05-80439

Libertad y Orden

REPÚBLICA DE COLOMBIA

DIVISIÓN DE PROPIEDAD INDUSTRIAL

PCT

PATENTE DE INVENCIÓN

Industria y Comercio
SUPERINTENDENCIA

05-80439

TITULO: ALCALOIDES DE TERPENO ANTIPARASITARIOS

SOLICITANTE: PFIZER INC.

CLASIFICACION INTERNACIONAL: A61K31/5365
A01N43/90
A61P33/10

DIRECCIÓN 235 East 42nd street, New York, NY 10017 E.U.A.

APODERADO CARLOS R. OLARTE

BOGOTÁ, Agosto 12 2005

OLARTERAISBECK

1

Industria y Comercio
SUPERINTENDENCIA

SUPERINDUSTRIA Y COMERCIO
Radicarion : 05000439 00000000
Fecha (AMD): 2005-08-12 10:30:00 Folios: 525
Tramite : 811 PCT-PATENT 379 FASE NACI 411 PRESENTAC
Perendencia: 2020 DIVISION DE NUEVAS SOLICITUDES

PETITORIO - FORMULARIO ÚNICO DE SOLICITUD
PATENTE PCT
ENTRADA EN FASE NACIONAL

SOLICITUD DE:

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

[ ] Capítulo I. [X] Capítulo II.

SOLICITANTE (71)

Nombre: PFIZER INC
Dirección: 235 East 42nd Street, New York, NY 10017 E.U.A.
Nacionalidad o Domicilio: ESTADOUNIDENSE
Lugar de Constitución: Delaware, Estados Unidos de América.
Teléfono: _____ **Fax:** _____
E-mail: _____

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

REPRESENTANTE O APODERADO

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E-mail: office@olarteraisbeck.com

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

INVENTOR (ES) (72)

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Nacionalidad o Domicilio: VER PAGINA ADJUNTA. folio 3

PCT (86)

Solicitud Internacional No. PCT/IB2004/000320 Fecha Febrero 3, 2004

Publicación Internacional No. WO 2004/072086 Fecha Agosto 26, 2004

Título (54) ALCALOIDES DE TERPENO ANTIPARASITARIOS

Clasificación Internacional (51) C07D 498/04 A61K31/5365 A61P33/10 A01N43/90

Prioridad SI [X] NO [ ]

(33) País de Origen	(32) Fecha	(31) Número de Solicitud
GB	Febrero 14, 2003	0303439.4

Comprobante de pago No. 60.519 **Fecha** Agosto 12, 2005

10 **ANEXOS**

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

11 **FIGURA CARACTERÍSTICA:**

12 Solicito la concesión de la patente,

NOMBRE: CARLOS R. OLARTE FIRMA:

C.C. 79.782.747 Btá T.P. 74.295

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

3

LISTA DE INVENTORES PCT/IB2004/000320

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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

RECIBO OFICIAL DE CAJA : 05 - 60.519
FECHA : AGOSTO 12 DE 2005

[illegible] RIA Y COMERCIO
Radicación : [illegible]
Fecha [illegible]: [illegible]
Tramite : [illegible]
Dependencia: [illegible]

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

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
OLARTE RAISBEGR	CONSIGNACION	BANCO POPULAR	050-00110-6	36579839	11/08/2005	4.518.000.00

C O N C E P T O

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01 SOLICITUDES	1 TRAMITES DE SOL. DE PATENTE DE IN	443.000.00
		TOTAL : $	443.000.00

SON: CUATROCIENTOS CUARENTA Y TRES MIL PESOS

RESPONSABLE : _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No._____

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

5

APOSTILLA EN PODER DE REPRESENTACIÓN DE

PFIZER INC.

Bilingüe inglés- español otorgado en Nueva York, Estados Unidos el 14 de julio de 2003 y firmado por J. Trevor Lumb, Vicepresidente de Pfizer Products Inc.

CERTIFICACION NOTARIAL

Bilingüe inglés- español, el 14 de julio de 2003 el suscrito notario Kenneth Greenwood certifica que J. Trevor Lumb, domiciliado en Nueva York ejercía funciones de Asistente General Consejero de Patentes la Compañía Pfizer Inc., con sede en Nueva York, Nueva York, Estados Unidos.

Firma del notario: Kenneth Greenwood

Sello notarial: certificado, verificado y autenticado en la Localidad de Egham en Surrey, 14 julio, 2003 por el Notario Kenneth Greenwood-Horne Engall & Freeman

Sello Notario Público en alto relieve rojo.

APOSTILLA

REINO UNIDO DE GRAN BRETAÑA E IRLANDA DEL NORTE

1. País :Reino Unido de Gran Bretaña e Irlanda del Norte
   Este documento Público
2. ha sido firmado por K. Greenwood
3. ejerce funciones de Notario Público
4. Lleva el sello de dicho Notario Público

CERTIFICADÓ

5. En Londres 6. El 17 de julio de 2003
7. Por el Secretario de Estado Principal de su Majestad [illegible] exteriores y de la mancomunidad
8. No. G210434
9. Sello del Secretario de Estado Principal de su Majestad para Asuntos exteriores y de la mancomunidad
10. Firma de R. Bawden - Por Secretario de Estado

Si el documento se usa en un país que no es parte de la convención de la Haya del 5 de octubre 1961, debe presentarse en sección consular de la misión que representa el país.

Es traducción fiel del inglés, con copia archivo para confrontación. Bogotá 25 de julio-2003. Marlen Neira C

MARLEN NEIRA CASTRO
Traductor e Intérprete Oficial
Inglés - Español - Inglés
Resolución No. 2117 del 7 Oct 1987

OLARTERAISBECK

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6

Power of Attorney

The undersigned,

Pfizer Inc.

domiciled in

235 East 42nd Street, New York, NY 10017 USA

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

Poder

El suscrito,

Pfizer Inc.

domiciliado en

235 East 42nd Street, New York, NY 10017 USA

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

Signature/Firma: _____

Date/Fecha: July 14, 2003

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

OLARTERAISBECK

OLARTE RAISBECK & FRIERI, LTDA.
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X

Notarial Certification

On this date,
July 14, 2003
The undersigned Notary Public certifies:

1. That J. Trevor Lumb
of legal age and domiciled in New York, USA
signed the foregoing document.

2. That the grantor has executed the foregoing document as Assistant General Patent Counsel of Pfizer Inc.

3. That Pfizer Inc.,
having its principal place of business located in New York, New York, U.S.A.
is duly incorporated, is currently in existence, and that the purposes for which the Power of Attorney is granted are within the scope of its corporate purposes.

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

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

Certificación Notarial

En esta fecha,

el Notario Público suscrito certifica:

1. Que
J. Trevor Lumb
mayor de edad y domiciliado
New York
suscribió el documento que antecede.

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

4. Que
con sede principal ubicada en

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

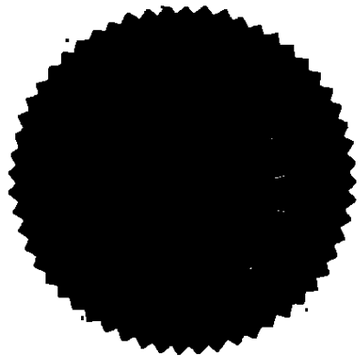
4. Que el otorgante tiene la representación para suscribir el poder, y que ésta es legítima.

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

NOTARY PUBLIC (Signature):

EXECUTION
Certified Verified and Authenticated
In The Town Of Egham In Surrey
This 14th Day Of July 2003

KENNETH GREENWOOD
NOTARY PUBLIC
HORNE ENGALL AND FREEMAN



APOSTILLE
(Hague Convention of 5 October 1961 / Convention de La Haye du 5 octobre 1961)

UNITED KINGDOM OF GREAT BRITAIN AND NORTHERN IRELAND

1. Country: United Kingdom of Great Britain and Northern Ireland
   Pays: Royaume-Uni de Grande-Bretagne et d'Irlande du Nord

   This public document / Le présent acte public

2. Has been signed by — K Greenwood
   a été signé par

3. Acting in the capacity of — Notary Public
   agissant en qualité de

4. Bears the seal/stamp of — The Said Notary Public
   est revêtu du sceau/timbre de

   Certified/Attesté
5. at London/à Londres — 6. the/le 17 July 2003

7. by Her Majesty's Principal Secretary of State for Foreign and Commonwealth Affairs /
   par le Secrétaire d'Etat Principal de Sa Majesté aux Affaires Etrangères et du Commonwealth.

8. Number/sous No — **G210434**

9. Stamp:
   timbre:

10. Signature: R. Bawden

For the Secretary of State / Pour le Secrétaire d'Etat

If this document is to be used in a country which is not party to the Hague Convention of 5 October 1961, it should be presented to the consular section of the mission representing that country.

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

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

To:

WOOD, David, J.
Pfizer Limited
Ramsgate Road
Sandwich
Kent, CT13 9NJ
ROYAUME-UNI

Date of mailing *(day/month/year)* 07 October 2004 (07.10.2004)	
Applicant's or agent's file reference PC10339A	**IMPORTANT NOTICE**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB2004/000320	03 February 2004 (03.02.2004)	14 February 2003 (14.02.2003)

Applicant
PFIZER LIMITED et al

The International Bureau transmits herewith the following documents:

☐ copy of the international application as published by the International Bureau on under No. WO

☑ copy of international application as republished by the International Bureau on 07 October 2004 (07.10.2004) under No. WO 2004/072086
For an explanation as to the reason for this republication of the international application, reference is made to INID codes (15), (48) or (88) (*as the case may be*) on the front page of the attached document.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Gabriele Bähr
Facsimile No.+41 22 740 14 35	Facsimile No.+41 22 338 70 60

Form PCT/IB/311 (January 2004)

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
26 August 2004 (26.08.2004)

PCT

(10) International Publication Number
WO 2004/072086 A3

(51) International Patent Classification[7]: C07D 498/04, A61K 31/5365, A01N 43/90, A61P 33/10

(21) International Application Number: PCT/IB2004/000320

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(30) Priority Data:
0303439.4 14 February 2003 (14.02.2003) GB

(71) Applicant (*for GB only*): PFIZER LIMITED [GB/GB]; Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(71) Applicant (*for all designated States except GB, US*): PFIZER INC. [US/US]; 235 East 42nd Street, New York, NY 10017 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): CHUBB, Nathan, Anthony, Logan [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). CRITCHER, Douglas, James [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). ESHELBY, James, John [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). LUNN, Graham [GB/GB]; Pfizer Global Research and Development, Sandwich, Kent CT13 9NJ (GB). RUDGE, Andrew, John [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). WALSHE, Nigel, Derek [IE/GB]; Pfizer Global Research and Development, Sandwich, Kent CT13 9NJ (GB). WIEDENAU, Paul, Heinrich [DE/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB). WILLIAMS, David, Howard [GB/GB]; Pfizer Global Research and Development, Ramsgate Road, Sandwich, Kent CT13 9NJ (GB).

(74) Agents: WOOD, David, J. et al.; Pfizer Limited, Ramsgate Road, Sandwich, Kent, CT13 9NJ (GB).

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

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

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

(88) Date of publication of the international search report:
7 October 2004

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

WO 2004/072086 A3

(54) Title: ANTIPARASITIC TERPENE ALKALOIDS

(57) Abstract: The present invention relates to novel terpene alkaloids and their use as antiparasitic agents. The present invention also relates to an antiparasitic agent which comprises a terpene alkaloid compound of this invention as an effective ingredient in an antiparasitic formulation. More particularly, the present invention relates to derivatives of the terpene alkaloid (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate. Pharmaceutical compositions comprising the same are also disclosed.

INTERNATI NAL SEARCH REPORT

In ional Application No
PCT/IB2004/000320

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D498/04 A61K31/5365 A01N43/90 A61P33/10

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D

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

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95/19363 A (BISHOP BERNARD F ;PFIZER PHARMA (JP); YAMAUCHI YUJI (JP); KOJIMA N) 20 July 1995 (1995-07-20) cited in the application the whole document	1-14
A	GB 2 240 100 A (PFIZER LTD) 24 July 1991 (1991-07-24) cited in the application the whole document	1-14

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

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 July 2004	[illegible] 2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Grassi, D

Form PCT/ISA/210 (second sheet) (January 2004)

INTERNATI NAL SEARCH REPORT

International application No.
PCT/IB2004/000320

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

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

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

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

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claim: 1(part)

R2 is alkyl.

2. claim: 1(part)

R2 is unsubstituted alkenyl.

3. claim: 1(part)

R2 is substituted alkenyl.

4. claim: 1(part)

R2 is a 5- or 6-membered heterocycle.

INTERNATI NAL SEARCH REPORT

International Application No
PCT/IB2004/000320

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9519363	A	20-07-1995	AT	173264 T	15-11-1998
			AU	684334 B2	11-12-1997
			AU	1424895 A	01-08-1995
			CA	2181168 A1	20-07-1995
			DE	69505946 D1	17-12-1998
			DE	69505946 T2	15-04-1999
			DK	739344 T3	26-07-1999
			EP	0739344 A1	30-10-1996
			ES	2123948 T3	16-01-1999
			WO	9519363 A1	20-07-1995
			JP	2767161 B2	18-06-1998
			JP	9500909 T	28-01-1997
			NZ	278143 A	24-11-1997
			US	5801023 A	01-09-1998
GB 2240100	A	24-07-1991	NONE		

PATENT COOPERATION TREATY

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

To:

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PFIZER LIMITED et al

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(54) Title: ANTIPARASITIC TERPENE ALKALOIDS

(57) Abstract: The present invention relates to novel terpene alkaloids and their use as antiparasitic agents. The present invention also relates to an antiparasitic agent which comprises a terpene alkaloid compound of this invention as an effective ingredient in an antiparasitic formulation. More particularly, the present invention relates to derivatives of the terpene alkaloid (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate. Pharmaceutical compositions comprising the same are also disclosed.

ANTIPARASITIC TERPENE ALKALOIDS

Technical Field

The present invention relates to novel terpene alkaloids and their use as antiparasitic agents. The present invention also relates to an antiparasitic treatment which comprises a terpene alkaloid compound of this invention as an effective ingredient in an antiparasitic formulation.

More particularly, the present invention relates to derivatives of the terpene alkaloid (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate. Processes for producing these compounds and pharmaceutical compositions comprising the same are also disclosed.

A further aspect of the invention is a novel binding assay which is used to assess the potential antiparasitic activity of these compounds by measuring how tightly they bind to membranes purified from parasite homogenates. The affinity is calculated according to how readily the compounds of the present invention displace a radiolabeled, reduced analogue of (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate from these membranes.

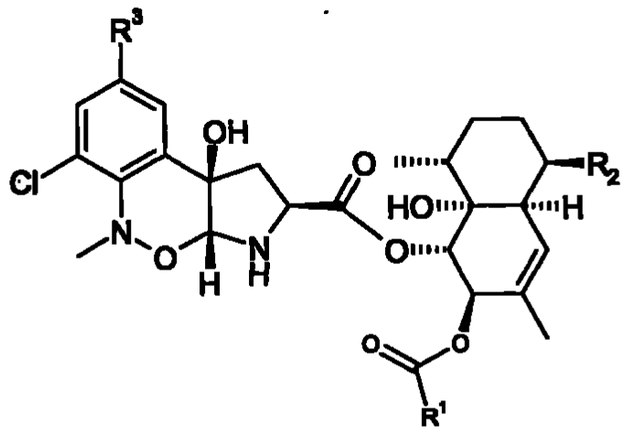
Certain terpene alkaloids, including (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate which can be isolated from the fermentation broths of certain microorganisms, are known to possess anthelmintic, ectoparasiticidal and insecticidal activity with utility in animal and human health, agriculture and horticulture (See WO 95/19363 and UK 2240100 respectively).

However, when administered to infected animals, their in vivo potencies were found to be too low as to preclude commercial development.

Surprisingly, we have found certain terpene alkaloid derivatives possess good in vivo activity and thus are effective as antiparasitic agents in animals. The present invention thus provides compounds that are effective as antiparasitic agents for use in animals and humans.

The compounds of the present invention may be formed by synthetic modification of (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate. The compounds of the invention show activity against insects, pests, acari, free living nematodes and endo- and ecto-parasites afflicting animals.

The present invention provides a compound of formula (I):



(I)

or a pharmaceutically or veterinarily acceptable salt or solvate thereof, wherein

R^1 is H, C_1-C_6 alkyl, C_2-C_6 haloalkyl, C_3-C_8 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, aryl or -OR^4, said C_1-C_6 alkyl, C_3-C_8 cycloalkyl and aryl being optionally substituted by one or more substituents selected from $COOR^{13}$, -$OCOR^{12}$, -$OCOOR^{13}$ and -$OCONR^{12}R^{12}$ and said C_2-C_6 alkenyl and C_2-C_6 alkynyl being optionally substituted by one or more halo;

R^2 is C_1-C_6 alkyl, C_2-C_6 alkenyl, or a 5- or 6-membered aromatic or non-aromatic heterocycle containing one or more atoms selected from N, O and S, said C_1-C_6 alkyl being optionally substituted by one or more substituents selected from
-NR^5R^6, -$CONR^5R^6$, -OR^{12}, -$OCOR^{12}$, -$OCOOR^{12}$, -$OCONR^{12}R^{14}$, =NOR^7 and halo, said C_2-C_6 alkenyl being optionally substituted by one or more substituents selected from halo and -$COOR^{13}$ and said 5- or 6-membered aromatic heterocycle containing one or more atoms selected from N, O and S being optionally substituted by one or more substituents selected from C_1-C_6 alkyl and aryl;

R^3 is H, halo, aryl, C_2-C_6 alkenyl, C_2-C_7 alkanoyl, or a 5- or 6-membered aromatic heterocycle containing one or more atoms selected from N, O and S;

R^4 is C_1-C_2 alkyl, C_2-C_6 alkenyl or C_2-C_6 alkynyl, each optionally substituted by one or more halo, or -$OC(O)OR^a$ where R^a is C_1-C_6 alkyl;

R^5 and R^6

either, when taken together with the nitrogen atom to which they are attached, represent a saturated, partially unsaturated or aromatic, mono-, bi- or tricyclic heterocycle of up to 16 atoms optionally containing 1 or more additional heteroatoms selected from O, N and S, said heterocycle being optionally fused to a benzene or pyridyl ring and optionally substituted (including the optional benzene or pyridyl ring) by one or more R^8 and optionally substituted (including the optional benzene or pyridyl ring) on any aromatic ring thereof by -$NR^{15}R^{16}$, with the proviso that the heterocycle may not contain an -NH- group;

or

R^5 and R^6 are each independently selected from H, C_1-C_8 alkyl, C_3-C_8 cycloalkyl, -CO-(C_3-C_8)cycloalkyl, $-COR^{10}$, C_2-C_7 alkanoyl, aryl, $-OR^{13}$, $-COOR^{13}$, $-CONR^{12}R^{12}$ or $-SO_2R^{13}$, said C_2-C_7 alkanoyl being optionally substituted by OR^{13} or halo, said C_1-C_8 alkyl and C_3-C_8 cycloalkyl being optionally substituted by one or more R^8 and said C_3-C_8 cycloalkyl being optionally fused to a saturated or unsaturated ring of from 5 to 6 atoms, optionally containing one or more O, N or S atoms, said fused ring being optionally substituted by one or more C_1-C_8 alkyl with the proviso that when R^5 is H or $-CH_3$, R^6 is not C_1-C_8 alkyl;

R^7 is C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl or aryl, said alkyl being optionally substituted by aryl;

R^8 is C_1-C_8 alkyl, C_3-C_8 cycloalkyl, R^9, R^{10}, $-OR^9$, $-OR^{10}$, COR^9, COR^{10}, -O-(C_1-C_8 alkyl)-R^{10}, C_2-C_8 alkenyl, $-OR^{13}$, $-SR^9$, $-SR^{10}$, $-SO_2R^{10}$, $-OCOR^{12}$, $-OCOOR^{12}$, $-OCONR^{12}R^{13}$, $-CONR^{12}OR^{13}$, $-CONR^{12}R^{13}$, $-NR^{12}COR^{12}$, $-NR^{12}COOR^{12}$, $-NR^{12}CONR^{12}R^{12}$, $-COOR^{13}$, $-COR^{12}$, oxo or halo, said C_3-C_8 cycloalkyl being optionally substituted by aryl, said C_1-C_8 alkyl being optionally substituted by one or more subetituents selected from C_3-C_8 cycloalkyl, R^9, R^{10}, $-OR^{10}$, $-OR^{13}$, $-SR^9$, $-SR^{11}$, $-OCOR^{12}$, $-OCOOR^{12}$, $-OCONR^{12}R^{12}$, $-NR^{12}COR^{12}$, $-NR^{12}COOR^{12}$, $-NR^{12}CONR^{12}R^{12}$, $-COR^{12}$ or halo, and said C_2-C_8 alkenyl being optionally substituted by one or more substituents selected from halo or aryl;

R^9 is

(a) a 5- or 6-membered aromatic heterocycle containing one or more atom(s) selected from N, O and S and optionally fused to a benzene ring, said aromatic heterocycle being optionally substituted (including on the optional benzene ring) by one or more subetituents selected from C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_3-C_8 cycloalkyl, $-OR^{13}$, $-NR^{12}R^{12}$, $-CO_2R^{13}$, cyano and halo, or

(b) a 4- to 8-membered saturated heterocycle containing one or more atoms selected from O and S and optionally fused to a benzene ring, said saturated heterocycle being optionally substituted (including on the optional benzene ring) by one or more substituents selected from C_1-C_6 alkyl and C_3-C_8 cycloalkyl;

R^{10} is aryl optionally substituted by one or more substituents selected from C_1-C_6 alkyl, C_1-C_6 haloalkyl, $-OR^{13}$, $-NR^{12}R^{12}$, $-CO_2R^{13}$, cyano or halo and optionally fused to a saturated or unsaturated ring of 5 or 6 atoms, optionally containing one or more O, N or S atoms, said fused ring being optionally substituted by one or more C_1-C_6 alkyl;

R^{11} is H, C_1-C_6 alkyl or C_3-C_8 cycloalkyl;

each R^{12} is independently H, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl or aryl, said C_1-C_6 alkyl being optionally substituted by aryl;

each R^{13} is independently C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl or aryl, said C_1-C_6 alkyl being optionally substituted by aryl;

R^{14} is C_1-C_6 alkyl, C_3-C_8 cycloalkyl or aryl, said C_1-C_6 alkyl each optionally substituted by aryl or -NHaryl;

R^{15} and R^{16} are either each independently selected from H, C_1-C_6 alkyl and C_3-C_8 cycloalkyl or, when taken together with the nitrogen atom to which they are attached, represent a 3- to 8-membered ring optionally containing one or more additional heteroatoms selected from O and S; and

'aryl' means phenyl or naphthyl;

with the proviso that when R^3 is H and R^1 is methyl, R^2 is not isopropenyl.

A preferred group of compounds of formula (I) is that wherein:

R^1 is C_1-C_8 alkyl, C_1-C_4 alkenyl, C_1-C_4 alkynyl, OC_1-C_8 alkyl, OC_1-C_4 alkenyl or OC_1-C_4 alkynyl; and

R^2 is a thiazole ring optionally substituted with C_1 to C_4 alkyl; a piperazine ring optionally substituted with C_1 to C_4 alkyl; an isopropenyl group optionally substituted by halo; or an isopropyl group optionally substituted by one or more halo; NR^7R^8 wherein R^7 and R^8 may be taken together to represent a ring of up to 7 atoms optionally containing oxygen or may be independently selected from H or C_1 to C_4 cycloalkyl; $=NOR^{17}$ wherein R^{17} may be selected from C_1 to C_8, C_1 to C_4 alkynyl or C_1 to C_4 alkenyl;

A more preferred group of compounds of formula (I) is that in which:

R^1 is $-CH_3$, -O-allyl or –O-propargyl;

R^2 is 2-ethylthiazol-4-yl, isopropyl, piperazinyl, 1,2-difluoropropen-2-yl, 1-oxoprop-2-yl methyl oxime, 1-oxoprop-2-yl propargyl oxime, 1-oxoprop-2-yl allyl oxime, 1-N-morpholinoprop-2-yl, 1-fluoroprop-2-yl, 1,1-difluoroprop-2-yl;

R^3 , R^4 and R^5 are H;

Particularly preferred individual compounds of the invention include compounds of formula (I) where R^3 , R^4 , and R^5 all are H, and R^1 and R^2 are as indicated below:

R1 =	R2 =
CH_3	2-Ethylthiazol-4-yl, isopropyl
CH_3	1,2-difluoropropen-2-yl
CH_3	1-oxoprop-2-yl methyl oxime
CH_3	1-oxoprop-2-yl propargyl oxime

CH_3	1-oxoprop-2-yl allyl oxime
CH_3	isopropyl
CH_3	1-N-morpholinoprop-2-yl
CH_3	1-fluoroprop-2-yl
CH_3	1,1-difluoroprop-2-yl
CH_3	piperazin-1-yl (optionally 4-substituted with C_1-C_6 alkyl, phenyl, benzyl each of which groups may optionally be halo-substituted by up to 3 halo atoms
Opropargyl	isopropenyl
Opropargyl	isopropyl
Oallyl	isopropyl

In the above definition, halo means fluoro, chloro, bromo or iodo.

The compounds of formula (I) may contain one or more chiral centres and therefore can exist as stereoisomers, i.e. as enantiomers or diastereoisomers, as well as mixtures thereof. The invention includes both the individual stereoisomers of the compounds of formula (I) together with mixtures thereof. Separation of diastereoisomers may be achieved by conventional techniques, e.g. by fractional crystallisation or chromatography (including HPLC) of a diastereoisomeric mixture of a compound of formula (I) or a suitable salt or derivative thereof. An individual enantiomer of a compound of formula (I) may be prepared from a corresponding optically pure intermediate or by resolution, either by HPLC of the racemate using a suitable chiral support or, where appropriate, by fractional crystallisation of the diastereoisomeric salts formed by reaction of the racemate with a suitable optically active acid.

Also included in the invention are radiolabelled derivatives of compounds of formula (I) which are suitable for biological studies.

The pharmaceutically, veterinarily and agriculturally acceptable salts of the compounds of formula (I) are, for example, non-toxic acid addition salts formed with inorganic acids such as hydrochloric, hydrobromic, sulphuric and phosphoric acid, with organo-carboxylic acids, or with organo-sulphonic acids. For a review of suitable salts, see J. Pharm. Sci., 1977, 66, 1.

In a further aspect, the present invention provides processes for the preparation of a compound of formula (I), or a pharmaceutically, veterinarily or agriculturally acceptable salt thereof, or a pharmaceutically, veterinarily or agriculturally acceptable solvate (including hydrate) of either entity, as illustrated below.

It will be appreciated by persons skilled in the art that, within certain of the processes described, the order of the synthetic steps employed may be varied and will depend inter alia on factors such as the nature of other functional groups present in a particular substrate, the availability of key intermediates, and the protecting group strategy (if any) to be adopted. Clearly, such factors will also influence the choice of reagent for use in the said synthetic steps. It will also be appreciated that various standard substituent or functional group interconversions and transformations within certain compounds of formula (I) will provide other compounds of formula (I).

Regarding the use of the compounds of the invention in humans, there is provided:

a pharmaceutical parasiticidal composition comprising a compound of formula (I), or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of either entity, together with a pharmaceutically acceptable diluent or carrier, which may be adapted for topical administration;

a compound of formula (I), or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of either entity, or a pharmaceutical composition containing any of the foregoing, for use as a medicament;

the use of a compound of formula (I), or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of either entity, or a pharmaceutical composition containing any of the foregoing, for the manufacture of a medicament for the treatment of a parasitic infestation;

and a method of treating a parasitic infestation in a human being which comprises treating said human being with an effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of either entity, or a pharmaceutical composition containing any of the foregoing.

With respect to their use in non-human animals, the compounds of the present invention may be administered alone or in a formulation appropriate to the specific use envisaged, the particular species of host animal being treated and the parasite involved. The methods by which the compounds may be administered include oral administration by capsule, bolus, tablet or drench, topical administration as a pour-on, spot-on, dip, spray, mousse, shampoo or powder formulation or, alternatively, they can be administered by injection (e.g. subcutaneously, intramuscularly or intravenously), or as an implant.

Such formulations are prepared in a conventional manner in accordance with standard veterinary practice. Thus capsules, boluses or tablets may be prepared by mixing the active ingredient with a suitable finely divided diluent or carrier additionally containing a disintegrating agent and/or binder such as starch, lactose, talc or magnesium stearate, etc. Oral drenches are prepared by dissolving or suspending the active ingredient in a suitable medium. Pour-on or spot-on formulations may be prepared by dissolving the active ingredient in an acceptable liquid carrier vehicle such as butyl digol, liquid paraffin or a non-volatile ester, optionally with the addition of a volatile component such as propan-2-ol. Alternatively, pour-on, spot-on or spray formulations can be prepared by encapsulation, to leave a residue of active agent on the surface of the animal. Injectable formulations may be prepared

in the form of a sterile solution which may contain other substances, for example enough salts or glucose to make the solution isotonic with blood. Acceptable liquid carriers include vegetable oils such as sesame oil, glycerides such as triacetin, esters such as benzyl benzoate, isopropyl myristate and fatty acid derivatives of propylene glycol, as well as organic solvents such as pyrrolidin-2-one and glycerol formal. The formulations are prepared by dissolving or suspending the active ingredient in the liquid carrier such that the final formulation contains from 0.01 to 10% by weight of the active ingredient.

These formulations will vary with regard to the weight of active compound contained therein, depending on the species of host animal to be treated, the severity and type of infection and the body weight of the host. For parenteral, topical and oral administration, typical dose ranges of the active ingredient are 0.01 to100 mg per kg of body weight of the animal. Preferably the range is 0.1 to 10mg per kg.

As an alternative the compounds may be administered with the animal feedstuff and for this purpose a concentrated feed additive or premix may be prepared for mixing with the normal animal feed.

The compounds of the invention are highly active antiparasitic agents having particular utility as anthelmintics, ectoparasiticides, insecticides and acaricides.

Thus the compounds are effective in treating a variety of conditions caused by endoparasites including, in particular, helminthiasis which is most frequently caused by a group of parasitic worms described as nematodes and which can cause severe economic losses in swine, sheep, horses and cattle as well as affecting domestic animals and poultry. The compounds are also effective against other nematodes which affect various species of animals including, for example, Dirofilaria in dogs and various parasites which can infect humans including gastro-intestinal parasites such as Ancylostoma, Necator, Ascaris, Strongyloides, Trichinella, Capillaria, Trichuris, Enterobius and parasites

which are found in the blood or other tissues and organs such as filarial worms and the extra intestinal stages of Strongyloides and Trichinella.

The compounds are also of value in treating ectoparasite infections including in particular arthropod ectoparasites of animals and birds such as ticks, mites, lice, fleas, blowfly, biting insects and migrating dipterous larvae which can affect cattle and horses.

The compounds are also insecticides active against household pests such as cockroach, clothes moth, carpet beetle and the housefly as well as being useful against insect pests of stored grain and of agricultural plants such as spider mites, aphids, caterpillars and migratory orthopterans such as locusts.

Therefore, according to a further aspect of the invention, there is provided a veterinary or agricultural formulation comprising a compound of formula (I), or a veterinarily or agriculturally acceptable salt thereof, or a veterinarily or agriculturally acceptable solvate of either entity, together with a veterinarily or agriculturally acceptable diluent or carrier. Preferably, the formulation is adapted for topical administration.

The invention further provides a compound of formula (I), or a veterinarily or agriculturally acceptable salt thereof, or a veterinarily or agriculturally acceptable solvate of either entity, or a veterinarily or agriculturally acceptable formulation containing any of the foregoing, for use as a parasiticide.

It also provides a method of treating a parasitic infestation at a locus, which comprises treatment of the locus with an effective amount of a compound of formula (I), or a veterinarily or agriculturally acceptable salt thereof, or a veterinarily or agriculturally acceptable solvate of either entity, or a veterinarily or agriculturally acceptable formulation containing any of the foregoing.

Preferably, the locus is the intestine, skin or fur of an animal.

It is to be appreciated that reference to treatment includes prophylaxis as well as the alleviation and/or cure of established symptoms of a parasitic infection. Treatment thus also includes palliative care.

Compound evaluation

The *in vitro* assay for measurement of compounds which displace ^{3}H-dihydro-(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate from fly head P_2 membranes represents another aspect of the invention and was performed as follows.

Novel antiparasitic compounds can be identified rapidly using a radiometric assay that measures the displacement of ^{3}H-dihydro-(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate from fly head P_2 membranes. This assay can be used to measure KI values and thereby identify structure activity relationships. It can also be used as a high throughput screen (testing synthetic small molecules or natural products generated by microorganism fermentation) to identify novel chemical entities with antiparasitic activity.

To prepare fly head P_2 membranes, *Lucilia sericata* pupae (or any other insect pest) are hatched in an insectory and snap frozen in liquid nitrogen. The flies are shaken in a sieve and tray unit to separate the bodies from the heads/wings/legs. A smaller diameter sieve then separates the heads from wings and legs. The sieve diameters are dependent on the size of the flies being harvested. The fly heads are then used to prepare the P_2 membrane.

The fly head membrane is prepared in buffer consisting of 50mM HEPES pH7.4, containing a cocktail of protease inhibitors (Boehringer Mannheim

Complete®). All steps are carried out on ice or at 4°C. The fly heads are homogenised in 5-10 volumes of buffer at 30 000 rpm using a Polytron homogeniser. The homogenate is then spun in a centrifuge at 1000 x g for 10 minutes and the supernatent filtered through gauze. The filtered supernatent is then spun at 20 000 x g for 1 hour and the P_2 membrane pellet resuspended in buffer and stored in aliquots at –80°C.

To measure binding of ^{3}H-dihydro-(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate to the fly head P_2 membranes, 400µl of protein at a concentration of 0.5mg/ml, is added to a deep well plate, containing ^{3}H-dihydro-CJ-12662 giving a final concentration of 1nM of the radioactive ligand. Control wells also contain either buffer or $5x10^{-6}$M (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (final concentration). Other wells contain the compound of interest serially diluted in 5 fold dilutions from $5x10^{-6}$M. For a high throughput screen, compounds are added at one concentration only to allow rapid screening of large numbers of compounds. The assay plate is incubated at 30°C for 90 minutes. The plate is then harvested onto glass fibre filters (pre-soaked in 0.5% Triton X-100) on a filtration manifold and rapidly washed under vacuum with 5 x 1ml washes of 50mM HEPES containing 0.25% Triton X-100. After drying, the radioactivity bound to the filters is measured using melted solid scintillant in a scintillation counter. Serially diluted wells are plotted as binding (counts per minute) vs. $\log_{10}$ (competitor concentration) and KI values (Kd=7nM) calculated and compared to (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate. In a high throughput screen, compounds showing ≥70% inhibition of ^{3}H-dihydro-

(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate binding are active.

Instruments used to acquire characterising data

Nuclear magnetic resonance (NMR) spectral data were obtained using Varian Inova 300, Varian Inova 400, Varian Unityplus 400, Bruker AC 300 MHz, Bruker AM 250 MHz, or Varian T60 MHz spectrometers, the observed chemical shifts (δ) being consistent with the proposed structures. Mass spectral (MS) data were obtained on a Finnigan Masslab Navigator, a Fisons Instruments Trio 1000, or a Hewlett Packard GCMS system model 5971 spectrometer. The calculated and observed ions quoted refer to the isotopic composition of lowest mass. HPLC means high performance liquid chromatography. Room temperature means 20 to 25°C.

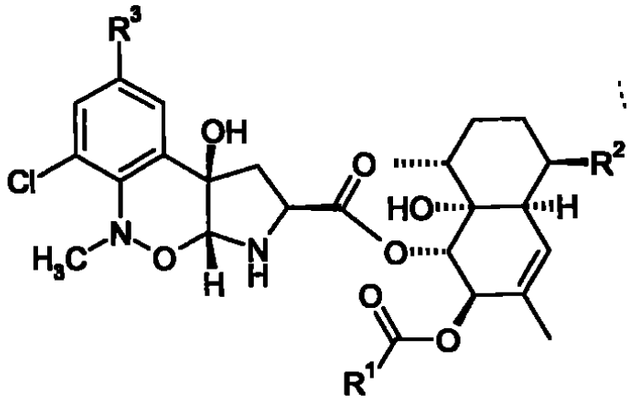
Salt preparations

Wherever applicable the hydrochloride salt can be prepared by dissolving the product in a mixture of methanol : ether (1:5) and adding hydrogen chloride (1 M solution in diethyl ether, 2 eq.). The mixture is concentrated *in vacuo* to give the hydrochloride salt.

Similarly, other salts such as trifluoroacetic acid salts and acetic acid salts can be prepared by dissolving the product in a suitable solvent such as ethyl acetate or methanol and adding the corresponding acid (2 eq). The reaction mixture can then be concentrated *in vacuo* to give the desired salt.

Stereochemistry

All stereoisomers of R^2 are within the scope of this invention, except where specifically described. The R^2 substituent may include single diastereomers as well as mixtures of stereoisomers.



Generic Procedures

Generic Process A

Methanol (3 ml) was added to the corresponding amine (0.39 mmol, 1.5 equiv.), which was placed in a Stem® Reaction Block. In those cases where the amine was an ammonium salt, triethylamine (55□l, 0.4 mmol) was added. A solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl)(2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 200mg, 0.26 mmol) in methanol (2 ml, analytical grade) was added, and the reaction mixtures were stoppered with a rubber septum and stirred for 5 hours at ambient temperature. Borohydride on Amberlite® IRA400 (200mg, 0.5 mmol) was added and the mixture stirred at room temperature for 18 h. The reaction mixture was then filtered through a filter cartridge (Isolute™, 6 ml), the residue washed with methanol (2 ml), and the filtrate concentrated under a stream of nitrogen. To the resulting crude product was added hydrogen chloride (4 N solution in dioxane, 2 ml), the mixture was agitated on an orbital shaker for 10 min, transferred to a hot plate (50 °C) and concentrated under a stream of nitrogen for 40 min. Triethylamine (20% v/v in dichloromethane, 2 ml) was added and the mixture was concentrated under a stream of nitrogen, followed by addition and evaporation of triethylamine (20% v/v in dichloromethane, 2ml). The crude reaction product was then dissolved in a acetonitrile :

dimethylsulfoxide (4:1, 1 ml) and purified by automated preparative liquid chromatography (Gilson system, 10 x 150 mm Phenomenex Magellen C18 5□ column) using a 0.1% aqueous trifluoroacetic acid : acetonitrile gradient (95:5 to 5:95). Evaporation of the eluant in a Genevac system gave the final product.

Generic Process B

To the corresponding amine (0.33 mmol, 1.5 equiv.) was added a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 170 mg, 0.22 mmol) in dichloromethane (2 ml). In those cases where the amine was an ammonium salt, triethylamine (55□l, 0.4 mmol) was added. Sodium triacetoxyborohydride (93 mg, 0.44 mmol) was added to the reaction, and the mixture was stirred in a Stem® reaction block for 18 h. The mixture was then diluted with dichloromethane (4 ml) and water (2 ml) and stirred vigorously for 20 min. The layers were separated by means of a filter cartridge with a hydrophobic frit (Whatman 12 ml 1PS filter media), and the organic filtrate concentrated under a stream of nitrogen. To the resulting crude product was added hydrogen chloride (4 N solution in dioxane, 2 ml), the mixture was agitated on an orbital shaker for 10 min, transferred to a hot plate (50 °C) and concentrated under a stream of nitrogen for 40 min. Triethylamine (20% v/v in dichloromethane, 2 ml) was added and the mixture concentrated under a stream of nitrogen, followed by addition and evaporation of further triethylamine (20% v/v in dichloromethane, 2 ml). The crude reaction product was then dissolved in a acetonitrile : dimethylsulfoxide mixture (4:1, 1 ml) and purified by automated preparative liquid chromatography (Gilson system, 10 x 150 mm Phenomenex Magellen C18 5□ column) using a 0.1% aqueous trifluoroacetic acid : acetonitrile gradient (95:5 to 5:95). Evaporation of the eluant in a Genevac system gave the final product.

Generic Process C

A solution of (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 141, 21 mg, 0.0375 mmol), the amine (0.1 mmol), tetramethylammonium triacetoxyborohydride (26 mg, 0.1 mmol), triethylamine (20 □l, 0.15 mmol) in 1-methyl-2-pyrrolidinone (0.9 ml) was shaken at ambient temperature for 18 h. The reaction mixture was then directly injected onto the HPLC column for purification using a 0.1% aqueous trifluoroacetic acid : acetonitrile gradient (95:5 to 5:95). The purified product was obtained after evaporation of the solvents in a Genevac system.

Autopurification was carried out using a Gilson HPLC system using a Phenomenex Magellen® 150mm x 10mm 5□ ODS column at ambient temperature. Elution was by gradient formed from 0.1% aqueous trifluoroacetic acid : acetonitrile (95:5 to 5 : 95) over 12 min. The products were detected by UV at 215nm. All fractions from autopurification were analysed by loop injection into a Micromass "Platform LC"® single-quadrupole mass spectrometer with APCI probe.

Generic Process D

To a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 200 mg, 0.26 mmol) in methanol (5 ml) was added the corresponding primary amine (0.52 mmol, 2 equiv.). Triethylamine (80 □l, 0.58 mmol) was added in those cases where the amine was an ammonium salt. The reaction mixture was stirred for 18 hours at ambient temperature in a Stem® reaction block. Then borohydride

on Amberlite® IRA400 (Aldrich, 2.5 mmol/g resin, 150 mg, 0.38 mmol) was added and the stirring continued for 2.5 days. The reaction mixture was filtered using a disposable filter cartridge (6 ml) and the residue rinsed with methanol. 4-Benzyloxybenzaldehyde, polymer-bound (Aldrich, 2.8 mmol/g resin, 180 mg, 0.5 mmol) was added to scavenge excess amine and the reaction mixture then stirred for 18 h at room temperature. The reaction solution was filtered using disposable filter cartridges (6 ml), the residue rinsed with methanol and the filtrate concentrated under a stream of nitrogen. The crude product was dissolved in dichloromethane (20 ml). Of this reaction mixture (5 ml) was added to anhydrous pyridine (8 □l, 0.10 mmol) and the corresponding acid chloride (0.1 mmol, 1.5 equiv.) added and the reaction stirred at room temperature for 3 hours. The solvents were evaporated under a stream of nitrogen. To the resulting crude product was added hydrogen chloride (4 N solution in dioxane, 2 ml), the mixture was stirred at room temperature for 45 min, transferred to a hot plate (50 °C) and concentrated under a stream of nitrogen. Triethylamine (20% v/v in dichloromethane, 2 ml) was added and the mixture was concentrated under a stream of nitrogen. The crude reaction product was then dissolved in acetonitrile : dimethylsulfoxide (8:1, 1 ml), filtered using a Whatman HPLC filter and purified by automated preparative liquid chromatography (Gilson system, 10 x 150 mm Phenomenex Magellen C18 5□ column), using a 0.1% aqueous trifluoroacetic acid : acetonitrile gradient ranging from 95:5 to 5:95. Evaporation of the eluant in a Genevac system gave the final product.

Generic Process E

To the solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-{[[(1,1-dimethylethyl)oxy]carbonyl]oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 100 mg, 0.13 mmol) in methanol (2 ml) was added the corresponding amine (0.52 mmol, 4 equiv.), and the mixture stirred at room temperature for 18 h. Borohydride on Amberlite® IRA400 (Aldrich, 2.5mmol/g resin, 77 mg, 0.19 mmol) was added

and the mixture agitated with an orbital shaker at room temperature for 18 h. Then benzyloxybenzaldehyde, polymer-bound (Aldrich, 2.8 mmol/g resin, 460 mg, 1.29 mmol) was added to scavenge excess amine and the reaction mixture was shaken for 18 h. The reaction mixture was filtered, the residue was washed with methanol and the filtrate concentrated to dryness under a stream of nitrogen. A solution of the crude product (0.064 mmol) in dichloromethane was placed into a 48-well-plate (Flexchem Synthesis Block), and polymer-bound *N*-methylmorpholine (3.0 mmol/g resin, 32 mg, 0.096 mmol) was added by means of a dispensing plate. The corresponding acid chloride (0.16 mmol, 2.5 eq.) was added and the reaction mixture shaken at room temperature for 18 h. Polymer-bound *tris*(2-aminoethyl)amine, (4.8 mmol/g resin, 41 mg, 0.2 mmol) was then added with a dispensing plate and the mixtures shaken at room temperature for 18 h. The reaction mixture was then filtered into another 48-well-block and the filtrates concentrated under a stream of nitrogen. The crude residue was dissolved in hydrogen chloride, (1 M solution in acetic acid, 0.5 ml), shaken at room temperature for 1 hour and then concentrated to dryness under a stream of nitrogen. The crude reaction product was then dissolved in a acetonitrile (1 ml) and purified by automated preparative liquid chromatography (Gilson system, 10 x 150 mm Phenomenex Magellen C18 5□ column), using a 0.1% aqueous trifluoroacetic acid : acetonitrile gradient (95:5 to 5:95). Evaporation of the eluant in a Genevac system gave the product.

Generic Process G

To a solution of (2R)-2-[(1R,4R,4aS,5R,6R)-5-({[(2S,3aR,9bR)-6-chloro-3-{[(1,1-dimethylethyl)oxy]carbonyl}-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazin-2-yl]carbonyl}oxy)-6-(acetyloxy)-4a-hydroxy-4,7-dimethyl-1,2,3,4,4a,5,6,8a-octahydronaphthalen-1-yl]propanoic acid (Preparation 181, 200 mg, 0.25 mmol) in dichloromethane (2 ml) was added 1-hydroxybenzotriazole (Aldrich, 58 mg, 0.38 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride salt (96 mg, 0.5 mmol), and the mixture was stirred at room temperature for 0.5 hours. The reaction mixture was added to a solution of th corresponding amine (0.38 mmol) in dichloromethane (2 ml) and stirred at

room temperature for 36 hours. The reaction mixture was diluted with dichloromethane (2 ml) and water (7 ml) and stirred vigorously for 45 min. The layers were separated by means of a filter cartridge with a hydrophobic frit (Whatman 12 ml 1PS filter media), and the organic filtrate concentrated under a stream of nitrogen followed by drying *in vacuo*. To a solution of the crude product in dioxane (1 ml) was added a hydrogen chloride (4M solution in dioxane solution, 2 ml) and the reaction mixture was stirred at room temperature for 25 min. The reaction mixture was concentrated under a stream of nitrogen for 40 min (hotplate 50°C), then a solution of triethylamine in dichloromethane (25% v/v, 2 ml) was added and the mixture again concentrated under reduced pressure. The crude reaction product was purified by automated preparative liquid chromatography (Gilson system, 10 x 150 mm Phenomenex Magellen C18 5□ column), using a 0.1% aqueous trifluoroacetic acid : acetonitrile gradient (95:5 to 5:95). Evaporation of the eluant in a Genevac system gave the product.

The Examples given in the following Table 1 were prepared by the methods referred to above and the Table includes physical characterising data for each compound synthesised. The synthesis of a number of representative compounds are also described in more detail after Table 2. Table 2 indicates the precursor compounds used in the synthesis of the compounds of the invention.

Table 1: Table of Examples

Ex No.	Compound Name	Data*
		*NMR data given for acetate or trifluoroacetate salts
1	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] = 563.3 C29H39ClN2O7 + H requires 563.25. NMR (CDCl3, selected data) : 0.6 (d, 3H), 0.9-1.1 (m, 7H), 1.9 (septet, 1H), 2.1 (s, 3H), 3.35 (s, 3H), 5.2 (s, 1H), 7.2 (d, 1H).

2	(1S,2R,4aS,5R,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-2-[(2-methylpropanoyl)oxy]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (TSP) : M/Z [MH+] = 589.6 C31H41ClN2O7 +H requires 589.3. NMR (CDCl3, selected data) : 0.6 (d, 3H), 1.18 (dd, 6H), 1.9 (septet, 1H), 1.8 (s, 3H), 3.4 (s, 3H), 4.75 (s, 1H), 5.0 (s, 1H), 5.1 (s, 1H), 5.25-5.3 (s, 2H), 5.4 (s, 1H), 7.2 (d, 1H).
3	(1S,2R,4aS,5R,8R,8aR)-2-(hexanoyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2, 3-c][2,1]benzoxazine-2-carboxylate	MS (TSP) : M/Z [MH+] = 617.3 C33H45ClN2O7 +H requires 617.3. NMR (CDCl3, selected data) : 0.55 (d, 3H), 0.9 (m, 3H), 1.85 (s, 3H), 2.3 (m, 3H), 3.35 (s, 3H), 5.2 (s, 1H), 7.2 (d, 1H).
4	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2-(acetyloxy)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexa hydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (TSP) : M/Z [MH+] = 621.2, C31H41ClN2O9 +H requires 621.3. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.0 (d, 3H), 2.0 (s, 3H), 2.1 (s, 3H), 2.3 (m, 3H), 3.35 (s, 3H), 5.25 (s, 1H), 7.2 (d, 1H).
5	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(2-methylpropanoyl)oxy]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3 ,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (TSP) : M/Z [MH+] = 649.2, C33H45ClN2O9 +H requires 649.3. NMR (CDCl3, selected data) : 0.6 (d, 3H), 1.1 (d, 3H), 1.6 (s, 3H), 2.1 (s, 3H), 2.1 (s, 3H), 2.3 (m, 3H), 3.35 (s, 3H), 5.25 (s, 1H), 7.0 (m, 1H), 7.2 (d, 1H), 7.4 (d, 1H).
6	(1S,2R,4aS,5R,8R,8aR)-2-[(cyclopropylcarbonyl)oxy]-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydro pyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] = 587.3, C31H39ClN2O7 +H requires 587.3. NMR (CDCl3, selected data) : 0.7 (d, 3H), 0.85 - 0.95 (m, 2H), 1.0 - 1.1 (m, 2H), 3.35 (s, 3H), 5.3 (s, 1H), 7.2 (d, 1H).
7	(1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethyl)-2-[[(prop-2-ynyloxy)carbonyl]oxy}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydro pyrrolo[2,3-c][2,1]benzoxazine-2-	MS (TSP) : M/Z [MH+] = 603.0, C31H39ClN2O8 +H requires 603.2. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.0 (m, 6H), 1.75 - 1.8 (m, 6H), 2.0

	carboxylate	(1H, septet), 3.1 (s, 1H), 3.35 (s, 3H), 4.8 (s, 2H), 5.25 (s, 1H), 7.2 (d, 1H).
8	(1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethyl)-2-({[(2,2,2-trichloroethyl)oxy]carbonyl}oxy)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9 b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (TSP) : M/Z [MH+] = 694.9, C30H38Cl4N2O8 +H requires 695.1. NMR (CDCl3, selected data) : 0.6 (d, 3H), 1.0 (m, 6H), 1.95 (1H, septet), 3.4 (s, 3H), 4.7 (d, 1H), 4.85 (d, 1H), 5.4 (s, 1H), 7.2 (d, 1H).
9	(1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-2-({[(1-methylethenyl)oxy]carbonyl}oxy)-5-(1-methylethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hex ahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (TSP) : M/Z [MH+] = 605.9, C31H41ClN2O8 +H requires 605.3. NMR (CDCl3, selected data) : 0.6 (m, 3H), 1.0 (m, 6H), 1.8 (s, 3H), 1.95 (1H, septet), 3.4 (s, 3H), 4.7 (s, 1H), 4.8 (s, 1H), 5.4 (s, 1H), 7.2 (d, 1H).
10	(1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethyl)-2-{[(prop-2-enyloxy)carbonyl]oxy}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydro pyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (TSP) : M/Z [MH+] = 605.5, C31H41ClN2O8 +H requires 605.3. NMR (CDCl3, selected data) : 0.65 (d, 3H), 1.0 (d, 6H), 1.95 (1H, septet), 3.4 (s, 3H), 4.65 (m, 2H), 5.25 - 5.35 (m, 4H), 5.9 (m, 1H), 7.25 (d, 1H).
11	(1S,2R,4aS,5S,8R,8aR)-1-({[(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazin-2-yl]carbonyl}oxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-2-yl methyl butanedioate	MS (ES) : M/Z [MH+] = 633.2, C32H41ClN2O9 +H requires 633.3. NMR (CDCl3, selected data) : 0.6 (d, 3H), 3.4 (s, 3H), 3.65 - 3.7 (m, 5H), 4.75 (s, 1H), 5.0 (s, 1H), 5.3 - 5.35 (m, 2H), 7.25 (d, 1H).
12	(1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-2-(pent-4-enoyloxy)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2 ,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] = 601.2, C32H41ClN2O7 +H requires 601.3. NMR (CDCl3, selected data) : 0.45 (d, 3H), 1.8 (s, 3H), 3.4 (s, 3H), 4.7 (s, 1H), 5.0 - 5.1 (m, 4H), 5.2 (s, 1H), 5.35 (s, 1H), 5.4 5.8 (s, 1H), 7.2 (d, 1H).

13	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[({[2-(naphthalen-1-ylamino)ethyl]amino}carbonyl)oxy]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chl oro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =791,2, C42H51ClN4O9 +H requires 791.3. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.0 (d, 3H), 2.1 (s, 3H), 3.2 (s, 3H), 3.2 - 3.5 (m, 4H), 5.3 (s, 1H), 6.5 (m, 1H), 6.9 - 7.5 (m, 7H), 7.7 - 7.8 (m, 2H).
14	(1S,2R,4aS,5R,8R,8aR)-2-{[(acetyloxy)acetyl]oxy}-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropy rrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =619.1, C31H39ClN2O9 +H requires 619.2. NMR (CDCl3, selected data) : 0.6 (d, 3H), 1.65 (s, 3H), 1.85 (s, 3H), 2.15 (s, 3H), 3.4 (s, 3H), 4.6 (dd, 2H), 5.25 (s, 1H), 7.2 (m, 1H).
15	(1S,2R,4aS,5R,8R,8aR)-2-(formyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] = 547.1, C28H35ClN2O7 +H requires 547.2. NMR (CDCl3, selected data) : 0.45 (d, 3H), 1.65 (s, 3H), 1.85 (s, 3H), 3.35 (s, 3H), 5.25 (s, 1H), 7.2 (d, 1H), 8.1 (s, 1H).
16	(1S,2R,4aS,5R,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-2-[(3,3,3-trifluoropropanoyl)oxy]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexa hydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] = 629.1, C30H36ClF3N2O7 +H requires 629.2. NMR (CDCl3, selected data) : 0.5 (d, 3H), 1.65 (s, 3H), 1.9 (s, 3H), 3.2 (dd, 2H), 3.35 (s, 3H), 5.25 (s, 1H), 7.2 (d, 1H).
17	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[4-(ethyloxy)-1-methyl-4-oxobut-2-enyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3 ,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] = 647.3, C33H43ClN2O9 +H requires 647.3. NMR (CDCl3, selected data) : 0.85 (d, 3H), 1.1 (t, 3H), 1.15 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.9 (m, 2H), 5.3 (s, 1H), 5.85 (d, 1H), 6.9 (dd, 1H), 7.25 (d, 1H).
18	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-(2,2-difluoro-1-methylethenyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropy rrolo[2,3-c][2,1]benzoxazine-2-	MS (TSP) : M/Z [MH+] = 597.2, C29H35ClF2N2O7 +H requires 597.2. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.2 (s, 3H),

	carboxylate	3.3 (s, 3H), 5.1 (s, 1H), 5.2 (s, 1H), 5.3 (s, 1H), 5.5 (s, 1H), 7.25 (m, 1H).
19	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2-fluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrr olo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (TSP) : M/Z [MH+] = 581.1, C29H38ClFN2O7 +H requires 581.2. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.1 (d, 3H), 1.6 (s, 3H), 2.1 (s, 3H), 2.2 (s, 3H), 3.3 (s, 3H), 4.3 - 4.7 (m, 2H), 5.4 (s, 1H), 7.25 (m, 1H).
20	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[(1-methyl-2-morpholin-4-ylethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexah ydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] = 648.3, C33H46ClN3O8 +H requires 648.3. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.05 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.4-2.6 (m, 5H), 3.4 (s, 3H), 3.6-3.8 (m, 4H), 5.3 (s, 1H), 7.25 (m, 1H).
21	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-(2-ethyl-1,3-thiazol-4-yl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrol o[2,3-c][2,1]benzoxazine-2-carboxylate	MS (TSP) : M/Z [MH+] = 631.7, C31H38ClN3O7S +H requires 632.2. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.3 (s, 3H), 1.4 (t, 3H), 2.1 (s, 3H), 3.0 (q, 2H), 3.35 (s, 3H), 5.2 (s, 1H), 7.25 (m, 1H), 7.7 (m, 1H).
21		
22	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2,2-difluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydro pyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (TSP) : M/Z [MH+] = 600.3, C29H37ClF2N2O7 +H requires 600.2. NMR (CDCl3, selected data) : 0.6 (d, 3H), 1.1 (d, 3H), 2.05 (s, 3H), 2.1 (s, 3H), 3.35 (s, 3H), 5.25-5.3 (m, 2H), 5.95 (t, 1H), 7.2 (d, 1H).

23	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2,2-difluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydro pyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (TSP) : M/Z [MH+] = 599.9, C29H37ClF2N2O7 +H requires 600.2. NMR (CDCl3, selected data) : 0.9 (d, 3H), 1.1 (d, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 5.4 (s, 1H), 5.9 (t, 1H), 7.2 (m, 1H).
24	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-(2,2-dichloro-1-methylethenyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropy rrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (TSP) : M/Z [MH+] = 629.2, C29H35Cl3N2O7 +H requires 629.2. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.25 (s, 3H), 1.95 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 5.1 (s, (1H), 5.2 (s, 1H), 5.3 (s, 1H), 5.4 (s, 1H), 7.2 (d, 1H).
25	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(phenylmethyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9 b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] = 668.308, C36H46ClN3O7 +H requires 668.310. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.1 (d, 3H), 1.65 (s, 3H), 2.05 (s, 3H), 3.25 (s, 3H), 4.05 (s, 2H), 5.2 (s, 1H), 7.2 (d, 1H), 7.3-7.5 (m, 5H).
26	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{[(2-chlorophenyl)methyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1, 2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] = 702.269, C36H45Cl2N3O7 +H requires 702.271. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.15 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 4.3 (s, 2H), 5.2 (s, 1H), 7.1-7.6 (m, 6H).
27	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(furan-2-ylmethyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a ,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] = 658.288, C34H44ClN3O8 +H requires 658.289. NMR (CDCl3, selected data) : 0.7 (m, 3H), 1.15 (d, 3H), 1.75 (s, 3H), 2.1 (s, 3H), 3.15 (s, 3H), 4.3 (m, 2H), 5.3 (s, 1H), 6.4 (m, 1H), 6.5 (m, 1H), 7.2 (m, 1H), 7.5 (m, 1H).

28	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-[[(2-methylphenyl)methyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1, 2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] = 682.323, C37H48ClN3O7 +H requires 682.326. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.1 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.4 (s, 3H), 3.3 (s, 3H), 4.1 (m, 2H), 5.2 (s, 1H), 7.1-7.3 (m, 5H), 7.45 (m, 1H).
29	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{[(1S)-1-phenylethyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3, 3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (AP) : M/Z [MH+] = 682.3252, C37H48ClN3O7 +H requires 682.3259. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.1 (d, 3H), 1.6 (s, 3H), 1.7 (d, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 5.2 (s, 1H), 6.8-7.6 (m, 8H).
30	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{[(3-chlorophenyl)methyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1, 2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =702.270, C36H45Cl2N3O7 +H requires 702.271. NMR (CDCl3, selected data) : 0.7 (d, 3H), 1.1 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.4 (s, 3H), 3.3 (s, 3H), 3.9-4.1 (m, 3H), 5.2 (s, 1H), 6.95 (m, 1H), 7.1-7.25 (m, 2H), 7.3-7.4 (m, 3H), 7.45 (m, 1H).
31	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-({[2-(methyloxy)phenyl]methyl}amino)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-meth yl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =698.323, C37H48ClN3O8 +H requires 698.321. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.1 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.85 (s, 3H), 4.05-4.3 (m, 2H), 5.2 (s, 1H), 6.85-7.0 (m, 5H), 7.2 (d, 1H), 7.4 (m, 1H).
32	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(4-pyridin-2-ylpiperazin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2 ,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =724.350, C38H50ClN5O7 +H requires 724.348. NMR (CDCl3, selected data) : 0.7 (d, 3H), 1.1 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H),

		2.2-2.4 (m, 4H), 3.3 (s, 3H), 3.4-3.6 (m, 4H), 5.2 (s, 1H), 6.6-6.7 (m, 2H), 7.0 (t, 1H), 7.2 (d, 1H), 7.35 (d, 1H), 7.5 (m, 1H), 8.2 (m, 1H).
33	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{bis[2-(methyloxy)ethyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2 ,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =694.347, C35H52ClN3O9 +H requires 694.347. NMR (CDCl3, selected data) : 0.65 (d, 3H), 1.0 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.4-2.8 (m, 8H), 3.3-3.4 (m, 9H), 3.4-3.5 (m, 4H), 5.2-5.3 (s, 2H), 7.2 (d, 1H).
34	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(2-thien-2-ylethyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3 a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =688.280, C35H46ClN3O7S +H requires 688.282. NMR (CDCl3, selected data) : 0.75 (d, 3H), 1.15 (d, 3H), 1.65 (s, 3H), 2.1 (s, 3H), 2.6-2.85 (m, 4H), 3.2-3.3 (m, 5H), 5.2 (s, 1H), 6.8-7.0 (m, 3H), 7.1-7.3 (m, 3H).
35	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-({[4-(trifluoromethyl)phenyl]methyl}amino)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =736.296, C37H45ClF3N3O7 +H requires 736.298. NMR (CDCl3, selected data) : 0.8 (m, 3H), 1.1 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.8-4.2 (m, 3H), 5.25 (s, 1H), 6.9 (t, 1H), 7.1 (d, 1H), 7.2 (d, 1H), 7.5-7.7 (m, 4H).
36	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[methyl(2-{[2-(methyloxy)phenyl]oxy}ethyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hy droxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =742.346, C39H52ClN3O9 +H requires 742.347. NMR (CDCl3, selected data) : 0.8 (m, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.0-3.2 (m, 3H), 3.3 (s, 3H), 3.4-3.9 (m, 4H), 3.85 (s, 3H), 5.2 (s, 1H), 6.8-7.0 (m, 4H), 7.0 (m, 1H),

		7.2 (d, 1H), 7.35 (d, 1H).
37	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{(1-methylethyl)[2-(phenylsulfonyl)ethyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hyd roxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =788.333, C40H54ClN3O9S +H requires 788.335. NMR (CDCl3, selected data) : 0.9 (d, 3H), 1.15 (d, 3H), 1.35 (d, 3H), 1.45 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.4-3.9 (m, 4H), 3.85 (s, 3H), 5.2 (s, 1H), 7.0 (t, 1H), 7.2 (d, 1H), 7.3 (d, 1H), 7.55-7.65 (m, 2H), 7.7 (m, 1H), 7.9 (m, 2H).
38	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(2,3-dihydro-1,4-benzodioxin-2-ylmethyl)(methyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chlor o-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =740.332, C39H50ClN3O9 +H requires 740.331. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (m, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.0 (s, 3H), 3.3 (s, 3H), 4.05-4.3 (m, 4H), 5.2 (s, 1H), 6.8-7.05 (m, 5H), 7.2-7.35 (m, 2H).
39	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(4-{[2-(methyloxy)phenyl]methyl}piperazin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hyd roxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =767.379, C41H55ClN4O8 +H requires 767.379. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.15 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.85 (s, 3H), 4.3 (s, 2H), 5.2 (s, 1H), 6.9-7.1 (m, 4H), 7.2-7.5 (m, 3H).
40	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(1,1-dimethylethyl)piperidin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-met hyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =702.3900, C38H56ClN3O7 +H requires 702.3885. NMR (CDCl3, selected data) : 0.8-0.95 (m, 12H), 0.9-1.1 (m, 3H), 1.65-1.75 (m, 3H), 2.1-2.15 (m, 3H), 2.2-2.5 (m, 8H), 3.3-3.35

		(s, 3H), 5.2 (s, 1H), 7.05 (m, 1H), 7.2 (m, 1H).
41	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[(phenylmethyl)oxy]piperidin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-met hyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =752.3678, C41H54ClN3O8 +H requires 752.3678. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.1 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.25-3.4 (m, 7H), 4.55 (s, 2H), 5.2 (s, 1H), 7.0 (m, 1H), 7.2-7.4 (m, 7H).
42	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[7,8-bis(methyloxy)-3,4-dihydroisoquinolin-2(1H)-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9 b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =754.3463, C40H52ClN3O9 +H requires 754.3470. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.1 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.0-3.35 (m, 8H), 3.3 (s, 3H), 3.8 (s, 3H), 3.9 (s, 3H), 4.55 (s, 2H), 5.2 (s, 1H), 6.8-6.9 (m, 2H), 7.0 (m, 1H), 7.2 (m, 1H), 7.35 (m, 1H).
43	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(methyl{[4-(methyloxy)phenyl]methyl}amino)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =712.3382, C38H50ClN3O8 +H requires 712.3365. NMR (CDCl3, selected data) : 0.85 (m, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.6-2.9 (m, 9H), 3.3 (s, 3H), 3.85 (s, 3H),4.15 (m, 2H), 5.2 (s, 1H), 6.9-7.1 (m, 3H), 7.2 (m, 1H), 7.2-7.25 (m, 2H).
44	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[(ethyloxy)carbonyl]-1,4-diazepan-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =733.3554, C37H53ClN4O9 +H requires 733.3579. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.3 (t, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.9-3.2 (m, 14H), 3.3 (s, 3H), 4.1-4.3 (m, 4H), 5.2 (s, 1H), 7.0 (m, 3H), 7.2-7.35 (m, 2H).

45	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(phenylmethyl)-1,4-diazepan-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-meth yl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =751.3840, C41H55ClN4O7 +H requires 751.3838. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.15 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.9-4.0 (m, 12H), 3.3 (s, 3H), 4.3 (s, 2H), 5.2 (s, 1H), 6.95 (m, 1H), 7.2 (d, 1H), 7.4-7.5 (m, 6H).
46	(1S,2R,4aS,5S,8R,8aR)-5-{2-[acetyl(ethyl)amino]-1-methylethyl}-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b -hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =649.0, C33H46ClN3O8 +H requires 648.3052. NMR (CDCl3, selected data) : 0.75-0.8 (m, 3H), 0.95-1.0 (m, 3H), 1.2-1.3 (m, 3H), 1.65-1.75 (m, 3H), 2.1 (s, 3H), 2.15 (s, 3H), 3.3 (s, 3H), 5.2 (s, 1H), 7.2 (d, 1H).
47	(1S,2R,4aS,5S,8R,8aR)-5-{2-[acetyl(cyclopropyl)amino]-1-methylethyl}-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3 a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =660.2, C34H46ClN3O8 +H requires 660.3052. NMR (CDCl3, selected data) : 0.7-0.8 (m, 5H), 0.9-1.0 (m, 6H), 1.7 (s, 3H), 2.1 (s, 3H), 2.2 (s, 3H), 3.3 (s, 3H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2 (d, 1H), 7.35 (d, 1H).
48	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{cyclopropyl[(methyloxy)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (TSP) : M/Z [MH+] =676.7, C34H46ClN3O9 +H requires 676.3001. NMR (CDCl3, selected data) : 0.6-0.7 (m, 5H), 0.7-0.9 (m, 3H), 1.0 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.2 (s, 3H), 3.35 (s, 3H), 3.7 (s, 3H), 5.25 (s, 1H), 7.0 (dd, 1H), 7.2 (d, 1H), 7.4 (d, 1H).
49	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{ethyl[(methyloxy)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (TSP) : M/Z [MH+] =664.4, C33H46ClN3O9 +H requires 664.3001. NMR (CDCl3, selected data) : 0.8 (t, 3H), 1.0 (m, 3H), 1.2 (m, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.35 (s, 3H), 3.65 (s, 3H), 5.2-

		5.25 (m, 2H), 7.0 (m, 1H), 7.2 (m, 1H), 7.4 (d, 1H).
50	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{[(2,5-dichlorophenyl)methyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (AP+) : M/Z [MH+] =736, C36H44Cl3N3O7 +H requires 736.2323. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.1 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 4.3 (s, 2H), 5.2 (s, 2H), 6.95 (dd, 1H), 7.2 (d, 1H), 7.3-7.4 (m, 3H), 7.6 (s, 1H).
51	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{[(3,5-dichlorophenyl)methyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (AP+) : M/Z [MH+] =736, C36H44Cl3N3O7 +H requires 736.2323. NMR (CDCl3, selected data) : 0.7 (m, 3H), 1.1 (m, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.9-4.1 (m, 2H), 5.3 (s, 1H), 6.9 (m, 1H), 7.1-7.4 (m, 5H).
52	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{cyclopropyl[(ethylamino)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5- methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =689.4, C35H49ClN4O8 +H requires 689.3317. NMR (CDCl3, selected data) : 0.7-0.8 (m, 5H), 0.8-0.9 (m, 3H), 0.95 (d, 3H), 1.1 (t, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.65-3.8 (m, 2H), 5.2 (s, 1H), 6.95 (dd, 1H), 7.2 (d, 1H), 7.3 (d, 1H).
53	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[methyl(phenylmethyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3, 3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =682, C37H48ClN3O7 +H requires 682.3259. NMR (CDCl3, selected data) : 0.8 (d, 3H), 0.85-1.1 (m, 3H), 1.6 (s, 3H), 2.1 (s, 3H), 2.65-2.75 (m, 3H), 3.1-3.15 (m, 3H), 4.2-4.6 (m, 3H), 5.2 (s, 1H), 6.9-7.4 (m, 3H), 7.45-7.6 (m, 5H).

54	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-[4-(phenylmethyl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1 ,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =737, C40H53ClN4O7 +H requires 737.3681. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.65 (s, 3H), 2.1 (s, 3H), 3.0-3.4 (m, 6H), 3.3 (s, 3H), 3.5-3.7 (m, 6H), 4.2 (s, 2H), 5.2 (s, 1H), 7.0 (m, 1H), 7.2 (m, 1H), 7.4-7.5 (m, 6H).
55	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(3-methylpiperidin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a, 5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =660, C35H50ClN3O7 +H requires 660.3416. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.0-1.05 (m, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.7-2.9 (m, 12H), 3.3 (s, 3H), 5.2 (s, 2H), 7.0 (m, 1H), 7.2 (m, 1H), 7.35 (d, 1H).
56	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(4-pyrimidin-2-ylpiperazin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1 ,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =725.2, C37H49ClN6O7 +H requires 725.3430. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.1 (d, 3H), 1.6 (s, 3H), 2.1 (s, 3H), 2.3-2.65 (m, 8H), 3.35 (s, 3H), 4.75-4.9 (m, 4H), 5.2 (m, 2H), 6.5 (m, 1H), 7.0 (dd, 1H), 7.2 (m, 1H), 7.4 (d, 1H), 8.3-8.35 (m, 2H).
57	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{methyl[2-(phenyloxy)ethyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =712, C38H50ClN3O8 +H requires 712.3365. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.6 (s, 3H), 2.1 (s, 3H), 2.9-3.05 (m, 4H), 3.3 (s, 3H), 4.4-4.5 (m, 2H), 5.2 (m, 1H), 6.85-7.0 (m, 3H), 7.0 (dd, 1H), 7.2 (m, 1H), 7.25-7.35 (m, 3H).
58	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-thiomorpholin-4-ylethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-h	MS (ES) : M/Z [MH+] =664, C33H46ClN3O7S +H requires 663.2745. NMR (CDCl3, selected data) : 0.85 (d, 3H), 1.2

	exahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	(d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.9-3.2 (m, 11H), 3.3 (s, 3H), 5.2 (m, 1H), 7.0 (dd, 1H), 7.2-7.3 (m, 2H).
59	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[cyclohexyl(methyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a ,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =674, C36H52ClN3O7 +H requires 674.3572. NMR (CDCl3, selected data) : 0.85 (d, 3H), 1.15-1.25 (m, 6H), 1.3-1.5 (m, 6H), 1.7 (s, 3H), 1.9-2.0 (m, 2H), 2.1 (s, 3H), 2.7-2.85 (m, 3H), 3.3 (s, 3H), 5.2 (m, 1H), 7.0 (m, 1H), 7.2 (m, 1H), 7.35 (dd, 1H).
60	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[methyl(pyridin-2-ylmethyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =683, C36H47ClN4O7 +H requires 683.3212. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.1 (d, 3H), 1. 65 (s, 3H), 2.1 (s, 3H), 2.95 (s, 3H), 3.3 (s, 3H), 4.45 (m, 2H), 5.2 (m, 1H), 7.0 (m, 1H), 7.2 (m, 1H), 7.35 (m, 1H), 7.5 (m, 1H), 7.65 (m, 1H), 7.85 (m, 1H), 8.65 (m, 1H).
61	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(3,6-dihydropyridin-1(2H)-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2, 3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =644, C34H46ClN3O7 +H requires 644.3103. NMR (CDCl3, selected data) : 0.85 (d, 3H), 1.15 (d, 3H), 1. 7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 4.45 (m, 2H), 5.1-5.2 (m, 2H), 5.7 (m, 1H), 6.0 (m, 1H), 7.0 (m, 1H), 7.35 (m, 1H).
62	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{[phenyl(pyridin-3-yl)methyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methy l-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =745, C41H49ClN4O7 +H requires 745.3. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.05 (d, 3H), 1. 6 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 4.45 (m, 2H), 5.0-5.15 (m, 3H), 6.9-7.6 (m, 9H), 8.1 (m, 1H), 8.6 (m, 1H), 8.8 (m, 1H).

63	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(2-phenylethyl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =751.3, C41H55ClN4O7 +H requires 751.3838. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.15 (d, 3H), 1. 7 (s, 3H), 2.1 (s, 3H), 3.25-3.35 (m, 4H), 3.55-3.65 (m, 6H), 5.2 (m, 1H), 7.0 (m, 1H), 7.2-7.4 (m, 7H).
64	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydr oxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =781, C41H53ClN4O9 +H requires 781.3579. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.15 (d, 3H), 1. 7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.5-3.75 (m, 9H), 5.2 (m, 1H), 6.0 (s, 2H), 6.8-6.85 (m, 2H), 6.9 (s, 1H), 7.0 (m, 1H), 7.2-7.3 (m, 2H).
65	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[3-(methyloxy)phenyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =753, C40H53ClN4O8 +H requires 753.3630. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.15 (d, 3H), 1. 7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.25-3.8 (m, 9H), 3.8 (s, 3H), 5.2 (m, 1H), 6.45 (m, 1H), 6.3-6.4 (m, 2H), 7.0 (m, 1H), 7.2-7.35 (m, 3H).
66	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(4-{[(4-chlorophenyl)methyl]oxy}piperidin-1-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hyd roxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =786, C41H53Cl2N3O8 +H requires 786.3288. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.1 (d, 3H), 1. 65 (s, 3H), 2.1 (s, 3H), 2.55-2.75 (m, 8H), 2.9-3.2 (m, 4H), 3.3 (s, 3H), 4.5 (s, 2H), 5.2 (s, 1H), 7.0 (m, 1H), 7.2-7.4 (m, 6H).
67	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[2-(methyloxy)phenyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =752, C40H53ClN4O8 +H requires 753.3630. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1. 7 (s, 3H), 2.1 (s, 3H), 3.0-3.6 (m, 11H),

		3.3 (s, 3H), 5.2 (s, 1H), 6.9 (m, 1H), 6.95-7.05 (m, 3H), 7.1 (m, 1H), 7.2-7.3 (m, 2H).
68	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(furan-2-ylmethyl)piperidin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-meth yl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =727, C39H52ClN3O8 +H requires 726.3521. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1. 7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.5-3.7 (m, 9H), 4.2 (m, 2H), 5.2 (s, 1H), 6.45 (m, 1H), 6.6 (m, 1H), 7.0 (m, 1H), 7.2-7.3 (m, 2H), 7.5 (m, 1H).
69	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[(3-methylphenyl)methyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =751, C41H55ClN4O7 +H requires 751.3838. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.15 (d, 3H), 1. 65 (s, 3H), 2.1 (s, 3H), 2.35 (s, 3H), 3.3 (s, 3H), 3.5-3.75 (m, 8H), 4.15 (m, 2H), 5.2 (s, 1H), 7.0 (m, 1H), 7.15-7.35 (m, 6H).
70	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(2,2-dimethylpropanoyl)(ethyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-met hyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =690, C36H52ClN3O8 +H requires 690.3521. NMR (CDCl3, selected data) : 0.85 (d, 3H), 0.95 (d, 3H), 1.25 (t, 3H), 1.3 (s, 9H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2 (m, 1H), 7.4 (d, 1H).
71	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[methyl(propanoyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a, 5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =648, C33H46ClN3O8 +H requires 648.3052. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.0 (d, 3H), 1.2 (m, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.1 (s, 3H), 3.3 (s, 3H), 5.2 (s, 1H), 7.0 (m, 1H), 7.2 (m, 1H), 7.4 (d, 1H).

72	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(1-methylethyl)(propanoyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =676, C35H50ClN3O8 +H requires 676.3365. NMR (CDCl3, selected data) : 0.8 (d, 3H), 0.9 (d, 3H), 1.2 (t, 3H), 1.3 (m, 6H), 1.7 (s, 3H), 2.1 (s, 3H), 3.1 (s, 3H), 3.3 (s, 3H), 4.15 (m, 2H), 5.2 (s, 1H), 7.0 (m, 1H), 7.2 (m, 1H), 7.4 (d, 1H).
73	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(2,2-dimethylpropanoyl)(1-methylethyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =704, C37H54ClN3O8 +H requires 704.3678. NMR (CDCl3, selected data) : 0.8-0.9 (m, 6H),1.2-1.25 (m, 6H), 1.3 (s, 9H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 5.2 (s, 1H), 6.95 (m, 1H), 7.2 (m, 1H), 7.35 (d, 1H).
74	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{(1-methylethyl)[(methyloxy)acetyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5 -methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =692, C35H50ClN3O9 +H requires 692.3314. NMR (CDCl3, selected data) : 0.8 (m, 3H), 0.95 (d, 3H), 1.2-1.3 (m, 6H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.4 (s, 3H), 4.15 (m, 2H), 5.2 (s, 1H), 7.0 (m, 1H), 7.2 (m, 1H), 7.35 (d, 1H).
75	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(2-chlorophenyl)methyl](propanoyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =758, C39H49Cl2N3O8 +H requires 758.2975. NMR (CDCl3, selected data) : 0.8 (m, 3H), 1.0 (d, 3H), 1.15 (t, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 4.65 (m, 2H), 5.2 (s, 1H), 6.95-7.1 (m, 2H), 7.2-7.45 (m, 5H).
76	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{[(2-chlorophenyl)methyl][(methyloxy)acetyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b- hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =774, C39H49Cl2N3O9 +H requires 774.2924. NMR (CDCl3, selected data) : 0.8 (m, 3H), 1.0 (m, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.4 (s, 3H), 4.0-4.2 (m, 3H),

		4.65 (m, 2H), 5.2 (s, 1H), 7.0 (m, 1H), 7.1 (m, 1H), 7.2-7.5 (m, 5H).
77	(1S,2R,4aS,5S,8R,8aR)-5-(2-{acetyl[(2-methylphenyl)methyl]amino}-1-methylethyl)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-met hyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =724, C39H50ClN3O8 +H requires 724.3365. NMR (CDCl3, selected data) : 0.75-0.8 (m, 3H), 1.0 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.3-2.35 (m, 3H), 3.3 (s, 3H), 5.25 (s, 1H), 6.95-7.1 (m, 2H), 7.2-7.4 (m, 5H).
78	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[[(2-methylphenyl)methyl](propanoyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =738, C40H52ClN3O8 +H requires 738.3521. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.05 (d, 3H), 1.1 (t, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.3 (s, 3H), 3.3 (s, 3H), 4.5 (m, 2H), 5.25 (s, 1H), 6.9-7.1 (m, 2H), 7.15-7.3 (m, 4H), 7.35 (m, 1H).
79	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{[(methyloxy)acetyl][(2-methylphenyl)methyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b- hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =754, C40H52ClN3O9 +H requires 754.3470. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.0 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.3 (s, 3H), 3.3-3.35 (m, 6H), 4.1 (m, 2H), 4.55 (m, 2H), 5.25 (s, 1H), 6.9-7.1 (m, 2H), 7.1-7.3 (m, 4H), 7.4 (m, 1H).
80	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(4-{[(4-fluorophenyl)methyl]oxy}piperidin-1-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hyd roxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =770, C41H53ClFN3O8 +H requires 770.3583. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 1.9-2.1 (m, 5H), 2.1 (s, 3H), 2.9-3.1 (m, 4H), 3.3 (s, 3H), 4.5 (s, 2H), 5.2 (s, 1H), 6.95-7.1 (m, 3H), 7.2-7.3 (m, 4H).

81	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[(4-chlorophenyl)methyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =771, C41H53Cl2N3O7 +H requires 770.3339. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 1.9-2.1 (m, 5H), 2.1 (s, 3H), 3.3 (s, 3H), 3.45-3.75 (m, 8H), 4.1 (s, 2H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2-7.35 (m, 2H), 7.35-7.45 (m, 4H).
82	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(3,4-dihydroisoquinolin-2(1H)-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =694, C38H48ClN3O7 +H requires 694.3. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (m, 3H), 3.0-3.5 (m, 5H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2-7.1-7.35 (m, 7H).
83	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-meth yl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =676, C35H50ClN3O8 +H requires 676.3365. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.2-1.3 (m, 6H), 1.7 (s, 3H), 2.1 (s, 3H), 3.1-3.3 (m, 6H), 3.3 (s, 3H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2-7.35 (m, 2H).
84	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[methyl(3,3,3-trifluoropropanoyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =702.2, C33H43ClF3N3O8 +H requires 702.2769. NMR (CDCl3, selected data) : 0.85 (m, 3H), 0.95 (m, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.1 (s, 3H), 3.4 (s, 3H), 5.2 (s, 1H), 7.0 (m, 1H), 7.2-7.4 (m, 2H).
85	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[[(2-methylphenyl)methyl](3,3,3-trifluoropropanoyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chl oro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =792.2, C40H49ClF3N3O8 +H requires 792.3239. NMR (CDCl3, selected data) : 0.8 (m, 3H), 1.05 (m, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.3 (s, 3H), 3.35 (s, 3H), 4.5 (m, 2H), 5.2

		(s, 1H), 6.9-7.4 (m, 7H).
86	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[(4-methylphenyl)methyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =751.2, C41H55ClN4O7 +H requires 751.3838. NMR (CDCl3, selected data) : 0.8 (m, 3H), 1.1 (m, 3H), 1.65 (s, 3H), 2.1 (s, 3H), 2.3 (s, 3H), 3.3 (s, 3H), 3.4-3.6 (m, 8H), 4.0-4.15 (m, 3H), 5.2 (s, 1H), 6.9 (dd, 1H), 7.1-7.3 (m, 6H).
87	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[6-(methyloxy)pyridazin-3-yl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hyd roxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =755, C38H51ClN6O8 +H requires 755.3535. NMR (CDCl3, selected data) : 0.8 (m, 3H), 1.1 (m, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.4-3.2 (m, 12H), 3.3 (s, 3H), 4.0 (s, 3H), 5.2 (s, 1H), 6.95-7.05 (m, 2H), 7.15 (m, 1H), 7.2-7.3 (m, 2H).
88	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(6-chloropyrazin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5- methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =759, C37H48Cl2N6O7 +H requires 759.3040. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.15 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.4-3.2 (m, 12H), 3.3 (s, 3H), 5.2 (s, 1H), 7.0 (m, 1H), 7.2 (m, 1H), 7.3 (d, 1H), 7.95 (s, 1H), 8.05 (s, 1H).
89	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(6-chloropyridin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5- methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =758.2, C38H49Cl2N5O7 +H requires 758.3087. NMR (CDCl3, selected data) : 0.75 (d, 3H), 1.1 (d, 3H), 1.6 (s, 3H), 1.95 (s, 3H), 2.4-2.8 (m, 10H), 3.1 (s, 3H), 5.1 (s, 1H), 6.45 (d, 1H), 6.55 (d, 1H), 6.95 (dd, 1H), 7.1 (d, 1H), 7.15 (d, 1H), 7.35 (dd, 1H).

90	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(4-phenylpiperazin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a, 5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =723, C39H51ClN4O7 +H requires 723.3525. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.1 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.45-2.8 (m, 8H), 3.15-3.25 (m, 5H), 3.3 (s, 3H), 5.1 (s, 1H), 6.85 (m, 1H), 6.9-6.95 (m, 2H), 7.0 (dd, 1H), 7.2-7.3 (m, 3H), 7.35 (dd, 1H).
91	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(cyclohexylmethyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-meth yl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =743.3, C40H59ClN4O7 +H requires 743.4151. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.1 (d, 3H), 1.7 (s, 3H), 1.7-1.85 (m, 8H), 2.1 (s, 3H), 3.3 (s, 3H), 3.6-3.8 (m, 8H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2-7.3 (m, 2H).
92	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(1,3-thiazol-2-yl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-meth yl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =730.2, C36H48ClN5O7S +H requires 730.3041. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.1 (d, 3H), 1.7 (s, 3H), 2.15 (s, 3H), 3.0-3.1 (m, 2H), 3.3 (s, 3H), 3.3-3.5 (m, 4H), 3.85-4.05 (m, 4H), 5.2 (s, 1H), 6.7 (s, 1H), 7.0 (dd, 1H), 7.2-7.25 (m, 2H), 7.3 (m, 1H).
93	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(3-chloropyridin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5- methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =758, C38H49Cl2N5O7 +H requires 758.3087. NMR (CDCl3, selected data) : 0.85 (d, 3H), 1.15 (d, 3H), 1.7 (s, 3H), 2.15 (s, 3H), 3.0-3.2 (m, 4H), 3.35 (s, 3H), 3.35-4.05 (m, 6H), 5.2 (s, 1H), 6.9 (m, 1H), 7.0 (dd, 1H), 7.2 (m, 1H), 7.3 (d, 1H), 7.6 (m, 1H), 8.2 (m, 1H).

