Q.F.

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
No. 11-065858- -00000-0000
Fecha: 2011-05-27 14:46:23 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 411 PRESENTACION Folios: 886

Industria y Comercio
SUPERINTENDENCIA
República de Colombia
Ministerio de Comercio, Industria y Turismo
PROPIEDAD INDUSTRIAL

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
INVENTARIO

Delegatura de Propiedad Industrial
División de Nuevas Creaciones

PCT

SOLICITUD DE

PATENTE DE INVENCION
PCT ENTRADA EN FASE NACIONAL

21. EXPEDIENTE No. 11-65858

54. TITULO: **NUEVAS OCTAHIDROCICLOPENTA[C]PIRROL-4-AMINAS SUSTITUIDAS COMO BLOQUEANTES DE LOS CANALES DE CALCIO**

52. CLASIFICACION INTERNACIONAL: **C07D 209/02, A61K 31/403**

71. SOLICITANTE: **ABBOTT LABORATORIES**

DOMICILIO: **100 Abbott Park Road, Abbott Park, Illinois 60064, ESTADOS UNIDOS DE AMERICA**

74. APODERADO: **Dra. MARGARITA CASTELLANOS A.**

22. BOGOTA, D.C., _____

26-05-2011

Industria y Comercio
SUPERINTENDENCIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

No. 11-065858- -00000-0000

ADM

Fecha: 2011-05-27 14:46:23 Dep: 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 411 PRESENTACION Folios: 886

PATENTE DE INVENCION [ ] **MODELO DE UTILIDAD** [ ] **Art. 33 Decisión 486/00**

- [ ] Indicación que se solicita una patente
- [ ] Datos de identificación del solicitante o de la persona que presenta la solicitud
- [ ] Descripción de la invención
- [ ] Dibujos de ser estos pertinentes
- [ ] Comprobante de pago de las tasas establecidas (de ser el caso formato de descuento)

Completa [ ] Incompleta [ ]

PATENTE DE INVENCION PCT [X] **MODELO DE UTILIDAD PCT** [ ] **Art. 33 Decisión 486/00 Circular Única**

- [X] Indicación que se solicita una PCT
- [X] Datos de identificación del solicitante o de la persona que presenta la solicitud
- [X] Copia de la solicitud en español, tal como fue presentada inicialmente (capítulo descriptivo, reivindicatorio, resumen)
- [ ] Dibujos de ser estos pertinentes
- [X] Comprobante de pago de las tasas establecidas (de ser el caso formato de descuento)

Completa [X] Incompleta [ ]

DISEÑO INDUSTRIAL [ ] **(Art. 119 Decisión 486/00)**

- [ ] Indicación que se solicita diseño industrial
- [ ] Datos de identificación del solicitante o de la persona que presenta la solicitud
- [ ] Representación gráfica y fotográfica del Diseño Industrial o muestra del material que incorpora el diseño
- [ ] Comprobante de pago de las tasas establecidas

Completa [ ] Incompleta [ ]

ESQUEMA DE TRAZADO [ ] **(Art. 92 Decisión 486/00)**

- [ ] Indicación que se solicita un esquema de trazado
- [ ] Datos de identificación del solicitante o de la persona que presenta la solicitud
- [ ] Representación gráfica de un esquema de trazado
- [ ] Comprobante de pago de las tasas establecidas

Completa [ ] Incompleta [ ]

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PETITORIO

Industria y Comercio
SUPERINTENDENCIA

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

No. 11-065858- -00000-0000 ción

Fecha: 2011-05-27 14:46:23 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 411 PRESENTACION Folios: 886

FORMULARIO UNICO DE SOLICITUD DE PATENTES
PCT
ENTRADA EN FASE NACIONAL

SOLICITUD DE:

(1)

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

[X] Capítulo I [ ] Capítulo II

(2) SOLICITANTE (71)

Nombre: **ABBOTT LABORATORIES**

Dirección: **100 Abbott Park Road**
Abbott Park, Illinois 60064
ESTADOS UNIDOS DE AMERICA

Domicilio: **Abbott Park, Illinois - ESTADOS UNIDOS DE AMERICA**

Lugar de Constitución: **ESTADOS UNIDOS DE AMERICA**

Teléfono: Fax:
E-mail:

IDENTIFICACIÓN

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

(3) REPRESENTANTE O APODERADO

Nombre: **MARGARITA CASTELLANOS A.**

Dirección: **CALLE 94A No. 7A-09**

Teléfono: **7560770** Fax: **7550158**

E-mail: info@castellanosyco.com

IDENTIFICACIÓN

C.C. [X] NIT [ ]
C.E. [ ] Otro [ ] Cual
Número **39'779.654** TPA **70.819**

(4) INVENTOR (ES) (72)

VER ANEXO # 1

(5) PCT (86)

Solicitud Internacional No. **PCT/US2009/065847** Fecha **25/11/2009**

Publicación Internacional No. **WO 2010/062927 A2** Fecha **03/06/2010**

(6) Título (54) **NUEVAS OCTAHIDROCICLOPENTA[C]PIRROL-4-AMINAS SUSTITUIDAS COMO BLOQUEANTES DE LOS CANALES DE CALCIO**

(7) Clasificación Internacional (51) **C07D 209/02, A61K 31/403**

(8) Prioridad

SI [X] NO [ ]

(33) País de Origen	(32) Fecha	(31) Número de Solicitud
US	26/11/2008	61/117,995

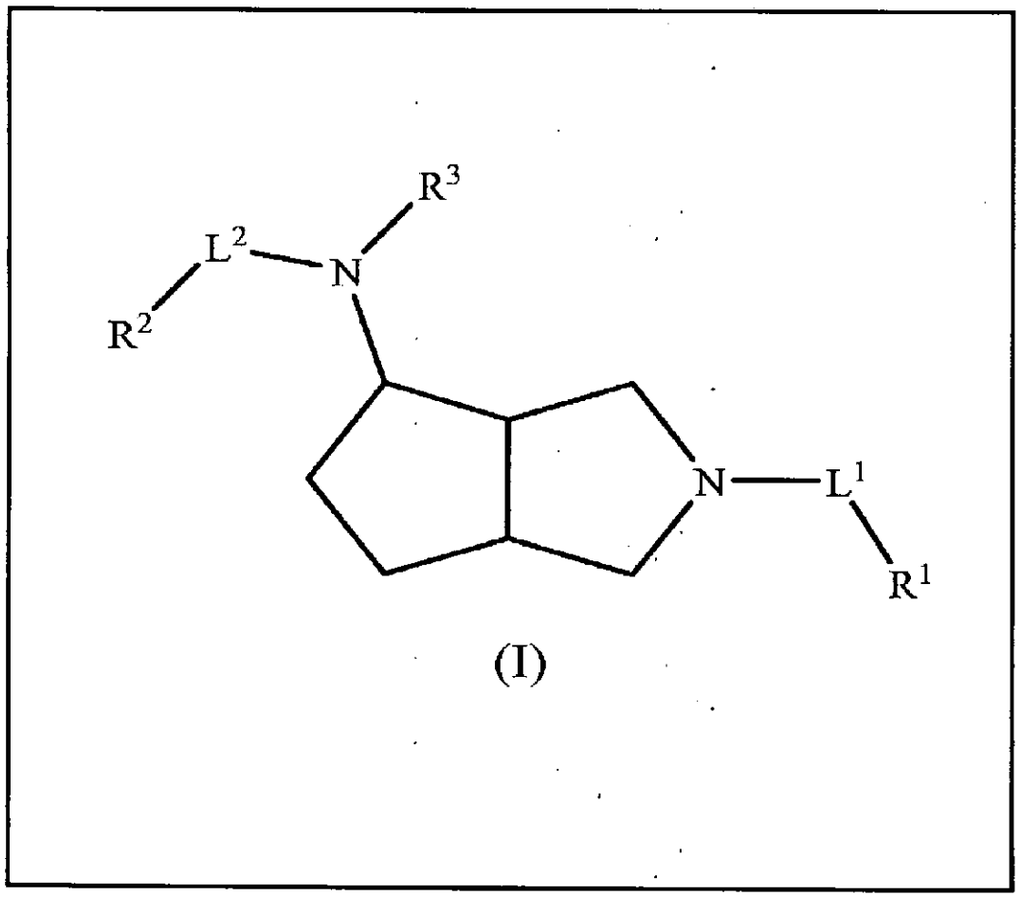
(9) Comprobantes de pago Nos. **11-0047000 y 11-0047004** **Fecha** **Mayo 17 de 2011**

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

(10) Anexos

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

(11) FIGURA CARACTERISTICA:



(I)

(12) Solicito la concesión de la patente,

NOMBRE: **MARGARITA CASTELLANOS ABONDANO**

FIRMA:

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

27 [illegible] 2011

Instrucciones para el diligenciamiento del presente formulario, ver reverso de esta página. - MCA/gcb - P2224

CASTELLANOS & CO LTDA
ABOGADOS
Calle 94 A No. 7 A-09
Bogotá, D.C. – COLOMBIA

ANEXO # 1
INVENTORES

1. **ANDREW STEWART**
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3. **DARIA DARCZAK**
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   Chicago, IL 60641
   ESTADOS UNIDOS DE AMERICA

4. **MING YEUNG**
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   Grayslake, IL 60030
   ESTADOS UNIDOS DE AMERICA

5. **STANLEY DIDOMENICO**
   10109 West Street
   Richmond, IL 60071
   ESTADOS UNIDOS DE AMERICA

P2224

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

Industria y Comercio
SUPERINTENDENCIA

RECIBO DE CAJA

No. 11 - 0047000

Bogotá D.C., Mayo 17 de 2011 - 14:35:26

RECIBIDO DE : CASTELLANOS Y Y CO NI 800.174.641

*** Soporte del Pago ***

TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PAGO	VR.PAGO
CONSIGNACION	BANCO DE BOGOTA	062754387	420512595	17/05/2011	2.581.000.00

*** Conceptos Pagados ***

CANT.	RENTISTICO	CONCEPTO	Vr.UNDITARIO	Vr.CONCEPTO
1	50005-01-01 SOLICITUDES	1 TRAMITES DE SOL. DE PATENTE DE INVENCION	571.000.00	571.000.00
				$571.000.00

SON: **QUINIENTOS SETENTA Y UN MIL PESOS MONEDA CORRIENTE***

Responsable: _____

Recibo de Caja Aplicado al Expediente No. _____

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
No. 11-065858- -00000-0000
Fecha: 2011-05-27 14:46:23 Dep. 2020 DIR.NUEVASCR
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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
NIT : 800.176.089-2
- / -

Industria y Comercio
SUPERINTENDENCIA

RECIBO DE CAJA

No. 11 - 0047004

Bogotá D.C., Mayo 17 de 2011 - 14:35:26

RECIBIDO DE : CASTELLANOS Y Y CO NI 800.174.641

*** Soporte del Pago ***

TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PAGO	VR.PAGO
CONSIGNACION	BANCO DE BOGOTA	062754387	420512595	17/05/2011	2.581.000.00

*** Conceptos Pagados ***

CANT.	RENTISTICO	CONCEPTO	Vr.UNDITARIO	Vr.CONCEPTO
11	50005-01-01 SOLICITUDES	1607 REIVINDICACION UNITARIA ADICIONAL A LAS 10 INICICIALES	27.000.00	297.000.00
				$297.000.00

SON: **DOSCIENTOS NOVENTA Y SIETE MIL PESOS MONEDA CORRIENTE***

Responsable: _____
*****

Recibo de Caja Aplicado al Expediente No. _____

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

No. 11-065858- -00000-0000

Fecha: 2011-05-27 14:46:23 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTE!YII Eve: 378 FASENACIONALI
Act. 411 PRESENTACION Folios: 886

El (los)

ABBOTT LABORATORIES

Domiciliados en

100 Abbott Park Road
Abbott Park
Illinois 60064
E.U.A.

Nombran por el presente a **XIMENA CASTELLANOS A. y/o MARGARITA CASTELLANOS A.** abogadas con oficinas en la Calle 94A No. 7A-09, Bogotá-Colombia para

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

a) Obtención de patentes de invención, modelos y dibujos industriales; registro de marcas de fabrica, de servicio, colectivas o defensivas y de denominaciones de origen, depósito de nombres y enseñas comerciales; su renovación, prórroga, inscripción de traspaso y cambio de nombre o domicilio, cancelación voluntaria y el registro de licencias de uso de esos derechos;
b) Para la obtención de registros sanitarios;
c) Acciones de oposición, observación, cancelación, nulidad, medidas cautelares y en general los juicios civiles, penales, administrativos o contencioso - administrativos que promovamos o se nos promuevan.

Pudiendo en todos los actos y gestiones arriba mencionados sustituir éste mandato, transigir, desistir, recibir, cancelar, renunciar, aceptar notificaciones y nombrar apoderados judiciales y extrajudiciales.

