein said aryl group is substituted by substituent(s) selected from the group consisting of

(a) a heterocyclic group optionally substituted by a C_{1-4} alkyl group or a C_{1-4} alkylcarbonyl group,

(b) a C_{3-7} cycloalkyl group optionally substituted by a hydroxyl group, an oxo group, a halogen atom or a C_{1-6} alkyl group,

(c) a carboxy group,

(d) a halogen atom,

(e) a C_{1-8} alkyl group,

(f) a C_{1-4} haloalkyl group,

(g) a C_{1-4} alkylamino group,

(h) a di(C_{1-4} alkyl)amino group,

(i) a C_{1-6} alkylthio group,

(j) a C_{1-4} alkoxy group, and

halógeno o un grupo alquilo de C_{1-6}, (2) un grupo arilo en donde el grupo arilo está sustituido por sustituyentes seleccionados del grupo que consiste de (a) un grupo heterocíclico sustituido opcionalmente por un grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4}, (b) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por un grupo hidroxilo, un grupo oxo, un átomo de halógeno o un grupo alquilo de C_{1-6}, (c) un grupo carboxi, (d) un átomo de halógeno, (e) un grupo alquilo de C_{1-6}, (f) un grupo haloalquilo de C_{1-4}, (g) un grupo alquilamino de C_{1-4}, (h) un grupo di(alquil de C_{1-4})amino, (i) un grupo alquiltio de C_{1-6}, (j) un grupo alcoxi de C_{1-4}, (k) un grupo alquilcarbonilo de C_{1-4} y (l) un grupo nitro, (3) un grupo anular heteroaromático en donde el grupo anular heteroaromático está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de (a) un grupo heterocíclico sustituido opcionalmente por un grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4}, (b) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por un grupo hidroxilo, un grupo oxo, un átomo de halógeno o un grupo alquilo de C_{1-6}, (c) un grupo carboxi, (d) un átomo de halógeno, (e) un grupo alquilo de C_{1-6}, (f) un grupo haloalquilo de C_{1-4}, (g) un grupo alquilamino de C_{1-4}, (h) un grupo di(alquil de C_{1-4})amino, (i) un grupo alquiltio de C_{1-6}, (j) un grupo alcoxi de C_{1-4}, (k) un grupo alquilcarbonilo de C_{1-4} y (l) un grupo arilo sustituido opcionalmente por un átomo de halógeno o un grupo haloalquilo de C_{1-4}, (4) un grupo indanilo o (5) un grupo piperacinilo en donde el grupo piperacinilo está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de (a) un grupo fenilo, (b) un grupo fenilalquilo de C_{1-4}, (c) un grupo

es 0 ó 1; A es un grupo alquileno de C_{1-4} sustituido opcionalmente por un grupo cicloalquilo de C_{3-7}; Z es (1) un grupo cicloalquilo de C_{3-7} en donde el grupo cicloalquilo de C_{3-7} está sustituido opcionalmente por un grupo arilo, en donde el grupo arilo está sustituido opcionalmente por un átomo de halógeno o un grupo alquilo de C_{1-6}, o un grupo anular heteroaromático en donde el grupo anular heteroaromático está sustituido opcionalmente por un átomo de halógeno o un grupo alquilo de C_{1-6}, (2) un grupo arilo en donde el grupo arilo está sustituido por sustituyentes seleccionados del grupo que consiste de (a) un grupo heterocíclico sustituido opcionalmente por un grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4}, (b) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por un grupo hidroxilo, un grupo oxo, un átomo de halógeno o un grupo alquilo de C_{1-6}, (c) un grupo carboxi, (d) un átomo de halógeno, (e) un grupo alquilo de C_{1-6}, (f) un grupo haloalquilo de C_{1-4}, (g) un grupo alquilamino de C_{1-4}, (h) un grupo di(alquil de C_{1-4})amino, (i) un grupo alquiltio de C_{1-6}, (j) un grupo alcoxi de C_{1-4}, y (k) un grupo alquilcarbonilo de C_{1-4}, (3) un grupo anular heteroaromático en donde el grupo anular heteroaromático está sustituido opcionalmente por sustituyentes seleccionados del grupo que consiste de (a) un grupo heterocíclico sustituido opcionalmente por un grupo alquilo de C_{1-4} o un grupo alquilcarbonilo de C_{1-4}, (b) un grupo cicloalquilo de C_{3-7} sustituido opcionalmente por un grupo hidroxilo, un grupo oxo, un átomo de halógeno o un grupo alquilo de C_{1-6}, (c) un grupo carboxi, (d) un átomo de halógeno, (e) un grupo alquilo de C_{1-6}, (f) un grupo haloalquilo de C_{1-4}, (g) un grupo alquilamino de C_{1-4}, (h) un grupo di(alquil de C_{1-4})amino, (i) un grupo