94	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-oxo-2-[(phenylmethyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3, 3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =682, C36H44ClN3O8 +H requires 682.2895. NMR (CDCl3, selected data) : 0.9 (m, 3H), 1.3 (m, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 4.2 (m, 2H), 5.3 (s, 1H), 7.0 (dd, 1H), 7.1-7.3 (m, 4H), 7.5 (m, 1H), 7.7 (m, 1H), 7.9 (m, 1H).
95	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-{2-[[(2-chlorophenyl)methyl](methyl)amino]-1-methyl-2-oxoethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =730, C37H45Cl2N3O8 +H requires 730.2662. NMR (CDCl3, selected data) : 0.9 (m, 3H), 1.3 (m, 3H), 1.75 (s, 3H), 2.1 (s, 3H), 3.1 (s, 3H), 3.3 (s, 3H), 5.15-5.2 (m, 2H), 6.8 (dd, 1H), 7.0-7.5 (m, 5H), 7.75 (m, 1H).
96	(1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethyl)-2-{[(phenylamino)carbonyl]oxy}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahy dropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (APCI) : M/Z [MH+] =640.2, C34H42ClN3O7 +H requires 640.2790. NMR (CDCl3, selected data) : 0.8 (m, 3H), 1.0 (m, 6H), 1.75 (s, 3H), 3.3 (s, 3H), 5.2 (s, 1H), 6.6 (s, 1H), 7.0 (dd, 1H), 7.1 (dd, 1H), 7.2 (m, 1H), 7.3-7.4 (m, 5H).
97	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(cycloheptylamino)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-h exahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (APCI) : M/Z [MH+] =674, C36H52ClN3O7 +H requires 674.3572. NMR (CDCl3, selected data) : 0.9 (m, 3H), 1.1 (m, 3H), 1.6-1.9 (m, 16H), 2.1 (s, 3H), 3.3 (s, 3H), 5.1-5.2 (m, 2H), 7.0 (dd, 1H), 7.2-7.4 (m, 2H).
98	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2-chloropyrimidin-4-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =759.1, C37H48Cl2N6O7 +H requires 759.3040. NMR (DMSO, selected data) : 0.8 (d, 3H), 1.1 (d, 3H), 1.6 (s, 3H), 2.1 (s, 3H), 2.5 (m, 2H), 2.95-3.1 (m, 2H), 3.15 (s, 3H), 3.2-3.8 (m, 6H), 5.1 (s, 1H), 7.0 (d, 1H), 7.1 (dd,

		1H), 7.3 (d, 1H), 7.35 (d, 1H), 8.2 (d, 1H).
99	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(5-chloropyridin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5- methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =758.2, C38H49Cl2N5O7 +H requires 758.3087. NMR (CDCl3, selected data) : 0.85 (d, 3H), 1.15 (m, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.4 (s, 3H),3.5-3.6 (m, 4H), 5.15-5.2 (m, 2H), 6.65 (d, 1H), 7.05 (dd, 1H), 7.2 (d, 1H), 7.3 (d, 1H), 7.5 (m, 1H), 8.15 (m, 1H).
100	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(5-chloropyrazin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5- methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =759.1, C37H48Cl2N6O7 +H requires 759.3040. NMR (CDCl3, selected data) : 0.85 (d, 3H), 1.25 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.3-2.8 (m, 9H), 3.3 (s, 3H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2 (d, 1H), 7.3 (d, 1H), 7.95 (s, 1H), 8.05 (s, 1H).
101	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(4-chlorophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl - 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =757.1, C39H50Cl2N4O7 +H requires 757.3135. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.05 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.45-2.8 (m, 7H), 3.1-3.25 (m, 4H), 3.3 (s, 3H), 5.2 (s, 1H), 6.8-6.85 (m, 2H), 7.0 (dd, 1H), 7.2-7.3 (m, 3H), 7.4 (d, 1H).
102	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(4-methylphenyl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl - 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =737.2, C40H53ClN4O7 +H requires 737.3681. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.25 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.3 (s, 3H), 3.0-3.2 (m, 4H), 3.3 (s, 3H), 5.2 (s, 1H), 6.85-6.9 (m, 2H), 7.0 (dd, 1H), 7.1-7.15 (m, 2H), 7.2-7.35 (d,

2H).

103	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2-chlorophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl -1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =757.1, C39H50Cl2N4O7 +H requires 757.3. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.25 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.0-3.5 (m, 11H), 5.2 (s, 1H), 6.95-7.1 (m, 3H), 7.15-7.4 (m, 4H).
104	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =792, C40H50ClF3N4O7 +H requires 791.3398. NMR (CDCl3, selected data) : 0.85 (d, 3H), 1.25 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.5-3.8 (m, 4H), 5.2 (s, 1H), 7.0-7.15 (m, 3H), 7.2-7.35 (m, 3H), 7.3 (dd, 1H).
105	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[4-(methyloxy)phenyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =753.2, C40H53ClN4O8 +H requires 753.3630. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.25 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.0-3.15 (m, 4H), 3.3 (s, 3H), 3.4-3.6 (m, 4H), 3.8 (s, 3H), 5.2 (s, 1H), 6.8-7.0 (m, 5H), 7.2-7.35 (m, 3H).
106	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[2-(trifluoromethyl)phenyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =791.2, C40H50ClF3N4O7 +H requires 791.3398. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.25 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.9-3.1 (m, 4H), 3.3 (s, 3H), 5.2 (s, 1H), 7.0-7.15 (m, 3H), 7.2-7.35 (m, 3H), 7.4 (m, 1H).

107	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[4-(trifluoromethyl)pyrimidin-2-yl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro- 9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =793.1, C38H48ClF3N6O7 +H requires 793.3303. NMR (CDCl3, selected data) : 0.6 (d, 3H), 1.1 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.5-2.8 (m, 10H), 3.35 (s, 3H), 3.6-3.8 (m, 2H), 3.8-4.0 (m, 4H), 5.2 (s, 1H), 6.7 (m, 1H), 7.0 (dd, 1H), 7.2 (m, 1H), 7.35 (d, 1H), 8.5 (m, 1H).
108	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2-fluorophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl - 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =741.2, C39H50ClFN4O7 +H requires 741.3430. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.0-3.2 (m, 4H), 3.3 (s, 3H), 3.3-3.55 (m, 4H), 3.6-3.8 (m, 2H), 5.2 (s, 1H), 6.9-7.15 (m, 5H), 7.2 (d, 1H), 7.3 (m, 1H).
109	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(6-methylpyridin-2-yl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5- methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =738.3, C39H52ClN5O7 +H requires 738.3634. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.65 (s, 3H), 3.0-3.2 (m, 2H), 3.3 (s, 3H), 3.3-3.6 (m, 4H), 4.0-4.2 (m, 5H), 5.2 (s, 1H), 6.8-6.85 (m, 3H), 7.0 (dd, 1H), 7.2 (d, 1H), 7.9 (m, 1H).
110	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(4-fluorophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl - 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =741.3, C39H50ClFN4O7 +H requires 741.3430. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.65 (s, 3H), 3.3 (s, 3H), 3.3-4.0 (m, 8H), 5.2 (s, 1H), 6.85-6.95 (m, 2H), 6.95-7.05 (m, 3H), 7.2-7.35 (m, 2H).

111	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(1,3-thiazol-2-ylcarbonyl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydrox y-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =758.2, C37H48ClN5O8S +H requires 758.2990. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.25 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.1-3.2 (m, 2H), 3.3 (s, 3H), 3.4-4.2 (m, 9H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2-7.35 (m, 2H), 7.6 (s, 1H), 7.9 (s, 1H).
112	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[(3-phenylpropyl)oxy]piperidin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =780.2, C43H58ClN3O8 +H requires 780.3991. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.25 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.4-3.1 (m, 10H), 3.3 (s, 3H), 3.3-3.5 (m, 8H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.1-7.3 (m, 7H).
113	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[5-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b -hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =792.2, C39H49ClF3N5O7 +H requires 792.3351. NMR (CDCl3, selected data) : 0.85 (d, 3H), 1.25 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.3-2.8 (m, 8H), 3.3 (s, 3H), 3.6-3.75 (m, 5H), 5.2 (s, 1H), 6.7 (d, 1H), 7.0 (dd, 1H), 7.2-7.35 (m, 2H), 7.75 (m, 1H), 8.45 (s, 1H).
114	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(phenylmethyl)piperidin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1 ,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =736.3, C41H54ClN3O7 +H requires 736.3729. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.4-3.1 (m, 15H), 3.3 (s, 3H), 3.7 (m, 2H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.1-7.15 (m, 2H), 7.2-7.35 (m, 5H).
115	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[3-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-	MS (ES) : M/Z [MH+] =792.2, C39H49ClF3N5O7 +H requires 792.3351. NMR (CDCl3, selected

	chloro-9b -hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.4-3.2 (m, 8H), 3.3 (s, 3H), 3.5-3.65 (m, 4H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.1 (m, 1H), 7.2-7.35 (m, 2H), 7.9 (d, 1H), 8.5 (m, 1H).
116	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[3-(trifluoromethyl)phenyl]piperidin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =790.2, C41H51ClF3N3O7 +H requires 790.3446. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.65 (s, 3H), 2.1 (s, 3H), 2.2-2.6 (m, 9H), 3.3 (s, 3H), 3.5-3.65 (m, 4H), 5.15 (s, 1H), 7.0 (dd, 1H), 7.2 (m, 1H), 7.25 (d, 1H), 7.35-7.55 (m, 4H).
117	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(4-{[3-(trifluoromethyl)phenyl]methyl}piperazin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro- 9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =805.2, C41H52ClF3N4O7 +H requires 805.3555. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.65 (s, 3H), 2.1 (s, 3H),3.2-3.3 (m, 4H), 3.3 (s, 3H), 3.9 (m, 2H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2-7.3 (m, 2H), 7.4-7.7 (m, 4H).
118	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[({3-[(ethyloxy)carbonyl]phenyl}methyl)oxy]piperidin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6 -chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =824.2, C44H58ClN3O10 +H requires 824.3889. NMR (CDCl3, selected data) : 0.75 (d, 3H), 1.15 (d, 3H), 1.35 (t, 3H), 1.75 (s, 3H), 2.1 (s, 3H), 2.85-3.15 (m, 9H), 3.3 (s, 3H), 4.3 (m, 2H), 4.5 (m, 2H), 5.15 (s, 1H), 6.95 (dd, 1H), 7.15 (d, 1H), 7.25 (m, 1H), 7.3-7.4 (m, 2H), 7.95-8.05 (m, 2H).
119	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(1,3-benzoxazol-2-yl)piperidin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-	MS (ES) : M/Z [MH+] =763.2, C41H51ClN4O8 +H requires 763.3474. NMR (CDCl3, selected data) : 0.85 (d, 3H), 1.2

	1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	(m, 3H), 1.75 (s, 3H), 2.1 (s, 3H), 2.9-3.3 (m, 11H), 3.3 (s, 3H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2-7.3 (m, 2H), 7.3-7.4 (m, 2H), 7.5 (m, 1H), 7.7 (m, 1H).
120	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(4-{[3,5-bis(trifluoromethyl)phenyl]methyl}piperazin-1-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-ch loro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =873.1, C42H51ClF6N4O7 +H requires 873.3429. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (m, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.9-3.1 (m, 6H), 3.3 (s, 3H), 4.8 (m, 2H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2-7.3 (m, 2H), 7.8-7.9 (m, 3H).
121	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[2-(methyloxy)phenyl]piperidin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =752.2, C41H54ClN3O8 +H requires 752.3678. NMR (CDCl3, selected data) : 0.8 (m, 3H), 1.25 (m, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.9-3.6 (m, 11H), 3.3 (s, 3H), 3.8 (s, 3H), 5.2 (s, 1H), 6.85-7.15 (m, 5H), 7.2-7.3 (m, 2H).
122	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[(4-fluorophenyl)methyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =755.3, C40H52ClN4O7 +H requires 755.3. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.4-3.7 (m, 8H), 4.1 (m, 2H), 5.2 (s, 1H), 7.0-7.45 (m, 7H).
123	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-[4-(4-cyanophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =755.3, C40H52ClFN4O7 +H requires 755.3587. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.4-3.7 (m, 8H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.1-7.15 (m, 2H), 7.2-7.3 (m, 2H), 7.4-7.5 (m, 2H).

124	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2,3-dihydro-1,4-benzodioxin-2-ylcarbonyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =809.3, C42H53ClN4O10 +H requires 809.3528. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.9-3.9 (m, 12H), 3.3 (s, 3H), 5.2 (s, 1H), 6.8-6.95 (m, 4H), 7.0 (dd, 1H), 7.2-7.35 (m, 2H).
125	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(4-bromophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =803.2, C39H50BrClN4O7 +H requires 801.2630. NMR (CDCl3, selected data) : 0.85 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.6-3.2 (m, 12H), 3.3 (s, 3H), 5.2 (s, 1H), 6.8 (m, 2H), 7.0 (dd, 1H), 7.2-7.35 (m, 2H), 7.4 (m, 2H).
126	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[4-(trifluoromethyl)phenyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =791.2, C40H50ClF3N4O7 +H requires 791.3398. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.6-3.3 (s, 3H), 3.4-3.9 (m, 6H), 5.2 (s, 1H), 6.9-7.05 (m, 3H), 7.15-7.35 (m, 2H), 7.5 (m, 2H).
127	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =759.2, C39H49ClF2N4O7 +H requires 759.3336. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.9-3.3 (m, 7H), 3.3 (s, 3H), 3.35-3.45 (m, 4H), 5.2 (s, 1H), 6.85-7.05 (m, 4H), 7.2 (d, 1H), 7.3 (m, 1H).
128	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(pyridin-4-ylmethyl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-	MS (ES) : M/Z [MH+] =738.3, C39H52ClN5O7 +H requires 738.3634. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d,

	1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.85-2.95 (m, 2H), 3.3 (s, 3H), 3.4-4.2 (m, 10H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2 (m, 1H), 7.3 (m, 1H), 7.5 (m, 2H), 8.7 (m, 2H).
129	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[5-chloro-2-(methyloxy)phenyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hy droxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =787.2, C40H52Cl2N4O8 +H requires 787.3240. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.0-3.6 (m, 10H), 3.3 (s, 3H), 3.85 (s, 3H), 5.2 (s, 1H), 6.8 (d, 1H), 6.85 (s, 1H), 6.95-7.05 (m, 2H), 7.2-7.3 (m, 2H).
130	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(3,5-dichlorophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =, C39H49Cl3N4O7 +H requires 791.2745. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.0-3.6 (m, 10H), 3.3 (s, 3H), 3.45-3.7 (m, 4H), 5.2 (s, 1H), 6.7-6.8 (m, 2H), 6.9-7.0 (m, 2H), 7.2-7.3 (m, 2H).
131	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[(2E)-3-phenylprop-2-enyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydrox y-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =763.3, C42H55ClN4O7 +H requires 763.3838. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.55-3.75 (m, 8H), 5.2 (s, 1H), 6.2 (m, 1H), 6.8 (d, 1H), 7.0 (dd, 1H), 7.2(d, 1H), 7.25 (m, 1H), 7.3-7.45 (m, 5H).
132	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(diphenylmethyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl - 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =813.3, C46H57ClN4O7 +H requires 813.3994. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.9-3.8 (m, 6H), 3.3 (s, 3H), 4.5 (s, 1H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.15-

		7.4 (m, 8H), 7.45-7.55 (m, 4H).
133	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =751.3, C41H55ClN4O7 +H requires 751.3838. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.2 (s, 3H), 2.3 (s, 3H), 3.0-3.2 (m, 10H), 3.3 (s, 3H), 4.5 (s, 1H), 5.2 (s, 1H), 6.9-7.05 (m, 4H), 7.25-7.35 (m, 2H).
134	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(4-cyclopentylpiperazin-1-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2, 3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =715.3, C38H55ClN4O7 +H requires 715.3838. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.6-1.7 (m, 4H), 1.7 (s, 3H), 1.8-2.0 (m, 5H), 2.1 (s, 3H), 3.3 (s, 3H), 3.6-3.8 (m, 8H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2-7.3 (m, 2H).
135	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2-ethylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =751.3, C41H55ClN4O7 +H requires 751.3838. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2-1.3 (m, 6H), 1.7 (s, 3H), 2.1 (s, 3H), 2.8-3.2 (m, 11H), 3.3 (s, 3H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.1-7.3 (m, 7H).
136	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[4-chloro-3-(trifluoromethyl)phenyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro -9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =825.2, C40H49Cl2F3N4O7 +H requires 825.3009. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.25 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.5-3.7 (m, 4H), 5.2 (s, 1H), 6.8-7.0 (m, 2H), 7.1-7.3 (m, 3H), 7.4 (d, 1H).

137	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(thien-2-ylcarbonyl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =757.2, C38H49ClN4O8S +H requires 757.3038. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.9-3.1 (m, 4H), 3.3 (s, 3H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.1 (m, 1H), 7.2-7.3 (m, 2H), 7.35 (m, 1H), 7.55 (m, 1H).
138	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(4-{[(butylamino)carbonyl]oxy}piperidin-1-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =761.3, C39H57ClN4O9 +H requires 761.3892. NMR (CDCl3, selected data) : 0.8 (d, 3H), 0.95 (t, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.15-3.3 (m, 4H), 3.3 (s, 3H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2 (m, 1H), 7.3 (m, 1H).
139	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2,4-dimethylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =751.3, C41H55ClN4O7 +H requires 751.3838. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.25 (s, 3H), 2.3 (s, 3H), 2.5-2.7 (m, 8H), 3.0-3.2 (m, 4H), 3.3 (s, 3H), 3.7-3.85 (m, 2H), 5.2 (s, 1H), 6.9-7.1 (m, 4H), 7.2-7.3 (m, 2H).
140	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2,5-dimethylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =751.4, C41H55ClN4O7 +H requires 751.3838. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.0 (s, 3H), 2.15 (s, 3H), 2.3 (s, 3H), 2.8-3.4 (m, 11H), 5.2 (s, 1H), 6.75-6.85 (m, 2H), 6.9-7.1 (m, 2H), 7.15 (m, 1H), 7.25 (m, 1H).
141	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(4-cyclopropylpiperazin-1-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2, 3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-	MS (ES) : M/Z [MH+] =687.3, C36H51ClN4O7 +H requires 687.3524. NMR (CDCl3, selected data) : 0.8 (d, 3H), 0.9-1.0 (m, 2H), 1.1-1.25 (m, 6H),

	carboxylate	1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.6-3.8 (m, 8H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2-7.3 (m, 2H).
142	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(cyclopentylcarbonyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =743.3, C39H55ClN4O8 +H requires 743.3787. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.75-2.9 (m, 6H), 3.0-3.2 (m, 2H), 3.3 (s, 3H), 3.5-4.2 (m, 11H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2-7.3 (m, 2H).
143	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[6-(methyloxy)pyridin-2-yl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =754.3, C39H52ClN5O8 +H requires 754.3583. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 3.4-3.9 (m, 10H), 3.85 (m, 3H), 5.2 (s, 1H), 6.15-6.25 (m, 2H), 7.0 (dd, 1H), 7.2-7.3 (m, 2H), 7.5 (m, 1H).
144	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =751.3, C41H55ClN4O7 +H requires 751.3838. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.3 (s, 6H), 3.3 (s, 3H), 3.3-3.9 (m, 8H), 5.2 (s, 1H), 6.8 (s, 2H), 6.9 (s, 1H), 7.0 (dd, 1H), 7.2-7.3 (m, 2H).
145	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(3,6-dimethylpyrazin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydrox y-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =753.3, C39H53ClN6O7 +H requires 753.3743. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.5 (s, 3H), 2.55 (s, 3H), 2.9-3.1 (m, 4H), 3.3 (s, 3H), 3.5-3.9 (m, 6H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2-7.3 (m, 2H), 8.05 (s, 1H).

146	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2,6-dimethylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =751.3, C41H55ClN4O7 +H requires 751.3838. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.25 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.3-2.4 (m, 6H), 2.8-3.1 (m, 10H), 3.3 (s, 3H), 5.2 (s, 1H), 6.9-7.1 (m, 4H), 7.2-7.3 (m, 2H).
147	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[(1S)-1-methyl-2-pyridin-3-ylethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahyd ropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =640.3, C34H42ClN3O7 +H requires 640.2790. NMR (CDCl3, selected data) : 0.8 (d, 3H), 0.9 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2-7.35 (m, 2H), 7.8 (dd, 1H), 8.2 (d, 1H), 8.7 (d, 1H), 8.75 (s, 1H).
148	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =688, C36H50ClN3O8 +H requires 688.3. HPLC: 3.99 mins.
149	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(4-methylpentanoyl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5 -methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =745, C39H57ClN4O8 +H requires 745.4. HPLC: 4.24 mins.
150	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(4-oxo-1,3,4,6,7,11b-hexahydro-2H-pyrazino[2,1-a]isoquinolin-2-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3 aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =763, C41H51ClN4O8 +H requires 763.3. HPLC: 6.46 mins.
151	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[3-[(ethyloxy)carbonyl]octahydroisoquinolin-2(1H)-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-	MS (ES) : M/Z [MH+] =772, C41H58ClN3O9 +H requires 772.4. HPLC: 5.64 mins.

carboxylate

152	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[3,5-bis(methyloxy)phenyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydrox y-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =783.1, C41H55ClN4O9 +H requires 783.3736. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.25 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.9-3.3 (m, 6H), 3.3 (s, 3H), 3.35-3.75 (m, 4H), 3.8 (s, 6H), 5.25 (s, 1H), 6.1 (s, 2H), 6.15 (s, 1H), 7.0 (dd, 1H), 7.2 (d, 1H), 7.3 (d, 1H).
153	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2-cyanophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =722.1, C40H50ClN5O7 +H requires 722.3572. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.25 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.3-3.25 (m, 15H), 3.3 (s, 3H), 5.25 (s, 1H), 7.0 (dd, 1H), 7.15-7.4 (m, 7H).
154	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(4-phenylpiperidin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a, 5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =748.1, C40H52ClN3O7 +H requires 748.3477. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.0-3.2 (m, 4H), 3.3 (s, 3H), 3.5-3.65 (m, 4H), 3.7-3.9 (m, 2H), 5.3 (s, 1H), 7.0 (dd, 1H), 7.15-7.3 (m, 4H), 7.55-7.65 (m, 2H).
155	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(3,4-dimethylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =751.1, C41H55ClN4O7 +H requires 751.3838. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.2 (s, 3H), 2.25 (s, 3H), 3.0-3.2 (m, 4H), 3.3 (s, 3H), 3.4-4.0 (m, 6H), 5.2 (s, 1H), 6.75 (d, 1H), 6.8 (s, 1H), 7.0 (dd, 1H),

		7.1 (d, 1H), 7.2 (d, 1H), 7.3 (d, 1H).
156	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[cyclopropyl(propanoyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2, 3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =674.3, C35H48ClN3O8 +H requires 674.3208. NMR (CDCl3, selected data) : 0.8 (d, 3H), 0.95 (d, 3H), 1.1 (t, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2 (d, 1H), 7.35 (d, 1H).
157	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(cyclopropylcarbonyl)(phenyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-meth yl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =722.3, C39H48ClN3O8 +H requires 722.3208. NMR (CDCl3, selected data) :0.5-0.7 (m, 2H), 0.8 (d, 3H), 0.95 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.3 (s, 3H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2-7.5 (m, 7H).
158	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(cyclohexylmethyl)(cyclopropylcarbonyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydr oxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =742.3, C40H56ClN3O8 +H requires 742.3834. NMR (CDCl3, selected data) : 0.7-0.8 (m, 2H), 0.85 (d, 3H), 0.9-1.1 (m, 8H), 1.7 (s, 3H), 2.1 (s, 3H), 2.4-2.7 (m, 7H), 3.3 (s, 3H), 5.2 (s, 1H), 6.9 (dd, 1H), 7.2-7.3 (m, 2H).
159	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(cyclohexylmethyl)(propanoyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-meth yl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =730.3, C39H56ClN3O8 +H requires 730.3834. NMR (CDCl3, selected data) : 0.85 (d, 3H), 0.95 (d, 3H), 1.6-1.9 (m, 9H), 2.1 (s, 3H), 3.3 (s, 3H), 5.2 (s, 1H), 6.9 (dd, 1H), 7.2-7.3 (m, 2H).
160	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(cyclopropylcarbonyl)(methyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-meth yl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =660.3, C34H46ClN3O8 +H requires 660.3052. NMR (CDCl3, selected data) : 0.7-0.85 (m, 2H), 0.85 (d, 3H), 0.9-1.1 (m, 6H), 1.7 (s, 3H), 2.1 (s,

		3H), 3.2 (s, 3H), 3.3 (s, 3H), 5.2 (s, 1H), 7.0 (dd, 1H), 7.2-7.3 (m, 2H).
161	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[methyl(phenylcarbonyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2, 3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =696.2, C37H46ClN3O8 +H requires 696.3052. NMR (CDCl3, selected data) : 0.8 (m, 3H), 1.1 (m, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 3.0 (s, 3H), 3.3 (s, 3H), 5.1-5.2 (m, 2H), 7.0 (dd, 1H), 7.2-7.4 (m, 7H).
162	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{methyl[(phenyloxy)acetyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1 ,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =726.2, C38H48ClN3O9 +H requires 726.3157. NMR (CDCl3, selected data) : 0.8-0.95 (m, 3H), 1.4-1.5 (m, 7H), 1.7 (s, 3H), 2.1 (s, 3H), 2.85 (s, 3H), 3.3 (s, 3H), 5.2 (m, 1H), 6.85-7.0 (m, 4H), 7.15-7.4 (m, 4H).
163	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(4-amino-5-cyano-6-methylpyrimidin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chlor o-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =779.2, C39H51ClN8O7 +H requires 779.3647. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.1 (d, 2H), 1.6 (s, 3H), 2.1 (s, 3H), 2.3 (s, 3H), 3.2 (s, 3H), 3.65-4.0 (m, 10H), 5.1 (s, 1H), 7.05 (dd, 1H), 7.2 (m, 1H), 7.4 (d, 1H).
164	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(2S,5R)-2,5-dimethyl-4-prop-2-enylpiperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro -9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =715, C38H55ClN4O7 +H requires 715.4. HPLC: 4.05 mins.
165	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(8-azabicyclo[3.2.1]oct-8-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl- 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxa- ɪɜ-2-carboxylate	MS (ES) : M/Z [MH+] =672, C36H50ClN3O7 +H requires 672.3. HPLC: 4.05 mins.

166	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(3S,8aR)-3-(phenylmethyl)hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3 aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =777, C43H57ClN4O7 +H requires 777.4. HPLC: 4.37 mins.
167	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(3-{[(3,4-difluorophenyl)methyl]oxy}piperidin-1-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chlor o-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =788, C41H52ClF2N3O8 +H requires 788.3. HPLC: 4.43 mins.
168	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(3R)-3-(methyloxy)piperidin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =676, C35H50ClN3O8 +H requires 676.3. HPLC: 7.16 mins.
169	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[1-methyl-6,7-bis(methyloxy)-3,4-dihydroisoquinolin-2(1H)-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9b R)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =768, C41H54ClN3O9 +H requires 768.3. HPLC: 4.11 mins.
170	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(2-methyl-4-piperidin-1-yl-5,8-dihydropyrido[3,4-d]pyrimidin-7(6H)-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =793, C42H57ClN6O7 +H requires 793.4. HPLC: 4.3 mins.
171	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(4-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9b R)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =793, C42H49Cl2N3O7S +H requires 810.

172	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(3-{[4-(methyloxy)phenyl]sulfanyl}-8-azabicyclo[3.2.1]oct-8-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR, 9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =810, C43H56ClN3O8S +H requires 810.4. HPLC: 4.49 mins.
173	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(4-methylpiperazin-1-yl)piperidin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydr oxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =744, C39H58ClN5O7 +H requires 744.4. HPLC: 1.71 mins.
174	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{3-[(3-chloropyridin-2-yl)oxy]piperidin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-h ydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =773, C39H50Cl2N4O8 +H requires 773.3. HPLC: 4.37 mins.
175	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(3-methylquinoxalin-2-yl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hyd roxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =789, C42H53ClN6O7 +H requires 789.4. HPLC: 4.3 mins.
176	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-[7-(hydroxymethyl)-3-azabicyclo[3.3.1]non-3-yl]-1-methylethyl}-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b -hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =716, C38H54ClN3O8 +H requires 716.4. HPLC: 3.99 mins.
177	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(3,11-diazatricyclo[7.3.1.0~2,7~]trideca-2,4,6-trien-11-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR) -6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =735, C40H51ClN4O7 +H requires 735.4. HPLC: 4.05 mins.
178	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(4,10-diazatricyclo[6.3.1.0~2,7~]dodeca-2,4,6-trien-10-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)- 6-	MS (ES) : M/Z [MH+] =721, C39H49ClN4O7 +H requires 721.3. HPLC: 3.67 mins.

	chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	
179	-	MS (ES) : M/Z [MH+] =748, C42H54ClN3O7 +H requires 748.4. HPLC: 4.56 mins.
180	(1S,2R,4aS,5S,8R,8aR)-5-{2-[(4aR,9aS)-2,3,4,4a,9,9a-hexahydro-1H-indeno[2,1-b]pyridin-1-yl]-1-methylethyl}-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR ,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =734, C41H52ClN3O7 +H requires 734.4. HPLC: 4.37 mins.
181	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(3-cyclohexyl-3-methylpiperidin-1-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5 -methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =742, C41H60ClN3O7 +H requires 742.4. HPLC: 4.68 mins.
182	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-(4-{2-[(2-hydroxyethyl)oxy]ethyl}piperazin-1-yl)-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9 b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =742, C41H60ClN3O7 +H requires 742.4. HPLC: 4.68 mins.
183	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(3-methyl-3-pyridin-2-ylpiperidin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy -5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =737, C40H53ClN4O7 +H requires 737.4. HPLC: 4.37 mins.
184	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(3,5-dichloropyridin-4-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hy droxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =793, C38H48Cl3N5O7 +H requires 792.3. HPLC: 4.37 mins.

185	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(3S)-3-methyl-3-phenylpiperidin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =736, C41H54ClN3O7 +H requires 736.4.
186	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{3-[(4-fluorophenyl)sulfanyl]-8-azabicyclo[3.2.1]oct-8-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)- 6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =798, C42H53ClFN3O7S +H requires 798.3. HPLC: 4.49 mins.
187	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[(pyridin-2-ylsulfanyl)methyl]piperidin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9 b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =769, C40H53ClN4O7S +H requires 769.3. HPLC: 4.3 mins.
188	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{3-[(pyridin-2-ylsulfanyl)methyl]piperidin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9 b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =769, C40H53ClN4O7S +H requires 769.3. HPLC: 4.3 mins.
189	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(2-{[methyl(methyloxy)amino]carbonyl}piperidin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chlo ro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =733, C37H53ClN4O9 +H requires 733.4. HPLC: 4.05 mins.
190	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[(3,4-dichlorophenyl)methyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b- hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =806, C40H51Cl3N4O7 +H requires 805.3. HPLC: 4.62 mins.

191	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[2-(2-piperidin-1-ylethyl)piperidin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =757, C41H61ClN4O7 +H requires 757.4. HPLC: 1.71 mins.
192	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(1-methylethyl)(2-{[2-(methyloxy)phenyl]oxy}ethyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6 -chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =770, C41H56ClN3O9 +H requires 770.4. HPLC: 4.3 mins.
193	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[methyl(2-phenylcyclopropyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =708, C39H50ClN3O7 +H requires 708.3. HPLC: 4.43 mins.
194	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{methyl[3-(1,2,4,5-tetrahydro-3H-3-benzazepin-3-yl)propyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR ,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =779, C43H59ClN4O7 +H requires 779.4. HPLC: 3.73 mins.
195	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[{2-[(2,6-dichlorophenyl)oxy]ethyl}(methyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro- 9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =781, C38H48Cl3N3O8 +H requires 780.3. HPLC: 4.43 mins.
196	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[[(4-chlorophenyl)methyl](ethyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =730, C38H49Cl2N3O7 +H requires 730.3. HPLC: 4.3 mins.
197	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{methyl[(3-methylthien-2-yl)methyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-	MS (ES) : M/Z [MH+] =702, C36H48ClN3O7S +H requires 702.3. HPLC: 4.24 mins.

	chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	
198	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(3-chloro-4-methylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hyd roxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =771, C40H52Cl2N4O7 +H requires 771.3. HPLC: 4.56 mins.
199	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(diphenylmethyl)(methyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methy l-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =758, C43H52ClN3O7 +H requires 758.4.
200	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[5-methyl-2-(methyloxy)phenyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9 b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =767, C41H55ClN4O8 +H requires 767.3. HPLC: 4.43 mins.
201	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[2-(ethyloxy)phenyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =767, C41H55ClN4O8 +H requires 767.3. HPLC: 4.43 mins.
202	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{(2S,4R)-4-methyl-2-[(methyloxy)carbonyl]piperidin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =718, C37H52ClN3O9 +H requires 718.3.
203	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-{2-[(2S)-2-(2-hydroxyethyl)piperidin-1-yl]-1-methylethyl}-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy -5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =690, C36H52ClN3O8 +H requires 690.4.

204	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(3S)-3-(methyloxy)piperidin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =676, C35H50ClN3O8 +H requires 676.3.
205	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{2-[(methyloxy)carbonyl]octahydro-1H-indol-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aS,9bS)-6-chloro-9 b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =744, C39H54ClN3O9 +H requires 744.4.
206	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(2S)-4-methyl-2-[(methyloxy)carbonyl]-3,6-dihydropyridin-1(2H)-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S, 3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =716, C37H50ClN3O9 +H requires 716.3.
207	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-(3-hydroxy-8-azabicyclo[3.2.1]oct-8-yl)-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy -5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =688, C36H50ClN3O8 +H requires 688.3.
208	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(3-methyl-3-phenylpiperidin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-met hyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =736, C41H54ClN3O7 +H requires 736.4.
209	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{(phenylmethyl)[2-(phenyloxy)ethyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] =788, C44H54ClN3O8 +H requires 788.4.

210	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-((1R)-1-methyl-2-{4-[4-(trifluoromethyl)-2-pyrimidinyl]-1-piperazinyl}ethyl)-1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenyl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate – TFA salt	MS (ES) : M/Z (M+H) 793.4; C38H48ClF3O7N6 + H requires 793.1. H-NMR (CDCl3, selected data): 0.85 (d, 3H), 3.30 (s, 3H), 4.30 (m, 1H), 5.20 (s, 1H), 5.25 (s, 1H), 5.40 (m, 1H), 5.50 (m, 1H), 6.90 (d, 1H), 7.05 (t, 1H), 7.25 (d, 1H), 7.45 (d, 1H), 8.55 (d, 1H)
211	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-((1R)-1-methyl-2-{4-[5-(trifluoromethyl)-2-pyridinyl]-1-piperazinyl}ethyl)-1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenyl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate– TFA salt	MS (ES) : M/Z (M+H) 792.5; C39H49ClF3O7N5 + H requires 792. 1H-NMR (CDCl3, selected data): 0.90 (d, 3H), 3.30 (s, 3H), 4.30 (m, 1H), 5.20 (s, 1H), 5.25 (s, 1H), 5.40 (m, 1H), 5.50 (m, 1H), 6.65 (d, 1H), 7.05 (t, 1H), 7.25 (d, 1H), 7.50 (d, 1H), 7.75 (d, 1H), 8.45 (s, 1H).
212	(1S,2R,5S,8R,8aR)-2-(acetyloxy)-5-((1R)-2-{4-[bis(4-fluorophenyl)methyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ESI) : M/Z [MH+] = 849.2, C46H55ClF2N4O7 + H requires 849.3806. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.7-3.20 (m, 12H), 3.3 (s, 3H), 4.1 (m, 1H), 4.4 (s, 1H), 5.1 (s, 1H), 5.2 (s, 1H), 5.3 (s, 1H), 5.5 (s, 1H), 7.00-7.5 (m, 11H).
213	(1S,2R,5S,8R,8aR)-2-(acetyloxy)-5-{(1R)-2-[4-(5-chloropyrimidin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ESI) : M/Z [MH+] = 759.1, C37H48Cl2N6O7 + H requires 759.3040. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.2 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.4-3.1 (m, 8H), 3.3 (s, 3H), 4.1 (m, 1H), 4.7-4.9 (m, 2H), 5.1 (s, 1H), 5.2 (s, 1H), 5.3 (s, 1H), 5.5 (s, 1H), 7.0-7.3 (m, 3H), 8.3 (s, 2H).

214	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{(1R)-2-[4-(5-bromopyrimidin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ESI) : M/Z [MH+] = 805.3, C37H48BrClN6O7 + H requires 803.2535. NMR (CDCl3, selected data) : 0.8 (d, 3H), 1.1 (d, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.3-2.6 (m, 8H), 3.3 (s, 3H), 3.6-3.8 (m, 5H), 4.1 (m, 1H), 5.1-5.2 (m, 2H), 5.3 (s, 1H), 5.6 (s, 1H), 7.0-7.4 (m, 3H), 8.3 (s, 2H).
215	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{(1R)-2-[4-(6-chloro-1,3-benzothiazol-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ESI) : M/Z [MH+] = 814.3, C40H49Cl2N5O7S + H requires 814.2808. NMR (CDCl3, selected data) : 0.8 (m, 3H), 1.1 (m, 3H), 1.7 (s, 3H), 2.1 (s, 3H), 2.3-2.8 (m, 8H), 3.3 (s, 3H), 3.5-3.8 (m, 4H), 4.1 (m, 1H), 5.1-5.4 (m, 4H), 5.6 (s, 1H), 7.0-7.6 (m, 6H).
216	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-((1R)-2-{4-[(3,4-dichlorophenyl)methyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	NMR (CDCl3, selected data) : 0.8 (m, 3H), 1.1 (m, 3H), 1.5 (s, 5H), 1.7 (s, 3H), 2.1 (s, 3H), 2.4-2.8 (m, 8H), 3.35 (s, 3H), 3.6 (s, 1H), 4.1 (m, 1H), 5.1-5.6 (m, 4H), 6.7-7.4 (m, 6H).
217	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-((1R)-1-methyl-2-{4-[5-(trifluoromethyl)pyrimidin-2-yl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ESI) : M/Z [MH+] = 793.4, C38H48ClF3N6O7 + H requires 793.3303. NMR (CDCl3, selected data) : 0.8 (m, 3H), 1.2 (m, 3H), 1.7 (s, 3H), 2.5 (m, 2H), 2.6 (s 3H), 2.8 (s, 1H), 3.1 (m, 2H), 3.3 (s, 3H), 4.1 (m, 1H), 5.1 (m, 2H), 5.3 (s, 1H), 5.5 (s, 1H), 7.0-7.1 (m, 1H), 7.2-7.4 (m, 3H), 8.6 (s, 2H).
218	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-((1R)-2-{4-[(4-chlorophenyl)oxy]piperidin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-	MS (ES) : M/Z [MH+] = 770, C40H51Cl2N3O8 + H requires 772.3131. NMR (CDCl3, selected data) : 0.8 (m, 3H), 1.1 (m, 3H), 1.3 (m, 4H), 1.7

	c][2,1]benzoxazine-2-carboxylate	(s, 3H), 2.1 (s, 3H), 2.2 (s, 1H), 3.1 (s, 1H), 3.3 (s, 3H), 3.6 (s, 1H), 4.1 (m, 1H), 4.25 (s, 1H), 5.1 (m, 2H), 5.3 (s, 1H), 5.6 (s, 1H), 6.8 (d, 2H), 7.0 (dd, 1H), 7.2-7.3 (m, 3H), 7.35 (d, 1H).

Table of precursors

Ex No.	Name of Terpene Alkaloid Precursor	Preparation Number of TA Precursor
1	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	1
2	(1S,2R,4aS,5R,8R,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzox azine-2-carboxylate	139
3	(1S,2R,4aS,5R,8R,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzox azine-2-carboxylate	139
4	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydr opyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	140

5	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydr opyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	140
6	(1S,2R,4aS,5R,8R,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzox azine-2-carboxylate	139
7	(1S,4aS,5S,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine -2-carboxylate	144
8	(1S,4aS,5S,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine -2-carboxylate	144
9	(1S,4aS,5S,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine -2-carboxylate	144
10	(1S,4aS,5S,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine -2-carboxylate	144

11	(1S,2R,4aS,5R,8R,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzox azine-2-carboxylate	139
12	(1S,2R,4aS,5R,8R,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzox azine-2-carboxylate	139
13	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-{2-[(1H-imidazol-1-ylcarbonyl)oxy]-1-methylethyl}-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	143
14	(1S,2R,4aS,5R,8R,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzox azine-2-carboxylate	139
15	(1S,2R,4aS,5R,8R,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzox azine-2-carboxylate	139
16	(1S,2R,4aS,5R,8R,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzox azine-2-carboxylate	139

17	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
18	2-[(1R,2R,4aS,5R,8S,8aS)-2-(acetyloxy)-5-(2,2-difluoro-1-methylvinyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenyl] 3-(tert-butyl) (2S,3aR,9bR)-9b-[(tert-butoxycarbonyl)oxy]-6-chloro-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	156
19	2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethyle thyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	157
20	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
21	(1S,2R,4aS,5R,8R,8aR)-5-(2-ethyl-1,3-thiazol-4-yl)-1,8a-dihydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-2-yl acetate	166
21	(2S,3aR,9bR)-6-chloro-3-[[(1,1-dimethylethyl)oxy]carbonyl]-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylic acid	153

22	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2,2-difluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimeth ylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	167
23	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2,2-difluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimeth ylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	168
24	2-[(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-(2,2-dichloro-1-methylethenyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl] 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethyl ethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	172
25	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
26	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

27	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
28	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
29	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
30	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
31	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

32	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
33	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
34	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
35	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
36	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

37	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
38	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
39	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
40	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
41	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

42	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
43	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
44	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
45	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
46	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

47	2-[(1S,2R,4aS,5S,8R,8aR)-5-{2-[acetyl(cyclopropyl)amino]-1-methylethyl}-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl] 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9 b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	177
48	2-[(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{cyclopropyl[(methyloxy)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl] 3-(1,1-dimethylethyl) (2S,3aR,9b R)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	179
49	2-[(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{ethyl[(methyloxy)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl] 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-c hloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	178
50	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

51	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
52	2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{cyclopropyl[(ethylamino)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl] 3-(1,1-dimethylethyl) (2S,3aR,9 bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	180
53	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
54	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

55	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
56	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
57	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
58	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

59	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
60	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
61	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
62	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

63	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
64	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
65	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
66	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

67	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
68	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
69	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
70	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

71	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
72	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
73	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
74	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

75	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
76	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
77	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
78	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

79	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
80	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
81	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
82	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

83	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
84	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
85	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
86	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

87	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
88	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
89	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
90	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

91	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
92	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
93	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
94	(2R)-2-[(1R,4R,4aS,5R,6R)-5-({[(2S,3aR,9bR)-6-chloro-3-{[(1,1-dimethylethyl)oxy]carbonyl}-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazin-2-yl] carbonyl}oxy)-6-(acetyloxy)-4a-hydroxy-4,7-dimethyl-1,2,3,4,4a,5,6,8a-octahydronaphthalen-1-yl]propanoic acid	181

95	(2R)-2-[(1R,4R,4aS,5R,6R)-5-({[(2S,3aR,9bR)-6-chloro-3-{[(1,1-dimethylethyl)oxy]carbonyl}-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazin-2-yl] carbonyl}oxy)-6-(acetyloxy)-4a-hydroxy-4,7-dimethyl-1,2,3,4,4a,5,6,8a-octahydronaphthalen-1-yl]propanoic acid	181
96	(1S,2R,4aR,8R,8aR)-8a-hydroxy-2-[(1H-imidazol-1-ylcarbonyl)oxy]-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	142
97	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
98	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

99	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
100	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
101	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
102	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

103	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
104	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
105	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
106	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

107	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
108	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
109	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
110	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

111	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
112	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
113	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
114	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

115	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
116	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
117	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
118	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

119	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
120	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
121	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
122	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

123	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
124	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
125	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
126	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

127	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
128	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
129	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
130	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

131	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
132	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
133	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
134	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

135	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
136	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
137	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
138	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

139	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
140	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
141	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
142	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

143	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
144	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
145	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
146	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

147	2-[(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl] 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carb onyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	152
148	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
149	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
150	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141

151	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
152	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
153	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
154	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
155	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

156	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
157	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
158	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
159	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

160	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
161	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
162	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
163	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

164	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
165	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
166	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
167	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141

168	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
169	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
170	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
171	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141

172	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
173	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
174	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
175	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141

176	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
177	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
178	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
179	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141

180	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
181	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
182	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
183	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141

184	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
185	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
186	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
187	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141

188	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
189	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
190	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
191	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141

192	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
193	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
194	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
195	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141

196	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
197	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
198	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
199	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141

200	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
201	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
202	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
203	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141

204	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
205	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
206	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
207	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141

208	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
209	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141
210	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	159
211	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	159

212	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
213	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
214	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
215	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160

216	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
217	2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate	160
218	(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyr rolo[2,3-c][2,1]benzoxazine-2-carboxylate	141

The synthesis of a number of representative compounds are now described in more detail and the remaining compounds may be prepared in an analogous manner.

Example 1 : (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2, 1]benzoxazine-2-carboxylate

To a solution of (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 1, 200 mg) in isopropanol (20 ml) was added platinum on carbon (10% w/w, 20 mg) and the resulting mixture was hydrogenated at room temperature with stirring under 1 atmosphere pressure of hydrogen for 18 hours. The mixture was filtered through celite and concentrated *in vacuo* to give a white solid. The solid was purified by preparative HPLC (1 inch diameter Ultrasphere C18 column, 2 injections, 70:30 acetonitrile:water) to give the product as a white solid (89 mg).

Example 2: (1S,2R,4aS,5R,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-2-[(2-methylpropanoyl)oxy]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of (1S,2R,4aS,5R,8R,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 139, 25mg, 0.05mmol) and 4-dimethylaminopyridine (6mg, 0.05mmol) in dichloromethane (2ml) was added *iso*butyric anhydride (17mg, 0.11mmol) and the resulting mixture stood at room temperature for 18 h. The crude product was purified by column chromatography on a Sepak® silica (1.5g) cartridge eluting with hexane : dichloromethane (1:1, 2ml) then hexane : ethyl acetate (4:1 then 2:1 then 1:1, 3ml each). The pure fractions were combined and concentrated *in vacuo* to give the title compound (11mg, 37%).

Example 3: (1S,2R,4aS,5R,8R,8aR)-2-(hexanoyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl

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(2S,3aR,9bR)-6-chl ro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2, 3-c][2,1]benzoxazine-2-carboxylate

To a solution of (1S,2R,4aS,5R,8R,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 139, 51mg, 0.10mmol) and 4-dimethylaminopyridine (14mg, 0.11mmol) in dichloromethane (5ml) was added hexanoic anhydride (43mg, 0.2mmol) and the resulting mixture stood at room temperature over a weekend. The crude product was purified by column chromatography over silica (10g) eluting with hexane : ethyl acetate (2:1). The pure fractions were combined and concentrated *in vacuo* to give the title compound (43mg, 97%).

Example 4: (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2-(acetyloxy)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexa hydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To ((1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 140, 63.8mg, 0.11mmol) in dichloromethane (1.1ml) was added acetic anhydride (22mg, 20□l, 0.22mmol) and 4-dimethylaminopyridine (14.3mg, 0.12mmol) and the reaction mixture stirred at room temperature for 18 hours. The reaction mixture was diluted with dichloromethane (20ml) and washed with aqueous citric acid solution, dried ($MgSO_4$) and concentrated *in vacuo* to give a gum. The crude product was purified by chromatography on silica eluting with hexane : ethyl acetate (60:40). The pure fractions were combined and concentrated *in vacuo* to give the title product as a white solid (42mg, 61%).

Example 5: (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(2-methylpropanoyl)oxy]ethyl}-1,2,4a,5,6,7,8,8a-

octahydronaphthalen-1-yl(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 140, 100mg, 0.17mmol) and 4-dimethylaminopyridine (21mg, 0.35mmol) in dichloromethane (5ml) at <0°C was added *i*sobutyric anhydride (0.06ml, 0.35mmol) and the resulting mixture allowed to warm to room temperature over 30 minutes. After 3 hours the reaction mixture was treated with water (5ml) and extracted with dichloromethane (2 x 5ml). The combined organic layers were washed with saturated aqueous sodium chloride solution and concentrated *in vacuo*. The crude product was purified by column chromatography on silica eluting with hexane : ethyl acetate (1:1 to 1:2).The pure fractions were combined and concentrated *in vacuo* to give the title compound (48mg, 43%).

Example 6: (1S,2R,4aS,5R,8R,8aR)-2-[(cyclopropylcarbonyl)oxy]-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of (1S,2R,4aS,5R,8R,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 139, 100mg, 0.19mmol) and 4-dimethylaminopyridine (30mg, 0.25mmol) in tetrahydrofuran (10ml) was added cyclopropanecarboxylic acid (400mg, 4.7mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (90mg, 0.58mmol) and the resulting mixture stirred at room temperature for 18 h. The reaction mixture was passed through a Sepak® cartridge (silica, 1.5g) to remove

insoluble material and the solvent removed *in vacuo*. The crude product was purified to give the title compound (20mg, 18%).

Example 7: (1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethyl)-2-{[(prop-2-ynyloxy)carbonyl]oxy}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydro pyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To (1S,4aS,5S,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 144, 500mg, 0.96mmol) and 4-dimethylaminopyridine (350mg, 2.9mmol) in dichloromethane (25ml) at 0°C under nitrogen was added propargyl chloroformate (170mg, 1.44mmol) and the resulting mixture stirred at 0°C for 30 minutes and at room temperature for 3 hours. The reaction mixture was diluted with dichloromethane (100ml) and washed with citric acid solution (3 x 50ml) and water (2 x 50ml), dried ($MgSO_4$) and concentrated *in vacuo* to give a solid. The crude product was purified by flash chromatography on silica (40g) eluting with hexane : ethyl acetate (3:2). The pure fractions were combined and concentrated *in vacuo* to give the title product (462mg, 80%).

Example 8: (1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethyl)-2-({[(2,2,2-trichloroethyl)oxy]carbonyl}oxy)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate
The title compound was prepared by the method of Example 9 substituting *iso*propenyl chloroformate with 2,2,2-trichloroethyl chloroformate (30.5mg, 0.14 mmol) to give the title product (55mg, 82%).

Example 9: (1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-2-({[(1-methylethenyl)oxy]carbonyl}oxy)-5-(1-methylethyl)-1,2,4a,5,6,7,8,8a-

octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To (1S,4aS,5S,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 144, 50mg, 0.096mmol) and 4-dimethylaminopyridine (35mg, 0.29mmol) in dichloromethane (5ml) at 0°C under nitrogen was added *isopropenyl* chloroformate (17.4mg, 0.144mmol) and the resulting mixture stirred at 0°C for 30 minutes and at room temperature for 2 hours. The reaction mixture was diluted with dichloromethane (25ml) and washed with citric acid solution (3 x 15ml), dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by chromatography on silica (5g) eluting with hexane : ethyl acetate (1:1). The pure fractions were combined and concentrated *in vacuo* to give the title product (56mg, 96%).

Example 10 : ((1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethyl)-2-{[(prop-2-enyloxy)carbonyl]oxy}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

Allyl chloroformate (17.4 mg) was added to a stirred, cooled (0 °C) solution of (1S,4aS,5S,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine -2-carboxylate (Preparation 144, 50 mg) and 4-dimethylaminopyridine (35 mg) in dichloromethane (5 ml) under an atmosphere of nitrogen. After 30 minutes, the reaction was allowed to warm to room temperature over 15 hours. The reaction mixture was diluted with dichloromethane (25 ml), washed with aqueous citric acid (10% w/w, 3 x 15 ml) and dried ($MgSO_4$). After evaporation of solvent *in vacuo*, the residue was purified by flash column chromatography

on silica (5 g) eluting with 1:1 ethyl acetate:hexane to give the product (44 mg, 76%).

Example 11: (1S,2R,4aS,5S,8R,8aR)-1-({[(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazin-2-yl]carbonyl}oxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a- octahydronaphthalen-2-yl methyl butanedioate

A mixture of (1S,2R,4aS,5R,8R,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 139, 100mg, 0.19mmol), commercially available 4-(methyloxy)-4-oxobutanoic acid (50mg, 0.38mmol), 4-dimethylaminopyridine (60mg, 0.5mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (90mg, 0.58mmol) and dichloromethane (5ml) was stirred for 18 h and the reaction mixture concentrated *in vacuo*. The crude product was purified by chromatography on a Biotage® 12M column eluting with dichloromethane : diethyl ether (4:1). The pure fractions were combined and the solvent removed *in vacuo* to give the title product (23mg, 18%).

Example 12: (1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-2-(pent-4-enoyloxy)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2 ,3-c][2,1]benzoxazine-2-carboxylate

The title compound was prepared by the method of Example 11 substituting 4-(methyloxy)-4-oxobutanoic acid with commercially available pent-4-enoic acid (50mg, 0.50mmol) to give the title compound (64mg, 56%).

Example 13: (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[({[2-(naphthalen-1-ylamino)ethyl]amino}carbonyl)oxy]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-{2-[(1H-imidazol-1-ylcarbonyl)oxy]-1-methylethyl}-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 143, 80 mg, 0.12 mmol) in pyridine (5 ml) was added 4-dimethylaminopyridine (16 mg, 0.13 mmol) followed by *N*-1-naphthyethylenediamine dihydrochloride salt (32 mg, 0.12 mmol). After stirring the reaction mixture for 48 h, the reaction mixture was concentrated *in vacuo* and purified by flash chromatography eluting with hexane : ethyl acetate (2 : 1 and then 1 : 1) to give the pure title compound.

Example 14: (1S,2R,4aS,5R,8R,8aR)-2-{[(acetyloxy)acetyl]oxy}-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To (1S,2R,4aS,5R,8R,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 139, 210mg, 0.4mmol) and 4-dimethylaminopyridine (65mg, 0.53mmol) in dichloromethane (10ml) was added (acetyloxy)acetic acid (60mg, 0.51mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (90mg, 0.58mmol). The resultant mixture was stirred at room temperature and upon completion was concentrated *in vacuo*. The crude product was purified by chromatography on a Biotage® 12M column eluting

with hexane : ethyl acetate (2:1). The pure fractions were combined and the solvent removed *in vacuo* to give the title product (150mg, 61%).

Example 15: (1S,2R,4aS,5R,8R,8aR)-2-(formyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

The title compound was prepared by the method of Example 14 substituting (acetyloxy)acetic acid with commercially available formic acid (20□l, 0.53mmol) to give the title compound (160mg, 73%).

Example 16: (1S,2R,4aS,5R,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-2-[(3,3,3-trifluoropropanoyl)oxy]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexa hydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

The title compound was prepared by the method of Example 14 substituting (acetyloxy)acetic acid with commercially available 3,3,3-trifluoropropionic acid to give the title compound (165mg, 66%).

Example 17: (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[4-(ethyloxy)-1-methyl-4-oxobut-2-enyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

A solution of ((1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 141, 94mg, 0.163mmol) and carbethoxymethylene triphenylphosphorane (68mg, 0.195mmol) in anhydrous toluene (5ml) was refluxed und r nitrogen for 3

hours and then stirred at room temperature for 18 h before concentrating *in vacuo*. The residue was treated with sulfuric acid (10%) and extracted with two aliquots of ethyl acetate. The combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate solution and saturated aqueous sodium chloride solution, dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was taken up in acetonitrile (1ml), filtered, and purified by preparative HPLC on a Dynamex®, 5mm x 21.6mm column, eluting with acetonitrile : water (60:40). The pure fractions were concentrated *in vacuo* to give the title product (7mg, 6%).

Example 18: (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-(2,2-difluoro-1-methylethenyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

A stirred solution of 2-[(1*R*,2*R*,4a*S*,5*R*,8*S*,8a*S*)-2-(acetyloxy)-5-(2,2-difluoro-1-methylvinyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenyl] 3-(*tert*-butyl) (2*S*,3a*R*,9b*R*)-9b-[(*tert*-butoxycarbonyl)oxy]-6-chloro-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3a*H*)-dicarboxylate (Preparation 156, 120 mg) in ethyl acetate (3 ml) was treated with concentrated hydrochloric acid (1 ml). After 50 minutes the homogenous mixture was diluted with ethyl acetate (50 ml) and washed with water (2 x 20 ml) followed by saturated, aqueous sodium chloride (20 ml). The combined organic extracts were dried (Na_2SO_4) and evaporated to give a white solid. The crude product was purified by flash column chromatography on silica gel eluting with ethyl acetate:hexane (1 : 1) to give a white solid (33 mg).

Example 19: (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2-fluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 157, 200mg, 0.26mmol) in dichloromethane at -78°C was added diethylaminosulfur trifluoride (45mg, 34□l, 0.28mmol) over 10 minutes. The resulting mixture was allowed to warm to room temperature and then stirred for 18 h. The reaction mixture was cooled to -78°C and diethylaminosulfur trifluoride (34□l, 0.28mmol) added. Again, the resulting mixture was allowed to warm to room temperature and stirred for 18 h. The reaction mixture was quenched with water and extracted with hexane : ether (1:2). The organic extract was washed with saturated aqueous sodium chloride solution, dried ($MgSO_4$) and concentrated *in vacuo* to give the Boc-protected intermediate 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2-fluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl)(2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate as a white solid (172mg, 86%).

To a solution of the Boc-protected intermediate 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2-fluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl}3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate in ethyl acetate (5ml) was added concentrated hydrochloric acid (12 N, 1.5ml) and the resulting mixture was stirred for 1 hour. The reaction mixture was diluted with ethyl acetate (50ml), washed with water (3 x 20ml) and saturated aqueous sodium chloride solution (20ml), dried ($MgSO_4$) and concentrated *in vacuo* to give a foam (125mg, 83%). The crude product was purified by chromatography on silica eluting with hexane : ethyl acetate (2:1 then 1:1). The pure fractions were combined and concentrated *in vacuo* to give a white

solid (50mg, 33%). This product was further purified by preparative HPLC using a 1inch "Microsorb" ODS column, eluting with water : acetonitrile (30:70) with a flow rate of 20ml per minute. The pure fractions were eluted at 10 to 10.5 minutes and were combined and concentrated *in vacuo* to give the title product as a white solid (15mg, 10%).

Example 20: ((1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[(1-methyl-2-morpholin-4-ylethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

A solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 200 mg, 0.26 mmol) and morpholine (33.6 mg, 0.39 mmol) in 1,2-dichloroethane (1.5 ml) was stirred for 20 min before adding sodium triacetoxyborohydride (0.11 mg, 0.28 mmol) and stirring for 15 h. The reaction mixture was poured into water (50 ml) and extracted with dichloromethane (3 x 30 ml). The combined organic extracts were washed with water (20 ml), dried (Na_2SO_4) and concentrated *in vacuo*. The crude residue was purified using a Biotage cartridge (8g, silica), eluting with methanol : dichloromethane gradient (2 : 98 to 6 : 94) to give the Boc-protected intermediate as a white foam (203 mg).

The Boc-protected intermediate (203 mg) in ethyl acetate (1.5 ml) was treated with concentrated hydrochloric acid (0.5 ml). After 20 minutes the reaction mixture was diluted with ethyl acetate (50 ml), washed with aqueous sodium hydrogen carbonate (10% w/w, 50 ml) and then water (30 ml). The combined organic extracts were dried (Na_2SO_4) and evaporated to give the title compound (114 mg).

Example 21: (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-(2-ethyl-1,3-thiazol-4-yl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of (1S,2R,4aS,5R,8R,8aR)-5-(2-ethyl-1,3-thiazol-4-yl)-1,8a-dihydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-2-yl acetate (Preparation 166, 94 mg), and (2S,9bR)-6-chloro-3-{[(1,1-dimethylethyl)oxy]carbonyl}-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylic acid (Preparation 153, 90 mg) in dichloromethane (4 ml) was added *N*-methylimidazole (0.05 ml) and 1-(2-mesitylenesulfonyl)-3-nitro-1H-1,2,4-triazole. The reaction mixture was stirred at room temperature for 3 hours before evaporating *in vacuo*. The crude mixture was purifying by flash column chromatography on silica gel eluting with ethyl acetate : hexane (20:80 to 50:50) to give the coupled intermediate as a gum (110 mg). A stirred solution of this intermediate (110 mg) in ethyl acetate (5 ml) was treated with concentrated hydrochloric acid (1 ml). After 40 minutes the homogenous mixture was diluted with ethyl acetate (50 ml), washed with dilute aqueous sodium chloride (50 ml), dried ($MgSO_4$) and evaporated. The crude product was purified by column chromatography on silica gel eluting with ethyl acetate : hexane (5 : 95 to 50 : 50) to give the title compound as a white solid (34 mg).

Example 22: (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2,2-difluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2,2-difluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 167, 35mg,

0.044mmol) in ethyl acetate (0.5ml) was added concentrated hydrochloric acid (0.5ml) and the resulting mixture stirred at room temperature for 20 minutes. The reaction mixture was poured into buffer solution (pH7, 15ml) and extracted with ethyl acetate. The organic phase was washed with water and saturated aqueous sodium chloride solution, dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified by flash column chromatography gradient eluting with hexane : ethyl acetate (2:1 to 1:1). The pure fractions were combined and concentrated *in vacuo* to give the title product (15mg, 57%).

Example 23: (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2,2-difluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydro pyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2,2-difluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 168, 135mg, 0.17mmol) in ethyl acetate (1.5ml) was added concentrated hydrochloric acid (1.5ml) and the resulting mixture stirred at room temperature for 20 minutes. The reaction mixture was poured into buffer solution (pH7, 30ml) and extracted with ethyl acetate. The organic phase was washed with water and saturated aqueous sodium chloride solution, dried (Na_2SO_4) and concentrated *in vacuo* to give a yellowish oil (145mg, 142%). The crude product was purified by flash column chromatography gradient eluting with hexane : ethyl acetate (2:1 to 1:1). The pure fractions were combined and concentrated *in vacuo* to give the title product (61mg, 60%).

Example 24 (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-(2,2-dichloro-1-methylethenyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-

octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

2-[(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-(2,2-dichloro-1-methylethenyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl] 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 172 0.10 g) was added to hydrogen chloride (1 M in acetic acid, 1 ml) and the resulting solution was stirred at room temperature. After 40 min, the crude mixture was diluted with diethyl ether (10 ml) and water (10 ml), the organic layer was separated and then washed with sodium hydrogen carbonate (5 x 10 ml), brine (10 ml) and dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by flash chromatography using a Bond ElutR cartridge eluting with a gradient of hexane : ethyl acetate (100 : 0 to then 50 : 50) to give the title compound.

Example 32: (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(4-pyridin-2-ylpiperazin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To 1-(2-pyridyl)piperazine (44.0mg, 0.39mmol) was added a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 200mg, 0.257mmol) in 1,2-dichloroethane. The resultant mixture was stirred at room temperature for 10 minutes before sodium triacetoxyborohydride (109mg, 0.51mmol) was added in one portion. The resultant reaction mixture was sealed and stirred for 60 hours. The reaction mixture was poured onto water (50ml) and extracted with dichloromethane (3 x 30ml). The combined extracts were washed with water (20ml), dried

(Na_2SO_4) and concentrated *in vacuo*. The crude *bis*-Boc protected product was purified by chromatography on a Biotage® cartridge (silica, 8g) eluting with methanol : dichloromethane (2:98) for 11 minutes then a gradient of methanol : dichloromethane (2:98 to 6:94) over 40 minutes then methanol : dichloromethane (6:94). The pure fractions were collected to give the *bis*-Boc protected intermediate as a colourless glass (104.4mg, 44%). Deprotection was effected by adding a solution of the intermediate in ethyl acetate (1.5ml) to concentrated aqueous hydrochloric acid (0.5ml). The resultant mixture was stirred for 20 minutes before pouring onto ethyl acetate (50ml) and aqueous sodium hydrogen carbonate solution (2N, 40ml). The aqueous layer was extracted with ethyl acetate (20ml) and the combined organic extracts washed with water (20ml), dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified by flash chromatography using a Biotage® silica (8g) cartridge gradient eluting with methanol : dichloromethane (2 : 98 to 6 : 98). The pure fractions were collected to give the title compound (20.50mg, 11%).

Example 33: (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{bis[2-(methyloxy)ethyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

The title compound was prepared by the method of Example 32 substituting 1-(2-pyridyl)piperazine with *bis*-(2-methoxyethyl)amine (51.3mg, 0.39mmol) to give the intermediate as a colourless glass (146.3mg, 64%) and the title compound (51.70mg, 29%).

Example 47: (1S,2R,4aS,5S,8R,8aR)-5-{2-[acetyl(cyclopropyl)amino]-1-methylethyl}-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

A solution of 2-[(1S,2R,4aS,5S,8R,8aR)-5-[2-[acetyl(cyclopropyl)amino]-1-methylethyl}-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 177, 91mg, 0.10mmol) in hydrochloric acid (4M solution in dioxane, 3ml) was stirred under nitrogen for 1 hour. The reaction mixture was cooled to 0°C and quenched with sodium hydrogen carbonate solution. The mixture was extracted with ethyl acetate and the combined organic fractions washed with sodium hydrogen carbonate solution, dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified by column chromatography on silica (3g) eluting with ethyl acetate : heptane (2:1). The pure fractions were recombined and concentrated *in vacuo* to give the title product as a yellow glassy solid (31mg, 47%).

Example 48: (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{cyclopropyl[(methyloxy)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

A solution of 2-[(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{cyclopropyl[(methyloxy)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 179, 108mg, 0.12mmol) in hydrogen chloride (4M solution in dioxane, 2ml) was stirred under nitrogen for 1 hour. The reaction mixture was cooled to 0°C and quenched with sodium hydrogen carbonate solution. The mixture was extracted with ethyl acetate and the combined organic fractions washed with sodium hydrogen carbonate solution, dried (Na_2SO_4) and

concentrated *In vacuo*. The crude product was purified by column chromatography on silica (2g) eluting with ethyl acetate : heptane (1:1). The pure fractions were recombined and concentrated *in vacuo* to give the title product as a yellow glassy solid (30mg, 37%).

Example 49: (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{ethyl[(methyloxy)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

The title compound was prepared by the method of Example 48 substituting 2-[(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{cyclopropyl[(methyloxy)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl] 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate with 2-[(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{ethyl[(methyloxy)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 178, 89mg, 0.10mmol) to give the title compound as a pale yellow solid (21mg, 31%).

Example 52: (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{cyclopropyl[(ethylamino)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

The title compound was prepared by the method of Example 47 substituting 2-[(1S,2R,4aS,5S,8R,8aR)-5-{2-[acetyl(cyclopropyl)amino]-1-methylethyl}-2-

(acetyloxy)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl] 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9 b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate with 2-[(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{cyclopropyl[(ethylamino)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]3-(1,1-dimethylethyl)(2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 180, 114mg, 0.13mmol) to give the title compound as an off white solid (25mg, 28%).

Example 96: (1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethyl)-2-[[(phenylamino)carbonyl]oxy]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To (1S,2R,4aR,8R,8aR)-8a-hydroxy-2-[(1H-imidazol-1-ylcarbonyl)oxy]-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 142, 510mg, 0.83mmol) in anhydrous pyridine (10ml) was added aniline hydrochloride (500mg, 3.8mmol) and 4-dimethylaminopyridine (240mg, 2.0mmol). The reaction mixture was stirred at room temperature under nitrogen for 4 days before pouring into dichloromethane (100ml) and washing with saturated aqueous citric acid solution (2 x 50ml). The organic fraction was dried (Na_2SO_4) and concentrated *in vacuo* to give a yellowish solid (490mg, 93%). The crude product was purified by flash column chromatography on silica gel eluting with a hexane : ethyl acetate gradient (1:1 to 1 : 5). The pure fractions were collected and concentrated *in vacuo* to give (1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-2-{[(phenylamino)carbonyl]oxy}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (440mg, 83%). To a

solution of the (1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-2-[[(phenylamino)carbonyl]oxy]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (100mg, 0.157mmol) in ethyl acetate (30ml) was added platinum(IV) oxide (10mg, 0.044mmol) and the resulting mixture was hydrogenated at room temperature under 60psi hydrogen for 10 hours. The reaction mixture was filtered and the filtrate concentrated *in vacuo* . The crude product was purified by flash column chromatography on silica gel eluting with hexane : ethyl acetate (1:1). The product was further purified to give the title product (19mg, 19%).

Example 101 : (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(4-chlorophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl -1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 620 mg, 0.80 mmol) in dichloromethane (8 ml) was added 1-(4-chlorophenyl) piperazine (Preparation 78, 254 mg, 1.08 mmol). After 10 min triethylamine (0.15 ml, 1.2 mmol) and sodium triacetoxyborohydride (110 mg, 0.52 mmol) were added and the reaction mixture stirred at room temperature under nitrogen for 16 h. The reaction mixture was diluted with dichloromethane (10 ml) and half-saturated aqueous sodium hydrogen carbonate solution (15 ml) and stirred for approximately 30 min. The aqueous layer re-extracted with dichloromethane (15 ml) and the combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo* to give the Boc protected intermediate.

To the Boc protected intermediate was added hydrogen chloride (4N in dioxane, 6ml). The reaction mixture was then stirred at room temperature for 45 min before addition of triethylamine (3 ml) accompanied by cooling in an ice bath. The reaction mixture was diluted with ethyl acetate (20 ml) and saturated aqueous sodium hydrogen carbonate solution (15 ml) and the layers separated. The aqueous layer was re-extracted with ethyl acetate (20 ml) and the combined organic layers washed with aqueous sodium hydrogen carbonate solution and brine, before being dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified to give the title compound (273 mg, 0.361 mmol).

Example 106 : (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[2-(trifluoromethyl)phenyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 600 mg, 0.77 mmol), 1-[2-(trifluoromethyl)phenyl]piperazine (Preparation 130, 300 mg, 1 mmol) and triethylamine (0.3 ml, 2 mmol) were dissolved in dichloromethane (6 ml) and sodium triacetoxyborohydride, (240 mg, 1.1 mmol) added. The reaction mixture was stirred at room temperature for 16 h before addition of saturated aqueous sodium hydrogen carbonate solution (5 ml). After further vigorous stirring for 15 min, the reaction mixture was diluted with dichloromethane (40 ml) and water (20 ml). The organic layer was separated and the aqueous layer re-extracted with dichloromethane (20 ml). The combined organic layers were washed with water, dried (Na_2SO_4) and evaporated to dryness to give the Boc protected intermediate.

To a solution of the Boc protected intermediate in ethyl acetate (6 ml) was added concentrated hydrochloric acid (2 ml) and the reaction mixture was stirred at room temperature for 25 min. Saturated aqueous sodium hydrogen carbonate solution (30 ml) was then added to adjust the reaction mixture to pH 8. After stirring for a further 10 min, the reaction mixture was diluted with ethyl acetate (30 ml) and the organic layer separated. The aqueous layer was re-extracted with ethyl acetate (2 x 30 ml) and the combined organic layers washed with NaCl solution, dried (Na_2SO_4) and concentrated *in vacuo*. Purification gave the title compound (133 mg).

Example 107 : (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[4-(trifluoromethyl)pyrimidin-2-yl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of 1-[5-(trifluoromethyl)pyrid-2-yl]piperazine (6.4 g, 28.0 mmol) and 1-(5-(trifluoromethyl)2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 15 g, 19 mmol) and 2-piperazin-1-yl-4-(trifluoromethyl)pyrimidine (4.5 g, 19 mmol) in dichloromethane (150 ml) was added sodium triacetoxyborohydride (6.0 g, 28 mmol) portionwise. The reaction mixture was stirred at room temperature for 40 h, before aqueous sodium hydrogen carbonate solution was added. After 15 min the layers were separated and the aqueous layer was re-extracted with dichloromethane (3 x 150 ml). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo to give the Boc protected intermediate as a white foam.

To a cooled solution of of the Boc protected intermediate (68 g, 62 mmol) in ethyl acetate (250 ml) was added concentrated hydrochloric acid (80 ml). The reaction mixture was stirred for 21 min before water (300 ml) was added and the layers separated. The aqueous layer was then extracted with dichloromethane (3 x 250 ml). The combined organic layers were washed with saturated aqueous sodium hydrogen carbonate, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was dissolved in warm acetonitrile (150 ml) and a solid was precipitated. The solid was washed with acetonitrile and dried *in vacuo* to give the title compound as a white solid (25.3 g, 51 %).

Example 113 (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[5-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b -

hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

A solution of 1-[5-(trifluoromethyl)pyrid-2-yl]piperazine (6.4 g, 28.0 mmol) and 1-(5-(trifluoromethyl)2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 19.5 g, 25.1 mmol) in dichloromethane (200 ml) was stirred for 30 min at room temperature. Sodium triacetoxyborohydride (7.9 g, 37.5 mmol) was added portionwise over 3 min and the reaction mixture was stirred for 18 h at room temperature. Saturated sodium hydrogen carbonate solution (200 ml) was added portionwise and the reaction mixture was stirred for 20 min. The layers were separated and the aqueous phase was re-extracted with dichloromethane (2 x 200 ml). The combined organic layers were washed with water (200 ml), dried (Na_2SO_4) and concentrated *in vacuo* to give the Boc protected intermediate as a white foam (26.2 g).

To a solution of the Boc protected intermediate (40 g) in ethyl acetate (210 ml) was added concentrated hydrochloric acid (70 ml) over 5 min and the reaction mixture was at room temperature for 30 min. Water (300 ml) was added and the product was extracted with dichloromethane (3 x 300 ml). The combined organic extracts were washed with sodium hydrogen carbonate solution and then dried ($MgSO_4$) and concentrated in vacuo to give the crude product as a yellow foam (19 g). The crude residue was dissolved in hot methanol (30 ml) and slowly cooled to room temperature, the solids were washed with cold methanol to give the product as a white solid (9.5 g), a second crop was obtained (5 g) as an off-white solid by reducing the volume of the filtrate.

Example 125 : (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(4-bromophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-

hydroxy-5-methyl- 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 170 mg, 0.22 mmol) in dichloromethane (2 ml) was added 1-(4-bromophenyl)-piperazine hydrochloride (91.0 mg, 0.33 mmol) and triethylamine (60 µl). The reaction mixture was stirred at room temperature for 1 h before addition of sodium triacetoxyborohydride (93 mg, 0.44 mmol). The reaction mixture was then stirred for a further 18 h. Dichloromethane (5 ml) and water (3 ml) were added, followed by vigorous stirring for 30 min, and the reaction mixture was filtered through a hydrophobic frit. The organic layer was separated and concentrated under a stream of nitrogen. To the residue was added hydrogen chloride (4N in dioxane, 2ml) before vigorous shaking for 15 min and concentration under a stream of nitrogen for 40 min. A mixture of triethylamine and dichloromethane (1:5, 2ml) was added and the resulting solution concentrated under a stream of nitrogen. The residue was dissolved in acetonitrile (900 µl) and filtered before purification to give the bis TFA salt of the title compound as an off white solid (55 mg).

Example 126 : (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[4-(trifluoromethyl)phenyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 170 mg, 0.22

mmol) in dichloromethane (2 ml) was added 1-(4-trifluoromethylphenyl) piperazine (75.5 mg, 0.33 mmol). The reaction mixture was stirred for 1 h at room temperature before addition of sodium triacetoxyborohydride (93 mg, 0.44 mmol). The reaction mixture was then stirred for a further 18 h. Dichloromethane (5 ml) and water (3 ml) were added, followed by vigorous stirring for 30 min, and the reaction mixture was filtered through a hydrophobic frit. The organic layer was separated and concentrated under a stream of nitrogen. To the residue was added hydrogen chloride (4N in dioxane, 2ml) before vigorous shaking for 15 min and concentration under a stream of nitrogen for 40 min. A mixture of triethylamine and dichloromethane (1:5, 2ml) was added and the resulting solution was concentrated under a stream of nitrogen. The residue was dissolved in acetonitrile (900 µl) and filtered before purification to give the bis TFA salt of the title compound as an off white solid (63 mg).

Example 127 : (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-[4-(2,4-difluorophenyl)piperazin-1-yl]-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

The title compound was prepared using method described in Example 126, substituting 1-(4-trifluoromethylphenyl) piperazine with 1-(2,4-difluorophenyl)piperazine (65 mg, 0.33 mmol) to give the desired compound (49 mg).

Example 130 : (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-[4-(3,5-dichlorophenyl)piperazin-1-yl]-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

The title compound was prepared using method described in Example 126, substituting 1-(4-trifluoromethylphenyl) piperazine with 1-(3,5-dichlorophenyl)piperazine (76 mg, 0.33 mmol) to give the desired compound (58 mg).

Example 135 : (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2-ethylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl- 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

The title compound was prepared using method described in Example 126, substituting 1-(4-trifluoromethylphenyl) piperazine with 1-(2-ethylphenyl)piperazine (62mg, 0.33 mmol) to give the desired compound (51 mg).

Example 147: (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[(1S)-1-methyl-2-pyridin-3-ylethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate - TFA salt

To a solution of 2-[(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl] 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 152, 600mg, 0.795mmol) in tetrahydrofuran (9ml) at 0°C was added 9-BBN (0.5M solution in tetrahydrofuran, 4.3ml, 2.12mmol) over 20 minutes and the resulting mixture was allowed to warm to room temperature with stirring over 3 hours. Potassium carbonate (440mg, 3.2mmol) was added and the reaction mixture

stirred for 15 minutes. A solution of (1,1'-*bis*(diphenylphosphino)ferrocene)palladium (II) chloride (130mg, 0.16mmol) and 3-iodopyridine (326mg, 1.59mmol) in anhydrous *N,N*-dimethylformamide (12ml) was degassed and added to the reaction mixture to give a deep red solution. The reaction mixture was heated under nitrogen to 50°C for 10 hours. After one hour the solution had become a pale orange colour and after ten hours it was a dark brown/red. The reaction was concentrated *in vacuo* and the residue dissolved in dichloromethane (400ml), washed with water (2 x 200ml), dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified twice by chromatography on a Biotage® cartridge (silica, 90g) eluting with ethyl acetate : hexane (1:9 to 1:1). The pure fractions were concentrated *in vacuo* to give the intermediate as an off-white foam (200mg, 29%). The intermediate was treated with hydrogen chloride (4M solution in dioxane, 2ml) and the resultant mixture shaken for 30 minutes before the mixture was concentrated by evaporation. The residue was treated with triethylamine (20% v/v in dichloromethane, 2ml), concentrated *in vacuo* and the residue taken up in acetonitrile (0.9ml) and filtered. The crude product was purified by HPLC on a Magellen 5□ C18, 150 x 21.2mm column at 40°C eluting with TFA (0.1% aqueous solution) : acetonitrile (95:5 for 3 minutes flow rate 20 ml/min, then to 2:98 over 15 minutes flow rate 23 ml/min, then 2:98 for 4 minutes flow rate 25 ml/min). The pure fractions were combined and concentrated *in vacuo* to give the title product as the mono trifluoroacetic acid salt as a white solid (35mg, 7%).

Example 210: (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-((1*R*)-1-methyl-2-{4-[4-(trifluoromethyl)-2-pyrimidinyl]-1-piperazinyl}ethyl)-1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenyl (2*S*,3a*R*,9b*R*)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-*c*][2,1]benzoxazine-2-carboxylate – TFA salt

2-[(1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-((1*R*)-1-methyl-2-{4-[4-(trifluoromethyl)-2-pyrimidinyl]-1-piperazinyl}ethyl)-

1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenyl] 3-*tert*-butyl (2*S*,3a*R*,9b*R*)-9b-[(*tert*-butoxycarbonyl)oxy]-6-chloro-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-*c*][2,1]benzoxazine-2,3(3a*H*)-dicarboxylate, (Preparation 187, 587 mg, 0.59 mmol) in ethyl acetate (10 ml) at room temperature was added concentrated hydrochloric acid (2 ml). The mixture was stirred vigorously for 30 min and then poured cautiously onto saturated aqueous sodium bicarbonate (30 ml). The mixture was diluted with ethyl acetate (50 ml) and the two layers were separated. The organic layer was washed with water (20 ml) and brine (20 ml) before being dried ($MgSO_4$), filtered and evaporated *in vacuo*. The residue was purified by preparative HPLC using a Phenomenex LUNA 2 column (5μm C_{18} silica, 21.2 x 150mm, temperature 40°C), eluting with a gradient of acetonitrile : 0.1% aqueous trifluoroacetic acid (30 : 70 for 14 mins, then 90 : 10 for 4 mins and then 30:70 for 2 mins), at a flow rate of 20 ml/min and UV detection at 220nm. The TFA salt of the title compound was obtained as a pale yellow solid (211 mg, 39%).

Example 211: (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-((1*R*)-1-methyl-2-{4-[5-(trifluoromethyl)-2-pyridinyl]-1-piperazinyl}ethyl)-1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenyl (2*S*,3a*R*,9b*R*)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-*c*][2,1]benzoxazine-2-carboxylate– TFA salt

To a solution of 2-[(1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-((1*R*)-1-methyl-2-{4-[5-(trifluoromethyl)-2-pyridinyl]-1-piperazinyl}ethyl)-1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenyl] 3-*tert*-butyl (2*S*,3a*R*,9b*R*)-9b-[(*tert*-butoxycarbonyl)oxy]-6-chloro-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3a*H*)-dicarboxylate, (Preparation 188, 660 mg, 0.65 mmol) in ethyl acetate (10 ml) at room temperature was added concentrated hydrochloric acid (2 ml). The mixture was stirred vigorously for 30 min and then poured cautiously onto saturated aqueous sodium bicarbonate (30 ml). The mixture was diluted with ethyl acetate (50 ml) and the two layers were separated. The organic layer was washed with

water (20 ml) and brine (20 ml) before being dried ($MgSO_4$) , filtered and evaporated *in vacuo*. The residue was purified by preparative HPLC using a Phenomenex LUNA 2 column (5µm C_{18} silica, 21.2 x 150mm, temperature 40°C), eluting with a gradient of acetonitrile : 0.1% aqueous trifluoroacetic acid (30 : 70 for 14 mins, then 90 : 10 for 4 mins and then 30:70 for 2 mins), at a flow rate of 20 ml/min and UV detection at 220nm. The TFA salt of the title compound was obtained as a pale yellow solid (220 mg, 36%).

Example 212 : (1S,2R,5S,8R,8aR)-2-(acetyloxy)-5-((1R)-2-{4-[bis(4-fluorophenyl)methyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 170 mg, 0.22 mmol) in dichloromethane (2 ml) was added 1-(4, 4'-difluorobenzhydryl) piperazine (94.6 mg, 0.33 mmol). The reaction mixture was stirred for 1 h at room temperature before addition of sodium triacetoxyborohydride (93 mg, 0.44 mmol). The reaction mixture was then stirred for a further 18 h. Dichloromethane (5 ml) and water (3 ml) were added, followed by vigorous stirring for 30 min, and the reaction mixture was filtered through a hydrophobic frit. The organic layer was separated and concentrated under a stream of nitrogen. To the residue was added hydrogen chloride (4N in dioxane, 2ml) before vigorous shaking for 15 min and concentration under a stream of nitrogen for 40 min. A mixture of triethylamine and dichloromethane (1:5, 2ml) was added and the resulting solution concentrated under a stream of nitrogen. The residue was dissolved in acetonitrile (900 µl) and filtered before

purification to give the bis TFA salt of the title compound as an off white solid (45 mg).

Example 213 : (1S,2R,5S,8R,8aR)-2-(acetyloxy)-5-{(1R)-2-[4-(5-chloropyrimidin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate, (Preparation 160, 550 mg, 0.71 mmol) and 5-chloro-2-piperazin-1-ylpyrimidine (Preparation 197, 200 mg, 1 mmol) in dichloromethane (8 ml) was added sodium triacetoxyborohydride (220 mg, 1 mmol). The reaction mixture was stirred at room temperature for 18 h before addition of saturated aqueous sodium hydrogen carbonate (5 ml). Vigorous stirring for 20 min was followed by separation of the layers using a filter cartridge fitted with a hydrophobic frit. The filtrate was evaporated under a stream of nitrogen to give the Boc-protected intermediate (800 mg, 0.83 mmol).

To a solution of the Boc protected intermediate, (800 mg) in ethyl acetate (7.5 ml) was added concentrated hydrochloric acid (2.5 ml). The reaction mixture was stirred at room temperature for 25 min before solid sodium hydrogen carbonate and saturated aqueous sodium hydrogen carbonate solution was added to adjust the reaction mixture to pH 5. The mixture was extracted with dichloromethane (2 x 20 ml) and the combined organic layers dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified to give the title compound (200 mg). The free base was obtained by dissolving in dichloromethane and shaking with aqueous sodium hydrogen carbonate

solution. The layers were separated using a hydrophobic filter cartridge and concentrated to give the title compound

Example 214 : (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{(1R)-2-[4-(5-bromopyrimidin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160,150 mg, 0.19 mmol) in dichloromethane (2.5 ml) was added 5-bromo-2-piperazin-1-ylpyrimidine (61 mg, 0.25 mmol) and sodium triacetoxyborohydride (65 mg, 0.3 mmol). The reaction mixture was shaken for 22 h and saturated aqueous sodium hydrogen carbonate was added followed by further vigorous stirring for 30 min. The organic and aqueous layers were separated using a hydrophobic filter cartridge and the filtrate was concentrated under a stream of nitrogen to give the Boc protected intermediate.