Finalmente, este poder ratifica la validez de todos los actos y solicitudes que, a nombre de la poderdante hubieren realizado los apoderados en relación con las facultades anteriormente enumeradas, antes de la suscripción del presente poder

Dado y firmado hoy 19 de Noviembre de 2008

en Abbott Park, Illinois,
ESTADOS UNIDOS DE AMERICA

por ABBOTT LABORATORIES
(firma ilegible) Paul D. Yasger

(El notario debe suscribir el documento en la pagina siguiente)

(Se requiere legalización consular o mediante apostilla)

I (we) the undersigned

ABBOTT LABORATORIES

Of

100 Abbott Park Road
Abbott Park
Illinois 60064
USA

hereby grant(s) Power of Attorney to **XIMENA CASTELLANOS A. and /or MARGARITA CASTELLANOS** a. attorneys residing at Calle 94A No. 7A-09, Bogotá- Colombia, to

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

a) Obtainment of patents, models and designs, registration of trademarks, service, collective and defensive marks, and of designations of origin; the deposit of trade names and ensigns; its renewal, extension, recordal of assignments, change of name or domicile, voluntary cancellation, and the registration of licenses of use of the above rights;
b) For the obtainment of Sanitary registrations;
c) Actions of opposition, cancellation, nullity, infringement, granting of licenses; and in general the civil, criminal and administrative suits related to those rights; actions and suits instituted by us or against us;

In all the above matters ~~they~~ may substitute this power of attorney, compromise, desist, cancel, receive, renounce, accept notifications and appoint attorneys in fact, in or out of court.

Finally, this power of attorney ratifies the validity of all acts and applications made by the representatives in the name of the signatory of this power of attorney, with regard to the faculties above given, before the execution of the present power of attorney.

Given and signed this 19 day of November, 2008

in Abbott Park, Illinois, USA 60064

by Paul D. Yasger, Assistant Secretary, DVP, Associate General Counsel

(Notary shall execute on the other side)

(Consular legalization or apostille is required)

Como Notario Veintiséis del Círculo de Bogotá, hago constar que esta copia coincide con el original que se ha presentado en esta D.C. Colombia.
20 MAY 2011
GUSTAVO SAMPER RODRIGUEZ
NOTARIO VEINTISEIS

* Abbott ex to sole discretion

CASTELLANOS & CO
ABOGADOS COLOMBIA
Calle 94A No. 7A-09- P.O.Box 6349 - Bogotá, Colombia
Tels.: (571) 610 74 20 / - Fax (571) 610 07 06 - e-mail info@castellanosyco.com

000007

Hoy 19de Nov. del año 2008
compareció (eron) personalmente
Paul D. Yasger

a quienes conozco como la(s) personas que firma(n) en representación de la Sociedad (Compañía) denominada **ABBOTT LABORATORIES**

Certifico :

a) Que **ABBOTT LABORATORIES**

es una sociedad/Compañía legalmente constituida y existente de acuerdo con las leyes de Estados Unidos de América

b) Que el domicilio de dicha Sociedad/Compañía es

100 Abbott Park Road
Abbott Park
Illinois 60064
EUA

c) Que el objeto u objetos para los cuales se otorga el presente poder están comprendidos dentro del objeto social de la mencionada Sociedad /Compañía.

d) Que el Sr. Paul D. Yasger

esta autorizado para otorgar el presente poder. Lo anterior esta probado por medio de los siguientes documentos, que certifico he visto*

(Ciudad) Abbott Park

(Estado) Illinois

Hoy 19del Noviembre de 2008

(Notario Público)

*Los documentos debe identificarse con fecha y origen.

On this 19 day of November of 2008
personally appeared Paul D. Yasger,
whom I know to be the person(s) who signed this document as representative(s) of the Corporation /Company named
ABBOTT LABORATORIES

I certify:

a) That **ABBOTT LABORATORIES**

is a corporation (Company legally constituted and in existence in accordance with the laws of United States of America

b) That the domicile of said Corporation/Company is

100 Abbott Park Road
Abbott Park
Illinois 60064
USA

c) That the purpose or purposes for which the present Power of Attorney is granted are comprised within the object set forth in the charter of the mentioned Corporation/Company.

d) That Mr. Paul D. Yasger

is (are) authorized to grant the present Power of Attorney. The aforementioned was duly proven through the following documents and I duly certify having seen them*:Appointment of Corporate Officer dated March 6, 2008 and signed by Mile D. White, Chairman of the Board and Chief Executive Office of Abbott Laboratories

(City) Abbott Park

(State) Illinois

this 19th day of November of the year 2008

(Notary Public)

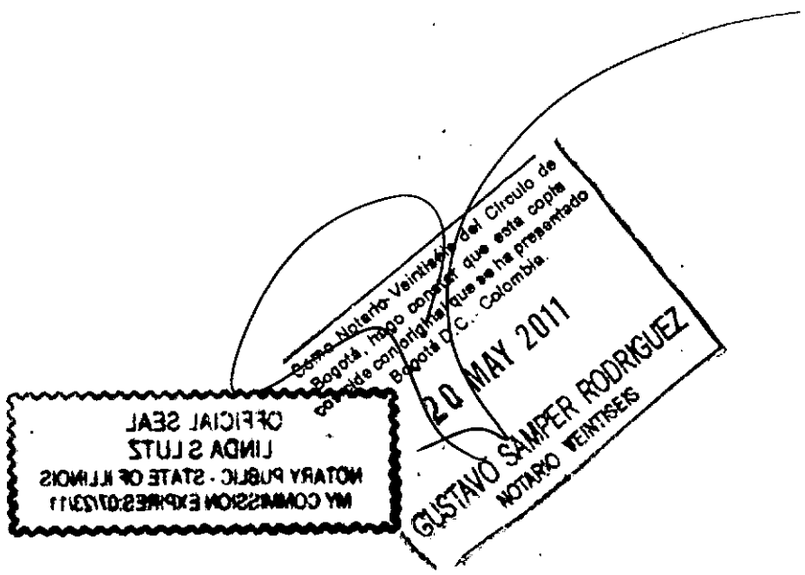
*Documents must be identified with date and origin

OFFICIAL SEAL
LINDA S LUTZ
NOTARY PUBLIC - STATE OF ILLINOIS
MY COMMISSION EXPIRES 07/03/11

20 MAY 2011

GUSTAVO SAMPER RODRIGUEZ
NOTARIO VEINTISEIS

CASTELLANOS & CO
ABOGADOS COLOMBIA
Calle 94A No. 7A-09- P.O.Box 6349 - Bogotá, Colombia
Tels.: (571) 610 74 20 / - Fax (571) 610 07 06 - e-mail info@castellanosyco.com


OFFICIAL SEAL
LINDA S LUTZ
NOTARY PUBLIC - STATE OF ILLINOIS
MY COMMISSION EXPIRES:07/23/11
Notaría Veintiséis del Círculo de Bogotá, hago constar que esta copia concuerda con el original que se ha presentado
Bogotá D.C., Colombia.
20 MAY 2011
GUSTAVO SAMPER RODRIGUEZ
NOTARIO VEINTISEIS

000008

STATE OF ILLINOIS

SECRETARY OF STATE

SPRINGFIELD, ILLINOIS

APOSTILLE

(Convention de La Haye du 5 Octobre 1961)

1. Country: United States of America

This public document

2. has been signed by LINDA S LUTZ
3. acting in the capacity of NOTARY PUBLIC, MCHENRY COUNTY
4. bears the seal/stamp of STATE OF ILLINOIS

Certified

5. Springfield, Illinois
6. NOVEMBER 26, 2008
7. by the Secretary of State, State of Illinois
8. No. S08DL14032
9. Seal/Stamp:

10. Signature:

JESSE WHITE
SECRETARY OF STATE
STATE OF ILLINOIS

Como Notario del Circuito de Bogotá, hago constar que esta copia coincide con original que se ha presentado en Bogotá D.C. Colombia.

20 MAY 2011

GUSTAVO SAMPER RODRIGUEZ
NOTARIO TREINTISEIS

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----------TRADUCCION OFICIAL No. 081205----------

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

(Adjunto a un documento de PODER de Abbott Laboratories)

(fdo) ilegible

Notario Público

SELLO OFICIAL

Notario Público – Estado de Illinois

LINDA S. LUTZ

Mi comisión vence 07/23/11

ESTADO DE ILLINOIS

Secretario de Estado

Springfield, Illinois

APOSTILLA

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

1. País: Estados Unidos de América

Este documento público

2. ha sido firmado por LINDA S. LUTZ
3. actuando en su calidad de Notario Público, Condado de McHenry
4. lleva el sello del Estado de Illinois

Como Notario Veintiseis del Circulo de Bogotá, hago constar que esta copia coincide con original que se ha presentado Bogotá D.C. Colombia.

20 MAY 2011

GUSTAVO SAMPER RODRIGUEZ
NOTARIO VEINTISEIS

CERTIFICADO

5. en Springfield, Illinois
6. El día 26 de Noviembre de 2008
7. Por el Secretario de Estado, Estado de Illinois
8. No. S08DL14032
9. Sello
10. Firma: (fdo) Jesse White

JESSE WHITE

Secretario de Estado

Estado de Illinois (Sello en oblea dorada)

ES TRADUCCION FIEL Y COMPLETA, a la cual me remito,

Bogotá, D. C., Diciembre 17, 2008

Como Notario Veintiseis del Circulo de Bogotá, hago constar que esta copia coincide con original que se ha presentado. Bogotá D.C. Colombia.

20 MAY 2011

GUSTAVO SAMPER RODRIGUEZ
NOTARIO VEINTISEIS

MINISTERIO D
RELACIONES EXTERIORES

2016 DIC 17 P 12:14

MRC
DE LEGALIZACIÓN
BOGOTÁ D.C.

Como Notario Veintiséis del Círculo de Bogotá, hago constar que esta copia coincide con original que se ha presentado
Bogotá D.C. Colombia
20 MAY 2011
GUSTAVO SAMPER RODRIGUEZ
NOTARIO VEINTISEIS

[illegible]
RESPONSABILIDAD
DEL TEXTO

854400

Doc Roque
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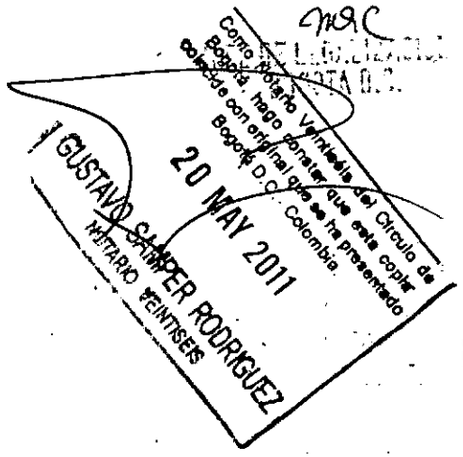
[illegible] PERA
AS FUNCIONES INDICADAS



12644754

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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
3 June 2010 (03.06.2010)

PCT

(10) International Publication Number
WO 2010/062927 A2

(51) International Patent Classification:
C07D 209/02 (2006.01) *A61K 31/403* (2006.01)

(21) International Application Number:
PCT/US2009/065847

(22) International Filing Date:
25 November 2009 (25.11.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/117,995 26 November 2008 (26.11.2008) US

(71) Applicant *(for all designated States except US)*: **ABBOTT LABORATORIES** [US/US]; 100 Abbott Park Road, D-377 AP6A-1, Abbott Park, IL 60064-6008 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **STEWART, Andrew** [US/US]; 1289 Thornbury Lane, Libertyville, IL 60048 (US). **SEARLE, Xenia** [US/US]; 38 N. Alleghany, Grayslake, IL 60030 (US). **DARCZAK, Daria** [US/US]; 3943 N. Kenneth Ave., Chicago, IL 60641 (US). **YEUNG, Ming** [US/US]; 34422 N. Tanguecay Drive, Grayslake, IL 60030 (US). **DIDOMENICO, Stanley** [US/US]; 10109 West Street, Richmond, IL 60071 (US).

(74) Agent: **MUELLER, Lisa**; Polsinelli Shughart PC, 700 W. 47th Street, Suite 1000, Kansas City, MO 64112 (US).