160
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SUPERINDUSTRIA Y COMERCIO
Radicacion : 05116118 00000000 Folios: 1167
Fecha (AMD): 2005-10-28 14:10:01
Tramite : 011 PCT-PATENT 379 FASE NACI 411 PRESENTAC
Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

REQUISITOS NECESARIOS PARA PRESENTACION Y AGILIZACION DEL TRAMITE

	USUARIO	RADICADOR
PATENTE DE INVENCIÓN PCT MODELO DE UTILIDAD	( )	( )
- Indicación de que se solicita la concesión de una patente.	( )	(X)
- Datos de identificación del solicitante o de la persona que se presenta la solicitud.	( )	(X)
- Descripción de la invención.	( )	(X)
- Dibujos de ser estos pertinentes.	( )	(X)
- Comprobante de Pago de las tasas establecidas.		
COMPLETA (X)	INCOMPLETA ( )	( )
DISEÑO INDUSTRIAL ( )		
- Indicación de que se solicita el registro de Diseño Industrial	( )	( )
- Datos de identificación del solicitante o de la persona que presenta	( )	( )
- la solicitud.		
- Representación gráfica o fotográfica del Diseño Industrial o muestra del Material que incorpora el diseño.	( )	( )
Comprobante de pago de las tasas establecidas	( )	( )
COMPLETA ( )	INCOMPLETA ( )	( )
ESQUEMA DE TRAZADO ( )		
- Indicación de que solicita el registro de un Esquema de trazado.	( )	( )
- Datos de identificación del solcitante o de la persona que presenta La solicitud.	( )	( )
Representación gráfica del esquema de trazado	( )	( )
Comprobante de pago de las tasas establecidas.	( )	( )
COMPLETA ( )	INCOMPLETA ( )	( )

Firma Responsable:

Fecha:

REPUBLICA DE COLOMBIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCI

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1160

Bogotá,
2020

Doctor(a)
CASTELLANOS ABONDANO MARGARITA
Apoderado(a) y/o Representante de
JAPAN TOBACCO INC

REFERENCIA	Radicación No.	5 110118
	Solicitud internacional	JP2004/005119
	Fecha inicio fase nacional	09/11/2005
	Trámite	11
	Evento	379
	Actuación	430
	Oficio No.	2651

Como resultado del examen de forma, realizado con fundamento en el artículo 38 de la Decisión 486 de la Comisión de la Comunidad Andina, artículo 27 del Tratado de Cooperación en Materia de Patentes (PCT), regla 51 bis del Reglamento y Circular Única de la Superintendencia de Industria y Comercio, se le comunica que:

1. Si fuere el caso, el solicitante debe adjuntar la traducción de los anexos del reporte de examen preliminar internacional (Art. 36.2.b) del tratado PCT.

En cumplimiento de lo dispuesto por el artículo 39 de la Decisión 486, se le requiere para que dentro del término de dos meses siguientes a la fecha de notificación del presente oficio, complete los requisitos anteriormente enunciados. En caso de no dar cumplimiento al presente requerimiento, la solicitud se considerará abandonada y perderá su prelación.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Unica No.10 de 2001.

ALIX CARMENZA CESPEDES DE VERGEL
Jefe de la división de Nuevas Creaciones

El anterior requerimiento fue notificado por fijación en lista de fecha 09 MAR. 2006
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