To the Boc protected intermediate was added hydrogen chloride (4N in dioxane, 2.5 ml) and the resulting solution was shaken at room temperature for 25 min. The reaction mixture was concentrated under a stream of nitrogen and quenched with a mixture of triethylamine and dichloromethane (2:3, 2 ml). The mixture was again concentrated under a stream of nitrogen. The residue was diluted with dichloromethane (5 ml) and water (5 ml) and the layers separated using a hydrophobic frit. The filtrate was concentrated under a stream of nitrogen and purified to give the title compound. The free base was dissolved in dichloromethane, shaken with saturated aqueous sodium hydrogen carbonate and filtered through a hydrophobic frit to give the title compound (51 mg).

Example 215 : (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{(1R)-2-[4-(6-chloro-1,3-benzothiazol-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 150 mg, 0.19 mmol) in dichloromethane (2.5 ml) was added 6-chloro-2-piperazino-1,3-benzothiazole (63 mg, 0.25 mmol, commercially available, Maybridge) and sodium triacetoxyborohydride (65 mg, 0.3 mmol). The reaction mixture was shaken for 22 h and saturated aqueous sodium hydrogen carbonate was added followed by further vigorous stirring for 30 min. Separation of the layers was achieved by filtering the solution through a hydrophobic filter cartridge and the filtrates were concentrated under a stream of nitrogen to give the Boc protected intermediate.

To the Boc protected intermediate was added hydrogen chloride (4N in dioxane 2.5 ml). The reaction mixture was shaken at room temperature for 25 min before concentrating under a stream of nitrogen for 20 min and quenching with a mixture of triethylamine and dichloromethane (2:3, 2 ml). The mixture was again concentrated under a stream of nitrogen and the residue was dissolved in dichloromethane (5 ml) and water (5 ml). The layers were separated using a hydrophobic frit and the filtrate was concentrated under a stream of nitrogen and purified to give the title compound. The free base was obtained by dissolving in dichloromethane and shaking with saturated aqueous sodium hydrogen carbonate. This solution was then filtered through a hydrophobic frit and the filtrate concentrated to give the title compound (58 mg).

Example 216 : (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-((1R)-2-{4-[(3,4-dichlorophenyl)methyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 150 mg, 0.19 mmol) and 1-(3, 4 – dichlorophenyl) piperazine hydrochloride salt (67 mg, 0.25 mmol) in dichloromethane (2.5 ml) was added triethylamine (50 µl) and sodium triacetoxyborohydride (65 mg, 0.3 mmol). The reaction mixture was stirred at room temperature for 20 h before saturated aqueous sodium hydrogen carbonate (3 ml) was added, followed by further vigorous stirring for 30 min. The reaction mixture was filtered through a hydrophobic filter cartridge and the filtrate evaporated under a stream of nitrogen to give Boc protected intermediate.

The Boc protected intermediate was dissolved in hydrogen chloride (4N dioxane, 2.5 ml) and stirred at room temperature for 25 min. The reaction mixture was concentrated under a stream of nitrogen (40 °C, 25 min) and quenched with a mixture of triethylamine and dichloromethane (2:3, 2 ml). The mixture was again concentrated under a stream of nitrogen and the residues were partitioned between dichloromethane (5 ml) and saturated aqueous sodium hydrogen carbonate. The combined phases were filtered through a hydrophobic filter cartridge and the filtrates were concentrated under a stream of nitrogen. Purification gave the title compound (44 mg).

Example 217 : (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-((1R)-1-methyl-2-{4-[5-(trifluoromethyl)pyrimidin-2-yl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 170 mg, 219 µmol) and 2-piperazin-1-yl-5-(trifluoromethyl)pyrimidine TFA salt, (Preparation 198, 68mg, 200 µmol) in dichloromethane (4 ml) was added sodium triacetoxyborohydride (93 mg, 440 mmol). The reaction mixture was stirred overnight and water added (5 ml). After further shaking, the layers were separated and the organic layer evaporated to dryness under a stream of nitrogen. The residue was dissolved in ethyl acetate (2 ml) and concentrated hydrochloric acid (1 ml) was added. After stirring for 20 min, saturated aqueous sodium hydrogen carbonate (20 ml) and ethyl acetate (20ml) were added and the mixture was shaken. The organic layer was separated, dried (Na_2SO_4) and evaporated before purification to give the title compound (37mg) as a TFA salt.

Example 218 : (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-((1R)-2-{4-[(4-chlorophenyl)oxy]piperidin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a solution of (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-

hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 141, 60 mg, 0.11 mmol) and 4-[(4-chlorophenyl)oxy]piperidine (Preparation 200, 25 mg, 0.1 mmol) was added dichloromethane (2 ml) and sodium triacetoxyborohydride (35 mg, 0.16 mmol), followed by triethylamine (0.02ml, 0.17mmol). The reaction mixture was stirred at room temperature for 17 h, before diluting with dichloromethane (5 ml) and saturated aqueous sodium hydrogen carbonate (3 ml). The reaction mixture was shaken vigorously and the layers were separated using a hydrophobic filter cartridge. The filtrate was concentrated under a stream of nitrogen and purified to give the title compound (26 mg).

Preparation 4: 1-(cyclopentylcarbonyl)piperazine.

Cyclopentane carboxylic acid (5.0 g, 44 mmol) was dissolved in chloroform (50 ml). Oxalyl chloride (4.6 ml, 52.5 mmol) was added dropwise under nitrogen and stirred at room temperature for 30 min. The reaction mixture was then heated under reflux for 1 h, before concentrating *in vacuo* to give cyclopentanecarbonyl chloride as a light yellow liquid.

Piperazine hexahydrate (8.55 g, 44.0 mmol) was dissolved in absolute ethanol (50 ml) and then refluxed for 10 min. Cyclopentanecarbonyl chloride (5.83 g, 44 mmol) was added dropwise at 65°C and the reaction mixture was refluxed for 30 min and then stirred at room temperature for 18 h. The reaction mixture was cooled, filtered and the filtrate was concentrated *in vacuo* to give ~20 ml of solution. The concentrate was cooled and then filtered again. Ethanolic hydrogen chloride was added to the mother liquor and the reaction mixture was concentrated to give a white solid, which was dissolved in water (15 ml). The solution was basified to pH 14 and the product was extracted with dichloromethane (7 x 50 ml). The extracts were dried (Na_2SO_4) and concentrated to give the title compound as a yellowish residue, which was distilled to give the product (1.28 g, 7.0 mmol, 16%)

Preparation 10 : 4-(8-azabicyclo[3.2.1]oct-3-ylsulfanyl)phenyl methyl ether

To a stirred solution of 2,2,2-trichloroethyl 3-[(4-methoxyphenyl)sulfanyl]-8-azabicyclo[3.2.1]octane-8-carboxylate (Preparation 11, 52.7 g, 0.12 moles) in tetrahydrofuran under nitrogen was added zinc dust (20 g,) and potassium hydrogenphosphate (1 M, 125 ml). The reaction mixture was stirred for 2 h at room temperature before adding more zinc dust (30 g) followed by heating on a steam bath for 30 min. The reaction mixture was cooled to room temperature and diluted with water (1l). Sodium carbonate was added to adjust the pH to 10. The reaction mixture was filtered and the filtrate was separated and then extracted with dichloromethane. The combined organic

extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give the title compound as a yellow oil (26.0 g, 84%). The oil was purified by column chromatography on silica gel (350 g) eluting with methanol : dichloromethane : 0.88 ammonia solution (10 : 90 : 1) to give the product as an oil which crystallised on standing (13 g, 42%). The solid was further purified by stirring in ether and filtering to give a light yellow solid (9 g, 29%).

Preparation 11 : 2,2,2-trichloroethyl 3-[(4-methoxyphenyl)sulfanyl]-8-azabicyclo[3.2.1]octane-8-carboxylate

To a solution of methyl 4-[(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)sulfanyl]phenyl ether (Preparation 12, 43.7 g, 0.16 moles) in benzene (400 ml) stirred under nitrogen was added potassium carbonate (24.3 g) and trichloroethylchloroformate (24.5 ml, 0.176 moles). The reactants were heated to reflux for 2 h before cooling, filtering and washing the collected solids with benzene. The mother liquor was concentrated *in vacuo* to give the crude product as an oil. The crude product was stirred with ethyl acetate : hexane (5 : 95) to precipitate the title compound as a white solid (51.5 g, 76%).

Preparation 12 : Methyl 4-[(8-methyl-8-azabicyclo[3.2.1]oct-3-yl)sulfanyl]phenyl ether

To a solution of methyl 8-methyl-8-azabicyclo[3.2.1]oct-3-yl sulfate (Preparation 13, 35 g, 0.16 mol) in tetrahydrofuran (300 ml) was added with cooling to 0°C sodium hydride (60% dispersion in oil, 7 g, 0.17 mol). After complete addition, 4-methoxybenzene thiol (23.8 g, 0.16 mol) was added in tetrahydrofuran (300 ml). The reaction mixture was heated under reflux for 2 h and then cooled to 30°C and water (250 ml) was added. The tetrahydrofuran was removed *in vacuo*, dichloromethane was added and the layers separated. The organic layer was washed with water, sodium hydroxide (1 M solution), water, and saturated brine before drying (Na_2SO_4).

The organic extracts were concentrated *in vacuo* to give the title compound (43.7 g, 100%).

Preparation 13 : **Methyl 8-methyl-8-azabicyclo[3.2.1]oct-3-yl sulfate**

To a solution of 8-methyl-8-azabicyclo[3.2.1]octan-3-ol (299 g, 2.12 moles) in dichloromethane (3.5 l) was added triethylamine (445 ml, 3.2 moles) and the reaction mixture was cooled to –40°C. Methanesulfonyl chloride (293 g, 2.55 moles) was added dropwise over 90 min and the reaction mixture was then allowed to warm to room temperature. Water (1 l) was added and the organic extract was washed with sodium hydroxide (0.5M) water and saturated sodium chloride solution. The organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give a yellow solid (262 g, 56%). The solid was recrystallised from hexane to give a first crop of the title compound as light yellow crystals (126.5 g, 27%), followed by a second crop (76.1 g, 16%).

Preparation 16 : **2,5-dimethyl-3-piperazin-1-ylpyrazine**

To a solution of 2,5-dimethyl-3-[4-(phenylmethyl)piperazin-1-yl]pyrazine (Preparation 17, 1.14 g, 4.04 mmol) in methanol (80 ml) was added ammonium formate (1.27 g, 20.2 mmol) followed by palladium (10% w/w on carbon, 0.17 g) under a nitrogen atmosphere. The reaction mixture was heated under reflux, after 2.5 h, more ammonium formate (0.64 g, 10.1 mmol) and palladium (0.06 g) were added. The reaction mixture was filtered through Celite® washed with methanol and concentrated *in vacuo*. The crude product was purified by flash chromatography using silica gel eluting with methanol : dichloromethane (8 : 92 and then 10 : 90) and then methanol : dichloromethane : 0.88 ammonia solution (10 : 90 : 1). The title compound was obtained as a white solid (0.35 g, 45%).

Preparation 17 : **2,5-dimethyl-3-[4-(phenylmethyl)piperazin-1-yl]pyrazine**

3-Chloro-2,5-dimethylpyrazine (1.0 g, 7.0 mmol) and *N*-benzylpiperazine (3.7 ml, 21.0 mmol) were mixed under nitrogen and heated to 125°C for 18 h. Saturated aqueous sodium hydrogen carbonate was added and the product was extracted with chloroform. The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give a yellow oil. The crude product was purified by flash chromatography using silica gel eluting with methanol : chloroform (2.5 : 97.5) to give the pure product as a yellow oil (1.14 g, 58%).

Preparation 18 : 2-methyl-3-piperazin-1-ylquinoxaline

To a solution of 2-methyl-3-[4-(phenylmethyl)piperazin-1-yl]quinoxaline (Preparation 19, 1.68 g, 5.28 mmol) in methanol (106 ml) was added ammonium formate (1.66 g, 26.4 mmol) followed by palladium (10% w/w on carbon, 0.25 g) under a nitrogen atmosphere. After 12.5 h, more ammonium formate (0.83 g, 13.2 mmol) and palladium (0.12 g) were added. The reaction mixture was filtered through Celite® and evaporated to a yellow oil. The crude product was purified by flash chromatography using silica gel eluting with methanol : dichloromethane (5 : 95 and then 10 : 90). The title compound was obtained as a pale yellow oil which crystallised upon standing (0.46 g, 38%).

Preparation 19 : 2-methyl-3-[4-(phenylmethyl)piperazin-1-yl]quinoxaline

2-Chloro-3-methylquinoxaline (1.0 g, 5.6 mmol) and *N*-benzylpiperazine (2.9 ml, 16.8 mmol) were mixed and heated to 125°C for 18 h. Saturated aqueous sodium hydrogen carbonate was added and the product was extracted with chloroform. The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give a dark red oil. The crude product was purified by flash chromatography using silica gel eluting with methanol : dichloromethane (15 : 85) to give the pure product as a red oil which solidified upon standing (1.63 g, 94%).

Preparation 15 : 3-chloro-2-pyridinyl 3-piperidinyl ether hydrochloride salt
To a stirred solution of racemic 3-hydroxypiperidine (1.12 g, 11.1 mmol) in tetrahydrofuran (20 ml) under nitrogen was added sodium hydride (60% dispersion in oil, 0.44 g, 11.1 mmol). The reaction mixture was stirred for 45 min before adding 2,3-chloropyridine (1.64 g, 11.1 mmol) and heating under reflux for 48 h. The reaction mixture was cooled to room temperature and quenched with water (5 ml) and extracted with ethyl acetate. The organic extracts were then washed with water, saturated aqueous ammonium chloride and brine before back washing with chloroform. The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to give a crude orange oil (2.5 g). The crude product was chromatographed eluting with chloroform : methanol (15 : 1 to 8 : 1) to give a pale yellow oil (2.3 g). A solution of hydrogen chloride (4M in dioxane, 5ml) was added to the pure product to give the hydrochloride salt upon concentration as a sticky yellow solid (2.27 g, 82%).

Preparation 21 : (+)-3,11-diazatricyclo[7.3.1.$0^{2,7}$]trideca-2,4,6-triene hydrochloride salt

Racemic 1,1-dimethylethyl 3,11-diazatricyclo[7.3.1.$0^{2,7}$]trideca-2,4,6-triene-11-carboxylate (Preparation 22, 0.47 g) was subjected to chiral preparative HPLC using a 5 cm x 25 cm Chiracel AD column, eluting with heptane : isopropyl alcohol (95 :5) at a flow rate of 120 ml/min over 20 min. The enantiomers were detected at 250 nm and were shown to have chiral purity of >98% enantiomeric excess, the first enantiomer to be eluted was designated enantiomer 1 and the second was designated enantiomer 2.

Enantiomer 2 of 1,1-dimethylethyl 3,11-diazatricyclo[7.3.1.$0^{2,7}$]trideca-2,4,6-triene-11-carboxylate was dissolved in ethyl acetate (5 ml) and treated with hydrochloric acid (3M, 2 ml) and then warmed to reflux for 18 h. The reaction mixture was cooled and filtered and the white precipitate was washed with ethyl acetate and hexane. The hydrochloride salt of enantiomer 2 was obtained as a white powder 0.12 g, 82%).

Preparation 22 : 1,1-dimethylethyl 3,11-diazatricyclo[7.3.1.$0^{2,7}$]trideca-2,4,6-triene-11-carboxylate

A solution of 11-(phenylmethyl)-3,11-diazatricyclo[7.3.1.$0^{2,7}$]trideca-2,4,6-triene (Preparation 23, 0.74 g, 2.81 mmol), ammonium formate (6.0 g, 95 mmol) and palladium hydroxide (10 wt % on carbon, 0.21 g) in methanol (30 ml) under nitrogen was heated under reflux for 1 h. The reaction mixture was filtered through a pad of Celite® and the pad was washed with hot methanol. The combined organic layers were concentrated *in vacuo*, dichloromethane (100 ml) was added and the mixture was filtered and then concentrated to an oil. The oil was dissolved in dichloromethane and di-tert-butyl dicarbonate (0.65 g, 3.09 mmol) was added. The reaction mixture was concentrated *in vacuo* and purified by flash chromatography eluting with ethyl acetate to give the title compound (0.23 g, 30%) and also 3,11-diazatricyclo[7.3.1.$0^{2,7}$]trideca-2,4,6-triene-11-carbaldehyde (0.36 g, 64%).

To 3,11-diazatricyclo[7.3.1.$0^{2,7}$]trideca-2,4,6-triene-11-carbaldehyde (0.36 g, 64%) was added sodium hydroxide (0.80 g, 20 mmol) in dioxane (7 ml) and water (3 ml) and the reaction mixture was heated under reflux for 9 h. More sodium hydroxide (0.40 g, 10 mmol) was added and the reaction mixture was refluxed for a further 9 h. The reaction mixture was cooled, diluted with saturated sodium hydrogen carbonate solution and extracted with dichloromethane. The organic extracts were dried and filtered and then di-tert-butyl dicarbonate (0.39 g, 1.83 mmol) was added and the reaction mixture was stirred for 2 h. The reaction mixture was washed with brine, dried (Na_2SO_4) and concentrated to give an oil which was purified by flash chromatography eluting with ethyl acetate to give the title product (0.24 g).

Thus the title compound was obtained (0.47 g, 61%) by combination of the two components described.

Preparation 23 : 11-(Phenylmethyl)-3,11-diazatricyclo[7.3.1.$0^{2,7}$]trideca-2,4,6-triene

To a solution of 3-azatricyclo[7.2.1.$0^{2,7}$]dodeca-2,4,6-triene-10,11-diol (Preparation 24, 1.16 g, 6.07 mmol) in ethanol (40 ml) was added sodium periodate (1.35 g, 6.07 mmol) in water (20 ml) to produce a yellow slurry. After 15 min, water and ethyl acetate were added and the layers were separated, the aqueous layer was washed with ethyl acetate (4 x 50 ml) and then dichloromethane. The combined organic extracts were dried (Na_2SO_4) to give an orange oil. The oil was diluted with dichloroethane (50 ml), benzylamine (0.65 g, 6.07 mmol) was added followed by sodium triacetoxyborohydride (4.12 g, 19.4 mmol). After 7 h, saturated sodium hydrogen carbonate solution (75 ml) and ethyl acetate (75 ml) were added and the reaction mixture was stirred for 20 min. The layers were separated and the aqueous layer was extracted with ethyl acetate (2 x 50 ml). The combined organic extracts were washed with water and brine, and then dried (Na_2SO_4) and concentrated *in vacuo* to give the crude product. Purification by flash chromatography produced the title compound as a light yellow oil (0.80 g, 50%).

Preparation 24 : 3-azatricyclo[7.2.1.$0^{2,7}$]dodeca-2,4,6-triene-10,11-diol

A mixture of 3-azatricyclo[7.2.1.$0^{2,7}$]dodeca-2,4,6,10-tetraene (Preparation 25, 0.96 g, 6.11 mmol), trimethylamine *N*-oxide dihydrate (0.75 g, 6.73 mmol) and osmium tetroxide (2.5 wt % solution in 2-methyl-2-propanol, 2 □l) in dichloromethane (15 ml) were stirred for 18 h. A further portion of osmium tetroxide (2.5 wt % solution in 2-methyl-2-propanol, ca. 1 □l) was added and the reaction mixture was stirred for a further 18 h. The reaction mixture was subjected to chromatography eluting with hexane and then ethyl acetate to give the title compound as a solid (1.16 g, 100%).

Preparation 25 : 3-azatricyclo[7.2.1.$0^{2,7}$]dodeca-2,4,6,10-tetraene

To a solution of 3-(cyclopent-3-en-1-ylmethyl)-1,2-dihydropyridin-2-yl trifluoromethanesulfonate (Preparation 26, 3.1 g, 10.1 mmol) in dimethylformamide (20 ml) stirred under nitrogen was added 1,3-*bis*(diphenylphosphino)propane (0.334 g, 0.8 mmol), triethylamine (1.52 g, 16.6 mmol) and palladium (II) acetate(0.072 g, 0.32 mmol). The reaction mixture was warmed to 100°C and stirred for 18 h. Triethylamine (1 ml) was added and the reaction mixture was warmed to 110°C for a further 6 h. The reaction mixture was cooled and poured into saturated brine solution (50%, 75 ml), and the product was extracted with ethyl acetate (4 x 30 ml). The combined organic extracts were washed with water (2 times), sodium hydrogen carbonate solution and brine before drying (Na_2SO_4) and concentrating *in vacuo*. The crude oil was purified by flash chromatography eluting with ethyl acetate : hexane (15 : 85) to give a colourless oil (1.07 g, 77%).

Preparation 26 : 3-(cyclopent-3-en-1-ylmethyl)-1,2-dihydropyridin-2-yl trifluoromethanesulfonate

To a solution of 3-(cyclopent-3-en-1-ylmethyl)pyridin-2(1*H*)-one (Preparation 27, 1.9 g, 10.8 mmol) in dichloromethane (50 ml) stirred at 0°C was added trifluoromethanesulfonic anhydride (2.38 ml, 14.1 mmol) and then 2,6-lutidine (2.2 ml, 19 mmol). The reaction mixture was allowed to warm to room temperature and then stirred for 1 h. The reaction mixture was diluted with dichloromethane and washed with water (2 times), then saturated aqueous sodium hydrogen carbonate solution and then brine. The crude product was purified by flash chromatography eluting with ethyl acetate : hexane (10 : 90) to give the product as a colourless liquid (3.1 g, 93%).

Preparation 27 : 3-(cyclopent-3-en-1-ylmethyl)pyridin-2(1*H*)-one

To a cloudy dispersion containing 3-(cyclopent-3-en-ylmethyl)-2-(methyloxy)pyridine (Preparation 28, 2.1 g, 11.1 mmol) and sodium iodide (4.1 g, 27.8 mmol) in anhydrous acetonitrile (25 ml) was added chlorotrimethylsilane (3.0 g, 27.8 mmol). A white precipitate formed which was stirred for 30 min at room temperature and then for 1 h at 70°C. The reaction mixture was cooled to room temperature and water was added, followed by ethyl acetate (200 ml), the organic layer was washed with water (4 x) and then with sodium hydrogen carbonate solution and brine before drying (Na_2SO_4) to give the title compound as a yellow solid (1.93 g, 100%).

Preparation 28 : 3-(Cyclopent-3-en-ylmethyl)-2-(methyloxy)pyridine

Cyclopent-3-en-yl[2-(methyloxy)pyridin-3-yl]methanone (Preparation 29, 10 g, 49.3 mmol), potassium hydroxide (85%, 16.8 g, 0.3 mol), and hydrazine (6.33 g, 198 mmol) in ethylene glycol (100 ml) were heated to 180°C and stirred for 18 h. Water was added and the product was extracted with hexane : ethyl acetate (50 : 50). The combined organic extracts were washed with brine and concentrated *in vacuo*. The crude oil was purified by flash chromatography eluting with ethyl acetate : hexane (10 : 90) to give a colourless oil (4.75 g, 51%).

Preparation 29 : Cyclopent-3-en-yl[2-(methyloxy)pyridin-3-yl]methanone

To 2-bromo-1,3,5-trimethylbenzene (16.9 g, 85 mmol) in tetrahydrofuran (340 ml) under a nitrogen atmosphere was added at –78°C over 30 min *tert*-butyl lithium (1.7 M solution, 100 ml, 170 mmol). A yellow precipitate formed and was stirred for 1 h at –78°C. 2-(methyloxy)pyridine (8.45 g, 77.3 mmol) in tetrahydrofuran (10 ml) was added and the reaction mixture was warmed to 0°C for 1 h and then to room temperature for 1 h. The reaction mixture was cooled to –70°C and *N*-methyl-*N*-(methyloxy)cyclopent-3-ene-1-carboxamide (Preparation 30, 12.4 g, 80 mmol) was added in tetrahydrofuran (20 ml), the

reaction mixture was allowed to gradually warm to room temperature over 18 h. Saturated aqueous sodium hydrogen carbonate (250 ml) was added and the mixture was stirred for 20 min, the product was extracted with diethyl ether (3 x 100 ml) the combined organic extracts were washed with water, then brine, and then dried (Na_2SO_4) and concentrated to give a yellow oil (26 g) . The crude oil was purified by flash chromatography using silica gel eluting with diethyl ether : hexane (10 : 90 and then 20 : 80). The title compound was obtained as a colourless oil (12.19 g, 75%).

Preparation 30 : N-methyl-N-(methyloxy)cyclopent-3-ene-1-carboxamide

To a solution of cyclopent-3-ene-1-carboxylic acid (80.0 g, 0.71 mol) in dichloromethane (300 ml) was added 1,1'-carbonyldiimidazole (127.5 g, 0.78 mol) slowly and the reaction mixture was stirred at room temperature for 1 h. N,O-dimethylhydroxylamine (76.7 g, 0.78 mol) was added and stirred for 18 h at room temperature. The reaction mixture was poured into water (300 ml) and extracted with dichloromethane (100 ml). The organic extracts were washed with hydrochloric acid (1N, 2 x 200 ml) and then with brine before filtering through cotton wool, drying and concentrating. The product was purified by flash chromatography using silica gel eluting with dichloromethane to give the title compound (116.78 g, 95%).

Preparation 31 : (-)-4,10-diazatricyclo[6.3.1.$0^{2,7}$]dodeca-2,4,6-triene hydrochloride salt

Racemic 10-(phenylmethyl)-4,10-diazatricyclo[6.3.1.$0^{2,7}$]dodeca-2,4,6-triene (Preparation 32, 1.9 g) was subjected to chiral preparative HPLC using a 5 cm x 25 cm Chiracel AD column, eluting with heptane : isopropyl alcohol (95 :5) at a flow rate of 120 ml/min over 30 min. The enantiomers were detected at 250 nm and were shown to have chiral purity of >98% enantiomeric excess, the first enantiomer to be eluted was designated enantiomer 1 and the second

was designated enantiomer 2. The eluants were concentrated to give enantiomer 1 (0.9 g) and enantiomer 2 (0.75 g).

Enantiomer 2 of 10-(phenylmethyl)-4,10-diazatricyclo[6.3.1.$0^{2,7}$]dodeca-2,4,6-triene (0.75 g) was dissolved in methanol (35 ml) and ammonium formate (4 g) was added followed by palladium hydroxide (10% wt on carbon, 0.20 g). The reaction mixture was heated under reflux for 2 h, cooled and filtered through a pad of Celite®, rinsing with methanol, the combined organic solutions were concentrated *in vacuo*. Dichloromethane was added and the resultant slurry was filtered and concentrated to give an oil (0.70 g). The oil was dissolved in methanol and hydrochloric acid (3 M, 6 ml) was added. The mixture was concentrated *in vacuo* to give a solid which was recrystallised by dissolving in methanol (20 ml) and adding diethyl ether until the reaction mixture went cloudy. The reaction mixture was stirred for 72 h before the solid was removed by filtration and washed with diethyl ether to give the pure hydrochloride salt of the title compound as a white solid (0.34 g).

Preparation 32 : 10-(phenylmethyl)-4,10-diazatricyclo[6.3.1.$0^{2,7}$]dodeca-2,4,6-triene

To a solution of 3-(phenylmethyl)-3-azabicyclo[3.2.1]octane-6,7-dicarbaldehye *bis* (O-methyloxime) (Preparation 33, 5.0 g, 15.2 mmol) in dichloroethane (150 ml) was added trifluoroacetic acid (17 ml) and the reaction mixture was stirred under nitrogen at room temperature for 20 min. The reaction mixture was heated under reflux for 2 h and then concentrated to give a brown oil. Ethyl acetate (100 ml) was added and the solution was treated with saturated sodium carbonate solution (70 ml) the layers were separated and the organic layer was washed with brine and dried (Na_2SO_4) and concentrated to give an oil (4.0 g). The crude oil was purified by flash chromatography using silica gel eluting with ethyl acetate to give the title compound as an orange oil (1.93 g, 51%).

Preparation 33 : 3-(phenylmethyl)-3-azabicyclo[3.2.1]octane-6,7-dicarbaldehye *bis* (O-methyloxime)

To a solution of 9-(phenylmethyl)-9-azatricyclo[5.3.1.$0^{2,6}$]undecane-3,4-diol (Preparation 34, 6.0 g, 21.9 mmol) in dioxane (100 ml) was added sodium periodate (5.0 g, 23.3 mmol) in water (50 ml). A thick slurry formed, water (50 ml) was added and the reaction mixture was stirred under nitrogen. Upon completion, the reaction mixture was diluted with water (150 ml) and saturated sodium carbonate (50 ml) and the product was extracted with ethyl acetate (2 x 150 ml). The combined organic extracts were washed with water, and then brine before drying (Na_2SO_4) and concentrating to give an orange oil (6.14 g). To the crude oil was added methanol (75 ml) and water (75 ml), followed by methoxylamine hydrochloride (7.34 g, 87.9 mmol) and sodium acetate (12.62 g, 153.8 mmol). The reaction mixture was shaken and then warmed on a steam bath for ca 15 min to give a clear solution, and was then stirred at room temperature for 18 h. Ethyl acetate (100 ml) and sodium carbonate solution (100 ml) were added and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 50 ml) and the combined organic extracts were washed with brine and dried (Na_2SO_4) and concentrated to give the title compound as an oil (5.0 g, 69%).

Preparation 34 : 9-(Phenylmethyl)-9-azatricyclo[5.3.1.$0^{2,6}$]undecane-3,4-diol

A solution of 9-(phenylmethyl)-9-azatricyclo[5.3.1.$0^{2,6}$]undec-3-ene (Preparation 35, 6.7 g, 28.0 mmol), *N*-methylmorpholine N-oxide (3.45 g, 29.45 mmol) and osmium tetroxide (2.5 wt % in 2-methyl-2-propanol, 2 □l) in acetone (50 ml) was stirred for 18 h. Florisil and aqueous sodium hydrogensulfite (4 ml) were added and the reaction mixture was stirred for 30 min and filtered. Methanol (50 ml) was added and the reaction mixture was concentrated to give an oil which was purified by flash chromatography eluting with ethyl acetate : hexane (50:50) to give an oil (6.2 g, 80%) which crystallises upon standing.

Preparation 35 : 9-(phenylmethyl)-9-azatricyclo[5.3.1.$0^{2,6}$]undec-3-ene

T a stirred solution of tricyclo[5.2.1.$0^{2,6}$]dec-3-ene-8,9-diol (Preparation 36, 6.24 g, 37.6 mmol) in dioxane (100 ml) was added sodium periodate (8.04 g, 37.6 mmol) in water (80 ml) and the reaction mixture was stirred vigorously for 45 min. The reaction mixture was extracted with ethyl acetate (4 x 100 ml) and the combined extracts were washed with brine, dried (Na_2SO_4) and concentrated *in vacuo*. The crude oil (6.1 g, 37.1 mmol) was diluted with dichloroethane (400 ml) and benzylamine (3.98 g, 37.1 mmol) was added. After 3 min, sodium triacetoxyborohydride (25.23 g, 119 mmol) was added and the reaction mixture was stirred at room temperature for 18 h. Saturated sodium carbonate solution (200 ml) was added, and after 30 min, the layers were separated and the aqueous layer was washed with dichloromethane (3 x 50 ml). The combined organic extracts were washed with brine, filtered and concentrated. The crude yellow oil was purified by flash chromatography eluting with ethyl acetate : dichloromethane (10 : 90) to give the title compound as a colourless oil (6.7 g, 75 %)

Preparation 36 : Tricyclo[5.2.1.$0^{2,6}$]dec-3-ene-8,9-diol

A slurry of tricyclo[5.2.1.$0^{2,6}$]deca-3,8-diene (26.5 g, 0.2 mol), trimethylamine N-oxide dihydrate (22.3 g, 0.2 mol) and osmium tetroxide (2.5 wt % solution in 2-methyl-2-propanol, 2 □l) in dichloromethane (200 ml) was stirred for 18 h. A further portion of osmium tetroxide (2.5 wt % solution in 2-methyl-2-propanol, ca. 2 □l) was added, water (25 ml) and acetone (50 ml) was added and the reaction mixture was stirred for a further 72 h. Pyridine (0.5 ml) and tetrabutylammonium acetate (0.5 g) were added. Florisil (10 g) and aqueous sodium hydrogensulfite solution was added and the reaction mixture was stirred for 20 min. The reaction mixture was filtered and the product was extracted with dichloromethane (3 times). The combined organic extracts were washed with water, brine and then concentrated to give an oil. The

crude oil was purified by flash chromatography eluting with ethyl acetate : hexane (10 : 90) and then ethyl acetate, to give a waxy solid (6.5 g, 19%).

Preparation 39 : 3-cyclohexyl-3-methylpiperidine hydrochloride salt

To a solution of 3-methyl-3-phenylpiperidine (500 mg, 2.85 mmol) in methanol (8 ml) was added concentrated hydrochloric acid (1 ml) and platinum (IV) oxide (500 mg). The reaction mixture was hydrogenated at 50 psi for 3 h before filtering through Celite® and concentrating. The crude residue was dissolved in dichloromethane and washed with sodium carbonate and concentrated to give a crude semi solid. The crude product was dissolved in diethyl ether (15 ml) and methanol (5 ml) and hydrogen chloride (1M in diethyl ether, 30 ml) was added to afford a white solid which was filtered to give the pure product (0.41 g, 66%).

Preparation 40 : 3-methyl-3-(2-pyridinyl)piperidine

To a dried flask under nitrogen was added borane tetrahydrofuran complex (1 M solution, 8.79 ml, 8.79 mmol), and tetrahydrofuran (10 ml). The solution was cooled to 0°C and a solution of 5-methyl-5-(2-pyridinyl)-2-piperidone (Preparation 41, 1 g, 5.26 mmol) in tetrahydrofuran (20 ml) was added. The reactants were warmed to room temperature and then heated at reflux for 6 h. Further borane tetrahydrofuran complex (1M solution, 8.79 ml, 8.79 mmol) was added and the reaction mixture was heated at reflux for 18 h. Thin layer chromatography still showed starting material was present so further borane tetrahydrofuran complex (1M solution, 8.79 ml, 8.79 mmol) was added and the reaction mixture was heated under reflux for 18 h. Upon completion hydrochloric acid (6M) was added to the reaction mixture and the mixture was stirred for 30 min. The reaction mixture was partially concentrated before adjusting to pH 11 with solid sodium hydroxide. The organic extracts were extracted with dichloromethane (5 x 20 ml) and dried (Na_2SO_4) to give a crude oil (0.45 g). The oil was purified by flash chromatography eluting with

dichloromethane : methanol : 0.88 ammonia solution (94 : 4 : 2) to give the title compound as an oil (0.20 g, 22%).

Preparation 41 : 5-methyl-5-(2-pyridinyl)-2-piperidone

To methyl 4-cyano-4-(2-pyridinyl)pentanoate (Preparation 42, 2.5 g, 11.4 mmol) in ethanol (30 ml) was added Raney nickel (3 g) and the reaction mixture was hydrogenated for 78 h. The reaction mixture was filtered through Celite® washing with ethanol (3.20 ml). The combined organic extracts were concentrated *in vacuo* to give the crude desired product (2.2 g) which was purified by flash chromatography eluting with dichloromethane : methanol (96 : 7) to give the pure product as an oil (1.1 g, 51%).

Preparation 42 : Methyl 4-cyano-4-(2-pyridinyl)pentanoate

To a dried flask under nitrogen was added 2-(2-pyridinyl)-propanenitrile (Preparation 43, 6.26 g, 47.4 mmol), t-butanol (30 ml), Triton B (6.66 g, 39.8 mmol) and methyl acrylate (6.12 g, 71.1 mmol). The reaction mixture was heated at reflux for 2.5 h. The solid was removed and the filtrate concentrated *in vacuo* to give a yellow oil. Water (30 ml) was added and the product was extracted with diethyl ether. The organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give a light yellow oil (4.32 g, 42%).

Preparation 43 : 2-(2-pyridinyl)-propanenitrile

To a dried flask under nitrogen was added dimethyl sulphoxide (100 ml) and tosmic (20.95 g, 107.3 mmol). The reaction mixture was cooled to 0°C before potassium t-butoxide (33.35 g, 297.1 mmol) was added. After 5 min, methanol (3.7 ml) was added followed by 1-(2-pyridinyl)ethanone (10 g, 32.5 mmol) and the reaction mixture was stirred at room temperature for 18 h. The reaction mixture was poured in brine : hexane : ethyl acetate (50 : 25 : 25). The organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to yield

a crude oil. The oil was purified by flash chromatography eluting with ethyl acetate : hexane (3 : 7) to give the title compound as a brown solid (8.26 g, 76%).

Preparation 46 : 2-[(4-piperidinylmethyl)sulfanyl]pyridine hydrochloride salt

tert-Butyl 4-[(2-pyridinylsulfanyl)methyl]-1-piperidinecarboxylate (Preparation 47, 0.90 g, 2.9 mmol) in hydrogen chloride (4 M solution in dioxane, 7.5 ml) was stirred under nitrogen at room temperature. After 20 min a white solid precipitated out of solution. Diethyl ether was added and the reaction mixture was filtered and the solid washed with diethyl ether. The title compound was obtained as a solid (0.70 g, 98%).

Preparation 47 : *tert*-butyl 4-[(2-pyridinylsulfanyl)methyl]-1-piperidinecarboxylate

To a stirred solution of *tert*-butyl 4-(hydroxymethyl)-1-piperidinecarboxylate (Preparation 48, 1.0 g, 5 mmol) in benzene (40 ml) under nitrogen was added triphenyl phosphine (1.44 g, 5.5 mmol). Diethyl azodicarboxylate (0.86 ml, 5.5 mmol) in benzene (4 ml) was added dropwise and the reaction mixture was stirred for 5 min. 2-mercapto pyridine (0.61 g, 5.5 mmol) was added and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was washed with sodium hydroxide (1M), water, and saturated brine. The organic extracts were dried (Na_2SO_4) and concentrated to an oil which was purified by flash chromatography on silica gel eluting with dichloromethane : ethyl acetate (9 : 1). The title compound was obtained as an oil (0.7 g, 58%).

Preparation 48 : *tert*-butyl 4-(hydroxymethyl)-1-piperidinecarboxylate

To a stirred solution of 1-*tert*-butyl 4-ethyl 1,4-piperidinedicarboxylate (Preparation 49, 12.8 g, 0.05 mol) in benzene (300 ml) under nitrogen was added slowly diisobutyl aluminium hydride (1 M solution, 100 ml, 0.1 mol). The reaction mixture was stirred at room temperature for 3 h before quenching by the addition of water (100 ml) followed by addition of hydrochloric acid (1 M) to adjust to pH 4. The organic layer was separated and the aqueous layer extracted with ethyl acetate. The combined organic extracts were dried (Na_2SO_4) and concentrated to give an oil. The crude oil was purified by flash chromatography on silica gel eluting with ethyl acetate : dichloromethane (6:4) to give the title compound as an oil (5.0 g, 46%).

Preparation 49 : 1-*tert*-butyl 4-ethyl 1,4-piperidinedicarboxylate

To a solution of ethyl 4-piperidinecarboxylate (15.4 ml, 0.1 mol) in dichloromethane (100 ml) stirred under nitrogen and cooled to 0°C was added di-*tert*-butyl dicarbonate (21.5 g, 0.1 mol). The reaction mixture was stirred at room temperature for 18 h before washing with water and then saturated brine. The organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give the title compound as an oil (25 g, 97%).

Preparation 50 : 2-[(3-piperidinylmethyl)sulfanyl]pyridine hydrochloride salt

tert-Butyl 3-[(2-pyridinylsulfanyl)methyl]-1-piperidinecarboxylate (Preparation 51, 1.0 g, 3.2 mmol) in hydrogen chloride (4 M solution in dioxane, 8.1 ml) was stirred under nitrogen at room temperature. After 25 min a white solid precipitated out of solution. Diethyl ether was added and the reaction mixture was filtered and the solid washed with diethyl ether. The title compound was obtained as a solid (0.81 g, 100%).

Preparation 51 : *tert*-butyl 3-[(2-pyridinylsulfanyl)methyl]-1-piperidinecarboxylate

To a stirred solution of *tert*-butyl 3-(hydroxymethyl)-1-piperidinecarboxylate (Preparation 52, 1.0 g, 5 mmol) in benzene (40 ml) under nitrogen was added triphenyl phosphine (1.44 g, 5.5 mmol). Diethyl azodicarboxylate (0.86 ml, 5.5 mmol) in benzene (4 ml) was added dropwise and the reaction mixture was stirred for 5 min. 2-mercapto pyridine (0.61 g, 5.5 mmol) was added and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was washed with sodium hydroxide (1M), water, and saturated brine. The organic extracts were dried (Na_2SO_4) and concentrated to an oil which was purified by flash chromatography on silica gel eluting with dichloromethane : ethyl acetate (9 : 1). The title compound was obtained as an oil (1.0 g, 65%).

Preparation 52 : *tert*-butyl 3-(hydroxymethyl)-1-piperidinecarboxylate

To a stirred solution of 3-piperidinylmethanol (5.06 g, 44 mmol) in dichloromethane (100 ml) under nitrogen was added di-*tert*-butyl dicarbonate (9.6 g, 44 mmol) and the reaction mixture was stirred at room temperature for 18 h. The reaction mixture was washed with water and then saturated brine. The organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give the title compound as an oil (9.0 g, 95%)

Preparation 56 : *N*-methoxy-*N*-methyl-2-piperidinecarboxamide

To ethyl 2-piperidincarboxylate (18.3 g, 0.12 mol) was added *N,O*-dimethylhydroxylamine hydrochloride (34.1 g, 0.35 mol) in dichloromethane (200 ml) followed by dropwise addition of triethylaluminium (1M solution in hexane, 350 ml, 0.35 mol). The reaction mixture was stirred for 3 h before quenching with tartaric acid (1 M solution, 25 ml) with cooling to maintain a temperature of ~20°C. The reaction mixture was stirred for 18 h and then filtered through Celite®, the filtrate was concentrated *in vacuo* to give a white solid (6.2 g). The Celite® plug was stirred with methanol, filtered and the

filtrate evaporated to dryness to give more solid (20 g). The solids were combined and purified by flash chromatography on silica gel eluting with dichloromethane and then dichloromethane : methanol (95 : 5) to give the pure product (15.8 g, 79%).

Preparation 67 : 1-(3-chloro-4-methylphenyl)piperazine

To a mixture of 3-chloro-4-methylaniline (105.5 g, 0.745 mol) and diethanolamine (78.1 g, 0.745 mol) was added slowly with stirring and cooling concentrated hydrochloric acid (c.a. 100 ml) to adjust the reaction mixture to pH 7. The reaction mixture was heated to remove water (66 ml), after standing for 18 h the mixture was heated to 240°C for 6 h. Sodium hydroxide (5N, solution, 236 ml) was added and the product was extracted with chloroform (4 x 100 ml). The combined organic extracts were concentrated to give a red oil which was purified by distillation to give the title compound (107.0 g, 68%)

Preparation 87 : Piperidin-4-yl butylcarbamate

1-(Phenylmethyl)piperidin-4-yl butylcarbamate (Preparation 109, 13.0 g) in ethanol (100 ml) containing palladium (5% on carbon) was hydrogenated at 60 psi to give the title compound as a green oil that solidified upon standing.

Preparation 89 : 2-methyl-4-piperidin-1-yl-5,6,7,8-tetrahydropyrido[3,4-d]pyrimidine

A solution of 2-methyl-7-(phenylmethyl)-4-piperidin-1-yl-5,6,7,8-tetrahydropyrido[3,4-d]pyrimidine (Preparation 88, 12 g) in ethanol (200 ml) was adjusted to pH 2 with concentrated hydrochloric acid, palladium (5% on carbon) was added and the reaction mixture was hydrogenated at 60 psi. The reaction mixture was filtered, and the filtrate concentrated *in vacuo*.

Chloroform and sodium hydroxide (2 M solution) were added and the organic extracts were dried, and concentrated *in vacuo*. The crude residue was dissolved in petroleum ether (30-40) and cooled in ice, the title compound was collected as a solid.

Preparation 88 : 2-methyl-7-(phenylmethyl)-4-piperidin-1-yl-5,6,7,8-tetrahydropyrido[3,4-d]pyrimidine

2-methyl-7-(phenylmethyl)-5,6,7,8-tetrahydropyrido[3,4-*d*]pyrimidin-4(4a*H*)-one (Preparation 85, 19 g) and phosphorous oxychloride (150 ml) was heated for 1.5 h. The reaction mixture was concentrated and poured onto ice. Sodium carbonate was added to adjust pH to 10, and the product was extracted with chloroform. The organic extracts were concentrated and then purified by passing through a thick pad of florisil (5 cm diameter) the product was eluted with chloroform. Evaporation gave a dark red oil which was dissolved in ethanol (100 ml) and piperidine (25 ml) was added. After 72 h, the reaction mixture was concentrated *in vacuo* then dissolved in chloroform and basified with sodium hydroxide (2 M solution). The reaction mixture was dried and concentrated before purifying by flash chromatography on florisil eluting the product with petroleum ether (30-40) to give the title compound (12.5 g)

Preparation 85 : 2-Methyl-7-(phenylmethyl)-5,6,7,8-tetrahydropyrido[3,4-*d*]pyrimidin-4(4a*H*)-one

Sodium metal (4.4 g, 0.19 mol) was dissolved in ethanol (300 ml) and acetamidine hydrochloride (9.3 g, 0.1 mol) was added. After 30 min, commercially available ethyl 3-oxo-1-(phenylmethyl)-piperidine-4-carboxylate hydrochloride (25 g, 0.084 mol) was added and the reaction mixture was refluxed for 18 h. The reaction mixture was filtered and the concentrated *in vacuo* to give the title compound (20 g).

Preparation 93 : 1-(1,3-thiazol-2-ylcarbonyl)piperazine

Piperazine (2.33 g) was dissolved in glacial acetic acid (25 ml) and the reaction mixture was heated to 60°C. A suspension of 1,3-thiazole-2-carbonyl chloride (Preparation 107, 4.0 g, 27.1 mmol) in glacial acetic acid (10 ml) was added dropwise over 10 min and the reaction mixture was stirred at 60°C for 30 min and then at room temperature for 18 h. The precipitated solid was filtered and dried, and the mother liquor was concentrated *in vacuo*. Water (50 ml) was added to the mother liquor and the solution was adjusted to pH 9 using sodium hydroxide solution (5M). The product was extracted with chloroform and the combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to give a yellow oil (1.85 g). The oil was dissolved in diethyl ether and hydrogen chloride (1 M solution in diethyl ether) was added, a white solid precipitated was filtered off and recrystallised from isopropanol to give the title compound as a white solid (0.5 g)

Preparation 107 : 1,3-thiazole-2-carbonyl chloride

1,3 thiazole-2-carboxylic acid (Preparation 92, 5.0 g, 39 mmol) was added to a solution containing sodium hydroxide (1.55 g), in water (26 ml). The solution was evaporated to dryness and the resultant solid was triturated with diethyl ether, filtered and dried in an oven at 60°C for 6 h to give a brown solid (5.5 g). The solid was added to thionyl chloride (25 ml) and heated on a steam bath for 2 h. The excess thionyl chloride was removed *in vacuo* and the resultant oil was triturated with petroleum ether (40-60, 3 x 30 ml) to give the title compound as an oily solid upon filtration and evaporation (4.0 g, 70%).

Preparation 92 : 1,3 thiazole-2-carboxylic acid

To a solution of 2-bromothiazole (16.4 g, 0.1 mol) in anhydrous diethyl ether (50 ml) at –70°C was added slowly *n*-butyl lithium (1.6 M solution in hexane, 75 ml). The reaction mixture was stirred at –70°C for 20 min and was then added portion-wise to powdered solid carbon dioxide (500 g). The reaction

mixture was stirred for 18 h, and the resultant mixture was dissolved in water (70 ml) filtered and extracted with diethyl ether (3 x 75 ml). The aqueous layer was acidified by the addition of sulphuric acid (10 M solution) and cooled to 0°C. A solid crystallised out and was removed by filtration, washed with cold water, and dried at 50°C for 6 h to give the title compound as a light brown solid (5.0 g).

Preparation 96 : 4-[[(4-fluorophenyl)methyl]oxy}piperidine oxalate salt

1-acetyl-4-[[(4-fluorophenyl)methyl]oxy}piperidine(Preparation 97, 9 g, 36 mmol) in methanol (60 ml) and sodium hydroxide solution (5 M, 100 ml) were refluxed on a steam bath for 4 h. After cooling the solution was extracted with chloroform (3 x 100ml) and the organic extracts were dried (Na_2SO_4) and concentrated to give an orange oil (8 g, 97%). A portion was dissolved in diethyl ether and treated with oxalic acid in ether to give a white solid which was recrystallised from ethanol to give needle crystals (3 g).

Preparation 97 : 1-acetyl-4-[[(4-fluorophenyl)methyl]oxy}piperidine

1-Acetylpiperidin-4-ol (Preparation 193, 10 g, 70 mmol) in *N,N*-dimethylformamide (50 ml) was added dropwise to a stirred suspension of sodium hydride (50% wt dispersion in oil, 3.8 g, 80 mmol) in *N,N*-dimethylformamide (50 ml) at room temperature under nitrogen. After stirring the reaction mixture for 3 hours, 4-fluorobenzyl chloride (10.1 g, 70 mmol) in *N,N*-dimethylformamide (50 ml) was added dropwise and the reaction mixture was stirred for a further 4 h. The reaction mixture was filtered and the filtrate was evaporated to give an orange oil. Water was added and the mixture was extracted with petroleum ether (3 x 100 ml) and then with diethyl ether (3 x 100 ml). The combined organic extracts were washed with sodium hydroxide solution (1 M, 3 x 100 ml), before drying (Na_2SO_4) and concentrating to give the title compound as an oil (10.1 g, 99%).

Preparation 98 : 4-{[(4-chlorophenyl)methyl]oxy}piperidine

1-acetyl-4-{[(4-chlorophenyl)methyl]oxy}piperidine (Preparation 99, 11 g, 41.1 mmol) in methanol (50 ml) and sodium hydroxide solution (5 M, 30 ml) were refluxed on a steam bath for 10 h. After cooling, methanol was removed and the remaining solution was extracted with petroleum ether (40-60, 3 x 30 ml). The organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give an white solid (5.8 g, 62%). A portion was recrystallised from petroleum ether to give needle crystals (3 g).

Preparation 99 : 1-acetyl-4-{[(4-chlorophenyl)methyl]oxy}piperidine

1-Acetylpiperidin-4-ol (Preparation 193, 10 g, 70 mmol) in *N,N*-dimethylformamide (50 ml) was added dropwise to a stirred suspension of sodium hydride (50% wt dispersion in oil, 4.8 g, 0.1 mol) in *N,N*-dimethylformamide (50 ml) at room temperature under nitrogen. After stirring the reaction mixture for 3 hours, 4-chlorobenzyl chloride (12.8 g, 80 mmol) in *N,N*-dimethylformamide (50 ml) was added dropwise and the reaction mixture was stirred for a further 4 h. The solution was filtered and the filtrate was evaporated to give an orange oil. Water was added and the mixture was extracted with petroleum ether (3 x 50 ml) and then with diethyl ether (3 x 50 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated to give the title compound as an orange oil (15.8 g, 84%).

Preparation 100 : ethyl 4-[(piperidin-4-yloxy)methyl]benzoate hydrochloride salt

4-[(Piperidin-4-yloxy)methyl]benzoic acid (Preparation 101, 7 g, 26 mmol) in ethanol (50 ml) and concentrated sulphuric acid (1 ml) were heated on a steam bath for 6 h. The solvent was removed *in vacuo* and the residue was dissolved in water, basified with sodium carbonate (5% w/v) and extracted with diethyl ether (3 x 50 ml). The organic extracts were dried (Na_2SO_4) and concentrated to give the title compound as a pale yellow oil (4.4 g, 64%). A portion (1 g) was dissolved in diethyl ether and treated with hydrogen chloride

(1 M solution in diethyl ether) to give a yellow solid which was recrystallised from ethanol and diethyl ether to give yellow platelets (0.5 g).

Preparation 101 : 4-[(piperidin-4-yloxy)methyl]benzoic acid

1-acetyl-4-[(piperidin-4-yloxy)methyl]benzoic acid (Preparation 102, 20 g, 72 mmol), aqueous sodium hydroxide solution (5 M, 75 ml), and methanol (75 ml) were heated to 100°C for 4 h, and then evaporated to give a thick suspension. The crystals were filtered off, dissolved in water and the pH adjusted to 1 with hydrochloric acid (2 M, 200 ml) at 0°C. The cloudy solution was evaporated to dryness and the white solid recrystallised from isopropyl alcohol to give the title compound (15.2 g, 90%).

Preparation 102 : 1-acetyl-4-[(piperidin-4-yloxy)methyl]benzoic acid

1-Acetylpiperidin-4-ol (Preparation 196, 20 g, 0.14 mol) in *N,N*-dimethylformamide (50 ml) was added dropwise to a stirred suspension of sodium hydride (50% wt dispersion in oil, 19.2 g, 0.40 mol) in *N,N*-dimethylformamide (50 ml) at room temperature under nitrogen. After stirring the reaction mixture for 3 hours, 4-(bromomethyl)benzoic acid (30.1 g, 0.14 mol) in *N,N*-dimethylformamide (50 ml) was added dropwise to the solution at 0°C and the reaction mixture was stirred for a further 4 h. The solution was diluted with water (200 ml) and then extracted with chloroform (3 x 150 ml). The aqueous layer was separated, cooled to 0°C and the pH adjusted to 1 with concentrated hydrochloric acid. The white solid was filtered off and dried to give the title compound (27 g, 74%).

Preparation 103 : 4-[(3-phenylpropyl)oxy]piperidine hydrochloride salt

A solution of 1-acetyl-4-[(3-phenylpropyl)oxy]piperidine (Preparation 104, 4 g) in sodium hydroxide (5 M solution, 20 ml) and methanol (20 ml) was heated

on a steam bath for 6 hours during which time the methanol was allowed to evaporate off. After cooling the solution the product was extracted with chloroform (3 x 30 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated to give a yellow oil (3.7 g, 88%). The product was dissolved in diethyl ether and treated with hydrogen chloride (1M solution in diethyl ether) to give a white solid which was filtered off and dried.

Preparation 104 : 1-acetyl-4-[(3-phenylpropyl)oxy]piperidine

1-Acetylpiperidin-4-ol (Preparation 193, 8 g, 60 mmol) in *N,N*-dimethylformamide (50 ml) was added dropwise to a stirred suspension of sodium hydride (50% wt dispersion in oil, 3.68 g, 80 mmol) in *N,N*-dimethylformamide (50 ml) at room temperature under nitrogen. After stirring the reaction mixture for 4 hours, 1-bromo-3-phenylpropane (12.94 g, 65 mmol) in *N,N*-dimethylformamide (50 ml) was added dropwise to the solution at 0°C and the reaction mixture was stirred for a further 4 h. The solution was diluted with isopropyl alcohol (20 ml) and water (100 ml) and then evaporated to give a semi solid. Water (100 ml) was added and the solution was extracted with petroleum ether (3 x 100 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give an orange oil (4.3 g, 27%).

Preparation 109 : 1-(phenylmethyl)piperidin-4-yl butylcarbamate

1-(Phenylmethyl)piperidin-4-ol (10 g, 52.2 mmol) was stirred in dioxane (90 ml) at room temperature. N-butyl isocyanate (5.0 g, 52.2 mmol) in dioxane (10 ml) was added and the reaction mixture was heated under reflux for 24 h. Water (20 ml) was added and the reaction mixture was concentrated *in vacuo* to give a brown oil. The crude product was partitioned between diethyl ether and water and the organic extracts were dried ($MgSO_4$) to give the title compound as an oil (14 g, 92%).

Preparation 128 : 1,1-dimethylethyl (3*R*)-3-hydroxypiperidine-1-carboxylate

To a solution of (3*R*)-piperidin-3-ol . (*S*) camphor sulphonic acid salt (Preparation 115, 5.03 g, 15.7 mmol) in dichloromethane (50 ml) and triethylamine (2.4 ml, 17.3 mmol) was added at 0°C a solution of di-*tert*-butyl dicarbonate (3.8 g, 17.3 mmol) dropwise in dichloromethane (10 ml). The reaction mixture was stirred at room temperature for 3 d, before ethyl acetate and water were added. The organic extracts were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give the title compound as a colourless oil (3.29 g, 100%).

Preparation 115 : (3*R*)-piperidin-3-ol . (*S*) camphor sulphonic acid salt

(*S*)-camphor sulphonic acid (109.4 g, 0.47 mol) and racemic piperidin-3-ol (48.5 g, 0.47 mol) were dissolved in butanone (400 ml) and the reaction mixture was heated under reflux and then allowed to cool to room temperature. After stirring for several hours, the resultant precipitate was filtered off, washed with butanone and then dried in a vacuum oven at 55°C. The title compound was obtained as a white powder (52.27 g, 35%).

Preparation 127 : 1,1-dimethylethyl (3S)-3-hydroxypiperidine-1-carboxylate

To a solution of (3*S*)-piperidin-3-ol . (*R*) camphor sulphonic acid salt (Preparation 116, 10.0 g, 31.4 mmol) in dichloromethane (80 ml) and triethylamine (5.0 ml, 35.3 mmol) was added at 0°C di-*tert*-butyl dicarbonate (3.8 g, 17.3 mmol) in one portion. The reaction mixture was stirred at room temperature for 2 d, before concentrating *in vacuo*. The residue was partitioned between ethyl acetate and water, the organic extracts were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give the product as a pale yellow oil (6.25 g). The oil was purified by flash chromatography on silica gel eluting with diethyl ether : hexane (2:1 and then 1:0) to give the title compound as a colourless oil 5.2 g, 83%).

Preparation 116 : (3*S*)-piperidin-3-ol . (*R*) camph r sulphonic acid salt

(*R*)-camphor sulphonic acid (32.6 g, 0.14 mol) and piperidin-3-ol (14.8 g, 0.14 mol) were dissolved in butanone (150 ml) and the reaction mixture was heated under reflux and then allowed to cool to room temperature. After stirring for 6 h, the resultant precipitate was filtered off, washed with butanone and then dried in a vacuum oven. The title compound was obtained as a white solid (16.2 g, 36%).

Preparation 117 : 1,1-dimethylethyl 3-hydroxypiperidine-1-carboxylate

To a solution of piperidin-3-ol hydrochloride salt (10.1 g, 0.1 mmol) in dichloromethane (30 ml) and triethylamine (13.3 ml, 95.4 mmol) was added a solution of di-*tert*-butyl dicarbonate (19.8 g, 90.9 mmol) dropwise in dichloromethane. Upon completion the reaction mixture was added to diethyl ether (120 ml) washed with hydrochloric acid (1 M) and then with brine. The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to give the title compound as a light yellow oil (17.7 g, 88%).

Preparation 126 : (1*S*,2*R*,4a*R*,5*R*,8*S*,8a*S*)-1,8a-dihydroxy-5-isopropenyl-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydro-2-naphthalenyl acetate and
Preparation 118 Methyl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

A solution of (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate, (Preparation 1, 100 g) and triethylamine (10 ml) in methanol (1000 ml) was stirred at room temperature for 3 hours. The reaction mixture was evaporated and the residue was crystallised from ethyl acetate/hexane to give a pure sample of the terpene, (1*S*,2*R*,4a*R*,5*R*,8*S*,8a*S*)-1,8a-dihydroxy-5-isopropenyl-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydro-2-naphthalenyl acetate (Preparation

126). The remaining solution was concentrated and purified by flash column chromatography on silica gel eluting with ethyl acetate : dichloromethane : hexane (2 : 1 : 7) to give further terpene moiety (1*S*,2*R*,4a*R*,5*R*,8*S*,8a*S*)-1,8a-dihydroxy-5-isopropenyl-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydro-2-naphthalenyl acetate as a white solid (Preparation 126, 43 g).
Further elution gave the alkaloid molety, methyl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate as a light yellow solid (Preparation 118, 50 g).

Preparation 125 : ethyl decahydroisoquinoline-3-carboxylate

2-(1,1-dimethylethyl) 3-ethyl octahydroisoquinoline-2,3(1*H*)-dicarboxylate (Preparation 124, 2.3 g, 7.4 mmol) was dissolved in ethyl acetate (220 ml) and then saturated with hydrogen chloride gas at 4°C. The reaction mixture was warmed to room temperature, stirred and then concentrated *in vacuo* to give the crude product which was triturated with diethyl ether. The resulting solid was filtered off and dried *in vacuo* to give the title compound (1.24 g, 68%).

Preparation 124 : 2-(1,1-dimethylethyl) 3-ethyl octahydroisoquinoline-2,3(1*H*)-dicarboxylate

2-(1,1-dimethylethyl) 3-ethyl 3,4-dihydroisoquinoline-2,3(1*H*)-dicarboxylate (Preparation 123, 3.1 g, 10.2 mmol) was dissolved in ethanol (250 ml) and rhodium (10% w/w on carbon, 0.3 g) was added. The reaction mixture was hydrogenated for 17 h at 50°C and 50 psi. More rhodium (10% w/w on carbon, 0.3 g) was added and the mixture was hydrogenated for a further 17 h. Again this procedure was repeated, with additional hydrogenation for 48 h. The catalyst was removed from the reaction mixture by filtration, upon concentration of the filtrate the crude product was obtained (2.96 g). The crude product was purified firstly by flash chromatography on silica gel (70 g) eluting with hexane : ethyl acetate (20 : 1 and then 10 : 1) and then by flash

chromatography on silica gel eluting with hexane : diethyl ether (5 : 1) to give the desired product (2.3 g, 73%).

Preparation 123 : 2-(1,1-dimethylethyl) 3-ethyl 3,4-dihydroisoquinoline-2,3(1*H*)-dicarboxylate

To a solution of ethyl 1,2,3,4-tetrahydroisoquinoline-3-carboxylate (Preparation 122, 3.64 g, 17.7 mmol) in tetrahydrofuran (50 ml) was added a stirred solution of sodium hydrogen carbonate (2.97 g, 35.4 mmol) in water (60 ml). Di-*tert*-butyl dicarbonate (5.8 g, 26.6 mmol) was added slowly and the reaction mixture was stirred for 18 h before concentrating *in vacuo*. The residue was dissolved and partitioned between ethyl acetate (200 ml) and aqueous sodium hydrogen carbonate solution (5%, 200 ml). The aqueous layer was washed with ethyl acetate (2 x 100 ml). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give the crude product which was purified by flash chromatography on silica gel (70 g) eluting with hexane : ethyl acetate (20 : 1 and then 10 : 1) to give the title compound (4.4 g, 81%).

Preparation 122 : ethyl 1,2,3,4-tetrahydroisoquinoline-3-carboxylate

1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid camphor sulphonic acid salt (Preparation 120, 6 g, 17.2 mmol) was dissolved in ethanol (140 ml) and saturated with hydrogen chloride (gas). The reaction mixture was heated under reflux for 18 h before concentrating *in vacuo*. The crude residue was dissolved in dichloromethane (150 ml) and washed with sodium hydrogen carbonate (150 ml). The organic layer was collected and washed again with sodium hydrogen carbonate (2 x 100 ml) before drying (Na_2SO_4) and concentrating *in vacuo* to give the title compound as a yellow oil (3.64 g, 100%).

Preparation 120 : 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

Phenylmethyl 1,2,3,4-tetrahydroisoquinoline-3-carboxylate camphor sulphonic acid salt (Preparation 121, 8.3 g, 18.9 mmol) was dissolved in ethanol (600 ml) and palladium on carbon (10%, 0.8 g) was added at room temperature under nitrogen. The reaction mixture was hydrogenated at room temperature at 30 psi for 3 h. The catalyst was removed by filtration and the filtrate was concentrated to give the title compound (6.6 g, 100%).

Preparation 121: Phenylmethyl (3*R*)-1,2,3,4-tetrahydroisoquinoline-3-carboxylate

D-Phenylalanine (50 g, 0.3 mol) concentrated hydrochloric acid (386 ml), and formalin (37% wt, 113.7 ml) were heated at 95°C with vigorous stirring for 4 h. The reaction mixture was cooled to room temperature and stirred for a further 2 h. The reaction mixture was filtered and the precipitate was washed with cold water to give (3*R*)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid as a white solid (25 g, 42%). Benzyl alcohol (64 g) and p-toluene sulphonic acid (26.9 g) were added and the reaction mixture was refluxed in benzene (400 ml) under Dean Stark conditions. The solvent was removed *in vacuo*, the crude residue was triturated with diethyl ether to give a solid which was then recrystallised from water and methanol to give the title compound as a white solid (28 g, 35%).

Preparation 139 : (1S,2R,4aS,5R,8R,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a stirred suspension of (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate, (Preparation 1, 1 g)

in methanol (25 ml) was added a solution of concentrated hydrochloric acid (2 ml) in methanol (25 ml). After 5 days the reaction mixture was diluted with dichloromethane (150 ml), washed with water (3 x 100 ml), filtered through cotton wool and evaporated to dryness to give a yellow, oily solid. This residue was partially dissolved in dichloromethane (25 ml) and hexane (50 ml) was slowly added. After 1 hour, the suspension was filtered to give the product as an off-white solid (900 mg).

Preparation 140 : (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

T a solution of (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 1, 500mg, 0.89mmol) in tetrahydrofuran (8ml) at -10°C under nitrogen was added borane (1M solution in tetrahydrofuran, 2ml, 2mmol) and the resulting mixture stirred and allowed to come to room temperature. After 5 hours borane (1M solution in tetrahydrofuran, 1ml, 1mmol) was added and the reaction stirred at room temperature for 18 h. To the reaction mixture was added 4-methylmorpholine *N*-oxide (600mg, 5.1mmol) and the mixture heated to gentle reflux for 3 hours. The reaction mixture was concentrated *in vacuo* and the residue treated with water (30ml) and extracted with ethyl acetate (2 x 30ml). The combined organic extracts were washed with saturated aqueous sodium chloride solution, dried ($MgSO_4$) and the solvent removed *in vacuo* to give an orange glass. The crude product was purified by column chromatography on silica eluting with hexane : ethyl acetate (2:1 then 1:1) and then ethyl acetate. The pure fractions were combined and concentrated *in vacuo* to give a the title product as a yellow solid (132mg, 26%).

Preparation 141 : (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To a stirred mixture of (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 140, 230mg, 0.40mmol) and 4Å molecular sieves in dichloromethane (18ml) was added tetrapropylammonium perruthenate (23mg, 0.065mmol) and N-methylmorpholine-N-oxide (180mg, 1.54mmol) in nine portions. The resulting mixture was stirred for 36 hours before diluting with dichloromethane and washing with aqueous sodium hydrogen sulfite solution and then saturated aqueous sodium chloride solution. The organic extracts were dried and concentrated *in vacuo*. The crude product was purified by column chromatography on silica eluting with ethyl acetate: hexane (1:1) to give the title product (50mg, 22%).

Preparation 142 : (1S,2R,4aR,8R,8aR)-8a-hydroxy-2-[(1H-imidazol-1-ylcarbonyl)oxy]-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To (1S,2R,4aS,5R,8R,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 139, 50 mg, 0.10 mmol) in dichloromethane (1 ml) was added carbonyl diimidazole (17 mg, 0.10 mmol) at room temperature. Upon completion the reaction mixture was purified by flash chromatography eluting with ethyl acetate : hexane (50 : 50 and then 100 : 0). The title compound was obtained as a white solid (36 mg).

Preparation 143 : (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-{2-[(1H-imidazol-1-ylcarbonyl)oxy]-1-methylethyl}-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methy l-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 140, 0.30 g, 0.52 mmol) in dichloromethane was added 1,1'-carbonyldiimidazole (0.92 g, 0.57 mmol) and the reaction mixture was stirred for 18 h. The reaction mixture was diluted with water and extracted with dichloromethane. The organic extracts were washed with brine, dried and then concentrated *in vacuo*. The crude product was purified by flash chromatography eluting with ethyl acetate : hexane (2 : 1) to give the title compound (0.16 g, 46%).

Preparation 144 : (1S,4aS,5S,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine -2-carboxylate

To a stirred suspension of (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetyloxy)-8a-hydroxy-5-isopropyl-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenyl-(2*S*,3a*R*,9b*R*)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Example 1, 887 mg) in methanol (25 ml) was added a solution of concentrated hydrochloric acid (1 ml) in methanol (25 ml). After 4 days the reaction mixture was diluted with dichloromethane (150 ml) and washed with water (3 x 100 ml). The combined aqueous layers were washed with dichloromethane (25 ml). All the organic phases were combined, dried and concentrated to yield a yellow solid (802

mg). Purification was achieved by flash column chromatography on silica gel eluting with 1:1 ethyl acetate:hexane to give the product (604 mg).

Preparation 145 : 1,1-dimethylethyl 3-[[(3,4-difluorophenyl)methyl]oxy}piperidine-1-carboxylate

To sodium hydride (60% w/w dispersion in oil, 0.62 g, 16.4 mmol) washed in pentane was added *N,N*-dimethylformamide (20 ml) and then 1,1-dimethylethyl 3-hydroxypiperidine-1-carboxylate (Preparation 117, 3.0 g, 14.9 mmol). The reaction mixture was stirred for 1 h, before adding 3,4-difluorobenzyl bromide (2.0 ml, 16.4 mmol) and stirring the reaction mixture for 18 h. The reaction mixture was concentrated *in vacuo* and the crude residue was dissolved in dichloromethane and washed with brine and dried ($MgSO_4$) before concentrating *in vacuo*. The crude residue was purified by flash chromatography to give the title compound (4.58 g, 94%).

Preparation 146 : 3-[[(3,4-difluorophenyl)methyl]oxy}piperidine

1,1-dimethylethyl 3-[[(3,4-difluorophenyl)methyl]oxy}piperidine-1-carboxylate (Preparation 145, 3.38 g, 10.3 mmol) was dissolved in methanol (100 ml) and cooled to 0°C, hydrogen chloride gas was bubbled into the reaction mixture for 3-5 min. The reaction mixture was concentrated *in vacuo* to give an oil, upon tituration with diethyl ether a white solid formed. The solid was separated by filtration to give the title compound (1.78 g, 65%) as the hydrochloride salt.

Preparation 152 : 2-[(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl] 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

A mixture of ((1S,2R,4aS,5R,6R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate, (Preparation 1, 200 mg), di-*tert*-butyl dicarbonate and 4-dimethylaminopyridine (10 mg) was heated at 65 °C for 1 hour during which time effervescence was noted. The reaction mixture was evaporated and purified by flash column chromatography eluting with ether:hexane (45 : 55) to give the product (244 mg).

Preparation: 153 : (2S,9bR)-6-chloro-3-{[(1,1-dimethylethyl)oxy]carbonyl}-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylic acid

A solution of (2*S*,3a*R*,9b*R*)-3-(*tert*-butoxycarbonyl)-9b-[(*tert*-butoxycarbonyl)oxy]-6-chloro-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylic acid (Preparation 150, 25.4 g) in ethyl acetate (200 ml) was treated with 10% palladium on charcoal (5 g) and stirred under 50 p.s.i. of hydrogen gas for 170 hours. The reaction mixture was filtered through celite, evaporated and purified by flash column chromatography eluting with ethyl acetate : hexane (1 : 4) to give the product as a white foam (17.5 g).

Preparation 150 : (2*S*,3a*R*,9b*R*)-3-(*tert*-butoxycarbonyl)-9b-[(*tert*-butoxycarbonyl)oxy]-6-chloro-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylic acid

A stirred mixture of 4-methoxybenzyl (2*S*,3a*R*,9b*R*)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 155, 29 g), di-*tert*-butyl dicarbonate (100 g) and 4-dimethylaminopyridine (200 mg) was heated at 60 °C for 3 hours and then left at room temperature for 18 h. The reaction mixture was purified by flash

chromatography using silica gel and eluting with a gradient of ethyl acetate : hexane (1 : 9 to 4 : 6) to give the product as a light yellow solid (25.4 g).

Preparation 155: 4-methoxybenzyl (2*S*,3a*R*,9b*R*)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

A stirred solution of methyl (2*S*,3a*R*,9b*R*)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 118 25g), *para*-methoxybenzyl alcohol (115 g) and titanium tetraethoxide (1.5 g) in toluene (300 ml) was heated at reflux for 1 hour. The reaction mixture was cooled, evaporated to a small volume and purified by flash column chromatography on silica gel eluting with a gradient of ethyl acetate : hexane (1 : 4 to 2 : 3) to give the product (29 g).

Preparation 157 : 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate **and diastereomer : Preparation 158** 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

To a stirred, cooled (0 °C) solution of the product of 2-[(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]3-(1,1-dimethylethyl)(2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 152, 6.15 g) in

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degassed tetrahydrofuran (100 ml) was added 9-borabicyclo[3.3.1]nonane (0.5M in tetrahydrofuran, 43.2 ml) dropwise over an hour. The reaction mixture was stirred for 3 hours at room temperature and quenched with a mixture of saturated aqueous sodium hydroxide (60 ml) and aqueous hydrogen peroxide (30%, 40 ml) which was added in portions with cooling. The reaction mixture was extracted with dichloromethane (3 x 400 ml) and the combined organic phases were washed with water (300 ml) and aqueous iron(II)sulfate (300 ml). The washed organic phases were dried (Na_2SO_4), evaporated and purified with Biotage® cartridges containing silica gel (2 x 80 g) using gradient elution ethyl acetate : hexane(1 : 4 to 2 : 3). The major hydroxy isomer 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate, Preparation 158, 4.45 g) and the minor hydroxy isomer 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl}3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate, (Preparation 157, 1.37 g) were both obtained as white foams.

Preparation 159 : 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl}3-(1,1-dimethylethyl)(2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

To a solution of 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl}3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-

c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 157, 780mg, 1mmol), dimethylsulfoxide (1.42ml, 20mmol) and triethylamine (1.39ml, 10mmol) in dichloromethane (10ml) at 0°C was added sulfur trioxide/pyridine complex (980mg, 6mmol) portion-wise over 10 minutes and the resulting mixture stirred for 3 hours at room temperature. The reaction mixture was diluted with water and dichloromethane and the organic layer washed with hydrochloric acid (0.5N solution in water, x2) and aqueous sodium hydrogen carbonate solution, dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified by column chromatography on silica eluting with hexane : ethyl acetate (2:1). The pure fractions were combined and concentrated *in vacuo* to give the title product (695mg, 89%) as a white solid.

Preparation 187 : 2-[(1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-((1*R*)-1-methyl-2-{4-[4-(trifluoromethyl)-2-pyrimidinyl]-1-piperazinyl}ethyl)-1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenyl] 3-*tert*-butyl (2*S*,3a*R*,9b*R*)-9b-[(*tert*-butoxycarbonyl)oxy]-6-chloro-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3a*H*)-dicarboxylate

To a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl}3-(1,1-dimethylethyl)(2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 159, 600 mg, 7.72 mmol) in dichloromethane (10 ml) was added 1[(4-trifluoromethyl)pyrimid-2-yl]piperazine (197 mg, 8.49 mmol) and triethylamine (0.16 ml, 1.16 mmol). After 30 min at room temperature sodium triacetoxyborohydride (213 mg, 1.00 mmol) was added and the reaction mixture was stirred at room temperature for 18 h. Saturated aqueous sodium hydrogen carbonate (10 ml) was added and stirred vigorously for 15 min, before adding water (10 ml) and dichloromethane (20 ml). The aqueous layer was separated and further washed with dichloromethane (2 x 10 ml), the combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to give a crude oil which was

purified by flash chromatography (silica) eluting with ethyl acetate hexane (1 : 1) to give the title compound as a colourless oil (587 mg).

Preparation 188 : 2-[(1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-((1*R*)-1-methyl-2-{4-[5-(trifluoromethyl)-2-pyridinyl]-1-piperazinyl}ethyl)-1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenyl] 3-*tert*-butyl (2*S*,3a*R*,9b*R*)-9b-[(*tert*-butoxycarbonyl)oxy]-6-chloro-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-*c*][2,1]benzoxazine-2,3(3a*H*)-dicarboxylate

To a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl}3-(1,1-dimethylethyl)(2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 159, 600 mg, 7.72 mmol) in dichloromethane (10 ml) was added1-[5-(trifluoromethyl)pyrid-2-yl]piperazine (196 mg, 8.49 mmol) and triethylamine (0.16 ml, 1.16 mmol). After 30 min at room temperature sodium triacetoxyborohydride (213 mg, 1.00 mmol) was added and the reaction mixture was stirred at room temperature for 18 h. Saturated aqueous sodium hydrogen carbonate (10 ml) was added and stirred vigorously for 15 min, before adding water (10 ml) and dichloromethane (20 ml). The aqueous layer was separated and further washed with dichloromethane (2 x 10 ml), the combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to give a crude oil which was purified by flash chromatography (silica) eluting with ethyl acetate : hexane (1 : 1) to give the title compound as a colourless oil (660 mg).

Preparation 160 : 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl)(2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

Dimethyl sulfoxide (6.02 g) and triethylamine (3.9 g) were added successively to a stirred, cooled (0°C) solution of 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl)(2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate) (Preparation 158, 3 g) in dichloromethane (30 ml). Sulfur trioxide pyridine complex (3.9 g) was then added in 5 portions over 10 minutes. After 2 hours the reaction mixture was diluted with water and extracted with dichloromethane. The combined organic layers were washed with water and aqueous hydrochloric acid (1M), dried (Na_2SO_4), evaporated and purified by flash column chromatography on silica gel (30 g) eluting with ethyl acetate : hexane (1 : 1) to give the title compound (2.82 g) as a white foam.

Preparation 161 : 2-[(1-methylethyl)oxy]ethyl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To methyl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 118, 0.20 g, 0.67 mmol) was added toluene (10 ml) titanium (IV) ethoxide (0.07 ml) and 2-isopropoxy ethanol. The reactants were stirred together and then heated under reflux for 1 h, before concentrating *in vacuo*. The crude residue was purified using a Sep Pak cartridge eluting with hexane and then hexane : ethyl acetate (50 : 50). Further purification by preparative HPLC was performed using a Magellan column 212 x 150 mm, flow rate 20 ml/min, eluting with a gradient of water : acetonitrile (55 : 45 to 90 : 10) over 8 min to yield the title compound (63.9 mg).

Preparation 163 : 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(ethylamino)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-

octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

To a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate] (Preparation 160, 1.0 g, 1.28 mmol) in anhydrous dichloromethane (10 ml) was added ethylamine hydrochloride (0.15 g, 1.93 mmol) and triethylamine (0.27 ml, 1.93 mmol) and the reaction mixture was stirred at room temperature for 20 min. Sodium triacetoxyborohydride (0.38 g, 1.8 mmol) was added and the reaction mixture was stirred for 18 h. The reaction mixture was diluted with ethyl acetate and washed with sodium hydrogen carbonate. The organic extracts were separated, dried (Na_2SO_4) and concentrated *in vacuo*.. The resultant residue was purified by flash chromatography using silica gel (20 g) eluting with ethyl acetate : methanol (100 : 0 and then 80 : 20) to give the title compound as a yellow foam (0.79 g, 77%).

Preparation 166 : (1S,2R,4aS,5R,8R,8aR)-5-(2-ethyl-1,3-thiazol-4-yl)-1,8a-dihydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-2-yl acetate

A solution of (3aS,4R,6aS,7R,10R,10aR)-7-(2-ethyl-1,3-thiazol-4-yl)-2,2,5,10-tetramethyl-4,6a,7,8,9,10-hexahydro-3aH-naphtho[1,8a-d][1,3]dioxol-4-yl acetate (Preparation 165, 345 mg) in methanolic *para*-toluenesulfonic acid (1% w/w, 10 ml) was stirred at room temperature for 12 days. The reaction mixture was partitioned between ethyl acetate and a mixture of dilute aqueous sodium chloride and saturated aqueous sodium hydrogen carbonate. The organic phase was dried ($MgSO_4$), evaporated and purified by flash column chromatography on silica gel using a gradient elution ethyl acetate : hexane (1 : 5 to 1 : 1) to give the product as a gum (94 mg).

Preparation 165 : (3aS,4R,6aS,7R,10R,10aR)-7-(2-ethyl-1\,3-thiazol-4-yl)-2,2,5,10-tetramethyl-4,6a,7,8,9,10-hexahydro-3aH-naphtho[1,8a-d][1,3]dioxol-4-yl acetate

To a stirred solution of (3a*S*,4*R*,6a*S*,7*R*,10*S*,10a*S*)-7-(2-bromoacetyl)-2,2,5,10-tetramethyl-4,6a,7,8,9,10-hexahydro-3a*H*-naphtho[1,8a-d][1,3]dioxol-4-yl acetate (Preparation 164, 500 mg) in ethanol (5 ml) was added thiopropionamide (110 mg). The reaction mixture was stirred at room temperature for 24 hours and then partitioned between saturated aqueous sodium chloride and ethyl acetate. The organic phase was dried ($MgSO_4$), evaporated and purified by flash column chromatography on silica gel eluting with ethyl acetate : hexane (1 : 4) to give the product as a gum (345 mg).

Preparation 164 : (3aS,4R,6aS,7R,10R,10aR)-7-(bromoacetyl)-2,2,5,10-tetramethyl-4,6a,7,8,9,10-hexahydro-3aH-naphtho[1,8a-d][1,3]dioxol-4-yl acetate

To a stirred, cooled (0 °C) solution of the product of (3a*S*,4*R*,6a*S*,7*R*,10*S*,10a*S*)-7-acetyl-2,2,5,10-tetramethyl-4,6a,7,8,9,10-hexahydro-3a*H*-naphtho[1,8a-d][1,3]dioxol-4-yl acetate (Preparation 148, 1.8 g) in diethyl ether (30 ml) was added triethylamine (1.8 ml) and trimethylsilyltrifluoromethanesulfonate (2.3 ml). After 30 minutes, *N*-bromosuccinimide (1.2 g) was added and the reaction mixture was allowed to warm to room temperature over three hours. The reaction mixture was partitioned between saturated aqueous sodium chloride and ethyl acetate. The organic phase was dried ($MgSO_4$), evaporated and purified by flash column chromatography on silica gel using a gradient elution ethyl acetate : hexane (1 : 9 to 2 : 8) to give the product as a gum (1.81 g).

Preparation 148 : (3a*S*,4*R*,6a*S*,7*R*,10*S*,10a*S*)-7-acetyl-2,2,5,10-tetramethyl-4,6a,7,8,9,10-hexahydro-3a*H*-naphtho[1,8a-d][1,3]dioxol-4-yl acetate

A solution of the product of (3a*S*,4*R*,6a*S*,7*R*,10*S*,10a*S*)-7-(1,2-dihydroxy-1-methylethyl)-2,2,5,10-tetramethyl-4,6a,7,8,9,10-hexahydro-3a*H*-naphtho[1,8a-d][1,3]dioxol-4-yl acetate (Preparation 147, 930 mg) in methanol (50 ml) was treated with sodium periodate (540 mg) and sonicated in an ultrasonic bath for 15 minutes. As the sodium periodate dissolved, a cloudy suspension formed. A further amount of sodium periodate (540 mg) was added and sonication was resumed for 15 min. After standing for 1 hour, the reaction mixture was diluted with water and solvent was evaporated. The residue was partitioned between water and dichloromethane and the organic phase was separated, washed with water and brine, dried (Na_2SO_4) and concentrated *in vacuo*. The residual oil was purified by flash column chromatography on silica gel eluting with ethyl acetate : hexane (1 : 4) to give the product as a colourless oil (680 mg).

Preparation 147 : (3a*S*,4*R*,6a*S*,7*R*,10*S*,10a*S*)-7-(1,2-dihydroxy-1-methylethyl)-2,2,5,10-tetramethyl-4,6a,7,8,9,10-hexahydro-3a*H*-naphtho[1,8a-d][1,3]dioxol-4-yl acetate

A solution of *N*-methylmorpholine-*N*-oxide (350 mg) in a minimum volume of isopropyl alcohol was added dropwise over 1 hour to a stirred solution of (3a*S*,4*R*,6a*R*,7*R*,10*S*,10a*S*)-7-isopropenyl-2,2,5,10-tetramethyl-4,6a,7,8,9,10-hexahydro-3a*H*-naphtho[1,8a-d][1,3]dioxol-4-yl acetate (Preparation 149, 1 g) and osmium tetroxide (2% in *tert*-butanol, 1ml) in acetone (10 ml). After 4 hours, further N-methylmorpholine-N-oxide (350 mg) was added and stirring was continued for 16 hours. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography on silica gel eluting with ethyl acetate : hexane (1 : 1) to give the product (950 mg).

Preparation 149 : (3a*S*,4*R*,6a*R*,7*R*,10*S*,10a*S*)-7-isopropenyl-2,2,5,10-tetramethyl-4,6a,7,8,9,10-hexahydro-3a*H*-naphtho[1,8a-d][1,3]dioxol-4-yl acetate

A stirred solution of (1*S*,2*R*,4a*R*,5*R*,8*S*,8a*S*)-1,8a-dihydroxy-5-isopropenyl-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydro-2-naphthalenyl acetate (Preparation 126, 10 g) in 2,2-dimethoxypropane (200 ml) was treated with *para*-toluenesulfonic acid (700 mg). After 3 days, the solution was concentrated *in vacuo* and the residue purified by flash column chromatography on silica gel eluting with ethyl acetate : hexane (5 : 95) to give the product (10.55 g).

Preparation 156 : 2-[(1*R*,2*R*,4a*S*,5*R*,8*S*,8a*S*)-2-(acetyloxy)-5-(2,2-difluoro-1-methylvinyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenyl] 3-(*tert*-butyl) (2*S*,3a*R*,9b*R*)-9b-[(*tert*-butoxycarbonyl)oxy]-6-chloro-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3a*H*)-dicarboxylate

Diethylisopropylamine (0.15 ml) was added to a stirred solution of (2S,9bR)-6-chloro-3-[[(1,1-dimethylethyl)oxy]carbonyl]-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylic acid (Preparation 153, 338 mg) and fluoro-*N,N,N'*-tetramethylformamidinium hexafluorophosphate (80%, 231 mg) in dichloromethane (2 ml). After 10 minutes, (1*S*,2*R*,4a*S*,5*R*,8*S*,8a*S*)- 5-(2,2-difluoro-1-methylvinyl)-1,8a-dihydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydro-2-naphthalenyl acetate (Preparation 154, 115 mg) and 4-dimethylaminopyridine (2 mg) were added and the reaction mixture was heated at reflux for 16 hours. The reaction mixture was diluted with dichloromethane (25 ml), washed with aqueous citric acid (10% w/w), dried (Na_2SO_4) and concentrated in vacuo. The solid residue was purified by flash column chromatography on silica gel eluting with ethyl acetate : hexane (1 : 4) to give the product as a gum (120 mg, 1:1 mixture of epimers).