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

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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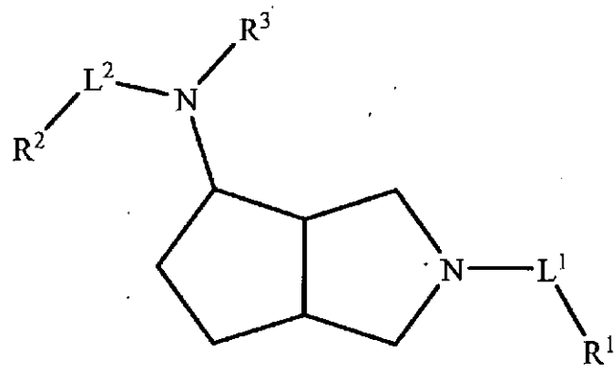

(I)

(57) Abstract: The present application relates to calcium channel inhibitors containing compounds of formula (I), wherein L^1, L^2, R^1, R^2, and R^3 are as defined in the specification. The present application also relates to compositions comprising such compounds, and methods of treating conditions and disorders using such compounds and compositions.

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NOVEL SUBSTITUTED OCTAHYDROCYCLOPENTA[C]PYRROL-4-AMINES AS CALCIUM CHANNEL BLOCKERS

TECHNICAL FIELD AND BACKGROUND

The present application relates to compounds that are calcium channel blockers, compositions comprising such compounds, and methods of treating conditions and disorders using such compounds and compositions.

Voltage-gated calcium channels (VGCC) play an integral role in the regulation of membrane ion conductance, neurotransmitter release, and cellular excitability. VGCC are composed of the pore-forming α1 subunit and auxiliary α2δ and β subunits that modulate channel expression and functional properties (Dolphin, A. C. A short history of voltage-gated calcium channels. British Journal of Pharmacology 2006, 147 (Suppl. 1), S56-S62.). These channels can be classified into low-voltage activated (LVA; T-type or $Ca_v3.x$) and high-voltage activated (HVA; L-type or $Ca_v1.x$ and N-, P/Q- and R-types or $Ca_v2.x$) channels. N-, P/Q and R channels typically activate at more positive membrane potentials (~ -30 mV) and are involved in "presynaptic" neurotransmission (McGivern J. G. Targeting N-type and T-type calcium channels for the treatment of pain. Drug Discovery Today 2006, 11, 245-253.). T-type channels are activated at relatively negative membrane potentials (~ -60 mV) and are primarily involved in "postsynaptic" excitability (Shin, H.-S.; et al. T-type Ca^{2+} channels as therapeutic targets in the nervous system. Curr. Opin. in Pharmacology 2008, 8, 33-41.).

N-type channel α_δ subunits are encoded by a single gene (α_1B or $Ca_v2.2$) in contrast to pharmacologically defined L- and T-type currents that are encoded by multiple α_1-subunit genes. A diversity of N-type channels arises due to extensive alternative splicing of the α subunit gene that generates variants with different expression patterns and GPCR-modulated biophysical properties (Gray, A. C.; et al. Neuronal calcium channels: splicing for optimal performance. Cell Calcium, 2007, 42(4-5), 409-417.). The primary sequence for $Ca_v2.2$ is highly conserved across species (rat and human share 91% identity at the amino acid level).

N-type channels are widely expressed in the central nervous system (CNS) (cortex, hippocampus, striatum, thalamus, brain stem nuclei and spinal cord) and in the peripheral nervous system (PNS) (adult sympathetic nervous system and dorsal root ganglia) (Ino, M.; et al. Functional disorders of the sympathetic nervous system in mice lacking the α_{1B} subunit ($Ca_v2.2$) of N-type calcium channels. Proc. Natl. Acad. Sci. USA 2001, 98(9), 5323-5328). In pain pathways, N-type channels are expressed in the rostral ventral medulla, an important

site of descending pain modulation (Urban, M. O.; et al. Medullary N-type and P/Q-type calcium channels contribute to neuropathy-induced allodynia. Neuroreport 2005, 16(6), 563-566.) and are a major contributor to the synaptic neurotransmission that occurs between C/Aδ nociceptors and spinal lamina I neurons (Bao, J.; et al: Differences in Ca^{2+} channels governing generation of miniature and evoked excitatory synaptic currents in spinal laminae I and II. J Neurosci. 1998, 18(21), 8740-50. Heinke, B.; et al. Pre- and postsynaptic contributions of voltage-dependent Ca^{2+} channels to nociceptive transmission in rat spinal lamina I neurons. Eur. J. Neurosci. 2004, 19(1), 103-111.). In contrast, P/Q type channels are expressed almost exclusively in laminae II-IV of the spinal cord and show little co-localization with Substance P and N-type channels (Westenbroek, R. E.; et al. Localization of Ca^{2+} channel subtypes on rat spinal motor neurons, interneurons, and nerve terminals. J. Neurosci. 1998, 18(16), 6319-6330.).

Following nerve injury there is increased expression of $Ca_v2.2$ (Westenbroek, R. E.; et al. Localization of Ca^{2+} channel subtypes on rat spinal motor neurons, interneurons, and nerve terminals. J. Neurosci. 1998, 18(16), 6319-6330. Cizkova, D.; et al. Localization of N-type Ca^{2+} channels in the rat spinal cord following chronic constrictive nerve injury. Exp. Brain Res. 2002, 147, 456-463. Yokoyama, K.; et al. Plastic change of N-type calcium channel expression after preconditioning is responsible for prostaglandin E2-induced long-lasting allodynia. Anesthesiology 2003, 99(6), 1364-1370.) and α2δ1 subunits (Luo, Z. D.; et al. Upregulation of dorsal root ganglion α2δ calcium channel subunit and its correlation with allodynia in spinal nerve-injured rats. J. Neurosci. 2001, 21(6), 1868-1875. Newton, R. A.; et al. Dorsal root ganglion neurons show increased expression of the calcium channel α2δ-1 subunit following partial sciatic nerve injury. Mol. Brain Res. 2001, 95(1-2), 1-8.) in addition to increases in the superficial layers of the dorsal horn of the spinal cord supporting a role for N-type channels in neuropathic pain. Recently a nociceptor-specific $Ca_v2.2$ splice variant has been identified in the dorsal root ganglion (Bell, T. J.; et al. Cell specific alternative splicing increases calcium channel density in the pain pathway. Neuron 2004, 41(1), 127-138.). These channels have distinct electrophysiological properties and current densities (Castiglioni, A. J.; et al. Alternative splicing in the C-terminus of $Ca_v2.2$ controls expression and gating of N-type calcium channels. J. Physiol. 2006, 576(Pt 1), 119-134.) compared to wildtype $Ca_v2.2$ channels. While G-protein coupled receptor inhibition of wildtype N-type channels is typically mediated by Gβγ and is voltage-dependent, the nociceptor specific splice variant is inhibited by GPCR activation (e.g. opioids) in a voltage-

independent fashion (Raingo, J.; et al. Alternative splicing controls G protein-dependent inhibition of N-type calcium channels in nociceptors. Nat. Neurosci. 2007, 10(3), 285-292.). This mechanism substantially increases the sensitivity of $Ca_v2.2$ channels to opiates and gamma-aminobutyric acid (GABA) suggesting that cell-specific alternative splicing of mRNA for $Ca_v2.2$ channels serves as a molecular switch that controls the sensitivity of N-type channels to neurotransmitters and drugs that modulate nociception. Collectively these data provide further support for the role of $Ca_v2.2$ channels in pain states.

The relative contributions of various HVA Ca^{2+} channels in nociceptive signaling have been evaluated using knockout mice studies. $Ca_v2.2$ knockout mice are healthy, fertile, and do not display overt neurological deficits (Ino, M.; et al. Functional disorders of the sympathetic nervous system in mice lacking the alpha 1B subunit ($Ca_v2.2$) of N-type calcium channels. Proc. Natl. Acad. Sci. USA 2001, 98(9), 5323-5328. Kim, C.; et al. Altered nociceptive response in mice deficient in the $alpha_{1B}$ subunit of the voltage-dependent calcium channel. Mol. Cell. Neurosci. 2001, 18(2), 235-245. Hatakeyama, S.; et al. Differential nociceptive responses in mice lacking the $alpha_{1B}$ subunit of N-type Ca^{2+} channels. Neuroreport 2001, 12(11), 2423-2427. Liu; L.; et al. In vivo analysis of voltage-dependent calcium channels. J. Bioenerg. Biomembr. 2003, 35(6), 671-685.). This finding suggests that other types of Ca_v channels are able to compensate for the lack of $Ca_v2.2$ channels at most synapses in these mice (Pietrobon, D. Function and dysfunction of synaptic calcium channels: insights from mouse models. Curr. Opin. Neurobiol. 2005, 15(3), 257-265.). $Ca_v2.2$ deficient mice are resistant to the development of inflammatory and neuropathic pain (Kim, C.; et al. Altered nociceptive response in mice deficient in the $alpha_{1B}$ subunit of the voltage-dependent calcium channel. Mol. Cell. Neurosci. 2001, 18(2), 235-245. Hatakeyama, S.; et al. Differential nociceptive responses in mice lacking the $alpha_{1B}$ subunit of N-type Ca^{2+} channels. Neuroreport 2001, 12(11), 2423-2427. Saegusa, H.; et al. Suppression of inflammatory and neuropathic pain symptoms in mice lacking the N-type calcium channel. EMBO J. 2001, 20(10), 2349-2356.), have decreased sympathetic nervous system function (Ino, M.; et al. Functional disorders of the sympathetic nervous system in mice lacking the alpha 1B subunit ($Ca_v2.2$) of N-type calcium channels. Proc. Natl. Acad. Sci. USA 2001, 98(9), 5323-5328.), and altered responses to both ethanol and anesthetics (Newton, R. A.; et al. Dorsal root ganglion neurons show increased expression of the calcium channel alpha2delta-1 subunit following partial sciatic nerve injury. Brain Res. Mol. Brain Res. 2001, 95(1-2), 1-8. Takei, R. et al. Increased sensitivity to halothane but decreased sensitivity to propofol in mice lacking the N-type Ca^{2+} channel. Neurosci. Lett.

2003, 350(1), 41-45.). Additional behavioral studies indicate that $Ca_v2.2$ knockout mice are less anxious, are hyperactive, and show enhanced vigilance compared to wild-type littermates (Beuckmann, C. T.; et al. N-type calcium channel $alpha_{1B}$ subunit($Ca_v2.2$) knock-out mice display hyperactivity and vigilance state differences. J. Neurosci. 2003, 23(17), 6793-6797.).

N- and P/Q-type channels are localized at neuronal synaptic junctions and contribute significantly to neurotransmitter release (Olivera, B. M.; et al. Calcium channel diversity and neurotransmitter release: the omega-conotoxins and omega agatoxins. Annu. Rev. Biochem. 1994, 63, 823-867. Miljanich, G. P.; et al. Antagonists of neuronal calcium channels: structure, function, and therapeutic implications. Annu. Rev. Pharmacol. Toxicol. 1995, 35, 707-734.). N-type channels play a major role in the release of glutamate, acetylcholine, dopamine, norepinephrine, GABA and calcitonin gene-related protein (CGRP). P/Q-type channels may be involved in the release of glutamate, aspartate, 5HT, GABA and probably glycine (Pietrobon, D. Function and dysfunction of synaptic calcium channels: insights from mouse models. Curr. Opin. Neurobiol. 2005, 15(3), 257-265.).