Preparation 154 : (1*S*,2*R*,4a*S*,5*R*,8*S*,8a*S*)- 5-(2,2-difluoro-1-methylvinyl)-1,8a-dihydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydro-2-naphthalenyl acetate

A solution of the product of (3a*S*,4*R*,6a*S*,7*R*,10*S*,10a*S*)-7-(2,2-difluoro-1-methylvinyl)-2,2,5,10-tetramethyl-4,6a,7,8,9,10-hexahydro-3a*H*-naphtho[1,8a-d][1,3]dioxol-4-yl acetate (Preparation 151, 400 mg) and *para*-toluenesulfonic acid in methanol (20 ml) was stirred at room temperature for 24 hours. The reaction mixture was quenched with excess aqueous sodium hydrogen carbonate, diluted with water and extracted with diethyl ether (2x). The combined organic phases were washed with concentrated aqueous sodium chloride, dried (Na_2SO_4) and evaporated. The solid residue was purified by flash column chromatography on silica gel eluting with ethyl acetate : hexane (5 : 95 and then 10 : 90) to give the product as a white solid (195 mg).

Preparation 151 : (3a*S*,4*R*,6a*S*,7*R*,10*S*,10a*S*)-7-(2,2-difluoro-1-methylvinyl)-2,2,5,10-tetramethyl-4,6a,7,8,9,10-hexahydro-3a*H*-naphtho[1,8a-d][1,3]dioxol-4-yl acetate

Dibromodifluoromethane (466 mg) was added dropwise to a stirred, cooled (0 °C) solution of hexamethylphosphorustriamide (85%, 850 mg) in freshly distilled triglyme (10 ml) forming a white slurry. After 10 minutes, a solution of (3a*S*,4*R*,6a*S*,7*R*,10*S*,10a*S*)-7-acetyl-2,2,5,10-tetramethyl-4,6a,7,8,9,10-hexahydro-3a*H*-naphtho[1,8a-d][1,3]dioxol-4-yl acetate (Preparation 148, 680 mg) in freshly distilled triglyme (10 ml) was added and the reaction mixture was stirred at room temperature for 16 hours. The reaction mixture was recooled to 0 °C and further hexamethylphosphorustriamide (850 mg) and dibromodifluoromethane (466 mg) were added. The reaction was allowed to warm to room temperature and stirred for 24 h. Further additions of hexamethylphosphorustriamide (1.7 g) and dibromodifluoromethane (1 g) were made at 0 °C and the reaction was stirred for 5 days. The reaction

mixture was diluted with water and extracted with ether (2 x). The combined organic phases were washed with water and then saturated aqueous sodium chloride, dried (Na_2SO_4) and concentrated. The gummy residue was purified by flash column chromatography on silica gel eluting with ethyl acetate:hexane (5 : 95) to give the product as an oil (400 mg).

Preparation 167 : 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2,2-difluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

To a solution of diethylaminosulfur trifluoride (41□l, 0.31mmol) in anhydrous dichloromethane (3ml) at -78°C was added a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl)(2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 200mg, 0.25mmol) in anhydrous dichloromethane (2ml) dropwise over 2 minutes. The resulting mixture was allowed to warm to room temperature and stirred for 18 h. The reaction mixture was diluted with dichloromethane (5ml), washed with water (5ml), dried (Na_2SO_4) and concentrated *in vacuo* to give the crude product (145mg, 59%). This crude product was purified by column chromatography on silica gel eluting with hexane : ethyl acetate (10:1 to 3:1). The pure fractions were combined and concentrated *in vacuo* to give the title product (38mg, 19%).

Preparation 168: 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2,2-difluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-

dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

To a solution of diethylaminosulfur trifluoride (0.1ml, 1.5mmol) in anhydrous dichloromethane (4ml) at -78°C was added a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl)(2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 159, 400mg, 0.5mmol) in anhydrous dichloromethane (6ml) dropwise over 2 minutes. The resulting mixture was allowed to warm to room temperature over 1½ hours and stirred for a further 2½ hours. The reaction mixture was diluted with dichloromethane (10ml), washed with water (10ml), dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified by flash chromatography on silica gel eluting with hexane : ethyl acetate (3:1 to 2:1). The pure fractions were combined and concentrated *in vacuo* to give the title product (145mg, 36%).

Preparation 170 : (3aS,4R,6aR,7R,10R,10aR)-7-(2,2-dichloro-1-methylethenyl)-2,2,5,10-tetramethyl-4,6a,7,8,9,10-hexahydro-3aH-naphtho[1,8a-d][1,3]dioxol-4-yl acetate

To dry lithium chloride (1.0 g) in tetrahydrofuran (45 ml) was added n-butyllithium (4.75 ml) at 0°C under a nitrogen atmosphere. The mixture was stirred for 10 min and then cooled to –78°C before adding diethylchloromethyl phosphonate (1.85 ml) in tetrahydrofuran (13 ml). After stirring for 10 min, carbon tetrachloride (1.15 ml) in tetrahydrofuran (13 ml) was added. After stirring for a further 10 min, a solution of 3aS,4R,6aS,7R,10S,10aS)-7-acetyl-2,2,5,10-tetramethyl-4,6a,7,8,9,10-hexahydro-3aH-naphtho[1,8a-d][1,3]dioxol-4-yl acetate (Preparation 148, 2g) in tetrahydrofuran (13 ml) was added and the solution was stirred for 2 h at –78°C. After this time the mixture was quenched into water (50 ml) and extracted with diethyl ether (3 x 50 ml). The

combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give an orange oil. The oil was purified by flash chromatography using a Biotage® cartridge (90 g) to give the title compound as a transparent oil (1.05 g, 45%).

Preparation 172 : 2-[(1S,2R,4aS,5R,6R,8aR)-2-(acetyloxy)-5-(2,2-dichloro-1-methylethenyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl] 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

(2S,9bR)-6-chloro-3-{[(1,1-dimethylethyl)oxy]carbonyl}-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylic acid (Preparation 153, 1.7 g), 1-methyl imidazole (0.39 g) and 1-(mesitylene-2-sulfonyl)-3-nitro-1,2,4-triazole (1.4 g) were stirred in dichloromethane at room temperature for 20 min. 5-(2,2-dichloro-1-methylethenyl)-1,8a-dihydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-2-yl acetate (Preparation 173, 0.85 g) was added and the resulting mixture was stirred at room temperature. After 1 h, the reaction mixture was concentrated *in vacuo*. The crude residue was dissolved in dichloromethane and preabsorbed onto silica gel before purifying by flash chromatography eluting with ethyl acetate : hexane (10 : 90, and then 30 : 70, and then 50 : 50 and then 100 : 0). The title compound was obtained as a white solid (0.71 g).

Preparation 173 : 5-(2,2-dichloro-1-methylethenyl)-1,8a-dihydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-2-yl acetate

To a stirred solution of (3aS,4R,6aR,7R,10R,10aR)-7-(2,2-dichloro-1-methylethenyl)-2,2,5,10-tetramethyl-4,6a,7,8,9,10-hexahydro-3aH-naphtho[1,8a-d][1,3]dioxol-4-yl acetate (Preparation 170, 0.95 g) in ethylene glycol (40 ml) and methanol (10 ml) was added *para*-toluenesulphonic acid

(95 mg). The reaction mixture was heated to 75°C, after 1.5 h the reaction mixture was concentrated *in vacuo* to remove the methanol. The resultant solution was diluted with diethyl ether (30 ml) and water (30 ml) and the organic layer separated and washed with sodium hydrogen carbonate (3 x 30 ml). The aqueous layers were back extracted with diethyl ether (2 x 20 ml) and the combined organic extracts were dried ($MgSO_4$) and concentrated to give the title compound as a white solid.

Preparation 176 : 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[(1R)-2-(cyclopropylamino)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

To 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 0.56 g, 0.73 mmol) in anhydrous dichloromethane (5 ml) was added cyclopropylamine (50□l, 0.73 mmol) and the reaction mixture was stirred at room temperature for 20 min. Sodium triacetoxyborohydride (0.21 g, 1.0 mmol) was added and the reaction mixture was stirred for 18 h. The reaction mixture was diluted with ethyl acetate and washed with sodium hydrogen carbonate solution. The organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give the title compound as a yellow foam (0.56 g, 96%).

Preparation 177 : 2-[(1S,2R,4aS,5S,8R,8aR)-5-{2-[acetyl(cyclopropyl)amino]-1-methylethyl}-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl] 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

To 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[(1R)-2-(cyclopropylamino)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 176, 0.10 g, 0.12 mmol) in anhydrous dichloromethane (3 ml) was added 4-dimethylaminopyridine (0.15 g, 0.12 mmol) and the reaction mixture was cooled to 0°C. Acetic anhydride (23□l, 0.24 mmol) was added dropwise and the reaction mixture was stirred under nitrogen for 1 h. The reaction mixture was diluted with dichloromethane and washed with water and then brine. The organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give the title compound as a pale yellow solid.

Preparation 178 : 2-[(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{ethyl[(methyloxy)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]3-(1,1-dimethylethyl)(2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(ethylamino)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 163, 99 mg, 0.12 mmol) and 4-dimethylaminopyridine (15 mg, 0.12 mmol) were dissolved in anhydrous dichloromethane (3 ml) and pyridine (50. □l, 0.61 mmol) was added. The reaction mixture was cooled to 0°C and methyl chloroformate (28 □l, 0.37 mmol) was added dropwise. After stirring for 18 h, the reaction mixture was diluted with ethyl acetate and washed with water, citric acid (20% w/v) and then again with water. The organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give the title compound as a yellow glassy solid (89 mg, 86%).

Preparation 179 : 2-[(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{cyclopropyl[(methyloxy)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

To 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[(1R)-2-(cyclopropylamino)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 176, 98 mg, 0.12 mmol) and 4-dimethylaminopyridine (15 mg, 0.12 mmol) in anhydrous dichloromethane (3 ml) was added pyridine (50. □l, 0.60 mmol) and the reaction mixture was cooled to 0°C. Methyl chloroformate was added dropwise and the reaction mixture was stirred for 18 h, before diluting with ethyl acetate and washing with water, citric acid (20% w/v) and water again. The organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give the title compound as a yellow glassy solid (108 mg, 100%).

Preparation 180 : 2-[(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{cyclopropyl[(ethylamino)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl] 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

To 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[(1R)-2-(cyclopropylamino)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 176, 0.16 g, 0.2 mmol) in anhydrous dichoromethane (5 ml) cooled to 0°C was added ethyl isocyanate (0.017 ml, 0.22 mmol) dropwise and the reaction mixture was

stirred under nitrogen. The reaction mixture was concentrated *in vacuo* and the crude yellow residue was purified by flash chroamtography on silica gel (8 g) eluting with ethyl acetate : hexane (1 : 1) to give the desired product as a white solid (114 mg, 61%).

Preparation 181 : 2-[(1R,4R,4aS,5R,6R)-5-({[(2S,3aR,9bR)-6-chloro-3-[[(1,1-dimethylethyl)oxy]carbonyl]-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazin-2-yl] carbonyl}oxy)-6-(acetyloxy)-4a-hydroxy-4,7-dimethyl-1,2,3,4,4a,5,6,8a-octahydronaphthalen-1-yl]propanoic acid

To a solution of 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 157, 500mg, 0.64mmol) in anhydrous *N,N*-dimethylformamide (5ml) was added pyridinium dichromate (845mg, 2.25mmol) and the resultant mixture stirred at room temperature under nitrogen for 4 hours. The reaction mixture was diluted with water (100ml) and extracted with diethyl ether (2 x 100ml). The organic extracts were washed with water (50ml), dried (Na_2SO_4) and concentrated *in vacuo*. The crude product was purified by column chromatography on a Biotage® silica (8g) column eluting with ethyl acetate : hexane (2:8) to give the title product as a white foam (240mg, 45%).

Preparation 182 : 1,1-dimethylethyl (3R)-3-(methyloxy)piperidine-1-carboxylate

To a solution of 1,1-dimethylethyl (3R)-3-hydroxypiperidine-1-carboxylate (Preparation 128, 1.6 g, 7.95 mmol) in anhydrous tetrahydrofuran (35 ml) was added sodium hydride (60% dispersion in oil, 0.32 g, 7.95 mmol) in portions.

The resulting mixture was stirred for 25 min then iodomethane (2.27 g, 16 mmol) was added dropwise and the reaction mixture was stirred for 17 h. The reaction mixture was diluted with ethyl acetate (150 ml) and washed with brine (5% solution,150 ml). The aqueous layer was extracted with ethyl acetate (2 x 50 ml) and the combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. The resulting yellow oil was purified by flash chromatography on silica gel (70 g) eluting with dichloromethane : methanol (100 : 1 and then 50 : 1) to give a yellow oil (1.68 g). The trace of iodine was removed by dissolving the product in ethyl acetate (50 ml) and washing with aqueous sodium metabisulphite (5% solution, 2 x 35 ml), water (35 ml) and aqueous sodium hydrogen carbonate (5% solution, 35 ml). The organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to give the desired product as a colourless oil (1.62 g).

Preparation 183 : (3R)-3-(methyloxy)piperidine

A solution of 1,1-dimethylethyl (3R)-3-(methyloxy)piperidine-1-carboxylate (Preparation 182, 1.55 g, 7.2 mmol) in anhydrous dichloromethane (60 ml) was cooled to 4°C and then saturated with hydrogen choride gas for about 10 min. The reaction mixture was stirred for 1.5 h before concentrating in vauco and azeotroping with anhydrous diethyl ethyl to produce the hydrochloride salt of the title compound as a white hydroscopic solid (0.90 g).

Preparation 184 : 1,1-dimethylethyl (3*S*)-3-(methyloxy)piperidine-1-carboxylate

To a solution of 1,1-dimethylethyl (3*S*)-3-hydroxypiperidine-1-carboxylate (Preparation 127, 1.8 g, 9.2 mmol) in anhydrous tetrahydrofuran (40 ml) was added sodium hydride (60% dispersion in oil, 0.39 g, 9.2 mmol) in portions. The resulting mixture was stirred for 25 min then iodomethane (2.83 g, 20 mmol) was added dropwise and the reaction mixture was stirred for 17 h. The reaction mixture was diluted with ethyl acetate (200 ml) and washed with brine

(5% solution, 200 ml). The aqueous layer was extracted with ethyl acetate (2 x 50 ml) and the combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. The resulting yellow oil was purified by flash chromatography on silica gel (100 g) eluting with dichloromethane : methanol (100 : 1 and then 50 : 1) to give a yellow oil. The trace of iodine was removed by dissolving the product in diethyl ether (60 ml) and washing with aqueous sodium metabisulphite (5% solution, 1 x 40 ml), water (2 x 40 ml) and aqueous sodium hydrogen carbonate (5% solution, 40 ml). The organic extracts were dried ($MgSO_4$) and concentrated *in vacuo* to give the desired product as a colourless oil (1.43 g).

Preparation 186 : (3*S*)-3-(methyloxy)piperidine

A solution of 1,1-dimethylethyl (3*S*)-3-(methyloxy)piperidine-1-carboxylate (Preparation 184, 1.35 g, 6.27 mmol) in anhydrous dichloromethane (50 ml) was cooled to 4°C and then saturated with hydrogen choride gas for about 10 min. The reaction mixture was stirred for 2 h before concentrating in vauco and azeotroping with anhydrous diethyl ethyl to produce the hydrochloride salt of the title compound as a white hydroscopic solid (0.82 g).

Preparation 185 : 4-amino-6-methyl-2-piperazin-1-ylpyrimidine-5-carbonitrile

A solution of 4-amino-2-chloro-2-methylpyrimidine-5-carbonitrile (Maybridge, 100 mg, 0.6 mmol), piperazine (207 mg, 2.4 mmol), and triethylamine (71 mg, 0.7 mmol) in *N*,*N*-dimethylacetamide (20 ml) was heated to 108 °C for 6 h. The reaction mixture was stirred at ambient temperature for 18 h before pouring into water (400 ml) and extracting with ethyl acetate (3 x 30 ml), and then dichloromethane (20 ml). The combined organic extracts were washed with water (3 x 150 ml), and then dried ($MgSO_4$) and concentrated to give a yellow solid (120 mg). The crude solid was pre-absorbed onto silica gel (250 mg) and then purified by flash chromatography on silica gel (20 g) eluting with ethyl acetate : methanol (90 : 10 and then 80 : 20) to give the title compound as a white solid (28 mg).

Preparation 198 : 2-piperazin-1-yl-5-(trifluoromethyl)pyrimidine

To a solution of 1-amidino-piperazine sulphate (760 mg, 4.3 mmol) and 1,1,5,5-tetramethyl-1,5-diaza-3-(trifluoromethyl)-1,3-pentadienium chloride (Preparation 199. 720 mg, 3.12 mmol) in acetonitrile (15 ml) was added sodium methoxide (25% in methanol, 1.2 ml). The reaction mixture was heated at 70°C for 1 h and allowed to cool overnight. The solvents were removed *in vacuo* and the residue was dissolved in dichloromethane (20 ml) and washed with saturated aqueous sodium hydrogen carbonate (30 ml) and water (10 ml). The reaction mixture was dried (Na_2SO_4) and the solvent removed *in vacuo* before the product was purified to give the title compound as a TFA salt (68 mg).

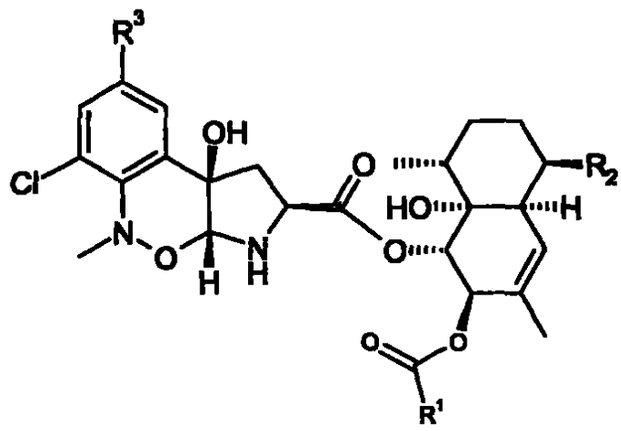
Preparation 200 : 4-[(4-chlorophenyl)oxy]piperidine

To a solution of tert-butyl 4-hydroxy-1-piperidinecarboxylate (500 mg, 2.48 mmol), 4-chlorophenol (320 mg, 2.48 mmol) and triphenylphosphine (650 mg, 2.48 mmol) in tetrahydrofuran (15 ml) at 0 °C was added dropwise diisopropylazodicarboxylate (490 µl, 2.48 mmol) in tetrahydrofuran (5 ml). The reaction mixture was allowed to warm to room temperature and stirred overnight in the absence of light. The solution was concentrated to give the Boc protected title compound.

The Boc protected title compound was dissolved in hydrogen chloride (4N in dioxane, 10 ml) and stirred at room temperature for 2 h. The reaction mixture was evaporated to dryness and partitioned between ethyl acetate and water. The layers were separated and to the aqueous layer was added sodium hydroxide solution (2 N) and ethyl acetate. The organic layers were separated, combined and dried (Na_2SO_4) before being filtered and evaporated to give the title compound.

Claims

1. A compound of formula (I):



(I)

or a pharmaceutically or veterinarily acceptable salt or solvate thereof, wherein

R^1 is H, C_1-C_6 alkyl, C_2-C_6 haloalkyl, C_3-C_8 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, aryl or $-OR^4$, said C_1-C_6 alkyl, C_3-C_8 cycloalkyl and aryl being optionally substituted by one or more substituents selected from $COOR^{13}$, $-OCOR^{12}$, $-OCOOR^{13}$ and $-OCONR^{12}R^{12}$ and said C_2-C_6 alkenyl and C_2-C_6 alkynyl being optionally substituted by one or more halo;

R^2 is C_1-C_6 alkyl, C_2-C_6 alkenyl, or a 5- or 6-membered aromatic or non-aromatic heterocycle containing one or more atoms selected from N, O and S, said C_1-C_6 alkyl being optionally substituted by one or more substituents selected from
$-NR^5R^6$, $-CONR^5R^6$, $-OR^{12}$, $-OCOR^{12}$, $-OCOOR^{12}$, $-OCONR^{12}R^{14}$, $=NOR^7$ and halo, said C_2-C_6 alkenyl being optionally substituted by one or more substituents selected from halo and $-COOR^{13}$ and said 5- or 6-membered aromatic heterocycle containing one or more atoms selected from N, O and S being optionally substituted by one or more substituents selected from C_1-C_6 alkyl and aryl;

R^3 is H, halo, aryl, C_2-C_6 alkenyl, C_2-C_7 alkanoyl, or a 5- or 6-membered aromatic heterocycle containing one or more atoms selected from N, O and S;

R^4 is C_1-C_2 alkyl, C_2-C_6 alkenyl or C_2-C_6 alkynyl, each optionally substituted by one or more halo, or $-OC(O)OR^a$ where R^a is C_1-C_6 alkyl;

R^5 and R^6

either, when taken together with the nitrogen atom to which they are attached, represent a saturated, partially unsaturated or aromatic, mono-, bi- or tricyclic heterocycle of up to 16 atoms optionally containing 1 or more additional heteroatoms selected from O, N and S, said heterocycle being optionally fused to a benzene or pyridyl ring and optionally substituted (including the optional benzene or pyridyl ring) by one or more R^8 and optionally substituted (including the optional benzene or pyridyl ring) on any aromatic ring thereof by $-NR^{15}R^{16}$, with the proviso that the heterocycle may not contain an -NH- group;

or

R^5 and R^6 are each independently selected from H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, $-CO-(C_3$-$C_8)$cycloalkyl, $-COR^{10}$, C_2-C_7 alkanoyl, aryl, $-OR^{13}$, $-COOR^{13}$, $-CONR^{12}R^{12}$ or $-SO_2R^{13}$, said C_2-C_7 alkanoyl being optionally substituted by OR^{13} or halo, said C_1-C_6 alkyl and C_3-C_8 cycloalkyl being optionally substituted by one or more R^8 and said C_3-C_8 cycloalkyl being optionally fused to a saturated or unsaturated ring of from 5 to 6 atoms, optionally containing one or more O, N or S atoms, said fused ring being optionally substituted by one or more C_1-C_6 alkyl with the proviso that when R^5 is H or $-CH_3$, R^6 is not C_1-C_6 alkyl;

R^7 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or aryl, said alkyl being optionally substituted by aryl;

R^8 is C_1-C_6 alkyl, C_3-C_8 cycloalkyl, R^9, R^{10}, -OR^9, -OR^{10}, COR^9, COR^{10}, -O-(C_1-C_6 alkyl)-R^{10}, C_2-C_6 alkenyl, -OR^{13}, -SR^9, -SR^{10}, -SO_2R^{10}, -$OCOR^{12}$, -$OCOOR^{12}$, -$OCONR^{12}R^{13}$, -$CONR^{12}OR^{13}$, -$CONR^{12}R^{13}$, -$NR^{12}COR^{12}$, -$NR^{12}COOR^{12}$, -$NR^{12}CONR^{12}R^{12}$, -$COOR^{13}$, -COR^{12}, oxo or halo, said C_3-C_8 cycloalkyl being optionally substituted by aryl, said C_1-C_6 alkyl being optionally substituted by one or more substituents selected from C_3-C_8 cycloalkyl, R^9, R^{10}, -OR^{10}, -OR^{13}, -SR^9, -SR^{11}, -$OCOR^{12}$, -$OCOOR^{12}$, -$OCONR^{12}R^{12}$, -$NR^{12}COR^{12}$, -$NR^{12}COOR^{12}$, -$NR^{12}CONR^{12}R^{12}$, -COR^{12} or halo, and said C_2-C_6 alkenyl being optionally substituted by one or more substituents selected from halo or aryl;

R^9 is

(a) a 5- or 6-membered aromatic heterocycle containing one or more atom(s) selected from N, O and S and optionally fused to a benzene ring, said aromatic heterocycle being optionally substituted (including on the optional benzene ring) by one or more substituents selected from C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl, -OR^{13}, -$NR^{12}R^{12}$, -CO_2R^{13}, cyano and halo, or

(b) a 4- to 8-membered saturated heterocycle containing one or more atoms selected from O and S and optionally fused to a benzene ring, said saturated heterocycle being optionally substituted (including on the optional benzene ring) by one or more substituents selected from C_1-C_6 alkyl and C_3-C_8 cycloalkyl;

R^{10} is aryl optionally substituted by one or more substituents selected from C_1-C_6 alkyl, C_1-C_6 haloalkyl, -OR^{13}, -$NR^{12}R^{12}$, -CO_2R^{13}, cyano or halo and optionally fused to a saturated or unsaturated ring of 5 or 6 atoms, optionally containing one or more O, N or S atoms, said fused ring being optionally substituted by one or more C_1-C_6 alkyl;

R^{11} is H, C_1-C_6 alkyl or C_3-C_8 cycloalkyl;

each R^{12} is independently H, C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_3-C_8 cycloalkyl or aryl, said C_1-C_8 alkyl being optionally substituted by aryl;

each R^{13} is independently C_1-C_8 alkyl, C_1-C_8 haloalkyl, C_3-C_8 cycloalkyl or aryl, said C_1-C_8 alkyl being optionally substituted by aryl;

R^{14} is C_1-C_8 alkyl, C_3-C_8 cycloalkyl or aryl, said C_1-C_8 alkyl each optionally substituted by aryl or -NHaryl;

R^{15} and R^{16} are either each independently selected from H, C_1-C_8 alkyl and C_3-C_8 cycloalkyl or, when taken together with the nitrogen atom to which they are attached, represent a 3- to 8-membered ring optionally containing one or more additional heteroatoms selected from O and S; and

'aryl' means phenyl or naphthyl;

with the proviso that when R^3 is H and R^1 is methyl, R^2 is not isopropenyl.

2. A compound as claimed in claim1, wherein:

R^1 is C_1-C_8 alkyl, C_1-C_4 alkenyl, C_1-C_4 alkynyl, OC_1-C_8 alkyl, OC_1-C_4 alkenyl or OC_1-C_4 alkynyl; and

R^2 is a thiazole ring optionally substituted with C_1 to C_4 alkyl; a piperazine ring optionally substituted with C_1 to C_4 alkyl; an isopropenyl group optionally substituted by halo; or an isopropyl group optionally substituted by one or more halo; NR^7R^8 wherein R^7 and R^8 may be taken together to represent a ring of up to 7 atoms optionally containing oxygen or may be independently selected from H or C_1 to C_4 cycloalkyl; $=NOR^{17}$ wherein R^{17} may be selected from C_1 to C_8, C_1 to C_4 alkynyl or C_1 to C_4 alkenyl;

3. A compound as claimed in claim 1 or 2, wherein:

R^1 is CH_3, -O-allyl or -O-propargyl;

R^2 is 2-ethylthiazol-4-yl, isopropyl, piperazinyl, 1,2-difluoropropen-2-yl, 1-oxoprop-2-yl methyl oxime, 1-oxoprop-2-yl propargyl oxime, 1-oxoprop-2-yl allyl oxime, 1-N-morpholinoprop-2-yl, 1-fluoroprop-2-yl, 1,1-difluoroprop-2-yl;

R^3, R^4 and R^5 are H;

4. A compound as claimed in any of claims 1, 2 or 3, wherein R^3, R^4, and R^5 all are H, and R^1 and R^2 are as indicated below:

R1 =	R2 =
CH_3	2-Ethylthiazol-4-yl, isopropyl
CH_3	1,2-difluoropropen-2-yl
CH_3	1-oxoprop-2-yl methyl oxime
CH_3	1-oxoprop-2-yl propargyl oxime
CH_3	1-oxoprop-2-yl allyl oxime
CH_3	isopropyl
CH_3	1-N-morpholinoprop-2-yl
CH_3	1-fluoroprop-2-yl
CH_3	1,1-difluoroprop-2-yl
CH_3	piperazin-1-yl (optionally 4-substituted with C_1-C_8 alkyl, phenyl, benzyl each of which groups may optionally be halo-substituted by up to 3 halo atoms
Opropargyl	Isopropenyl
Opropargyl	isopropyl
Oallyl	isopropyl

5. A pharmaceutical parasiticidal composition comprising a compound of formula (I) as defined in any of claims 1 to 4, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of either entity, together with a pharmaceutically acceptable diluent or carrier, which may be adapted for topical administration.

6. A formulation as claimed in claim 5 in the form of a formulation suitable for oral administration by capsule, bolus, tablet or drench, topical administration as a pour-on, spot-on, dip, spray, mousse, shampoo or powder formulation or, by injection (e.g. subcutaneously, intramuscularly or intravenously), or as an implant, or the compounds may be administered with the animal feedstuff and for this purpose a concentrated feed additive or premix may be prepared for mixing with the normal animal feed.

7. A compound of formula (I) as defined in any of claims 1 to 4, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of either entity, or a pharmaceutical composition containing any of the foregoing, for use as a medicament;

8. The use of a compound of formula (I) as defined in any of claims 1 to 4, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of either entity, or a pharmaceutical composition containing any of the foregoing, for the manufacture of a medicament for the treatment of a parasitic infestation;

9. A method of treating a parasitic infestation in a human being which comprises treating said human being with an effective amount of a compound of formula (I) as defined in any of claims 1 to 4, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of either entity, or a pharmaceutical composition containing any of the foregoing.

10. A veterinary or agricultural formulation comprising a compound of formula (I) as defined in any of claims 1 to 4, or a veterinarily or agriculturally

acceptable salt thereof, or a veterinarily or agriculturally acceptable solvate of either entity, together with a veterinarily or agriculturally acceptable diluent or carrier. Preferably, the formulation is adapted for topical administration.

11. A compound of formula (I) as defined in any of claims 1 to 4, or a veterinarily or agriculturally acceptable salt thereof, or a veterinarily or agriculturally acceptable solvate of either entity, or a veterinarily or agriculturally acceptable formulation containing any of the foregoing, for use as a parasiticide.

12. A method of treating a parasitic infestation at a locus, which comprises treatment of the locus with an effective amount of a compound of formula (I) as defined in any of claims 1 to 4, or a veterinarily or agriculturally acceptable salt thereof, or a veterinarily or agriculturally acceptable solvate of either entity, or a veterinarily or agriculturally acceptable formulation containing any of the foregoing.

13. A method as claimed in claim 12, wherein the locus is the intestine, skin or fur of an animal.

14. A compound selected from the group comprising:

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2, 1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-2-[(2-methylpropanoyl)oxy]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-2-(hexanoyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2, 3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2-(acetyloxy)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexa hydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(2-methylpropanoyl)oxy]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3 ,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-2-[(cyclopropylcarbonyl)oxy]-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydro pyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethyl)-2-{[(prop-2-ynyloxy)carbonyl]oxy}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydro pyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethyl)-2-({[(2,2,2-trichloroethyl)oxy]carbonyl}oxy)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9 b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-2-({[(1-methylethenyl)oxy]carbonyl}oxy)-5-(1-methylethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hex ahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethyl)-2-{[(prop-2-enyloxy)carbonyl]oxy}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydro pyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-1-({[(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazin-2-yl]carbonyl}oxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-2-yl methyl butanedioate

(1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-2-(pent-4-enoyloxy)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2 ,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[({[2-(naphthalen-1-ylamino)ethyl]amino}carbonyl)oxy]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-2-{[(acetyloxy)acetyl]oxy}-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-2-(formyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-2-[(3,3,3-trifluoropropanoyl)oxy]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[4-(ethyloxy)-1-methyl-4-oxobut-2-enyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-(2,2-difluoro-1-methylethenyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2-fluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[(1-methyl-2-morpholin-4-ylethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-(2-ethyl-1,3-thiazol-4-yl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2,2-difluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2,2-difluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydro pyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-(2,2-dichloro-1-methylethenyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropy rrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(phenylmethyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9 b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{[(2-chlorophenyl)methyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1, 2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(furan-2-ylmethyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a ,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{[(2-methylphenyl)methyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1, 2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{[(1S)-1-phenylethyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3, 3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{[(3-chlorophenyl)methyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1, 2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-({[2-(methyloxy)phenyl]methyl}amino)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-meth yl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(4-pyridin-2-ylpiperazin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2 ,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{bis[2-(methyloxy)ethyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2 ,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(2-thien-2-ylethyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3 a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-({[4-(trifluoromethyl)phenyl]methyl}amino)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[methyl(2-{[2-(methyloxy)phenyl]oxy}ethyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hy droxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{(1-methylethyl)[2-(phenylsulfonyl)ethyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hyd roxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(2,3-dihydro-1,4-benzodioxin-2-ylmethyl)(methyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chlor o-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(4-{[2-(methyloxy)phenyl]methyl}piperazin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hyd roxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(1,1-dimethylethyl)piperidin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-met hyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[(phenylmethyl)oxy]piperidin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-met hyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[7,8-bis(methyloxy)-3,4-dihydroisoquinolin-2(1H)-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9 b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(methyl{[4-(methyloxy)phenyl]methyl}amino)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[(ethyloxy)carbonyl]-1,4-diazepan-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(phenylmethyl)-1,4-diazepan-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-meth yl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-5-{2-[acetyl(ethyl)amino]-1-methylethyl}-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b - hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-5-{2-[acetyl(cyclopropyl)amino]-1-methylethyl}-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3 a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{cyclopropyl[(methyloxy)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{ethyl[(methyloxy)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl- 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{[(2,5-dichlorophenyl)methyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methy l-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{[(3,5-dichlorophenyl)methyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methy l-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{cyclopropyl[(ethylamino)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5- methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[methyl(phenylmethyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3, 3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(phenylmethyl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1 ,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(3-methylpiperidin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a, 5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(4-pyrimidin-2-ylpiperazin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1 ,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{methyl[2-(phenyloxy)ethyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl- 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-thiomorpholin-4-ylethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-h exahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[cyclohexyl(methyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a ,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[methyl(pyridin-2-ylmethyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl- 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(3,6-dihydropyridin-1(2H)-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2, 3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

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(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{[phenyl(pyridin-3-yl)methyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methy l-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(2-phenylethyl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl- 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydr oxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[3-(methyloxy)phenyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(4-{[(4-chlorophenyl)methyl]oxy}piperidin-1-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hyd roxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[2-(methyloxy)phenyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(furan-2-ylmethyl)piperidin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-meth yl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[(3-methylphenyl)methyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(2,2-dimethylpropanoyl)(ethyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-met hyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[methyl(propanoyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a, 5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(1-methylethyl)(propanoyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl- 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(2,2-dimethylpropanoyl)(1-methylethyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{(1-methylethyl)[(methyloxy)acetyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5 -methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[[(2-chlorophenyl)methyl](propanoyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{[(2-chlorophenyl)methyl][(methyloxy)acetyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-5-(2-{acetyl[(2-methylphenyl)methyl]amino}-1-methylethyl)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-met hyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[[(2-methylphenyl)methyl](propanoyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{[(methyloxy)acetyl][(2-methylphenyl)methyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b- hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-(4-{[(4-fluorophenyl)methyl]oxy}piperidin-1-yl)-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hyd roxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[(4-chlorophenyl)methyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(3,4-dihydroisoquinolin-2(1H)-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl- 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(2R,6S)-2,6-dimethylmorpholin-4-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-meth yl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[methyl(3,3,3-trifluoropropanoyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[[(2-methylphenyl)methyl](3,3,3-trifluoropropanoyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chl oro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[(4-methylphenyl)methyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[6-(methyloxy)pyridazin-3-yl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hyd roxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(6-chloropyrazin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5- methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(6-chloropyridin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5- methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(4-phenylpiperazin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a, 5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(cyclohexylmethyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-meth yl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(1,3-thiazol-2-yl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-meth yl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(3-chloropyridin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5- methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-oxo-2-[(phenylmethyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3, 3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-{2-[[(2-chlorophenyl)methyl](methyl)amino]-1-methyl-2-oxoethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethyl)-2-{[(phenylamino)carbonyl]oxy}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahy dropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(cycloheptylamino)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-h exahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2-chloropyrimidin-4-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(5-chloropyridin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5- methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(5-chloropyrazin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5- methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(4-chlorophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl -1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(4-methylphenyl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl -1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2-chlorophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl -1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[4-(methyloxy)phenyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[2-(trifluoromethyl)phenyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[4-(trifluoromethyl)pyrimidin-2-yl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro- 9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2-fluorophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl -1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(6-methylpyridin-2-yl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5- methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(4-fluorophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl -1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(1,3-thiazol-2-ylcarbonyl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydrox y-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[(3-phenylpropyl)oxy]piperidin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[5-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b -hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(phenylmethyl)piperidin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1 ,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[3-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b -hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[3-(trifluoromethyl)phenyl]piperidin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(4-{[3-(trifluoromethyl)phenyl]methyl}piperazin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro- 9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[({3-[(ethyloxy)carbonyl]phenyl}methyl)oxy]piperidin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6 -chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(1,3-benzoxazol-2-yl)piperidin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(4-{[3,5-bis(trifluoromethyl)phenyl]methyl}piperazin-1-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-ch loro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[2-(methyloxy)phenyl]piperidin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[(4-fluorophenyl)methyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(4-cyanophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl- 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2,3-dihydro-1,4-benzodioxin-2-ylcarbonyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6- chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(4-bromophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl- 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[4-(trifluoromethyl)phenyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2,4-difluorophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(pyridin-4-ylmethyl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[5-chloro-2-(methyloxy)phenyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hy droxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(3,5-dichlorophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[(2E)-3-phenylprop-2-enyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydrox y-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(diphenylmethyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl -1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2,3-dimethylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(4-cyclopentylpiperazin-1-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2, 3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2-ethylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl- 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[4-chloro-3-(trifluoromethyl)phenyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro -9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(thien-2-ylcarbonyl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(4-{[(butylamino)carbonyl]oxy}piperidin-1-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2,4-dimethylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2,5-dimethylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(4-cyclopropylpiperazin-1-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2, 3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(cyclopentylcarbonyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[6-(methyloxy)pyridin-2-yl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(3,5-dimethylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(3,6-dimethylpyrazin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydrox y-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2,6-dimethylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[(1S)-1-methyl-2-pyridin-3-ylethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahyd ropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(3-oxa-9-azabicyclo[3.3.1]non-9-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-m ethyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(4-methylpentanoyl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5 -methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(4-oxo-1,3,4,6,7,11b-hexahydro-2H-pyrazino[2,1-a]isoquinolin-2-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3 aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[3-[(ethyloxy)carbonyl]octahydroisoquinolin-2(1H)-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[3,5-bis(methyloxy)phenyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(2-cyanophenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl- 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(4-phenylpiperidin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a, 5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(3,4-dimethylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[cyclopropyl(propanoyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2, 3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(cyclopropylcarbonyl)(phenyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(cyclohexylmethyl)(cyclopropylcarbonyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(cyclohexylmethyl)(propanoyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(cyclopropylcarbonyl)(methyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

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(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[methyl(phenylcarbonyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2, 3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{methyl[(phenyloxy)acetyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1 ,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(4-amino-5-cyano-6-methylpyrimidin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chlor o-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(2S,5R)-2,5-dimethyl-4-prop-2-enylpiperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro -9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(8-azabicyclo[3.2.1]oct-8-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl- 1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(3S,8aR)-3-(phenylmethyl)hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3 aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(3-{[(3,4-difluorophenyl)methyl]oxy}piperidin-1-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chlor o-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(3R)-3-(methyloxy)piperidin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[1-methyl-6,7-bis(methyloxy)-3,4-dihydroisoquinolin-2(1H)-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9b R)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(2-methyl-4-piperidin-1-yl-5,8-dihydropyrido[3,4-d]pyrimidin-7(6H)-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(4-chlorophenyl)-6,7-dihydrothieno[3,2-c]pyridin-5(4H)-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9b R)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(3-{[4-(methyloxy)phenyl]sulfanyl}-8-azabicyclo[3.2.1]oct-8-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR, 9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(4-methylpiperazin-1-yl)piperidin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydr oxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{3-[(3-chloropyridin-2-yl)oxy]piperidin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-h ydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[4-(3-methylquinoxalin-2-yl)piperazin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hyd roxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-{2-[7-(hydroxymethyl)-3-azabicyclo[3.3.1]non-3-yl]-1-methylethyl}-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b -hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(3,11-diazatricyclo[7.3.1.0~2,7~]trideca-2,4,6-trien-11-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR) -6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(4,10-diazatricyclo[6.3.1.0~2,7~]dodeca-2,4,6-trien-10-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)- 6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-5-{2-[(4aR,9aS)-2,3,4,4a,9,9a-hexahydro-1H-indeno[2,1-b]pyridin-1-yl]-1-methylethyl}-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR ,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[2-(3-cyclohexyl-3-methylpiperidin-1-yl)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5 -methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-(4-{2-[(2-hydroxyethyl)oxy]ethyl}piperazin-1-yl)-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9 b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(3-methyl-3-pyridin-2-ylpiperidin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy -5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(3,5-dichloropyridin-4-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hy droxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(3S)-3-methyl-3-phenylpiperidin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{3-[(4-fluorophenyl)sulfanyl]-8-azabicyclo[3.2.1]oct-8-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)- 6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[(pyridin-2-ylsulfanyl)methyl]piperidin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9 b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{3-[(pyridin-2-ylsulfanyl)methyl]piperidin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9 b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(2-{[methyl(methyloxy)amino]carbonyl}piperidin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chlo ro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[(3,4-dichlorophenyl)methyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b- hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[2-(2-piperidin-1-ylethyl)piperidin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(1-methylethyl)(2-{[2-(methyloxy)phenyl]oxy}ethyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6 -chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[methyl(2-phenylcyclopropyl)amino]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{methyl[3-(1,2,4,5-tetrahydro-3H-3-benzazepin-3-yl)propyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR ,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[{2-[(2,6-dichlorophenyl)oxy]ethyl}(methyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro- 9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(4-chlorophenyl)methyl](ethyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{methyl[(3-methylthien-2-yl)methyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[4-(3-chloro-4-methylphenyl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hyd roxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{2-[(diphenylmethyl)(methyl)amino]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methy l-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{4-[5-methyl-2-(methyloxy)phenyl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9 b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{4-[2-(ethyloxy)phenyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy- 5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{(2S,4R)-4-methyl-2-[(methyloxy)carbonyl]piperidin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6- chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-{2-[(2S)-2-(2-hydroxyethyl)piperidin-1-yl]-1-methylethyl}-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy -5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(3S)-3-(methyloxy)piperidin-1-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-me thyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{2-[(methyloxy)carbonyl]octahydro-1H-indol-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aS,9bS)-6-chloro-9 b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(2S)-4-methyl-2-{(methyloxy)carbonyl}-3,6-dihydropyridin-1(2H)-yl]ethyl}-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S, 3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-(3-hydroxy-8-azabicyclo[3.2.1]oct-8-yl)-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy -5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-(3-methyl-3-phenylpiperidin-1-yl)ethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-met hyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methyl-2-{(phenylmethyl)[2-(phenyloxy)ethyl]amino}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydro xy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-((1R)-1-methyl-2-{4-[4-(trifluoromethyl)-2-pyrimidinyl]-1-piperazinyl}ethyl)-1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenyl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate – TFA salt

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-((1R)-1-methyl-2-{4-[5-(trifluoromethyl)-2-pyridinyl]-1-piperazinyl}ethyl)-1,2,4a,5,6,7,8,8a-octahydro-1-naphthalenyl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate– TFA salt

(1S,2R,5S,8R,8aR)-2-(acetyloxy)-5-((1R)-2-{4-[bis(4-fluorophenyl)methyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,5S,8R,8aR)-2-(acetyloxy)-5-{(1R)-2-[4-(5-chloropyrimidin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{(1R)-2-[4-(5-bromopyrimidin-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-{(1R)-2-[4-(6-chloro-1,3-benzothiazol-2-yl)piperazin-1-yl]-1-methylethyl}-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-((1R)-2-{4-[(3,4-dichlorophenyl)methyl]piperazin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-((1R)-1-methyl-2-{4-[5-(trifluoromethyl)pyrimidin-2-yl]piperazin-1-yl}ethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-((1R)-2-{4-[(4-chlorophenyl)oxy]piperidin-1-yl}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

ALCALOIDES DE TERPENO ANTIPARASITARIOS

Campo Técnico

La presente invención se refiere a nuevos alcaloides de terpeno y a su uso como agentes antiparasitarios. La presente invención también se refiere a un tratamiento antiparasitario que comprende un compuesto alcaloide de terpeno de esta invención como ingrediente eficaz en una formulación antiparasitaria.

Más particularmente, la presente invención se refiere a derivados del alcaloide de terpeno (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo. También se describen procedimientos para producir estos compuestos y composiciones farmacéuticas que comprenden los mismos.

Un aspecto más de la invención es un nuevo ensayo de unión que se usa para evaluar la potencial actividad antiparasitaria de estos compuestos midiendo lo bien que se unen a las membranas purificadas de los homogenados de los parásitos. La afinidad se calcula de acuerdo con la facilidad con la que los compuestos de la presente invención desplazan un análogo reducido y radiomarcado de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo desde estas membranas.

Ciertos alcaloides de terpeno, incluyendo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-

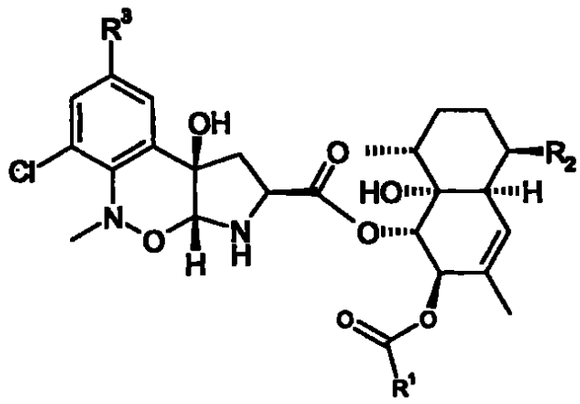
hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,6*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo que pueden aislarse de los caldos de fermentación de ciertos microorganismos, se conocen por poseer actividad antihelmíntica, ectoparasiticida e insecticida con utilidad en la salud animal y humana, agricultura y horticultura (Véanse los documentos WO 95/19363 y UK 2240100 respectivamente).

Sin embargo, se descubrió que cuando se administran a animales infectados, sus potencias in vivo eran demasiado bajas como para excluir el desarrollo comercial.

Sorprendentemente, se ha descubierto que ciertos derivados de alcaloides de terpeno poseen buena actividad in vivo y de esta manera son eficaces como agentes antiparasitarios en animales. La presente invención proporciona por tanto compuestos que son eficaces como agentes antiparasitarios para uso en animales y seres humanos.

Los compuestos de la presente invención pueden formarse por modificación sintética de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,6*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo. Los compuestos de la invención muestran actividad contra insectos, plagas, ácaros, nematodos que viven libres y animales afectados por endo- y ecto-parásitos.

La presente invención proporciona un compuesto de fórmula (I):



(I)

o una sal o solvato farmacéutica o veterinariamente aceptable del mismo, en la que

R^1 es H, alquilo C_1-C_6, haloalquilo C_2-C_6, cicloalquilo C_3-C_8, alquenilo C_2-C_6, alquinilo C_2-C_6, arilo o $-OR^4$, estando dicho alquilo C_1-C_6, cicloalquilo C_3-C_8 y arilo opcionalmente sustituidos con uno o más sustituyentes seleccionados entre $COOR^{13}$, $-OCOR^{12}$, $-OCOOR^{13}$ y $-OCONR^{12}R^{12}$ y estando dicho alquenilo C_2-C_6 y alquinilo C_2-C_6 opcionalmente sustituidos con uno o más halo;

R^2 es alquilo C_1-C_6, alquenilo C_2-C_6 o un heterociclo aromático o no aromático de 5 ó 6 miembros que contiene uno o más átomos seleccionados entre N, O y S, estando dicho alquilo C_1-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados entre $-NR^5R^6$, $-CONR^5R^6$, $-OR^{12}$, $-OCOR^{12}$, $-OCOOR^{12}$, $-OCONR^{12}R^{14}$, $=NOR^7$ y halo, estando dicho alquenilo C_2-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados entre halo y $-COOR^{13}$ y estando dicho heterociclo aromático de 5 ó 6 miembros que contiene uno o más átomos seleccionados entre N, O y S opcionalmente sustituido con uno o más sustituyentes seleccionados entre alquilo C_1-C_6 y

arilo;

R^3 es H, halo, arilo, alquenilo C_2-C_6, alcanoílo C_2-C_7 o un heterociclo aromático de 5 ó 6 miembros que contiene uno o más átomos seleccionados entre N, O y S;

R^4 es alquilo C_1-C_2, alquenilo C_2-C_6 o alquinilo C_2-C_6, cada uno opcionalmente sustituido con uno o más halo, o -OC(O)OR^a donde R^a es alquilo C_1-C_6;

R^5 y R^6, cuando se toman junto con el átomo de nitrógeno al que están unidos, representan un heterociclo mono-, bi- o tricíclico, saturado, parcialmente insaturado o aromático de hasta 16 átomos que contiene opcionalmente 1 o más heteroátomos adicionales seleccionados entre O, N y S, estando dicho heterociclo opcionalmente condensado con un anillo de benceno o piridilo y opcionalmente sustituido (incluyendo el anillo de benceno o piridilo opcional) con uno o más R^8 y opcionalmente sustituido (incluyendo el anillo de benceno o piridilo opcional) en cualquier anillo aromático del mismo con -$NR^{15}R^{16}$, con la condición de que el heterociclo puede no contener un grupo -NH-;

o

cada uno de R^5 y R^6 se selecciona independientemente entre H, alquilo C_1-C_6, cicloalquilo C_3-C_8, -CO-cicloalquilo (C_3-C_8), -COR^{10}, alcanoílo C_2-C_7, arilo, -OR^{13}, -$COOR^{13}$, -$CONR^{12}R^{12}$ o -SO_2R^{13}, estando dicho alcanoílo C_2-C_7 opcionalmente sustituido con OR^{13} o halo, estando dicho alquilo C_1-C_6 y cicloalquilo C_3-C_8 opcionalmente sustituido con uno o más R^8 y estando dicho cicloalquilo C_3-C_8 opcionalmente condensado con un anillo saturado o insaturado de 5 a 6 átomos, que contiene opcionalmente uno o más átomos de

O, N o S, estando dicho anillo condensado opcionalmente sustituido con uno o más alquilo C_1-C_6 con la condición de que cuando R^5 sea H o $-CH_3$, R^6 no sea alquilo C_1-C_6;

R^7 es alquilo C_1-C_6, alquenilo C_2-C_6, alquinilo C_2-C_6 o arilo, estando dicho alquilo opcionalmente sustituido con arilo;

R^8 es alquilo C_1-C_6, cicloalquilo C_3-C_8, R^9, R^{10}, $-OR^9$, $-OR^{10}$, COR^9, COR^{10}, -O-(alquil C_1-C_6)-R^{10}, alquenilo C_2-C_6, $-OR^{13}$, $-SR^9$, $-SR^{10}$, $-SO_2R^{10}$, $-OCOR^{12}$, $-OCOOR^{12}$, $-OCONR^{12}R^{13}$, $-CONR^{12}OR^{13}$, $-CONR^{12}R^{13}$, $-NR^{12}COR^{12}$, $-NR^{12}COOR^{12}$, $-NR^{12}CONR^{12}R^{12}$, $-COOR^{13}$, $-COR^{12}$, oxo o halo, estando dicho cicloalquilo C_3-C_8 opcionalmente sustituido con arilo, estando dicho alquilo C_1-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados entre cicloalquilo C_3-C_8, R^9, R^{10}, $-OR^{10}$, $-OR^{13}$, $-SR^9$, $-SR^{11}$, $-OCOR^{12}$, $-OCOOR^{12}$, $-OCONR^{12}R^{12}$, $-NR^{12}COR^{12}$, $-NR^{12}COOR^{12}$, $-NR^{12}CONR^{12}R^{12}$, $-COR^{12}$ o halo y estando dicho alquenilo C_2-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados entre halo o arilo;

R^9 es

(a) un heterociclo aromático de 5 ó 6 miembros que contiene uno o más átomo(s) seleccionado(s) entre N, O y S y opcionalmente condensado con un anillo de benceno, estando dicho heterociclo aromático opcionalmente sustituido (incluyendo en el anillo de benceno opcional) con uno o más sustituyentes seleccionados entre alquilo C_1-C_6, haloalquilo C_1-C_6, cicloalquilo C_3-C_8, $-OR^{13}$, $-NR^{12}R^{12}$, $-CO_2R^{13}$, ciano y halo, o

(b) un heterociclo saturado de 4 a 8 miembros que contiene uno o más átomos seleccionados entre O y S y opcionalmente condensado con un anillo de benceno, estando dicho heterociclo saturado opcionalmente sustituido

(incluyendo en el anillo de benceno opcional) con uno o más sustituyentes seleccionados entre alquilo C_1-C_6 y cicloalquilo C_3-C_6;

R^{10} es arilo opcionalmente sustituido con uno o más sustituyentes seleccionados entre alquilo C_1-C_6, haloalquilo C_1-C_6, -OR^{13}, -$NR^{12}R^{12}$, -CO_2R^{13}, ciano o halo y opcionalmente condensado con un anillo saturado o insaturado de 5 ó 6 átomos, que contiene opcionalmente uno o más átomos de O, N o S, estando dicho anillo condensado opcionalmente sustituido con uno o más alquilo C_1-C_6;

R^{11} es H, alquilo C_1-C_6 o cicloalquilo C_3-C_6;

cada R^{12} es independientemente H, alquilo C_1-C_6, haloalquilo C_1-C_6, cicloalquilo C_3-C_6 o arilo, estando dicho alquilo C_1-C_6 opcionalmente sustituido con arilo;

cada R^{13} es independientemente alquilo C_1-C_6, haloalquilo C_1-C_6, cicloalquilo C_3-C_6 o arilo, estando dicho alquilo C_1-C_6 opcionalmente sustituido con arilo;

R^{14} es alquilo C_1-C_6, cicloalquilo C_3-C_6 o arilo, cada uno de dichos alquilo C_1-C_6 opcionalmente sustituido con arilo o -NHarilo;

cada uno de R^{15} y R^{16} se selecciona independientemente entre H, alquilo C_1-C_6 y cicloalquilo C_3-C_6 o, cuando se toman junto con el átomo de nitrógeno al que están unidos, representan un anillo de 3 a 8 miembros que contiene opcionalmente uno o más heteroátomos adicionales seleccionados entre O y S; y

"arilo" significa fenilo o naftilo;

con la condición de que cuando R^3 sea H y R^1 sea metilo, R^2 no sea isopropenilo.

Un grupo preferido de compuestos de fórmula (I) es aquel en el que:

R^1 es alquilo C_1-C_8, alquenilo C_1-C_4, alquinilo C_1-C_4, O-alquilo C_1-C_8, O-alquenilo C_1-C_4 u O-alquinilo C_1-C_4; y

R^2 es un anillo de tiazol opcionalmente sustituido con alquilo de C_1 a C_4; un anillo de piperazina opcionalmente sustituido con alquilo de C_1 a C_4; un grupo isopropenilo opcionalmente sustituido con halo; o un grupo isopropilo opcionalmente sustituido con uno o más halo; NR^7R^8 donde R^7 y R^8 pueden tomarse conjuntamente para representar un anillo de hasta 7 átomos que contiene opcionalmente oxígeno o pueden seleccionarse independientemente entre H o cicloalquilo de C_1 a C_4; $=NOR^{17}$ donde R^{17} puede seleccionarse entre alquinilo de C_1 a C_8, de C_1 a C_4 o alquenilo de C_1 a C_4;

Un grupo más preferido de compuestos de fórmula (I) es aquel en el que:

R^1 es $-CH_3$, -O-alilo o -O-propargilo;

R^2 es 2-etiltiazol-4-ilo, isopropilo, piperazinilo, 1,2-difluoropropen-2-ilo, 1-oxoprop-2-il-metil-oxima, 1-oxoprop-2-il-propargil-oxima, 1-oxoprop-2-il-alil-oxima, 1-*N*-morfolinoprop-2-ilo, 1-fluoroprop-2-ilo, 1,1-difluoroprop-2-ilo;

R^3, R^4 y R^5 son H;

Los compuestos individuales particularmente preferidos de la invención incluyen compuestos de fórmula (I) en la que R^3, R^4 y R^5 son todos H, y R^1 y R^2 son como se indica a continuación:

R1 =	R2 =
CH_3	2-Etiltiazol-4-ilo, isopropilo
CH_3	1,2-difluoropropen-2-ilo
CH_3	1-oxoprop-2-il-metil-oxima

CH_3	1-oxoprop-2-il-propargil-oxima
CH_3	1-oxoprop-2-il-alil-oxima
CH_3	isopropilo
CH_3	1-*N*-morfolinoprop-2-ilo
CH_3	1-fluoroprop-2-ilo
CH_3	1,1-difluoroprop-2-ilo
CH_3	piperazin-1-ilo (opcionalmente 4-sustituido con alquilo C_1-C_6, fenilo, bencilo donde cada uno de los grupos puede estar opcionalmente halo-sustituido con hasta 3 átomos de halo
Opropargilo	isopropenilo
Opropargilo	isopropilo
Oalilo	isopropilo

En la definición anterior, halo significa fluoro, cloro, bromo o yodo.

Los compuestos de fórmula (I) pueden contener uno o más centros quirales y por lo tanto pueden existir como estereoisómeros, es decir, como enantiómeros o diastereómeros, así como mezclas de los mismos. La invención incluye estereoisómeros individuales de los compuestos de fórmula (I) junto con mezclas de los mismos. La separación de diastereoisómeros puede conseguirse mediante técnicas convencionales, por ejemplo por cristalización fraccionada o cromatografía (incluyendo HPLC) de una mezcla diastereoisomérica de un compuesto de fórmula (I) o una sal adecuada o derivado de la misma. Un enantiómero individual de un compuesto de fórmula

(I) puede prepararse a partir de un intermedio ópticamente puro correspondiente o por resolución, por HPLC del racemato usando un soporte quiral adecuado o, cuando sea apropiado, por cristalización fraccionada de las sales diastereoisoméricas formadas mediante la reacción del racemato con un ácido ópticamente activo adecuado.

También se incluyen en la invención derivados radiomarcados de compuestos de fórmula (I) que son adecuados para estudios biológicos.

Las sales farmacéutica, veterinaria y agrícolamente aceptables de los compuestos de fórmula (I) son, por ejemplo, sales de adición de ácidos no tóxicas formadas con ácidos inorgánicos tales como ácido clorhídrico, bromhídrico, sulfúrico y fosfórico, con ácidos organo-carboxílicos, o con ácidos organo-sulfónicos. Para un análisis de las sales adecuadas, véase J. Pharm. Sci., 1977, 66, 1.

En un aspecto más, la presente invención proporciona procedimientos para la preparación de un compuesto de fórmula (I), o una sal farmacéutica, veterinaria o agrícolamente aceptable del mismo, o un solvato farmacéutica, veterinaria o agrícolamente aceptable (incluyendo hidrato) de tal entidad, como se ilustra a continuación.

Se apreciará por parte de los especialistas en la técnica que, en algunos de los procedimientos descritos, el orden de las etapas sintéticas empleadas puede variar y dependerá entre otros de factores tales como la naturaleza de otros grupos funcionales presentes en un sustrato particular, la disponibilidad de los intermedios clave y la estrategia del grupo protector (si la hubiera) a adoptar. Evidentemente, tales factores también influirán en la elección del reactivo para uso en dichas etapas sintéticas. También se apreciará que

diversas interconversiones y transformaciones de sustituyentes o grupos funcionales convencionales en ciertos compuestos de fórmula (I) proporcionarán otros compuestos de fórmula (I).

Con respecto al uso de los compuestos de la invención en seres humanos, se proporciona:

una composición farmacéutica parasiticida que comprende un compuesto de fórmula (I), o una sal farmacéuticamente aceptable del mismo, o un solvato farmacéuticamente aceptable de cualquier entidad, junto con un diluyente o vehículo farmacéuticamente aceptable, que puede adaptarse para administración tópica;

un compuesto de fórmula (I), o una sal farmacéuticamente aceptable del mismo, o un solvato farmacéuticamente aceptable de cualquier entidad, o una composición farmacéutica que contiene cualquiera de los anteriores, para uso como un medicamento;

el uso de un compuesto de fórmula (I), o una sal farmacéuticamente aceptable, o un solvato farmacéuticamente aceptable de cualquier entidad, o una composición farmacéutica que contiene cualquiera de los anteriores, para la fabricación de un medicamento para el tratamiento de una infestación parasitaria;

y un procedimiento para tratar una infestación parasitaria en un ser humano que comprende tratar a dicho ser humano con una cantidad eficaz de un compuesto de fórmula (I), o una sal farmacéuticamente aceptable del mismo, o un solvato farmacéuticamente aceptable de tal entidad, o una composición farmacéutica que contiene cualquiera de los anteriores.

Con respecto a su uso en animales no humanos, los compuestos de la

presente invención pueden administrarse solos o en una formulación apropiada para el uso específico previsto, la especie particular de animal huésped que se está tratando y el parásito implicado. Los procedimientos mediante los que se pueden administrar los compuestos incluyen administración oral mediante cápsula, bolo, comprimido o brebaje, administración tópica en forma de una formulación de vertido, aplicación puntual, inmersión, pulverización, espuma, champú o en polvo o, como alternativa, pueden administrarse por inyección (por ejemplo, por vía subcutánea, intramuscular o intravenosa), o en forma de un implante.

Tales formulaciones se preparan de manera convencional de acuerdo con la práctica veterinaria convencional. De esta manera, las cápsulas, bolos o comprimidos pueden prepararse mezclando el ingrediente activo con un diluyente o vehículo dividido finamente adecuado que contiene además un agente disgregante y/o aglutinante tal como almidón, lactosa, talco o estearato de magnesio, etc. Los brebajes orales se preparan disolviendo o suspendiendo el ingrediente activo en un medio adecuado. Las formulaciones de vertido o de aplicación puntual pueden prepararse disolviendo el ingrediente activo en un vehículo líquido aceptable tal como butildigol, parafina líquida o un éster no volátil, opcionalmente con la adición de un componente volátil tal como propan-2-ol. Como alternativa, las formulaciones de vertido, aplicación puntual o pulverización pueden prepararse por encapsulación, para dejar un resto de agente activo en la superficie del animal. Las formulaciones inyectables pueden prepararse en forma de una solución estéril que puede contener otras sustancias, por ejemplo suficientes sales o glucosa para hacer que la solución sea isotónica con la sangre. Los vehículos líquidos aceptables incluyen aceites

vegetales tales como aceite de sésamo, glicéridos tales como triacetina, ésteres tales como benzoato de bencilo, miristato de isopropilo y derivados de ácidos grasos de propilenglicol, así como disolventes orgánicos tales como pirrolidin-2-ona y glicerol formal. Las formulaciones se preparan disolviendo o suspendiendo el ingrediente activo en el vehículo líquido de forma que la formulación final contenga del 0,01 a 10% en peso del ingrediente activo.

Estas formulaciones variarán con respecto al peso del compuesto activo contenido en ellas, dependiendo de la especie del animal huésped a tratar, la gravedad y tipo de infección y el peso corporal del huésped. Para administración parenteral, tópica y oral, son intervalos de dosificación típicos del ingrediente activo de 0,01 a 100 mg por kg de peso corporal del animal. Preferiblemente, el intervalo es de 0,1 a 10 mg por kg.

Como alternativa, los compuestos pueden administrarse con el pienso del animal y para este propósito puede prepararse un aditivo o premezcla de pienso concentrado para mezclar con el pienso normal del animal.

Los compuestos de la invención son agentes antiparasitarios altamente activos que tienen utilidad particular como antihelmínticos, ectoparasiticidas, insecticidas y acaricidas.

De esta manera, los compuestos son eficaces en el tratamiento de diversas afecciones provocadas por endoparásitos incluyendo, en particular, helmintiasis que se provoca más frecuentemente por un grupo de gusanos parasitarios descritos como nematodos y que pueden provocar graves pérdidas económicas en cerdos, ovejas, caballos y ganado así como afectar a animales domésticos y aves. Los compuestos también son eficaces contra otros nematodos que afectan a diversas especies de animales incluyendo, por

ejemplo, Dirofilaria en perros y diversos parásitos que pueden infectar a seres humanos incluyendo parásitos gastro-intestinales tales como Ancylostoma, Necator, Ascaris, Strongyloides, Trichinella. Capillaria, Trichuris, Enterobius y parásitos que se encuentran en la sangre u otros tejidos y órganos tales como gusanos filariales y las etapas extra-intestinales de Strongyloides y Trichinella.

Los compuestos también son de valor en el tratamiento de infecciones por ectoparásitos incluyendo en particular ectoparásitos artrópodos de animales y pájaros tales como garrapatas, ácaros, piojos, mosca azul, insectos que pican, moscas, y larvas de dípteros migradores que pueden afectar al ganado y a los caballos.

Los compuestos también son insecticidas activos contra pestes domésticas tales como cucarachas, polillas, escarabajo de alfombras, y la mosca así como útiles contra pestes de insectos del grano almacenado de plantas agrícolas tales como ácaros arácnidos, áfidos, orugas y ortópteros migradores tales como langostas.

Por lo tanto, de acuerdo con otro aspecto de la invención, se proporciona una formulación veterinaria o agrícola que comprende un compuesto de fórmula (I), o una sal veterinaria o agrícolamente aceptable del mismo, o un solvato veterinaria o agrícolamente aceptable de cualquier entidad, junto con un diluyente o vehículo veterinaria o agrícolamente aceptable. Preferiblemente, la formulación se adapta para administración tópica.

La invención también proporciona un compuesto de fórmula (I), o una sal veterinaria o agrícolamente aceptable del mismo, o un solvato veterinaria o agrícolamente aceptable de tal entidad, o una formulación veterinaria o agrícolamente aceptable que contenga cualquiera de los anteriores, para uso

como parasiticida.

También se proporciona un procedimiento para tratar una infestación parasitaria en un lugar, que comprende el tratamiento del lugar con una cantidad eficaz de un compuesto de fórmula (I), o una sal veterinaria o agrícolamente aceptable del mismo, o un solvato veterinaria o agrícolamente aceptable de cualquier entidad, o una formulación veterinaria o agrícolamente aceptable que contiene cualquiera de los anteriores.

Preferiblemente, el lugar es el intestino, la piel o pelaje de un animal.

Se apreciará que la referencia a tratamiento incluye profilaxis así como alivio y/o curación de los síntomas establecidos de una infección parasitaria. De esta manera, el tratamiento también incluye cuidado paliativo.

Evaluación del compuesto

El ensayo in vitro para la medición de los compuestos que desplazan (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de ^{3}H-dihidro-(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo de las membranas P_2 de cabeza de mosca representa otro aspecto de la invención y se realizó como se indica a continuación.

Los nuevos compuestos antiparasitarios pueden identificarse fácilmente usando un ensayo radiométrico que mide el desplazamiento de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrol[2,3-c][2,1]benzoxazin-2-carboxilato de ^{3}H-dihidro-(1*S*,2*R*,4*aS*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4a,5,6,7,8,8*a*-octahidronaftalen-1-ilo de membranas P_2 de cabeza de mosca. Este ensayo puede usarse para medir los valores de Ki y por lo tanto para identificar las relaciones de la actividad de la estructura.

como parasiticida.

También se proporciona un procedimiento para tratar una infestación parasitaria en un lugar, que comprende el tratamiento del lugar con una cantidad eficaz de un compuesto de fórmula (I), o una sal veterinaria o agrícolamente aceptable del mismo, o un solvato veterinaria o agrícolamente aceptable de cualquier entidad, o una formulación veterinaria o agrícolamente aceptable que contiene cualquiera de los anteriores.

Preferiblemente, el lugar es el intestino, la piel o pelaje de un animal.

Se apreciará que la referencia a tratamiento incluye profilaxis así como alivio y/o curación de los síntomas establecidos de una infección parasitaria. De esta manera, el tratamiento también incluye cuidado paliativo.

Evaluación del compuesto

El ensayo in vitro para la medición de los compuestos que desplazan (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de ^{3}H-dihidro-(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo de las membranas P_2 de cabeza de mosca representa otro aspecto de la invención y se realizó como se indica a continuación.

Los nuevos compuestos antiparasitarios pueden identificarse fácilmente usando un ensayo radiométrico que mide el desplazamiento de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrol[2,3-c][2,1]benzoxazin-2-carboxilato de ^{3}H-dihidro-(1*S*,2*R*,4*aS*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4a,5,6,7,8,8*a*-octahidronaftalen-1-ilo de membranas P_2 de cabeza de mosca. Este ensayo puede usarse para medir los valores de Ki y por lo tanto para identificar las relaciones de la actividad de la estructura.

También puede usarse como una selección de alto rendimiento (ensayando las moléculas pequeñas sintéticas o productos naturales generados por fermentación de microorganismos) para identificar nuevas entidades químicas con actividad antiparasitaria.

Para preparar las membranas P_2 de cabeza de mosca, las pupas de *Lucilia sericata* (o cualquier otra plaga de insectos) se incuban en una cámara para insectos y se congelan rápidamente en nitrógeno líquido. Las moscas se agitan en un tamiz y un platillo unitario para separar los cuerpos de las cabezas/alas/patas. Después un tamiz de diámetro más pequeño separa las cabezas de las alas y patas. Los diámetros de tamiz dependen del tamaño de las moscas que se recojan. Después las cabezas de las moscas se usan para preparar la membrana P_2.

La membrana de la cabeza de la mosca se prepara en tampón que consite en HEPES 50 mM, pH 7,4, que contiene un cóctel de inhibidores de proteasa (Boehringer Mannheim Complete®). Todas las etapas se realizan en hielo o a 4ºC. Las cabezas de las moscas se homogeneizan en 5-10 volúmenes de tampón a 30.000 rpm usando un homogeneizador Polytron. Después, el homogeneizado se centrifuga en una centrífuga a 1000 x g durante 10 minutos y el sobrenadante se filtra a través de una gasa. Después, el sobrenadante filtrado se centrifuga a 20.000 x g durante 1 hora y el sedimento de la membrana P_2 se vuelve a suspender en tampón y se almacena en alícuotas a -80ºC.

Para medir la unión de (2*S*,3*aR*,9*bR*)-6-cloro-9b-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrol[2,3-*c*][2,1]benzoxazin-2-carboxilato de ^{3}*H*-dihidro-(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-

1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo a las membranas P_2 de cabeza de mosca, se añaden 400 µl de proteína a una concentración de 0,5 mg/ml, a una placa de pocillos profundos, que contiene ^{3}*H*-dihidro-CJ-12662 que da una concentración final de 1 nM del ligando radiactivo. Los pocillos de control también contienen tampón o (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrol[2,3-*c*][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo $5x10^{-6}$M (concentración final). Otros pocillos contienen el compuesto de interés diluido en serie en diluciones de 5 veces a partir de $5x10^{-6}$M. Para una selección de alto rendimiento los compuestos se añaden a una concentración sólo para permitir una selección rápida de grandes cantidades de compuestos. La placa de ensayo se incuba a 30ºC durante 90 minutos. Después, la placa se recoge en filtros de fibra de vidrio (prehumedecidos en Triton X-100 al 0,5%) sobre un colector de filtración y se lava rápidamente al vacío con 5 x 1 ml de lavados de HEPES 50 mM que contiene Triton X-100 al 0,25%. Después de secar, la radiactividad unida a los filtros se mide usando una escintilación sólida fundida en un contador de escintilación. Los pocillos diluidos en serie se representan gráficamente como unión (cuentas por minuto) contra valores de $\log_{10}$ (concentración competidora) y valores de Ki (Kd=7 nM) calculados y comparados con (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrol[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo. En una selección de alto rendimiento, los compuestos que muestran inhibición ≥ 70% de la unión de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrol[2,3-

c][2,1]benzoxazin-2-carboxilato de ^{3}H-dihidro-(1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo son activos.

Instrumentos usados para adquirir los datos de caracterización

Los datos espectrales de resonancia magnética nuclear (RMN) se obtuvieron usando espectrómetros Varian Inova 300, Varian Inova 400, Varian Unityplus 400, Bruker AC 300 MHz, Bruker AM 250 MHz o Varian T60 MHz, los desplazamientos químicos observados (δ) fueron coherentes con las estructuras propuestas. Los datos de espectro de masas (EM) se obtuvieron en un espectrómetro Finnigan Masslab Navigator, Fisons Instruments Trio 1000 o un sitema Hewlett Packard GCMS modelo 5971. Los iones calculados y observados citados se refieren a la composición isotópica de menor masa. HPLC significa cromatografía líquida de alta resolución. Temperatura ambiente significa de 20 a 25°C.

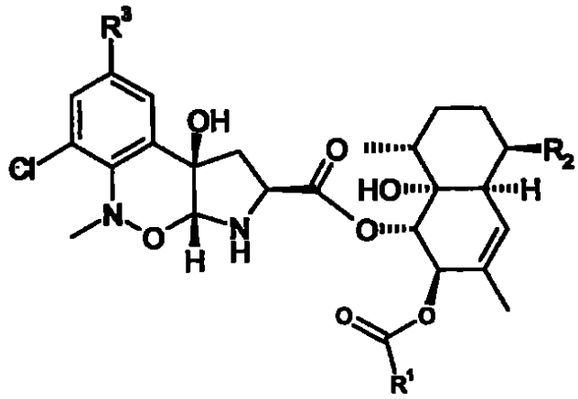
Preparación de sal

Cuando sea aplicable, la sal clorhidrato puede prepararse disolviendo el producto en una mezcla de metanol:éter (1:5) y añadiendo cloruro de hidrógeno (solución 1 M en éter dietílico, 2 equiv.). La mezcla se concentra al vacío, dando la sal clorhidrato.

De igual forma, pueden prepararse otras sales tales como sales de ácido trifluoroacético y sales de ácido acético disolviendo el producto en un disolvente adecuado tal como acetato de etilo o metanol y añadiendo el ácido correspondiente (2 equiv.). Después, la mezcla de reacción puede concentrarse al vacío, dando la sal deseada.

Estereoquímica

Todos los estereoisómeros de R^2 están dentro del alcance de esta invención, excepto cuando se describa específicamente. El sustituyente R^2 puede incluir diastereómeros unitarios así como mezclas de diastereómeros.



Procedimientos Genéricos

Procedimiento Genérico A

Se añadió metanol (3 ml) a la amina correspondiente (0,39 mmol, 1,5 equiv.), que se pone en un bloque de reacción Stem®. En los casos en los que la amina era una sal amónica, se añadió trietilamina (55 µl, 0,4 mmol). Se añadió una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 200 mg, 0,26 mmol) en metanol (2 ml, calidad analítica) y las mezclas de reacción se taparon con un tapón septum de caucho y se agitaron durante 5 horas a temperatura ambiente. Se añadió hidruro de boro sobre Amberlite® IRA400 (200 mg, 0,5 mmol) y la mezcla se agitó a temperatura ambiente durante 18 h. Después, la mezcla de reacción se filtró a través de un cartucho de filtro (Isolute™, 6 ml), el

residuo se lavó con metanol (2 ml) y el filtrado se concentró en una corriente de nitrógeno. Al producto bruto resultante se le añadió cloruro de hidrógeno (solución 4 N en dioxano, 2 ml), la mezcla se agitó en un agitador orbital durante 10 min, se transfirió a una placa caliente (50ºC) y se concentró en una corriente de nitrógeno durante 40 min. Se añadió trietilamina (20% v/v en diclorometano, 2 ml) y la mezcla se concentró en una corriente de nitrógeno, seguido de la adición y evaporación de trietilamina (20% v/v en diclorometano, 2 ml). Después, el producto de reacción bruto se disolvió en acetonitrilo:dimetilsulfóxido (4:1, 1 ml) y se purificó por cromatografía líquida preparativa automatizada (sistema Gilson, columna de 10 x 150 mm Phenomenex Magellen C18 de 5 µ) usando un gradiente acuoso de ácido trifluoroacético al 0,1%:acetonitrilo (de 95:5 a 5:95). La evaporación del eluyente en un sistema Genevac dio el producto final.

Procedimiento Genérico B

A la amina correspondiente (0,33 mmol, 1,5 equiv.) se le añadió una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3a*H*)-dicarboxilato de 2-{(1*S*,2*R*,4a*S*,5*R*,6*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4a,5,6,7,8,8a-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 170 mg, 0,22 mmol) en diclorometano (2 ml). En los casos en los que la amina era una sal amónica, se añadió trietilamina (55 µl, 0,4 mmol). A la reacción se le añadió triacetoxiborohidruro sódico (93 mg, 0,44 mmol) y la mezcla se agitó en un bloque de reacción Stem® durante 18 h. Después, la mezcla se diluyó con diclorometano (4 ml) y agua (2 ml) y se agitó vigorosamente durante 20 min. Las fases se separaron por medio de un

cartucho de filtro con una frita hidrófoba (medio de filtro Whatman de 12 ml 1PS) y el filtrado orgánico se concentró en una corriente de nitrógeno. Al producto bruto resultante se le añadió cloruro de hidrógeno (solución 4 N en dioxano, 2 ml), la mezcla se agitó en un agitador orbital durante 10 min, se transfirió a una placa caliente (50°C) y se concentró en una corriente de nitrógeno durante 40 min. Se añadió trietilamina (al 20% v/v en diclorometano, 2 ml) y la mezcla se concentró en una corriente de nitrógeno, seguido de la adición y evaporación de más trietilamina (al 20% v/v en diclorometano, 2 ml). Después, el producto de reacción bruto se disolvió en una mezcla de acetonitrilo:dimetilsulfóxido (4:1, 1 ml) y se purificó por cromatografía líquida preparativa automatizada (sistema Gilson, columna de 10 x 150 mm Phenomenex Magellen C18 de 5 µ) usando un gradiente de ácido trifluoroacético acuoso al 0,1%:acetonitrilo (de 95:5 a 5:95). La evaporación del eluyente en un sistema Genevac dio el producto final.

Procedimiento Genérico C

Una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 141, 21 mg, 0,0375 mmol), la amina (0,1 mmol), triacetoxiborohidruro de tetrametilamonio (26 mg, 0,1 mmol), trietilamina (20 µl, 0,15 mmol) en 1-metil-2-pirrolidinona (0,9 ml) se agitó a temperatura ambiente durante 18 h. Después, la mezcla de reacción se inyectó directamente en la columna de HPLC para la purificación usando un gradiente de ácido trifluoroacético acuoso al 0,1%:acetonitrilo (de 95:5 a 5:95). El producto purificado se obtuvo después de la evaporación de los disolventes

en un sistema Genevac.

La autopurificación se realizó usando un sistema de HPLC Gilson usando una columna Phenomenex Magellen® de 150 mm x 10 mm 5 µ ODS a temperatura ambiente. La elución se formó en gradientes a partir de ácido trifluoroacético acuoso al 0,1%:acetonitrilo (de 95:5 a 5:95) durante 12 min. Los productos se detectaron por UV a 215 nm. Todas las fracciones de la autopurificación se analizaron por inyección en bucle en un espectrómetro de masas de un único cuadripolo Micromass "Platform LC"® con sonda de IQPA.

Procedimiento Genérico D

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-{[[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 200 mg, 0,26 mmol) en metanol (5 ml) se le añadió la amina primaria correspondiente (0,52 mmol, 2 equiv.). Se añadió trietilamina (80 µl, 0,58 mmol) en los casos en los que la amina era una sal amónica. La mezcla de reacción se agitó durante 18 horas a temperatura ambiente en un bloque de reacción Stem®. Después, se añadió hidruro de boro sobre Amberlite® IRA400 (Aldrich, resina de 2,5 mmol/g, 150 mg, 0,38 mmol) y la agitación continuó durante 2,5 días. La mezcla de reacción se filtró usando un cartucho de filtro desechable (6 ml) y el residuo se aclaró con metanol. Se añadió 4-benciloxibenzaldehído, unido a polímero (Aldrich, resina de 2,8 mmol/g, 180 mg, 0,5 mmol) para eliminar el exceso de amina y después la mezcla de reacción se agitó durante 18 h a temperatura ambiente. La solución de reacción se filtró usando cartuchos de filtro desechables (6 ml),

el residuo se aclaró con metanol y el filtrado se concentró en una corriente de nitrógeno. El producto bruto se disolvió en diclorometano (20 ml). De esta mezcla de reacción se añadieron (5 ml) a piridina anhidra (8 µl, 0,10 mmol) y se añadió el cloruro de ácido correspondiente (0,1 mmol, 1,5 equiv.) y la reacción se agitó a temperatura ambiente durante 3 horas. Los disolventes se evaporaron en una corriente de nitrógeno. Al producto bruto resultante se le añadió cloruro de hidrógeno (solución 4 N en dioxano, 2 ml), la mezcla se agitó a temperatura ambiente durante 45 min, se transfirió a una placa caliente (50ºC) y se concentró en una corriente de nitrógeno. Se añadió trietilamina (al 20% v/v en diclorometano, 2 ml) y la mezcla se concentró en una corriente de nitrógeno. Después, el producto de reacción bruto se disolvió en acetonitrilo:dimetilsulfóxido (8:1, 1 ml), se filtró usando un filtro de HPLC Whatman y se purificó por cromatografía líquida preparativa automatizada (sistema Gilson, columna de 10 x 150 mm Phenomenex Magellen C18 de 5 µ), usando un gradiente de ácido trifluoroacético acuoso al 0,1%:acetonitrilo variando de 95:5 a 5:95, La evaporación del eluyente en un sistema Genevac dio el producto final.

<u>Procedimiento Genérico E</u>

A la solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 100 mg, 0,13 mmol) en metanol (2 ml) se le añadió la amina correspondiente (0,52 mmol, 4 equiv.) y la mezcla se agitó a temperatura ambiente durante 18 h. Se añadió hidruro de

boro sobre Amberlite® IRA400 (Aldrich, resina de 2,5 mmol/g, 77 mg, 0,19 mmol) y la mezcla se agitó con un agitador orbital a temperatura ambiente durante 18 h. Después, se añadió benciloxibenzaldehído, unido a polímero (Aldrich, resina de 2,8 mmol/g, 460 mg, 1,29 mmol) para eliminar el exceso de amina y la mezcla de reacción se agitó durante 18 h. La mezcla de reacción se filtró, el residuo se lavó con metanol y el filtrado se concentró a sequedad en una corriente de nitrógeno. Una solución del producto bruto (0,064 mmol) en diclorometano se puso en una placa de 48 pocillos (Flexchem Synthesis Block) y se añadió *N*-metilmorfolina unida a polímero (resina de 3,0 mmol/g, 32 mg, 0,096 mmol) por medio de una placa de administración. Se añadió el cloruro de ácido correspondiente (0,16 mmol, 2,5 equiv.) y la mezcla de reacción se agitó a temperatura ambiente durante 18 h. Después, se añadió *tris*(2-aminoetil)amina unida a polímero (resina de 4,8 mmol/g, 41 mg, 0,2 mmol) con una placa de administración y las mezclas se agitaron a temperatura ambiente durante 18 h. Después, la mezcla de reacción se filtró en otro bloque de 48 pocillos y los filtrados se concentraron en una corriente de nitrógeno. El residuo bruto se disolvió en cloruro de hidrógeno (solución 1 M en ácido acético, 0,5 ml), se agitó a temperatura ambiente durante 1 hora y después se concentró a sequedad en una corriente de nitrógeno. Después, el producto de reacción bruto se disolvió en acetonitrilo (1 ml) y se purificó por cromatografía líquida preparativa automatizada (sistema Gilson, columna de 10 x 150 mm Phenomenex Magellen C18 5µ), usando un gradiente de ácido trifluoroacético acuoso al 0,1%:acetonitrilo (de 95:5 a 5:95). La evaporación del eluyente en un sistema Genevac dio el producto.

Procedimiento Genérico G

A una solución del ácido (2*R*)-2-[(1*R*,4*R*,4*aS*,5*R*,6*R*)-5-({[(2*S*,3*aR*,9*bR*)-6-cloro-3-{[(1,1-dimetiletil)oxi]carbonil}-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-*c*][2,1]benzoxazin-2-il]carbonil}oxi)-6-(acetiloxi)-4*a*-hidroxi-4,7-dimetil-1,2,3,4,4*a*,5,6,8*a*-octahidronaftalen-1-il]propanoico (Preparación 181, 200 mg, 0,25 mmol) en diclorometano (2 ml) se le añadieron 1-hidroxibenzotriazol (Aldrich, 58 mg, 0,38 mmol) y sal clorhidrato de 1-(3-dimetilaminopropil)-3-etilcarbodiimida (96 mg, 0,5 mmol) y la mezcla se agitó a temperatura ambiente durante 0,5 horas. La mezcla de reacción se añadió a una solución de la amina correspondiente (0,38 mmol) en diclorometano (2 ml) y se agitó a temperatura ambiente durante 36 horas. La mezcla de reacción se diluyó con diclorometano (2 ml) y agua (7 ml) y se agitó vigorosamente durante 45 min. Las fases se separaron por medio de un cartucho de filtro con una frita hidrófoba (medio de filtro Whatman de 12 ml 1PS) y el filtrado orgánico se concentró en una corriente de nitrógeno seguido del secado al vacío. A una solución del producto bruto en dioxano (1 ml) se le añadió cloruro de hidrógeno (solución 4 M en una solución de dioxano, 2 ml) y la mezcla de reacción se agitó a temperatura ambiente durante 25 min. La mezcla de reacción se concentró en una corriente de nitrógeno durante 40 min (placa caliente a 50°C), después se añadió una solución de trietilamina en diclorometano (al 25% v/v, 2 ml) y la mezcla se concentró de nuevo a presión reducida. El producto de reacción bruto se purificó por cromatografía líquida preparativa automatizada (sistema Gilson, columna de 10 x 150 mm Phenomenex Magellen C18 5 μ), usando un gradiente de ácido trifluoroacético acuoso al 0,1%:acetonitrilo (de 95:5 a 5:95). La evaporación del eluyente en un sistema Genevac dio el producto.

Los Ejemplos dados en la siguiente Tabla 1 se prepararon mediante los procedimientos indicados anteriormente y la Tabla incluye los datos de caracterización física para cada compuesto sintetizado. La síntesis de diversos compuestos representativos también se describe con más detalle después de la Tabla 2. La Tabla 2 indica los compuestos precursores usados en la síntesis de los compuestos de la invención.

Tabla 1: Tabla de Ejemplos

Ej. Nº	Nombre del Compuesto	Datos*
1	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	datos de *RMN dados para las sales acetato o trifluoroacetato EM (EN): M/Z [MH+] = 563,3 C29H39ClN2O7 + H requiere 563,25. RMN (CDCl3, datos seleccionados): 0,6 (d, 3H), 0,9-1,1 (m, 7H), 1,9 (septuplete, 1H), 2,1 (s, 3H), 3,35 (s, 3H), 5,2 (s, 1H), 7,2 (d, 1H).
2	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de	EM (TSP): M/Z [MH+] = 589,6 C31H41ClN2O7 +H

	(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-2-[(2-metilpropanoil)oxi]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	requiere 589,3. RMN (CDCl3, datos seleccionados): 0,6 (d, 3H), 1,18 (dd, 6H), 1,9 (septuplete, 1H), 1,8 (s, 3H), 3,4 (s, 3H), 4,75 (s, 1H), 5,0 (s, 1H), 5,1 (s, 1H), 5,25-5,3 (s, 2H), 5,4 (s, 1H), 7,2 (d, 1H).
3	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2, 3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(hexanoiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (TSP): M/Z [MH+] = 617,3 C33H45ClN2O7 +H requiere 617,3. RMN (CDCl3, datos seleccionados): 0,55 (d, 3H), 0,9 (m, 3H), 1,85 (s, 3H), 2,3 (m, 3H), 3,35 (s, 3H), 5,2 (s, 1H), 7,2 (d, 1H).
4	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-	EM (TSP): M/Z [MH+] = 621,2, C31H41ClN2O9 +H requiere 621,3. RMN

	(acetiloxi)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	(CDCl3, datos seleccionados): 0,8 (d, 3H), 1,0 (d, 3H), 2,0(s, 3H), 2,1 (s, 3H), 2,3 (m, 3H), 3,35 (s, 3H), 5,25 (s, 1H), 7,2 (d, 1H).
5	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3 ,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-[(2-metilpropanoil)oxi]etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (TSP): M/Z [MH+] = 649,2, C33H45ClN2O9 +H requiere 649,3. RMN (CDCl3, datos seleccionados): 0,6 (d, 3H), 1,1 (d, 3H), 1,6 (s, 3H), 2,1 (s, 3H), 2,1 (s, 3H), 2,3 (m, 3H), 3,35 (s, 3H), 5,25 (s, 1H), 7,0 (m, 1H), 7,2 (d, 1H), 7,4 (d, 1H).
6	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-[(ciclopropilcarbonil)oxi]-8*a*-hidroxi-3,8-	EM (EN): M/Z [MH+] = 587,3, C31H39ClN2O7 +H requiere 587,3. RMN (CDCl3, datos

	dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	seleccionados): 0,7 (d, 3H), 0,85-0,95 (m, 2H), 1,0-1,1 (m, 2H), 3,35 (s, 3H), 5,3 (s, 1H), 7,2 (d, 1H).
7	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletil)-2-{[(prop-2-iniloxi)carbonil]oxi}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (TSP): M/Z [MH+] = 603,0, C31H39ClN2O8 +H requiere 603,2. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,0 (m, 6H), 1,75-1,8 (m, 6H), 2,0 (1H, septuplete), 3,1 (s, 1H), 3,35 (s, 3H), 4,8 (s, 2H), 5,25 (s, 1H), 7,2 (d, 1H).
8	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9 b-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletil)-2-({[(2,2,2-tricloroetil)oxi]carbonil}oxi)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (TSP): M/Z [MH+] = 694,9, C30H38Cl4N2O8 +H requiere 695,1. RMN (CDCl3, datos seleccionados): 0,6 (d, 3H), 1,0 (m, 6H), 1,95 (1H, septuplete),

		3,4 (s, 3H), 4,7 (d, 1H), 4,85 (d, 1H), 5,4 (s, 1H), 7,2 (d, 1H).
9	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-2-({[(1-metiletenil)oxi]carbonil}oxi)-5-(1-metiletil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (TSP): M/Z [MH+] = 605,9, C31H41ClN2O8 +H requiere 605,3. RMN (CDCl3, datos seleccionados): 0,6 (m, 3H), 1,0 (m, 6H), 1,8 (s, 3H), 1,95 (1H, septuplete), 3,4 (s, 3H), 4,7 (s, 1H), 4,8 (s, 1H), 5,4 (s, 1H), 7,2 (d, 1H).
10	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*- hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletil)-2-{[(prop-2-eniloxi)carbonil]oxi}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (TSP): M/Z [MH+] = 605,5, C31H41ClN2O8 +H requiere 605,3. RMN (CDCl3, datos seleccionados): 0,65 (d, 3H), 1,0 (d, 6H), 1,95 (1H, septuplete), 3,4 (s, 3H), 4,65 (m, 2H), 5,25-5,35 (m,

		4H), 5,9 (m, 1H), 7,25 (d, 1H).
11	metilbutanodioato de (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-1-({[(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-il]carbonil}oxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-2-ilo	EM (EN): M/Z [MH+] = 633,2, C32H41ClN2O9 +H requiere 633,3. RMN (CDCl3, datos seleccionados): 0,6 (d, 3H), 3,4 (s, 3H), 3,65-3,7 (m, 5H), 4,75 (s, 1H), 5,0 (s, 1H), 5,3-5,35 (m, 2H), 7,25 (d, 1H).
12	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-2-(pent-4-enoiloxi)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 601,2, C32H41ClN2O7 +H requiere 601,3. RMN (CDCl3, datos seleccionados): 0,45 (d, 3H), 1,8 (s, 3H), 3,4 (s, 3H), 4,7 (s, 1H), 5,0-5,1 (m, 4H), 5,2 (s, 1H), 5,35 (s, 1H), 5,4 5,8 (s, 1H), 7,2 (d, 1H).

13	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[({[2-(naftalen-1-ilamino)etil]amino}carbonil)oxi]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 791,2, C42H51ClN4O9 +H requiere 791,3. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,0 (d, 3H), 2,1 (s, 3H), 3,2 (s, 3H), 3,2-3,5 (m, 4H), 5,3 (s, 1H), 6,5 (m, 1H), 6,9-7,5 (m, 7H), 7,7-7,8 (m, 2H).
14	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-{[(acetiloxi)acetil]oxi}-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 619,1, C31H39ClN2O9 +H requiere 619,2. RMN (CDCl3, datos seleccionados): 0,6 (d, 3H), 1,65 (s, 3H), 1,85 (s, 3H), 2,15 (s, 3H), 3,4 (s, 3H), 4,6 (dd, 2H), 5,25 (s, 1H), 7,2 (m, 1H).
15	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(formiloxi)-8*a*-	EM (EN): M/Z [MH+] = 547,1, C28H35ClN2O7 +H requiere 547,2. RMN (CDCl3, datos

	hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	seleccionados): 0,45 (d, 3H), 1,65 (s, 3H), 1,85 (s, 3H), 3,35 (s, 3H), 5,25 (s, 1H), 7,2 (d, 1H), 8,1 (s, 1H).
16	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-2-[(3,3,3-trifluoropropanoil)oxi]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 629,1, C30H36ClF3N2O7 +H requiere 629,2. RMN (CDCl3, datos seleccionados): 0,5 (d, 3H), 1,65 (s, 3H), 1,9 (s, 3H), 3,2 (dd, 2H), 3,35 (s, 3H), 5,25 (s, 1H), 7,2 (d, 1H).
17	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3 ,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[4-(etiloxi)-1-metil-4-oxobut-2-enil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 647,3, C33H43ClN2O9 +H requiere 647,3. RMN (CDCl3, datos seleccionados): 0,85 (d, 3H), 1,1 (t, 3H), 1,15 (d, 3H), 1,7 (s, 3H), 2,1 (*S*, 3H), 3,3 (s, 3H), 3,9 (m, 2H), 5,3 (s, 1H), 5,85 (d, 1H),

		6,9 (dd, 1H), 7,25 (d, 1H).
18	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-(2,2-difluoro-1-metiletenil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (TSP): M/Z [MH+] = 597,2, C29H35ClF2N2O7 +H requiere 597,2. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,2 (s, 3H), 3,3 (s, 3H), 5,1 (s, 1H), 5,2 (s, 1H), 5,3 (s, 1H), 5,5 (s, 1H), 7,25 (m, 1H).
19	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2;1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-fluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (TSP): M/Z [MH+] = 581,1, C29H38ClFN2O7 +H requiere 581,2. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,1 (d, 3H), 1,6 (s, 3H), 2,1 (s, 3H), 2,2 (s, 3H), 3,3 (s, 3H), 4,3-4,7 (m, 2H), 5,4 (s, 1H), 7,25

		(m, 1H).
20	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[(1-metil-2-morfolin-4-iletil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 648,3, C33H46ClN3O8 +H requiere 648,3. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,05 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,4-2,6 (m, 5H), 3,4 (s, 3H), 3,6-3,8 (m, 4H), 5,3 (s, 1H), 7,25 (m, 1H).
21	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-etil-1,3-tiazol-4-il)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (TSP): M/Z [MH+] = 631,7, C31H38ClN3O7S +H requiere 632,2. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,3 (s, 3H), 1,4 (t, 3H), 2,1 (s, 3H), 3,0 (c, 2H), 3,35 (s, 3H), 5,2 (s, 1H), 7,25 (m, 1H), 7,7 (m, 1H).

22	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2,2-difluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (TSP): M/Z [MH+] = 600,3, C29H37ClF2N2O7 +H requiere 600,2. RMN (CDCl3, datos seleccionados): 0,6 (d, 3H), 1,1 (d, 3H), 2,05 (s, 3H), 2,1 (s, 3H), 3,35 (s, 3H), 5,25-5,3 (m, 2H), 5,95 (t, 1H), 7,2 (d, 1H).
23	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2,2-difluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (TSP): M/Z [MH+] = 599,9. C29H37ClF2N2O7 +H requiere 600,2. RMN (CDCl3, datos seleccionados): 0,9 (d, 3H), 1,1 (d, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 5,4 (s, 1H), 5,9 (t, 1H), 7,2 (m, 1H).
24	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-(2,2-	EM (TSP); M/Z [MH+] = 629,2, C29H35Cl3N2O7 +H requiere 629,2. RMN

	dicloro-1-metiletenil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	(CDCl3, datos seleccionados): 0,8 (d, 3H), 1,25 (s, 3H), 1,95 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 5,1 (s, (1H), 5,2 (s, 1H), 5,3 (s, 1H), 5,4 (s, 1H), 7,2 (d, 1H).
25	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9b-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[(fenilmetil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 668,308, C36H46ClN3O7 +H requiere 668,310. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,1 (d, 3H), 1,65 (s, 3H), 2,05 (s, 3H), 3,25 (s, 3H), 4,05 (s, 2H), 5,2 (s, 1H), 7,2 (d, 1H), 7,3-7,5 (m, 5H).
26	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{[(2-clorofenil)metil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 702,269, C36H45Cl2N3O7 +H requiere 702,271. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,15 (d, 3H), 1,7

		(s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 4,3 (s, 2H), 5,2 (s, 1H), 7,1-7,6 (m, 6H).
27	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(furan-2-ilmetil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 658,288, C34H44ClN3O8 +H requiere 658,289. RMN (CDCl3, datos seleccionados): 0,7 (m, 3H), 1,15 (d, 3H), 1,75 (s, 3H), 2,1 (s, 3H), 3,15 (s, 3H), 4,3 (m, 2H), 5,3 (s, 1H), 6,4 (m, 1H), 6,5 (m, 1H), 7,2 (m, 1H), 7,5 (m, 1H).
28	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{[(2-metilfenil)metil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 682,323, C37H48ClN3O7 +H requiere 682,326. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,1 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,4

		(s, 3H), 3,3 (s, 3H), 4,1 (m, 2H), 5,2 (s, 1H), 7,1-7,3 (m, 5H), 7,45 (m, 1H).
29	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{[(1S)-1-feniletil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (PA): M/Z [MH+] = 682,3252, C37H48ClN3O7 +H requiere 682,3259. RMN (CDCl3, datos seleccionados) : 0,8 (d, 3H), 1,1 (d, 3H), 1,6 (s, 3H), 1,7 (d, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 5,2 (s, 1H), 6,8-7,6 (m, 8H).
30	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{[(3-clorofenil)metil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 702,270, C36H45Cl2N3O7 +H requiere 702,271. RMN (CDCl3, datos seleccionados): 0,7 (d, 3H), 1,1 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,4 (s, 3H), 3,3 (s, 3H), 3,9-4,1 (m, 3H),

		5,2 (s, 1H), 6,95 (m, 1H), 7,1-7,25 (m, 2H), 7,3-7,4 (m, 3H), 7,45 (m, 1H).
31	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-({[2-(metiloxi)fenil]metil}amino)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 698,323, C37H48ClN3O8 +H requiere 698,321. RMN (CDCl3, datos seleccionados) : 0,8 (d, 3H), 1,1 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,85 (s, 3H), 4,05-4,3 (m, 2H), 5,2 (s, 1H), 6,85-7,0 (m, 5H), 7,2 (d, 1H), 7,4 (m, 1H).
32	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(4-piridin-2-ilpiperazin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 724,350, C38H50ClN5O7 +H requiere 724,348. RMN (CDCl3, datos seleccionados) : 0,7 (d, 3H), 1,1 (d, 3H), 1,7 (s, 3H), 2,1 (s,

		3H), 2,2-2,4 (m, 4H), 3,3 (s, 3H), 3,4-3,6 (m, 4H), 5,2 (s, 1H), 6,6-6,7 (m, 2H), 7,0 (t, 1H), 7,2 (d, 1H), 7,35 (d, 1H), 7,5 (m, 1H). 8,2 (m, 1H).
33	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{*bis*[2-(metiloxi)etil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 694,347, C35H52ClN3O9 +H requiere 694,347. RMN (CDCl3, datos seleccionados): 0,65 (d, 3H), 1,0 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,4-2,8 (m, 8H), 3,3-3,4 (m, 9H), 3,4-3,5 (m, 4H), 5,2-5,3 (s, 2H), 7,2 (d, 1H).
34	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3 a,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-[(2-tien-2-iletil)amino]etil]-1,2,4*a*,5,6,7,8,8*a*-	EM (EN): M/Z [MH+] = 688,280, C35H46ClN3O7S +H requiere 688,282. RMN (CDCl3, datos seleccionados): 0,75

	octahidronaftalen-1-ilo	(d, 3H), 1,15 (d, 3H) 1,65 (s, 3H), 2,1 (s, 3H), 2,6-2,85 (m, 4H), 3,2-3,3 (m, 5H), 5,2 (s, 1H), 6,8-7,0 (m, 3H), 7,1-7,3 (m, 3H).
35	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo-[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-({[4-(trifluorometil)fenil]metil}amino)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 736,296, C37H45ClF3N3O7 +H requiere 736,298. RMN (CDCl3, datos seleccionados): 0,8 (m, 3H), 1,1 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,8-4,2 (m, 3H), 5,25 (s, 1H), 6,9 (t, 1H), 7,1 (d, 1H), 7,2 (d, 1H), 7,5-7,7 (m, 4H).
36	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[metil(2-{[2-(metiloxi)fenil]oxi}etil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 742,346, C39H52ClN3O9 +H requiere 742,347. RMN (CDCl3, datos seleccionados):- 0,8 (m, 3H), 1,2 (d, 3H),

		1,7 (s, 3H), 2,1 (s, 3H), 3,0-3,2 (m, 3H), 3,3 (s, 3H), 3,4-3,9 (m, 4H), 3,85 (s, 3H), 5,2 (s, 1H), 6,8-7,0 (m, 4H), 7,0 (m, 1H), 7,2 (d, 1H), 7,35 (d, 1H).
37	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{(1-metiletil)[2-(fenilsulfonil)etil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 788,333, C40H54ClN3O9S +H requiere 788,335. RMN (CDCl3, datos seleccionados): 0,9 (d, 3H), 1,15 (d, 3H), 1,35 (d, 3H), 1,45 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,4-3,9 (m, 4H), 3,85 (s, 3H), 5,2 (s, 1H), 7,0 (t, 1H), 7,2 (d, 1H), 7,3 (d, 1H), 7,55-7,65 (m, 2H), 7,7 (m, 1H), 7,9 (m, 2H).
38	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-	EM (EN): M/Z [MH+] = 740,332,

	c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(2,3-dihidro-1,4-benzodioxin-2-ilmetil)(metil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	C39H50ClN3O9 +H requiere 740,331. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (m, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,0 (s, 3H), 3,3 (s, 3H), 4,05-4,3 (m, 4H), 5,2 (s, 1H), 6,8-7,05 (m, 5H), 7,2-7,35 (m, 2H).
39	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(4-{[2-(metiloxi)fenil]metil}piperazin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 767,379, C41H55ClN4O8+H requiere 767,379. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,15 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,85 (s, 3H), 4,3 (s, 2H), 5,2 (s, 1H), 6,9-7,1 (m, 4H), 7,2-7,5 (m, 3H).
40	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-	EM (EN): M/Z [MH+] =

	1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(1,1-dimetiletil)piperidin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	702,3900, C38H56ClN3O7 +H requiere 702,3885. RMN (CDCl3, datos seleccionados): 0,8-0,95 (m, 12H), 0,9-1,1 (m, 3H), 1,65-1,75 (m, 3H), 2,1-2,15 (m, 3H), 2,2-2,5 (m, 8H), 3,3-3,35 (s, 3H), 5,2 (s, 1H), 7,05 (m, 1H), 7,2 (m, 1H).
41	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[(fenilmetil)oxi]piperidin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 752,3678, C41H54ClN3O8+H requiere 752,3678. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,1 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,25-3,4 (m, 7H), 4,55 (s, 2H), 5,2 (s, 1H), 7,0 (m, 1H), 7,2-7,4 (m, 7H).
42	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-	EM (EN): M/Z [MH+] =

	1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[7,8-*bis*(metiloxi)-3,4-dihidroisoquinolin-2(1*H*)-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	754,3463, C40H52ClN3O9 +H requiere 754,3470. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,1 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,0-3,35 (m, 8H), 3,3 (s, 3H), 3,8 (s, 3H), 3,9 (s, 3H), 4,55 (s, 2H), 5,2 (s, 1H), 6,8-6,9 (m, 2H), 7,0 (m, 1H), 7,2 (m, 1H), 7,35 (m, 1H).
43	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(metil{[4-(metiloxi)fenil]metil}amino)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 712,3382, C38H50ClN3O8 +H requiere 712,3365. RMN (CDCl3, datos seleccionados): 0,85 (m, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,6-2,9 (m, 9H), 3,3 (s, 3H), 3,85 (s, 3H), 4,15 (m, 2H), 5,2 (s, 1H), 6,9-7,1 (m, 3H), 7,2 (m, 1H), 7,2-

		7,25 (m, 2H).
44	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[(etiloxi)carbonil]-1,4-diazepan-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 733,3554, C37H53ClN4O9 +H requiere 733,3579. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,3(t, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,9-3,2 (m, 14H), 3,3 (s, 3H), 4,1-4,3 (m, 4H), 5,2 (s, 1H), 7,0 (m, 3H), 7,2-7,35 (m, 2H).
45	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(fenilmetil)-1,4-diazepan-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 751,3840, C41H55ClN4O7+H requiere 751,3838. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,15 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,9-4,0 (m, 12H), 3,3 (s, 3H), 4,3 (s, 2H), 5,2 (s, 1H), 6,95 (m, 1H),

		7,2 (d, 1H), 7,4-7,5 (m, 6H).
46	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-5-{2-[acetil(etil)amino]-1-metiletil}-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 649,0, C33H46ClN3O8 +H requiere 648,3052. RMN (CDCl3, datos seleccionados): 0,75-0,8 (m, 3H), 0,95-1,0 (m, 3H), 1,2-1,3 (m, 3H), 1,65-1,75 (m, 3H), 2,1 (s, 3H), 2,15 (s, 3H), 3,3 (s, 3H), 5,2 (s, 1H), 7,2 (d, 1H).
47	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3 a,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-5-{2-[acetil(ciclopropil)amino]-1-metiletil}-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 660,2, C34H46ClN3O8 +H requiere 660,3052. RMN (CDCl3, datos seleccionados): 0,7-0,8 (m, 5H), 0,9-1,0 (m, 6H), 1,7 (s, 3H), 2,1 (s, 3H), 2,2 (s, 3H), 3,3 (s, 3H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2 (d, 1H), 7,35 (d, 1H).
48	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-	EM (TSP): M/Z [MH+]

	1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{ciclopropil[(metiloxi)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	= 676,7, C34H46ClN3O9 +H requiere 676,3001. RMN (CDCl3, datos seleccionados): 0,6-0,7 (m, 5H), 0,7-0,9 (m, 3H), 1,0 (d, 3H),1,7 (s, 3H), 2,1 (s, 3H), 2,2 (s, 3H), 3,35 (s, 3H), 3,7 (s, 3H), 5,25 (s, 1H), 7,0 (dd, 1H), 7,2 (d, 1H), 7,4(d, 1H).
49	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{etil[(metiloxi)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (TSP): M/Z [MH+] = 664,4, C33H46ClN3O9 +H requiere 664,3001. RMN (CDCl3, datos seleccionados): 0,8 (t, 3H), 1,0 (m 3H), 1,2 (m, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,35 (s, 3H), 3,65 (s, 3H), 5,2-5,25 (m, 2H), 7,0 (m, 1H), 7,2 (m, 1H), 7,4(d, 1H).

50	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{[(2,5-diclorofenil)metil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (PA+): M/Z [MH+] = 736, C36H44Cl3N3O7 +H requiere 736,2323. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,1 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 4,3 (s, 2H), 5,2 (s, 2H), 6,95 (dd, 1H), 7,2 (d, 1H), 7,3-7,4 (m, 3H), 7,6 (s, 1H).
51	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{[(3,5-diclorofenil)metil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (PA+): M/Z [MH+] = 736, C36H44Cl3N3O7 +H requiere 736,2323. RMN (CDCl3, datos seleccionados): 0,7 (m, 3H), 1,1 (m, 3H),1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,9-4,1 (m, 2H), 5,3 (s, 1H), 6,9 (m, 1H), 7,1-7,4 (m, 5H).

52	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{ciclopropil[(etilamino)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 689,4, C35H49ClN4O8 +H requiere 689,3317. RMN (CDCl3, datos seleccionados): 0,7-0,8 (m, 5H), 0,8-0,9 (m, 3H), 0,95 (d, 3H), 1,1 (t, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,65-3,8 (m, 2H), 5,2 (s, 1H), 6,95 (dd, 1H), 7,2 (d, 1H), 7,3 (d, 1H).
53	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[metil(fenilmetil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 682, C37H48ClN3O7 +H requiere 682,3259. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 0,85-1,1 (m, 3H), 1,6 (s, 3H), 2,1 (s, 3H), 2,65-2,75 (m, 3H), 3,1-3,15 (m, 3H), 4,2-4,6 (m, 3H), 5,2 (s, 1H), 6,9-7,4 (m, 3H), 7,45-7,6 (m, 5H).
54	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-	EM (EN): M/Z [MH+] =

	1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-[4-(fenilmetil)piperazin-1-il]etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	737, C40H53ClN4O7 +H requiere 737,3681. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,65 (s, 3H), 2,1 (s, 3H), 3,0-3,4 (m, 6H), 3,3 (s, 3H), 3,5-3,7 (m, 6H), 4,2 (s, 2H), 5,2 (s, 1H), 7,0 (m, 1H), 7,2 (m, 1H), 7,4-7,5 (m, 6H).
55	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(3-metilpiperidin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 660, C35H50ClN3O7 +H requiere 660,3416. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,0-1,05 (m, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,7-2,9 (m, 12H), 3,3 (s, 3H), 5,2 (s, 2H), 7,0 (m, 1H), 7,2 (m, 1H), 7,35 (d, 1H).
56	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-	EM (EN): M/Z [MH+] = 725,2, C37H49ClN6O7

	c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(4-pirimidin-2-ilpiperazin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	+H requiere 725,3430. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,1 (d, 3H),1,6 (s, 3H), 2,1 (s, 3H), 2,3-2,65 (m, 8H), 3,35 (s, 3H), 4,75-4,9 (m, 4H), 5,2 (m, 2H), 6,5 (m, 1H), 7,0 (dd, 1H), 7,2 (m, 1H), 7,4 (d, 1H), 8,3-8,35 (m, 2H).
57	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{metil[2-(feniloxi)etil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 712, C38H50ClN3O8 +H requiere 712,3365. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d. 3H),1,6 (s, 3H), 2,1 (s, 3H), 2,9-3,05 (m, 4H), 3,3 (s, 3H), 4,4-4,5 (m, 2H), 5,2 (m, 1H), 6,85-7,0 (m, 3H), 7,0 (dd, 1H), 7,2 (m, 1H), 7,25-7,35 (m, 3H).
58	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-	EM (EN): M/Z [MH+] =

	1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-tiomorfolin-4-iletil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	664, C33H46ClN3O7S +H requiere 663,2745. RMN (CDCl3, datos seleccionados): 0,85 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,9-3,2 (m, 11H), 3,3 (s, 3H), 5,2 (m, 1H), 7,0 (dd, 1H), 7,2-7,3 (m, 2H).
59	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[ciclohexil(metil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 674, C36H52ClN3O7 +H requiere 674,3572. RMN (CDCl3, datos seleccionados): 0,85 (d, 3H), 1,15-1,25 (m, 6H), 1,3-1,5 (m, 6H), 1,7 (s, 3H), 1,9-2,0 (m, 2H), 2,1 (s, 3H), 2,7-2,85 (m, 3H), 3,3 (s, 3H), 5,2 (m, 1H), 7,0 (m, 1H), 7,2 (m, 1H), 7,35 (dd, 1H).
60	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-	EM (EN): M/Z [MH+] = 683, C36H47ClN4O7

	c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[metil(piridin-2-ilmetil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	+H requiere 683,3212. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,1 (d 3H), 1,65 (s, 3H), 2,1 (s 3H), 2,95 (s, 3H), 3,3 (s, 3H), 4,45 (m, 2H), 5,2 (m 1H), 7,0 (m, 1H), 7,2 (m, 1H), 7,35 (m, 1H), 7,5 (m 1H), 7,65 (m, 1H), 7,85 (m, 1H), 8,65 (m, 1H).
61	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(3,6-dihidropiridin-1(2*H*)-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 644, C34H46ClN3O7 +H requiere 644,3103. RMN (CDCl3, datos seleccionados): 0,85 (d, 3H), 1,15 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 4,45 (m, 2H), 5,1-5,2 (m, 2H), 5,7 (m, 1H), 6,0 (m, 1H), 7,0 (m, 1H), 7,35 (m, 1H)
62	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-	EM (EN): M/Z [MH+] =

	1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{[fenil(piridin-3-il)metil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	745,C41H49ClN4O7 +H requiere 745,3. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,05 (d, 3H), 1,6 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 4,45 (m, 2H), 5,0-5,15 (m, 3H) 6,9-7,6 (m, 9H), 8,1 (m, 1H), 8,6 (m, 1H),8,8 (m, 1H).
63	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(2-feniletil)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 751,3, C41H55ClN4O7 +H requiere 751,3838. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,15 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,25-3,35 (m, 4H), 3,55-3,65 (m, 6H), 5,2 (m, 1H), 7,0 (m, 1H), 7,2-7,4 (m, 7H).
64	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-	EM (EN): M/Z [MH+] =

	1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(1,3-benzodioxol-5-ilmetil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	781, C41H53ClN4O9 +H requiere 781,3579. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,15 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,5-3,75 (m, 9H), 5,2 (m, 1H), 6,0 (s, 2H), 6,8-6,85 (m, 2H), 6,9 (s, 1H), 7,0 (m, 1H), 7,2-7,3 (m, 2H).
65	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[3-(metiloxi)fenil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 753, C40H53ClN4O8 +H requiere 753,3630. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,15 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,25-3,8 (m, 9H), 3,8 (s, 3H), 5,2 (m, 1H), 6,45 (m, 1H), 6,3-6,4 (m, 2H), 7,0 (m, 1H), 7,2-7,35 (m, 3H).

66	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(4-{[(4-clorofenil)metil]oxi}piperidin-1-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 786, C41H53Cl2N3O8 +H requiere 786,3288. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,1 (d, 3H), 1,65 (s, 3H), 2,1 (s, 3H), 2,55-2,75 (m, 8H), 2,9-3,2 (m, 4H), 3,3 (s, 3H), 4,5 (s, 2H), 5,2 (s, 1H), 7,0 (m, 1H), 7,2-7,4 (m, 6H).
67	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[2-(metiloxi)fenil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 752, C40H53ClN4O8 +H requiere 753,3630. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,0-3,6 (m, 11H), 3,3 (s, 3H), 5,2 (s, 1H), 6,9 (m, 1H), 6,95-7,05 (m 3H), 7,1 (m, 1H), 7,2-7,3 (m, 2H).
68	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-	EM (EN): M/Z [MH+] =

	1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(furan-2-ilmetil)piperidin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	727, C39H52ClN3O8 +H requiere 726,3521. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,5-3,7 (m, 9H), 4,2 (m, 2H), 5,2 (s, 1H), 6,45 (m, 1H), 6,6 (m, 1H), 7,0 (m, 1H), 7,2-7,3 (m, 2H), 7,5 (m, 1H)
69	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[(3-metilfenil)metil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 751,C41H55ClN4O7 +H requiere 751,3838. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,15 (d, 3H), 1,65 (s, 3H), 2,1 (s, 3H), 2,35 (s, 3H), 3,3 (s, 3H), 3,5-3,75 (m, 8H), 4,15 (m, 2H), 5,2 (s, 1H), 7,0 (m, 1H), 7,15-7,35 (m, 6H).
70	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-	EM (EN): M/Z [MH+] =

	1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(2,2-dimetilpropanoil)(etil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	690, C36H52ClN3O8 +H requiere 690,3521. RMN (CDCl3, datos seleccionados): 0,85 (d, 3H), 0,95 (d, 3H), 1,25 (t, 3H), 1,3 (s,9H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 5,2 (s 1H), 7,0 (dd, 1H), 7,2 (m 1H), 7,4 (d, 1H).
71	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[metil(propanoil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 648, C33H46ClN3O8 +H requiere 648,3052. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,0 (d 3H), 1,2 (m, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,1 (s, 3H), 3,3 (s, 3H), 5,2 (s, 1H), 7,0 (m, 1H), 7,2 (m, 1H), 7,4 (d, 1H).
72	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-	EM (EN): M/Z [MH+] = 676, C35H50ClN3O8 +H requiere 676,3365. RMN (CDCl3, datos

	hidroxi-3,8-dimetil-5-[1-metil-2-[(1-metiletil)(propanoil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	seleccionados): 0,8 (d, 3H), 0,9 (d, 3H), 1,2 (t, 3H), 1,3 (m, 6H), 1,7 (s, 3H), 2,1 (s, 3H), 3,1 (s, 3H), 3,3 (s, 3H), 4,15 (m, 2H), 5,2 (s, 1H), 7,0 (m, 1H), 7,2 (m, 1H), 7,4(d, 1H).
73	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[(2,2-dimetilpropanoil)(1-metiletil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 704, C37H54ClN3O8 +H requiere 704,3678. RMN (CDCl3, datos seleccionados): 0,8-0,9 (m, 6H),1,2-1,25 (m, 6H), 1,3 (s,9H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 5,2 (s, 1H), 6,95 (m, 1H), 7,2 (m, 1H), 7,35 (d, 1H).
74	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-[(1-metiletil)[(metiloxi)acetil]amino}etil)-	EM (EN): M/Z [MH+] = 692, C35H50ClN3O9 +H requiere 692,3314. RMN (CDCl3, datos seleccionados): 0,8 (m, 3H), 0,95 (d, 3H), 1,2-

	1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	1,3 (m, 6H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,4 (s, 3H), 4,15 (m, 2H), 5,2 (s, 1H), 7,0 (m, 1H), 7,2 (m, 1H), 7,35 (d, 1H).
75	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[[(2-clorofenil)metil](propanoil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 758, C39H49Cl2N3O8 +H requiere 758,2975. RMN (CDCl3, datos seleccionados): 0,8 (m, 3H), 1,0 (d, 3H), 1,15 (t, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 4,65 (m, 2H), 5,2 (s, 1H), 6,95-7,1 (m, 2H), 7,2-7,45 (m, 5H).
76	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{[(2-clorofenil)metil][(metiloxi)acetil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 774, C39H49Cl2N3O9 +H requiere 774,2924. RMN (CDCl3, datos seleccionados): 0,8 (m, 3H), 1,0 (m, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,4 (s. 3H),

		4,0-4,2 (m, 3H), 4,65 (m, 2H), 5,2 (s, 1H), 7,0 (m, 1H), 7,1 (m, 1H), 7,2-7,5 (m, 5H).
77	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-5-(2-{acetil[(2-metilfenil)metil]amino}-1-metiletil)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 724, C39H50ClN3O8 +H requiere 724,3365. RMN (CDCl3, datos seleccionados): 0,75-0,8 (m, 3H), 1,0 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,3-2,35 (m, 3H), 3,3 (s, 3H), 5,25 (s, 1H), 6,95-7,1 (m, 2H), 7,2-7,4 (m, 5H).
78	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[[(2-metilfenil)metil](propanoil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 738, C40H52ClN3O8 +H requiere 738,3521. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,05 (d, 3H), 1,1 (t, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,3 (s, 3H), 3,3 (s, 3H), 4,5 (m, 2H), 5,25 (s, 1H), 6,9-7,1

		(m, 2H), 7,15-7,3 (m, 4H) 7,35 (m, 1H).
79	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{[(metiloxi)acetil][(2-metilfenil)metil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 754, C40H52ClN3O9 +H requiere 754,3470. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,0 (d, 3H),1,7 (s, 3H), 2,1 (s, 3H), 2,3 (s, 3H), 3,3-3,35 (m, 6H), 4,1 (m, 2H), 4,55 (m, 2H), 5,25 (s, 1H), 6,9-7,1 (m, 2H), 7,1-7,3 (m, 4H), 7,4 (m, 1H).
80	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(4-{[(4-fluorofenil)metil]oxi}piperidin-1-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 770, C41H53ClFN3O8 +H requiere 770,3583. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 1,9-2,1 (m, 5H), 2,1 (s, 3H), 2,9-3,1 (m, 4H), 3,3 (s, 3H), 4,5 (s, 2H), 5,2 (s, 1H), 6,95-7,1 (m, 3H), 7,2-7,3

		(m, 4H).
81	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[(4-clorofenil)metil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 771,C41H53Cl2N3O7 +H requiere 770,3339. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 1,9-2,1 (m, 5H), 2,1 (s, 3H), 3,3 (s, 3H), 3,45-3,75 (m, 8H), 4,1 (s, 2H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2-7,35 (m, 2H), 7,35-7,45 (m, 4H).
82	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(3,4-dihidroisoquinolin-2(1*H*)-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 694, C38H48ClN3O7 +H requiere 694,3. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (m, 3H), 3,0-3,5 (m, 5H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2-7,1-7,35 (m, 7H).
83	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-	EM (EN): M/Z [MH+] = 676, C35H50ClN3O8

	c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(2*R*,6*S*)-2,6-dimetilmorfolin-4-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	+H requiere 676,3365. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,2-1,3 (m, 6H), 1,7 (s, 3H), 2,1 (s, 3H),3,1-3,3 (m, 6H), 3,3 (s, 3H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2-7,35 (m, 2H).
84	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[metil(3,3,3-trifluoropropanoil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 702,2, C33H43ClF3N3O8 +H requiere 702,2769. RMN (CDCl3, datos seleccionados): 0,85 (m, 3H), 0,95 (m, 3H), 1,7 (s, 3H), 2,1 (s, 3H),3,1 (s, 3H), 3,4 (s, 3H), 5,2 (s, 1H), 7,0 (m, 1H), 7,2-7,4 (m, 2H).
85	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-	EM (EN): M/Z [MH+] = 792,2, C40H49ClF3N3O8 +H requiere 792,3239.

	hidroxi-3,8-dimetil-5-{1-metil-2-[[(2-metilfenil)metil](3,3,3-trifluoropropanoil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	RMN (CDCl3, datos seleccionados): 0,8 (m, 3H), 1,05 (m, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,3 (s, 3H), 3,35 (s, 3H), 4,5 (m, 2H), 5,2 (s, 1H), 6,9-7,4 (m, 7H).
86	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[(4-metilfenil)metil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 751,2, C41H55ClN4O7 +H requiere 751,3838. RMN (CDCl3, datos seleccionados): 0,8 (m, 3H), 1,1 (m, 3H), 1,65 (s, 3H), 2,1 (s, 3H), 2,3 (s, 3H), 3,3 (s 3H), 3,4-3,6 (m, 8H), 4,0-4,15 (m, 3H), 5,2 (s, 1H), 6,9 (dd, 1H), 7,1-7,3 (m, 6H).
87	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[6-(metiloxi)piridazin-3-il]piperazin-1-il}etil)-	EM (EN): M/Z [MH+] = 755, C38H51ClN6O8 +H requiere 755,3535. RMN (CDCl3, datos seleccionados): 0,8 (m, 3H), 1,1 (m, 3H), 1,7

	1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	(s, 3H), 2,1 (s, 3H), 2,4-3,2 (m, 12H), 3,3 (s, 3H), 4,0 (s, 3H), 5,2 (s, 1H), 6,95-7,05 (m, 2H), 7,15 (m, 1H), 7,2-7,3 (m, 2H).
88	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(6-cloropirazin-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 759, C37H48Cl2N6O7 +H requiere 759,3040. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,15 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,4-3,2 (m,12H), 3,3 (s, 3H), 5,2 (s, 1H), 7,0 (m, 1H), 7,2 (m, 1H), 7,3 (d, 1H), 7,95 (s, 1H), 8,05 (s, 1H).
89	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(6-cloropiridin-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 758,2, C38H49Cl2N5O7 +H requiere 758,3087. RMN (CDCl3, datos seleccionados): 0,75 (d, 3H), 1,1 (d, 3H), 1,6

		(s, 3H), 1,95 (s, 3H), 2,4-2,8 (m, 10H), 3,1 (s, 3H), 5,1 (s, 1H), 6,45 (d, 1H), 6,55 (d, 1H) 6,95 (dd, 1H), 7,1 (d, 1H) 7,15 (d, 1H), 7,35 (dd, 1H).
90	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(4-fenilpiperazin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 723, C39H51ClN4O7 +H requiere 723,3525. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,1 (d, 3H),1,7 (s, 3H), 2,1 (s, 3H), 2,45-2,8 (m, 8H), 3,15-3,25 (m, 5H), 3,3 (s, 3H), 5,1 (s, 1H), 6,85 (m, 1H), 6,9-6,95 (m, 2H), 7,0 (dd, 1H), 7,2-7,3 (m, 3H), 7,35 (dd, 1H).
91	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[4-(ciclohexilmetil)piperazin-1-il]-1-metiletil]-	EM (EN): M/Z [MH+] = 743,3, C40H59ClN4O7 +H requiere 743,4151. RMN (CDCl3, datos seleccionados): 0,8 (d,

	8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	3H), 1,1 (d, 3H), 1,7 (s, 3H), 1,7-1,85 (m, 8H), 2,1 (s, 3H), 3,3 (s, 3H), 3,6-3,8 (m, 8H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2-7,3 (m, 2H).
92	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(1,3-tiazol-2-il)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 730,2, C36H48ClN5O7S +H requiere 730,3041. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,1 (d, 3H), 1,7 (s, 3H), 2,15 (s, 3H), 3,0-3,1 (m, 2H), 3,3 (s, 3H), 3,3-3,5 (m, 4H), 3,85-4,05 (m, 4H), 5,2 (s, 1H), 6,7 (s, 1H), 7,0 (dd, 1H), 7,2-7,25 (m, 2H), 7,3 (m, 1H).
93	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(3-cloropiridin-2-il)piperazin-1-il]-1-	EM (EN): M/Z [MH+] = 758, C38H49Cl2N5O7 +H requiere 758,3087. RMN (CDCl3, datos seleccionados): 0,85

	metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	(d, 3H), 1,15 (d, 3H), 1,7 (s, 3H), 2,15 (s, 3H), 3,0-3,2 (m, 4H), 3,35 (s, 3H), 3,35-4,05 (m, 6H), 5,2 (s, 1H), 6,9 (m, 1H), 7,0 (dd, 1H), 7,2 (m, 1H), 7,3 (d, 1H), 7,6 (m, 1H), 8,2 (m, 1H).
94	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-oxo-2-[(fenilmetil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 682, C36H44ClN3O8 +H requiere 682,2895. RMN (CDCl3, datos seleccionados): 0,9 (m, 3H), 1,3 (m, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 4,2 (m, 2H), 5,3 (s, 1H), 7,0 (dd, 1H), 7,1-7,3 (m, 4H), 7,5 (m, 1H), 7,7 (m, 1H), 7,9 (m, 1H).
95	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-	EM (EN): M/Z [MH+] = 730, C37H45Cl2N3O8 +H requiere 730,2662. RMN (CDCl3, datos

	[[(2-clorofenil)metil](metil)amino]-1-metil-2-oxoetil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	seleccionados): 0,9 (m, 3H), 1,3 (m, 3H), 1,75 (s, 3H), 2,1 (s, 3H), 3,1 (s, 3H), 3,3 (s, 3H), 5,15-5,2 (m, 2H), 6,8 (dd, 1H), 7,0-7,5 (m, 5H), 7,75 (m, 1H).
96	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletil)-2-{[(fenilamino)carbonil]oxi}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (IQPA): M/Z [MH+] = 640,2, C34H42ClN3O7 +H requiere 640,2790. RMN (CDCl3, datos seleccionados): 0,8 (m, 3H), 1,0 (m, 6H), 1,75 (s, 3H), 3,3 (s, 3H), 5,2 (s, 1H), 6,6 (s, 1H), 7,0 (dd, 1H), 7,1 (dd, 1H), 7,2 (m, 1H), 7,3-7,4 (m, 5H).
97	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(cicloheptilamino)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-	EM (IQPA): M/Z [MH+] = 674, C36H52ClN3O7 +H requiere 674,3572. RMN (CDCl3, datos seleccionados): 0,9 (m, 3H), 1,1 (m, 3H), 1,6-

	1-ilo	1,9 (m, 16H), 2,1 (s, 3H), 3,3 (s, 3H), 5,1-5,2 (m, 2H), 7,0 (dd, 1H), 7,2-7,4 (m, 2H).
98	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[4-(2-cloropirimidin-4-il)piperazin-1-il]-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 759,1, C37H48Cl2N6O7 +H requiere 759,3040. RMN (DMSO, datos seleccionados): 0,8 (d, 3H), 1,1 (d, 3H),1,6 (s, 3H), 2,1 (s, 3H), 2,5 (m, 2H), 2,95-3,1 (m, 2H), 3,15 (s, 3H), 3,2-3,8 (m, 6H), 5,1 (s, 1H), 7,0 (d, 1H), 7,1(dd, 1H), 7,3 (d, 1H), 7,35 (d, 1H), 8,2 (d, 1H).
99	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[4-(5-cloropiridin-2-il)piperazin-1-il]-1-metiletil]-8*a*-hidroxi-3,8-dimetil-	EM (EN): M/Z [MH+] = 758,2, C38H49Cl2N5O7 +H requiere 758,3087. RMN (CDCl3, datos seleccionados): 0,85

	1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	(d, 3H), 1,15 (m, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,4 (s, 3H),3,5-3,6 (m, 4H), 5,15-5,2 (m 2H), 6,65 (d, 1H), 7,05 (dd, 1H), 7,2 (d, 1H), 7,3 (d, 1H), 7,5 (m, 1H), 8,15 (m, 1H).
100	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(5-cloropirazin-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 759,1, C37H48Cl2N6O7 +H requiere 759,3040. RMN (CDCl3, datos seleccionados): 0,85 (d, 3H), 1,25 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,3-2,8 (m, 9H), 3,3 (s, 3H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2 (d, 1H), 7,3 (d, 1H), 7,95 (s, 1H), 8,05 (s, 1H).
101	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-	EM (EN): M/Z [MH+] = 757,1, C39H50Cl2N4O +H requiere 757,3135. RMN (CDCl3, datos

	[4-(4-clorofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	seleccionados): 0,8 (d, 3H), 1,05 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,45-2,8 (m, 7H) 3,1-3,25 (m, 4H), 3,3 (s, 3H), 5,2 (s, 1H), 6,8-6,85 (m, 2H), 7,0 (dd, 1H), 7,2 7,3 (m, 3H), 7,4 (d, 1H).
102	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(4-metilfenil)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 737,2, C40H53ClN4O7 +H requiere 737,3681. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,25 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,3 (s, 3H), 3,0-3,2 (m, 4H), 3,3 (s, 3H). 5,2 (s, 1H), 6,85-6,9 (m 2H), 7,0 (dd, 1H), 7,1-7,15 (m, 2H), 7,2-7,35 (d, 2H).
103	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de	EM (EN): M/Z [MH+] = 757,1, C39H50Cl2N4O7

	(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(2-clorofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	+H requiere 757,3. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,25 (d, 3H),1,7 (s, 3H), 2,1 (s, 3H), 3,0-3,5 (m, 11H), 5,2 (s, 1H), 6,95-7,1 (m, 3H), 7,15-7,4 (m, 4H).
104	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[3-(trifluorometil)fenil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 792, C40H50ClF3N4O7 +H requiere 791,3398. RMN (CDCl3, datos seleccionados): 0,85 (d, 3H), 1,25 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,5-3,8 (m, 4H), 5,2 (s, 1H), 7,0-7,15 (m, 3H), 7,2-7,35 (m, 3H), 7,3 (dd, 1H).
105	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-	EM (EN): M/Z [MH+] = 753,2,

	c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[4-(metiloxi)fenil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	C40H53ClN4O8 +H requiere 753,3630. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,25 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,0-3,15 (m, 4H), 3,3 (s, 3H), 3,4-3,6 (m, 4H), 3,8 (s, 3H), 5,2 (s, 1H), 6,8-7,0 (m, 5H), 7,2-7,35 (m, 3H).
106	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[2-(trifluorometil)fenil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 791,2, C40H50ClF3N4O7 +H requiere 791,3398,- RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,25 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,9-3,1 (m, 4H), 3,3 (s, 3H), 5,2 (s, 1H), 7,0-7,15 (m, 3H), 7,2-7,35 (m, 3H), 7,4

		(m, 1H).
107	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[4-(trifluorometil)pirimidin-2-il]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN) : M/Z [MH+] = 793,1, C38H48ClF3N6O7 +H requiere 793,3303. RMN (CDCl3, datos seleccionados): 0,6 (d, 3H), 1,1 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,5-2,8 (m, 10H), 3,35 (s, 3H), 3,6-3,8 (m, 2H), 3,8-4,0 (m, 4H), 5,2 (s, 1H), 6,7 (m, 1H), 7,0 (dd, 1H), 7,2 (m, 1H), 7,35 (d, 1H),8,5 (m, 1H).
108	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(2-fluorofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 741,2, C39H50ClFN4O7 +H requiere 741,3430. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,0-3,2 (m, 4H), 3,3 (s,

		3H), 3,3-3,55 (m, 4H), 3,6-3,8 (m, 2H), 5,2 (s, 1H), 6,9-7,15 (m, 5H), 7,2 (d, 1H), 7,3(m, 1H).
109	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(6-metilpiridin-2-il)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 738,3, C39H52ClN5O7 +H requiere 738,3634. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H),1,7 (s, 3H), 2,1 (s, 3H), 2,65 (s, 3H), 3,0-3,2 (m, 2H), 3,3 (s, 3H), 3,3-3,6 (m, 4H), 4,0-4,2 (m, 5H), 5,2 (s, 1H), 6,8-6,85 (m, 3H), 7,0 (dd, 1H), 7,2 (d, 1H), 7,9 (m, 1H).
110	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(4-fluorofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 741,3, C39H50ClFN4O7 +H requiere 741,3430. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s,

		3H), 2,1 (s, 3H), 2,65 (s, 3H), 3,3 (s, 3H), 3,3-4,0 (m, 8H), 5,2 (s, 1H), 6,85-6,95 (m, 2H), 6,95-7,05 (m, 3H), 7,2-7,35 (m, 2H).
111	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(1,3-tiazol-2-ilcarbonil)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 758,2, C37H48ClN5O8S +H requiere 758,2990. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,25 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,1-3,2 (m, 2H), 3,3 (s, 3H), 3,4-4,2 (m, 9H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2-7,35 (m, 2H), 7,6 (s, 1H), 7,9 (s, 1H).
112	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[(3-fenilpropil)oxi]piperidin-1-il}etil)-	EM (EN): M/Z [MH+] = 780,2, C43H58ClN3O8 +H requiere 780,3991. RMN (CDCl3, datos seleccionados): 0,8

	1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	(d, 3H), 1,25 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,4-3,1 (m, 10H), 3,3 (s, 3H), 3,3-3,5 (m, 8H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,1-7,3 (m, 7H).
113	(2*S*,3*aR*,9*bR*)-6-cloro-9*b* -hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[5-(trifluorometil)piridin-2-il]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 792,2, C39H49ClF3N5O7 +H requiere 792,3351. RMN (CDCl3, datos seleccionados): 0,85 (d, 3H), 1,25 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,3-2,8 (m, 8H), 3,3 (s, 3H), 3,6-3,75 (m, 5H), 5,2 (s, 1H), 6,7 (d, 1H), 7,0 (dd, 1H), 7,2-7,35 (m, 2H), 7,75 (m, 1H), 8,45 (s, 1H).
114	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-	EM (EN): M/Z [MH+] = 736,3, C41H54ClN3O7 +H requiere 736,3729.

	hidroxi-3,8-dimetil-5-[1-metil-2-[4-(fenilmetil)piperidin-1-il]etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,4-3,1 (m, 15H), 3,3 (s, 3H), 3,7 (m, 2H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,1-7,15 (m, 2H), 7,2-7,35 (m, 5H).
115	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[3-(trifluorometil)piridin-2-il]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 792,2, C39H49ClF3N5O7 +H requiere 792,3351. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,4-3,2 (m, 8H), 3,3 (s, 3H), 3,5-3,65 (m, 4H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,1 (m, 1H), 7,2-7,35 (m, 2H), 7,9 (d, 1H), 8,5 (m, 1H).

116	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[3-(trifluorometil)fenil]piperidin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 790,2, C41H51ClF3N3O7+H requiere 790,3446. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,65 (s, 3H), 2,1 (s, 3H), 2,2-2,6 (m, 9H), 3,3 (s, 3H), 3,5-3,65 (m, 4H), 5,15 (s, 1H), 7,0 (dd, 1H), 7,2 (m,-1*H*), 7,25 (d, 1H), 7,35-7,55 (m, 4H).
117	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(4-{[3-(trifluorometil)fenil]metil}piperazin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 805,2, C41H52ClF3N4O7+H requiere 805,3555. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,65 (s, 3H), 2,1 (s, 3H),3,2-3,3 (m, 4H), 3,3 (s, 3H), 3,9 (m, 2H), 5,2 (s, 1H), 7,0

		(dd, 1H), 7,2-7,3 (m, 2H), 7,4-7,7 (m, 4H).
118	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c]2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[({3-[(etiloxi)carbonil]fenil}metil)oxi]piperidin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 824,2, C44H58ClN3O10 +H requiere 824,3889. RMN (CDCl3, datos seleccionados): 0,75 (d, 3H), 1,15 (d, 3H), 1,35 (t, 3H), 1,75 (s, 3H), 2,1 (s, 3H), 2,85-3,15 (m,9H), 3,3 (s, 3H), 4,3 (m, 2H), 4,5 (m, 2H), 5,15 (s, 1H), 6,95 (dd, 1H), 7,15 (d, 1H), 7,25 (m, 1H), 7,3-7,4 (m, 2H), 7,95-8,05 (m, 2H).
119	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(1,3-benzoxazol-2-il)piperidin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 763,2, C41H51ClN4O8 +H requiere 763,3474. RMN (CDCl3, datos seleccionados): 0,85 (d, 3H), 1,2 (m, 3H),

		1,75 (s, 3H), 2,1 (s, 3H), 2,9-3,3 (m, 11H), 3,3 (s, 3H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2-7,3 (m, 2H), 7,3-7,4 (m, 2H), 7,5 (m, 1H), 7,7 (m, 1H).
120	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(4-{[3,5-*bis*(trifluorometil)fenil]metil}piperazin-1-il)-1-metiletil]-8a-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 873,1, C42H51ClF6N4O7+H requiere 873,3429. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (m, 3H),1,7 (s, 3H), 2,1 (s, 3H), 2,9-3,1 (m, 6H), 3,3 (s, 3H), 4,8 (m, 2H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2-7,3 (m, 2H), 7,8-7,9 (m, 3H).
121	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[2-	EM (EN): M/Z [MH+] = 752,2, C41H54ClN3O8 +H requiere 752,3678. RMN (CDCl3, datos seleccionados): 0,8 (m,

	(metiloxi)fenil]piperidin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	3H), 1,25 (m, 3H),1,7 (s, 3H), 2,1 (s, 3H), 2,9-3,6 (m, 11H), 3,3 (s, 3H), 3,8 (s, 3H), 5,2 (s, 1H), 6,85-7,15 (m, 5H), 7,2-7,3 (m, 2H).
122	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[(4-fluorofenil)metil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 755,3, C40H52ClN4O7 +H requiere 755,3. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,4-3,7 (m, 8H), 4,1 (m, 2H), 5,2 (s, 1H), 7,0-7,45 (m, 7H).
123	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(4-cianofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 755,3, C40H52ClFN4O7 +H requiere 755,3587. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,4-3,7 (m,8H),

		5,2 (s, 1H), 7,0 (dd, 1H), 7,1-7,15 (m, 2H), 7,2-7,3 (m, 2H), 7,4-7,5 (m, 2H).
124	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(2,3-dihidro-1,4-benzodioxin-2-ilcarbonil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 809,3, C42H53ClN4O10 +H requiere 809,3528. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,9-3,9 (m, 12H),3,3 (s, 3H), 5,2 (s, 1H), 6,8-6,95 (m, 4H), 7,0 (dd, 1H), 7,2-7,35 (m, 2H).
125	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(4-bromofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 803,2, C39H50BrClN4O7 +H requiere 801,2630. RMN (CDCl3, datos seleccionados): 0,85 (d, 3H), 1,2 (d, 3H),

		1,7 (s, 3H), 2,1 (s, 3H), 2,6-3,2 (m, 12H), 3,3 (s, 3H), 5,2 (s, 1H), 6,8 (m, 2H), 7,0 (dd, 1H), 7,2-7,35 (m, 2H), 7,4 (m, 2H).
126	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-[4-[4-(trifluorometil)fenil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 791,2, C40H50ClF3N4O7 +H requiere 791,3398. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,6-3,3 (s, 3H), 3,4-3,9 (m, 6H), 5,2 (s, 1H), 6,9-7,05 (m, 3H), 7,15-7,35 (m, 2H), 7,5 (m, 2H).
127	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[4-(2,4-difluorofenil)piperazin-1-il]-1-	EM (EN): M/Z [MH+] = 759,2, C39H49ClF2N4O7 +H requiere 759,3336. RMN

	metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	(CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H),1,7 (s, 3H), 2,1 (s, 3H), 2,9-3,3 (m, 7H), 3,3 (s, 3H), 3,35-3,45 (m, 4H), 5,2 (s, 1H), 6,85-7,05 (m, 4H), 7,2 (d, 1H), 7,3 (m, 1H).
128	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(piridin-4-ilmetil)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 738,3, C39H52ClN5O7 +H requiere 738,3634. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,85-2,95 (m, 2H), 3,3 (s, 3H), 3,4-4,2 (m, 10H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2 (m, 1H), 7,3 (m, 1H), 7,5 (m, 2H), 8,7 (m, 2H).

129	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[5-cloro-2-(metiloxi)fenil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 787,2, C40H52Cl2N4O8 +H requiere 787,3240. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,0-3,6 (m, 10H), 3,3 (s, 3H), 3,85 (s, 3H), 5,2 (s, 1H), 6,8 (d, 1H), 6,85 (s, 1H), 6,95-7,05 (m, 2H), 7,2-7,3 (m, 2H).
130	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[4-(3,5-diclorofenil)piperazin-1-il]-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = , C39H49Cl3N4O7 +H requiere 791,2745. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,0-3,6 (m, 10H), 3,3 (s, 3H), 3,45-3,7 (m, 4H), 5,2 (s, 1H), 6,7-6,8 (m, 2H), 6,9-7,0 (m, 2H),

		7,2-7,3 (m, 2H).
131	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[(2*E*)-3-fenilprop-2-enil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 763,3, C42H55ClN4O7 +H requiere 763,3838. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H),1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,55-3,75 (m, 8H), 5,2 (s, 1H), 6,2 (m, 1H), 6,8 (d, 1H), 7,0 (dd, 1H), 7,2 (d, 1H), 7,25 (m, 1H), 7,3-7,45 (m, 5H).
132	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(difenilmetil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 813,3, C46H57ClN4O7 +H requiere 813,3994. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,9-3,8 (m, 6H), 3,3 (s, 3H), 4,5 (s, 1H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,15-7,4 (m, 8H), 7,45-7,55

		(m 4H).
133	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[4-(2,3-dimetilfenil)piperazin-1-il]-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 751,3, C41H55ClN4O7 +H requiere 751,3838. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,2 (s, 3H), 2,3 (s, 3H), 3,0-3,2 (m, 10H), 3,3 (s, 3H), 4,5 (s, 1H), 5,2 (s, 1H), 6,9-7,05 (m, 4H), 7,25-7,35 (m, 2H).
134	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(4-ciclopentilpiperazin-1-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 715,3, C38H55ClN4O7 +H requiere 715,3838. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,6-1,7 (m, 4H), 1,7 (s, 3H), 1,8-2,0 (m, 5H), 2,1 (s, 3H), 3,3 (s, 3H), 3,6-3,8 (m, 8H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2-7,3 (m, 2H).

135	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[4-(2-etilfenil)piperazin-1-il]-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 751,3, C41H55ClN4O7 +H requiere 751,3838. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2-1,3 (m, 6H), 1,7 (s, 3H), 2,1 (s, 3H), 2,8-3,2 (m, 11H), 3,3 (s, 3H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,1-7,3 (m, 7H).
136	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[4-cloro-3-(trifluorometil)fenil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 825,2, C40H49Cl2F3N4O7 +H requiere 825,3009. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,25 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,5-3,7 (m, 4H), 5,2 (s, 1H), 6,8-7,0 (m, 2H), 7,1-7,3 (m, 3H), 7,4 (d, 1H).
137	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-	EM (EN): M/Z [MH+] = 757,2,

	c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(tien-2-ilcarbonil)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	C38H49ClN4O8S +H requiere 757,3038. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H),1,7 (s, 3H), 2,1 (s, 3H), 2,9-3,1 (m, 4H), 3,3 (s, 3H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,1 (m, 1H), 7,2-7,3 (m, 2H), 7,35 (m, 1H), 7,55 (m, 1H).
138	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(4-{[(butilamino)carbonil]oxi}piperidin-1-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 761,3, C39H57ClN4O9 +H requiere 761,3892. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 0,95 (t, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,15-3,3 (m, 4H), 3,3 (s, 3H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2 (m, 1H), 7,3 (m, 1H).
139	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-	EM (EN): M/Z [MH+] =

	1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(2,4-dimetilfenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	751,3, C41H55ClN4O7 +H requiere 751,3838. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H),1,7 (s, 3H), 2,1 (s, 3H), 2,25 (s, 3H), 2,3 (s, 3H), 2,5-2,7 (m, 8H), 3,0-3,2 (m, 4H), 3,3 (s, 3H), 3,7-3,85 (m, 2H), 5,2 (s, 1H), 6,9-7,1 (m, 4H), 7,2-7,3 (m, 2H).
140	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(2,5-dimetilfenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 751,4, C41H55ClN4O7 +H requiere 751,3838. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H),1,7 (s, 3H), 2,0(s, 3H), 2,15 (s, 3H), 2,3 (s, 3H), 2,8-3,4 (m, 11H), 5,2 (s, 1H), 6,75-6,85 (m,

		2H), 6,9-7,1 (m, 2H), 7,15 (m, 1H), 7,25 (m, 1H).
141	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2- carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(4-ciclopropilpiperazin-1-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 687,3, C36H51ClN4O7 +H requiere 687,3524. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 0,9-1,0 (m, 2H), 1,1-1,25 (m, 6H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,6-3,8 (m, 8H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2-7,3 (m, 2H).
142	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[4-(ciclopentilcarbonil)piperazin-1-il]-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 743,3, C39H55ClN4O8 +H requiere 743,3787. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,75-2,9 (m, 6H),

		3,0-3,2 (m, 2H), 3,3 (s, 3H), 3,5-4,2 (m, 11H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2-7,3 (m, 2H).
143	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[6-(metiloxi)piridin-2-il]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 754,3, C39H52ClN5O8 +H requiere 754,3583. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 3,4-3,9 (m, 10H), 3,85 (m, 3H), 5,2 (s, 1H), 6,15-6,25 (m, 2H), 7,0 (dd, 1H), 7,2-7,3 (m, 2H), 7,5 (m, 1H).
144	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(3,5-dimetilfenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-	EM (EN): M/Z [MH+] = 751,3,C41H55ClN4O7 +H requiere 751,3838. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H),1,7

	octahidronaftalen-1-ilo	(s, 3H), 2,1 (s, 3H), 2,3 (s, 6H), 3,3 (s, 3H), 3,3-3,9 (m, 8H), 5,2 (s, 1H), 6,8 (s, 2H), 6,9 (s, 1H), 7,0 (dd, 1H), 7,2-7,3 (m, 2H).
145	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(3,6-dimetilpirazin-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 753,3, C39H53ClN6O7 +H requiere 753,3743. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H),1,7 (s, 3H), 2,1 (s, 3H), 2,5 (s, 3H), 2,55 (s, 3H), 2,9-3,1 (m, 4H), 3,3 (s, 3H), 3,5-3,9 (m, 6H), 5,2 (s, 1H), 7,0 (dd. 1H), 7,2-7,3 (m, 2H), 8,05 (s, 1H).
146	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1] benzoxazin-2-carboxilato de	EM (EN): M/Z [MH+] = 751,3, C41H55ClN4O7 +H

	(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(2,6-dimetilfenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	requiere 751,3838. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,25 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,3-2,4 (m, 6H), 2,8-3,1 (m, 10H), 3,3 (s, 3H), 5,2 (s, 1H), 6,9-7,1 (m, 4H), 7,2-7,3 (m, 2H).
147	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[(1*S*)-1-metil-2-piridin-3-iletil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 640,3, C34H42ClN3O7 +H requiere 640,2790. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 0,9 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2-7,35 (m, 2H), 7,8 (dd, 1H),8,2 (d, 1H),8,7 (d, 1H), 8,75 (s, 1H).
148	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de	EM (EN): M/Z [MH+] = 688, C36H50ClN3O8 +H requiere 688,3,

	(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(3-oxa-9-azabiciclo[3,3,1]non-9-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	HPLC: 3,99 min.
149	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(4-metilpentanoil)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 745, C39H57ClN4O8 +H requiere 745,4, HPLC: 4,24 min.
150	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(4-oxo-1,3,4,6,7,11 b-hexahidro-2H-pirazino[2,1-a]isoquinolin-2-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 763, C41H51ClN4O8 +H requiere 763,3, HPLC: 6,46 min.
151	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[3-[(etiloxi)carbonil]octahidroisoquinolin-2(1*H*)-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-	EM (EN): M/Z [MH+] = 772, C41H58ClN3O9 +H requiere 772,4, HPLC: 5,64 min.

	1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
152	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[3,5-*bis*(metiloxi)fenil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 783,1, C41H55ClN4O9 +H requiere 783,3736. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,25 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,9-3,3 (m, 6H), 3,3 (s, 3H), 3,35-3,75 (m, 4H), 3,8 (s, 6H), 5,25 (s, 1H), 6,1 (s, 2H), 6,15 (s, 1H), 7,0 (dd, 1H), 7,2 (d, 1H), 7,3 (d, 1H).
153	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[4-(2-cianofenil)piperazin-1-il]-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 722,1, C40H50ClN5O7 +H requiere 722,3572. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,25 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,3-3,25 (m, 15H), 3,3

		(s, 3H), 5,25 (s, 1H), 7,0 (dd, 1H), 7,15-7,4 (m, 7H).
154	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(4-fenilpiperidin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 748,1, C40H52ClN3O7 +H requiere 748,3477. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,0-3,2 (m, 4H), 3,3 (s, 3H), 3,5-3,65 (m, 4H), 3,7-3,9 (m, 2H), 5,3 (s, 1H), 7,0 (dd, 1H), 7,15-7,3 (m, 4H), 7,55-7,65 (m, 2H).
155	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(3,4-dimetilfenil)piperazin-1-il]-1-metil etil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 751,1, C41H55ClN4O7 +H requiere 751,3838. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H),1,7 (s, 3H), 2,1 (s, 3H), 2,2 (s, 3H), 2,25 (s, 3H),

		3,0-3,2 (m, 4H), 3,3 (s, 3H), 3,4-4,0 (m, 6H), 5,2 (s, 1H), 6,75 (d, 1H), 6,8 (s, 1H), 7,0 (dd, 1H), 7,1 (d, 1H), 7,2 (d, 1H), 7,3 (d, 1H).
156	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetiloxi)-5-{2-[ciclopropil(propanoil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 674,3, C35H48ClN3O8 +H requiere 674,3208. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 0,95 (d, 3H),1,1 (t, 3H),1,7 (s, 3H), 2,1 (s, 3H), 3,3 (s, 3H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2 (d, 1H), 7,35 (d, 1H).
157	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetiloxi)-5-{2-[(ciclopropilcarbonil)(fenil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 722,3, C39H48ClN3O8 +H requiere 722,3208. RMN (CDCl3, datos seleccionados): 0,5-0,7 (m, 2H), 0,8 (d, 3H), 0,95 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H),3,3 (s,

		3H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2-7,5 (m, 7H).
158	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(ciclohexilmetil)(ciclopropilcarbonil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 742,3, C40H56ClN3O8 +H requiere 742,3834. RMN (CDCl3, datos seleccionados): 0,7-0,8 (m, 2H), 0,85 (d, 3H), 0,9-1,1 (m, 8H),1,7 (s, 3H), 2,1 (s, 3H), 2,4-2,7 (m, 7H), 3,3 (s, 3H), 5,2 (s, 1H), 6,9 (dd, 1H), 7,2-7,3 (m, 2H).
159	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(ciclohexilmetil)(propanoil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 730,3, C39H56ClN3O8 +H requiere 730,3834. RMN (CDCl3, datos seleccionados): 0,85 (d, 3H), 0,95 (d, 3H), 1,6-1,9 (m, 9H), 2,1 (s, 3H), 3,3 (s, 3H), 5,2 (s, 1H), 6,9 (dd, 1H), 7,2-7,3 (m, 2H).

160	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(ciclopropilcarbonil)(metil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 660,3, C34H46ClN3O8 +H requiere 660,3052. RMN (CDCl3, datos seleccionados): 0,7-0,85 (m, 2H), 0,85 (d, 3H), 0,9-1,1 (m, 6H), 1,7 (s, 3H), 2,1 (s, 3H), 3,2 (s, 3H), 3,3 (s, 3H), 5,2 (s, 1H), 7,0 (dd, 1H), 7,2-7,3 (m, 2H).
161	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[metil(fenilcarbonil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 696,2, C37H46ClN3O8 +H requiere 696,3052. RMN (CDCl3, datos seleccionados): 0,8 (m, 3H), 1,1 (m, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 3,0 (s, 3H), 3,3 (s, 3H), 5,1-5,2 (m, 2H), 7,0 (dd, 1H), 7,2-7,4 (m, 7H).
162	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de	EM (EN): M/Z [MH+] = 726,2, C38H48ClN3O9 +H requiere 726,3157.

	(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{metil[(feniloxi)acetil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	RMN (CDCl3, datos seleccionados): 0,8-0,95 (m, 3H), 1,4-1,5 (m, 7H), 1,7 (s, 3H), 2,1 (s, 3H), 2,85 (s, 3H), 3,3 (s, 3H), 5,2 (m, 1H), 6,85-7,0 (m, 4H), 7,15-7,4 (m, 4H).
163	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(4-amino-5-ciano-6-metilpirimidin-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 779,2, C39H51ClN8O7 +H requiere 779,3647. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,1 (d, 2H), 1,6 (s, 3H), 2,1 (s, 3H), 2,3 (s, 3H), 3,2 (s, 3H), 3,65-4,0 (m, 10H), 5,1 (s, 1H), 7,05 (dd, 1H), 7,2 (m, 1H), 7,4 (d, 1H).
164	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(2*S*,5R)-2,5-dimetil-4-prop-2-enilpiperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-	EM (EN): M/Z [MH+] = 715, C38H55ClN4O7 +H requiere 715,4, HPLC: 4,05 min.

	1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
165	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(8-azabiciclo[3.2.1]oct-8-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 672, C36H50ClN3O7 +H requiere 672,3, HPLC: 4,05 min.
166	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(3*S*,8*aR*)-3-(fenilmetil)hexahidropirrolo[1,2-a]pirazin-2(1*H*)-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 777, C43H57ClN4O7 +H requiere 777,4, HPLC: 4,37 min.
167	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(3-{[(3,4-difluorofenil)metil]oxi}piperidin-1-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 788, C41H52ClF2N3O8 +H requiere 788,3, HPLC: 4,43 min.

168	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[(3*R*)-3-(metiloxi)piperidin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 676, C35H50ClN3O8 +H requiere 676,3, HPLC: 7,16 min.
169	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[1-metil-6,7-*bis*(metiloxi)-3,4-dihidroisoquinolin-2(1*H*)-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 768, C41H54ClN3O9 +H requiere 768,3, HPLC: 4,11 min.
170	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(2-metil-4-piperidin-1-il-5,8-dihidropirido[3,4-d]pirimidin-7(6H)-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 793, C42H57ClN6O7 +H requiere 793,4, HPLC: 4,3 min.
171	(2*S*,3*aR*,9*b* R)-6-cloro-9*b*-hidroxi-5-metil-	EM (EN): M/Z [MH+] =

	1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(4-clorofenil)-6,7-dihidrotieno[3,2-c]piridin-5(4*H*)-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	793, C42H49Cl2N3O7S +H requiere 810,
172	(2*S*,3*aR*, 9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(3-[[4-(metiloxi)fenil]sulfanil}-8-azabiciclo[3.2.1]oct-8-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 810,C43H56ClN3O8S +H requiere 810,4, HPLC: 4,49 min.
173	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(4-metilpiperazin-1-il)piperidin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 744, C39H58ClN5O7 +H requiere 744,4, HPLC: 1,71 min.
174	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3a,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-	EM (EN): M/Z [MH+] = 773, C39H50Cl2N4O8 +H requiere 773,3,

	{3-[(3-cloropiridin-2-il)oxi]piperidin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	HPLC: 4,37 min.
175	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(3-metilquinoxalin-2-il)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 789, C42H53ClN6O7 +H requiere 789,4, HPLC: 4,3 min.
176	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-[7-(hidroximetil)-3-azabiciclo[3,3,1]non-3-il]-1-metiletil}-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 716, C38H54ClN3O8 +H requiere 716,4, HPLC: 3,99 min.
177	(2*S*,3*aR*,9*bR*)-6-cloro-9b-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(3,11-diazatriciclo[7.3.1.0~2,7~]trideca-2,4,6-trien-11-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-	EM (EN): M/Z [MH+] = 735,C40H51ClN4O7 +H requiere 735,4, HPLC: 4,05 min.

	1-ilo	
178	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(4,10-diazatriciclo[6.3.1.0~2,7~]dodeca-2,4,6-trien-10-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 721,C39H49ClN4O7 +H requiere 721,3, HPLC: 3,67 min.
179	-	EM (EN) : M/Z [MH+] = 748, C42H54ClN3O7 +H requiere 748,4, HPLC: 4,56 min.
180	(2*S*,3*aR* ,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-5-{2-[(4*aR*,9*aS*)-2,3,4,4*a*,9,9*a*-hexahidro-1*H*-indeno[2,1-b]piridin-1-il]-1-metiletil}-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 734, C41H52ClN3O7 +H requiere 734,4, HPLC: 4,37 min.
181	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de	EM (EN): M/Z [MH+] = 742, C41H60ClN3O7 +H

	(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(3-ciclohexil-3-metilpiperidin-1-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	requiere 742,4, HPLC: 4,68 min.
182	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-(4-{2-[(2-hidroxietil)oxi]etil}piperazin-1-il)-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 742,C41H60ClN3O7 +H requiere 742,4, HPLC: 4,68 min.
183	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(3-metil-3-piridin-2-ilpiperidin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 737, C40H53ClN4O7 +H requiere 737,4, HPLC: 4,37 min.
184	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(3,5-dicloropiridin-4-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-	EM (EN): M/Z [MH+] = 793, C38H48Cl3N5O7 +H requiere 792,3, HPLC: 4,37 min.

	1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
185	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[(3*S*)-3-metil-3-fenilpiperidin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 736, C41H54ClN3O7 +H requiere 736,4,
186	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{3-[(4-fluorofenil)sulfanil]-8-azabiciclo[3.2.1]oct-8-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 798, C42H53ClFN3O7S +H requiere 798,3, HPLC: 4,49 min.
187	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[(piridin-2-ilsulfanil)metil]piperidin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 769, C40H53ClN4O7S +H requiere 769,3, HPLC: 4,3 min.
188	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-	EM (EN): M/Z [MH+] = 769,

	c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{3-[(piridin-2-ilsulfanil)metil]piperidin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	C40H53ClN4O7S +H requiere 769,3, HPLC: 4,3 min.
189	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(2-{[metil(metiloxi)amino]carbonil}piperidin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 733, C37H53ClN4O9 +H requiere 733,4, HPLC: 4,05 min.
190	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[(3,4-diclorofenil)metil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 806, C40H51Cl3N4O7 +H requiere 805,3, HPLC: 4,62 min.
191	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[2-(2-	EM (EN): M/Z [MH+] = 757, C41H61ClN4O7 +H requiere 757,4, HPLC: 1,71 min.

	piperidin-1-iletil)piperidin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
192	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[(1-metiletil)(2-{[2-(metiloxi)fenil]oxi}etil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 770,C41H56ClN3O9 +H requiere 770,4, HPLC: 4,3 min.
193	(2S,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[metil(2-fenilciclopropil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 708, C39H50ClN3O7 +H requiere 708,3, HPLC: 4,43 min.
194	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{metil[3-(1,2,4,5-tetrahidro-3H-3-benzazepin-3-il)propil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN) : M/Z [MH+] = 779, C43H59ClN4O7 +H requiere 779,4, HPLC: 3,73 min.

195	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[{2-[(2,6-diclorofenil)oxi]etil}(metil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 781,C38H48Cl3N3O8 +H requiere 780,3, HPLC: 4,43 min.
196	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[[(4-clorofenil)metil](etil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 730, C38H49Cl2N3O7 +H requiere 730,3, HPLC: 4,3 min.
197	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{metil[(3-metiltien-2-il)metil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 702, C36H48ClN3O7S +H requiere 702,3, HPLC: 4,24 min.
198	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-	EM (EN): M/Z [MH+] = 771,C40H52Cl2N4O7 +H requiere 771,3, HPLC: 4,56 min.

	[4-(3-cloro-4-metilfenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
199	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(difenilmetil)(metil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 758, C43H52ClN3O7 +H requiere 758,4,
200	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[5-metil-2-(metiloxi)fenil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 767, C41H55ClN4O8 +H requiere 767,3, HPLC: 4,43 min.
201	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[2-(etiloxi)fenil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 767, C41H55ClN4O8 +H requiere 767,3, HPLC: 4,43 min.

202	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{(2*S*,4R)-4-metil-2-[(metiloxi)carbonil]piperidin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 718, C37H52ClN3O9 +H requiere 718,3,
203	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-{2-[(2S)-2-(2-hidroxietil)piperidin-1-il]-1-metiletil}-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 690, C36H52ClN3O8 +H requiere 690,4.
204	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[(3S)-3-(metiloxi)piperidin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 676, C35H50ClN3O8 +H requiere 676,3.
205	(2*S*,3*aS*,9*bS*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de	EM (EN): M/Z [MH+] = 744, C39H54ClN3O9 +H requiere 744,4.

	(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{2-[(metiloxi)carbonil]octahidro-1*H*-indol-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
206	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[(2S)-4-metil-2-[(metiloxi)carbonil]-3,6-dihidropiridin-1(2*H*)-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 716, C37H50ClN3O9 +H requiere 716,3.
207	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi -5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-(3-hidroxi-8-azabiciclo[3.2.1]oct-8-il)-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 688, C36H50ClN3O8 +H requiere 688,3.
208	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-	EM (EN): M/Z [MH+] = 736, C41H54ClN3O7 +H requiere 736,4.

	hidroxi-3,8-dimetil-5-[1-metil-2-(3-metil-3-fenilpiperidin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
209	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{(fenilmetil)[2-(feniloxi)etil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 788, C44H54ClN3O8 +H requiere 788,4.
210	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-((1*R*)-1-metil-2-{4-[4-(trifluorometil)-2-pirimidinil]-1-piperazinil}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidro-1-naftalenilo, sal TFA	EM (EN): M/Z (M+H) 793,4; C38H48ClF3O7N6 + H requiere 793,1, H-RMN (CDCl3, datos seleccionados): 0,85 (d, 3H), 3,30 (s, 3H), 4,30 (m, 1H), 5,20 (s, 1H), 5,25 (s, 1H), 5,40 (m, 1H), 5,50 (m, 1H), 6,90 (d, 1H), 7,05 (t, 1H), 7,25 (d, 1H), 7,45 (d, 1H), 8,55 (d, 1H)
211	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-	EM (EN): M/Z (M+H) 792,5;

	c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-((1*R*)-1-metil-2-{4-[5-(trifluorometil)-2-piridinil]-1-piperazinil}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidro-1-naftalenilo, sal TFA	C39H49ClF3O7N5 + H requiere 792, 1H RMN (CDCl3, datos seleccionados): 0,90 (d, 3H), 3,30 (s, 3H), 4,30 (m, 1H), 5,20 (s, 1H), 5,25 (s, 1H), 5,40 (m, 1H), 5,50 (m, 1H), 6,65 (d, 1H), 7,05 (t, 1H), 7,25 (d, 1H), 7,50 (d, 1H), 7,75 (d, 1H), 8,45 (s, 1H).
212	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-((1*R*)-2-{4-[*bis*(4-fluorofenil)metil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (IEN): M/Z [MH+] = 849,2, C46H55ClF2N4O7 + H requiere 849,3806. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,7-3,20 (m,12H), 3,3 (s, 3H), 4,1 (m, 1H), 4,4 (s, 1H), 5,1 (s, 1H), 5,2 (s, 1H), 5,3 (s, 1H), 5,5 (s, 1H), 7,00-7,5 (m,

		11H).
213	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{(1*R*)-2-[4-(5-cloropirimidin-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (IEN): M/Z [MH+] = 759,1, C37H48Cl2N6O7 + H requiere 759,3040. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,2 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,4-3,1 (m, 8H), 3,3 (s, 3H), 4,1(m, 1H), 4,7-4,9 (m, 2H), 5,1 (s, 1H), 5,2 (s, 1H), 5,3 (s, 1H), 5,5 (s, 1H), 7,0-7,3 (m, 3H), 8,3 (s, 2H).
214	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{(1*R*)-2-[4-(5-bromopirimidin-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (IEN): M/Z [MH+] = 805,3, C37H48BrClN6O7 + H requiere 803,2535. RMN (CDCl3, datos seleccionados): 0,8 (d, 3H), 1,1 (d, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,3-2,6 (m, 8H), 3,3 (s,

		3H), 3,6-3,8 (m, 5H), 4,1 (m, 1H), 5,1-5,2 (m, 2H), 5,3 (s, 1H), 5,6 (s, 1H), 7,0-7,4 (m, 3H), 8,3 (s, 2H).
215	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{(1*R*)-2-[4-(6-cloro-1,3-benzotiazol-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (IEN): M/Z [MH+] = 814,3, C40H49Cl2N5O7S + H requiere 814,2808. RMN (CDCl3, datos seleccionados): 0,8 (m, 3H), 1,1 (m, 3H), 1,7 (s, 3H), 2,1 (s, 3H), 2,3-2,8 (m, 8H), 3,3 (s, 3H), 3,5-3,8 (m, 4H), 4,1 (m, 1H), 5,1-5,4 (m, 4H), 5,6 (s, 1H), 7,0-7,6 (m, 6H).
216	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-((1*R*)-2-{4-[(3,4-diclorofenil)metil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	RMN (CDCl3, datos seleccionados): 0,8 (m, 3H), 1,1 (m, 3H), 1,5 (s, 5H), 1,7 (s, 3H), 2,1 (s, 3H), 2,4-2,8 (m, 8H), 3,35 (s, 3H), 3,6 (s, 1H), 4,1 (m, 1H),

		5,1-5,6 (m, 4H), 6,7-7,4 (m, 6H).
217	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-((1*R*)-1-metil-2-{4-[5-(trifluorometil)pirimidin-2-il]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (IEN): M/Z [MH+] = 793,4, C38H48ClF3N6O7 + H requiere 793,3303. RMN (CDCl3, datos seleccionados): 0,8 (m, 3H), 1,2 (m, 3H), 1,7 (s, 3H), 2,5 (m, 2H), 2,6 (s, 3H), 2,8 (s, 1H), 3,1 (m, 2H), 3,3 (s, 3H), 4,1 (m, 1H), 5,1 (m, 2H), 5,3 (s, 1H), 5,5 (s, 1H), 7,0-7,1 (m, 1H), 7,2-7,4 (m, 3H), 8,6 (s, 2H).
218	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-((1*R*)-2-{4-[(4-clorofenil)oxi]piperidin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	EM (EN): M/Z [MH+] = 770, C40H51Cl2N3O8 + H requiere 772,3131. RMN (CDCl3, datos seleccionados): 0,8 (m, 3H), 1,1 (m, 3H), 1,3 (m, 4H), 1,7 (s, 3H), 2,1 (s, 3H), 2,2 (s,

1H),3,1 (s, 1H),3,3 (s, 3H), 3,6 (s, 1H), 4,1 (m, 1H), 4,25 (s, 1H), 5,1 (m, 2H), 5,3 (s, 1H), 5,6 (s, 1H), 6,8 (d, 2H), 7,0 (dd, 1H), 7,2-7,3 (m, 3H), 7,35 (d, 1H).