L, P/Q and N-type channels are blocked by channel specific antagonists i.e., dihydropyridines, ω-agatoxin IVA and ω-conotoxin MVIIA/ ziconotide, respectively. Agatoxin IVa has been shown to block excitatory (Luebke, J. I.; et al. Multiple calcium channel types control glutamatergic synaptic transmission in the hippocampus. Neuron 1993, 11(5), 895-902.) as well as inhibitory neurotransmission (Takahashi, T.; et al. Different types of calcium channels mediate central synaptic transmission. Nature 1993, 366(6451), 156-158.). Intrathecal injection of selective N-type channel blockers (e.g. conotoxin-derived peptides such as GVIA, MVIIA (ziconotide), and CVID) significantly attenuates pain responses in animal models of neuropathic pain, formalin-induced pain, and post-operative pain (Chaplan, S. R.; et al. Role of voltage-dependent calcium channel subtypes in experimental tactile allodynia. J. Pharmacol. Exp. Ther. 1994,269(3), 1117-1123. Malmberg, A. B.; et al. Voltage-sensitive calcium channels in spinal nociceptive processing: blockade of N-and P-type channels inhibits formalin-induced nociception. J. Neurosci. 1994, 14(8), 4882-4890. Bowersox, S. S.; et al. Selective N-type neuronal voltage-sensitive calcium channel blocker, SNX-111, produced spinal antinociception in rat models of acute, persistent and neuropathic pain. J. Pharmacol. Exp. Ther. 1996, 279(3), 1243-1249. Wang, Y. X.; et al. Effects of intrathecal administration of ziconotide, a selective neuronal N-type calcium channel blocker, on mechanical allodynia and heat

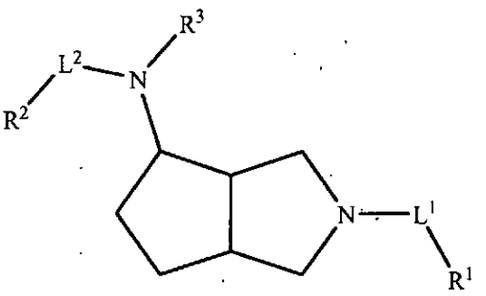
hyperalgesia in a rat model of postoperative pain. Pain 2000, 84(2-3), 151-158. Scott, D. A.; et al. Actions of intrathecal omega-conotoxins CVID, GVIA, MVIIA, and morphine in acute and neuropathic pain in the rat. Eur. J. Pharmacol. 2002, 451(3), 279-286.). These peptide blockers bind to the pore region of the channel, do not show voltage- or frequency-dependent activity, and show irreversible channel block (Feng, Z. P.; et al. Determinants of inhibition of transiently expressed voltage-gated calcium channels by omega-conotoxins GVIA and MVIIA. J. Biol. Chem. 2003, 278(22), 20171-20178.). Ziconotide potently blocks neurotransmitter release in the spinal cord dorsal horn (Matthews, E. A.; et al. Effects of spinally delivered N-and P-type voltage-dependent calcium channel antagonists on dorsal horn neuronal responses in a rat model of neuropathy. Pain 2001, 92(1-2), 235-246. Smith, M. T.; et al. The novel N-type calcium channel blocker, AM336, produces potent dose-dependent antinociception after intrathecal dosing in rats and inhibits substance P release in rat spinal cord slices. Pain 2002, 96(1-2), 119-127. Heinke, B.; et al. Pre- and postsynaptic contributions of voltage-dependent Ca^{2+} channels to nociceptive transmission in rat spinal lamina I neurons. Eur. J. Neurosci. 2004, 19(1), 103-111.) and in dorsal root ganglion (DRG) neurons (Evans, A. R.; et al. Differential regulation of evoked peptide release by voltage-sensitive calcium channels in rat sensory neurons. Brain Res. 1996, 712(2), 265-273. Smith, M. T.; et al. The novel N-type calcium channel blocker, AM336, produces potent dose-dependent antinociception after intrathecal dosing in rats and inhibits substance P release in rat spinal cord slices. Pain 2002, 96(1-2), 119-127.). It also potently and fully blocks depolarization-induced release of substance P from rat spinal cord slices. In contrast, intrathecal delivery of the selective P/Q type blocker ω-agatoxin IVA had no effects on mechanical allodynia in the spinal nerve ligation model (Chaplan, S. R.; et al. Role of voltage-dependent calcium channel subtypes in experimental tactile allodynia. J. Pharmacol. Exp. Ther. 1994, 269(3), 1117-1123.) or thermal hyperalgesia in the chronic constriction injury model (Yamamoto, T.; et al. Differential effects of intrathecally administered N- and P-type voltage-sensitive calcium channel blockers upon two models of experimental mononeuropathy in the rat. Brain Res. 1998, 794(2), 329-332.) of neuropathic pain.

Pain is the most common symptom of disease and the most frequent complaint with which patients present to physicians. Inadequate pain management across the spectrum of pain etiologies remains a major public health problem. Going forward, the development of novel therapeutics with new mechanisms of action for the treatment of pain including calcium channel blockade will have a significant impact on the ongoing struggle to balance

efficacy and safety for those patients most in need. The compounds of the present invention are novel calcium channel blockers that have utility in treating pain, amongst other conditions.

SUMMARY OF THE INVENTION

The invention is directed to compounds of formula (I)



(I),

or a pharmaceutically acceptable salt, prodrug, salt of a prodrug, or a combination thereof, wherein

L^1 is C(O), $S(O)_2$, $SO_2N(R^4)$, C(O)O or $-(CR^aR^b)_m-$;

R^1 is alkyl, G^1, $-CH(G^1)_2$, $-(CR^aR^b)_m-G^1$, $-(CR^aR^b)_m-CH(G^1)_2$, $-(CR^eR^f)_n-N(R^5)_2$, $-(CR^eR^f)_n-N(R^5)-C(O)O(alkyl)$, $-(CR^eR^f)_n-N(R^5)-C(O)(alkyl)$, or $-(CR^eR^f)_n-N(R^5)-SO_2R^6$; or

L^1-R^1 taken together are hydrogen, alkyl, hydroxyalkyl, G^1, or $-CH(G^1)_2$;

L^2 is $-(CR^cR^d)_p-$, C(O), $C(O)N(R^4)$, $S(O)_2$, $SO_2N(R^5)$, or C(O)O;

R^2 is alkyl, G^2, $-C(R^c)(G^2)(G^3)$, $-(CR^cR^d)_p-G^2$, $-(CR^cR^d)_p-CH(G^2)(G^3)$, $-(CR^gR^h)_q-N(R^5)-C(O)O(alkyl)$, $-(CR^gR^h)_q-N(R^5)-C(O)O-G^2$, $-(CR^gR^h)_q-N(R^5)-C(O)(alkyl)$, $-(CR^gR^h)_q-N(R^5)-SO_2R^6$, $-(CR^gR^h)_q-N(R^4)(R^5)$, $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-(alkyl)$, or $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-G^2$; or

L^2-R^2 taken together are alkyl, G^2, or $-C(R^c)(G^2)(G^3)$;

m and p, at each occurrence, are each independently 1, 2, 3, 4, 5, or 6;

n and q, at each occurrence, are each independently 1, 2, 3, 4, or 5;

R^a, R^b, R^c, and R^d, at each occurrence, are each independently hydrogen, alkyl, arylalkyl, halogen, haloalkyl or OR^7; or

R^a and R^b, or R^c and R^d, together with the carbon atom to which they are attached, optionally form a C_{3-6} cycloalkyl ring;

R^e, R^f, R^g, and R^h, at each occurrence, are each independently hydrogen, alkyl, halogen, haloalkyl, OR^7, cycloalkylalkyl, heteroaryl, arylalkyl, or heteroarylalkyl; wherein the aryl, cycloalkyl and heteroaryl groups of aryl, cycloalkyl and heteroaryl are each

independently unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of alkyl and haloalkyl;

G^1, G^2, and G^3 at each occurrence, are each independently aryl, cycloalkyl, cycloalkenyl, heteroaryl, or heterocycle; wherein G^1, G^2, and G^3 at each occurrence are each independently unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected form the group consisting of alkyl, alkenyl, alkynyl, cyano, haloalkyl, halogen, nitro, oxo, phenyl, $N(R^7)_2$, $N(R^7)C(O)R^7$, OR^7, $C(O)R^7$, $C(O)OR^7$, $C(O)N(R^7)_2$, SO_2R^8, and $SO_2N(R^7)_2$; and wherein G^1 is other than quinoline, quinazolinedione, or pyridopyrimidinedione;

R^3 is hydrogen, alkyl, haloalkyl, cycloalkyl, or cycloalkylalkyl;

R^4, R^5, and R^7, at each occurrence, are each independently hydrogen, alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, or haloalkyl; wherein said aryl, the aryl of arylalkyl and cycloalkyl are independently unsubstituted or substituted with 1, 2 3, 4, or 5 substituents independently selected from the group consisting of alkyl, haloalkyl, and halogen;

R^6 is alkyl, aryl, cycloalkyl, cycloalkenyl, heteroaryl, or heterocycle; wherein said aryl, heteroaryl, and heterocycle are independently unsubstituted or substituted with 1, 2 3, 4, or 5 substituents independently selected from the group consisting of alkyl, haloalkyl, and halogen;

R^8 is alkyl or haloalkyl;

with the proviso that L^1-R^1 and L^2-R^2 are not both alkyl at the same time;

and with the proviso that when L^1-R^1 is alkyl, L^2-R^2 is other than $C(O)N(R^4)$, wherein R^4 is alkyl;

and with the further proviso that the compound is other than:

N-(2-trityloctahydrocyclopenta[*c*]pyrrol-4-yl)acetamide;

N-(octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide

N-methyl-*N*-(2-trityloctahydrocyclopenta[*c*]pyrrol-4-yl)acetamide;

N-methyl-*N*-(octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide;

6-(2-(2-(3-fluoro-6-methoxy-1,5-naphthyridin-4-yl)ethyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)methyl-2*H*-pyrido[3,2-*b*][1,4]thiazin-3(4*H*)-one;

tert-butyl 2-(2-(3-fluoro-6-methoxy-1,5-naphthyridin-4-yl)ethyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate;

tert-butyl 2-benzyl octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate; or

tert-butyl octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate.

Another aspect of the invention relates to pharmaceutical compositions comprising therapeutically effective amount of compound(s) of the invention or pharmaceutically acceptable salts thereof, in combination with one or more pharmaceutically acceptable carrier. Such compositions can be administered in accordance with a method of the invention, typically as part of a therapeutic regimen for treatment or prevention of conditions and disorders related to calcium channels. More particularly, the method is useful for treating conditions related to a method of treating pain in a subject in need thereof. The method comprises administering to the subject a therapeutically suitable amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof. Conditions related to pain include acute pain, chronic pain, neuropathic pain, inflammatory pain, visceral pain, cancer pain, allodynia, fibromyalgia, sciatica, back pain, and headache pain including migraine, or combinations thereof.

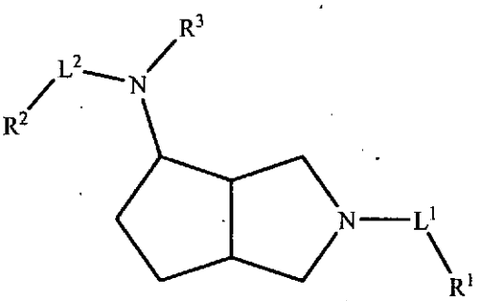
Another aspect of the invention provides a method of treating disorders of the central nervous system in a subject in need thereof. The method comprising the step of: administering a therapeutically suitable amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof. The disorders of the central nervous system include stroke, epilepsy, manic depression, bipolar disorders, depression, anxiety, schizophrenia, migraine, and psychoses; neural degenerative disorders including Alzheimer's disease, AIDS related dementia, Parkinson's disease, neuropathy caused by head injury, and dementia caused by cerebrovascular disorders; disorders of the lower urinary tract including overactive bladder, prostatis, prostadynia, interstitial cystitis, and benign prostatic hyperplasia; disorders caused by psychogenic stress including bronchial asthma, unstable angina, and hypersensitive colon inflammation; cardiovascular disorders including hypertension, atherosclerosis, heart failure, and cardiac arrhythmias; drug addiction withdrawal symptoms, including ethanol addiction withdrawal symptoms; skin disorders including pruritis and allergic dermatitis, inflammatory bowel disease; cancer; diabetes; and infertility and sexual dysfunction, or combinations thereof.

The compounds, compositions comprising the compounds, and methods for treating or preventing conditions and disorders by administering the compounds are further described herein.

These and other objects of the invention are described in the following paragraphs. These objects should not be deemed to narrow the scope of the invention.

DETAILED DESCRIPTION

Compounds of formula (I) are disclosed in this invention



(I),

wherein L^1, L^2, R^1, R^2, and R^3 are as defined above in the Summary of the Invention. Compositions comprising such compounds and methods for treating conditions and disorders using such compounds and compositions are also disclosed.

In various embodiments, the present invention provides at least one variable that occurs more than one time in any substituent or in the compound of the invention or any other formulae herein. Definition of a variable on each occurrence is independent of its definition at another occurrence. Further, combinations of substituents are permissible only if such combinations result in stable compounds. Stable compounds are compounds, which can be isolated from a reaction mixture.

a. Definitions

As used in the specification and the appended claims, unless specified to the contrary, the following terms have the meaning indicated:

The term "alkenyl" as used herein, means a straight or branched hydrocarbon chain containing from 2 to 10 carbons and containing at least one carbon-carbon double bond formed by the removal of two hydrogens. Representative examples of alkenyl include, but are not limited to, ethenyl, 2-propenyl, 2-methyl-2-propenyl, 3-butenyl, 4-pentenyl, 5-hexenyl, 2-heptenyl, 2-methyl-1-heptenyl, and 3-decenyl.

The term "alkenylene" denotes a divalent group derived from a straight or branched chain hydrocarbon of 2 to 4 carbon atoms and contains at least one carbon-carbon double. Representative examples of alkylene include, but are not limited to, -CH=CH- and $-CH_2CH=CH-$.

The term "alkyl" as used herein, means a straight or branched, saturated hydrocarbon chain containing from 1 to 10 carbon atoms. The term "lower alkyl" or "C_{1-6} alkyl" means a straight or branched chain hydrocarbon containing 1 to 6 carbon atoms. The term "C_{1-3} alkyl" means a straight or branched chain hydrocarbon containing 1 to 3 carbon atoms. Representative examples of alkyl include, but are not limited to, methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, iso-butyl, *tert*-butyl, n-pentyl, isopentyl, neopentyl, n-hexyl, 3-methylhexyl, 2,2-dimethylpentyl, 2,3-dimethylpentyl, n-heptyl, n-octyl, n-nonyl, and n-decyl.

The term "alkylene" denotes a divalent group derived from a straight or branched chain hydrocarbon 1 to 10 carbon atoms. Representative examples of alkylene include, but are not limited to, $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2-$, and $-CH_2CH(CH_3)CH_2-$.

The term "alkynyl" as used herein, means a straight or branched chain hydrocarbon group containing from 2 to 10 carbon atoms and containing at least one carbon-carbon triple bond. Representative examples of alkynyl include, but are not limited, to acetylenyl, 1-propynyl, 2-propynyl, 3-butynyl, 2-pentynyl, and 1-butynyl.

The term "aryl" as used herein, means phenyl or a bicyclic aryl. The bicyclic aryl is naphthyl, or a phenyl fused to a monocyclic cycloalkyl, or a phenyl fused to a monocyclic cycloalkenyl. Representative examples of the aryl groups include, but are not limited to, dihydroindenyl, indenyl, naphthyl, dihydronaphthalenyl, and tetrahydronaphthalenyl. The bicyclic aryl is attached to the parent molecular moiety through any carbon atom contained within the bicyclic ring system. The aryl groups of the present invention can be unsubstituted or substituted.

The term "arylalkyl" as used herein, means an aryl group, as defined herein, appended to the parent molecular moiety through an alkylene group, as defined herein. Representative examples of arylalkyl include, but are not limited to, benzyl, 2-phenylethyl, 3-phenylpropyl, and 2-naphth-2-ylethyl.

The term "cyano" as used herein, means a -CN group.

The term "cycloalkyl" or "cycloalkane" as used herein, means a monocyclic, a bicyclic, or a tricyclic cycloalkyl. The monocyclic cycloalkyl is a carbocyclic ring system containing three to eight carbon atoms, zero heteroatoms and zero double bonds. Examples of monocyclic ring systems include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl. The bicyclic cycloalkyl is a monocyclic cycloalkyl fused to a monocyclic cycloalkyl ring, or a bridged monocyclic ring system in which two non-adjacent carbon atoms of the monocyclic ring are linked by an alkylene bridge containing one, two,

three, or four carbon atoms. Representative examples of bicyclic ring systems include, but are not limited to, bicyclo[3.1.1]heptane, bicyclo[2.2.1]heptane, bicyclo[2.2.2]octane, bicyclo[3.2.2]nonane, bicyclo[3.3.1]nonane, and bicyclo[4.2.1]nonane. Tricyclic cycloalkyls are exemplified by a bicyclic cycloalkyl fused to a monocyclic cycloalkyl, or a bicyclic cycloalkyl in which two non-adjacent carbon atoms of the ring systems are linked by an alkylene bridge of 1, 2, 3, or 4 carbon atoms. Representative examples of tricyclic-ring systems include, but are not limited to, tricyclo[3.3.1.$0^{3,7}$]nonane (octahydro-2,5-methanopentalene or noradamantane), and tricyclo[3.3.1.$1^{3,7}$]decane (adamantane). The monocyclic, bicyclic, and tricyclic cycloalkyls can be unsubstituted or substituted, and are attached to the parent molecular moiety through any substitutable atom contained within the ring system.

The term "cycloalkylalkyl" as used herein, means a cycloalkyl group appended to the parent molecular moiety through an alkyl group, as defined herein.

The term "cycloalkenyl" or "cycloalkene" as used herein, means a monocyclic or a bicyclic hydrocarbon ring system. The monocyclic cycloalkenyl has four-, five-, six-, seven- or eight carbon atoms and zero heteroatoms. The four-membered ring systems have one double bond, the five-or six-membered ring systems have one or two double bonds, and the seven- or eight-membered ring systems have one, two or three double bonds. Representative examples of monocyclic cycloalkenyl groups include, but are not limited to, cyclobutenyl, cyclopentenyl, cyclohexenyl, cycloheptenyl and cyclooctenyl. The bicyclic cycloalkenyl is a monocyclic cycloalkenyl fused to a monocyclic cycloalkyl group, or a monocyclic cycloalkenyl fused to a monocyclic cycloalkenyl group. The monocyclic or bicyclic cycloalkenyl ring may contain one or two alkylene bridges, each consisting of one, two or three carbon atoms, each linking two non-adjacent carbon atoms of the ring system. Representative examples of the bicyclic cycloalkenyl groups include, but are not limited to, 4,5,6,7-tetrahydro-3aH-indene, octahydronaphthalenyl and 1,6-dihydro-pentalene. The monocyclic and bicyclic cycloalkenyl can be attached to the parent molecular moiety through any substitutable atom contained within the ring systems, and can be unsubstituted or substituted.

The term "halo" or "halogen" as used herein, means Cl, Br, I, or F.

The term "haloalkyl" as used herein, means an alkyl group, as defined herein, in which one, two, three, four, five or six hydrogen atoms are replaced by halogen. Representative examples of haloalkyl include, but are not limited to, chloromethyl, 2-

fluoroethyl, 2,2,2-trifluoroethyl, trifluoromethyl, difluoromethyl, pentafluoroethyl, 2-chloro-3-fluoropentyl, and trifluoropropyl such as 3,3,3-trifluoropropyl.

The term "heterocycle" or "heterocyclic" as used herein, means a monocyclic heterocycle, a bicyclic heterocycle, or a tricyclic heterocycle. The monocyclic heterocycle is a three-, four-, five-, six-, seven-, or eight-membered ring containing at least one heteroatom independently selected from the group consisting of O, N, and S. The three- or four-membered ring contains zero or one double bond, and one heteroatom selected from the group consisting of O, N, and S. The five-membered ring contains zero or one double bond and one, two or three heteroatoms selected from the group consisting of O, N and S. The six-membered ring contains zero, one or two double bonds and one, two, or three heteroatoms selected from the group consisting of O, N, and S. The seven- and eight-membered rings contains zero, one, two, or three double bonds and one, two, or three heteroatoms selected from the group consisting of O, N, and S. Representative examples of monocyclic heterocycles include, but are not limited to, azetidinyl, azepanyl, aziridinyl, diazepanyl, 1,3-dioxanyl, 1,3-dioxolanyl, 1,3-dithiolanyl, 1,3-dithianyl, imidazolinyl, imidazolidinyl, isothiazolinyl, isothiazolidinyl, isoxazolinyl, isoxazolidinyl, morpholinyl, oxadiazolinyl, oxadiazolidinyl, oxazolinyl, oxazolidinyl, piperazinyl, piperidinyl, pyranyl, pyrazolinyl, pyrazolidinyl, pyrrolinyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydropyranyl, tetrahydropyridinyl, tetrahydrothienyl, thiadiazolinyl, thiadiazolidinyl, 1,2-thiazinanyl, 1,3-thiazinanyl, thiazolinyl, thiazolidinyl, thiomorpholinyl, 1,1-dioxidothiomorpholinyl (thiomorpholine sulfone), thiopyranyl, and trithianyl. The bicyclic heterocycle is a monocyclic heterocycle fused to a phenyl group, or a monocyclic heterocycle fused to a monocyclic cycloalkyl, or a monocyclic heterocycle fused to a monocyclic cycloalkenyl, or a monocyclic heterocycle fused to a monocyclic heterocycle, or a bridged monocyclic heterocycle ring system in which two non adjacent atoms of the ring are linked by an alkylene bridge of 1, 2, 3, or 4 carbon atoms, or an alkenylene bridge of two, three, or four carbon atoms. Representative examples of bicyclic heterocycles include, but are not limited to, benzopyranyl, benzothiopyranyl, chromanyl, 2,3-dihydrobenzofuranyl, 2,3-dihydrobenzothienyl, 2,3-dihydroisoquinoline, azabicyclo[2.2.1]heptyl (including 2-azabicyclo[2.2.1]hept-2-yl), 2,3-dihydro-1H-indolyl, isoindolinyl, octahydrocyclopenta[*c*]pyrrolyl, octahydropyrrolopyridinyl, and tetrahydroisoquinolinyl. Tricyclic heterocycles are exemplified by a bicyclic heterocycle fused to a phenyl group, or a bicyclic heterocycle fused to a monocyclic cycloalkyl, or a bicyclic heterocycle fused to a monocyclic cycloalkenyl, or a bicyclic heterocycle fused to a monocyclic heterocycle, or a

bicyclic heterocycle in which two non adjacent atoms of the bicyclic ring are linked by an alkylene bridge of 1, 2, 3, or 4 carbon atoms, or an alkenylene bridge of two, three, or four carbon atoms. Examples of tricyclic heterocycles include, but not limited to, octahydro-2,5-epoxypentalene, hexahydro-2*H*-2,5-methanocyclopenta[*b*]furan, hexahydro-1*H*-1,4-methanocyclopenta[*c*]furan, aza-adamantane (1-azatricyclo[3.3.1.$1^{3,7}$]decane), and oxa-adamantane (2-oxatricyclo[3.3.1.$1^{3,7}$]decane). The monocyclic, bicyclic, and tricyclic heterocycles are connected to the parent molecular moiety through any carbon atom or any nitrogen atom contained within the rings, and can be unsubstituted or substituted.

The term "heteroaryl" as used herein, means a monocyclic heteroaryl or a bicyclic heteroaryl. The monocyclic heteroaryl is a five- or six-membered ring. The five-membered ring contains two double bonds. The five-membered ring may contain one heteroatom selected from O or S; or one, two, three, or four nitrogen atoms and optionally one oxygen or sulfur atom. The six-membered ring contains three double bonds and one, two, three or four nitrogen atoms. Representative examples of monocyclic heteroaryl include, but are not limited to, furanyl, imidazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, 1,3-oxazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, pyrazolyl, pyrrolyl, tetrazolyl, thiadiazolyl, 1,3-thiazolyl, thienyl, triazolyl, and triazinyl. The bicyclic heteroaryl consists of a monocyclic heteroaryl fused to a phenyl, or a monocyclic heteroaryl fused to a monocyclic cycloalkyl, or a monocyclic heteroaryl fused to a monocyclic cycloalkenyl, or a monocyclic heteroaryl fused to a monocyclic heteroaryl, or a monocyclic heteroaryl fused to a monocyclic heterocycle. Representative examples of bicyclic heteroaryl groups include, but are not limited to, benzofuranyl, benzothienyl, benzoxazolyl, benzimidazolyl, benzoxadiazolyl, 6,7-dihydro-1,3-benzothiazolyl, imidazo[1,2-*a*]pyridinyl, indazolyl, indolyl, isoindolyl, isoquinolinyl, naphthyridinyl, pyridoimidazolyl, quinolinyl, thiazolo[5,4-b]pyridin-2-yl, thiazolo[5,4-d]pyrimidin-2-yl, and 5,6,7,8-tetrahydroquinolin-5-yl. The monocyclic and bicyclic heteroaryl groups of the present invention can be substituted or unsubstituted and are connected to the parent molecular moiety through any carbon atom or any nitrogen atom contained within the ring systems.

The term "heteroarylalkyl," as used herein, means a heteroaryl group appended to the parent molecular moiety through an alkyl group, as defined herein.

The term "heteroatom" as used herein, means a nitrogen, oxygen, or sulfur atom.

The term "hydroxyl" or "hydroxy" as used herein, means an -OH group.

The term "hydroxyalkyl" as used herein, means at least one hydroxy group, as defined herein, is appended to the parent molecular moiety through an alkylene group, as defined

herein. Representative examples of hydroxyalkyl include, but are not limited to, hydroxymethyl, 2-hydroxyethyl, 3-hydroxypropyl, 2,3-dihydroxypentyl, and 2-ethyl-4-hydroxyheptyl.

The term "nitro" as used herein, means a $-NO_2$ group.

The term "oxo" as used herein, means a =O group.

b. Compounds

Compounds of the invention have the formula (I) as described above.

Particular values of variable groups in compounds of formula (I) are as follows. Such values may be used where appropriate with any of the other values, definitions, claims or embodiments defined hereinbefore or hereinafter.

More particularly, compound of formula (I) can include, but are not limited to compounds wherein L^1-R^1 taken together are hydrogen, alkyl, hydroxyalkyl, G^1, or $CH(G^1)_2$.

In another embodiment, compound of formula (I) can include, but are not limited to compounds wherein L^1 is C(O), $S(O)_2$, $SO_2N(R^4)$, C(O)O or $-(CR^aR^b)_m-$; wherein m is 1,2,3, 4, 5, or 6.

In a further embodiment, compound of formula (I) can include, but are not limited to compounds wherein L^1 is C(O), $S(O)_2$, or $-(CR^aR^b)_m-$.