Tabla de Precursores

Ej. Nº	Nombre del Precursor Alcaloide de Terpeno	Número de Preparación del Precursor Alcaloide de Terpeno (TA)
1	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*R*,6*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	1
2	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*R*,6*R*,8a*R*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletenil)-	139

	1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
3	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	139
4	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-hidroxi-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	140
5	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-hidroxi-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	140
6	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2,8*a*-dihidroxi-	139

	3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
7	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,4*aS*,5*S*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	144
8	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,4*aS*,5*S*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	144
9	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,4*aS*,5*S*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	144
10	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,4*aS*,5*S*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletil)-1,2,4*a*,5,6,7,8,8*a*-	144

	octahidronaftalen-1-ilo	
11	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	139
12	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	139
13	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-{2-[(1*H*-imidazol-1-ilcarbonil)oxi]-1-metiletil}-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-	143

	ilo	
14	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	139
15	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	139
16	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,6*R*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	139
17	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-	141

	c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
18	(2*S*,3*aR*,9*bR*)-9*b*-[(*terc*-butoxicarbonil)oxi]-6-cloro-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*R*,2*R*,4*aS*,5*R*,8*S*,8*aS*)-2-(acetiloxi)-5-(2,2-difluoro-1-metilvinil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidro-1-naftalenil]-3-(*terc*-butilo)	156
19	3-(1,1-dimetiletilo) (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-hidroxi-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo}	157
20	3-(1,1-dimetiletilo) (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato	160

	de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo}	
21	acetato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-5-(2-etil-1,3-tiazol-4-il)-1,8*a*-dihidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-2-ilo	166
21	ácido (2*S*,3*aR*,9*bR*)-6-cloro-3-[[(1,1-dimetiletil)oxi]carbonil}-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxílico	153
22	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2,2-difluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-*il*}-3-(1,1-dimetiletilo)	167
23	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-	168

	1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2,2-difluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8a-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
24	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-(2,2-dicloro-1-metiletenil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo)	172
25	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160

26	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
27	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
28	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
29	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-	160

	dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
30	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
31	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
32	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-	160

	1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
33	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
34	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-	160

	dimetiletilo)	
35	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8a-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
36	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
37	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-	160

	dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
38	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
39	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-	160

	dimetiletilo)	
40	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3a*H*)-dicarboxilato de 2-{(1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4a,5,6,7,8,8a-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
41	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3a*H*)-dicarboxilato de 2-{(1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4a,5,6,7,8,8a-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
42	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3a*H*)-	160

	dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
43	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
44	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-	160

	dimetiletilo)	
45	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
46	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
47	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-	177

	dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-5-{2-[acetil(ciclopropil)amino]-1-metiletil}-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo)	
48	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{ciclopropil[(metiloxi)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo)	179
49	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{etil[(metiloxi)carbonil]amino}-1-	178

	metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo)	
50	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
51	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
52	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-	180

	1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{ciclopropil[(etilamino)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo)	
53	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5R,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
54	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-	160

	8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
55	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
56	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
57	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-	160

	dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8a-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
58	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
59	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-	160

	(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
60	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
61	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
62	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-	160

	dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
63	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
64	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-	160

	octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
65	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
66	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
67	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-	160

	c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
68	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5R,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8a-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
69	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-	160

	octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
70	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
71	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
72	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-	160

	c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
73	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
74	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-	160

	octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
75	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
76	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
77	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-	160

	c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
78	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
79	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-	160

	octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
80	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
81	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
82	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-	160

	c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
83	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
84	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-	160

	octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
85	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
86	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
87	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-	160

	c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
88	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
89	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-	160

	octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
90	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
91	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
92	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-	160

	c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
93	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
94	ácido (2R)-2-[(1*R*,4*R*,4*aS*,5*R*,6*R*)-5-({[(2*S*,3*aR*,9*bR*)-6-cloro-3-{[(1,1-dimetiletil)oxi]carbonil}-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-il]carbonil}oxi)-6-(acetiloxi)-4*a*-hidroxi-4,7-dimetil-1,2,3,4,4*a*,5,6,8*a*-octahidronaftalen-	181

	1-il]propanoico	
95	ácido (2R)-2-[(1*R*,4*R*,4a*S*,5*R*,6*R*)-5-({[(2*S*,3a*R*,9b*R*)-6-cloro-3-{[(1,1-dimetiletil)oxi]carbonil}-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-il]carbonil}oxi)-6-(acetiloxi)-4*a*-hidroxi-4,7-dimetil-1,2,3,4,4*a*,5,6,8*a*-octahidronaftalen-1-il]propanoico	181
96	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*R*,8*R*,8a*R*)-8a-hidroxi-2-[(1*H*-imidazol-1-ilcarbonil)oxi]-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	142
97	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-	160

	c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
98	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
99	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160

100	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
101	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
102	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-	160

	{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
103	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
104	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160

105	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
106	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
107	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-	160

	{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
108	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
109	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160

110	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5R,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
111	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
112	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-	160

	{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
113	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
114	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160

115	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
116	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
117	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-	160

	{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
118	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
119	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160

120	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
121	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
122	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-	160

	{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
123	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
124	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160

125	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8a-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
126	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8a-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
127	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-	160

	hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
128	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
129	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
130	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-	160

	1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
131	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
132	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-	160

	metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
133	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
134	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
135	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-	160

	1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
136	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
137	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-	160

	metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
138	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
139	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
140	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-	160

	1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
141	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
142	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-	160

	metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
143	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
144	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
145	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-	160

	dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
146	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
147	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-	152

	dimetiletilo)	
148	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
149	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
150	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141

151	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
152	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-{[[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
153	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-([[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-	160

	metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
154	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
155	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
156	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-	160

	1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
157	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
158	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-	160

	[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
159	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
160	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
161	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-	160

	dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
162	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
163	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-	160

	dimetiletilo)	
164	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
165	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
166	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141

167	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
168	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
169	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2- carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
170	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-	141

	metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
171	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
172	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
173	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-	141

	metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
174	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
175	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141

176	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
177	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
178	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
179	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-	141

	metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
180	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
181	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
182	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-	141

	hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4a,5,6,7,8,8a-octahidronaftalen-1-ilo	
183	(2*S*,3a*R*,9b*R*)-6-cloro-9b-hidroxi-5-metil-1,2,3,3a,5,9b-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4a,5,6,7,8,8a-octahidronaftalen-1-ilo	141
184	(2*S*,3a*R*,9b*R*)-6-cloro-9b-hidroxi-5-metil-1,2,3,3a,5,9b-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4a,5,6,7,8,8a-octahidronaftalen-1-ilo	141
185	(2*S*,3a*R*,9b*R*)-6-cloro-9b-hidroxi-5-metil-1,2,3,3a,5,9b-hexahidropirrolo[2,3-	141

	c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
186	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
187	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
188	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de	141

	(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
189	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
190	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
191	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-	141

	8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,*4a*,5,6,7,8,8a-octahidronaftalen-1-ilo	
192	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
193	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
194	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-	141

	[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
195	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,*4a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
196	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
197	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-	141

	octahidronaftalen-1-ilo	
198	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
199	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
200	(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141

201	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
202	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
203	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
204	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-	141

	metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	
205	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
206	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141
207	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-	141

	hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4a,5,6,7,8,8a-octahidronaftalen-1-ilo	
208	(2*S*,3a*R*,9b*R*)-6-cloro-9b-hidroxi-5-metil-1,2,3,3a,5,9b-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4a,5,6,7,8,8a-octahidronaftalen-1-ilo	141
209	(2*S*,3a*R*,9b*R*)-6-cloro-9b-hidroxi-5-metil-1,2,3,3a,5,9b-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4a,5,6,7,8,8a-octahidronaftalen-1-ilo	141
210	(2*S*,3a*R*,9b*R*)-6-cloro-9b-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9b-tetrahidropirrolo[2,3-	159

	c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
211	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	159
212	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-	160

	octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
213	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
214	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
215	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-	160

	c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
216	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	160
217	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-	160

	octahidronaftalen-1-il}-3-(1,1-dimetiletilo)	
218	(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo	141

La síntesis de diversos compuestos representativos se describe ahora con más detalle y los compuestos restantes pueden prepararse de manera análoga.

Ejemplo 1: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-(1-metiletil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 1, 200 mg) en isopropanol (20 ml) se le añadió platino sobre carbono (al 10% p/p, 20 mg) y la mezcla resultante se hidrogenó a temperatura ambiente con agitación a una presión de 1 atmósfera (101,325 kPa) de hidrógeno durante 18 horas. La mezcla se filtró a través de celite y se concentró al vacío, dando un sólido

blanco. El sólido se purificó por HPLC preparativa (columna C18 Ultrasphere de 2,54 cm (1 pulgada) de diámetro, 2 inyecciones, 70:30 de acetonitrilo:agua), dando el producto en forma de un sólido blanco (89 mg).

Ejemplo 2: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-2-[(2-metilpropanoil)oxi]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 139, 25 mg, 0,05 mmol) y 4-dimetilaminopiridina (6 mg, 0,05 mmol) en diclorometano (2 ml) se le añadió anhídrido isobutírico (17 mg, 0,11 mmol) y la mezcla resultante permaneció a temperatura ambiente durante 18 h. El producto bruto se purificó por cromatografía en columna sobre un cartucho de sílice Sepak® (1,5 g) eluyendo con hexano:diclorometano (1:1, 2 ml) y después con hexano:acetato de etilo (4:1 después 2:1 después 1:1, 3 ml cada uno). Las fracciones puras se combinaron y se concentraron al vacío, dando el compuesto del título (11 mg, 37%).

Ejemplo 3: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(hexanoiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2,8a-dihidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4a,5,6,7,8,8a-octahidronaftalen-1-ilo (Preparación 139, 51 mg, 0,10 mmol) y 4-dimetilaminopiridina (14 mg, 0,11 mmol) en diclorometano (5 ml) se le añadió anhídrido hexanoico (43 mg, 0,2 mmol) y la mezcla resultante permaneció a temperatura ambiente durante un fin de semana. El producto bruto se purificó por cromatografía en columna sobre sílice (10 g) eluyendo con hexano:acetato de etilo (2:1). Las fracciones puras se combinaron y se concentraron al vacío, dando el compuesto del título (43 mg, 97%).

Ejemplo 4: (2*S*,3a*R*,9b*R*)-6-cloro-9b-hidroxi-5-metil-1,2,3,3a,5,9b-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-5-[2-(acetiloxi)-1-metiletil]-8a-hidroxi-3,8-dimetil-1,2,4a,5,6,7,8,8a-octahidronaftalen-1-ilo

A (2*S*,3a*R*,9b*R*)-6-cloro-9b-hidroxi-5-metil-1,2,3,3a,5,9b-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de ((1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-5-[2-hidroxi-1-metiletil]-3,8-dimetil-1,2,4a,5,6,7,8,8a-octahidronaftalen-1-ilo (Preparación 140, 63,8 mg, 0,11 mmol) en diclorometano (1,1 ml) se le añadieron anhídrido acético (22 mg, 20 µl, 0,22 mmol) y 4-dimetilaminopiridina (14,3 mg, 0,12 mmol) y la mezcla de reacción se agitó a temperatura ambiente durante 18 horas. La mezcla de reacción se diluyó con diclorometano (20 ml) y se lavó con una solución acuosa de ácido cítrico, se secó ($MgSO_4$) y se concentró al vacío, dando una goma. El producto bruto se purificó por cromatografía sobre sílice eluyendo con hexano:acetato de etilo (60:40). Las fracciones puras se combinaron y se concentraron al vacío, dando el producto del título en forma de un sólido blanco (42 mg, 61%).

Ejemplo 5: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[(2-metilpropanoil)oxi]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-hidroxi-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 140, 100 mg, 0,17 mmol) y 4-dimetilaminopiridina (21 mg, 0,35 mmol) en diclorometano (5 ml) a <0ºC se le añadió anhídrido isobutírico (0,06 ml, 0,35 mmol) y la mezcla resultante se dejó calentar a temperatura ambiente durante 30 minutos. Después de 3 horas, la mezcla de reacción se trató con agua (5 ml) y se extrajo con diclorometano (2 x 5 ml). Las fases orgánicas combinadas se lavaron con una solución saturada acuosa de cloruro sódico y se concentraron al vacío. El producto bruto se purificó por cromatografía en columna sobre sílice eluyendo con hexano:acetato de etilo (de 1:1 a 1:2). Las fracciones puras se combinaron y se concentraron al vacío, dando el compuesto del título (48 mg, 43%).

Ejemplo 6: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-[(ciclopropilcarbonil)oxi]-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 139, 100 mg, 0,19 mmol)

y 4-dimetilaminopiridina (30 mg, 0,25 mmol) en tetrahidrofurano (10 ml) se le añadieron ácido ciclopropanocarboxílico (400 mg, 4,7 mmol) y clorhidrato de 1-(3-dimetilaminopropil)-3-etilcarbodiimida (90 mg, 0,58 mmol) y la mezcla resultante se agitó a temperatura ambiente durante 18 h. La mezcla de reacción se pasó a través de un cartucho Sepak® (sílice, 1,5 g) para retirar el material insoluble y el disolvente se retiró al vacío. El producto bruto se purificó, dando el compuesto del título (20 mg, 18%).

Ejemplo 7: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletil)-2-{[(prop-2-iniloxi)carbonil]oxi}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,4*aS*,5*S*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 144, 500 mg, 0,96 mmol) y 4-dimetilaminopiridina (350 mg, 2,9 mmol) en diclorometano (25 ml) a 0ºC en atmósfera de nitrógeno se le añadió cloroformiato de propargilo (170 mg, 1,44 mmol) y la mezcla resultante se agitó a 0ºC durante 30 minutos y a temperatura ambiente durante 3 horas. La mezcla de reacción se diluyó con diclorometano (100 ml) y se lavó con una solución de ácido cítrico (3 x 50 ml) y agua (2 x 50 ml), se secó ($MgSO_4$) y se concentró al vacío, dando un sólido. El producto bruto se purificó por cromatografía ultrarrápida sobre sílice (40 g) eluyendo con hexano:acetato de etilo (3:2). Las fracciones puras se combinaron y se concentraron al vacío, dando el producto del título (462 mg, 80%).

Ejemplo 8: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-

hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletil)-2-({[(2,2,2-tricloroetil)oxi]carbonil}oxi)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

El compuesto del título se preparó mediante el procedimiento del Ejemplo 9 sustituyendo cloroformiato de isopropenilo con cloroformiato de 2,2,2-tricloroetilo (30,5 mg, 0,14 mmol), dando el producto del título (55 mg, 82%).

Ejemplo 9: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-2-({[(1-metiletenil)oxi]carbonil}oxi)-5-(1-metiletil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,4*aS*,5*S*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 144, 50 mg, 0,096 mmol) y 4-dimetilaminopiridina (35 mg, 0,29 mmol) en diclorometano (5 ml) a 0ºC en atmósfera de nitrógeno se le añadió cloroformiato de isopropenilo (17,4 mg, 0,144 mmol) y la mezcla resultante se agitó a 0ºC durante 30 minutos y a temperatura ambiente durante 2 horas. La mezcla de reacción se diluyó con diclorometano (25 ml) y se lavó con una solución de ácido cítrico (3 x 15 ml), se secó ($MgSO_4$) y se concentró al vacío. El producto bruto se purificó por cromatografía sobre sílice (5 g) eluyendo con hexano:acetato de etilo (1:1). Las fracciones puras se combinaron y se concentraron al vacío, dando el producto del título (56 mg, 96%).

Ejemplo 10: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-

hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de ((1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletil)-2-{[(prop-2-eniloxi)carbonil]oxi}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

Se añadió cloroformiato de alilo (17,4 mg) a una solución agitada y enfriada (0ºC) de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]-benzoxazin-2-carboxilato de (1*S*,4*aS*,5*S*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 144, 50 mg) y 4-dimetilaminopiridina (35 mg) en diclorometano (5 ml) en una atmósfera de nitrógeno. Después de 30 minutos, la reacción se dejó calentar a temperatura ambiente durante 15 horas. La mezcla de reacción se diluyó con diclorometano (25 ml), se lavó con ácido cítrico acuoso (al 10% p/p, 3 x 15 ml) y se secó ($MgSO_4$). Después de la evaporación del disolvente al vacío, el residuo se purificó por cromatografía ultrarrápida en columna sobre sílice (5 g) eluyendo con 1:1 acetato de etilo:hexano, dando el producto (44 mg, 76%).

Ejemplo 11: metilbutanodioato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-1-({[(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-il]carbonil}oxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-2-ilo

Una mezcla de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 139, 100 mg, 0,19 mmol), ácido 4-(metiloxi)-4-oxobutanoico disponible en el mercado (50 mg, 0,38 mmol), 4-dimetilaminopiridina (60 mg, 0,5 mmol), clorhidrato de 1-(3-

dimetilaminopropil)-3-etilcarbodiimida (90 mg, 0,58 mmol) y diclorometano (5 ml) se agitó durante 18 h y la mezcla de reacción se concentró al vacío. El producto bruto se purificó por cromatografía sobre una columna Biotage® 12 M eluyendo con diclorometano:éter dietílico (4:1). Las fracciones puras se combinaron y el disolvente se retiró al vacío, dando el producto del título (23 mg, 18%).

Ejemplo 12: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-2-(pent-4-enoiloxi)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

El compuesto del título se preparó mediante el procedimiento del Ejemplo 11 sustituyendo el ácido 4-(metiloxi)-4-oxobutanoico con ácido pent-4-enoico disponible en el mercado (50 mg, 0,50 mmol), dando el compuesto del título (64 mg, 56%).

Ejemplo 13: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[({[2-(naftalen-1-ilamino)etil]amino}carbonil)oxi]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-{2-[(1*H*-imidazol-1-ilcarbonil)oxi]-1-metiletil}-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 143, 80 mg, 0,12 mmol) en piridina (5 ml) se le añadió 4-dimetilaminopiridina (16 mg, 0,13 mmol) seguido de la sal diclorhidrato de *N*-1-

naftietilendiamina (32 mg, 0,12 mmol). Después de agitar la mezcla de reacción durante 48 h, la mezcla de reacción se concentró al vacío y se purificó por cromatografía ultrarrápida eluyendo con hexano:acetato de etilo (de 2:1 y después 1:1), dando el compuesto del título puro.

Ejemplo 14: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-{[(acetiloxi)acetil]oxi}-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 139, 210 mg, 0,4 mmol) y 4-dimetilaminopiridina (65 mg, 0,53 mmol) en diclorometano (10 ml) se le añadieron ácido (acetiloxi)acético (60 mg, 0,51 mmol) y clorhidrato de 1-(3-dimetilaminopropil)-3-etilcarbodiimida (90 mg, 0,58 mmol). La mezcla resultante se agitó a temperatura ambiente y después de que se completara se concentró al vacío. El producto bruto se purificó por cromatografía sobre una columna Biotage® 12 M eluyendo con hexano:acetato de etilo (2:1). Las fracciones puras se combinaron y el disolvente se retiró al vacío, dando el producto del título (150 mg, 61%).

Ejemplo 15: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(formiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

El compuesto del título se preparó mediante el procedimiento del Ejemplo 14 sustituyendo el ácido (acetiloxi)acético con ácido fórmico disponible en el mercado (20 µl, 0,53 mmol), dando el compuesto del título (160 mg, 73%).

Ejemplo 16: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-2-[3,3,3-trifluoropropanoil)oxi]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

El compuesto del título se preparó mediante el procedimiento del Ejemplo 14 sustituyendo ácido (acetiloxi)acético con ácido 3,3,3-trifluoropropiónico disponible en el mercado, dando el compuesto del título (165 mg, 66%).

Ejemplo 17: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[4-(etiloxi)-1-metil-4-oxobut-2-enil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

Una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de ((1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 141, 94 mg, 0,163 mmol) y carbetoximetilen trifenilfosforano (68 mg, 0,195 mmol) en tolueno anhidro (5 ml) se calentó a reflujo en atmósfera de nitrógeno durante 3 horas y después se agitó a temperatura ambiente durante 18 h antes de concentrarse al vacío. El residuo se trató con ácido sulfúrico (al 10%) y se extrajo con dos alícuotas de acetato de etilo. Los extractos orgánicos combinados se lavaron con una solución saturada acuosa de carbonato ácido

sódico y una solución saturada acuosa de cloruro sódico, se secó ($MgSO_4$) y se concentró al vacío. El producto bruto se recogió en acetonitrilo (1 ml), se filtró y se purificó por HPLC preparativa sobre una columna Dynamex®, 5 mm x 21,6 mm, eluyendo con acetonitrilo:agua (60:40). Las fracciones puras se concentraron al vacío, dando el producto del título (7 mg, 6%).

Ejemplo 18: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-(2,2-difluoro-1-metiletenil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

Una solución agitada de (2*S*,3*aR*,9*bR*)-9*b*-[(*terc*-butoxicarbonil)oxi]-6-cloro-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*R*,2*R*,4*aS*,5*R*,8*S*,8*aS*)-2-(acetiloxi)-5-(2,2-difluoro-1-metilvinil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidro-1-naftalenil]-3-(*terc*-butilo) (Preparación 156, 120 mg) en acetato de etilo (3 ml) se trató con ácido clorhídrico concentrado (1 ml). Después de 50 minutos, la mezcla homogénea se diluyó con acetato de etilo (50 ml) y se lavó con agua (2 x 20 ml) seguido de cloruro sódico saturado acuoso (20 ml). Los extractos orgánicos combinados se secaron (Na_2SO_4) y se evaporaron, dando un sólido blanco. El producto bruto se purificó por cromatografía en columna ultrarrápida sobre gel de sílice eluyendo con acetato de etilo:hexano (1:1), dando un sólido blanco (33 mg).

Ejemplo 19: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-fluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-hidroxi-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 157, 200 mg, 0,26 mmol) en diclorometano a -78ºC se le añadió trifluoruro de dietilaminoazufre (45 mg, 34 µl, 0,28 mmol) durante 10 minutos. La mezcla resultante se dejó calentar a temperatura ambiente y después se agitó durante 18 h. La mezcla de reacción se enfrió a -78ºC y se le añadió trifluoruro de dietilaminoazufre (34 µl, 0,28 mmol). De nuevo, la mezcla resultante se dejó calentar a temperatura ambiente y se agitó durante 18 h. La mezcla de reacción se inactivó con agua y se extrajo con hexano:éter (1:2). El extracto orgánico se lavó con una solución saturada acuosa de cloruro sódico, se secó ($MgSO_4$) y se concentró al vacío, dando el intermedio Boc-protegido (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-fluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) en forma de un sólido blanco (172 mg, 86%).

A una solución del intermedio Boc-protegido (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-fluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) en acetato de etilo (5 ml) se le añadió ácido clorhídrico concentrado (12 N, 1,5 ml) y la mezcla resultante se agitó durante 1 hora. La mezcla de reacción se diluyó con acetato de etilo (50 ml), se

lavó con agua (3 x 20 ml) y una solución saturada acuosa de cloruro sódico (20 ml), se secó ($MgSO_4$) y se concentró al vacío, dando una espuma (125 mg, 83%). El producto bruto se purificó por cromatografía sobre sílice eluyendo con hexano:acetato de etilo (2:1 y después 1:1). Las fracciones puras se combinaron y se concentraron al vacío, dando un sólido blanco (50 mg, 33%). Este producto se purificó de nuevo por HPLC preparativa usando una columna "Microsorb" ODS de 2,54 cm (1 pulgada), eluyendo con agua:acetonitrilo (30:70) con un caudal de 20 ml por minuto. Las fracciones puras se eluyeron durante un período de 10 a 10,5 minutos y se combinaron y se concentraron al vacío, dando el producto del título en forma de un sólido blanco (15 mg, 10%).

Ejemplo 20: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de ((1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[(1-metil-2-morfolin-4-iletil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

Una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 200 mg, 0,26 mmol) y morfolina (33,6 mg, 0,39 mmol) en 1,2-dicloroetano (1,5 ml) se agitó durante 20 min antes de que se añadiera triacetoxiborohidruro sódico (0,11 mg, 0,28 mmol) y de que se agitara durante 15 h. La mezcla de reacción se vertió en agua (50 ml) y se extrajo con diclorometano (3 x 30 ml). Los extractos orgánicos combinados se lavaron con agua (20 ml), se secaron (Na_2SO_4) y se concentraron al vacío. El residuo bruto se purificó usando un cartucho Biotage

(8 g, sílice), eluyendo con un gradiente de metanol:diclorometano (de 2:98 a 6:94), dando el intermedio Boc-protegido en forma de una espuma blanca (203 mg).

El intermedio Boc-protegido (203 mg) en acetato de etilo (1,5 ml) se trató con ácido clorhídrico concentrado (0,5 ml). Después de 20 minutos, la mezcla de reacción se diluyó con acetato de etilo (50 ml), se lavó con carbonato ácido sódico acuoso (al 10% p/p, 50 ml) y después con agua (30 ml). Los extractos orgánicos combinados se secaron (Na_2SO_4) y se evaporaron, dando el compuesto del título (114 mg).

Ejemplo 21: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-etil-1,3-tiazol-4-il)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de acetato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-5-(2-etil-1,3-tiazol-4-il)-1,8*a*-dihidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-2-ilo (Preparación 166, 94 mg) y ácido (2*S*,9*bR*)-6-cloro-3-{[(1,1-dimetiletil)oxi]carbonil}-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]-benzoxazin-2-carboxílico (Preparación 153, 90 mg) en diclorometano (4 ml) se le añadieron *N*-metilimidazol (0,05 ml) y 1-(2-mesitilensulfonil)-3-nitro-1*H*-1,2,4-triazol. La mezcla de reacción se agitó a temperatura ambiente durante 3 horas antes de evaporarse al vacío. La mezcla bruta se purificó por cromatografía ultrarrápida en columna sobre gel de sílice eluyendo con acetato de etilo:hexano (de 20:80 a 50:50), dando el intermedio acoplado en forma de una goma (110 mg). Una solución agitada de este intermedio (110 mg) en acetato de etilo (5 ml) se trató

con ácido clorhídrico concentrado (1 ml). Después de 40 minutos, la mezcla homogénea se diluyó con acetato de etilo (50 ml), se lavó con cloruro sódico acuoso diluido (50 ml), se secó ($MgSO_4$) y se evaporó. El producto bruto se purificó por cromatografía en columna sobre gel de sílice eluyendo con acetato de etilo:hexano (de 5:95 a 50:50), dando el compuesto del título en forma de un sólido blanco (34 mg).

Ejemplo 22: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2,2-difluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-{[[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2,2-difluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 167, 35 mg, 0,044 mmol) en acetato de etilo (0,5 ml) se le añadió ácido clorhídrico concentrado (0,5 ml) y la mezcla resultante se agitó a temperatura ambiente durante 20 minutos. La mezcla de reacción se vertió en una solución tampón (pH 7, 15 ml) y se extrajo con acetato de etilo. La fase orgánica se lavó con agua y una solución saturada acuosa de cloruro sódico, se secó (Na_2SO_4) y se concentró al vacío. El producto bruto se purificó por cromatografía en columna ultrarrápida eluyendo con un gradiente de hexano:acetato de etilo (de 2:1 a 1:1). Las fracciones puras se combinaron y se concentraron al vacío, dando el producto del título (15 mg, 57%).

Ejemplo 23: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2,2-difluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2,2-difluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 168, 135 mg, 0,17 mmol) en acetato de etilo (1,5 ml) se le añadió ácido clorhídrico concentrado (1,5 ml) y la mezcla resultante se agitó a temperatura ambiente durante 20 minutos. La mezcla de reacción se vertió en una solución tampón (pH 7, 30 ml) y se extrajo con acetato de etilo. La fase orgánica se lavó con agua y una solución saturada acuosa de cloruro sódico, se secó (Na_2SO_4) y se concentró al vacío, dando un aceite amarillento (145 mg, 142%). El producto bruto se purificó por cromatografía en columna ultrarrápida eluyendo con un gradiente de hexano:acetato de etilo (de 2:1 a 1:1). Las fracciones puras se combinaron y se concentraron al vacío, dando el producto del título (61 mg, 60%).

Ejemplo 24: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-(2,2-dicloro-1-metiletenil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

Se añadió (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-(2,2-dicloro-1-metiletenil)-8*a*-hidroxi-

3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo) (Preparación 172, 0,10 g) a cloruro de hidrógeno (1 M en ácido acético, 1 ml) y la solución resultante se agitó a temperatura ambiente. Después de 40 min, la mezcla bruta se diluyó con éter dietílico (10 ml) y agua (10 ml), la fase orgánica se separó y después se lavó con carbonato ácido sódico (5 x 10 ml) y salmuera (10 ml), se secó ($MgSO_4$) y se concentró al vacío. El producto bruto se purificó por cromatografía ultrarrápida usando un cartucho Bond ElutR eluyendo con un gradiente de hexano:acetato de etilo (de 100:0 a, después, 50:50), dando el compuesto del título.

Ejemplo 32: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(4-piridin-2-ilpiperazin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A 1-(2-piridil)piperazina (44,0 mg, 0,39 mmol) se le añadió una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 200 mg, 0,257 mmol) en 1,2-dicloroetano. La mezcla resultante se agitó a temperatura ambiente durante 10 minutos antes de que se le añadiera en una porción triacetoxiborohidruro sódico (109 mg, 0,51 mmol). La mezcla de reacción resultante se cerró herméticamente y se agitó durante 60 horas. La mezcla de reacción se vertió sobre agua (50 ml) y se extrajo con diclorometano (3 x 30 ml). Los extractos combinados se lavaron con agua (20 ml), se secaron (Na_2SO_4) y se concentraron al vacío. El producto *bis*-Boc-protegido bruto se

purificó por cromatografía sobre un cartucho Biotage® (sílice, 8 g) eluyendo con metanol:diclorometano (2:98) durante 11 minutos, después con un gradiente de metanol:diclorometano (de 2:98 a 6:94) durante 40 minutos y después con metanol:diclorometano (6:94). Las fracciones puras se recogieron, dando el intermedio *bis*-Boc-protegido en forma de un vidrio incoloro (104,4 mg, 44%). La desprotección se realizó añadiendo una solución del intermedio en acetato de etilo (1,5 ml) a ácido clorhídrico concentrado acuoso (0,5 ml). La mezcla resultante se agitó durante 20 minutos antes de verterse en acetato de etilo (50 ml) y una solución acuosa de carbonato ácido sódico (2 N, 40 ml). La fase acuosa se extrajo con acetato de etilo (20 ml) y los extractos orgánicos combinados se lavaron con agua (20 ml), se secaron (Na_2SO_4) y se concentraron al vacío. El producto bruto se purificó por cromatografía ultrarrápida usando un cartucho de sílice Biotage® (8 g) eluyendo con un gradiente de metanol:diclorometano (de 2:98 a 6:98). Las fracciones puras se recogieron, dando el compuesto del título (20,50 mg, 11%).

Ejemplo 33: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{*bis*[2-(metiloxi)etil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

El compuesto del título se preparó mediante el procedimiento del Ejemplo 32 sustituyendo 1-(2-piridil)piperazina con *bis*-(2-metoxietil)amina (51,3 mg, 0,39 mmol), dando el intermedio en forma de un vidrio incoloro (146,3 mg, 64%) y el compuesto del título (51,70 mg, 29%).

Ejemplo 47: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-5-{2-[acetil(ciclopropil)amino]-1-metiletil}-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

Una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-5-{2-[acetil(ciclopropil)amino]-1-metiletil}-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo) (Preparación 177, 91 mg, 0,10 mmol) en ácido clorhídrico (solución 4 M en dioxano, 3 ml) se agitó en atmósfera de nitrógeno durante 1 hora. La mezcla de reacción se enfrió a 0ºC y se inactivó con una solución de carbonato ácido sódico. La mezcla se extrajo con acetato de etilo y las fracciones orgánicas combinadas se lavaron con una solución de carbonato ácido sódico, se secaron (Na_2SO_4) y se concentraron al vacío. El producto bruto se purificó por cromatografía en columna sobre sílice (3 g) eluyendo con acetato de etilo:heptano (2:1). Las fracciones puras se combinaron de nuevo y se concentraron al vacío, dando el producto del título en forma de un sólido vidrioso amarillo (31 mg, 47%).

Ejemplo 48: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-{ciclopropil[(metiloxi)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

Una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-{ciclopropil[(metiloxi)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo) (Preparación

179, 108 mg, 0,12 mmol) en cloruro de hidrógeno (solución 4 M en dioxano, 2 ml) se agitó en atmósfera de nitrógeno durante 1 hora. La mezcla de reacción se enfrió a 0ºC y se inactivó con una solución de carbonato ácido sódico. La mezcla se extrajo con acetato de etilo y las fracciones orgánicas combinadas se lavaron con una solución de carbonato ácido sódico, se secaron (Na_2SO_4) y se concentraron al vacío. El producto bruto se purificó por cromatografía en columna sobre sílice (2 g) eluyendo con acetato de etilo:heptano (1:1). Las fracciones puras se combinaron de nuevo y se concentraron al vacío, dando el producto del título en forma de un sólido vidrioso amarillo (30 mg, 37%).

Ejemplo 49: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{etil[(metiloxi)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

El compuesto del título se preparó mediante el procedimiento del Ejemplo 48 sustituyendo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{ciclopropil[(metiloxi)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo) con (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{etil[(metiloxi)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo) (Preparación 178, 89 mg, 0,10 mmol), dando el compuesto del título en forma de un sólido amarillo pálido (21 mg, 31%).

Ejemplo 52: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{ciclopropil[(etilamino)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

El compuesto del título se preparó mediante el procedimiento del Ejemplo 47 sustituyendo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-5-[2-[acetil(ciclopropil)amino]-1-metiletil}-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo) con (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{ciclopropil[(etilamino)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo) (Preparación 180, 114 mg, 0,13 mmol), dando el compuesto del título en forma de un sólido blanquecino (25 mg, 28%).

Ejemplo 96: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletil)-2-{[(fenilamino)carbonil]oxi}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aR*,8*R*,8*aR*)-8*a*-hidroxi-2-[(1*H*-imidazol-1-ilcarbonil)oxi]-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 142, 510 mg, 0,83 mmol)

en piridina anhidra (10 ml) se le añadieron clorhidrato de anilina (500 mg, 3,8 mmol) y 4-dimetilaminopiridina (240 mg, 2,0 mmol). La mezcla de reacción se agitó a temperatura ambiente en atmósfera de nitrógeno durante 4 días antes de verterse en diclorometano (100 ml) y de lavarse con una solución saturada acuosa de ácido cítrico (2 x 50 ml). La fracción orgánica se secó (Na_2SO_4) y se concentró al vacío, dando un sólido amarillento (490 mg, 93%). El producto bruto se purificó por cromatografía en columna ultrarrápida sobre gel de sílice eluyendo con un gradiente de hexano:acetato de etilo (de 1:1 a 1:5). Las fracciones puras se recogieron y se concentraron al vacío, dando (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-2-{[(fenilamino)carbonil]oxi}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (440 mg, 83%). A una solución del (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-2-{[(fenilamino)carbonil]oxi}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (100 mg, 0,157 mmol) en acetato de etilo (30 ml) se le añadió óxido de platino (IV) (10 mg, 0,044 mmol) y la mezcla resultante se hidrogenó a temperatura ambiente a 413,685 kPa (60 psi) de hidrógeno durante 10 horas. La mezcla de reacción se filtró y el filtrado se concentró al vacío. El producto bruto se purificó por cromatografía en columna ultrarrápida sobre gel de sílice eluyendo con hexano:acetato de etilo (1:1). El producto se purificó adicionalmente, dando el producto del título (19 mg, 19%).

Ejemplo 101: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[4-(4-clorofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 620 mg, 0,80 mmol) en diclorometano (8 ml) se le añadió 1-(4-clorofenil)piperazina (Preparación 78, 254 mg, 1,08 mmol). Después de 10 min, se añadieron trietilamina (0,15 ml, 1,2 mmol) y triacetoxiborohidruro sódico (110 mg, 0,52 mmol) y la mezcla de reacción se agitó a temperatura ambiente en atmósfera de nitrógeno durante 16 h. La mezcla de reacción se diluyó con diclorometano (10 ml) y una solución semi-saturada acuosa de carbonato ácido sódico (15 ml) y se agitó durante aproximadamente 30 min. La fase acuosa se extrajo de nuevo con diclorometano (15 ml) y las fases orgánicas combinadas se secaron (Na_2SO_4) y se concentraron al vacío, dando el intermedio Boc-protegido.

Al intermedio Boc-protegido se le añadió cloruro de hidrógeno (4 N en dioxano, 6 ml). Después, la mezcla de reacción se agitó a temperatura ambiente durante 45 min antes de la adición de trietilamina (3 ml) acompañada de refrigeración en un baño de hielo. La mezcla de reacción se diluyó con acetato de etilo (20 ml) y una solución saturada acuosa de carbonato ácido sódico (15 ml) y las fases se separaron. La fase acuosa se extrajo de nuevo con acetato de etilo (20 ml) y las fases orgánicas combinadas se lavaron con una solución acuosa de carbonato ácido sódico y salmuera, antes de secarse

(Na_2SO_4) y de concentrarse al vacío. El producto bruto se purificó, dando el compuesto del título (273 mg, 0,361 mmol).

Ejemplo 106: (2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[2-(trifluorometil)fenil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

Se disolvieron (2*S*,3a*R*,9b*R*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3a*H*)-dicarboxilato de 2-{(1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 600 mg, 0,77 mmol), 1-[2-(trifluorometil)fenil]piperazina (Preparación 130, 300 mg, 1 mmol) y trietilamina (0,3 ml, 2 mmol) en diclorometano (6 ml) y se añadió triacetoxiborohidruro sódico (240 mg, 1,1 mmol). La mezcla de reacción se agitó a temperatura ambiente durante 16 h antes de la adición de una solución saturada acuosa de carbonato ácido sódico (5 ml). Después de otra agitación vigorosa durante 15 min, la mezcla de reacción se diluyó con diclorometano (40 ml) y agua (20 ml). La fase orgánica se separó y la fase acuosa se extrajo de nuevo con diclorometano (20 ml). Las fases orgánicas combinadas se lavaron con agua, se secaron (Na_2SO_4) y se evaporaron a sequedad, dando el intermedio Boc-protegido.

A una solución del intermedio Boc-protegido en acetato de etilo (6 ml) se le añadió ácido clorhídrico concentrado (2 ml) y la mezcla de reacción se agitó a temperatura ambiente durante 25 min. Después, se añadió una solución saturada acuosa de carbonato ácido sódico (30 ml) para ajustar la mezcla de

reacción a pH 8. Después de agitar durante 10 min más, la mezcla de reacción se diluyó con acetato de etilo (30 ml) y la fase orgánica se separó. La fase acuosa se extrajo de nuevo con acetato de etilo (2 x 30 ml) y las fases orgánicas combinadas se lavaron con una solución de NaCl, se secaron (Na_2SO_4) y se concentraron al vacío. La purificación dio el compuesto del título (133 mg).

Ejemplo 107: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[4-(trifluorometil)pirimidin-2-il]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de 1-[5-(trifluorometil)pirid-2-il]piperazina (6,4 g, 28,0 mmol), (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 1-(5-(trifluorometil)-2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 15 g, 19 mmol) y 2-piperazin-1-il-4-(trifluorometil)pirimidina (4,5 g, 19 mmol) en diclorometano (150 ml) se le añadió en porciones triacetoxiborohidruro sódico (6,0 g, 28 mmol). La mezcla de reacción se agitó a temperatura ambiente durante 40 h, antes de que se añadiera una solución acuosa de carbonato ácido sódico. Después de 15 min, las fases se separaron y la fase acuosa se extrajo de nuevo con diclorometano (3 x 150 ml). Los extractos orgánicos combinados se secaron ($MgSO_4$) y se concentraron al vacío, dando el intermedio Boc-protegido en forma de una espuma blanca.

A una solución enfriada del intermedio Boc-protegido (68 g, 62 mmol) en acetato de etilo (250 ml) se le añadió ácido clorhídrico concentrado (80 ml). La mezcla de reacción se agitó durante 21 min antes de que se le añadiera agua (300 ml) y las fases se separaron. Después, la fase acuosa se extrajo con diclorometano (3 x 250 ml). Las fases orgánicas combinadas se lavaron con carbonato ácido sódico saturado acuoso, se secaron ($MgSO_4$) y se concentraron al vacío. El residuo se disolvió en acetonitrilo caliente (150 ml) y se precipitó un sólido. El sólido se lavó con acetonitrilo y se secó al vacío, dando el compuesto del título en forma de un sólido blanco (25,3 g, 51%).

Ejemplo 113: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[5-(trifluorometil)piridin-2-il]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

Una solución de 1-[5-(trifluorometil)pirid-2-il]piperazina (6,4 g, 28,0 mmol) y (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 1-(5-(trifluorometil)-2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 19,5 g, 25,1 mmol) en diclorometano (200 ml) se agitó durante 30 min a temperatura ambiente. Se añadió en porciones triacetoxiborohidruro sódico (7,9 g, 37,5 mmol) durante 3 min y la mezcla de reacción se agitó durante 18 h a temperatura ambiente. Se añadió en porciones una solución saturada de carbonato ácido sódico (200 ml) y la mezcla de reacción se agitó durante 20 min. Las fases se separaron y la fase acuosa se

extrajo de nuevo con diclorometano (2 x 200 ml). Las fases orgánicas combinadas se lavaron con agua (200 ml), se secaron (Na_2SO_4) y se concentraron al vacío, dando el intermedio Boc-protegido en forma de una espuma blanca (26,2 g).

A una solución del intermedio Boc-protegido (40 g) en acetato de etilo (210 ml) se le añadió ácido clorhídrico concentrado (70 ml) durante 5 min y la mezcla de reacción se agitó a temperatura ambiente durante 30 min. Se añadió agua (300 ml) y el producto se extrajo con diclorometano (3 x 300 ml). Los extractos orgánicos combinados se lavaron con una solución de carbonato ácido sódico y después se secaron ($MgSO_4$) y se concentraron al vacío, dando el producto bruto en forma de una espuma amarilla (19 g). El residuo bruto se disolvió en metanol caliente (30 ml) y se enfrió lentamente a temperatura ambiente, los sólidos se lavaron con metanol frío, dando el producto en forma de un sólido blanco (9,5 g), se obtuvo un segundo cultivo (5 g) en forma de un sólido blanquecino reduciendo el volumen del filtrado.

Ejemplo 125: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(4-bromofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 170 mg, 0,22 mmol) en diclorometano (2 ml) se le añadieron clorhidrato de 1-(4-bromofenil)-

piperazina (91,0 mg, 0,33 mmol) y trietilamina (60 µl). La mezcla de reacción se agitó a temperatura ambiente durante 1 h antes de la adición de triacetoxiborohidruro sódico (93 mg, 0,44 mmol). Después, la mezcla de reacción se agitó durante 18 h más. Se añadieron diclorometano (5 ml) y agua (3 ml), seguido de agitación vigorosa durante 30 min, y la mezcla de reacción se filtró a través de una frita hidrófoba. La fase orgánica se separó y se concentró en una corriente de nitrógeno. Al residuo se le añadió cloruro de hidrógeno (4 N en dioxano, 2 ml) antes de agitarse vigorosamente durante 15 min y de concentrarse en una corriente de nitrógeno durante 40 min. Se añadió una mezcla de trietilamina y diclorometano (1:5, 2 ml) y la solución resultante se concentró en una corriente de nitrógeno. El residuo se disolvió en acetonitrilo (900 µl) y se filtró antes de la purificación, dando la sal *bis*-TFA del compuesto del título en forma de un sólido blanquecino (55 mg).

Ejemplo 126: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[4-(trifluorometil)fenil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 170 mg, 0,22 mmol) en diclorometano (2 ml) se le añadió 1-(4-trifluorometilfenil)piperazina (75,5 mg, 0,33 mmol). La mezcla de reacción se agitó durante 1 h a temperatura ambiente antes de la adición de triacetoxiborohidruro sódico (93 mg, 0,44

mmol). Después, la mezcla de reacción se agitó durante 18 h más. Se añadieron diclorometano (5 ml) y agua (3 ml), seguido de agitación vigorosa durante 30 min y la mezcla de reacción se filtró a través de una frita hidrófoba. La fase orgánica se separó y se concentró en una corriente de nitrógeno. Al residuo se le añadió cloruro de hidrógeno (4 N en dioxano, 2 ml) antes de agitarse vigorosamente durante 15 min y de concentrarse en una corriente de nitrógeno durante 40 min. Se añadió una mezcla de trietilamina y diclorometano (1:5, 2 ml) y la solución resultante se concentró en una corriente de nitrógeno. El residuo se disolvió en acetonitrilo (900 µl) y se filtró antes de la purificación, dando la sal *bis*-TFA del compuesto del título en forma de un sólido blanquecino (63 mg).

Ejemplo 127: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(2,4-difluorofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

El compuesto del título se preparó usando el procedimiento descrito en el Ejemplo 126, sustituyendo 1-(4-trifluorometilfenil)piperazina con 1-(2,4-difluorofenil)piperazina (65 mg, 0,33 mmol), dando el compuesto deseado (49 mg).

Ejemplo 130: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(3,5-diclorofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

El compuesto del título se preparó usando el procedimiento descrito en el Ejemplo 126, sustituyendo 1-(4-trifluorometilfenil)piperazina con 1-(3,5-

diclorofenil)piperazina (76 mg, 0,33 mmol), dando el compuesto deseado (58 mg).

Ejemplo 135: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(2-etilfenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

El compuesto del título se preparó usando el procedimiento descrito en el Ejemplo 126, sustituyendo 1-(4-trifluorometilfenil)piperazina con 1-(2-etilfenil)piperazina (62 mg, 0,33 mmol), dando el compuesto deseado (51 mg).

Ejemplo 147: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[(1*S*)-1-metil-2-piridin-3-iletil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo - sal TFA

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo) (Preparación 152, 600 mg, 0,795 mmol) en tetrahidrofurano (9 ml) a 0ºC se le añadió 9-BBN (solución 0,5 M en tetrahidrofurano, 4,3 ml, 2,12 mmol) durante 20 minutos y la mezcla resultante se dejó calentar a temperatura ambiente con agitación durante 3 horas. Se añadió carbonato potásico (440 mg, 3,2 mmol) y la mezcla de reacción se agitó durante 15 minutos. Una solución de cloruro de (1,1'-*bis*(difenilfosfino)ferroceno)paladio (II) (130 mg, 0,16 mmol) y 3-yodopiridina (326 mg, 1,59 mmol) en *N*,*N*-dimetilformamida anhidra (12 ml) se desgasificó y

se añadió a la mezcla de reacción, dando una solución de color rojo oscuro. La mezcla de reacción se calentó en atmósfera de nitrógeno a 50ºC durante 10 horas. Después de una hora, la solución se volvió de color naranja pálido y después de diez horas era de color pardo/rojo oscuro. La reacción se concentró al vacío y el residuo se disolvió en diclorometano (400 ml), se lavó con agua (2 x 200 ml), se secó (Na_2SO_4) y se concentró al vacío. El producto bruto se purificó dos veces por cromatografía sobre un cartucho Biotage® (sílice, 90 g) eluyendo con acetato de etilo:hexano (de 1:9 a 1:1). Las fracciones puras se concentraron al vacío, dando el intermedio en forma de una espuma blanquecina (200 mg, 29%). El intermedio se trató con cloruro de hidrógeno (solución 4 M en dioxano, 2 ml) y la mezcla resultante se agitó durante 30 minutos antes de que la mezcla se concentrase por evaporación. El residuo se trató con trietilamina (al 20% v/v en diclorometano, 2 ml), se concentró al vacío y el residuo se recogió en acetonitrilo (0,9 ml) y se filtró. El producto bruto se purificó por HPLC sobre una columna C18 Magellen 5µ, de 150 x 21,2 mm a 40ºC eluyendo con TFA (solución acuosa al 0,1%):acetonitrilo (95:5 durante 3 minutos caudal 20 ml/min, después a 2:98 durante 15 minutos caudal 23 ml/min, después 2:98 durante 4 minutos caudal 25 ml/min). Las fracciones puras se combinaron y se concentraron al vacío, dando el producto del título en forma de la sal del ácido mono-trifluoroacético en forma de un sólido blanco (35 mg, 7%).

Ejemplo 210: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-((1*R*)-1-metil-2-(4-

[4-(trifluorometil)-2-pirimidinil]-1-piperazinil}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidro-1-naftalenilo - sal TFA

A (2*S*,3*aR*,9*bR*)-9*b*-[(*terc*-butoxicarbonil)oxi]-6-cloro-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-((1*R*)-1-metil-2-{4-[4-(trifluorometil)-2-pirimidinil]-1-piperazinil}etil)-1,2,4a,5,6,7,8,8*a*-octahidro-1-naftalenil]-3-*terc*-butilo (Preparación 187, 587 mg, 0,59 mmol) en acetato de etilo (10 ml) a temperatura ambiente se le añadió ácido clorhídrico concentrado (2 ml). La mezcla se agitó vigorosamente durante 30 min y después se vertió cuidadosamente en bicarbonato sódico saturado acuoso (30 ml). La mezcla se diluyó con acetato de etilo (50 ml) y las dos fases se separaron. La fase orgánica se lavó con agua (20 ml) y salmuera (20 ml) antes de secarse ($MgSO_4$), filtrarse y evaporarse al vacío. El residuo se purificó por HPLC preparativa usando una columna Phenomenex LUNA 2 (columna de sílice C_{18} de 5µm, 21,2 x 150 mm, temperatura 40°C), eluyendo con un gradiente de acetonitrilo:ácido trifluoroacético acuoso al 0,1% (30:70 durante 14 min, después 90:10 durante 4 min y después 30:70 durante 2 min), a un caudal de 20 ml/min y detección UV a 220 nm. La sal TFA del compuesto del título se obtuvo en forma de un sólido amarillo pálido (211 mg, 39%).

Ejemplo 211: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-((1*R*)-1-metil-2-{4-[5-(trifluorometil)-2-piridinil]-1-piperazinil}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidro-1-naftalenilo - sal TFA

A una solución de (2*S*,3*aR*,9*bR*)-9*b*-[(*terc*-butoxicarbonil)oxi]-6-cloro-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-((1*R*)-1-metil-2-{4-[5-(trifluorometil)-2-piridinil]-1-piperazinil}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidro-1-naftalenil]-3-*terc*-butilo (Preparación 188, 660 mg, 0,65 mmol) en acetato de etilo (10 ml) a temperatura ambiente se le añadió ácido clorhídrico concentrado (2 ml). La mezcla se agitó vigorosamente durante 30 min y después se vertió cuidadosamente en bicarbonato sódico saturado acuoso (30 ml). La mezcla se diluyó con acetato de etilo (50 ml) y las dos fases se separaron. La fase orgánica se lavó con agua (20 ml) y salmuera (20 ml) antes de secarse ($MgSO_4$), filtrarse y evaporarse al vacío. El residuo se purificó por HPLC preparativa usando una columna Phenomenex LUNA 2 (columna de sílice C_{18} de 5 µm, 21,2 x 150 mm, temperatura 40ºC), eluyendo con un gradiente de acetonitrilo:ácido trifluoroacético acuoso al 0,1% (30:70 durante 14 min, después 90:10 durante 4 min y después 30:70 durante 2 min), a un caudal de 20 ml/min y detección UV a 220 nm. La sal TFA del compuesto del título se obtuvo en forma de un sólido amarillo pálido (220 mg, 36%).

Ejemplo 212: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-((1*R*)-2-{4-[*bis*(4-fluorofenil)metil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-

octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 170 mg, 0,22 mmol) en diclorometano (2 ml) se le añadió 1-(4,4'-difluorobenzohidril)piperazina (94,6 mg, 0,33 mmol). La mezcla de reacción se agitó durante 1 h a temperatura ambiente antes de la adición de triacetoxiborohidruro sódico (93 mg, 0,44 mmol). Después, la mezcla de reacción se agitó durante 18 h más. Se añadieron diclorometano (5 ml) y agua (3 ml), seguido de agitación vigorosa durante 30 min y la mezcla de reacción se filtró a través de una frita hidrófoba. La fase orgánica se separó y se concentró en una corriente de nitrógeno. Al residuo se le añadió cloruro de hidrógeno (4 N en dioxano, 2 ml) antes de agitarse vigorosamente durante 15 min y de concentrarse en una corriente de nitrógeno durante 40 min. Se añadió una mezcla de trietilamina y diclorometano (1:5, 2 ml) y la solución resultante se concentró en una corriente de nitrógeno. El residuo se disolvió en acetonitrilo (900 µl) y se filtró antes de la purificación, dando la sal *bis*-TFA del compuesto del título en forma de un sólido blanquecino (45 mg).

Ejemplo 213: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[(1*R*)-2-[4-(5-cloropirimidin-2-il)piperazin-1-il]-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 550 mg, 0,71 mmol) y 5-cloro-2-piperazin-1-ilpirimidina (Preparación 197, 200 mg, 1 mmol) en

diclorometano (8 ml) se le añadió triacetoxiborohidruro sódico (220 mg, 1 mmol). La mezcla de reacción se agitó a temperatura ambiente durante 18 h antes de la adición de carbonato ácido sódico saturado acuoso (5 ml). A la agitación vigorosa durante 20 min le siguió la separación de las fases usando un cartucho de filtro equipado con una frita hidrófoba. El filtrado se evaporó en una corriente de nitrógeno, dando el intermedio Boc-protegido (800 mg, 0,83 mmol).

A una solución del intermedio Boc-protegido (800 mg) en acetato de etilo (7,5 ml) se le añadió ácido clorhídrico concentrado (2,5 ml). La mezcla de reacción se agitó a temperatura ambiente durante 25 min antes de que se le añadieran carbonato ácido sódico sólido y una solución saturada acuosa de carbonato ácido sódico para ajustar la mezcla de reacción a pH 5. La mezcla se extrajo con diclorometano (2 x 20 ml) y las fases orgánicas combinadas se secaron (Na_2SO_4) y se concentraron al vacío. El residuo se purificó, dando el compuesto del título (200 mg). La base libre se obtuvo disolviendo en diclorometano y agitando con una solución acuosa de carbonato ácido sódico. Las fases se separaron usando un cartucho de filtro hidrófobo y se concentraron, dando el compuesto del título.

Ejemplo 214: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{(1*R*)-2-[4-(5-bromopirimidin-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-

c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 150 mg, 0,19 mmol) en diclorometano (2,5 ml) se le añadieron 5-bromo-2-piperazin-1-ilpirimidina (61 mg, 0,25 mmol) y triacetoxiborohidruro sódico (65 mg, 0,3 mmol). La mezcla de reacción se agitó durante 22 h y se le añadió carbonato ácido sódico saturado acuoso seguido de agitación vigorosa adicional durante 30 min. Las fases orgánica y acuosa se separaron usando un cartucho de filtro hidrófobo y el filtrado se concentró en una corriente de nitrógeno, dando el intermedio Boc-protegido.

Al intermedio Boc-protegido se le añadió cloruro de hidrógeno (4 N en dioxano, 2,5 ml) y la solución resultante se agitó a temperatura ambiente durante 25 min. La mezcla de reacción se concentró en una corriente de nitrógeno y se inactivó con una mezcla de trietilamina y diclorometano (2:3, 2 ml). La mezcla se concentró de nuevo en una corriente de nitrógeno. El residuo se diluyó con diclorometano (5 ml) y agua (5 ml) y las fases se separaron usando una frita hidrófoba. El filtrado se concentró en una corriente de nitrógeno y se purificó, dando el compuesto del título. La base libre se disolvió en diclorometano, se agitó con carbonato ácido sódico saturado acuoso y se filtró a través de una frita hidrófoba, dando el compuesto del título (51 mg).

Ejemplo 215: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{(1*R*)-2-[4-(6-cloro-1,3-benzotiazol-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3a*R*,9b*R*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3a*H*)-dicarboxilato de 2-{(1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4a,5,6,7,8,8a-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 150 mg, 0,19 mmol) en diclorometano (2,5 ml) se le añadieron 6-cloro-2-piperazino-1,3-benzotiazol (63 mg, 0,25 mmol, disponible en el mercado, Maybridge) y triacetoxiborohidruro sódico (65 mg, 0,3 mmol). La mezcla de reacción se agitó durante 22 h y se le añadió carbonato ácido sódico saturado acuoso seguido de agitación vigorosa durante 30 min. La separación de las fases se consiguió filtrando la solución a través de un cartucho de filtro hidrófobo y los filtrados se concentraron en una corriente de nitrógeno, dando el intermedio Boc-protegido.

Al intermedio Boc-protegido se le añadió cloruro de hidrógeno (4 N en dioxano 2,5 ml). La mezcla de reacción se agitó a temperatura ambiente durante 25 min antes de concentrarse en una corriente de nitrógeno durante 20 min y de inactivarse con una mezcla de trietilamina y diclorometano (2:3, 2 ml). La mezcla se concentró de nuevo en una corriente de nitrógeno y el residuo se disolvió en diclorometano (5 ml) y agua (5 ml). Las fases se separaron usando una frita hidrófoba y el filtrado se concentró en una corriente de nitrógeno y se purificó, dando el compuesto del título. La base libre se obtuvo disolviendo en diclorometano y agitando con carbonato ácido sódico saturado acuoso. Después, esta solución se filtró a través de una frita hidrófoba y el filtrado se concentró, dando el compuesto del título (58 mg).

Ejemplo 216: (2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3a,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-((1*R*)-2-{4-[(3,4-diclorofenil)metil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160,150 mg, 0,19 mmol) y sal clorhidrato de 1-(3,4-diclorofenil)piperazina (67 mg, 0,25 mmol) en diclorometano (2,5 ml) se le añadieron trietilamina (50 µl) y triacetoxiborohidruro sódico (65 mg, 0,3 mmol). La mezcla de reacción se agitó a temperatura ambiente durante 20 h antes de que se le añadiera carbonato ácido sódico saturado acuoso (3 ml), seguido de agitación vigorosa adicional durante 30 min. La mezcla de reacción se filtró a través de un cartucho de filtro hidrófobo y el filtrado se evaporó en una corriente de nitrógeno, dando el intermedio Boc-protegido.

El intermedio Boc-protegido se disolvió en cloruro de hidrógeno (4 N en dioxano, 2,5 ml) y se agitó a temperatura ambiente durante 25 min. La mezcla de reacción se concentró en una corriente de nitrógeno (40ºC, 25 min) y se inactivó con una mezcla de trietilamina y diclorometano (2:3, 2 ml). La mezcla se concentró de nuevo en una corriente de nitrógeno y los residuos se repartieron entre diclorometano (5 ml) y carbonato ácido sódico saturado acuoso. Las fases combinadas se filtraron a través de un cartucho de filtro hidrófobo y los filtrados se concentraron en una corriente de nitrógeno. La purificación dio el compuesto del título (44 mg).

Ejemplo 217: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-((1*R*)-1-metil-2-{4-[5-(trifluorometil)pirimidin-2-il]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 170 mg, 219 μmol) y sal TFA de 2-piperazin-1-il-5-(trifluorometil)pirimidina (Preparación 198, 68 mg, 200 μmol) en diclorometano (4 ml) se le añadió triacetoxiborohidruro sódico (93 mg, 440 mmol). La mezcla de reacción se agitó durante una noche y se le añadió agua (5 ml). Después de más agitación, las fases se separaron y la fase orgánica se evaporó a sequedad en una corriente de nitrógeno. El residuo se disolvió en acetato de etilo (2 ml) y se le añadió ácido clorhídrico concentrado (1 ml). Después de agitar durante 20 min, se añadieron carbonato ácido sódico saturado acuoso (20 ml) y acetato de etilo (20 ml) y la mezcla se agitó. La fase orgánica se separó, se secó (Na_2SO_4) y se evaporó antes de la purificación, dando el compuesto del título (37 mg) en forma de una sal TFA.

Ejemplo 218: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-((1*R*)-2-{4-[(4-clorofenil)oxi]piperidin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 141, 60 mg, 0,11 mmol) y 4-[(4-clorofenil)oxi]piperidina (Preparación 200, 25 mg, 0,1 mmol) se le añadieron diclorometano (2 ml) y triacetoxiborohidruro sódico (35 mg, 0,16 mmol), seguido de trietilamina (0,02 ml, 0,17 mmol). La mezcla de reacción se agitó a temperatura ambiente durante 17 h, antes de diluirse con diclorometano (5 ml) y carbonato ácido sódico saturado acuoso (3 ml). La mezcla de reacción se agitó vigorosamente y las fases se separaron usando un cartucho de filtro hidrófobo. El filtrado se concentró en una corriente de nitrógeno y se purificó, dando el compuesto del título (26 mg).

Preparación 4: 1-(ciclopentilcarbonil)piperazina.

Se disolvió ácido ciclopentanocarboxílico (5,0 g, 44 mmol) en cloroformo (50 ml). Se añadió gota a gota cloruro de oxalilo (4,6 ml, 52,5 mmol) en atmósfera de nitrógeno y se agitó a temperatura ambiente durante 30 min. Después, la mezcla de reacción se calentó a reflujo durante 1 h, antes de concentrarse al vacío, dando cloruro de ciclopentanocarbonilo en forma de un líquido amarillo claro.

Se disolvió piperazina hexahidrato (8,55 g, 44,0 mmol) en etanol absoluto (50 ml) y después se calentó a reflujo durante 10 min. Se añadió gota a gota cloruro de ciclopentanocarbonilo (5,83 g, 44 mmol) a 65ºC y la mezcla de reacción se calentó a reflujo durante 30 min y después se agitó a temperatura ambiente durante 18 h. La mezcla de reacción se enfrió, se filtró y el filtrado se concentró al vacío, dando ~20 ml de una solución. El concentrado

se enfrió y después se filtró de nuevo. Se añadió cloruro de hidrógeno etanólico a las aguas madre y la mezcla de reacción se concentró, dando un sólido blanco, que se disolvió en agua (15 ml). La solución se basificó a pH 14 y el producto se extrajo con diclorometano (7 x 50 ml). Los extractos se secaron (Na_2SO_4) y se concentraron, dando el compuesto del título en forma de un residuo amarillento, que se destiló, dando el producto (1,28 g, 7,0 mmol, 16%)

Preparación 10: 4-(8-azabiciclo[3.2.1]oct-3-ilsulfanil)fenil metil éter

A una solución agitada de 3-[(4-metoxifenil)sulfanil]-8-azabiciclo[3.2.1]octano-8-carboxilato de 2,2,2-tricloroetilo (Preparación 11, 52,7 g, 0,12 mol) en tetrahidrofurano en atmósfera de nitrógeno se le añadieron polvo de cinc (20 g) e hidrogenofosfato potásico (1 M, 125 ml). La mezcla de reacción se agitó durante 2 h a temperatura ambiente antes de añadirse más polvo de cinc (30 g) seguido de calentamiento en un baño de vapor durante 30 min. La mezcla de reacción se enfrió a temperatura ambiente y se diluyó con agua (1 l). Se añadió carbonato sódico para ajustar el pH a 10. La mezcla de reacción se filtró y el filtrado se separó y después se extrajo con diclorometano. Los extractos orgánicos combinados se secaron (Na_2SO_4) y se concentraron al vacío, dando el compuesto del título en forma de un aceite amarillo (26,0 g, 84%). El aceite se purificó por cromatografía en columna sobre gel de sílice (350 g) eluyendo con una solución de metanol:diclorometano:amoniaco 0,88 (10:90:1), dando el producto en forma de un aceite que cristalizó tras el reposo (13 g, 42%). El sólido se purificó de nuevo agitando en éter y filtrando, dando un sólido amarillo claro (9 g, 29%).

Preparación 11: 3-[(4-metoxifenil)sulfanil]-8-azabiciclo[3.2.1]octano-8-carboxilato de 2,2,2-tricloroetilo

A una solución de metil 4-[(8-metil-8-azabiciclo[3.2.1]oct-3-il)sulfanil]fenil éter (Preparación 12, 43,7 g, 0,16 mol) en benceno (400 ml) agitada en atmósfera de nitrógeno se le añadieron carbonato potásico (24,3 g) y cloroformiato de tricloroetilo (24,5 ml, 0,176 mol). Los reactivos se calentaron a reflujo durante 2 h antes de enfriar, filtrar y lavar los sólidos recogidos con benceno. Las aguas madre se concentraron al vacío, dando el producto bruto en forma de un aceite. El producto bruto se agitó con acetato de etilo:hexano (5:95), precipitando el compuesto del título en forma de un sólido blanco (51,5 g, 76%).

Preparación 12: Metil 4-[(8-metil-8-azabiciclo[3.2.1]oct-3-il)sulfanil]fenil éter

A una solución de 8-metil-8-azabiciclo[3.2.1]oct-3-il-sulfato de metilo (Preparación 13, 35 g, 0,16 mol) en tetrahidrofurano (300 ml) se le añadió con refrigeración a 0ºC hidruro sódico (dispersión al 60% en aceite, 7 g, 0,17 mol). Después de que se completara la adición, se añadió 4-metoxibencenotiol (23,8 g, 0,16 mol) en tetrahidrofurano (300 ml). La mezcla de reacción se calentó a reflujo durante 2 h y después se enfrió a 30ºC y se añadió agua (250 ml). El tetrahidrofurano se retiró al vacío, se añadió diclorometano y las fases se separaron. La fase orgánica se lavó con agua, hidróxido sódico (solución 1 M), agua y salmuera saturada antes de secarse (Na_2SO_4). Los extractos orgánicos se concentraron al vacío, dando el compuesto del título (43,7 g, 100%).

Preparación 13: 8-Metil-8-azabiciclo[3.2.1]oct-3-il-sulfato de metilo

A una solución de 8-metil-8-azabiciclo[3.2.1]octan-3-ol (299 g, 2,12 mol) en diclorometano (3,5 l) se le añadió trietilamina (445 ml, 3,2 mol) y la mezcla de reacción se enfrió a -40ºC. Se añadió gota a gota cloruro de metanosulfonilo (293 g, 2,55 mol) durante 90 min y después la mezcla de reacción se dejó

calentar a temperatura ambiente. Se añadió agua (1 l) y el extracto orgánico se lavó con hidróxido sódico (0,5 M), agua y una solución saturada de cloruro sódico. Los extractos orgánicos se secaron (Na_2SO_4) y se concentraron al vacío, dando un sólido amarillo (262 g, 56%). El sólido se recristalizó en hexano, dando un primer cultivo del compuesto del título en forma de cristales amarillos claros (126,5 g, 27%), seguido de un segundo cultivo (76,1 g, 16%).

Preparación 16: 2,5-dimetil-3-piperazin-1-ilpirazina

A una solución de 2,5-dimetil-3-[4-(fenilmetil)piperazin-1-il]pirazina (Preparación 17, 1,14 g, 4,04 mmol) en metanol (80 ml) se le añadió formiato amónico (1,27 g, 20,2 mmol) seguido de paladio (al 10% p/p sobre carbono, 0,17 g) en una atmósfera de nitrógeno. La mezcla de reacción se calentó a reflujo, y después de 2,5 h, se añadieron más formiato amónico (0,64 g, 10,1 mmol) y paladio (0,06 g). La mezcla de reacción se filtró a través de Celite®, se lavó con metanol y se concentró al vacío. El producto bruto se purificó por cromatografía ultrarrápida usando gel de sílice eluyendo con metanol:diclorometano (8:92 y después 10:90) y después una solución de metanol:diclorometano:amoniaco 0,88 (10:90:1). El compuesto del título se obtuvo en forma de un sólido blanco (0,35 g, 45%).

Preparación 17: 2,5-dimetil-3-[4-(fenilmetil)piperazin-1-il]pirazina

Se mezclaron 3-cloro-2,5-dimetilpirazina (1,0 g, 7,0 mmol) y *N*-bencilpiperazina (3,7 ml, 21,0 mmol) en atmósfera de nitrógeno y se calentaron a 125ºC durante 18 h. Se añadió carbonato ácido sódico saturado acuoso y el producto se extrajo con cloroformo. Los extractos orgánicos combinados se secaron (Na_2SO_4) y se concentraron al vacío, dando un aceite amarillo. El producto bruto se purificó por cromatografía ultrarrápida usando gel de sílice

eluyendo con metanol:cloroformo (2,5:97,5), dando el producto puro en forma de un aceite amarillo (1,14 g, 58%).

Preparación 18: 2-metil-3-piperazin-1-ilquinoxalina

A una solución de 2-metil-3-[4-(fenilmetil)piperazin-1-il]quinoxalina (Preparación 19, 1,68 g, 5,28 mmol) en metanol (106 ml) se le añadió formiato amónico (1,66 g, 26,4 mmol) seguido de paladio (al 10% p/p sobre carbono, 0,25 g) en una atmósfera de nitrógeno. Después de 12,5 h, se añadieron más formiato amónico (0,83 g, 13,2 mmol) y paladio (0,12 g). La mezcla de reacción se filtró a través de Celite® y se evaporó hasta un aceite amarillo. El producto bruto se purificó por cromatografía ultrarrápida usando gel de sílice eluyendo con metanol:diclorometano (5:95 y después 10:90). El compuesto del título se obtuvo en forma de un aceite amarillo pálido que cristalizó tras el reposo (0,46 g, 38%).

Preparación 19: 2-metil-3-[4-(fenilmetil)piperazin-1-il]quinoxalina

Se mezclaron 2-cloro-3-metilquinoxalina (1,0 g, 5,6 mmol) y *N*-bencilpiperazina (2,9 ml, 16,8 mmol) y se calentaron a 125ºC durante 18 h. Se añadió carbonato ácido sódico saturado acuoso y el producto se extrajo con cloroformo. Los extractos orgánicos combinados se secaron (Na_2SO_4) y se concentraron al vacío, dando un aceite rojo oscuro. El producto bruto se purificó por cromatografía ultrarrápida usando gel de sílice eluyendo con metanol:diclorometano (15:85), dando el producto puro en forma de un aceite rojo que se solidificó tras el reposo (1,63 g, 94%).

Preparación 15: sal clorhidrato de 3-cloro-2-piridinil 3-piperidinil éter

A una solución agitada de 3-hidroxipiperidina racémica (1,12 g, 11,1 mmol) en tetrahidrofurano (20 ml) en atmósfera de nitrógeno se le añadió

hidruro sódico (dispersión al 60% en aceite, 0,44 g, 11,1 mmol). La mezcla de reacción se agitó durante 45 min antes de añadirse 2,3-cloropiridina (1,64 g, 11,1 mmol) y de calentarse a reflujo durante 48 h. La mezcla de reacción se enfrió a temperatura ambiente, se inactivó con agua (5 ml) y se extrajo con acetato de etilo. Después, los extractos orgánicos se lavaron con agua, cloruro amónico saturado acuoso y salmuera antes de lavarse de nuevo con cloroformo. Los extractos orgánicos combinados se secaron ($MgSO_4$) y se concentraron al vacío, dando un aceite naranja bruto (2,5 g). El producto bruto se cromatografió eluyendo con cloroformo:metanol (de 15:1 a 8:1), dando un aceite amarillo pálido (2,3 g). Al producto puro se le añadió una solución de cloruro de hidrógeno (4 M en dioxano, 5 ml), dando la sal clorhidrato después de la concentración en forma de un sólido amarillo pegajoso (2,27 g, 82%).

Preparación 21: sal clorhidrato de (+)-3,11-diazatriciclo[7.3.1.$0^{2,7}$]trideca-2,4,6-trieno

Se sometió 3,11-diazatriciclo[7.3.1.$0^{2,7}$]trideca-2,4,6-trieno-11-carboxilato de 1,1-dimetiletilo racémico (Preparación 22, 0,47 g) a HPLC preparativa quiral usando una columna Chiracel AD de 5 cm x 25 cm, eluyendo con heptano:alcohol isopropílico (95:5) a un caudal de 120 ml/min durante 20 min. Los enantiómeros se detectaron a 250 nm y se demostró que tenían una pureza quiral de >98% de exceso enantiomérico, el primer enantiómero en eluir se denominó enantiómero 1 y el segundo se denominó enantiómero 2.

El enantiómero 2 de 3,11-diazatriciclo[7.3.1.$0^{2,7}$]trideca-2,4,6-trieno-11-carboxilato de 1,1-dimetiletilo se disolvió en acetato de etilo (5 ml) y se trató con ácido clorhídrico (3 M, 2 ml) y después se calentó a reflujo durante 18 h. La mezcla de reacción se enfrió y se filtró y el precipitado blanco se lavó con

acetato de etilo y hexano. La sal clorhidrato del enantiómero 2 se obtuvo en forma de un polvo blanco (0,12 g, 82%).

Preparación 22: 3,11-diazatriciclo[7.3.1.$0^{2,7}$]trideca-2,4,6-trieno-11-carboxilato de 1,1-dimetiletilo

Una solución de 11-(fenilmetil)-3,11-diazatriciclo[7.3.1.$0^{2,7}$]trideca-2,4,6-trieno (Preparación 23, 0,74 g, 2,81 mmol), formiato amónico (6,0 g, 95 mmol) e hidróxido de paladio (al 10% en peso sobre carbono, 0,21 g) en metanol (30 ml) en atmósfera de nitrógeno se calentó a reflujo durante 1 h. La mezcla de reacción se filtró a través de una capa de Celite® y la capa se lavó con metanol caliente. Las fases orgánicas combinadas se concentraron al vacío, se añadió diclorometano (100 ml) y la mezcla se filtró y después se concentró hasta un aceite. El aceite se disolvió en diclorometano y se añadió dicarbonato de di-*terc*-butilo (0,65 g, 3,09 mmol). La mezcla de reacción se concentró al vacío y se purificó por cromatografía ultrarrápida eluyendo con acetato de etilo, dando el compuesto del título (0,23 g, 30%) y también 3,11-diazatriciclo[7.3.1.$0^{2,7}$]trideca-2,4,6-trieno-11-carbaldehído (0,36 g, 64%).

A 3,11-diazatriciclo[7.3.1.$0^{2,7}$]trideca-2,4,6-trieno-11-carbaldehído (0,36 g, 64%) se le añadieron hidróxido sódico (0,80 g, 20 mmol) en dioxano (7 ml) y agua (3 ml) y la mezcla de reacción se calentó a reflujo durante 9 h. Se añadió más hidróxido sódico (0,40 g, 10 mmol) y la mezcla de reacción se calentó a reflujo durante 9 h más. La mezcla de reacción se enfrió, se diluyó con una solución saturada de carbonato ácido sódico y se extrajo con diclorometano. Los extractos orgánicos se secaron y se filtraron y después se añadió dicarbonato de di-*terc*-butilo (0,39 g, 1,83 mmol) y la mezcla de reacción se agitó durante 2 h. La mezcla de reacción se lavó con salmuera, se secó

(Na_2SO_4) y se concentró, dando un aceite que se purificó por cromatografía ultrarrápida eluyendo con acetato de etilo, dando el producto del título (0,24 g).

De esta manera, el compuesto del título (0,47 g, 61%) se obtuvo por combinación de los dos componentes descritos.

Preparación 23: 11-(Fenilmetil)-3,11-diazatriciclo[7.3.1.$0^{2,7}$]trideca-2,4,6-trieno

A una solución de 3-azatriciclo[7.2.1.$0^{2,7}$]dodeca-2,4,6-trieno-10,11-diol (Preparación 24, 1,16 g, 6,07 mmol) en etanol (40 ml) se le añadió peryodato sódico (1,35 g, 6,07 mmol) en agua (20 ml), produciendo una suspensión amarilla. Después de 15 min, se añadieron agua y acetato de etilo y las fases se separaron y la fase acuosa se lavó con acetato de etilo (4 x 50 ml) y después con diclorometano. Los extractos orgánicos combinados se secaron (Na_2SO_4), dando un aceite naranja. El aceite se diluyó con dicloroetano (50 ml) y se añadió bencilamina (0,65 g, 6,07 mmol) seguido de triacetoxiborohidruro sódico (4,12 g, 19,4 mmol). Después de 7 h, se añadieron una solución saturada de carbonato ácido sódico (75 ml) y acetato de etilo (75 ml) y la mezcla de reacción se agitó durante 20 min. Las fases se separaron y la fase acuosa se extrajo con acetato de etilo (2 x 50 ml). Los extractos orgánicos combinados se lavaron con agua y salmuera y después se secaron (Na_2SO_4) y se concentraron al vacío, dando el producto bruto. La purificación por cromatografía ultrarrápida produjo el compuesto del título en forma de un aceite amarillo claro (0,80 g, 50%).

Preparación 24: 3-azatriciclo[7.2.1.$0^{2,7}$]dodeca-2,4,6-trieno-10,11-diol

Una mezcla de 3-azatriciclo[7.2.1.$0^{2,7}$]dodeca-2,4,6,10-tetraeno (Preparación 25, 0,96 g, 6,11 mmol), *N*-óxido de trimetilamina dihidrato (0,75 g, 6,73 mmol) y tetróxido de osmio (solución al 2,5% en peso en 2-metil-2-

propanol, 2 µl) en diclorometano (15 ml) se agitó durante 18 h. Se añadió una porción más de tetróxido de osmio (solución al 2,5% en peso en 2-metil-2-propanol, aprox. 1 µl) y la mezcla de reacción se agitó durante 18 h más. La mezcla de reacción se sometió a cromatografía eluyendo con hexano y después con acetato de etilo, dando el compuesto del título en forma de un sólido (1,16 g, 100%).

Preparación 25: 3-azatriciclo[7.2.1.$0^{2,7}$]dodeca-2,4,6,10-tetraeno

A una solución de trifluorometanosulfonato de 3-(ciclopent-3-en-1-ilmetil)-1,2-dihidropiridin-2-ilo (Preparación 26, 3,1 g, 10,1 mmol) en dimetilformamida (20 ml) agitada en atmósfera de nitrógeno se le añadieron 1,3-*bis*(difenilfosfino)propano (0,334 g, 0,8 mmol), trietilamina (1,52 g, 16,6 mmol) y acetato de paladio (II) (0,072 g, 0,32 mmol). La mezcla de reacción se calentó a 100ºC y se agitó durante 18 h. Se añadió trietilamina (1 ml) y la mezcla de reacción se calentó a 110ºC durante 6 h más. La mezcla de reacción se enfrió y se vertió en una solución saturada de salmuera (al 50%, 75 ml) y el producto se extrajo con acetato de etilo (4 x 30 ml). Los extractos orgánicos combinados se lavaron con agua (2 veces), una solución de carbonato ácido sódico y salmuera antes de secarse (Na_2SO_4) y de concentrarse al vacío. El aceite bruto se purificó por cromatografía ultrarrápida eluyendo con acetato de etilo:hexano (15:85), dando un aceite incoloro (1,07 g, 77%).

Preparación 26: trifluorometanosulfonato de 3-(ciclopent-3-en-1-ilmetil)-1,2-dihidropiridin-2-ilo

A una solución de 3-(ciclopent-3-en-1-ilmetil)piridin-2(1*H*)-ona (Preparación 27, 1,9 g, 10,8 mmol) en diclorometano (50 ml) agitada a 0ºC se le añadió anhídrido trifluorometanosulfónico (2,38 ml, 14,1 mmol) y después

2,6-lutidina (2,2 ml, 19 mmol). La mezcla de reacción se dejó calentar a temperatura ambiente y después se agitó durante 1 h. La mezcla de reacción se diluyó con diclorometano y se lavó con agua (2 veces), después con una solución saturada acuosa de carbonato ácido sódico y después con salmuera. El producto bruto se purificó por cromatografía ultrarrápida eluyendo con acetato de etilo:hexano (10:90), dando el producto en forma de un líquido incoloro (3,1 g, 93%).

Preparación 27: 3-(ciclopent-3-en-1-ilmetil)piridin-2(1*H*)-ona

A una dispersión turbia que contenía 3-(ciclopent-3-en-ilmetil)-2-(metiloxi)piridina (Preparación 28, 2,1 g, 11,1 mmol) y yoduro sódico (4,1 g, 27,8 mmol) en acetonitrilo anhidro (25 ml) se le añadió clorotrimetilsilano (3,0 g, 27,8 mmol). Se formó un precipitado blanco que se agitó durante 30 min a temperatura ambiente y después durante 1 h a 70ºC. La mezcla de reacción se enfrió a temperatura ambiente y se añadió agua, seguido de acetato de etilo (200 ml), la fase orgánica se lavó con agua (4 x) y después con una solución de carbonato ácido sódico y salmuera antes de secarse (Na_2SO_4), dando el compuesto del título en forma de un sólido amarillo (1,93 g, 100%).

Preparación 28: 3-(Ciclopent-3-en-ilmetil)-2-(metiloxi)piridina

Se calentaron ciclopent-3-en-il[2-(metiloxi)piridin-3-il]metanona (Preparación 29, 10 g, 49,3 mmol), hidróxido potásico (al 85%, 16,8 g, 0,3 mol) e hidrazina (6,33 g, 198 mmol) en etilenglicol (100 ml) a 180ºC y se agitaron durante 18 h. Se añadió agua y el producto se extrajo con hexano:acetato de etilo (50:50). Los extractos orgánicos combinados se lavaron con salmuera y se concentraron al vacío. El aceite bruto se purificó por cromatografía ultrarrápida

eluyendo con acetato de etilo:hexano (10:90), dando un aceite incoloro (4,75 g, 51%).

Preparación 29: Ciclopent-3-en-il[2-(metiloxi)piridin-3-il]metanona

A 2-bromo-1,3,5-trimetilbenceno (16,9 g, 85 mmol) en tetrahidrofurano (340 ml) en una atmósfera de nitrógeno se le añadió a -78ºC durante 30 min *terc*-butillitio (solución 1,7 M, 100 ml, 170 mmol). Se formó un precipitado amarillo y se agitó durante 1 h a -78ºC. Se añadió 2-(metiloxi)piridina (8,45 g, 77,3 mmol) en tetrahidrofurano (10 ml) y la mezcla de reacción se calentó a 0ºC durante 1 h y después a temperatura ambiente durante 1 h. La mezcla de reacción se enfrió a -70ºC y se añadió *N*-metil-*N*-(metiloxi)ciclopent-3-eno-1-carboxamida (Preparación 30, 12,4 g, 80 mmol) en tetrahidrofurano (20 ml) y la mezcla de reacción se dejó calentar gradualmente a temperatura ambiente durante 18 h. Se añadió carbonato ácido sódico saturado acuoso (250 ml) y la mezcla se agitó durante 20 min, el producto se extrajo con éter dietílico (3 x 100 ml) y los extractos orgánicos combinados se lavaron con agua y después con salmuera y después se secaron (Na_2SO_4) y se concentraron, dando un aceite amarillo (26 g) . El aceite bruto se purificó por cromatografía ultrarrápida usando gel de sílice eluyendo con éter dietílico:hexano (10:90 y después 20:80). El compuesto del título se obtuvo en forma de un aceite incoloro (12,19 g, 75%).

Preparación 30: *N*-metil-*N*-(metiloxi)ciclopent-3-eno-1-carboxamida

A una solución de ácido ciclopent-3-eno-1-carboxílico (80,0 g, 0,71 mol) en diclorometano (300 ml) se le añadió lentamente 1,1'-carbonildiimidazol (127,5 g, 0,78 mol) y la mezcla de reacción se agitó a temperatura ambiente durante 1 h. Se añadió *N,O*-dimetilhidroxilamina (76,7 g, 0,78 mol) y se agitó

durante 18 h a temperatura ambiente. La mezcla de reacción se vertió en agua (300 ml) y se extrajo con diclorometano (100 ml). Los extractos orgánicos se lavaron con ácido clorhídrico (1 N, 2 x 200 ml) y después con salmuera antes de filtrarse a través de lana de algodón, secarse y concentrarse. El producto se purificó por cromatografía ultrarrápida usando gel de sílice eluyendo con diclorometano, dando el compuesto del título (116,78 g, 95%).

Preparación 31: sal clorhidrato de (-)-4,10-diazatriciclo[6.3.1.$0^{2,7}$]dodeca-2,4,6-trieno

Se sometió 10-(fenilmetil)-4,10-diazatriciclo[6.3.1.$0^{2,7}$]dodeca-2,4,6-trieno racémico (Preparación 32, 1,9 g) a HPLC preparativa quiral usando una columna Chiracel AD de 5 cm x 25 cm, eluyendo con heptano:alcohol isopropílico (95:5) a un caudal de 120 ml/min durante 30 min. Los enantiómeros se detectaron a 250 nm y demostraron que tenían una pureza quiral de >98% de exceso enantiomérico, el primer enantiómero en eluir se denominó enantiómero 1 y el segundo se denominó enantiómero 2. Los eluyentes se concentraron, dando el enantiómero 1 (0,9 g) y el enantiómero 2 (0,75 g).

El enantiómero 2 de 10-(fenilmetil)-4,10-diazatriciclo[6.3.1.$0^{2,7}$]dodeca-2,4,6-trieno (0,75 g) se disolvió en metanol (35 ml) y se añadió formiato amónico (4 g) seguido de hidróxido de paladio (al 10% en peso sobre carbono, 0,20 g). La mezcla de reacción se calentó a reflujo durante 2 h, se enfrió y se filtró a través de una capa de Celite®, aclarando con metanol, las soluciones orgánicas combinadas se concentraron al vacío. Se añadió diclorometano y la suspensión resultante se filtró y se concentró, dando un aceite (0,70 g). El aceite se disolvió en metanol y se añadió ácido clorhídrico (3 M, 6 ml). La mezcla se concentró al vacío, dando un sólido que se recristalizó disolviendo

en metanol (20 ml) y añadiendo éter dietílico hasta que la mezcla de reacción fue turbia. La mezcla de reacción se agitó durante 72 h antes de que el sólido se retirase por filtración y se lavase con éter dietílico, dando la sal clorhidrato pura del compuesto del título en forma de un sólido blanco (0,34 g).

Preparación 32: 10-(fenilmetil)-4,10-diazatriciclo[6.3.1.$0^{2,7}$]dodeca-2,4,6-trieno

A una solución de *bis*(*O*-metiloxima) de 3-(fenilmetil)-3-azabiciclo[3.2.1]octano-6,7-dicarbaldehído (Preparación 33, 5,0 g, 15,2 mmol) en dicloroetano (150 ml) se le añadió ácido trifluoroacético (17 ml) y la mezcla de reacción se agitó en atmósfera de nitrógeno a temperatura ambiente durante 20 min. La mezcla de reacción se calentó a reflujo durante 2 h y después se concentró, dando un aceite pardo. Se añadió acetato de etilo (100 ml) y la solución se trató con una solución saturada de carbonato sódico (70 ml) las fases se separaron y la fase orgánica se lavó con salmuera, se secó (Na_2SO_4) y se concentró, dando un aceite (4,0 g). El aceite bruto se purificó por cromatografía ultrarrápida usando gel de sílice eluyendo con acetato de etilo, dando el compuesto del título en forma de un aceite naranja (1,93 g, 51%).

Preparación 33: *bis*(*O*-metiloxima) de 3-(fenilmetil)-3-azabiciclo[3.2.1]octano-6,7-dicarbaldehído

A una solución de 9-(fenilmetil)-9-azatriciclo[5.3.1.$0^{2,6}$]undecano-3,4-diol (Preparación 34, 6,0 g, 21,9 mmol) en dioxano (100 ml) se le añadió peryodato sódico (5,0 g, 23,3 mmol) en agua (50 ml). Se formó una suspensión densa, se añadió agua (50 ml) y la mezcla de reacción se agitó en atmósfera de nitrógeno. Después de que se completara, la mezcla de reacción se diluyó con agua (150 ml) y carbonato sódico saturado (50 ml) y el producto se extrajo con acetato de etilo (2 x 150 ml). Los extractos orgánicos combinados se lavaron

con agua, y después con salmuera antes de secarse (Na_2SO_4) y concentrarse, dando un aceite naranja (6,14 g). Al aceite bruto se le añadieron metanol (75 ml) y agua (75 ml), seguido de clorhidrato de metoxilamina (7,34 g, 87,9 mmol) y acetato sódico (12,62 g, 153,8 mmol). La mezcla de reacción se agitó y después se calentó en un baño de vapor durante aprox. 15 min, dando una solución transparente, y después se agitó a temperatura ambiente durante 18 h. Se añadieron acetato de etilo (100 ml) y una solución de carbonato sódico (100 ml) y las fases se separaron. La fase acuosa se extrajo con acetato de etilo (3 x 50 ml) y los extractos orgánicos combinados se lavaron con salmuera, se secaron (Na_2SO_4) y se concentraron, dando el compuesto del título en forma de un aceite (5,0 g, 69%).