In another embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^1 is alkyl, G^1, $CH(G^1)_2$, $-(CR^aR^b)_m-G^1$, $-(CR^aR^b)_m-CH(G^1)_2$, $-(CR^eR^f)_n-N(R^5)_2$, $-(CR^eR^f)_n-N(R^5)-C(O)O(alkyl)$, $-(CR^eR^f)_n-N(R^5)-C(O)(alkyl)$, or $-(CR^eR^f)_n-N(R^5)-SO_2R^6$; wherein m is 1, 2, 3, 4, 5, or 6; and wherein n is 1, 2, 3, 4, or 5.

In a further embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^1 is G^1, $CH(G^1)_2$, $-(CR^aR^b)_m-G^1$, $-(CR^aR^b)_m-CH(G^1)_2$.

In one embodiment, compound of formula (I) can include, but are not limited to compounds wherein L^2-R^2 taken together are alkyl, G^2, or $C(R^c)(G^2)(G^3)$.

In a further embodiment, compound of formula (I) can include, but are not limited to compounds wherein L^2-R^2 together are alkyl, aryl, cycloalkyl, heteroaryl or $-C(R^c)(G^2)(G^3)$, wherein R^c is hydrogen and G^2 and G^3 are each aryl or heteroaryl.

In another embodiment, compound of formula (I) can include, but are not limited to compounds wherein L^2 is $-(CR^cR^d)_p-$, C(O), $C(O)N(R^4)$, $S(O)_2$, $SO_2N(R^5)$, or C(O)O; wherein p is 1, 2, 3, 4, 5, or 6.

In a further embodiment, compound of formula (I) can include, but are not limited to compounds wherein L^2 is $-(CR^cR^d)_p-$, C(O), $C(O)N(R^4)$, or $S(O)_2$, wherein p is 1.

In another embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^2 is alkyl, G^2, $-C(R^c)(G^2)(G^3)$, $-(CR^cR^d)_p-G^2$, $-(CR^cR^d)_p-CH(G^2)(G^3)$, $-(CR^gR^h)_q-N(R^5)-C(O)O(alkyl)$, $-(CR^gR^h)_q-N(R^5)-C(O)O-G^2$, $-(CR^gR^h)_q-N(R^5)-C(O)(alkyl)$, $-(CR^gR^h)_q-N(R^5)-SO_2R^6$, $-(CR^gR^h)_q-N(R^4)(R^5)$, $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-(alkyl)$, or $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-G^2$; wherein q is 1, 2, 3, 4, or 5; and wherein p is 1, 2, 3, 4, 5, or 6.

In another embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^a and R^b, at each occurrence, are each independently hydrogen, alkyl, arylalkyl, halogen, or haloalkyl or OR^7.

In a further embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^a and R^b, at each occurrence, are each independently hydrogen, alkyl, or arylalkyl.

In yet another embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^a and R^b, together with the carbon atom to which they are attached, optionally form a C_{3-6} cycloalkyl ring.

In another embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^c and R^d, at each occurrence, are each independently hydrogen, alkyl, arylalkyl, halogen, or haloalkyl or OR^7.

In a further embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^c and R^d, at each occurrence, are each independently hydrogen, alkyl, arylalkyl, or OR^7, wherein R^7 is hydrogen.

In yet another embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^c and R^d, together with the carbon atom to which they are attached, optionally form a C_{3-6} cycloalkyl ring.

In one embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^e and R^f, at each occurrence, are each independently hydrogen, alkyl, halogen, haloalkyl, OR^7, cycloalkylalkyl, heteroaryl, arylalkyl, or heteroarylalkyl; wherein the aryl, cycloalkyl and heteroaryl groups of aryl, cycloalkyl and heteroaryl are each independently unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of alkyl and haloalkyl.

In another embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^g, and R^h, at each occurrence, are each independently hydrogen, alkyl, halogen, haloalkyl, OR^7, cycloalkylalkyl, heteroaryl, arylalkyl, or heteroarylalkyl; wherein the aryl, cycloalkyl and heteroaryl groups of aryl, cycloalkyl and heteroaryl are each

independently unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of alkyl and haloalkyl.

In a further embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^g, and R^h, at each occurrence, are each independently hydrogen, alkyl, arylalkyl or cycloalkyl.

In one embodiment, compound of formula (I) can include, but are not limited to compounds wherein G^1 at each occurrence, is independently aryl, cycloalkyl, cycloalkenyl, heteroaryl, or heterocycle; wherein G^1 at each occurrence is independently unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected form the group consisting of alkyl, alkenyl, alkynyl, cyano, haloalkyl, halogen, nitro, oxo, phenyl, $N(R^7)_2$, $N(R^7)C(O)R^7$, OR^7, $C(O)R^7$, $C(O)OR^7$, $C(O)N(R^7)_2$, SO_2R^8, and $SO_2N(R^7)_2$.

In another embodiment, compound of formula (I) can include, but are not limited to compounds wherein G^1 at each occurrence, is independently aryl, cycloalkyl, or heteroaryl; wherein G^1 at each occurrence is independently unsubstituted or substituted with 1, 2, or 3 substituents selected form the group consisting of alkyl, cyano, haloalkyl, halogen, or OR^7.

In one embodiment, compound of formula (I) can include, but are not limited to compounds wherein G^2 at each occurrence, is independently aryl, cycloalkyl, cycloalkenyl, heteroaryl, or heterocycle; wherein G^2 at each occurrence is independently unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected form the group consisting of alkyl, alkenyl, alkynyl, cyano, haloalkyl, halogen, nitro, oxo, phenyl, $N(R^7)_2$, $N(R^7)C(O)R^7$, OR^7, $C(O)R^7$, $C(O)OR^7$, $C(O)N(R^7)_2$, SO_2R^8, and $SO_2N(R^7)_2$.

In a further embodiment, compound of formula (I) can include, but are not limited to compounds wherein G^2 at each occurrence, is independently aryl, cycloalkyl, heteroaryl or heterocycle; wherein G^2 at each occurrence is independently unsubstituted or substituted with 1, 2, or 3 substituents selected form the group consisting of alkyl, cyano, haloalkyl, halogen, nitro, oxo, OR^7, $C(O)R^7$, $C(O)OR^7$ or SO_2R^8,

In one embodiment, compound of formula (I) can include, but are not limited to compounds wherein G^3 at each occurrence, is independently aryl, cycloalkyl, cycloalkenyl, heteroaryl, or heterocycle; wherein G^2 at each occurrence is independently unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected form the group consisting of alkyl, alkenyl, alkynyl, cyano, haloalkyl, halogen, nitro, oxo, phenyl, $N(R^7)_2$, $N(R^7)C(O)R^7$, OR^7, $C(O)R^7$, $C(O)OR^7$, $C(O)N(R^7)_2$, SO_2R^8, and $SO_2N(R^7)_2$.

In a further embodiment, compound of formula (I) can include, but are not limited to compounds wherein G^3 at each occurrence, is independently aryl, cycloalkyl, heteroaryl or

heterocycle; wherein G^2 at each occurrence is independently unsubstituted or substituted with 1, 2, or 3 substituents selected form the group consisting of alkyl, cyano, haloalkyl, halogen, nitro, oxo, OR^7, $C(O)R^7$, $C(O)OR^7$ or SO_2R^8,

In one embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^3 is hydrogen, alkyl, haloalkyl, cycloalkyl, or cycloalkylalkyl.

In a further embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^3 is hydrogen, alkyl, or cycloalkyl.

In one embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^4 and R^5, at each occurrence, are each independently hydrogen, alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, or haloalkyl; wherein said aryl, the aryl of arylalkyl and cycloalkyl are independently unsubstituted or substituted with 1, 2 3, 4, or 5 substituents independently selected from the group consisting of alkyl, haloalkyl, and halogen.

In a further embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^4 and R^5, at each occurrence, are each independently hydrogen, alkyl, arylalkyl, cycloalkyl or cycloalkylalkyl.

In one embodiment; compound of formula (I) can include, but are not limited to compounds wherein R^6 is alkyl, aryl, cycloalkyl, cycloalkenyl, heteroaryl, or heterocycle; wherein said aryl, heteroaryl, and heterocycle are independently unsubstituted or substituted with 1, 2 3, 4, or 5 substituents independently selected from the group consisting of alkyl, haloalkyl, and halogen.

In another embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^6 is alkyl or cycloalkyl.

In one embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^7, at each occurrence, is independently hydrogen, alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, or haloalkyl; wherein said aryl, the aryl of arylalkyl and cycloalkyl are independently unsubstituted or substituted with 1, 2 3, 4, or 5 substituents independently selected from the group consisting of alkyl, haloalkyl, and halogen.

In a further embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^7, at each occurrence, is independently hydrogen or alkyl.

In one embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^8 is alkyl or haloalkyl.

In a further embodiment, compound of formula (I) can include, but are not limited to compounds wherein R^8 is alkyl.

In one embodiment, in a compound of formula (I), L^1 is $-(CR^aR^b)_m-$; R^a and R^b are each hydrogen; m is 1; R^1 is G^1, wherein G^1 is aryl; L^2 is C(O); R^2 is $-(CR^cR^d)_p-G^2$, wherein G^2 is aryl and p is 1; R^c and R^d, together with the carbon atom to which they are attached form a C_{3-6} cycloalkyl ring; and R^3 is hydrogen.

In another embodiment, in a compound of formula (I), L^1-R^1 together are alkyl; or L^1 is $-(CR^aR^b)_m-$ or C(O); and R^1 is G^1; wherein G^1 is aryl, cycloalkyl, or heteroaryl; L^2 is C(O); R^2 is $-(CR^cR^d)_p-G^2$; wherein G^2 is aryl and p is 1 or 2; R^a, R^b, R^c, and R^d, at each occurrence are independently hydrogen, alkyl or arylalkyl; and R^3 is hydrogen or alkyl.

In one embodiment, in a compound of formula (I), L^1 is $-(CR^aR^b)_m-$; m is 1 or 2; R^a and R^b are each hydrogen; R^1 is G^1, wherein G^1 is aryl; L^2 is $C(O)N(R^4)$, wherein R^4 is alkyl; R^2 is G^2, wherein G^2 is aryl; and R^3 is hydrogen.

In another embodiment, in a compound of formula (I), L^1 is $-(CR^aR^b)_m-$, C(O), or $S(O)_2$; R^a and R^b at each occurrence are each hydrogen; m is 1; R^1 is alkyl or G^1, wherein G^1 is aryl or cycloalkyl; L^2 is C(O); and R^2 is $-(CR^cR^d)_p-G^2$; wherein Rc and Rd at each occurrence are independently hydrogen, alkyl or OR^7; p is 1; G^2 is cycloalkyl or heterocycle; wherein said cycloalkyl or heterocycle is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of alkyl, haloalkyl, halogen, oxo C(O)OR^7; R^7 is hydrogen;; and R^3 is hydrogen.

In one embodiment, in a compound of formula (I), L^1 is $-(CR^aR^b)_m-$; R^a and R^b are each hydrogen; m is 1; R^1 is G^1; wherein G^1 is aryl; L^2-R^2 together are cycloalkyl; and R^3 is hydrogen or cycloalkyl.

In another embodiment, in a compound of formula (I), L^1 is $-(CR^aR^b)_m-$; R^a and R^b are each hydrogen; m is 1; R^1 is G^1; wherein G^1 is aryl; L^2 is C(O); R^2 is $-C(R^c)(G^2)(G^3)$ or $-(CR^cR^d)_p-CH(G^2)(G^3)$; wherein G^2 is aryl and G^3 is aryl or cycloalkyl; R^c and R^d, at each occurrence, are each independently hydrogen; p is 1, 2, 3, 4, or 5; and R^3 is hydrogen.

In a further embodiment, in a compound of formula (I), L^1-R^1 together are hydrogen or $-CH(G^1)_2$; wherein each G^1 is aryl or heteroaryl; or L^1 is $-(CR^aR^b)_m-$, C(O), or $S(O)_2$; and R^1 is G^1, $-CH(G^1)_2$, $-(CR^aR^b)_m-G^1$, $-(CR^aR^b)_m-CH(G^1)_2$, $-(CR^eR^f)_n-N(R^5)_2$, wherein each G^1 is aryl or heteroaryl; R^a and R^b at each occurrence, are each independently hydrogen; R^e and R^f at each occurrence, are each independently hydrogen or alkyl; m is 1, 2, 3, 4, or 5; n is 1 or 2; R^5 is hydrogen or alkyl; L^2 is C(O); R^2 is $-C(R^c)(G^2)(G^3)$; wherein G^2 and G^3 are each cycloalkyl; R^c is hydrogen or OR^7, R^7 is hydrogen; and R^3 is hydrogen.

In one embodiment, in a compound of formula (I), L^1 is $-(CR^aR^b)_m-$; R^a and R^b are each hydrogen; m is 1; R^1 is G^1, wherein G^1 is aryl; L^2 is C(O); R^2 is alkyl or G^2; wherein G^2 is cycloalkyl or heterocycle; R^3 is hydrogen.

In another embodiment, in a compound of formula (I), L^1 is $-(CR^aR^b)_m-$, C(O) or $S(O)_2$, wherein R^a and R^b are each hydrogen and m is 1 or 2; R^1 is G^1, $-CH(G^1)_2$ or $-(CR^aR^b)_m-G^1$, wherein G^1 at each occurrence is aryl or heteroaryl; L^2 is C(O); R^2 is $-(CR^gR^h)_q-N(R^5)-C(O)O(alkyl)$, $-(CR^gR^h)_q-N(R^5)--C(O)O-G^2$, $-(CR^gR^h)_q-N(R^5)-C(O)(alkyl)$, $-(CR^gR^h)_q-N(R^5)-SO_2R^6$, $-(CR^gR^h)_q-N(R^4)(R^5)$, $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-(alkyl)$, or $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-G^2$; q is 1 or 2; R^g and R^h, at each occurrence, are each independently hydrogen, alkyl, arylalkyl or cycloalkylalkyl; R^4 and R^5 at each occurrence, are each independently hydrogen, alkyl, arylalkyl, or cycloalkyl; R^6 is alkyl, aryl, or cycloalkyl; G^2 is aryl or cycloalkyl; and R^3 is hydrogen, alkyl, cycloalkyl or cycloalkylalkyl.

In one embodiment, in a compound of formula (I), L^1-R^1 together are hydroxyalkyl; or L^1 is $-(CR^aR^b)_m-$, C(O) or $S(O)_2$; and R^1 is G^1 or $-CH(G^1)^2$, wherein G^1 is aryl or heteroaryl, and wherein R^a and R^b, at each occurrence, are each independently hydrogen or alkyl; m is 1, 2, 3, 4, or 5; L^2 is $S(O)_2$; R^2 is G^2, wherein G^2 is aryl or heteroaryl; and R^3 is hydrogen, alkyl or cycloalkyl.

In a further embodiment, in a compound of formula (I), L^1 is $-(CR^aR^b)_m-$; R^a and R^b, at each occurrence, are each independently hydrogen; m is 1, 2, 3, 4, or 5; L^2 is C(O); R^2 is $-(CR^cR^d)_p-G^2$; wherein G^2 is aryl; p is 1; R^c and R^d, at each occurrence, are each independently hydrogen or alkyl; and R^3 is hydrogen.

In another embodiment, in a compound of formula (I), L^1 is C(O), $S(O)_2$ or $-(CR^aR^b)_m-$; R^a and R^b, at each occurrence, are independently hydrogen or alkyl; m is 1; R^1 is G^1 or $-(CR^aR^b)_m-G^1$, wherein G^1 is aryl or heteroaryl; L^2 is $-(CR^cR^d)_p-$; R^c and R^d are each hydrogen; p is 1; R^2 is G^2, wherein G^2 is aryl, cycloalkyl or heteroaryl; or L^2-R^2 taken together are alkyl, G^2, or $-C(R^c)(G^2)(G^3)$, wherein G^2 and G^3 are each aryl or heteroaryl and R^c is hydrogen; and R^3 is hydrogen or alkyl.

In a further embodiment, in a compound of formula (I), L^1 is C(O); R^1 is $-(CR^eR^f)_n-N(R^5)_2$; n is 1 or 2; R^e and R^f at each occurrence are each independently hydrogen or alkyl; R^5 at each occurrence is independently hydrogen or alkyl; L^2 is C(O) or $S(O)_2$; R^2 is G^2 or $-C(R^c)(G^2)(G^3)$, wherein G^2 and G^3 are each aryl or heteroaryl and R^c is hydrogen; and R^3 is hydrogen, alkyl, or cycloalkyl. In an additional embodiment, in a compound of formula (I), L^1 is C(O); R^1 is $-(CR^eR^f)_n-N(R^5)_2$ or $-(CR^eR^f)_n-N(R^5)C(O)O(alkyl)$; n is 1 or 2; R^e and R^f at each occurrence are each independently hydrogen, alkyl, or arylalkyl; R^5 at each

occurrence is independently hydrogen, alkyl or cycloalkyl; L^2 is C(O); R^2 is $-(CR^gR^h)_qN(R^4)(R^5)$ or $-(CR^gR^h)_q-N(R^5)C(O)O(alkyl)$; q is 1 or 2; R^4 is hydrogen or alkyl; R^g and R^h at each occurrence are each independently hydrogen or alkyl; and R^3 is hydrogen.

In another embodiment, in a compound of formula (I), L^1-R^1 taken together are hydrogen, G^1 or $CH(G^1)_2$, wherein G^1 is aryl or heteroaryl; L^2 is C(O); R^2 is $-(CR^gR^h)_qN(R^4)(R^5)$ or $-(CR^gR^h)_q-N(R^5)C(O)O(alkyl)$; q is 1 or 2; R^4 is hydrogen, alkyl, or cycloalkylalkyl; R^5 is hydrogen or alkyl; R^g and R^h at each occurrence are each independently hydrogen or alkyl; and R^3 is hydrogen. In a further embodiment, in a compound of formula (I), L^1-R^1 taken together are G^1, wherein G^1 is aryl or heteroaryl; L^2 is C(O); R^2 is G^2, wherein G^2 is aryl or heteroaryl; and R^3 is hydrogen or alkyl.

Specific embodiments of compounds contemplated as part of the invention include, but are not limited to:

N-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclopentanecarboxamide;

N-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclopentanecarboxamide;

N-[(3a*R**,4*R**,6a*S**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclohexyl-2-phenylacetamide;

N-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclohexyl-2-phenylacetamide;

N-[(3a*R**,4*R**,6a*S**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*R**,4*S**,6a*S**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclopentyl-2-phenylacetamide;

N-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclopentyl-2-phenylacetamide;

N-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclohexanecarboxamide;

N-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclohexanecarboxamide;

N-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide;

(2*S*)-2-(3-benzoylphenyl)-*N*-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]propanamide;

(2*S*)-2-(3-benzoylphenyl)-*N*-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]propanamide;

N-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclopentyl-2-phenylacetamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylpropanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-propylpentanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]cycloheptanecarboxamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(4-isobutylphenyl)propanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclohexanecarboxamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,3-diphenylpropanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-methyl-3-phenylpropanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-methyl-2-phenylpropanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclopropanecarboxamide;

2-benzyl-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethylbutanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethyl-2-phenylbutanamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethyl-2-phenylbutanamide;

(2*R*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethyl-2-phenylbutanamide;

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclopentyl-2-phenylacetamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

(2*R*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide;

(2*R*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylpropanamide;

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylpropanamide;

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(4-isobutylphenyl)propanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclopropyl-2-phenylacetamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclobutyl-2-phenylacetamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(4-chlorophenyl)-3-methylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-ethyl-2-phenylpentanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(4-hydroxyphenyl)-3-methylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclohexanecarboxamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-methyl-2-phenylpropanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclopropanecarboxamide;

2-benzyl-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,3-diphenylpropanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-methyl-3-phenylpropanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethyl-2-phenylbutanamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(2-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[4-fluoro-3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-fluoro-4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

N-{(3a*S*,4*S*,6a*R*)-2-[3,5-bis(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[2-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-methylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(4-methylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethoxy)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

N-{(3a*S*,4*S*,6a*R*)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide;

N-{(3a*S*,4*S*,6a*R*)-2-[6,6-bis(4-fluorophenyl)hexyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide;

N-{(3a*S*,4*S*,6a*R*)-2-[3-(3-chlorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(3-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-phenylpropyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-((3a*S*,4*S*,6a*R*)-2-{3-[4-(trifluoromethyl)phenyl]propyl}octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(pyridin-4-ylmethyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(pyridin-3-ylmethyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

N-{(3a*S*,4*R*,6a*R*)-2-[3,5-bis(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide;

N-{(3a*S*,4*R*,6a*R*)-2-[6,6-bis(4-fluorophenyl)hexyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*R*,6a*R*)-2-(3,3-diphenylpropyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

N-{(3a*S*,4*R*,6a*R*)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide;

N-{(3a*S*,4*R*,6a*R*)-2-[4,4-bis(4-fluorophenyl)butyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide;

3-methyl-2-phenyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(cyclohexylmethyl)octahydrocyclopenta[c]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-2-methyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(2-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(3-chlorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(3-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

3-methyl-2-phenyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(3-methoxybenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(3-methylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide;

3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(2-methylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(2,6-dimethylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(2-methoxybenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(4-*tert*-butylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(4-methoxybenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(3-cyanobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

3-methyl-2-phenyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

3-methyl-2-phenyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[2-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[4-fluoro-3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[3-fluoro-4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

3-methyl-2-phenyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(thien-2-ylmethyl)octahydrocyclopenta[*c*]pyrrol-4-yl]butanamide;

3-methyl-2-phenyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(pyridin-4-ylmethyl)octahydrocyclopenta[*c*]pyrrol-4-yl]butanamide;

3-methyl-2-phenyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(2-phenylethyl)octahydrocyclopenta[*c*]pyrrol-4-yl]butanamide;

3-methyl-2-phenyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(3-phenylpropyl)octahydrocyclopenta[*c*]pyrrol-4-yl]butanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[3-(4-*tert*-butylphenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[6,6-bis(4-fluorophenyl)hexyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

3-methyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(2-methylphenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2-phenylbutanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[3-(3-chlorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

3-methyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(3-methylphenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2-phenylbutanamide;

3-methyl-2-phenyl-*N*-((3a*R*,4*S*,6a*S*)-2-{3-[3-(trifluoromethyl)phenyl]propyl}octahydrocyclopenta[*c*]pyrrol-4-yl)butanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[3-(3-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

3-methyl-2-phenyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(4-phenylbutyl)octahydrocyclopenta[*c*]pyrrol-4-yl]butanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[3-(3-chloro-5-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

3-methyl-2-phenyl-*N*-((3a*R*,4*S*,6a*S*)-2-{3-[4-(trifluoromethyl)phenyl]propyl}octahydrocyclopenta[*c*]pyrrol-4-yl)butanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(3,3-diphenylpropyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[4,4-bis(4-fluorophenyl)butyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[5,5-bis(4-fluorophenyl)pentyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

N-[(3a*S*,4*S*,6a*R*)-2-benzhydryloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzhydryloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide;

3-methyl-2-phenyl-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

3,3-dimethyl-2-phenyl-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

2,2-dicyclohexyl-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2-ethyl-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

2-propyl-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}pentanamide;

N-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}cyclohexanecarboxamide;

N-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}cycloheptanecarboxamide;

N-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}cyclopentanecarboxamide;

6,6-bis(4-fluorophenyl)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}hexanamide;

3,3-diphenyl-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}propanamide;

5,5-bis(4-fluorophenyl)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}pentanamide;

3,3-bis(4-fluorophenyl)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[c]pyrrol-4-yl}propanamide;

4,4-bis(4-fluorophenyl)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

2,2-diphenyl-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-bis(4-fluorophenyl)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

6,6-bis(4-fluorophenyl)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}hexanamide;

3,3-diphenyl-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}propanamide;

5,5-bis(4-fluorophenyl)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}pentanamide;

3,3-bis(4-fluorophenyl)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}propanamide;

4,4-bis(4-fluorophenyl)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

2,2-diphenyl-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-bis(4-fluorophenyl)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

3,3-dimethyl-2-phenyl-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide;

2,2-dicyclohexyl-2-hydroxy-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

2,2-dicyclohexyl-2-hydroxy-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

2,2-dicyclohexyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-{(3a*R*,4*R*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^2-methyl-N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^2-methyl-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide;

N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[c]pyrrol-4-yl}-L-leucinamide;

N^2-methyl-N^2-(methylsulfonyl)-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-N^2-(methylsulfonyl)-L-leucinamide;

N^2-methyl-N^2-(methylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(methylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(methylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^2-(cyclopropylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(isobutylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(cyclopropylsulfonyl)-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-acetyl-N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(2,2-dimethylpropanoyl)-N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(2,2-dimethylpropanoyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

isobutyl (*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

cyclopentyl (*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

N^2-[(*tert*-butylamino)carbonyl]-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-[(cyclopentylamino)carbonyl]-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

3-(trifluoromethyl)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide;

3-(trifluoromethyl)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide;

3-(trifluoromethyl)-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide;

3-(trifluoromethyl)-*N*-{(3a*R*,4*R*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide;

3-(trifluoromethyl)-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide;

N-{(3a*S*,4*R*,6a*R*)-2-[6,6-bis(4-fluorophenyl)hexyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-(trifluoromethyl)benzenesulfonamide;