Preparación 34: 9-(Fenilmetil)-9-azatriciclo[5.3.1.$0^{2,6}$]undecano-3,4-diol

Una solución de 9-(fenilmetil)-9-azatriciclo[5.3.1.$0^{2,6}$]undec-3-eno (Preparación 35, 6,7 g, 28,0 mmol), *N*-óxido de *N*-metilmorfolina (3,45 g, 29,45 mmol) y tetróxido de osmio (al 2,5% en peso en 2-metil-2-propanol, 2 µl) en acetona (50 ml) se agitó durante 18 h. Se añadieron florisil e hidrogenosulfito sódico acuoso (4 ml) y la mezcla de reacción se agitó durante 30 min y se filtró. Se añadió metanol (50 ml) y la mezcla de reacción se concentró, dando un aceite que se purificó por cromatografía ultrarrápida eluyendo con acetato de etilo:hexano (50:50), dando un aceite (6,2 g, 80%) que cristaliza después del reposo.

Preparación 35: 9-(fenilmetil)-9-azatriciclo[5.3.1.$0^{2,6}$]undec-3-eno

A una solución agitada de triciclo[5.2.1.$0^{2,6}$]dec-3-eno-8,9-diol (Preparación 36, 6,24 g, 37,6 mmol) en dioxano (100 ml) se le añadió peryodato sódico (8,04 g, 37,6 mmol) en agua (80 ml) y la mezcla de reacción

se agitó vigorosamente durante 45 min. La mezcla de reacción se extrajo con acetato de etilo (4 x 100 ml) y los extractos combinados se lavaron con salmuera, se secaron (Na_2SO_4) y se concentraron al vacío. El aceite bruto (6,1 g, 37,1 mmol) se diluyó con dicloroetano (400 ml) y se añadió bencilamina (3,98 g, 37,1 mmol). Después de 3 min, se añadió triacetoxiborohidruro sódico (25,23 g, 119 mmol) y la mezcla de reacción se agitó a temperatura ambiente durante 18 h. Se añadió una solución saturada de carbonato sódico (200 ml), y después de 30 min las fases se separaron y la fase acuosa se lavó con diclorometano (3 x 50 ml). Los extractos orgánicos combinados se lavaron con salmuera, se filtraron y se concentraron. El aceite amarillo bruto se purificó por cromatografía ultrarrápida eluyendo con acetato de etilo:diclorometano (10:90), dando el compuesto del título en forma de un aceite incoloro (6,7 g, 75%)

Preparación 36: Triciclo[5.2.1.$0^{2,6}$]dec-3-eno-8,9-diol

Una suspensión de triciclo[5.2.1.$0^{2,6}$]deca-3,8-dieno (26,5 g, 0,2 mol), *N*-óxido de trimetilamina dihidrato (22,3 g, 0,2 mol) y tetróxido de osmio (solución al 2,5% en peso en 2-metil-2-propanol, 2 µl) en diclorometano (200 ml) se agitó durante 18 h. Se añadió una porción más de tetróxido de osmio (solución al 2,5% en peso en 2-metil-2-propanol, aprox. 2 µl), se añadieron agua (25 ml) y acetona (50 ml) y la mezcla de reacción se agitó durante 72 h más. Se añadieron piridina (0,5 ml) y acetato de tetrabutilamonio (0,5 g). Se añadieron florisil (10 g) y una solución acuosa de hidrogenosulfito sódico y la mezcla de reacción se agitó durante 20 min. La mezcla de reacción se filtró y el producto se extrajo con diclorometano (3 veces). Los extractos orgánicos combinados se lavaron con agua y salmuera y después se concentraron, dando un aceite. El aceite bruto se purificó por cromatografía ultrarrápida eluyendo con acetato de

etilo:hexano (10:90) y después con acetato de etilo, dando un sólido ceroso (6,5 g, 19%).

Preparación 39: **sal clorhidrato de 3-ciclohexil-3-metilpiperidina**

A una solución de 3-metil-3-fenilpiperidina (500 mg, 2,85 mmol) en metanol (8 ml) se le añadieron ácido clorhídrico concentrado (1 ml) y óxido de platino (IV) (500 mg). La mezcla de reacción se hidrogenó a 344,737 kPa (50 psi) durante 3 h antes de filtrarse a través de Celite® y de concentrarse. El residuo bruto se disolvió en diclorometano, se lavó con carbonato sódico y se concentró, dando un semisólido bruto. El producto bruto se disolvió en éter dietílico (15 ml) y metanol (5 ml) y se añadió cloruro de hidrógeno (1 M en éter dietílico, 30 ml), produciendo un sólido blanco que se filtró, dando el producto puro (0,41 g, 66%).

Preparación 40: **3-metil-3-(2-piridinil)piperidina**

A un matraz seco en atmósfera de nitrógeno se le añadieron complejo de borano-tetrahidrofurano (solución 1 M, 8,79 ml, 8,79 mmol) y tetrahidrofurano (10 ml). La solución se enfrió a 0ºC y se añadió una solución de 5-metil-5-(2-piridinil)-2-piperidona (Preparación 41, 1 g, 5,26 mmol) en tetrahidrofurano (20 ml). Los reactivos se calentaron a temperatura ambiente y después se calentaron a reflujo durante 6 h. Se añadió más complejo de borano-tetrahidrofurano (solución 1 M, 8,79 ml, 8,79 mmol) y la mezcla de reacción se calentó a reflujo durante 18 h. La cromatografía de capa fina mostró que aún quedaba material de partida por lo que se añadió más complejo de borano-tetrahidrofurano (solución 1 M, 8,79 ml, 8,79 mmol) y la mezcla de reacción se calentó a reflujo durante 18 h. Después de que se completase, a la mezcla se le añadió ácido clorhídrico (6 M) de reacción y la

mezcla se agitó durante 30 min. La mezcla de reacción se concentró parcialmente antes de ajustarse a pH 11 con hidróxido sódico sólido. Los extractos orgánicos se extrajeron con diclorometano (5 x 20 ml) y se secaron (Na_2SO_4), dando un aceite bruto (0,45 g). El aceite se purificó por cromatografía ultrarrápida eluyendo con una solución de diclorometano:metanol:amoniaco 0,88 (94:4:2), dando el compuesto del título en forma de un aceite (0,20 g, 22%).

Preparación 41: **5-metil-5-(2-piridinil)-2-piperidona**

A 4-ciano-4-(2-piridinil)pentanoato de metilo (Preparación 42, 2,5 g, 11,4 mmol) en etanol (30 ml) se le añadió níquel Raney (3 g) y la mezcla de reacción se hidrogenó durante 78 h. La mezcla de reacción se filtró a través de Celite® lavando con etanol (3,20 ml). Los extractos orgánicos combinados se concentraron al vacío, dando el producto bruto deseado (2,2 g) que se purificó por cromatografía ultrarrápida eluyendo con diclorometano:metanol (96:7), dando el producto puro en forma de un aceite (1,1 g, 51%).

Preparación 42: 4-Ciano-4-(2-piridinil)pentanoato de metilo

A un matraz seco en atmósfera de nitrógeno se le añadieron 2-(2-piridinil)-propanonitrilo (Preparación 43, 6,26 g, 47,4 mmol), *t*-butanol (30 ml), Triton B (6,66 g, 39,8 mmol) y acrilato de metilo (6,12 g, 71,1 mmol). La mezcla de reacción se calentó a reflujo durante 2,5 h. El sólido se retiró y el filtrado se concentró al vacío, dando un aceite amarillo. Se añadió agua (30 ml) y el producto se extrajo con éter dietílico. Los extractos orgánicos se secaron (Na_2SO_4) y se concentraron al vacío, dando un aceite amarillo claro (4,32 g, 42%).

Preparación 43: 2-(2-piridinil)-propanonitrilo

A un matraz seco en atmósfera de nitrógeno se le añadió dimetilsulfóxido (100 ml) y tosmic (20,95 g, 107,3 mmol). La mezcla de reacción se enfrió a 0ºC antes de que se le añadiera *t*-butóxido potásico (33,35 g, 297,1 mmol). Después de 5 min, se añadió metanol (3,7 ml) seguido de 1-(2-piridinil)etanona (10 g, 32,5 mmol) y la mezcla de reacción se agitó a temperatura ambiente durante 18 h. La mezcla de reacción se vertió en salmuera:hexano:acetato de etilo (50:25:25). Los extractos orgánicos se secaron (Na_2SO_4) y se concentraron al vacío, produciendo un aceite bruto. El aceite se purificó por cromatografía ultrarrápida eluyendo con acetato de etilo:hexano (3:7), dando el compuesto del título en forma de un sólido pardo (8,26 g, 76%).

Preparación 46: sal clorhidrato de 2-[(4-piperidinilmetil)sulfanil]piridina

Se agitó 4-[(2-piridinilsulfanil)metil]-1-piperidincarboxilato de *terc*-butilo (Preparación 47, 0,90 g, 2,9 mmol) en cloruro de hidrógeno (solución 4 M en dioxano, 7,5 ml) en atmósfera de nitrógeno a temperatura ambiente. Después de 20 min, precipitó un sólido blanco de la solución. Se añadió éter dietílico y la mezcla de reacción se filtró y el sólido se lavó con éter dietílico. El compuesto del título se obtuvo en forma de un sólido (0,70 g, 98%).

Preparación 47: 4-[(2-piridinilsulfanil)metil]-1-piperidincarboxilato de *terc*-butilo

A una solución agitada de 4-(hidroximetil)-1-piperidincarboxilato de *terc*-butilo (Preparación 48, 1,0 g, 5 mmol) en benceno (40 ml) en atmósfera de nitrógeno se le añadió trifenilfosfina (1,44 g, 5,5 mmol). Se añadió gota a gota dietilazodicarboxilato (0,86 ml, 5,5 mmol) en benceno (4 ml) y la mezcla de reacción se agitó durante 5 min. Se añadió 2-mercapto-piridina (0,61 g, 5,5 mmol) y la mezcla de reacción se agitó a temperatura ambiente durante 2 h. La

mezcla de reacción se lavó con hidróxido sódico (1M), agua y salmuera saturada. Los extractos orgánicos se secaron (Na_2SO_4) y se concentraron hasta un aceite que se purificó por cromatografía ultrarrápida sobre gel de sílice eluyendo con diclorometano:acetato de etilo (9:1). El compuesto del título se obtuvo en forma de un aceite (0,7 g, 58%).

Preparación 48: 4-(hidroximetil)-1-piperidincarboxilato de *terc*-butilo

A una solución agitada de 1,4-piperidindicarboxilato de 1-*terc*-butilo 4-etilo (Preparación 49, 12,8 g, 0,05 mol) en benceno (300 ml) en atmósfera de nitrógeno se le añadió lentamente hidruro de diisobutilaluminio (solución 1 M, 100 ml, 0,1 mol). La mezcla de reacción se agitó a temperatura ambiente durante 3 h antes de inactivarse mediante la adición de agua (100 ml) seguido de la adición de ácido clorhídrico (1 M) para ajustar el pH a 4. La fase orgánica se separó y la fase acuosa se extrajo con acetato de etilo. Los extractos orgánicos combinados se secaron (Na_2SO_4) y se concentraron, dando un aceite. El aceite bruto se purificó por cromatografía ultrarrápida sobre gel de sílice eluyendo con acetato de etilo:diclorometano (6:4), dando el compuesto del título en forma de un aceite (5,0 g, 46%).

Preparación 49: 1,4-piperidindicarboxilato de 1-*terc*-butilo 4-etilo

A una solución de 4-piperidincarboxilato de etilo (15,4 ml, 0,1 mol) en diclorometano (100 ml) agitada en atmósfera de nitrógeno y enfriada a 0°C se le añadió dicarbonato de di-*terc*-butilo (21,5 g, 0,1 mol). La mezcla de reacción se agitó a temperatura ambiente durante 18 h antes de lavarse con agua y después con salmuera saturada. Los extractos orgánicos se secaron (Na_2SO_4) y se concentraron al vacío, dando el compuesto del título en forma de un aceite (25 g, 97%).

Preparación 50: sal clorhidrato de 2-[(3-piperidinilmetil)sulfanil]piridina

Se agitó 3-[(2-piridinilsulfanil)metil]-1-piperidincarboxilato de *terc*-butilo (Preparación 51, 1,0 g, 3,2 mmol) en cloruro de hidrógeno (solución 4 M en dioxano, 8,1 ml) en atmósfera de nitrógeno a temperatura ambiente. Después de 25 min, un sólido blanco precipitó de la solución. Se añadió éter dietílico y la mezcla de reacción se filtró y el sólido se lavó con éter dietílico. El compuesto del título se obtuvo en forma de un sólido (0,81 g, 100%).

Preparación 51: 3-[(2-piridinilsulfanil)metil]-1-piperidincarboxilato de *terc*-butilo

A una solución agitada de 3-(hidroximetil)-1-piperidincarboxilato de *terc*-butilo (Preparación 52, 1,0 g, 5 mmol) en benceno (40 ml) en atmósfera de nitrógeno se le añadió trifenilfosfina (1,44 g, 5,5 mmol). Se añadió gota a gota dietilazodicarboxilato (0,86 ml, 5,5 mmol) en benceno (4 ml) y la mezcla de reacción se agitó durante 5 min. Se añadió 2-mercapto-piridina (0,61 g, 5,5 mmol) y la mezcla de reacción se agitó a temperatura ambiente durante 2 h. La mezcla de reacción se lavó con hidróxido sódico (1M), agua y salmuera saturada. Los extractos orgánicos se secaron (Na_2SO_4) y se concentraron hasta un aceite que se purificó por cromatografía ultrarrápida sobre gel de sílice eluyendo con diclorometano:acetato de etilo (9:1). El compuesto del título se obtuvo en forma de un aceite (1,0 g, 65%).

Preparación 52: 3-(hidroximetil)-1-piperidincarboxilato de *terc*-butilo

A una solución agitada de 3-piperidinilmetanol (5,06 g, 44 mmol) en diclorometano (100 ml) en atmósfera de nitrógeno se le añadió dicarbonato de di-*terc*-butilo (9,6 g, 44 mmol) y la mezcla de reacción se agitó a temperatura ambiente durante 18 h. La mezcla de reacción se lavó con agua y después salmuera saturada. Los extractos orgánicos se secaron (Na_2SO_4) y se

concentraron al vacío, dando el compuesto del título en forma de un aceite (9,0 g, 95%).

Preparación 56: *N*-metoxi-*N*-metil-2-piperidincarboxamida

A 2-piperidincarboxilato de etilo (18,3 g, 0,12 mol) se le añadió clorhidrato de *N,O*-dimetilhidroxilamina (34,1 g, 0,35 mol) en diclorometano (200 ml) seguido de la adición gota a gota de trietilaluminio (solución 1 M en hexano, 350 ml, 0,35 mol). La mezcla de reacción se agitó durante 3 h antes de inactivarse con ácido tartárico (solución 1 M, 25 ml) con refrigeración para mantener una temperatura de ~20°C. La mezcla de reacción se agitó durante 18 h y después se filtró a través de Celite®, el filtrado se concentró al vacío, dando un sólido blanco (6,2 g). El lecho corto de Celite® se agitó con metanol, se filtró y el filtrado se evaporó a sequedad, dando más sólido (20 g). Los sólidos se combinaron y se purificaron por cromatografía ultrarrápida sobre gel de sílice eluyendo con diclorometano y después diclorometano:metanol (95:5), dando el producto puro (15,8 g, 79%).

Preparación 67: 1-(3-cloro-4-metilfenil)piperazina

A una mezcla de 3-cloro-4-metilanilina (105,5 g, 0,745 mol) y dietanolamina (78,1 g, 0,745 mol) se le añadió lentamente con agitación y refrigeración ácido clorhídrico concentrado (aprox. 100 ml) para ajustar la mezcla de reacción a pH 7. La mezcla de reacción se calentó para retirar el agua (66 ml) y después de reposar durante 18 h, la mezcla se calentó a 240°C durante 6 h. Se añadió hidróxido sódico (solución 5 N, 236 ml) y el producto se extrajo con cloroformo (4 x 100 ml). Los extractos orgánicos combinados se concentraron, dando un aceite rojo que se purificó por destilación, dando el compuesto del título (107,0 g, 68%)

Preparación 87: Butilcarbamato de piperidin-4-ilo

Se hidrogenó butilcarbamato de 1-(fenilmetil)piperidin-4-ilo (Preparación 109, 13,0 g) en etanol (100 ml) que contenía paladio (al 5% sobre carbono) a 413,685 kPa (60 psi), dando el compuesto del título en forma de un aceite verde que solidificó tras el reposo.

Preparación 89: 2-metil-4-piperidin-1-il-5,6,7,8-tetrahidropirido[3,4-d]pirimidina

Una solución de 2-metil-7-(fenilmetil)-4-piperidin-1-il-5,6,7,8-tetrahidropirido[3,4-d]pirimidina (Preparación 88, 12 g) en etanol (200 ml) se ajustó a pH 2 con ácido clorhídrico concentrado, se añadió paladio (al 5% sobre carbono) y la mezcla de reacción se hidrogenó a 413,685 kPa (60 psi). La mezcla de reacción se filtró y el filtrado se concentró al vacío. Se añadieron cloroformo e hidróxido sódico (solución 2 M) y los extractos orgánicos se secaron y se concentraron al vacío. El residuo bruto se disolvió en éter de petróleo (30-40), se enfrió en hielo y el compuesto del título se recogió en forma de un sólido.

Preparación 88: 2-metil-7-(fenilmetil)-4-piperidin-1-il-5,6,7,8-tetrahidropirido[3,4-d]pirimidina

Se calentó 2-metil-7-(fenilmetil)-5,6,7,8-tetrahidropirido[3,4-*d*]pirimidin-4(4a*H*)-ona (Preparación 85, 19 g) y oxicloruro de fósforo (150 ml) durante 1,5 h. La mezcla de reacción se concentró y se vertió en hielo. Se añadió carbonato sódico para ajustar el pH a 10 y el producto se extrajo con cloroformo. Los extractos orgánicos se concentraron y después se purificaron pasándolos a través de una capa densa de florisil (5 cm de diámetro) y el producto se eluyó con cloroformo. La evaporación dio un aceite rojo oscuro que se disolvió en etanol (100 ml) y se añadió piperidina (25 ml). Después de 72 h,

la mezcla de reacción se concentró al vacío, después se disolvió en cloroformo y se basificó con hidróxido sódico (solución 2 M). La mezcla de reacción se secó y se concentraron antes de purificarse por cromatografía ultrarrápida sobre florisil eluyendo el producto con éter de petróleo (30-40), dando el compuesto del título (12,5 g)

Preparación 85: 2-Metil-7-(fenilmetil)-5,6,7,8-tetrahidropirido[3,4-*d*]pirimidin-4(4*aH*)-ona

Se disolvió sodio metal (4,4 g, 0,19 mol) en etanol (300 ml) y se añadió clorhidrato de acetamidina (9,3 g, 0,1 mol). Después de 30 min, se añadió clorhidrato de 3-oxo-1-(fenilmetil)-piperidin-4-carboxilato de etilo disponible en el mercado (25 g, 0,084 mol) y la mezcla de reacción se calentó a reflujo durante 18 h. La mezcla de reacción se filtró y se concentró al vacío, dando el compuesto del título (20 g).

Preparación 93: 1-(1,3-tiazol-2-ilcarbonil)piperazina

Se disolvió piperazina (2,33 g) en ácido acético glacial (25 ml) y la mezcla de reacción se calentó a 60ºC. Se añadió gota a gota una suspensión de cloruro de 1,3-tiazol-2-carbonilo (Preparación 107, 4,0 g, 27,1 mmol) en ácido acético glacial (10 ml) durante 10 min y la mezcla de reacción se agitó a 60ºC durante 30 min y después a temperatura ambiente durante 18 h. El sólido precipitado se filtró y se secó y el agua madre se concentró al vacío. Se añadió agua (50 ml) a las aguas madre y la solución se ajustó a pH 9 usando una solución de hidróxido sódico (5 M). El producto se extrajo con cloroformo y los extractos orgánicos combinados se secaron ($MgSO_4$) y se concentraron al vacío, dando un aceite amarillo (1,85 g). El aceite se disolvió en éter dietílico y se añadió cloruro de hidrógeno (solución 1 M en éter dietílico), un sólido blanco

precipitado se retiró por filtración y se recristalizó en isopropanol, dando el compuesto del título en forma de un sólido blanco (0,5 g)

Preparación 107: cloruro de 1,3-tiazol-2-carbonilo

Se añadió ácido 1,3-tiazol-2-carboxílico (Preparación 92, 5,0 g, 39 mmol) a una solución que contenía hidróxido sódico (1,55 g), en agua (26 ml). La solución se evaporó a sequedad y el sólido resultante se trituró con éter dietílico, se filtró y se secó en una estufa a 60ºC durante 6 h, dando un sólido pardo (5,5 g). El sólido se añadió a cloruro de tionilo (25 ml) y se calentó en un baño de vapor durante 2 h. El exceso de cloruro de tionilo se retiró al vacío y el aceite resultante se trituró con éter de petróleo (40-60, 3 x 30 ml), dando el compuesto del título en forma de un sólido oleoso después de la filtración y la evaporación (4,0 g, 70%).

Preparación 92: ácido 1,3 tiazol-2-carboxílico

A una solución de 2-bromotiazol (16,4 g, 0,1 mol) en éter dietílico anhidro (50 ml) a -70ºC se le añadió lentamente *n*-butillitio (solución 1,6 M en hexano, 75 ml). La mezcla de reacción se agitó a -70ºC durante 20 min y después se añadió en porciones a dióxido de carbono sólido en polvo (500 g). La mezcla de reacción se agitó durante 18 h y la mezcla resultante se disolvió en agua (70 ml), se filtró y se extrajo con éter dietílico (3 x 75 ml). La fase acuosa se acidificó mediante la adición de ácido sulfúrico (solución 10 M) y se enfrió a 0ºC. Se cristalizó un sólido y se retiró por filtración, se lavó con agua fría y se secó a 50ºC durante 6 h, dando el compuesto del título en forma de un sólido pardo claro (5,0 g).

Preparación 96: sal oxalato de 4-{[(4-fluorofenil)metil]oxi}piperidina

Se calentaron a reflujo 1-acetil-4-{[(4-fluorofenil)metil]oxi}piperidina (Preparación 97, 9 g, 36 mmol) en metanol (60 ml) y una solución de hidróxido sódico (5 M, 100 ml) en un baño de vapor durante 4 h. Después de enfriar, la solución se extrajo con cloroformo (3 x 100 ml) y los extractos orgánicos se secaron (Na_2SO_4) y se concentraron, dando un aceite naranja (8 g, 97%). Una porción se disolvió en éter dietílico y se trató con ácido oxálico en éter, dando un sólido blanco que se recristalizó en etanol, dando cristales en forma de agujas (3 g).

Preparación 97: 1-acetil-4-{[(4-fluorofenil)metil]oxi}piperidina

Se añadió gota a gota 1-acetilpiperidin-4-ol (Preparación 193, 10 g, 70 mmol) en *N,N*-dimetilformamida (50 ml) a una suspensión agitada de hidruro sódico (dispersión al 50% en peso en aceite, 3,8 g, 80 mmol) en *N,N*-dimetilformamida (50 ml) a temperatura ambiente en atmósfera de nitrógeno. Después de agitar la mezcla de reacción durante 3 horas, se añadió gota a gota cloruro de 4-fluorobencilo (10,1 g, 70 mmol) en *N,N*-dimetilformamida (50 ml) y la mezcla de reacción se agitó durante 4 h más. La mezcla de reacción se filtró y el filtrado se evaporó, dando un aceite naranja. Se añadió agua y la mezcla se extrajo con éter de petróleo (3 x 100 ml) y después con éter dietílico (3 x 100 ml). Los extractos orgánicos combinados se lavaron con una solución de hidróxido sódico (1 M, 3 x 100 ml), antes de secarse (Na_2SO_4) y concentrarse, dando el compuesto del título en forma de un aceite (10,1 g, 99%).

Preparación 98: 4-{[(4-clorofenil)metil]oxi}piperidina

Se calentaron a reflujo 1-acetil-4-{[(4-clorofenil)metil]oxi}piperidina (Preparación 99, 11 g, 41,1 mmol) en metanol (50 ml) y una solución de

hidróxido sódico (5 M, 30 ml) en un baño de vapor durante 10 h. Después de enfriar, el metanol se retiró y la solución restante se extrajo con éter de petróleo (40-60, 3 x 30 ml). Los extractos orgánicos se secaron (Na_2SO_4) y se concentraron al vacío, dando un sólido blanco (5,8 g, 62%). Se recristalizó una porción en éter de petróleo, dando cristales en forma de agujas (3 g).

Preparación 99: 1-acetil-4-[[(4-clorofenil)metil]oxi}piperidina

Se añadió gota a gota 1-acetilpiperidin-4-ol (Preparación 193, 10 g, 70 mmol) en *N,N*-dimetilformamida (50 ml) a una suspensión agitada de hidruro sódico (dispersión al 50% en peso en aceite, 4,8 g, 0,1 mol) en *N,N*-dimetilformamida (50 ml) a temperatura ambiente en atmósfera de nitrógeno. Después de agitar la mezcla de reacción durante 3 horas, se añadieron gota a gota cloruro de 4-clorobencilo (12,8 g, 80 mmol) en *N,N*-dimetilformamida (50 ml) y la mezcla de reacción se agitó durante 4 h más. La solución se filtró y el filtrado se evaporó, dando un aceite naranja. Se añadió agua y la mezcla se extrajo con éter de petróleo (3 x 50 ml) y después con éter dietílico (3 x 50 ml). Los extractos orgánicos combinados se secaron (Na_2SO_4) y se concentraron, dando el compuesto del título en forma de un aceite naranja (15,8 g, 84%).

Preparación 100: sal clorhidrato de 4-[(piperidin-4-iloxi)metil]benzoato de etilo

Se calentaron ácido 4-[(piperidin-4-iloxi)metil]benzoico (Preparación 101, 7 g, 26 mmol) en etanol (50 ml) y ácido sulfúrico concentrado (1 ml) en un baño de vapor durante 6 h. El disolvente se retiró al vacío y el residuo se disolvió en agua, se basificó con carbonato sódico (al 5% p/v) y se extrajo con éter dietílico (3 x 50 ml). Los extractos orgánicos se secaron (Na_2SO_4) y se concentraron, dando el compuesto del título en forma de un aceite amarillo pálido (4,4 g,

64%). Se disolvió una porción (1 g) en éter dietílico y se trató con cloruro de hidrógeno (solución 1 M en éter dietílico), dando un sólido amarillo que se recristalizó en etanol y éter dietílico, dando placas amarillas (0,5 g).

Preparación 101: ácido 4-[(piperidin-4-iloxi)metil]benzoico

Se calentaron ácido 1-acetil-4-[(piperidin-4-iloxi)metil]benzoico (Preparación 102, 20 g, 72 mmol), una solución acuosa de hidróxido sódico (5 M, 75 ml) y metanol (75 ml) a 100ºC durante 4 h y después se evaporaron, dando una suspensión densa. Los cristales se retiraron por filtración, se disolvieron en agua y el pH se ajustó a 1 con ácido clorhídrico (2 M, 200 ml) a 0ºC. La solución turbia se evaporó a sequedad y el sólido blanco se recristalizó en alcohol isopropílico, dando el compuesto del título (15,2 g, 90%).

Preparación 102: ácido 1-acetil-4-[(piperidin-4-iloxi)metil]benzoico

Se añadió gota a gota 1-acetilpiperidin-4-ol (Preparación 196, 20 g, 0,14 mol) en *N,N*-dimetilformamida (50 ml) a una suspensión agitada de hidruro sódico (dispersión al 50% en peso en aceite, 19,2 g, 0,40 mol) en *N,N*-dimetilformamida (50 ml) a temperatura ambiente en atmósfera de nitrógeno. Después de agitar la mezcla de reacción durante 3 horas, a la solución se le añadió gota a gota ácido 4-(bromometil)benzoico (30,1 g, 0,14 mol) en *N,N*-dimetilformamida (50 ml) a 0ºC y la mezcla de reacción se agitó durante 4 h más. La solución se diluyó con agua (200 ml) y después se extrajo con cloroformo (3 x 150 ml). La fase acuosa se separó, se enfrió a 0ºC y el pH se ajusto a 1 con ácido clorhídrico concentrado. El sólido blanco se retiró por filtración y se secó, dando el compuesto del título (27 g, 74%).

Preparación 103: sal clorhidrato de 4-[(3-fenilpropil)oxi]piperidina

Una solución de 1-acetil-4-[(3-fenilpropil)oxi]piperidina (Preparación 104, 4 g) en hidróxido sódico (solución 5 M, 20 ml) y metanol (20 ml) se calentó en un baño de vapor durante 6 horas, tiempo durante el cual el metanol se dejó retirar por evaporación. Después de enfriar la solución, el producto se extrajo con cloroformo (3 x 30 ml). Los extractos orgánicos combinados se secaron (Na_2SO_4) y se concentraron, dando un aceite amarillo (3,7 g, 88%). El producto se disolvió en éter dietílico y se trató con cloruro de hidrógeno (solución 1 M en éter dietílico), dando un sólido blanco que se retiró por filtración y se secó.

Preparación 104: 1-acetil-4-[(3-fenilpropil)oxi]piperidina

Se añadió gota a gota 1-acetilpiperidin-4-ol (Preparación 193, 8 g, 60 mmol) en *N,N*-dimetilformamida (50 ml) a una suspensión agitada de hidruro sódico (dispersión al 50% en peso en aceite, 3,68 g, 80 mmol) en *N,N*-dimetilformamida (50 ml) a temperatura ambiente en atmósfera de nitrógeno. Después de agitar la mezcla de reacción durante 4 horas, a la solución se le añadió gota a gota 1-bromo-3-fenilpropano (12,94 g, 65 mmol) en *N,N*-dimetilformamida (50 ml) a 0ºC y la mezcla de reacción se agitó durante 4 h más. La solución se diluyó con alcohol isopropílico (20 ml) y agua (100 ml) y después se evaporó, dando un semisólido. Se añadió agua (100 ml) y la solución se extrajo con éter de petróleo (3 x 100 ml). Los extractos orgánicos combinados se secaron (Na_2SO_4) y se concentraron al vacío, dando un aceite naranja (4,3 g, 27%).

Preparación 109: butilcarbamato de 1-(fenilmetil)piperidin-4-ilo

Se agitó 1-(fenilmetil)piperidin-4-ol (10 g, 52,2 mmol) en dioxano (90 ml) a temperatura ambiente. Se añadió isocianato de *N*-butilo (5,0 g, 52,2 mmol) en dioxano (10 ml) y la mezcla de reacción se calentó a reflujo durante 24 h. Se

añadió agua (20 ml) y la mezcla de reacción se concentró al vacío, dando un aceite pardo. El producto bruto se repartió entre éter dietílico y agua y los extractos orgánicos se secaron ($MgSO_4$), dando el compuesto del título en forma de un aceite (14 g, 92%).

Preparación 128: (3*R*)-3-hidroxipiperidin-1-carboxilato de 1,1-dimetiletilo

A una solución de sal del ácido (*S*)-alcanforsulfónico de (3*R*)-piperidin-3-ol (Preparación 115, 5,03 g, 15,7 mmol) en diclorometano (50 ml) y trietilamina (2,4 ml, 17,3 mmol) se le añadió gota a gota a 0ºC una solución de dicarbonato de di-*terc*-butilo (3,8 g, 17,3 mmol) en diclorometano (10 ml). La mezcla de reacción se agitó a temperatura ambiente durante 3 d, antes de que se añadieran acetato de etilo y agua. Los extractos orgánicos se lavaron con salmuera, se secaron ($MgSO_4$) y se concentraron al vacío, dando el compuesto del título en forma de un aceite incoloro (3,29 g, 100%).

Preparación 115: sal del ácido (S)-alcanforsulfónico de (3*R*)-piperidin-3-ol

Se disolvieron ácido (S)-alcanforsulfónico (109,4 g, 0,47 mol) y piperidin-3-ol racémico (48,5 g, 0,47 mol) en butanona (400 ml) y la mezcla de reacción se calentó a reflujo y después se dejó enfriar a temperatura ambiente. Después de agitar durante varias horas, el precipitado resultante se retiró por filtración, se lavó con butanona y después se secó en una estufa de vacío a 55ºC. El compuesto del título se obtuvo en forma de un polvo blanco (52,27 g, 35%).

Preparación 127: (3S)-3-hidroxipiperidin-1-carboxilato de 1,1-dimetiletilo

A una solución de sal del ácido (*R*)-alcanforsulfónico de (3*S*)-piperidin-3-ol (Preparación 116, 10,0 g, 31,4 mmol) en diclorometano (80 ml) y trietilamina (5,0 ml, 35,3 mmol) se le añadió en una porción a 0ºC dicarbonato de di-*terc*-butilo (3,8 g, 17,3 mmol). La mezcla de reacción se agitó a temperatura

ambiente durante 2 d, antes de concentrarse al vacío. El residuo se repartió entre acetato de etilo y agua, los extractos orgánicos se lavaron con salmuera, se secaron ($MgSO_4$) y se concentraron al vacío, dando el producto en forma de un aceite amarillo pálido (6,25 g). El aceite se purificó por cromatografía ultrarrápida sobre gel de sílice eluyendo con éter dietílico:hexano (2:1 y después 1:0), dando el compuesto del título en forma de un aceite incoloro (5,2 g, 83%).

Preparación 116: sal del ácido (*R*)-alcanforsulfónico de (3S)-piperidin-3-ol

Se disolvieron ácido (*R*)-alcanforsulfónico (32,6 g, 0,14 mol) y piperidin-3-ol (14,8 g, 0,14 mol) en butanona (150 ml) y la mezcla de reacción se calentó a reflujo y después se dejó enfriar a temperatura ambiente. Después de agitar durante 6 h, el precipitado resultante se retiró por filtración, se lavó con butanona y después se secó en una estufa de vacío. El compuesto del título se obtuvo en forma de un sólido blanco (16,2 g, 36%).

Preparación 117: 3-hidroxipiperidin-1-carboxilato de 1,1-dimetiletilo

A una solución de sal clorhidrato de piperidin-3-ol (10,1 g, 0,1 mmol) en diclorometano (30 ml) y trietilamina (13,3 ml, 95,4 mmol) se le añadió gota a gota una solución de dicarbonato de di-*terc*-butilo (19,8 g, 90,9 mmol) en diclorometano. Después de que se completara, la mezcla de reacción se añadió a éter dietílico (120 ml), se lavó con ácido clorhídrico (1 M) y después con salmuera. Los extractos orgánicos combinados se secaron ($MgSO_4$) y se concentraron al vacío, dando el compuesto del título en forma de un aceite amarillo claro (17,7 g, 88%).

Preparación 126: acetato de (1*S*,2*R*,4*aR*,5*R*,8*S*,8*aS*)-1,8*a*-dihidroxi-5-isopropenil-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidro-2-naftalenilo acetato y

Preparación 118: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de metilo

Una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4a,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 1, 100 g) y trietilamina (10 ml) en metanol (1000 ml) se agitó a temperatura ambiente durante 3 horas. La mezcla de reacción se evaporó y el residuo se cristalizó en acetato de etilo/hexano, dando una muestra pura del terpeno, acetato de (1*S*,2*R*,4*aR*,5*R*,8*S*,8*aS*)-1,8*a*-dihidroxi-5-isopropenil-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidro-2-naftalenilo (Preparación 126). La solución restante se concentró y se purificó por cromatografía ultrarrápida en columna sobre gel de sílice eluyendo con acetato de etilo:diclorometano:hexano (2:1:7), dando más resto terpeno acetato de (1*S*,2*R*,4*aR*,5*R*,8*S*,8*aS*)-1,8*a*-dihidroxi-5-isopropenil-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidro-2-naftalenilo en forma de un sólido blanco (Preparación 126, 43 g). Otra elución dio el resto alcaloide, (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de metilo en forma de un sólido amarillo claro (Preparación 118, 50 g).

Preparación 125: decahidroisoquinolin-3-carboxilato de etilo

Se disolvió octahidroisoquinolin-2,3(1*H*)-dicarboxilato de 2-(1,1-dimetiletilo) 3-etilo (Preparación 124, 2,3 g, 7,4 mmol) en acetato de etilo (220 ml) y después se saturó con gas cloruro de hidrógeno a 4ºC. La mezcla de reacción se calentó a temperatura ambiente, se agitó y después se concentró al vacío, dando el producto bruto que se trituró con éter dietílico. El sólido

resultante se retiró por filtración y se secó al vacío, dando el compuesto del título (1,24 g, 68%).

Preparación 124: octahidroisoquinolin-2,3(1*H*)-dicarboxilato de 2-(1,1-dimetiletilo) 3-etilo

Se disolvió 3,4-dihidroisoquinolin-2,3(1*H*)-dicarboxilato de 2-(1,1-dimetiletilo) 3-etilo (Preparación 123, 3,1 g, 10,2 mmol) en etanol (250 ml) y se le añadió rodio (al 10% p/p sobre carbono, 0,3 g). La mezcla de reacción se hidrogenó durante 17 h a 50ºC y a 344,737 kPa (50 psi). Se añadió más rodio (al 10% p/p sobre carbono, 0,3 g) y la mezcla se hidrogenó durante 17 h más. Este procedimiento se volvió a repetir con más hidrogenación durante 48 h. El catalizador se retiró de la mezcla de reacción por filtración y después de la concentración del filtrado se obtuvo el producto bruto (2,96 g). El producto bruto se purificó primero por cromatografía ultrarrápida sobre gel de sílice (70 g) eluyendo con hexano:acetato de etilo (20:1 y después 10:1) y después por cromatografía ultrarrápida sobre gel de sílice eluyendo con hexano:éter dietílico (5:1), dando el producto deseado (2,3 g, 73%).

Preparación 123: 3,4-dihidroisoquinolin-2,3(1*H*)-dicarboxilato de 2-(1,1-dimetiletilo) 3-etilo

A una solución de 1,2,3,4-tetrahidroisoquinolin-3-carboxilato de etilo (Preparación 122, 3,64 g, 17,7 mmol) en tetrahidrofurano (50 ml) se le añadió una solución agitada de carbonato ácido sódico (2,97 g, 35,4 mmol) en agua (60 ml). Se añadió lentamente dicarbonato de di-*terc*-butilo (5,8 g, 26,6 mmol) y la mezcla de reacción se agitó durante 18 h antes de concentrarse al vacío. El residuo se disolvió y se repartió entre acetato de etilo (200 ml) y una solución acuosa de carbonato ácido sódico (al 5%, 200 ml). La fase acuosa se lavó con

acetato de etilo (2 x 100 ml). Los extractos orgánicos combinados se secaron (Na_2SO_4) y se concentraron al vacío, dando el producto bruto que se purificó por cromatografía ultrarrápida sobre gel de sílice (70 g) eluyendo con hexano:acetato de etilo (20:1 y después 10:1), dando el compuesto del título (4,4 g, 81%).

Preparación 122: 1,2,3,4-tetrahidroisoquinolin-3-carboxilato de etilo

Se disolvió sal del ácido alcanforsulfónico del ácido 1,2,3,4-tetrahidroisoquinolin-3-carboxílico (Preparación 120, 6 g, 17,2 mmol) en etanol (140 ml) y se saturó con cloruro de hidrógeno (gas). La mezcla de reacción se calentó a reflujo durante 18 h antes de concentrarse al vacío. El residuo bruto se disolvió en diclorometano (150 ml) y se lavó con carbonato ácido sódico (150 ml). La fase orgánica se recogió y se lavó de nuevo con carbonato ácido sódico (2 x 100 ml) antes de secarse (Na_2SO_4) y concentrarse al vacío, dando el compuesto del título en forma de un aceite amarillo (3,64 g, 100%).

Preparación 120: ácido 1,2,3,4-tetrahidroisoquinolin-3-carboxílico

Se disolvió sal del ácido alcanforsulfónico de 1,2,3,4-tetrahidroisoquinolin-3-carboxilato de fenilmetilo (Preparación 121, 8,3 g, 18,9 mmol) en etanol (600 ml) y se añadió paladio sobre carbono (al 10%, 0,8 g) a temperatura ambiente en atmósfera de nitrógeno. La mezcla de reacción se hidrogenó a temperatura ambiente a 206,842 kPa (30 psi) durante 3 h. El catalizador se retiró por filtración y el filtrado se concentró, dando el compuesto del título (6,6 g, 100%).

Preparación 121: (3*R*)-1,2,3,4-tetrahidroisoquinolin-3-carboxilato de fenilmetilo

Se calentaron *D*-fenilalanina (50 g, 0,3 mol), ácido clorhídrico concentrado (386 ml) y formalina (al 37% en peso, 113,7 ml) a 95ºC con

agitación vigorosa durante 4 h. La mezcla de reacción se enfrió a temperatura ambiente y se agitó durante 2 h más. La mezcla de reacción se filtró y el precipitado se lavó con agua fría, dando el ácido (3*R*)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico en forma de un sólido blanco (25 g, 42%). Se añadieron alcohol bencílico (64 g) y ácido *p*-toluenosulfónico (26,9 g) y la mezcla de reacción se calentó a reflujo en benceno (400 ml) en condiciones de Dean Stark. El disolvente se retiró al vacío y el residuo bruto se trituró con éter dietílico, dando un sólido que después se recristalizó en agua y metanol, dando el compuesto del título en forma de un sólido blanco (28 g, 35%).

Preparación 139: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una suspensión agitada de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 1, 1 g) en metanol (25 ml) se le añadió una solución de ácido clorhídrico concentrado (2 ml) en metanol (25 ml). Después de 5 días, la mezcla de reacción se diluyó con diclorometano (150 ml), se lavó con agua (3 x 100 ml), se filtró a través de lana de algodón y se evaporó a sequedad, dando un sólido oleoso amarillo. Este residuo se disolvió parcialmente en diclorometano (25 ml) y se añadió lentamente hexano (50 ml). Después de 1 hora, la suspensión se filtró, dando el producto en forma de un sólido blanquecino (900 mg).

Preparación 140: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-hidroxi-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 1, 500 mg, 0,89 mmol) en tetrahidrofurano (8 ml) a -10ºC en atmósfera de nitrógeno se le añadió borano (solución 1 M en tetrahidrofurano, 2 ml, 2 mmol) y la mezcla resultante se agitó y se dejó volver a temperatura ambiente. Después de 5 horas, se añadió borano (solución 1 M en tetrahidrofurano, 1 ml, 1 mmol) y la reacción se agitó a temperatura ambiente durante 18 h. A la mezcla de reacción se le añadió *N*-óxido de 4-metilmorfolina (600 mg, 5,1 mmol) y la mezcla se calentó a suave reflujo durante 3 horas. La mezcla de reacción se concentró al vacío y el residuo se trató con agua (30 ml) y se extrajo con acetato de etilo (2 x 30 ml). Los extractos orgánicos combinados se lavaron con una solución saturada acuosa de cloruro sódico, se secaron ($MgSO_4$) y el disolvente se retiró al vacío, dando un vidrio naranja. El producto bruto se purificó por cromatografía en columna sobre sílice eluyendo con hexano:acetato de etilo (2:1 y después 1:1) y después acetato de etilo. Las fracciones puras se combinaron y se concentraron al vacío, dando el producto del título en forma de un sólido amarillo (132 mg, 26%).

Preparación 141: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una mezcla agitada de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-hidroxi-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 140, 230 mg, 0,40 mmol) y tamices moleculares 4 Å en diclorometano (18 ml) se le añadieron en nueve porciones perrutenato de tetrapropilamonio (23 mg, 0,065 mmol) y *N*-óxido de *N*-metilmorfolina (180 mg, 1,54 mmol). La mezcla resultante se agitó durante 36 horas antes de diluirse con diclorometano y lavarse con una solución acuosa de sulfito ácido sódico y después con una solución saturada acuosa de cloruro sódico. Los extractos orgánicos se secaron y se concentraron al vacío. El producto bruto se purificó por cromatografía en columna sobre sílice eluyendo con acetato de etilo:hexano (1:1), dando el producto del título (50 mg, 22%).

Preparación 142: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aR*,8*R*,8*aR*)-8*a*-hidroxi-2-[(1*H*-imidazol-1-ilcarbonil)oxi]-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 139, 50 mg, 0,10 mmol) en diclorometano (1 ml) se le añadió carbonildiimidazol (17 mg, 0,10 mmol) a temperatura ambiente. Después de que se completara, la mezcla de reacción

se purificó por cromatografía ultrarrápida eluyendo con acetato de etilo:hexano (50:50 y después 100:0). El compuesto del título se obtuvo en forma de un sólido blanco (36 mg).

Preparación 143: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-{2-[(1*H*-imidazol-1-ilcarbonil)oxi]-1-metiletil}-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-hidroxi-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 140, 0,30 g, 0,52 mmol) en diclorometano se le añadió 1,1'-carbonildiimidazol (0,92 g, 0,57 mmol) y la mezcla de reacción se agitó durante 18 h. La mezcla de reacción se diluyó con agua y se extrajo con diclorometano. Los extractos orgánicos se lavaron con salmuera, se secaron y después se concentraron al vacío. El producto bruto se purificó por cromatografía ultrarrápida eluyendo con acetato de etilo:hexano (2:1), dando el compuesto del título (0,16 g, 46%).

Preparación 144: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,4*aS*,5*S*,8*aR*)-2,8*a*-dihidroxi-3,8-dimetil-5-(1-metiletil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

A una suspensión agitada de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-isopropil-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidro-1-naftalenilo (Ejemplo 1, 887 mg) en metanol (25 ml) se le añadió una solución de ácido clorhídrico concentrado (1 ml) en

metanol (25 ml). Después de 4 días, la mezcla de reacción se diluyó con diclorometano (150 ml) y se lavó con agua (3 x 100 ml). Las fases acuosas combinadas se lavaron con diclorometano (25 ml). Todas las fases orgánicas se combinaron, se secaron y se concentraron, produciendo un sólido amarillo (802 mg). La purificación se realizó por cromatografía ultrarrápida en columna sobre gel de sílice eluyendo con 1:1 acetato de etilo:hexano, dando el producto (604 mg).

Preparación 145: 3-{[(3,4-difluorofenil)metil]oxi}piperidin-1-carboxilato de 1,1-dimetiletilo

A hidruro sódico (dispersión al 60% p/p en aceite, 0,62 g, 16,4 mmol) lavado en pentano se le añadió *N*,*N*-dimetilformamida (20 ml) y después 3-hidroxipiperidin-1-carboxilato de 1,1-dimetiletilo (Preparación 117, 3,0 g, 14,9 mmol). La mezcla de reacción se agitó durante 1 h, antes de que se le añadiera bromuro de 3,4-difluorobencilo (2,0 ml, 16,4 mmol) y se agitara la mezcla de reacción durante 18 h. La mezcla de reacción se concentró al vacío y el residuo bruto se disolvió en diclorometano, se lavó con salmuera y se secó ($MgSO_4$) antes de concentrarse al vacío. El residuo bruto se purificó por cromatografía ultrarrápida, dando el compuesto del título (4,58 g, 94%).

Preparación 146: 3-{[(3,4-difluorofenil)metil]oxi}piperidina

Se disolvió 3-{[(3,4-difluorofenil)metil]oxi}piperidin-1-carboxilato de 1,1-dimetiletilo (Preparación 145, 3,38 g, 10,3 mmol) en metanol (100 ml), se enfrió a 0°C y se burbujeó gas cloruro de hidrógeno en la mezcla de reacción durante 3-5 min. La mezcla de reacción se concentró al vacío, dando un aceite y después de la trituración con éter dietílico se formó un sólido blanco. El sólido

se separó por filtración, dando el compuesto del título (1,78 g, 65%) en forma de la sal clorhidrato.

Preparación 152: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo)

Una mezcla de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de ((1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (Preparación 1, 200 mg), dicarbonato de di-*terc*-butilo y 4-dimetilaminopiridina (10 mg) se calentó a 65ºC durante 1 hora, tiempo durante el cual se observó efervescencia. La mezcla de reacción se evaporó y se purificó por cromatografía ultrarrápida en columna eluyendo con éter:hexano (45:55), dando el producto (244 mg).

Preparación 153: ácido (2*S*,9*bR*)-6-cloro-3-{[(1,1-dimetiletil)oxi]carbonil}-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxílico

Una solución de ácido (2*S*,3*aR*,9*bR*)-3-(*terc*-butoxicarbonil)-9*b*-[(*terc*-butoxicarbonil)oxi]-6-cloro-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxílico (Preparación 150, 25,4 g) en acetato de etilo (200 ml) se trató con paladio al 10% sobre carbono (5 g) y se agitó a 344,737 kPa (50 psi) de gas hidrógeno durante 170 horas. La mezcla de reacción se filtró a través de celite, se evaporó y se purificó por cromatografía en columna ultrarrápida eluyendo con acetato de etilo:hexano (1:4), dando el producto en forma de una espuma blanca (17,5 g).

Preparación 150: ácido (2*S*,3*aR*,9*bR*)-3-(*terc*-butoxicarbonil)-9*b*-[(*terc*-butoxicarbonil)oxi]-6-cloro-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxílico

Una mezcla agitada de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de 4-metoxibencilo (Preparación 155, 29 g), dicarbonato de di-*terc*-butilo (100 g) y 4-dimetilaminopiridina (200 mg) se calentó a 60ºC durante 3 horas y después se dejó a temperatura ambiente durante 18 h. La mezcla de reacción se purificó por cromatografía ultrarrápida usando gel de sílice y eluyendo con un gradiente de acetato de etilo:hexano (de 1:9 a 4:6), dando el producto en forma de un sólido amarillo claro (25,4 g).

Preparación 155: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de 4-metoxibencilo

Una solución agitada de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de metilo (Preparación 118 25 g), *para*-metoxibencilalcohol (115 g) y tetraetóxido de titano (1,5 g) en tolueno (300 ml) se calentó a reflujo durante 1 hora. La mezcla de reacción se enfrió, se evaporó hasta un pequeño volumen y se purificó por cromatografía en columna ultrarrápida sobre gel de sílice eluyendo con un gradiente de acetato de etilo:hexano (de 1:4 a 2:3), dando el producto (29 g).

Preparación 157: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-hidroxi-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) y el diastereómero: **Preparación 158:** (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-

dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-hidroxi-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)

A una solución agitada y enfriada (0ºC) del producto de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo) (Preparación 152, 6,15 g) en tetrahidrofurano desgasificado (100 ml) se le añadió gota a gota 9-borabiciclo[3,3,1]nonano (0,5 M en tetrahidrofurano, 43,2 ml) durante una hora. La mezcla de reacción se agitó durante 3 horas a temperatura ambiente y se inactivó con una mezcla de hidróxido sódico saturado acuoso (60 ml) y peróxido de hidrógeno acuoso (al 30%, 40 ml) que se añadió en porciones con refrigeración. La mezcla de reacción se extrajo con diclorometano (3 x 400 ml) y las fases orgánicas combinadas se lavaron con agua (300 ml) y sulfato de hierro (II) acuoso (300 ml). Las fases orgánicas lavadas se secaron (Na_2SO_4), se evaporaron y se purificaron con cartuchos Biotage® que contenían gel de sílice (2 x 80 g) usando un gradiente de elución de acetato de etilo:hexano (de 1:4 a 2:3). El isómero hidroxi principal (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-hidroxi-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 158, 4,45 g) y el isómero hidroxi minoritario (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-

metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-hidroxi-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 157,1,37 g) se obtuvieron en forma de espumas blancas.

Preparación 159: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-hidroxi-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 157, 780 mg, 1 mmol), dimetilsulfóxido (1,42 ml, 20 mmol) y trietilamina (1,39 ml, 10 mmol) en diclorometano (10 ml) a 0ºC se le añadió en porciones complejo de trióxido de azufre/piridina (980 mg, 6 mmol) durante 10 minutos y la mezcla resultante se agitó durante 3 horas a temperatura ambiente. La mezcla de reacción se diluyó con agua y diclorometano y la fase orgánica se lavó con ácido clorhídrico (solución 0,5 N en agua, x 2) y una solución acuosa de carbonato ácido sódico, se secó (Na_2SO_4) y se concentró al vacío. El producto bruto se purificó por cromatografía en columna sobre sílice eluyendo con hexano:acetato de etilo (2:1). Las fracciones puras se combinaron y se concentraron al vacío, dando el producto del título (695 mg, 89%) en forma de un sólido blanco.

Preparación 187: (2*S*,3*aR*,9*bR*)-9*b*-[(*terc*-butoxicarbonil)oxi]-6-cloro-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-

[(1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-((1*R*)-1-metil-2-{4-[4-(trifluorometil)-2-pirimidinil]-1-piperazinil}etil)-1,2,4a,5,6,7,8,8a-octahidro-1-naftalenil]-3-*terc*-butilo

A una solución de (2*S*,3a*R*,9b*R*)-6-cloro-9b-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9b-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3a*H*)-dicarboxilato de 2-{(1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4a,5,6,7,8,8a-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 159, 600 mg, 7,72 mmol) en diclorometano (10 ml) se le añadieron 1-[(4-trifluorometil)pirimid-2-il]piperazina (197 mg, 8,49 mmol) y trietilamina (0,16 ml, 1,16 mmol). Después de 30 min a temperatura ambiente, se añadió triacetoxiborohidruro sódico (213 mg, 1,00 mmol) y la mezcla de reacción se agitó a temperatura ambiente durante 18 h. Se añadió carbonato ácido sódico saturado acuoso (10 ml) y se agitó vigorosamente durante 15 min, antes de que se añadieran agua (10 ml) y diclorometano (20 ml). La fase acuosa se separó y se lavó adicionalmente con diclorometano (2 x 10 ml), los extractos orgánicos combinados se secaron ($MgSO_4$) y se concentraron al vacío, dando un aceite bruto que se purificó por cromatografía ultrarrápida (sílice) eluyendo con acetato de etilo hexano (1:1), dando el compuesto del título en forma de un aceite incoloro (587 mg).

Preparación 188: (2*S*,3a*R*,9b*R*)-9b-[(*terc*-butoxicarbonil)oxi]-6-cloro-5-metil-1,2,5,9b-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3a*H*)-dicarboxilato de 2-[(1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-((1*R*)-1-metil-2-{4-[5-(trifluorometil)-2-piridinil]-1-piperazinil}etil)-1,2,4a,5,6,7,8,8a-octahidro-1-naftalenil]-3-*terc*-butilo

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 159, 600 mg, 7,72 mmol) en diclorometano (10 ml) se le añadieron 1-[5-(trifluorometil)pirid-2-il]piperazina (196 mg, 8,49 mmol) y trietilamina (0,16 ml, 1,16 mmol). Después de 30 min a temperatura ambiente, se añadió triacetoxiborohidruro sódico (213 mg, 1,00 mmol) y la mezcla de reacción se agitó a temperatura ambiente durante 18 h. Se añadió carbonato ácido sódico saturado acuoso (10 ml) y se agitó vigorosamente durante 15 min, antes de que se añadieran agua (10 ml) y diclorometano (20 ml). La fase acuosa se separó y se lavó además con diclorometano (2 x 10 ml), los extractos orgánicos combinados se secaron ($MgSO_4$) y se concentraron al vacío, dando un aceite bruto que se purificó por cromatografía ultrarrápida (sílice) eluyendo con acetato de etilo:hexano (1:1), dando el compuesto del título en forma de un aceite incoloro (660 mg).

Preparación 160: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1-c]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)

Se añadieron sucesivamente dimetilsulfóxido (6,02 g) y trietilamina (3,9 g) a una solución agitada y enfriada (0ºC) de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato) de 2-{(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-hidroxi-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-

octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 158, 3 g) en diclorometano (30 ml). Después, se añadió en 5 porciones complejo de trióxido de azufre-piridina (3,9 g) durante 10 minutos. Después de 2 horas, la mezcla de reacción se diluyó con agua y se extrajo con diclorometano. Las fases orgánicas combinadas se lavaron con agua y ácido clorhídrico acuoso (1 M), se secaron (Na_2SO_4), se evaporaron y se purificaron por cromatografía en columna ultrarrápida sobre gel de sílice (30 g) eluyendo con acetato de etilo:hexano (1:1), dando el compuesto del título (2,82 g) en forma de una espuma blanca.

Preparación 161: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de 2-[(1-metiletil)oxi]etilo

A (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de metilo (Preparación 118, 0,20 g, 0,67 mmol) se le añadieron tolueno (10 ml), etóxido de titano (IV) (0,07 ml) y 2-isopropoxietanol. Los reactivos se agitaron juntos y después se calentaron a reflujo durante 1 h, antes de concentrarse al vacío. El residuo bruto se purificó usando un cartucho Sep Pak eluyendo con hexano y después hexano:acetato de etilo (50:50). Otra purificación por HPLC preparativa se realizó usando una columna Magellan de 212 x 150 mm, caudal 20 ml/min, eluyendo con un gradiente de agua:acetonitrilo (de 55:45 a 90:10) durante 8 min, produciendo el compuesto del título (63,9 mg).

Preparación 163: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(etilamino)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)

A una solución de (2*S*,3a*R*,9b*R*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3a*H*)-dicarboxilato] de 2-{(1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4a,5,6,7,8,8a-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 1,0 g, 1,28 mmol) en diclorometano anhidro (10 ml) se le añadieron clorhidrato de etilamina (0,15 g, 1,93 mmol) y trietilamina (0,27 ml, 1,93 mmol) y la mezcla de reacción se agitó a temperatura ambiente durante 20 min. Se añadió triacetoxiborohidruro sódico (0,38 g, 1,8 mmol) y la mezcla de reacción se agitó durante 18 h. La mezcla de reacción se diluyó con acetato de etilo y se lavó con carbonato ácido sódico. Los extractos orgánicos se separaron, se secaron (Na_2SO_4) y se concentraron al vacío. El residuo resultante se purificó por cromatografía ultrarrápida usando gel de sílice (20 g) eluyendo con acetato de etilo:metanol (100:0 y después 80:20), dando el compuesto del título en forma de una espuma amarilla (0,79 g, 77%).

Preparación 166: acetato de (1*S*,2*R*,4a*S*,5*R*,8*R*,8a*R*)-5-(2-etil-1,3-tiazol-4-il)-1,8a-dihidroxi-3,8-dimetil-1,2,4a,5,6,7,8,8a-octahidronaftalen-2-ilo

Una solución de acetato de (3a*S*,4*R*,6a*S*,7*R*,10*R*,10a*R*)-7-(2-etil-1,3-tiazol-4-il)-2,2,5,10-tetrametil-4,6a,7,8,9,10-hexahidro-3a*H*-nafto[1,8a-d][1,3]dioxol-4-ilo (Preparación 165, 345 mg) en ácido *para*-toluenosulfónico metanólico (al 1% p/p, 10 ml) se agitó a temperatura ambiente durante 12 días. La mezcla de reacción se repartió entre acetato de etilo y una mezcla de cloruro sódico acuoso diluido y carbonato ácido sódico saturado acuoso. La fase orgánica se secó ($MgSO_4$), se evaporó y se purificó por cromatografía en columna ultrarrápida sobre gel de sílice usando un gradiente de elución de

acetato de etilo:hexano (de 1:5 a 1:1), dando el producto en forma de una goma (94 mg).

Preparación 165: acetato de (3*aS*,4*R*,6*aS*,7*R*,10*R*,10*aR*)-7-(2-etil-1,3-tiazol-4-il)-2,2,5,10-tetrametil-4,6*a*,7,8,9,10-hexahidro-3*aH*-nafto[1,8*a*-d][1,3]dioxol-4-ilo

A una solución agitada de acetato de (3*aS*,4*R*,6*aS*,7*R*,10*S*,10*aS*)-7-(2-bromoacetil)-2,2,5,10-tetrametil-4,6*a*,7,8,9,10-hexahidro-3*aH*-nafto[1,8*a*-d][1,3]dioxol-4-ilo (Preparación 164, 500 mg) en etanol (5 ml) se le añadió tiopropionamida (110 mg). La mezcla de reacción se agitó a temperatura ambiente durante 24 horas y después se repartió entre cloruro sódico saturado acuoso y acetato de etilo. La fase orgánica se secó ($MgSO_4$), se evaporó y se purificó por cromatografía en columna ultrarrápida sobre gel de sílice eluyendo con acetato de etilo:hexano (1:4), dando el producto en forma de una goma (345 mg).

Preparación 164: acetato de (3*aS*,4*R*,6*aS*,7*R*,10*R*,10*aR*)-7-(bromoacetil)-2,2,5,10-tetrametil-4,6*a*,7,8,9,10-hexahidro-3*aH*-nafto[1,8*a*-d][1,3]dioxol-4-ilo

A una solución agitada y enfriada (0ºC) del producto de acetato de (3*aS*,4*R*,6*aS*,7*R*,10*S*,10*aS*)-7-acetil-2,2,5,10-tetrametil-4,6*a*,7,8,9,10-hexahidro-3*aH*-nafto[1,8*a*-d][1,3]dioxol-4-ilo acetato (Preparación 148, 1,8 g) en éter dietílico (30 ml) se le añadieron trietilamina (1,8 ml) y trifluorometanosulfonato de trimetilsililo (2,3 ml). Después de 30 minutos, se añadió *N*-bromosuccinimida (1,2 g) y la mezcla de reacción se dejó calentar a temperatura ambiente durante tres horas. La mezcla de reacción se repartió entre cloruro sódico saturado acuoso y acetato de etilo. La fase orgánica se secó ($MgSO_4$), se evaporó y se purificó por cromatografía en columna ultrarrápida sobre gel de sílice usando un gradiente de elución de acetato de

etilo:hexano (de 1:9 a 2:8), dando el producto en forma de una goma (1,81 g).

Preparación 148: acetato de (3*aS*,4*R*,6*aS*,7*R*,10*S*,10*aS*)-7-acetil-2,2,5,10-tetrametil-4,6*a*,7,8,9,10-hexahidro-3*aH*-nafto[1,8*a*-d][1,3]dioxol-4-ilo

Una solución del producto de acetato de (3*aS*,4*R*,6*aS*,7*R*,10*S*,10*aS*)-7-(1,2-dihidroxi-1-metiletil)-2,2,5,10-tetrametil-4,6*a*,7,8,9,10-hexahidro-3*aH*-nafto[1,8*a*-d][1,3]dioxol-4-ilo (Preparación 147, 930 mg) en metanol (50 ml) se trató con peryodato sódico (540 mg) y se sonicó en un baño ultrasónico durante 15 minutos. Cuando se disolvió el peryodato sódico, se formó una suspensión turbia. Se añadió una cantidad más de peryodato sódico (540 mg) y la sonicación se reanudó durante 15 min. Después de reposar durante 1 hora, la mezcla de reacción se diluyó con agua y el disolvente se evaporó. El residuo se repartió entre agua y diclorometano y la fase orgánica se separó, se lavó con agua y salmuera, se secó (Na_2SO_4) y se concentró al vacío. El aceite residual se purificó por cromatografía en columna ultrarrápida sobre gel de sílice eluyendo con acetato de etilo:hexano (1:4), dando el producto en forma de un aceite incoloro (680 mg).

Preparación 147: acetato de (3*aS*,4*R*,6*aS*,7*R*,10*S*,10*aS*)-7-(1,2-dihidroxi-1-metiletil)-2,2,5,10-tetrametil-4,6*a*,7,8,9,10-hexahidro-3*aH*-nafto[1,8*a*-d][1,3]dioxol-4-ilo

Una solución de *N*-óxido de *N*-metilmorfolina (350 mg) en un volumen mínimo de alcohol isopropílico se añadió gota a gota durante 1 hora a una solución agitada de acetato de (3*aS*,4*R*,6*aR*,7*R*,10*S*,10*aS*)-7-isopropenil-2,2,5,10-tetrametil-4,6*a*,7,8,9,10-hexahidro-3*aH*-nafto[1,8*a*-d][1,3]dioxol-4-ilo (Preparación 149, 1 g) y tetróxido de osmio (al 2% en *terc*-butanol, 1 ml) en acetona (10 ml). Después de 4 horas, se añadió más *N*-óxido de *N*-

metilmorfolina (350 mg) y la agitación se continuó durante 16 horas. La mezcla de reacción se concentró al vacío y se purificó por cromatografía en columna ultrarrápida sobre gel de sílice eluyendo con acetato de etilo:hexano (1:1), dando el producto (950 mg).

Preparación 149: acetato de (3*aS*,4*R*,6*aR*,7*R*,10*S*,10*aS*)-7-isopropenil-2,2,5,10-tetrametil-4,6*a*,7,8,9,10-hexahidro-3*aH*-nafto[1,8*a*-d][1,3]dioxol-4-ilo

Una solución agitada de acetato de (1*S*,2*R*,4*aR*,5*R*,8*S*,8*aS*)-1,8*a*-dihidroxi-5-isopropenil-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidro-2-naftalenilo (Preparación 126, 10 g) en 2,2-dimetoxipropano (200 ml) se trató con ácido *para*-toluenosulfónico (700 mg). Después de 3 días, la solución se concentró al vacío y el residuo se purificó por cromatografía en columna ultrarrápida sobre gel de sílice eluyendo con acetato de etilo:hexano (5:95), dando el producto (10,55 g).

Preparación 156: (2*S*,3*aR*,9*bR*)-9*b*-[(*terc*-butoxicarbonil)oxi]-6-cloro-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*R*,2*R*,4*aS*,5*R*,8*S*,8*aS*)-2-(acetiloxi)-5-(2,2-difluoro-1-metilvinil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidro-1-naftalenil]-3-(*terc*-butilo)

Se añadió dietilisopropilamina (0,15 ml) a una solución agitada de ácido (2*S*,9*bR*)-6-cloro-3-{[(1,1-dimetiletil)oxi]carbonil}-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxílico (Preparación 153, 338 mg) y hexafluorofosfato de fluoro-*N*,*N*,*N'*-tetrametilformamidinio (al 80%, 231 mg) en diclorometano (2 ml). Después de 10 minutos, se añadieron acetato de (1*S*,2*R*,4*aS*,5*R*,8*S*,8*aS*)-5-(2,2-difluoro-1-metilvinil)-1,8*a*-dihidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidro-2-naftalenilo (Preparación 154, 115 mg) y 4-dimetilaminopiridina (2

mg) y la mezcla de reacción se calentó a reflujo durante 16 horas. La mezcla de reacción se diluyó con diclorometano (25 ml), se lavó con ácido cítrico acuoso (al 10% p/p), se secó (Na_2SO_4) y se concentró al vacío. El residuo sólido se purificó por cromatografía en columna ultrarrápida sobre gel de sílice eluyendo con acetato de etilo:hexano (1:4), dando el producto en forma de una goma (120 mg, mezcla 1:1 de epímeros).

Preparación 154: acetato de (1*S*,2*R*,4*aS*,5*R*,8*S*,8*aS*)-5-(2,2-difluoro-1-metilvinil)-1,8*a*-dihidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidro-2-naftalenilo

Una solución del producto de acetato de (3*aS*,4*R*,6*aS*,7*R*,10*S*,10*aS*)-7-(2,2-difluoro-1-metilvinil)-2,2,5,10-tetrametil-4,6*a*,7,8,9,10-hexahidro-3*aH*-nafto[1,8*a*-d][1,3]dioxol-4-ilo (Preparación 151, 400 mg) y ácido *para*-toluenosulfónico en metanol (20 ml) se agitó a temperatura ambiente durante 24 horas. La mezcla de reacción se inactivó con exceso de carbonato ácido sódico acuoso, se diluyó con agua y se extrajo con éter dietílico (2 x). Las fases orgánicas combinadas se lavaron con cloruro sódico acuoso concentrado, se secaron (Na_2SO_4) y se evaporaron. El residuo sólido se purificó por cromatografía en columna ultrarrápida sobre gel de sílice eluyendo con acetato de etilo:hexano (5:95 y después 10:90), dando el producto en forma de un sólido blanco (195 mg).

Preparación 151: acetato de (3*aS*,4*R*,6*aS*,7*R*,10*S*,10*aS*)-7-(2,2-difluoro-1-metilvinil)-2,2,5,10-tetrametil-4,6*a*,7,8,9,10-hexahidro-3*aH*-nafto[1,8*a*-d][1,3]dioxol-4-ilo

Se añadió gota a gota dibromodifluorometano (466 mg) a una solución agitada y enfriada (0°C) de hexametiltriamida de fósforo (al 85%, 850 mg) en triglime destilado recientemente (10 ml) formando una suspensión blanca.

Después de 10 minutos, se añadió una solución de acetato de (3*aS*,4*R*,6*aS*,7*R*,10*S*,10*aS*)-7-acetil-2,2,5,10-tetrametil-4,6*a*,7,8,9,10-hexahidro-3*aH*-nafto[1,8*a*-d][1,3]dioxol-4-ilo (Preparación 148, 680 mg) en triglime destilado recientemente (10 ml) y la mezcla de reacción se agitó a temperatura ambiente durante 16 horas. La mezcla de reacción se enfrió de nuevo a 0°C y se le añadieron más hexametiltriamida de fósforo (850 mg) y dibromodifluorometano (466 mg). La reacción se dejó calentar a temperatura ambiente y se agitó durante 24 h. Se realizaron más adiciones de hexametiltriamida de fósforo (1,7 g) y dibromodifluorometano (1 g) a 0°C y la reacción se agitó durante 5 días. La mezcla de reacción se diluyó con agua y se extrajo con éter (2 x). Las fases orgánicas combinadas se lavaron con agua y después con cloruro sódico acuoso saturado, se secaron (Na_2SO_4) y se concentraron. El residuo gomoso se purificó por cromatografía en columna ultrarrápida sobre gel de sílice eluyendo con acetato de etilo:hexano (5:95), dando el producto en forma de un aceite (400 mg).

Preparación 167: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2,2-difluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)

A una solución de trifluoruro de dietilaminoazufre (41 µl, 0,31 mmol) en diclorometano anhidro (3 ml) a -78°C se le añadió gota a gota una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación

160, 200 mg, 0,25 mmol) en diclorometano anhidro (2 ml) durante 2 minutos. La mezcla resultante se dejó calentar a temperatura ambiente y se agitó durante 18 h. La mezcla de reacción se diluyó con diclorometano (5 ml), se lavó con agua (5 ml), se secó (Na_2SO_4) y se concentró al vacío, dando el producto bruto (145 mg, 59%). Este producto bruto se purificó por cromatografía en columna sobre gel de sílice eluyendo con hexano:acetato de etilo (de 10:1 a 3:1). Las fracciones puras se combinaron y se concentraron al vacío, dando el producto del título (38 mg, 19%).

Preparación 168: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2,2-difluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)

A una solución de trifluoruro de dietilaminoazufre (0,1 ml, 1,5 mmol) en diclorometano anhidro (4 ml) a -78ºC se le añadió gota a gota una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 159, 400 mg, 0,5 mmol) en diclorometano anhidro (6 ml) durante 2 minutos. La mezcla resultante se dejó calentar a temperatura ambiente durante 1 hora ½ y se agitó durante 2 horas ½ más. La mezcla de reacción se diluyó con diclorometano (10 ml), se lavó con agua (10 ml), se secó (Na_2SO_4) y se concentró al vacío. El producto bruto se purificó por cromatografía ultrarrápida sobre gel de sílice eluyendo con hexano:acetato de etilo (de 3:1 a 2:1). Las

fracciones puras se combinaron y se concentraron al vacío, dando el producto del título (145 mg, 36%).

Preparación 170: acetato de (3*aS*,4*R*,6*aR*,7*R*,10*R*,10*aR*)-7-(2,2-dicloro-1-metiletenil)-2,2,5,10-tetrametil-4,6*a*,7,8,9,10-hexahidro-3*aH*-nafto[1,8*a*-d][1,3]dioxol-4-ilo

A cloruro de litio seco (1,0 g) en tetrahidrofurano (45 ml) se le añadió *n*-butillitio (4,75 ml) a 0ºC en una atmósfera de nitrógeno. La mezcla se agitó durante 10 min y después se enfrió a -78ºC antes de añadirse fosfonato de dietilclorometilo (1,85 ml) en tetrahidrofurano (13 ml). Después de agitar durante 10 min, se añadió tetracloruro de carbono (1,15 ml) en tetrahidrofurano (13 ml). Después de agitar durante 10 min más, se añadió una solución de acetato de (3*aS*,4*R*,6*aS*,7*R*,10*S*,10*aS*)-7-acetil-2,2,5,10-tetrametil-4,6*a*,7,8,9,10-hexahidro-3*aH*-nafto[1,8*a*-d][1,3]dioxol-4-ilo (Preparación 148, 2 g) en tetrahidrofurano (13 ml) y la solución se agitó durante 2 h a -78ºC. Después de este tiempo, la mezcla se inactivó en agua (50 ml) y se extrajo con éter dietílico (3 x 50 ml). Las fases orgánicas combinadas se secaron ($MgSO_4$) y se concentraron al vacío, dando un aceite naranja. El aceite se purificó por cromatografía ultrarrápida usando un cartucho Biotage® (90 g), dando el compuesto del título en forma de un aceite transparente (1,05 g, 45%).

Preparación 172: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-(2,2-dicloro-1-metiletenil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo)

Se agitaron ácido (2*S*,9*bR*)-6-cloro-3-[(1,1-dimetiletil)oxi]carbonil}-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-

c][2,1]benzoxazin-2-carboxílico (Preparación 153, 1,7 g), 1-metilimidazol (0,39 g) y 1-(mesitilen-2-sulfonil)-3-nitro-1,2,4-triazol (1,4 g) en diclorometano a temperatura ambiente durante 20 min. Se añadió acetato de 5-(2,2-dicloro-1-metiletenil)-1,8*a*-dihidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-2-ilo (Preparación 173, 0,85 g) y la mezcla resultante se agitó a temperatura ambiente. Después de 1 h, la mezcla de reacción se concentró al vacío. El residuo bruto se disolvió en diclorometano y se preabsorbió en gel de sílice antes de purificarse por cromatografía ultrarrápida eluyendo con acetato de etilo:hexano (10:90, después 30:70, después 50:50 y después 100:0). El compuesto del título se obtuvo en forma de un sólido blanco (0,71 g).

Preparación 173: acetato de 5-(2,2-dicloro-1-metiletenil)-1,8*a*-dihidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-2-ilo

A una solución agitada de acetato de (3*aS*,4*R*,6*aR*,7*R*,10*R*,10*aR*)-7-(2,2-dicloro-1-metiletenil)-2,2,5,10-tetrametil-4,6*a*,7,8,9,10-hexahidro-3*aH*-nafto[1,8*a*-d][1,3]dioxol-4-ilo (Preparación 170, 0,95 g) en etilenglicol (40 ml) y metanol (10 ml) se le añadió ácido *para*-toluenosulfónico (95 mg). La mezcla de reacción se calentó a 75ºC y después de 1,5 h la mezcla de reacción se concentró al vacío para retirar el metanol. La solución resultante se diluyó con éter dietílico (30 ml) y agua (30 ml) y la fase orgánica se separó y se lavó con carbonato ácido sódico (3 x 30 ml). Las fases acuosas se extrajeron de nuevo con éter dietílico (2 x 20 ml) y los extractos orgánicos combinados se secaron ($MgSO_4$) y se concentraron, dando el compuesto del título en forma de un sólido blanco.

Preparación 176: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de

2-{(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[(1*R*)-2-(ciclopropilamino)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo)

A (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-oxoetil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 160, 0,56 g, 0,73 mmol) en diclorometano anhidro (5 ml) se le añadió ciclopropilamina (50 µl, 0,73 mmol) y la mezcla de reacción se agitó a temperatura ambiente durante 20 min. Se añadió triacetoxiborohidruro sódico (0,21 g, 1,0 mmol) y la mezcla de reacción se agitó durante 18 h. La mezcla de reacción se diluyó con acetato de etilo y se lavó con una solución de carbonato ácido sódico. Los extractos orgánicos se secaron (Na_2SO_4) y se concentraron al vacío, dando el compuesto del título en forma de una espuma amarilla (0,56 g, 96%).

Preparación 177: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-5-[2-[acetil(ciclopropil)amino]-1-metiletil]-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo)

A (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[(1*R*)-2-(ciclopropilamino)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 176, 0,10 g, 0,12 mmol) en diclorometano anhidro (3

ml) se le añadió 4-dimetilaminopiridina (0,15 g, 0,12 mmol) y la mezcla de reacción se enfrió a 0ºC. Se añadió gota a gota anhídrido acético (23 µl, 0,24 mmol) y la mezcla de reacción se agitó en atmósfera de nitrógeno durante 1 h. La mezcla de reacción se diluyó con diclorometano y se lavó con agua y después con salmuera. Los extractos orgánicos se secaron (Na_2SO_4) y se concentraron al vacío, dando el compuesto del título en forma de un sólido amarillo pálido.

Preparación 178: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{etil[(metiloxi)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo)

Se disolvieron (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(etilamino)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo) (Preparación 163, 99 mg, 0,12 mmol) y 4-dimetilaminopiridina (15 mg, 0,12 mmol) en diclorometano anhidro (3 ml) y se añadió piridina (50 µl, 0,61 mmol). La mezcla de reacción se enfrió a 0ºC y se añadió gota a gota cloroformiato de metilo (28 µl, 0,37 mmol). Después de agitar durante 18 h, la mezcla de reacción se diluyó con acetato de etilo y se lavó con agua, ácido cítrico (al 20% p/v) y después de nuevo con agua. Los extractos orgánicos se secaron (Na_2SO_4) y se concentraron al vacío, dando el compuesto del título en forma de un sólido vidrioso amarillo (89 mg, 86%).

Preparación 179: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3-(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{ciclopropil[(metiloxi)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo)

A (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[(1*R*)-2-(ciclopropilamino)-1-metietil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 176, 98 mg, 0,12 mmol) y 4-dimetilaminopiridina (15 mg, 0,12 mmol) en diclorometano anhidro (3 ml) se le añadió piridina (50 µl, 0,60 mmol) y la mezcla de reacción se enfrió a 0ºC. Se añadió gota a gota cloroformiato de metilo y la mezcla de reacción se agitó durante 18 h, antes de diluirse con acetato de etilo y lavarse con agua, ácido cítrico (al 20% p/v) y de nuevo con agua. Los extractos orgánicos se secaron (Na_2SO_4) y se concentraron al vacío, dando el compuesto del título en forma de un sólido vidrioso amarillo (108 mg, 100%).

Preparación 180: (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-[(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{ciclopropil[(etilamino)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il]-3-(1,1-dimetiletilo)

A (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[(1*R*)-2-(ciclopropilamino)-1-metiletil]-

8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8a-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 176, 0,16 g, 0,2 mmol) en diclorometano anhidro (5 ml) enfriado a 0°C se le añadió gota a gota isocianato de etilo (0,017 ml, 0,22 mmol) y la mezcla de reacción se agitó en atmósfera de nitrógeno. La mezcla de reacción se concentró al vacío y el residuo amarillo bruto se purificó por cromatografía ultrarrápida sobre gel de sílice (8 g) eluyendo con acetato de etilo:hexano (1:1), dando el producto deseado en forma de un sólido blanco (114 mg, 61%).

Preparación 181: ácido 2-[(1*R*,4*R*,4*aS*,5*R*,6*R*)-5-({[(2*S*,3*aR*,9*bR*)-6-cloro-3-{[(1,1-dimetiletil)oxi]carbonil}-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-il]carbonil}oxi)-6-(acetiloxi)-4*a*-hidroxi-4,7-dimetil-1,2,3,4,4*a*,5,6,8*a*-octahidronaftalen-1-il]propanoico

A una solución de (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-({[(1,1-dimetiletil)oxi]carbonil}oxi)-5-metil-1,2,5,9*b*-tetrahidropirrolo[2,3-c][2,1]benzoxazin-2,3(3*aH*)-dicarboxilato de 2-{(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-hidroxi-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-il}-3-(1,1-dimetiletilo) (Preparación 157, 500 mg, 0,64 mmol) en *N*,*N*-dimetilformamida anhidra (5 ml) se le añadió dicromato de piridinio (845 mg, 2,25 mmol) y la mezcla resultante se agitó a temperatura ambiente en atmósfera de nitrógeno durante 4 horas. La mezcla de reacción se diluyó con agua (100 ml) y se extrajo con éter dietílico (2 x 100 ml). Los extractos orgánicos se lavaron con agua (50 ml), se secaron (Na_2SO_4) y se concentraron al vacío. El producto bruto se purificó por cromatografía en columna sobre una columna de sílice Biotage® (8 g) eluyendo con acetato de etilo:hexano (2:8),

dando el producto del título en forma de una espuma blanca (240 mg, 45%).

Preparación 182: (3*R*)-3-(metiloxi)piperidin-1-carboxilato de 1,1-dimetiletilo

A una solución de (3*R*)-3-hidroxipiperidin-1-carboxilato de 1,1-dimetiletilo (Preparación 128, 1,6 g, 7,95 mmol) en tetrahidrofurano anhidro (35 ml) se le añadió en porciones hidruro sódico (dispersión al 60% en aceite, 0,32 g, 7,95 mmol). La mezcla resultante se agitó durante 25 min y después se añadió gota a gota yodometano (2,27 g, 16 mmol) y la mezcla de reacción se agitó durante 17 h. La mezcla de reacción se diluyó con acetato de etilo (150 ml) y se lavó con salmuera (solución al 5%,150 ml). La fase acuosa se extrajo con acetato de etilo (2 x 50 ml) y los extractos orgánicos combinados se secaron ($MgSO_4$) y se concentraron al vacío. El aceite amarillo resultante se purificó por cromatografía ultrarrápida sobre gel de sílice (70 g) eluyendo con diclorometano:metanol (100:1 y después 50:1), dando un aceite amarillo (1,68 g). La pequeña cantidad de yodo se retiró disolviendo el producto en acetato de etilo (50 ml) y lavando con metabisulfito sódico acuoso (solución al 5%, 2 x 35 ml), agua (35 ml) y carbonato ácido sódico acuoso (solución al 5%, 35 ml). Los extractos orgánicos se secaron ($MgSO_4$) y se concentraron al vacío, dando el producto deseado en forma de un aceite incoloro (1,62 g).

Preparación 183: (3*R*)-3-(metiloxi)piperidina

Una solución de (3*R*)-3-(metiloxi)piperidin-1-carboxilato de 1,1-dimetiletilo (Preparación 182, 1,55 g, 7,2 mmol) en diclorometano anhidro (60 ml) se enfrió a 4ºC y después se saturó con gas cloruro de hidrógeno durante aproximadamente 10 min. La mezcla de reacción se agitó durante 1,5 h antes de concentrarse al vacío y destilarse azeotrópicamente con dietiletilo anhidro,

produciendo la sal clorhidrato del compuesto del título en forma de un sólido hidroscópico blanco (0,90 g).

Preparación 184: (3*S*)-3-(metiloxi)piperidin-1-carboxilato de 1,1-dimetiletilo

A una solución de (3*S*)-3-hidroxipiperidin-1-carboxilato de 1,1-dimetiletilo (Preparación 127, 1,8 g, 9,2 mmol) en tetrahidrofurano anhidro (40 ml) se le añadió en porciones hidruro sódico (dispersión al 60% en aceite, 0,39 g, 9,2 mmol). La mezcla resultante se agitó durante 25 min y después se añadió gota a gota yodometano (2,83 g, 20 mmol) y la mezcla de reacción se agitó durante 17 h. La mezcla de reacción se diluyó con acetato de etilo (200 ml) y se lavó con salmuera (solución al 5%, 200 ml). La fase acuosa se extrajo con acetato de etilo (2 x 50 ml) y los extractos orgánicos combinados se secaron ($MgSO_4$) y se concentraron al vacío. El aceite amarillo resultante se purificó por cromatografía ultrarrápida sobre gel de sílice (100 g) eluyendo con diclorometano:metanol (100:1 y después 50:1), dando un aceite amarillo. La cantidad pequeña de yodo se retiró disolviendo el producto en éter dietílico (60 ml) y lavando con metabisulfito sódico acuoso (solución al 5%, 1 x 40 ml), agua (2 x 40 ml) y carbonato ácido sódico acuoso (solución al 5%, 40 ml). Los extractos orgánicos se secaron ($MgSO_4$) y se concentraron al vacío, dando el producto deseado en forma de un aceite incoloro (1,43 g).

Preparación 186: (3*S*)-3-(metiloxi)piperidina

Una solución de (3*S*)-3-(metiloxi)piperidin-1-carboxilato de 1,1-dimetiletilo (Preparación 184, 1,35 g, 6,27 mmol) en diclorometano anhidro (50 ml) se enfrió a 4°C y después se saturó con gas cloruro de hidrógeno durante aproximadamente 10 min. La mezcla de reacción se agitó durante 2 h antes de concentrarse al vacío y de destilarse formándose un azeótropo con dietiletilo

anhidro, produciendo la sal clorhidrato del compuesto del título en forma de un sólido hidroscópico blanco (0,82 g).

Preparación 185: 4-amino-6-metil-2-piperazin-1-ilpirimidin-5-carbonitrilo

Una solución de 4-amino-2-cloro-2-metilpirimidin-5-carbonitrilo (Maybridge, 100 mg, 0,6 mmol), piperazina (207 mg, 2,4 mmol) y trietilamina (71 mg, 0,7 mmol) en *N,N*-dimetilacetamida (20 ml) se calentó a 108ºC durante 6 h. La mezcla de reacción se agitó a temperatura ambiente durante 18 h antes de verterse en agua (400 ml) y de extraerse con acetato de etilo (3 x 30 ml) y después con diclorometano (20 ml). Los extractos orgánicos combinados se lavaron con agua (3 x 150 ml) y después se secaron ($MgSO_4$) y se concentraron, dando un sólido amarillo (120 mg). El sólido bruto se pre-absorbió sobre gel de sílice (250 mg) y después se purificó por cromatografía ultrarrápida sobre gel de sílice (20 g) eluyendo con acetato de etilo:metanol (90:10 y después 80:20), dando el compuesto del título en forma de un sólido blanco (28 mg).

Preparación 198: 2-piperazin-1-il-5-(trifluorometil)pirimidina

A una solución de sulfato de 1-amidino-piperazina (760 mg, 4,3 mmol) y cloruro de 1,1,5,5-tetrametil-1,5-diaza-3-(trifluorometil)-1,3-pentadienio (Preparación 199, 720 mg, 3,12 mmol) en acetonitrilo (15 ml) se le añadió metóxido sódico (al 25% en metanol, 1,2 ml). La mezcla de reacción se calentó a 70ºC durante 1 h y se dejó enfriar durante una noche. Los disolventes se retiraron al vacío y el residuo se disolvió en diclorometano (20 ml) y se lavó con carbonato ácido sódico saturado acuoso (30 ml) y agua (10 ml). La mezcla de reacción se secó (Na_2SO_4) y el disolvente se retiró al vacío antes de que el producto se purificara, dando el compuesto del título en forma de una sal TFA

(68 mg).

Preparación 200: 4-[(4-clorofenil)oxi]piperidina

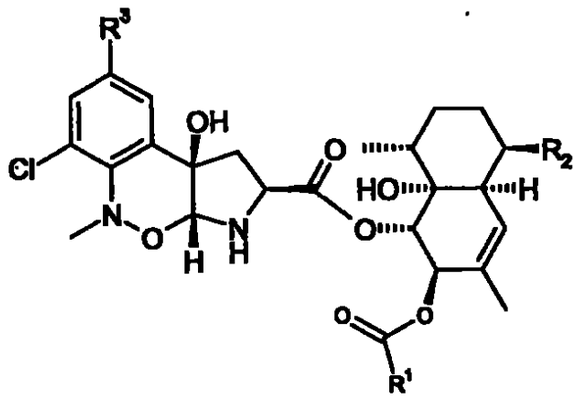
A una solución de 4-hidroxi-1-piperidincarboxilato de *terc*-butilo (500 mg, 2,48 mmol), 4-clorofenol (320 mg, 2,48 mmol) y trifenilfosfina (650 mg, 2,48 mmol) en tetrahidrofurano (15 ml) a 0ºC se le añadió gota a gota diisopropilazodicarboxilato (490 µl, 2,48 mmol) en tetrahidrofurano (5 ml). La mezcla de reacción se dejó calentar a temperatura ambiente y se agitó durante una noche en ausencia de luz. La solución se concentró, dando el compuesto del título Boc-protegido.

El compuesto del título Boc-protegido se disolvió en cloruro de hidrógeno (4 N en dioxano, 10 ml) y se agitó a temperatura ambiente durante 2 h. La mezcla de reacción se evaporó a sequedad y se repartió entre acetato de etilo y agua. Las fases se separaron y a la fase acuosa se le añadió una solución de hidróxido sódico (2 N) y acetato de etilo. Las fases orgánicas se separaron, se combinaron y se secaron (Na_2SO_4) antes de filtrarse y evaporarse, dando el compuesto del título.

Habiendo descrito la invención como antecede, se declara como propiedad lo contenido en las siguientes

REIVINDICACIONES

1. Un compuesto de fórmula (I):



(I)

o una sal o solvato farmacéutica o veterinariamente aceptable del mismo, en la que

R^1 es H, alquilo C_1-C_8, haloalquilo C_2-C_8, cicloalquilo C_3-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, arilo o -OR^4, estando dicho alquilo C_1-C_8, cicloalquilo C_3-C_8 y arilo opcionalmente sustituidos con uno o más sustituyentes seleccionados entre $COOR^{13}$, -$OCOR^{12}$, -$OCOOR^{13}$ y -$OCONR^{12}R^{12}$ y estando dicho alquenilo C_2-C_8 y alquinilo C_2-C_8 opcionalmente sustituidos con uno o más halo;

R^2 es alquilo C_1-C_8, alquenilo C_2-C_8 o un heterociclo aromático o no aromático de 5 ó 6 miembros que contiene uno o más átomos seleccionados entre N, O y S, estando dicho alquilo C_1-C_8 opcionalmente sustituido con uno o

más sustituyentes seleccionados entre $-NR^5R^6$, $-CONR^5R^6$, $-OR^{12}$, $-OCOR^{12}$, $-OCOOR^{12}$, $-OCONR^{12}R^{14}$, $=NOR^7$ y halo, estando dicho alquenilo C_2-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados entre halo y $-COOR^{13}$ y estando dicho heterociclo aromático de 5 ó 6 miembros que contiene uno o más átomos seleccionados entre N, O y S opcionalmente sustituido con uno o más sustituyentes seleccionados entre alquilo C_1-C_6 y arilo;

R^3 es H, halo, arilo, alquenilo C_2-C_6, alcanoílo C_2-C_7 o un heterociclo aromático de 5 ó 6 miembros que contiene uno o más átomos seleccionados entre N, O y S;

R^4 es alquilo C_1-C_2, alquenilo C_2-C_6 o alquinilo C_2-C_6, cada uno opcionalmente sustituido con uno o más halo, o $-OC(O)OR^a$ donde R^a es alquilo C_1-C_6;

R^5 y R^6, cuando se toman junto con el átomo de nitrógeno al que están unidos, representan un heterociclo mono-, bi- o tricíclico, saturado, parcialmente insaturado o aromático de hasta 16 átomos que contiene opcionalmente 1 o más heteroátomos adicionales seleccionados entre O, N y S, estando dicho heterociclo opcionalmente condensado con un anillo de benceno o piridilo y opcionalmente sustituido (incluyendo el anillo de benceno o piridilo opcional) con uno o más R^8 y opcionalmente sustituido (incluyendo el anillo de benceno o piridilo opcional) en cualquier anillo aromático del mismo con $-NR^{15}R^{16}$, con la condición de que el heterociclo puede no contener un grupo -NH-;

o

cada uno de R^5 y R^6 se selecciona independientemente entre H, alquilo

C_1-C_6, cicloalquilo C_3-C_8, -CO-cicloalquilo (C_3-C_8), -COR^{10}, alcanoílo C_2-C_7, arilo, -OR^{13}, -$COOR^{13}$, -$CONR^{12}R^{12}$ o -SO_2R^{13}, estando dicho alcanoílo C_2-C_7 opcionalmente sustituido con OR^{13} o halo, estando dicho alquilo C_1-C_6 y cicloalquilo C_3-C_8 opcionalmente sustituido con uno o más R^8 y estando dicho cicloalquilo C_3-C_8 opcionalmente condensado con un anillo saturado o insaturado de 5 a 6 átomos, que contiene opcionalmente uno o más átomos de O, N o S, estando dicho anillo condensado opcionalmente sustituido con uno o más alquilo C_1-C_6 con la condición de que cuando R^5 sea H o -CH_3, R^6 no sea alquilo C_1-C_6;

R^7 es alquilo C_1-C_6, alquenilo C_2-C_6, alquinilo C_2-C_6 o arilo, estando dicho alquilo opcionalmente sustituido con arilo;

R^8 es alquilo C_1-C_6, cicloalquilo C_3-C_8, R^9, R^{10}, -OR^9, -OR^{10}, COR^9, COR^{10}, -O-(alquil C_1-C_6)-R^{10}, alquenilo C_2-C_6, -OR^{13}, -SR^9, -SR^{10}, -SO_2R^{10}, -$OCOR^{12}$, -$OCOOR^{12}$, -$OCONR^{12}R^{13}$, -$CONR^{12}OR^{13}$, -$CONR^{12}R^{13}$, -$NR^{12}COR^{12}$, -$NR^{12}COOR^{12}$, -$NR^{12}CONR^{12}R^{12}$, -$COOR^{13}$, -COR^{12}, oxo o halo, estando dicho cicloalquilo C_3-C_8 opcionalmente sustituido con arilo, estando dicho alquilo C_1-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados entre cicloalquilo C_3-C_8, R^9, R^{10}, -OR^{10}, -OR^{13}, -SR^9, -SR^{11}, -$OCOR^{12}$, -$OCOOR^{12}$, -$OCONR^{12}R^{12}$, -$NR^{12}COR^{12}$, -$NR^{12}COOR^{12}$, -$NR^{12}CONR^{12}R^{12}$, -COR^{12} o halo y estando dicho alquenilo C_2-C_6 opcionalmente sustituido con uno o más sustituyentes seleccionados entre halo o arilo;

R^9 es

(a) un heterociclo aromático de 5 ó 6 miembros que contiene uno o más átomo(s) seleccionado(s) entre N, O y S y opcionalmente condensado con un anillo de benceno, estando dicho heterociclo aromático opcionalmente

sustituido (incluyendo en el anillo de benceno opcional) con uno o más sustituyentes seleccionados entre alquilo C_1-C_6, haloalquilo C_1-C_6, cicloalquilo C_3-C_8, $-OR^{13}$, $-NR^{12}R^{12}$, $-CO_2R^{13}$, ciano y halo, o

(b) un heterociclo saturado de 4 a 8 miembros que contiene uno o más átomos seleccionados entre O y S y opcionalmente condensado con un anillo de benceno, estando dicho heterociclo saturado opcionalmente sustituido (incluyendo en el anillo de benceno opcional) con uno o más sustituyentes seleccionados entre alquilo C_1-C_6 y cicloalquilo C_3-C_8;

R^{10} es arilo opcionalmente sustituido con uno o más sustituyentes seleccionados entre alquilo C_1-C_6, haloalquilo C_1-C_6, $-OR^{13}$, $-NR^{12}R^{12}$, $-CO_2R^{13}$, ciano o halo y opcionalmente condensado con un anillo saturado o insaturado de 5 ó 6 átomos, que contiene opcionalmente uno o más átomos de O, N o S, estando dicho anillo condensado opcionalmente sustituido con uno o más alquilo C_1-C_6;

R^{11} es H, alquilo C_1-C_6 o cicloalquilo C_3-C_8;

cada R^{12} es independientemente H, alquilo C_1-C_6, haloalquilo C_1-C_6, cicloalquilo C_3-C_8 o arilo, estando dicho alquilo C_1-C_6 opcionalmente sustituido con arilo;

cada R^{13} es independientemente alquilo C_1-C_6, haloalquilo C_1-C_6, cicloalquilo C_3-C_8 o arilo, estando dicho alquilo C_1-C_6 opcionalmente sustituido con arilo;

R^{14} es alquilo C_1-C_6, cicloalquilo C_3-C_8 o arilo, cada uno de dicho alquilo C_1-C_6 opcionalmente sustituido con arilo o -NHarilo;

cada uno de R^{15} y R^{16} se selecciona independientemente entre H, alquilo C_1-C_6 y cicloalquilo C_3-C_8 o, cuando se toman junto con el átomo de nitrógeno

al que están unidos, representan un anillo de 3 a 8 miembros que contiene opcionalmente uno o más heteroátomos adicionales seleccionados entre O y S; y

"arilo" significa fenilo o naftilo;

con la condición de que cuando R^3 sea H y R^1 sea metilo, R^2 no sea isopropenilo.

2. Un compuesto de acuerdo con la reivindicación 1, en el que:

R^1 es alquilo C_1-C_6, alquenilo C_1-C_4, alquinilo C_1-C_4, O-alquilo C_1-C_6, O-alquenilo C_1-C_4 u O-alquinilo C_1-C_4; y

R^2 es un anillo de tiazol opcionalmente sustituido con alquilo de C_1 a C_4; un anillo de piperazina opcionalmente sustituido con alquilo de C_1 a C_4; un grupo isopropenilo opcionalmente sustituido con halo; o un grupo isopropilo opcionalmente sustituido con uno o más halo; NR^7R^8 donde R^7 y R^8 pueden tomarse conjuntamente para representar un anillo de hasta 7 átomos que contiene opcionalmente oxígeno o pueden seleccionarse independientemente entre H o cicloalquilo de C_1 a C_4; $=NOR^{17}$ donde R^{17} puede seleccionarse entre alquinilo de C_1 a C_6, de C_1 a C_4 o alquenilo de C_1 a C_4.

3. Un compuesto de acuerdo con la reivindicación 1 ó 2, en el que:

R^1 es $-CH_3$, -O-alilo o -O-propargilo;

R^2 es 2-etiltiazol-4-ilo, isopropilo, piperazinilo, 1,2-difluoropropen-2-ilo, 1-oxoprop-2-il-metil-oxima, 1-oxoprop-2-il-propargil-oxima, 1-oxoprop-2-il-alil-oxima, 1-*N*-morfolinoprop-2-ilo, 1-fluoroprop-2-ilo, 1,1-difluoroprop-2-ilo;

R^3, R^4 y R^5 son H;

4. Un compuesto de acuerdo con cualquiera de las reivindicaciones 1, 2 ó 3, en el que R^3, R^4 y R^5 son todos H, y R^1 y R^2 son como se indica a continuación:

R1 =	R2 =
CH_3	2-Etiltiazol-4-ilo, isopropilo
CH_3	1,2-difluoropropen-2-ilo
CH_3	1-oxoprop-2-il-metil-oxima
CH_3	1-oxoprop-2-il-propargil-oxima
CH_3	1-oxoprop-2-il-alil-oxima
CH_3	isopropilo
CH_3	1-*N*-morfolinoprop-2-ilo
CH_3	1-fluoroprop-2-ilo
CH_3	1,1-difluoroprop-2-ilo
CH_3	piperazin-1-ilo (opcionalmente 4-sustituido con alquilo C_1-C_6, fenilo, bencilo donde cada uno de los grupos puede estar opcionalmente halo-sustituido con hasta 3 átomos de halo
Opropargilo	isopropenilo
Opropargilo	isopropilo
Oalilo	isopropilo

5. Una composición parasiticida farmacéutica que comprende un compuesto de fórmula (I) como se define en una cualquiera de las

reivindicaciones 1 a 4, o una sal farmacéuticamente aceptable del mismo, o un solvato farmacéuticamente aceptable de cualquier entidad, junto con un diluyente o vehículo farmacéuticamente aceptable, que puede adaptarse para administración tópica.

6. Una formulación de acuerdo con la reivindicación 5 en forma de una formulación adecuada para administración oral por cápsula, bolo, comprimido o brebaje, para administración tópica en forma de formulación de vertido, aplicación puntual, inmersión, pulverización, espuma, champú o en polvo o, por inyección (por ejemplo, por vía subcutánea, intramuscular o intravenosa), o en forma de un implante, o los compuestos pueden administrarse con el pienso del animal y para este propósito puede prepararse un aditivo o premezcla de pienso concentrado para mezclar con el pienso animal normal.

7. Un compuesto de fórmula (I) como se define en cualquiera de las reivindicaciones 1 a 4, o una sal farmacéuticamente aceptable del mismo, o un solvato farmacéuticamente aceptable de cualquier entidad, o una composición farmacéutica que contiene cualquiera de los anteriores, para uso como medicamento.

8. El uso de un compuesto de fórmula (I) como se define en cualquiera de las reivindicaciones 1 a 4, o una sal farmacéuticamente aceptable del mismo, o un solvato farmacéuticamente aceptable de cualquier entidad, o una composición farmacéutica que contiene cualquiera de los anteriores, para la fabricación de un medicamento para el tratamiento de una infestación

parasitaria.

9. Un procedimiento para tratar una infestación parasitaria en un ser humano que comprende tratar dicho ser humano con una cantidad eficaz de un compuesto de fórmula (I) como se define en cualquiera de las reivindicaciones 1 a 4, o una sal farmacéuticamente aceptable del mismo, o un solvato farmacéuticamente aceptable de cualquier entidad, o una composición farmacéutica que contiene cualquiera de los anteriores.

10. Una formulación veterinaria o agrícola que comprende un compuesto de fórmula (I) como se define en cualquiera de las reivindicaciones 1 a 4, o una sal veterinaria o agrícolamente aceptable del mismo, o un solvato veterinaria o agrícolamente aceptable de cualquier entidad, junto con un diluyente o vehículo veterinaria o agrícolamente aceptable. Preferiblemente, la formulación se adapta para administración tópica.

11. Un compuesto de fórmula (I) como se define en cualquiera de las reivindicaciones 1 a 4, o una sal veterinaria o agrícolamente aceptable del mismo, o un solvato veterinaria o agrícolamente aceptable de cualquier entidad, o una formulación veterinaria o agrícolamente aceptable que contiene cualquiera de los anteriores, para uso como parasiticida.

12. Un procedimiento para tratar una infestación parasitaria en un lugar, que comprende el tratamiento del lugar con una cantidad eficaz de un compuesto de fórmula (I) como se define en cualquiera de las reivindicaciones 1 a 4, o una

sal veterinaria o agrícolamente aceptable del mismo, o un solvato veterinaria o agrícolamente aceptable de cualquier entidad, o una formulación veterinaria o agrícolamente aceptable que contiene cualquiera de los anteriores.

13. Un procedimiento de acuerdo con la reivindicación 12, en el que el lugar es el intestino, la piel o el pelaje de un animal.

14. Un compuesto seleccionado entre el grupo que comprende:

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-2-[(2-metilpropanoil)oxi]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(hexanoiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(acetiloxi)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[(2-metilpropanoil)oxi]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-[(ciclopropilcarbonil)oxi]-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletil)-2-{[(prop-2-iniloxi)carbonil]oxi}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9b-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletil)-2-({[(2,2,2-tricloroetil)oxi]carbonil}oxi)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-2-({[(1-metiletenil)oxi]carbonil}oxi)-5-(1-metiletil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletil)-2-{[(prop-2-eniloxi)carbonil]oxi}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

metilbutanodioato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-1-({[(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-il]carbonil}oxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-2-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-2-(pent-4-enoiloxi)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[({[2-(naftalen-1-ilamino)etil]amino}carbonil)oxi]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-{[(acetiloxi)acetil]oxi}-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(formiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletenil)-2-[(3,3,3-trifluoropropanoil)oxi]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[4-(etiloxi)-1-metil-4-oxobut-2-enil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-(2,2-difluoro-1-metiletenil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-fluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[(1-metil-2-morfolin-4-iletil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-etil-1,3-tiazol-4-il)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2,2-difluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-[2,2-difluoro-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-(2,2-dicloro-1-metiletenil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[(fenilmetil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{[(2-clorofenil)metil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(furan-2-ilmetil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{[(2-metilfenil)metil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{[(1S)-1-feniletil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{[(3-clorofenil)metil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-({[2-(metiloxi)fenil]metil}amino)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(4-piridin-2-ilpiperazin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{*bis*[2-(metiloxi)etil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3a,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[(2-tien-2-iletil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo-[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-({[4-(trifluorometil)fenil]metil}amino)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[metil(2-{[2-(metiloxi)fenil]oxi}etil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{(1-metiletil)[2-(fenilsulfonil)etil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(2,3-dihidro-1,4-benzodioxin-2-ilmetil)(metil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(4-{[2-(metiloxi)fenil]metil}piperazin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(1,1-dimetiletil)piperidin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[(fenilmetil)oxi]piperidin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[7,8-*bis*(metiloxi)-3,4-dihidroisoquinolin-2(1*H*)-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(metil{[4-(metiloxi)fenil]metil}amino)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[(etiloxi)carbonil]-1,4-diazepan-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(fenilmetil)-1,4-diazepan-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-5-[2-[acetil(etil)amino]-1-metiletil]-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3a,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-5-[2-[acetil(ciclopropil)amino]-1-metiletil]-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{ciclopropil[(metiloxi)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{etil[(metiloxi)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{[(2,5-diclorofenil)metil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{[(3,5-diclorofenil)metil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-

{ciclopropil[(etilamino)carbonil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[metil(fenilmetil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(fenilmetil)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(3-metilpiperidin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(4-pirimidin-2-ilpiperazin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{metil[2-(feniloxi)etil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-tiomorfolin-4-iletil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[ciclohexil(metil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[metil(piridin-2-ilmetil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(3,6-dihidropiridin-1(2*H*)-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{[fenil(piridin-3-il)metil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(2-feniletil)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(1,3-benzodioxol-5-

ilmetil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[3-(metiloxi)fenil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(4-{[(4-clorofenil)metil]oxi}piperidin-1-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[2-(metiloxi)fenil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(furan-2-ilmetil)piperidin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[(3-metilfenil)metil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(2,2-dimetilpropanoil)(etil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[metil(propanoil)amino]etil}- 1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[(1-metiletil)(propanoil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(2,2-dimetilpropanoil)(1-metiletil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{(1-metiletil)[(metiloxi)acetil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[[(2-clorofenil)metil](propanoil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{[(2-clorofenil)metil][(metiloxi)acetil]amino}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-5-(2-{acetil[(2-metilfenil)metil]amino}-1-metiletil)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[(2-metilfenil)metil](propanoil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{[(metiloxi)acetil][(2-metilfenil)metil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(4-{[(4-fluorofenil)metil]oxi}piperidin-1-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[(4-clorofenil)metil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(3,4-dihidroisoquinolin-2(1*H*)-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil- 1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(2*R*,6*S*)-2,6-dimetilmorfolin-4-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[metil(3,3,3-trifluoropropanoil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[[(2-metilfenil)metil](3,3,3-trifluoropropanoil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[(4-metilfenil)metil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[6-

(metiloxi)piridazin-3-il]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(6-cloropirazin-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(6-cloropiridin-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(4-fenilpiperazin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(ciclohexilmetil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(1,3-tiazol-2-il)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(3-cloropiridin-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-oxo-2-[(fenilmetil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*R*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[[(2-clorofenil)metil](metil)amino]-1-metil-2-oxoetil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-(1-metiletil)-2-{[(fenilamino)carbonil]oxi}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(cicloheptilamino)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(2-cloropirimidin-4-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(5-cloropiridin-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(5-cloropirazin-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(4-clorofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(4-metilfenil)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(2-clorofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[3-(trifluorometil)fenil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[4-(metiloxi)fenil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[2-(trifluorometil)fenil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[4-(trifluorometil)pirimidin-2-il]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(2-fluorofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(6-metilpiridin-2-il)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(4-fluorofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(1,3-tiazol-2-ilcarbonil)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[(3-fenilpropil)oxi]piperidin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[5-(trifluorometil)piridin-2-il]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(fenilmetil)piperidin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[3-(trifluorometil)piridin-2-il]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[3-(trifluorometil)fenil]piperidin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(4-[[3-(trifluorometil)fenil]metil}piperazin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c]2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[({3-[(etiloxi)carbonil]fenil}metil)oxi]piperidin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(1,3-benzoxazol-2-il)piperidin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(4-[[3,5-*bis*(trifluorometil)fenil]metil}piperazin-1-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[2-(metiloxi)fenil]piperidin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[(4-fluorofenil)metil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(4-cianofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(2,3-dihidro-1,4-benzodioxin-2-ilcarbonil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(4-bromofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[4-(trifluorometil)fenil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(2,4-difluorofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(piridin-4-ilmetil)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[5-cloro-2-(metiloxi)fenil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(3,5-diclorofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[(2*E*)-3-fenilprop-2-enil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(difenilmetil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(2,3-dimetilfenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(4-ciclopentilpiperazin-1-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[4-(2-etilfenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[4-cloro-3-(trifluorometil)fenil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(tien-2-ilcarbonil)piperazin-1-il]etil}- 1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(4-{[(butilamino)carbonil]oxi}piperidin-1-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[4-(2,4-dimetilfenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[4-(2,5-dimetilfenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(4-ciclopropilpiperazin-1-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[4-(ciclopentilcarbonil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[6-(metiloxi)piridin-2-il]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[4-(3,5-dimetilfenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-[4-(3,6-dimetilpirazin-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(2,6-dimetilfenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[(1S)-1-metil-2-piridin-3-iletil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(3-oxa-9-azabiciclo[3,3,1]non-9-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(4-metilpentanoil)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(4-oxo-1,3,4,6,7,11b-hexahidro-2H-pirazino[2,1-a]isoquinolin-2-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[3-[(etiloxi)carbonil]octahidroisoquinolin-2(1*H*)-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[3,5-*bis*(metiloxi)fenil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(2-cianofenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(4-fenilpiperidin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(3,4-dimetilfenil)piperazin-1-il]-1-metil etil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[ciclopropil(propanoil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(ciclopropilcarbonil)(fenil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(ciclohexilmetil)(ciclopropilcarbonil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(ciclohexilmetil)(propanoil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(ciclopropilcarbonil)(metil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[metil(fenilcarbonil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-{metil[(feniloxi)acetil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(4-amino-5-ciano-6-metilpirimidin-

2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(2*S*,5R)-2,5-dimetil-4-prop-2-enilpiperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(8-azabiciclo[3.2.1]oct-8-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(3*S*,8*aR*)-3-(fenilmetil)hexahidropirrolo[1,2-a]pirazin-2(1*H*)-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(3-{[(3,4-difluorofenil)metil]oxi}piperidin-1-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[(3*R*)-3-(metiloxi)piperidin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[1-metil-6,7-*bis*(metiloxi)-3,4-dihidroisoquinolin-2(1*H*)-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-(2-metil-4-piperidin-1-il-5,8-dihidropirido[3,4-d]pirimidin-7(6H)-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*b*R)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(4-clorofenil)-6,7-dihidrotieno[3,2-c]piridin-5(4H)-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(3-[[4-(metiloxi)fenil]sulfanil}-8-azabiciclo[3.2.1]oct-8-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(4-metilpiperazin-1-il)piperidin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{3-[(3-cloropiridin-2-il)oxi]piperidin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[4-(3-metilquinoxalin-2-il)piperazin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-{2-[7-(hidroximetil)-3-azabiciclo[3,3,1]non-3-il]-1-metiletil}-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9b-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(3,11-diazatriciclo[7.3.1.0~2,7~]trideca-2,4,6-trien-11-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(4,10-diazatriciclo[6.3.1.0~2,7~]dodeca-2,4,6-trien-10-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8a-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-5-{2-[(4*aR*,9*aS*)-2,3,4,4*a*,9,9*a*-hexahidro-1*H*-indeno[2,1-b]piridin-1-il]-1-metiletil}-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-[2-(3-ciclohexil-3-metilpiperidin-1-il)-1-metiletil]-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-(4-{2-[(2-hidroxietil)oxi]etil}piperazin-1-il)-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(3-metil-3-piridin-2-ilpiperidin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(3,5-dicloropiridin-4-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[(3S)-3-metil-3-fenilpiperidin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{3-[(4-fluorofenil)sulfanil]-8-azabiciclo[3.2.1]oct-8-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[(piridin-2-ilsulfanil)metil]piperidin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{3-[(piridin-2-ilsulfanil)metil]piperidin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(2-{[metil(metiloxi)amino]carbonil}piperidin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[(3,4-diclorofenil)metil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-{1-metil-2-[2-(2-piperidin-1-iletil)piperidin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-{1-metil-2-[(1-metiletil)(2-{[2-(metiloxi)fenil]oxi}etil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2S,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-{1-metil-2-[metil(2-fenilciclopropil)amino]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetiloxi)-8a-hidroxi-3,8-dimetil-5-(1-metil-2-{metil[3-(1,2,4,5-tetrahidro-3H-3-benzazepin-3-il)propil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4a*S*,5*S*,8*R*,8a*R*)-2-(acetiloxi)-5-{2-[{2-[(2,6-diclorofenil)oxi]etil}(metil)amino]-1-metiletil}-8a-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3a*R*,9b*R*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[[(4-clorofenil)metil](etil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{metil[(3-metiltien-2-il)metil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[4-(3-cloro-4-metilfenil)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{2-[(difenilmetil)(metil)amino]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{4-[5-metil-2-(metiloxi)fenil]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de

(1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-(2-{4-[2-(etiloxi)fenil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{(2*S*,4R)-4-metil-2-[(metiloxi)carbonil]piperidin-1-il}etil)-1,2,4*a*,5,6,7,8,8a-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-{2-[(2S)-2-(2-hidroxietil)piperidin-1-il]-1-metiletil}-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[(3S)-3-(metiloxi)piperidin-1-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aS*,9*b*S)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{2-[(metiloxi)carbonil]octahidro-1*H*-indol-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-{1-metil-2-[(2S)-4-metil-2-[(metiloxi)carbonil]-3,6-dihidropiridin-1(2*H*)-il]etil}-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-5-[2-(3-hidroxi-8-azabiciclo[3.2.1]oct-8-il)-1-metiletil]-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-[1-metil-2-(3-metil-3-fenilpiperidin-1-il)etil]-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-(1-metil-2-{(fenilmetil)[2-(feniloxi)etil]amino}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-((1*R*)-1-metil-2-{4-[4-(trifluorometil)-2-pirimidinil]-1-piperazinil}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidro-1-naftalenilo, sal TFA

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-((1*R*)-1-metil-2-{4-[5-(trifluorometil)-2-piridinil]-1-piperazinil}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidro-1-naftalenilo, sal TFA

(2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,5*S*,8*R*,8*aR*)-2-

(acetiloxi)-5-((1*R*)-2-{4-[*bis*(4-fluorofenil)metil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{(1*R*)-2-[4-(5-cloropirimidin-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1 ,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{(1*R*)-2-[4-(5-bromopirimidin-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-{(1*R*)-2-[4-(6-cloro-1,3-benzotiazol-2-il)piperazin-1-il]-1-metiletil}-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-((1*R*)-2-{4-[(3,4-diclorofenil)metil]piperazin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-8*a*-hidroxi-3,8-dimetil-5-((1*R*)-1-metil-2-{4-

[5-(trifluorometil)pirimidin-2-il]piperazin-1-il}etil)-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-((1*R*)-2-[4-[(4-clorofenil)oxi]piperidin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo (2*S*,3*aR*,9*bR*)-6-cloro-9*b*-hidroxi-5-metil-1,2,3,3*a*,5,9*b*-hexahidropirrolo[2,3-c][2,1]benzoxazin-2-carboxilato de (1*S*,2*R*,4*aS*,5*S*,8*R*,8*aR*)-2-(acetiloxi)-5-((1*R*)-2-[4-[(4-clorofenil)oxi]piperidin-1-il}-1-metiletil)-8*a*-hidroxi-3,8-dimetil-1,2,4*a*,5,6,7,8,8*a*-octahidronaftalen-1-ilo

TRATADO DE COOPERACIÓN DE PATENTES
PCT
NOTIFICACIÓN DE TRANSMISIÓN DEL REPORTE DE EXAMEN PRELIMINAR INTERNACIONAL
(PCT Regla 71.1)
De: AUTORIDAD DE REVISION PRELIMINAR INTERNACIONAL

Para:
WOOD, David J.
PFIZER LIMITED
Ramsgate Road
Sandwich
Kent, CT13 9NJ
Gran Bretaña

Sello de recibido de fecha 5 de mayo de 2005 Oficina Europea de Patentes.

Fecha de expedición: 03.05.2005
Referencia del expediente del solicitante o mandatario: PC10339A
Solicitud Internacional No.: PCT/IB2004/000320
Fecha de presentación internacional: 03.02.2004
Fecha de prioridad: 14.02.2003
Solicitante: PFIZER LIMITED.

1. Se notifica al solicitante que la Administración Encargada del Examen Preliminar Internacional ha emitido el informe de examen preliminar internacional para la solicitud internacional y se lo transmite adjunto, acompañado, si procede, de sus anexos.

2. Se transmite una copia del presente informe y, si procede, de sus anexos, a la Oficina Internacional para comunicación a todas las Oficinas elegidas.

3. Si alguna Oficina elegida lo exige, la Oficina Internacional realizará una traducción en inglés del informe (con exclusión de sus anexos) y la transmitirá a las Oficinas interesadas.

4. **RECORDATORIO**

   Para iniciar la fase nacional ante cada Oficina elegida, el solicitante debe cumplir ciertos actos (presentación de la traducción y pago de las tasas nacionales) en el plazo de 30 meses desde la fecha de prioridad (o más tarde por lo que respecta a ciertas oficinas) (Artículo 39.1) (véase también el recordatorio enviado por la Oficina Internacional en el formulario PCT/IB/301).

Cuando deba entregarse una traducción de la solicitud internacional o una oficina elegida, se incluirá la traducción de cualquier anexo de informe de Examen Preliminar Internacional. Corresponde al solicitante preparar la traducción en cuestión y entregarla directamente a cada Oficina elegida interesada

Para más amplios detalles en lo relativo a los plazos aplicables y las exigencias de las oficinas elegidas, véase el volumen II de la guía del solicitante PCT.

Se llama la atención del solicitante sobre el Artículo 33(5) que prevé que los criterios de novedad, actividad inventiva y de aplicación industrial definidos en el Artículo 33(2) a (4) sólo servirán a los efectos del examen preliminar internacional, y que "todo Estado contratante puede aplicar criterios adicionales o diferentes al objeto de decidir, en ese Estado, si la invención es patentable o no" (véase también el Artículo 27(5)). Tales criterios adicionales pueden afectar, por ejemplo, a las excepciones de patentabilidad, requisitos específicos relativos a la divulgación, la claridad de las reivindicaciones.

Nombre y dirección postal de la Administración encargada del Examen Preliminar Internacional:
Oficina de Patentes Europea
D-80298 – Munich
Tel: +49-89 2399 - 0, Tx: 523656 epmu d
Fax: +49-89 2399 – 4465.

Funcionario Autorizado: Hebert, W.
Tel: + 49 89 2399-2152

TRATADO DE COOPERACIÓN DE PATENTES
PCT
INFORME PRELIMINAR INTERNACIONAL SOBRE PATENTABILIDAD
(Capítulo II del Tratado de Cooperación en materia de Patentes)
(PCT Artículo 36 y Regla 70)

Referencia del expediente del solicitante o mandatario: PC10339A
Solicitud Internacional No.: PCT/IB2004/000320
Fecha de presentación internacional: 03.02.2004
Fecha de prioridad: 14.02.2003
Clasificación Internacional de Patentes (IPC) o la vez clasificación nacional e IPC: C07D498/04, C07D498
Solicitante: PFIZER LIMITED

1. El presente informe preliminar internacional sobre patentabilidad, se establece por esta Administración encargada del examen preliminar internacional según el Artículo 35 y se transmite al solicitante conforme el Artículo 36.

2. Este INFORME consta de un total de 6 hojas, incluida la presente hoja de portada.

3. Este informe también contiene ANEXOS, que comprenden.

a. ☒ (*remitido al solicitante y a la oficina internacional*) un total de 16 hojas,
descritas a continuación:
☐ hojas de la descripción, las reivindicaciones y/o los dibujos que han sido modificadas y que sirven de base al presente informe, y/o de hojas que contienen rectificaciones autorizadas por esta Administración (véase la Regla 70.16 y la Instrucción Administrativa 607 del PCT).

☐ hojas que reemplazan a otras hojas anteriores, pero que esta Administración considera que contienen modificaciones que se extienden más allá de la divulgación de la invención tal como fue originalmente presentada, según se indica en el punto 4 del Reglamento I y en el Recuadro Suplementario.

b. ☐ (remitido únicamente a la Oficina Internacional) un total de (indicar tipo y soporte(s) electrónico(s)) , que contienen una lista de secuencias y/o tabla(s) relativa(s), solo en formato legible por ordenador, como se indica en el Recuadro Suplementario relativo a Listas de Secuencias (ver Instrucción Administrativa 802).

4. El presente informe contiene indicaciones relativas a los siguientes puntos:

☒	Recuadro I	Base de este informe
☐	Recuadro II	Prioridad
☒	Recuadro III	Ninguna formulación de opinión sobre la novedad, la actividad inventiva y la aplicación industrial
☒	Recuadro IV	Falta de unidad de Invención
☒	Recuadro V	Declaración motivada según el Artículo 35(2) sobre la novedad, la actividad inventiva y la aplicación industrial, citas y explicaciones en apoyo de esta declaración
☐	Recuadro VI	Ciertos documentos citados
☐	Recuadro VII	Defectos en la Solicitud Internacional
☐	Recuadro VIII	Observaciones relativas a la solicitud internacional

Fecha de radicación de la demanda: 27.02.2004
Fecha de elaboración de este reporte: 03.05.2005

Nombre y dirección postal de la Administración encargada del Examen Preliminar Internacional:
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Fax: +49-89 2399 – 4465.

Funcionario Autorizado: Grassi, D
Tel: + 49 89 2399-8499

Recuadro No. I Base de este informe

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1. Por lo que respecta al **idioma**, este informe se ha establecido sobre la base de la solicitud internacional en el idioma en el cual se depositó, salvo indicación en contra señalada a continuación.

☐ Este informe está basado en una traducción del idioma original al siguiente idioma____, que es el de una traducción proporcionada a los fines de:
- ☐ búsqueda internacional (según Reglas 12.3 y 23.1 (b))
- ☐ publicación de la solicitud internacional (según Regla 12.4)
- ☐ examen preliminar internacional (según Reglas 55.2 y/o 55.3)

2. Por lo que respecta a los **elementos** de la solicitud internacional, esta opinión se ha establecido sobre la base de (*las hojas de reemplazo que hayan sido enviadas a la Oficina receptora en respuesta a un requerimiento según el Artículo 14 se las denomina en este informe como "inicialmente presentadas" y no se anexan al informe):*

Descripción, Páginas

1-5, 7-14, 21-118, 120-124, 126, 128-158, 160-163, 166-197, 199, 200, 202, 204-207	tal como se presentaron inicialmente
6, 15-20, 119, 125, 127, 159, 164, 165, 198, 201, 203	recibida el 14.12.2004 con carta del 10.12.2004

Reivindicaciones, Números

1 – 14 tal como se presentaron inicialmente

☐ una lista de secuencias y/o tabla(s) relativa(s) – ver Recuadro Suplementario relativo a Listas de Secuencias

3. Las modificaciones ha ocasionado la cancelación de:

☐ la descripción, páginas
☐ las reivindicaciones, Nos.
☐ los dibujos, hojas/fig.
☐ la lista de secuencias (especificar):
☐ tabla(s) relativa(s) a la lista de secuencias (especificar):

4. ☐ El presente informe ha sido establecido como si no se hubiesen presentado (algunas de) las modificaciones anexadas a este informe y listadas abajo, ya que se ha considerado que iban más allá de la divulgación de la invención tal como fue presentada, como se indica en el Recuadro Suplementario (Regla 70.2(c)).

☐ la descripción, páginas
☐ las reivindicaciones, Nos.
☐ los dibujos, hojas/fig.
☐ la lista de secuencias (especificar):
☐ tabla(s) relativa(s) a la lista de secuencias (especificar):

* Si se utiliza el punto 4, algunas o todas estas páginas pueden llevar el sello de "sustituida".

Recuadro No. III. Ninguna formulación de opinión sobre la novedad, la actividad inventiva y la aplicación industrial

1. Las preguntas con respecto a si el invento reivindicado parece ser novedoso, implica una actividad inventiva (no ser evidente), o ser susceptible de aplicación industrial, por lo que respecta.

☐ al conjunto de la solicitud internacional,
☒ a las reivindicaciones Nos. 9, 12, 13

debido a que:

☒ la solicitud internacional, o las reivindicaciones Nos. (con respecto a la aplicación industrial) en cuestión se refieren al objeto, respecto del cual no requiere examen preliminar internacional (especifique):

Ver hoja separada

☐ a descripción, reivindicaciones, o los dibujos (indíquese cuales a continuación) o tales reivindicaciones Nos. en cuestión no son claras, de manera que no es posible formular una opinión significativa (especifique):

☐ las reivindicaciones, o las reivindicaciones Nos. en cuestión no son claras, de manera que no es posible formular una opinión significativa.

☐ no se ha emitido informe de búsqueda internacional para dichas reivindicaciones Nos.

☐ la lista de de secuencias nucleótidas y/o de aminoácidos no cumplen la norma estándar prevista en el Anexo C de las Instrucciones Administrativas por que:

La lista en papel
☐ no se presentó
☐ no cumple con la norma estándar

La lista en formato legible por ordenador
☐ no se presentó
☐ no cumple con la norma estándar

☐ las tablas relativas a las listas de secuencias de nucleótidas y/o de aminoácidos, si únicamente se han presentado en formato legible por ordenador, no cumplen con los requisitos técnicos previstos en el Anexo C-*bis* de las Instrucciones Administrativas.

☐ Ver recuadro suplementario para más detalles.

Recuadro No. IV Falta de unidad de Invención

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1. ☒ En respuesta al requerimiento para limitar las reivindicaciones o pagar tasas adicionales, el solicitante:

   ☐ ha limitado las reivindicaciones
   ☐ ha pagado tasas adicionales
   ☐ ha pagado tasas adicionales bajo protesta
   ☒ no ha limitado las reivindicaciones ni pagado las tasas adicionales.

2. ☐ Esta Administración considera que no se cumple la exigencia de unidad de la invención por los motivos indicados a continuación, y con forme a la regla 68.1, decide no requerir al solicitante para limitar las reivindicaciones o pagar tasas adicionales.

3. Esta Administración considera que el requerimiento de unidad de invención según las reglas 13.1, 13.2 y 13.3:

   ☐ se cumple
   ☐ no se cumple por las siguientes razones:

4. En consecuencia, el presente informe se ha establecido con relación a las partes siguientes de la solicitud internacional:

   ☐ todas las partes de la solicitud

   ☒ las partes relativas a la reivindicaciones Nos. 1-14 (parte)

Recuadro No. V Declaración razonada según el Artículo 35(2) con respecto a la novedad, nivel inventivo o aplicación industrial: anterioridades y explicaciones que soportan tal declaración

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1. Declaración

Novedad (N)	Si:	Reivindicaciones 1-14
	No:	Reivindicaciones
Nivel Inventivo (NI)	Si:	Reivindicaciones
	No:	Reivindicaciones 1-14
Aplicación Industrial (AI)	Si:	Reivindicaciones 1-8, 10, 11, 14
	No:	Reivindicaciones

2. Citas y explicaciones (Regla 70.7)

ver hoja adjunta.

REPORTE DE EXAMEN PRELIMINAR INTERNACIONAL – HOJA ANEXA
Solicitud Internacional No. PCT/IB04/000320

Se hace referencia a los siguientes documentos:
D1: WO 95/19363

Ítem III
Las reivindicaciones 9, 12 y 13 se relacionan con materia considerada por esta Autoridad cubierta por las provisiones establecidas en la Regla 67.1 (iv) del PCT. Por lo tanto, no se formulará ninguna opinión con respecto a la aplicación industrial de la materia de estas reivindicaciones (Artículo 34(4)(a)(I) del PCT).

La Autoridad Internacional de Evaluación encontró múltiples (grupos) inventos en esta solicitud internacional. No se cancelaron tarifas requeridas de evaluación adicional por parte del solicitante. Por lo tanto, este concepto escrito se limita únicamente al primer invento.

Ítem IV

D1 divulga pirrolobenzoxazinas antiparasitarias.
El problema técnico a resolverse en la presente solicitud es proporcionar compuestos antiparasitarios alternos.
En vista de los compuestos de D1, los cuales muestran la misma estructura básica de los compuestos presentes, las diferentes alternativas abarcadas por las presentes reivindicaciones no comparten una característica técnica especial en común tal como se requiere en la Regla 13.2 del PCT.
El hecho de negar los compuestos de D1 no puede establecer unidad entre los diferentes grupos de inventos.

Esta Autoridad Internacional de Búsqueda encontró múltiples (grupos) inventos en esta solicitud internacional, y son los siguientes:

1. Reivindicación: 1(parte) R2 es alquilo.
2. Reivindicación: 1(parte) R2 es alquenilo no sustituido.
3. Reivindicación: 1(parte) R2 es alquenilo sustituido.
4. Reivindicación: 1(parte) R2 es un heterociclo de 5 ó 6 miembros.

Ítem V

1) Las modificaciones parecen estar conformes con el Artículo 34(2)b) del PCT.

Sin embargo, la corrección realizada en la página 6, también debería hacerse en la presente reivindicación 2.

2) La materia de las reivindicaciones 1-14 es novedosa (Artículo 33(2) del PCT).
Los presentes compuestos difieren de los compuestos de D1 en que el R2 residual es alquilo y no alquenilo. En consecuencia, los usos y métodos de las composiciones son novedosos.

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3) La materia de las reivindicaciones 1-14 no posee nivel inventivo (Artículo 33(3) del PCT).

D1 representa la anterioridad más relevante y divulga pirrolobenzoxazinas antiparasitarias. Los presentes compuestos difieren de los compuestos de D1 en que el R2 residual es alquilo y no alquenilo.

El problema técnico que sostiene las reivindicaciones 1-4, 7, 11, y 14 es proporcionar compuestos antiparasitarios alternos los cuales exhiban mayor actividad in vivo en comparación con los compuestos de D1 (comparar con la página 2, líneas 1-8 de la solicitud).

La solicitud parece no contener no datos farmacológicos ni pruebas comparativas. Consecuentemente, no puede decidirse si el problema técnico es resuelto o no y por lo tanto no puede reconocerse nivel inventivo.

Las reivindicaciones relacionadas con las composiciones que contienen los compuestos de la reivindicación 1 (reivindicaciones 5, 6 y 10) o con el uso de dichos compuestos (reivindicaciones 8, 9, 12 y 13) tampoco poseen consecuentemente nivel inventivo.

Observación adicional:
El solicitante debió citar el estado de la técnica anterior dando origen a las dos condiciones en la reivindicación en la página 209 (Regla 5.1(a)(ii) del PCT).

Un grupo preferido de compuestos de fórmula (I) es aquel en donde:

R1 es alquilo C1-6, alquenilo C1-4, alquinilo C1-4, alquilo OC1-6, alquenilo OC1-4 ó alquinilo OC1-4; y

R2 es un anillo de tiazol opcionalmente sustituido con alquilo C1-4; un anillo de piperazina opcionalmente sustituido con alquilo C1-4; un grupo isopropenilo opcionalmente sustituido por halo; o un grupo isopropilo opcionalmente sustituido por uno o más halo, NR7R8, en donde R7 y R8 pueden tomarse de manera conjunta para representar un anillo de hasta siete átomos opcionalmente conteniendo oxígeno o pueden ser seleccionados de manera independiente entre H o cicloalquilo C1-4, =NOR17, en donde R17 puede seleccionarse entre alquinilo C1-6, C1-4 ó alquenilo C1-4.

Un grupo más preferido de compuestos de fórmula (I) es aquel en donde:

R1 es –CH3, -O-alilo ó –O-propargilo;

R2 es 2-etiltiazol-4-ilo, isopropilo, piperazinilo, 1,2-difluoropropen-2-ilo, 1-oxoprop-2-il metiloxima, 1-oxoprop-2-il propargiloxima, 1-oxoprop-2-il aliloxima, 1-N-morfolinoprop-2-ilo, 1-fluoroprop-2-ilo, 1,1-difluoroprop-2-ilo;

R3, R4, y R5 son H;

Compuestos individuales particularmente preferidos del invento incluyen compuestos de fórmula (I) en donde R3, R4, y R5 todos son H, y R1 y R2 son tal como se ilustran abajo:

R1=	R2=
CH_3	2-etiltiazol-4-ilo, isopropilo
CH_3	1,2-difluoropropen-2-ilo
CH_3	1-oxoprop-2-il metiloxima
CH_3	1-oxoprop-2-il propargiloxima

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

WOOD, David, J.
Pfizer Limited
Ramsgate Road
Sandwich
Kent, CT13 9NJ
GRANDE BRETAGNE

EUROPEAN PHARMA PATENT DEPARTMENT
05 MAY 2005

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	03.05.2005
Applicant's or agent's file reference: PC10339A	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB2004/000320	03.02.2004	14.02.2003

Applicant
PFIZER LIMITED

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the *international preliminary report on patentability and its annexes, if any, established on the international* application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

   The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

   Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

   For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

   The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

FILING ✓
DEPT
REC

Name and mailing address of the international preliminary examining authority:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer:
Hebert, W
Tel. +49 89 2399-2152

Form PCT/IPEA/416 (January 2004)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PC10339A	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/IB2004/000320	International filing date *(day/month/year)* 03.02.2004	Priority date *(day/month/year)* 14.02.2003
International Patent Classification (IPC) or national classification and IPC C07D498/04, C07D498		
Applicant PFIZER LIMITED		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 16 sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
27.02.2004	03.05.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Grassi, D Telephone No. +49 89 2399-8499

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No. PCT/IB2004/000320

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-5, 7-14, 21-118, 120-124, 126, 128-158, 160-163, 166-197, 199, 200, 202, 204-207	as originally filed
6, 15-20, 119, 125, 127, 159, 164, 165, 198, 201, 203	received on 14.12.2004 with letter of 10.12.2004

Claims, Numbers

1-14	as originally filed

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 9,12,13

because:

☒ the said international application, or the said claims Nos. (with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees, the applicant has:
   - ☐ restricted the claims.
   - ☐ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☒ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☐ not complied with for the following reasons:

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-14(part) .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-14
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-14
Industrial applicability (IA)	Yes:	Claims	1-8,10,11,14
	No:	Claims	

2. Citations and explanations (Rule 70.7):

   see separate sheet

Reference is made to the following documents:
D1: WO 95/19363 (cited in the application)

Re Item III
Claims 9, 12 and 13 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

The International Examining Authority found multiple (groups of) inventions in this international application. No required additional examination fees were paid by the applicant. Consequently, this written opinion is restricted to the first invention.

Re Item IV

D1, discloses antiparasitic pyrrolobenzoxazines.
The technical problem underlying the present application is seen in the provision of alternative antiparasitic compounds.
In view of the compounds of D1, showing the same core structure as the present compounds, the different alternatives encompassed by the present claims do not share a common special technical feature as required by Rule 13.2 PCT.
The fact that the compounds of D1 are disclaimed cannot establish unity among the different groups of inventions.

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

1. Claim : 1(part) R2 is alkyl.
2. Claim : 1(part) R2 is unsubstituted alkenyl.
3. Claim : 1(part) R2 is substituted alkenyl.
4. Claim : 1(part) R2 is a 5- or 6-membered heterocycle.

Re Item V

1) The amendments appear to be in conformity with Art. 34(2)b) PCT.

However, the correction carried out on page 6, should also be carried out in present claim 2.

2) The subject-matter of present claims 1-14 is new (Article 33(2) PCT).
The present compounds differ from the compounds of D1 in that the residue R2 is alkyl and not alkenyl. The compositions uses and methods are novel by consequence.

3) The subject-matter of claims 1-14 does not involve an inventive step (Article 33(3) PCT).

D1 represents the most relevant prior art and discloses antiparasitic pyrrolobenzoxazines. The present compounds differ from the compounds of D1 in that the residue R2 is alkyl and not alkenyl.

The technical problem underlying the present claims 1-4, 7, 11 and 14 is seen in the provision of alternative antiparasitic compounds exhibiting higher in vivo activity compared to the compounds of D1 (cf. page 2, lines 1-8 of the application).

The application appears to contain neither pharmacological data nor comparative tests. Consequently, it cannot be decided whether the technical problem is solved or not and inventive activity cannot be acknowledged.

The claims relating to the compositions containing the compounds of claim 1 (claims 5, 6, and 10) or to the use of the said compounds (claims 8, 9, 12 and 13) do, by consequence, also not involve inventive activity.

Additional remark:
The applicant should have cited the prior art giving rise to the two provisos on claim page 209 (Rule 5.1(a)(ii) PCT).

A preferred group of compounds of formula (I) is that wherein:

R^1 is C_1-C_6 alkyl, C_1-C_4 alkenyl, C_1-C_4 alkynyl, OC_1-C_6 alkyl, OC_1-C_4 alkenyl or OC_1-C_4 alkynyl; and

R^2 is a thiazole ring optionally substituted with C_1 to C_4 alkyl; a piperazine ring optionally substituted with C_1 to C_4 alkyl; an isopropenyl group optionally substituted by halo; or an isopropyl group optionally substituted by one or more halo, NR^7R^8, wherein R^7 and R^8 may be taken together to represent a ring of up to 7 atoms optionally containing oxygen or may be independently selected from H or C_1 to C_4 cycloalkyl, $=NOR^{17}$, wherein R^{17} may be selected from C_1 to C_6, C_1 to C_4 alkynyl or C_1 to C_4 alkenyl.

A more preferred group of compounds of formula (I) is that in which:

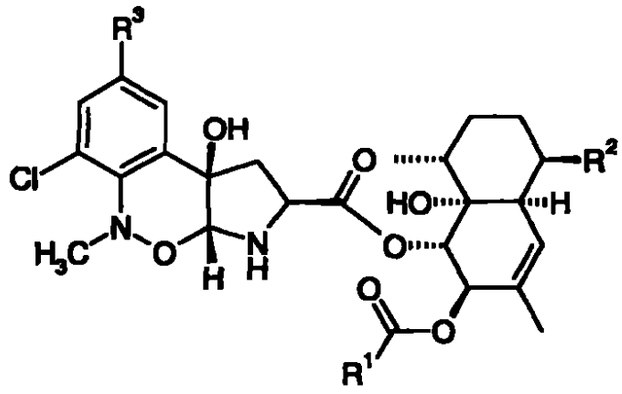
R^1 is $-CH_3$, -O-allyl or –O-propargyl;

R^2 is 2-ethylthiazol-4-yl, isopropyl, piperazinyl, 1,2-difluoropropen-2-yl, 1-oxoprop-2-yl methyl oxime, 1-oxoprop-2-yl propargyl oxime, 1-oxoprop-2-yl allyl oxime, 1-N-morpholinoprop-2-yl, 1-fluoroprop-2-yl, 1,1-difluoroprop-2-yl;

R^3 , R^4 and R^5 are H;

Particularly preferred individual compounds of the invention include compounds of formula (I) where R^3 , R^4 , and R^5 all are H, and R^1 and R^2 are as indicated below:

R1 =	R2 =
CH_3	2-Ethylthiazol-4-yl, isopropyl
CH_3	1,2-difluoropropen-2-yl
CH_3	1-oxoprop-2-yl methyl oxime
CH_3	1-oxoprop-2-yl propargyl oxime



Generic Procedures

Generic Process A

Methanol (3 ml) was added to the corresponding amine (0.39 mmol, 1.5 equiv.), which was placed in a Stem® Reaction Block. In those cases where the amine was an ammonium salt, triethylamine (55µl, 0.4 mmol) was added. A solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl)(2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 200mg, 0.26 mmol) in methanol (2 ml, analytical grade) was added, and the reaction mixtures were stoppered with a rubber septum and stirred for 5 hours at ambient temperature. Borohydride on Amberlite® IRA400 (200mg, 0.5 mmol) was added and the mixture stirred at room temperature for 18 h. The reaction mixture was then filtered through a filter cartridge (Isolute™, 6 ml), the residue washed with methanol (2 ml), and the filtrate concentrated under a stream of nitrogen. To the resulting crude product was added hydrogen chloride (4 N solution in dioxane, 2 ml), the mixture was agitated on an orbital shaker for 10 min, transferred to a hot plate (50 °C) and concentrated under a stream of nitrogen for 40 min. Triethylamine (20% v/v in dichloromethane, 2 ml) was added and the mixture was concentrated under a stream of nitrogen, followed by addition and evaporation of triethylamine (20% v/v in dichloromethane, 2ml). The crude reaction product was then dissolved in a acetonitrile :

dimethylsulfoxide (4:1, 1 ml) and purified by automated preparative liquid chromatography (Gilson system, 10 x 150 mm Phenomenex Magellen C18 5µ column) using a 0.1% aqueous trifluoroacetic acid : acetonitrile gradient (95:5 to 5:95). Evaporation of the eluant in a Genevac system gave the final product.

Generic Process B

To the corresponding amine (0.33 mmol, 1.5 equiv.) was added a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 170 mg, 0.22 mmol) in dichloromethane (2 ml). In those cases where the amine was an ammonium salt, triethylamine (55µl, 0.4 mmol) was added. Sodium triacetoxyborohydride (93 mg, 0.44 mmol) was added to the reaction, and the mixture was stirred in a Stem® reaction block for 18 h. The mixture was then diluted with dichloromethane (4 ml) and water (2 ml) and stirred vigorously for 20 min. The layers were separated by means of a filter cartridge with a hydrophobic frit (Whatman 12 ml 1PS filter media), and the organic filtrate concentrated under a stream of nitrogen. To the resulting crude product was added hydrogen chloride (4 N solution in dioxane, 2 ml), the mixture was agitated on an orbital shaker for 10 min, transferred to a hot plate (50 °C) and concentrated under a stream of nitrogen for 40 min. Triethylamine (20% v/v in dichloromethane, 2 ml) was added and the mixture concentrated under a stream of nitrogen, followed by addition and evaporation of further triethylamine (20% v/v in dichloromethane, 2 ml). The crude reaction product was then dissolved in a acetonitrile : dimethylsulfoxide mixture (4:1, 1 ml) and purified by automated preparative liquid chromatography (Gilson system, 10 x 150 mm Phenomenex Magellen C18 5µ column) using a 0.1% aqueous trifluoroacetic acid : acetonitrile gradient (95:5 to 5:95). Evaporation of the eluant in a Genevac system gave the final product.

Generic Process C

A solution of (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 141, 21 mg, 0.0375 mmol), the amine (0.1 mmol), tetramethylammonium triacetoxyborohydride (26 mg, 0.1 mmol), triethylamine (20 µl, 0.15 mmol) in 1-methyl-2-pyrrolidinone (0.9 ml) was shaken at ambient temperature for 18 h. The reaction mixture was then directly injected onto the HPLC column for purification using a 0.1% aqueous trifluoroacetic acid : acetonitrile gradient (95:5 to 5:95). The purified product was obtained after evaporation of the solvents in a Genevac system.

Autopurification was carried out using a Gilson HPLC system using a Phenomenex Magellen® 150mm x 10mm 5µ ODS column at ambient temperature. Elution was by gradient formed from 0.1% aqueous trifluoroacetic acid : acetonitrile (95:5 to 5 : 95) over 12 min. The products were detected by UV at 215nm. All fractions from autopurification were analysed by loop injection into a Micromass "Platform LC"® single-quadrupole mass spectrometer with APCI probe.

Generic Process D

To a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 200 mg, 0.26 mmol) in methanol (5 ml) was added the corresponding primary amine (0.52 mmol, 2 equiv.). Triethylamine (80 µl, 0.58 mmol) was added in those cases where the amine was an ammonium salt. The reaction mixture was stirred for 18 hours at ambient temperature in a Stem® reaction block. Then borohydride

on Amberlite® IRA400 (Aldrich, 2.5 mmol/g resin, 150 mg, 0.38 mmol) was added and the stirring continued for 2.5 days. The reaction mixture was filtered using a disposable filter cartridge (6 ml) and the residue rinsed with methanol. 4-Benzyloxybenzaldehyde, polymer-bound (Aldrich, 2.8 mmol/g resin, 180 mg, 0.5 mmol) was added to scavenge excess amine and the reaction mixture then stirred for 18 h at room temperature. The reaction solution was filtered using disposable filter cartridges (6 ml), the residue rinsed with methanol and the filtrate concentrated under a stream of nitrogen. The crude product was dissolved in dichloromethane (20 ml). Of this reaction mixture (5 ml) was added to anhydrous pyridine (8 µl, 0.10 mmol) and the corresponding acid chloride (0.1 mmol, 1.5 equiv.) added and the reaction stirred at room temperature for 3 hours. The solvents were evaporated under a stream of nitrogen. To the resulting crude product was added hydrogen chloride (4 N solution in dioxane, 2 ml), the mixture was stirred at room temperature for 45 min, transferred to a hot plate (50 °C) and concentrated under a stream of nitrogen. Triethylamine (20% v/v in dichloromethane, 2 ml) was added and the mixture was concentrated under a stream of nitrogen. The crude reaction product was then dissolved in acetonitrile : dimethylsulfoxide (8:1, 1 ml), filtered using a Whatman HPLC filter and purified by automated preparative liquid chromatography (Gilson system, 10 x 150 mm Phenomenex Magellen C18 5µ column), using a 0.1% aqueous trifluoroacetic acid : acetonitrile gradient ranging from 95:5 to 5:95. Evaporation of the eluant in a Genevac system gave the final product.

Generic Process E

To the solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 100 mg, 0.13 mmol) in methanol (2 ml) was added the corresponding amine (0.52 mmol, 4 equiv.), and the mixture stirred at room temperature for 18 h. Borohydride on Amberlite® IRA400 (Aldrich, 2.5mmol/g resin, 77 mg, 0.19 mmol) was added

and the mixture agitated with an orbital shaker at room temperature for 18 h. Then benzyloxybenzaldehyde, polymer-bound (Aldrich, 2.8 mmol/g resin, 460 mg, 1.29 mmol) was added to scavenge excess amine and the reaction mixture was shaken for 18 h. The reaction mixture was filtered, the residue was washed with methanol and the filtrate concentrated to dryness under a stream of nitrogen. A solution of the crude product (0.064 mmol) in dichloromethane was placed into a 48-well-plate (Flexchem Synthesis Block), and polymer-bound *N*-methylmorpholine (3.0 mmol/g resin, 32 mg, 0.096 mmol) was added by means of a dispensing plate. The corresponding acid chloride (0.16 mmol, 2.5 eq.) was added and the reaction mixture shaken at room temperature for 18 h. Polymer-bound *tris*(2-aminoethyl)amine, (4.8 mmol/g resin, 41 mg, 0.2 mmol) was then added with a dispensing plate and the mixtures shaken at room temperature for 18 h. The reaction mixture was then filtered into another 48-well-block and the filtrates concentrated under a stream of nitrogen. The crude residue was dissolved in hydrogen chloride, (1 M solution in acetic acid, 0.5 ml), shaken at room temperature for 1 hour and then concentrated to dryness under a stream of nitrogen. The crude reaction product was then dissolved in a acetonitrile (1 ml) and purified by automated preparative liquid chromatography (Gilson system, 10 x 150 mm Phenomenex Magellen C18 5µ column), using a 0.1% aqueous trifluoroacetic acid : acetonitrile gradient (95:5 to 5:95). Evaporation of the eluant in a Genevac system gave the product.

Generic Process G

To a solution of (2R)-2-[(1R,4R,4aS,5R,6R)-5-({[(2S,3aR,9bR)-6-chloro-3-{[(1,1-dimethylethyl)oxy]carbonyl}-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazin-2-yl]carbonyl}oxy)-6-(acetyloxy)-4a-hydroxy-4,7-dimethyl-1,2,3,4,4a,5,6,8a-octahydronaphthalen-1-yl]propanoic acid (Preparation 181, 200 mg, 0.25 mmol) in dichloromethane (2 ml) was added 1-hydroxybenzotriazole (Aldrich, 58 mg, 0.38 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride salt (96 mg, 0.5 mmol), and the mixture was stirred at room temperature for 0.5 hours. The reaction mixture was added to a solution of the corresponding amine (0.38 mmol) in dichloromethane (2 ml) and stirred at

room temperature for 36 hours. The reaction mixture was diluted with dichloromethane (2 ml) and water (7 ml) and stirred vigorously for 45 min. The layers were separated by means of a filter cartridge with a hydrophobic frit (Whatman 12 ml 1PS filter media), and the organic filtrate concentrated under a stream of nitrogen followed by drying *in vacuo*. To a solution of the crude product in dioxane (1 ml) was added a hydrogen chloride (4M solution in dioxane solution, 2 ml) and the reaction mixture was stirred at room temperature for 25 min. The reaction mixture was concentrated under a stream of nitrogen for 40 min (hotplate 50°C), then a solution of triethylamine in dichloromethane (25% v/v, 2 ml) was added and the mixture again concentrated under reduced preasure. The crude reaction product was purified by automated preparative liquid chromatography (Gilson system, 10 x 150 mm Phenomenex Magellen C18 5µ column), using a 0.1% aqueous trifluoroacetic acid : acetonitrile gradient (95:5 to 5:95). Evaporation of the eluant in a Genevac system gave the product.

The Examples given in the following Table 1 were prepared by the methods referred to above and the Table includes physical characterising data for each compound synthesised. The synthesis of a number of representative compounds are also described in more detail after Table 2. Table 2 indicates the precursor compounds used in the synthesis of the compounds of the invention.

Table 1: Table of Examples

Ex No.	Compound Name	Data*
		*NMR data given for acetate or trifluoroacetate salts
1	(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate	MS (ES) : M/Z [MH+] = 563.3 C29H39ClN2O7 + H requires 563.25. NMR (CDCl3, selected data) : 0.6 (d, 3H), 0.9-1.1 (m, 7H), 1.9 (septet, 1H), 2.1 (s, 3H), 3.35 (s, 3H), 5.2 (s, 1H), 7.2 (d, 1H).

(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2, 3-c][2,1]benzoxazine-2-carboxylate

To a solution of (1S,2R,4aS,5R,8R,8aR)-2,8a-dihydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 139, 51mg, 0.10mmol) and 4-dimethylaminopyridine (14mg, 0.11mmol) in dichloromethane (5ml) was added hexanoic anhydride (43mg, 0.2mmol) and the resulting mixture stood at room temperature over a weekend. The crude product was purified by column chromatography over silica (10g) eluting with hexane : ethyl acetate (2:1). The pure fractions were combined and concentrated *in vacuo* to give the title compound (43mg, 97%).

Example 4: (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2-(acetyloxy)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexa hydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

To ((1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 140, 63.8mg, 0.11mmol) in dichloromethane (1.1ml) was added acetic anhydride (22mg, 20µl, 0.22mmol) and 4-dimethylaminopyridine (14.3mg, 0.12mmol) and the reaction mixture stirred at room temperature for 18 hours. The reaction mixture was diluted with dichloromethane (20ml) and washed with aqueous citric acid solution, dried ($MgSO_4$) and concentrated *in vacuo* to give a gum. The crude product was purified by chromatography on silica eluting with hexane : ethyl acetate (60:40). The pure fractions were combined and concentrated *in vacuo* to give the title product as a white solid (42mg, 61%).

Example 5: (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-{1-methyl-2-[(2-methylpropanoyl)oxy]ethyl}-1,2,4a,5,6,7,8,8a-

with hexane : ethyl acetate (2:1). The pure fractions were combined and the solvent removed *in vacuo* to give the title product (150mg, 61%).

Example 15: (1S,2R,4aS,5R,8R,8aR)-2-(formyloxy)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl(2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

The title compound was prepared by the method of Example 14 substituting (acetyloxy)acetic acid with commercially available formic acid (20µl, 0.53mmol) to give the title compound (160mg, 73%).

Example 16: (1S,2R,4aS,5R,8R,8aR)-8a-hydroxy-3,8-dimethyl-5-(1-methylethenyl)-2-[(3,3,3-trifluoropropanoyl)oxy]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexa hydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

The title compound was prepared by the method of Example 14 substituting (acetyloxy)acetic acid with commercially available 3,3,3-trifluoropropionic acid to give the title compound (165mg, 66%).

Example 17: (1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[4-(ethyloxy)-1-methyl-4-oxobut-2-enyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate

A solution of ((1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6-chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate (Preparation 141, 94mg, 0.163mmol) and carbethoxymethylene triphenylphosphorane (68mg, 0.195mmol) in anhydrous toluene (5ml) was refluxed under nitrogen for 3

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To 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-8a-hydroxy-5-[2-hydroxy-1-methylethyl]-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 157, 200mg, 0.26mmol) in dichloromethane at -78°C was added diethylaminosulfur trifluoride (45mg, 34µl, 0.28mmol) over 10 minutes. The resulting mixture was allowed to warm to room temperature and then stirred for 18 h. The reaction mixture was cooled to -78°C and diethylaminosulfur trifluoride (34µl, 0.28mmol) added. Again, the resulting mixture was allowed to warm to room temperature and stirred for 18 h. The reaction mixture was quenched with water and extracted with hexane : ether (1:2). The organic extract was washed with saturated aqueous sodium chloride solution, dried ($MgSO_4$) and concentrated *in vacuo* to give the Boc-protected intermediate 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2-fluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl)(2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate as a white solid (172mg, 86%).

To a solution of the Boc-protected intermediate 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2-fluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl}3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate in ethyl acetate (5ml) was added concentrated hydrochloric acid (12 N, 1.5ml) and the resulting mixture was stirred for 1 hour. The reaction mixture was diluted with ethyl acetate (50ml), washed with water (3 x 20ml) and saturated aqueous sodium chloride solution (20ml), dried ($MgSO_4$) and concentrated *in vacuo* to give a foam (125mg, 83%). The crude product was purified by chromatography on silica eluting with hexane : ethyl acetate (2:1 then 1:1). The pure fractions were combined and concentrated *in vacuo* to give a white

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Preparation 23 : 11-(Phenylmethyl)-3,11-diazatricyclo[7.3.1.$0^{2,7}$]trideca-2,4,6-triene

To a solution of 3-azatricyclo[7.2.1.$0^{2,7}$]dodeca-2,4,6-triene-10,11-diol (Preparation 24, 1.16 g, 6.07 mmol) in ethanol (40 ml) was added sodium periodate (1.35 g, 6.07 mmol) in water (20 ml) to produce a yellow slurry. After 15 min, water and ethyl acetate were added and the layers were separated, the aqueous layer was washed with ethyl acetate (4 x 50 ml) and then dichloromethane. The combined organic extracts were dried (Na_2SO_4) to give an orange oil. The oil was diluted with dichloroethane (50 ml), benzylamine (0.65 g, 6.07 mmol) was added followed by sodium triacetoxyborohydride (4.12 g, 19.4 mmol). After 7 h, saturated sodium hydrogen carbonate solution (75 ml) and ethyl acetate (75 ml) were added and the reaction mixture was stirred for 20 min. The layers were separated and the aqueous layer was extracted with ethyl acetate (2 x 50 ml). The combined organic extracts were washed with water and brine, and then dried (Na_2SO_4) and concentrated *in vacuo* to give the crude product. Purification by flash chromatography produced the title compound as a light yellow oil (0.80 g, 50%).

Preparation 24 : 3-azatricyclo[7.2.1.$0^{2,7}$]dodeca-2,4,6-triene-10,11-diol

A mixture of 3-azatricyclo[7.2.1.$0^{2,7}$]dodeca-2,4,6,10-tetraene (Preparation 25, 0.96 g, 6.11 mmol), trimethylamine *N*-oxide dihydrate (0.75 g, 6.73 mmol) and osmium tetroxide (2.5 wt % solution in 2-methyl-2-propanol, 2 µl) in dichloromethane (15 ml) were stirred for 18 h. A further portion of osmium tetroxide (2.5 wt % solution in 2-methyl-2-propanol, ca. 1 µl) was added and the reaction mixture was stirred for a further 18 h. The reaction mixture was subjected to chromatography eluting with hexane and then ethyl acetate to give the title compound as a solid (1.16 g, 100%).

Preparation 33 : 3-(phenylmethyl)-3-azabicyclo[3.2.1]octane-6,7-dicarbaldehye *bis* (*O*-methyloxime)

To a solution of 9-(phenylmethyl)-9-azatricyclo[5.3.1.$0^{2,6}$]undecane-3,4-diol (Preparation 34, 6.0 g, 21.9 mmol) in dioxane (100 ml) was added sodium periodate (5.0 g, 23.3 mmol) in water (50 ml). A thick slurry formed, water (50 ml) was added and the reaction mixture was stirred under nitrogen. Upon completion, the reaction mixture was diluted with water (150 ml) and saturated sodium carbonate (50 ml) and the product was extracted with ethyl acetate (2 x 150 ml). The combined organic extracts were washed with water, and then brine before drying (Na_2SO_4) and concentrating to give an orange oil (6.14 g). To the crude oil was added methanol (75 ml) and water (75 ml), followed by methoxylamine hydrochloride (7.34 g, 87.9 mmol) and sodium acetate (12.62 g, 153.8 mmol). The reaction mixture was shaken and then warmed on a steam bath for ca 15 min to give a clear solution, and was then stirred at room temperature for 18 h. Ethyl acetate (100 ml) and sodium carbonate solution (100 ml) were added and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 x 50 ml) and the combined organic extracts were washed with brine and dried (Na_2SO_4) and concentrated to give the title compound as an oil (5.0 g, 69%).

Preparation 34 : 9-(Phenylmethyl)-9-azatricyclo[5.3.1.$0^{2,6}$]undecane-3,4-diol

A solution of 9-(phenylmethyl)-9-azatricyclo[5.3.1.$0^{2,6}$]undec-3-ene (Preparation 35, 6.7 g, 28.0 mmol), *N*-methylmorpholine N-oxide (3.45 g, 29.45 mmol) and osmium tetroxide (2.5 wt % in 2-methyl-2-propanol, 2 µl) in acetone (50 ml) was stirred for 18 h. Florisil and aqueous sodium hydrogensulfite (4 ml) were added and the reaction mixture was stirred for 30 min and filtered. Methanol (50 ml) was added and the reaction mixture was concentrated to give an oil which was purified by flash chromatography eluting with ethyl acetate : hexane (50:50) to give an oil (6.2 g, 80%) which crystallises upon standing.

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Preparation 35 : 9-(phenylmethyl)-9-azatricyclo[5.3.1.$0^{2,6}$]undec-3-ene

T a stirred solution of tricyclo[5.2.1.$0^{2,6}$]dec-3-ene-8,9-diol (Preparation 36, 6.24 g, 37.6 mmol) in dioxane (100 ml) was added sodium periodate (8.04 g, 37.6 mmol) in water (80 ml) and the reaction mixture was stirred vigorously for 45 min. The reaction mixture was extracted with ethyl acetate (4 x 100 ml) and the combined extracts were washed with brine, dried (Na_2SO_4) and concentrated *in vacuo*. The crude oil (6.1 g, 37.1 mmol) was diluted with dichloroethane (400 ml) and benzylamine (3.98 g, 37.1 mmol) was added. After 3 min, sodium triacetoxyborohydride (25.23 g, 119 mmol) was added and the reaction mixture was stirred at room temperature for 18 h. Saturated sodium carbonate solution (200 ml) was added, and after 30 min, the layers were separated and the aqueous layer was washed with dichloromethane (3 x 50 ml). The combined organic extracts were washed with brine, filtered and concentrated. The crude yellow oil was purified by flash chromatography eluting with ethyl acetate : dichloromethane (10 : 90) to give the title compound as a colourless oil (6.7 g, 75 %)

Preparation 36 : Tricyclo[5.2.1.$0^{2,6}$]dec-3-ene-8,9-diol

A slurry of tricyclo[5.2.1.$0^{2,6}$]deca-3,8-diene (26.5 g, 0.2 mol), trimethylamine N-oxide dihydrate (22.3 g, 0.2 mol) and osmium tetroxide (2.5 wt % solution in 2-methyl-2-propanol, 2 µl) in dichloromethane (200 ml) was stirred for 18 h. A further portion of osmium tetroxide (2.5 wt % solution in 2-methyl-2-propanol, ca. 2 µl) was added, water (25 ml) and acetone (50 ml) was added and the reaction mixture was stirred for a further 72 h. Pyridine (0.5 ml) and tetrabutylammonium acetate (0.5 g) were added. Florisil (10 g) and aqueous sodium hydrogensulfite solution was added and the reaction mixture was stirred for 20 min. The reaction mixture was filtered and the product was extracted with dichloromethane (3 times). The combined organic extracts were washed with water, brine and then concentrated to give an oil. The

mixture was diluted with water and extracted with ether (2 x). The combined organic phases were washed with water and then saturated aqueous sodium chloride, dried (Na_2SO_4) and concentrated. The gummy residue was purified by flash column chromatography on silica gel eluting with ethyl acetate:hexane (5 : 95) to give the product as an oil (400 mg).

Preparation 167 : 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2,2-difluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

To a solution of diethylaminosulfur trifluoride (41µl, 0.31mmol) in anhydrous dichloromethane (3ml) at -78°C was added a solution of 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl)(2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 200mg, 0.25mmol) in anhydrous dichloromethane (2ml) dropwise over 2 minutes. The resulting mixture was allowed to warm to room temperature and stirred for 18 h. The reaction mixture was diluted with dichloromethane (5ml), washed with water (5ml), dried (Na_2SO_4) and concentrated *in vacuo* to give the crude product (145mg, 59%). This crude product was purified by column chromatography on silica gel eluting with hexane : ethyl acetate (10:1 to 3:1). The pure fractions were combined and concentrated *in vacuo* to give the title product (38mg, 19%).

Preparation 168: 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-5-[2,2-difluoro-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-

(95 mg). The reaction mixture was heated to 75°C, after 1.5 h the reaction mixture was concentrated *in vacuo* to remove the methanol. The resultant solution was diluted with diethyl ether (30 ml) and water (30 ml) and the organic layer separated and washed with sodium hydrogen carbonate (3 x 30 ml). The aqueous layers were back extracted with diethyl ether (2 x 20 ml) and the combined organic extracts were dried ($MgSO_4$) and concentrated to give the title compound as a white solid.

Preparation 176 : 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[(1R)-2-(cyclopropylamino)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

T 2-{(1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-[1-methyl-2-oxoethyl]-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 160, 0.56 g, 0.73 mmol) in anhydrous dichloromethane (5 ml) was added cyclopropylamine (50µl, 0.73 mmol) and the reaction mixture was stirred at room temperature for 20 min. Sodium triacetoxyborohydride (0.21 g, 1.0 mmol) was added and the reaction mixture was stirred for 18 h. The reaction mixture was diluted with ethyl acetate and washed with sodium hydrogen carbonate solution. The organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give the title compound as a yellow foam (0.56 g, 96%).

Preparation 177 : 2-[(1S,2R,4aS,5S,8R,8aR)-5-{2-[acetyl(cyclopropyl)amino]-1-methylethyl}-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl] 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

Preparation 179 : 2-[(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{cyclopropyl[(methyloxy)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl]3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

To 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[(1R)-2-(cyclopropylamino)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 176, 98 mg, 0.12 mmol) and 4-dimethylaminopyridine (15 mg, 0.12 mmol) in anhydrous dichloromethane (3 ml) was added pyridine (50. µl, 0.60 mmol) and the reaction mixture was cooled to 0°C. Methyl chloroformate was added dropwise and the reaction mixture was stirred for 18 h, before diluting with ethyl acetate and washing with water, citric acid (20% w/v) and water again. The organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give the title compound as a yellow glassy solid (108 mg, 100%).

Preparation 180 : 2-[(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-(2-{cyclopropyl[(ethylamino)carbonyl]amino}-1-methylethyl)-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl] 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate

To 2-{(1S,2R,4aS,5S,8R,8aR)-2-(acetyloxy)-5-[(1R)-2-(cyclopropylamino)-1-methylethyl]-8a-hydroxy-3,8-dimethyl-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl} 3-(1,1-dimethylethyl) (2S,3aR,9bR)-6-chloro-9b-({[(1,1-dimethylethyl)oxy]carbonyl}oxy)-5-methyl-1,2,5,9b-tetrahydropyrrolo[2,3-c][2,1]benzoxazine-2,3(3aH)-dicarboxylate (Preparation 176, 0.16 g, 0.2 mmol) in anhydrous dichoromethane (5 ml) cooled to 0°C was added ethyl isocyanate (0.017 ml, 0.22 mmol) dropwise and the reaction mixture was

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(54) Title: ANTIPARASITIC TERPENE ALKALOIDS

(57) Abstract: The present invention relates to novel terpene alkaloids and their use as antiparasitic agents. The present invention also relates to an antiparasitic agent which comprises a terpene alkaloid compound of this invention as an effective ingredient in an antiparasitic formulation. More particularly, the present invention relates to derivatives of the terpene alkaloid (1S,2R,4aS,5R,8R,8aR)-2-(acetyloxy)-8a-hydroxy-3,8-dimethyl-5-(1methylethenyl)-1,2,4a,5,6,7,8,8a-octahydronaphthalen-1-yl (2S,3aR,9bR)-6chloro-9b-hydroxy-5-methyl-1,2,3,3a,5,9b-hexahydropyrrolo[2,3-c][2,1]benzoxazine-2-carboxylate. Pharmaceutical compositions comprising the same are also disclosed.

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EPO-Internal, CHEM ABS Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 95/19363 A (BISHOP BERNARD F ;PFIZER PHARMA (JP); YAMAUCHI YUJI (JP); KOJIMA N) 20 July 1995 (1995-07-20) cited in the application the whole document	1-14
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☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 July 2004	[illegible] 2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Grassi, D

Form PCT/ISA/210 (second sheet) (January 2004)

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2004/000320

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

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

1. [ ] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

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

see additional sheet

1. [X] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[X] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claim: 1(part)

R2 is alkyl.

2. claim: 1(part)

R2 is unsubstituted alkenyl.

3. claim: 1(part)

R2 is substituted alkenyl.

4. claim: 1(part)

R2 is a 5- or 6-membered heterocycle.

INTERNATI NAL SEARCH REP RT

International Application No
PCT/IB2004/000320

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9519363 A	20-07-1995	AT 173264 T	15-11-1998
		AU 684334 B2	11-12-1997
		AU 1424895 A	01-08-1995
		CA 2181168 A1	20-07-1995
		DE 69505946 D1	17-12-1998
		DE 69505946 T2	15-04-1999
		DK 739344 T3	26-07-1999
		EP 0739344 A1	30-10-1996
		ES 2123948 T3	16-01-1999
		WO 9519363 A1	20-07-1995
		JP 2767161 B2	18-06-1998
		JP 9500909 T	28-01-1997
		NZ 278143 A	24-11-1997
		US 5801023 A	01-09-1998
GB 2240100 A	24-07-1991	NONE	

WO 2004/072086
PCT/IB2004/000320

DSL PCT.

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

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

To:

WOOD, David, J.
Pfizer Limited
Ramsgate Road
Sandwich
Kent, CT13 9NJ
ROYAUME-UNI

EUROPEAN PHARMA PATENT DEPARTMENT
31 AUG 2004

Date of mailing (day/month/year)	
26 August 2004 (26.08.2004)	
Applicant's or agent's file reference: PC10339A	IMPORTANT NOTICE

International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/IB2004/000320	03 February 2004 (03.02.2004)	14 February 2003 (14.02.2003)

Applicant: PFIZER LIMITED et al

The International Bureau transmits herewith the following documents:

☑ copy of the international application as published by the International Bureau on 26 August 2004 (26.08.2004) under No. WO 2004/072086

☐ copy of international application as republished by the International Bureau on under No. WO

For an explanation as to the reason for this republication of the international application, reference is made to INID codes (15), (48) or (88) (*as the case may be*) on the front page of the attached document.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Gabriele Bähr
Facsimile No.+41 22 740 14 35	Facsimile No.+41 22 338 70 60

Form PCT/IB/311 (January 2004)

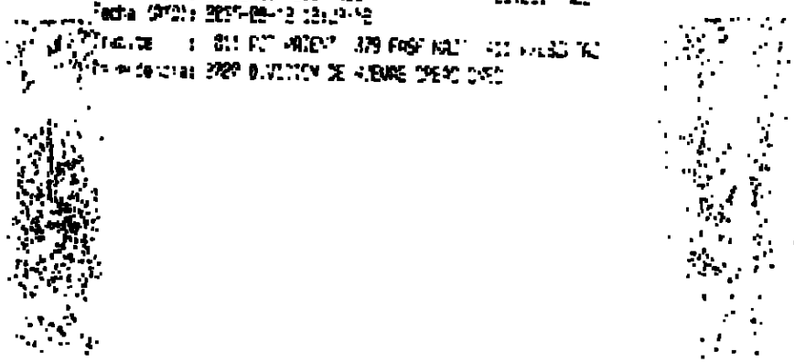
REQUISITOS NECESARIOS PARA PRESENTACION Y AGILIZACION DEL TRAMITE

	USUARIO	RADICADOR
PATENTE DE INVENCIÓN MODELO DE UTILIDAD	( )	( )
- Indicación de que se solicita la concesión de una patente.	( )	
- Datos de identificación del solicitante o de la persona que se presenta la solicitud.	( )	
- Descripción de la invención.	( )	
- Dibujos de ser estos pertinentes.	( )	
- Comprobante de Pago de las tasas establecidas.		
COMPLETA ( )	INCOMPLETA ( )	( )
DISEÑO INDUSTRIAL ( )		
- Indicación de que se solicita el registro de Diseño Industrial	( )	( )
- Datos de identificación del solicitante o de la persona que presenta	( )	( )
- la solicitud.		
- Representación gráfica o fotográfica del Diseño Industrial o muestra del Material que incorpora el diseño.	( )	( )
Comprobante de pago de las tasas establecidas	( )	( )
COMPLETA ( )	INCOMPLETA ( )	( )
ESQUEMA DE TRAZADO ( )		
- Indicación de que solicita el registro de un Esquema de trazado.	( )	( )
- Datos de identificación del solicitante o de la persona que presenta La solicitud.	( )	( )
Representación gráfica del esquema de trazado	( )	( )
Comprobante de pago de las tasas establecidas.	( )	( )
COMPLETA ( )	INCOMPLETA ( )	( )

Firma Responsable:

Fecha:

SUPERINDUSTRIA Y COMERCIO



S27

REPUBLICA DE COLOMBIA
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

Bogotá,
2020

Doctor(a)
OLARTE GARCIA CARLOS REINALDO

REFERENCIA	Radicación No.	5 80439
	Solicitud internacional	IB2004/000320
	Fecha inicio fase nacional	14/09/2005
	Trámite	11
	Evento	379
	Actuación	430
	Oficio No.	0-09724

Como resultado del examen de forma, realizado con fundamento en el artículo 38 de la Decisión 486 de la Comisión de la Comunidad Andina, artículo 27 del Tratado de Cooperación en Materia de Patentes (PCT), regla 51 bis del Reglamento y Circular Única de la Superintendencia de Industria y Comercio, se le comunica que:

1. La solicitud no contiene la traducción de los anexos del reporte de examen preliminar internacional (Art. 36.2.b) del tratado PCT.

2. La solicitud no contiene la copia del documento en que consta la cesión del derecho a la patente del inventor al solicitante o a su causante. (Art. 26-k) Decisión 486.

3. Aclarar el motivo por el cual el Señor J. Trevor Lumb aparece con diferentes cargos en distintas compañías: Secretario Asistente con Pharmacia & Upjohn Company, Vicepresidente con Pfizer Products Inc, Asistente General Consejero de Patentes en Pfizer Inc, Secretario Asistente con Warner Lambert Company LLC.

En cumplimiento de lo dispuesto por el artículo 39 de la Decisión 486, se le requiere para que dentro del término de dos meses siguientes a la fecha de notificación del presente oficio, complete los requisitos anteriormente enunciados. En caso de no dar cumplimiento al presente requerimiento, la solicitud se considerará abandonada y perderá su prelación.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Unica No.10 de 2001.

ALIX CARMENZA CESPEDES DE VERGEL
Jefe de la división de Nuevas Creaciones

El anterior requerimiento fue notificado por fijación en lista de fecha 21 OCT. 2005
adpal