N-{(3a*S*,4*R*,6a*R*)-2-[3,5-bis(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-(trifluoromethyl)benzenesulfonamide;

N-{(3a*S*,4*R*,6a*R*)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-(trifluoromethyl)benzenesulfonamide;

N-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-(trifluoromethyl)benzenesulfonamide;

N-[(3a*S*,4*S*,6a*R*)-2-(4-hydroxybutyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide;

(3a*S**,4*S**,6a*R**)-*N*,*N*-dicyclopropyl-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*S**,4*R**,6a*R**)-2-benzyl-*N*-cyclopropyloctahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*S**,4*S**,6a*R**)-2-benzyl-*N*-cyclopropyloctahydrocyclopenta[*c*]pyrrol-4-amine;

N-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*-cyclopropyl-3-(trifluoromethyl)benzenesulfonamide;

N-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*-cyclopropyl-3-(trifluoromethyl)benzenesulfonamide;

N-cyclopropyl-*N*-[(3a*S**,4*S**,6a*R**)-octahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide;

N-{(3a*S**,4*S**,6a*R**)-2-[6,6-bis(4-fluorophenyl)hexyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-*N*-cyclopropyl-3-(trifluoromethyl)benzenesulfonamide;

N-{(3a*S**,4*S**,6a*R**)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-*N*-cyclopropyl-3-(trifluoromethyl)benzenesulfonamide;

N-cyclopropyl-3-(trifluoromethyl)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide;

2,2-dicyclohexyl-*N*-((3a*S*,4*S*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[(2-phenylethyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-((3a*S*,4*S*,6a*R*)-2-{[2-(1-naphthyl)ethyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide;

2,2-dicyclohexyl-*N*-((3a*S*,4*S*,6a*R*)-2-{[3-(trifluoromethyl)benzyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide;

2,2-dicyclohexyl-*N*-((3a*S*,4*S*,6a*R*)-2-{[2-(4-fluorophenyl)ethyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide;

(2*S*)-2-phenyl-*N*-{(3a*R*,4*R*,6a*S*)-2-[(1*S*)-1-phenylethyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

(2*S*)-2-phenyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[(1*S*)-1-phenylethyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

(2*S*)-2-phenyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[(1*S*)-1-phenylethyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

(2*S*)-2-phenyl-*N*-{(3a*S*,4*R*;6a*R*)-2-[(1*S*)-1-phenylethyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*,3-dimethyl-2-phenylbutanamide;

N-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*,3-dimethyl-2-phenylbutanamide;

(3a*R**,4*S**,6a*S**)-*N*-benzyl-2-(3-methyl-2-phenylbutanoyl)octahydrocyclopenta[*c*]pyrrol-4-amine;

2,2-dicyclohexyl-*N*-[(3a*S*,4*R*,6a*R*)-2-(*N*,*N*-dimethyl-D-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzoyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N'-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*-isopropyl-*N*-phenylurea;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-ylcarbamate;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(ethyl)carbamate;

tert-butyl (2*S*,3*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3,3-dimethyl-1-oxobutan-2-ylcarbamate;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-ylcarbamate;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxohexan-2-yl(methyl)carbamate;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-bis(4-fluorophenyl)acetamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-isopropyl-3-methylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methylbutanamide;

tert-butyl (2*S*)-2-({[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]amino}carbonyl)piperidine-1-carboxylate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxobutan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3,3-dimethyl-1-oxobutan-2-ylcarbamate;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-isopropyl-3-methylbutanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methylbutanamide;

2-cyclohexyl-2-hydroxy-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

tert-butyl (*S*)-1-((3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate;

S-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(methylsulfonyl)-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(methylsulfonyl)-L-leucinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-neopentyl-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-neopentyl-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-neopentyl-L-norvalinamide;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-morpholin-4-ylpentanamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-pyrrolidin-1-ylpentanamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-piperidin-1-ylpentanamide;

N^2-neopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-neopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-neopentyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-neopentyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-neopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-neopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N-(*tert*-butoxycarbonyl)-*N*-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

N^2-neopentyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-neopentyl-L-leucinamide;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(5-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

isopropyl (*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(5-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(6-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

tert-butyl (*S*)-4,4-dimethyl-1-((3a*R*,4*S*,6a*S*)-2-(2-(methylsulfonyl)pyrimidin-5-yl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-ylcarbamate;

(*S*)-*tert*-butyl 2-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamoyl)pyrrolidine-1-carboxylate;

tert-butyl (1*R*)-1-isopropyl-3-oxo-3-[((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]propylcarbamate;

tert-butyl (2*S*)-2-{[((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]carbonyl}piperidine-1-carboxylate;

N-(*tert*-butoxycarbonyl)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide;

N-(*tert*-butoxycarbonyl)-*N*-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide;

(*S*)-*tert*-butyl 2-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamoyl)pyrrolidine-1-carboxylate;

tert-butyl (1*R*)-1-isopropyl-3-oxo-3-[((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]propylcarbamate;

tert-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate;

tert-butyl (2*S*)-2-{[((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]carbonyl}piperidine-1-carboxylate;

tert-butyl (3*S*)-3-{[((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]carbonyl}-3,4-dihydroisoquinoline-2(1*H*)-carboxylate;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)hexan-2-yl)carbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

isopropyl (*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

isopropyl (*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

(3a*S*,4*R*,6a*R*)-*N*-neopentyl-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*-neopentyl-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*-isopropyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}-*N*-isopropyloctahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*S*,4*R*,6a*R*)-*N*-(4-fluorobenzyl)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*-(4-fluorobenzyl)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*-(4-fluorobenzyl)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*-ethyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*,*N*-diethyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*-propyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*,*N*-dipropyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*-(cyclopropylmethyl)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}-*N*-ethyloctahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}-*N*,*N*-diethyloctahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}-*N*-[5-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-amine;

tert-butyl (*S*)-1-(ethyl((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-(propyl((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)pentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((cyclopropylmethyl)((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate;

2-nitro-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)benzenesulfonamide;

N-methyl-2-nitro-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)benzenesulfonamide;

(3a*R*,4*S*,6a*S*)-*N*-methyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

tert-butyl (*S*)-4,4-dimethyl-1-(methyl((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)-1-oxopentan-2-yl(methyl)carbamate;

(2*S*)-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}pentanamide;

2-isopropyl-3-methyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

2-isopropyl-3-methyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

tert-butyl (*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

tert-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl ethyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(3-fluoro-4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluoro-3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate;

(2*S*)-4-methyl-2-morpholin-4-yl-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide;

(2*S*)-4-methyl-2-pyrrolidin-1-yl-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide;

(2*S*)-4-methyl-2-piperidin-1-yl-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide;

tert-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl ethyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluoro-3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*R*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*R*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((2*S*,3*S*)-3-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((2*S*,3*S*)-3-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((2*S*,3*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((2*S*,3*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate;

tert-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate;

tert-butyl (*S*)-3,3-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-ylcarbamate;

tert-butyl (*S*)-3,3-dimethyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-ylcarbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)hexan-2-yl)carbamate;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

(2*S*)-4-methyl-2-pyrrolidin-1-yl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzoyl]octahydrocyclopenta[*c*]pyrrol-4-yl}pentanamide;

(2*S*)-4-methyl-*N*-[(3a*S*,4*R*,6a*R*)-2-(methylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-2-pyrrolidin-1-ylpentanamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-(cyclopropylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-pyrrolidin-1-ylpentanamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide;

tert-butyl methyl((*S*)-4-methyl-1-((3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl)carbamate;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]piperidine-2-carboxamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-valinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-isoleucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-isoleucinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2,4-dimethyl-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-L-valinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-L-valinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2,4-dimethyl-L-leucinamide;

N^1-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide;

N^1-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-L-leucinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norleucinamide;

N^1-[(3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide;

N^1-[(3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide;

N^2-ethyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-valinamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]piperidine-2-carboxamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-valinamide;

(2*S*)-*N*-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}piperidine-2-carboxamide;

N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide;

N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-valinamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[4-fluoro-3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide;

N^2-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide;

N^2-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide;

N^2-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide;

N^2-ethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide;

N-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide;

N-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-prolinamide;

(3*R*)-3-amino-4-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide;

(2*S*)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)piperidine-2-carboxamide;

(3*S*)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide;

4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norleucinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-prolinamide;

(3*R*)-3-amino-4-methyl-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide;

(2*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)piperidine-2-carboxamide;

(2*S*)-*N*-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}piperidine-2-carboxamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-valinamide;

(2*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)piperidine-2-carboxamide;

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide;

N^1-((3a*S*,4*R*,6a*R*)-2-{[4-fluoro-3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-methyl-L-leucinamide;

3-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide;

3-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-isoleucinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-isoleucinamide;

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-isoleucinamide;

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-isoleucinamide;

N^2,4-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2,4-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2,4-dimethyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2,4-dimethyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norleucinamide;

4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-methyl-N^1-((3a*R*,4*R*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-methyl-N^1-((3a*R*,4*R*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

3-cyclohexyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-alaninamide;

3-cyclohexyl-N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-alaninamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-5-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-L-leucinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-L-leucinamide;

N-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2,4-dimethyl-L-leucinamide;

N-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-*N*-methyl-L-phenylalaninamide;

N^1-cyclopropyl-N^2,4-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^1-ethyl-N^2,4-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2,4-dimethyl-N^1-propyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^1-(cyclopropylmethyl)-N^2,4-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^1,N^2,4-trimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^1,N^2-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^1,N^2,4-trimethyl-L-leucinamide;

4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamido;

4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[2-(methylsulfonyl)pyrimidin-5-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3,4-difluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3,5-difluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-chlorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide;

N^2-methyl-N^1-[(3a*S*,4*R*,6a*R*)-2-(phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-leucinamide;

N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-valinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-4-methyl-L-leucinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norleucinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide;

N^2-methyl-N^1-((3a*S*,4*S*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-methyl-N^1-((3a*S*,4*S*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

2,2-bis(4-fluorophenyl)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-bis(4-fluorophenyl)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-methyl-L-norvalyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

N-[(3a*R*,4*S*,6a*S*)-2-(*N*,4-dimethyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-bis(4-fluorophenyl)acetamide;

2,2-bis(4-fluorophenyl)-*N*-[(3a*R*,4*S*,6a*S*)-2-(4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-4-((*S*)-2-(*tert*-butoxycarbonylamino)-4,4-dimethylpentanamido)hexahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)-4,4-dimethyl-1-oxopentan-2-ylcarbamate;

4-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-leucinamide;

4-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-L-phenylalanyloctahydrocyclopenta[*c*]pyrrol-4-yl]-L-leucinamide;

(3a*R*,4*S*,6a*S*)-*N*-benzhydryl-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*S*,4*R*,6a*R*)-*N*-benzhydryl-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*-benzhydryl-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzhydryloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide;

4-methyl-N^2-propyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-(cyclopropylmethyl)-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-(cyclobutylmethyl)-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-isobutyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-(cyclopentylmethyl)-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-(cyclohexylmethyl)-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-butyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-ethyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-(cyclopropylmethyl)-4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(cyclopropylmethyl)-4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-isopropyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-isopropyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-isopropyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-isopropyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-isopropyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

3-cyclohexyl-N^2-isopropyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-alaninamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-5-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-isopropyl-4-methyl-L-leucinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-isopropyl-4-methyl-L-leucinamide;

N^2-isopropyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropyl-4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-L-leucinamide;

N^2-isopropyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropyl-L-phenylalanyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-L-leucinamide;

N^2-isopropyl-4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-isopropyl-4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

2,2-bis(4-fluorophenyl)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropyl-4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

N^2-isopropyl-4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[2-(methylsulfonyl)pyrimidin-5-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-isopropyl-L-norvalinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-isopropyl-L-norvalinamide;

N^2-isopropyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2,N^2-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

(3*R*)-3-(dimethylamino)-4-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide;

N^2-cyclopropyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2,N^2-dicyclopropyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-cyclopentyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-cyclohexyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-(1-ethylpropyl)-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-cyclobutyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

4-methyl-N^2-neopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-cyclopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-cyclohexyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-cyclopentyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-cyclopentyl-4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-L-leucinamide;

N^2,N^2-dimethyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-N^2-neopentyl-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(3,3-dimethylbutyl)-N^2-methyl-L-leucinamide;

N^2,N^2-dimethyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(4-fluorobenzyl)-N^2-methyl-L-leucinamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-(methylsulfonyl)piperidine-2-carboxamide;

(3*R*)-4-methyl-3-[(methylsulfonyl)amino]-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide;

N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^2-ethyl-N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

4-methyl-N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

3-methyl-N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-valinamide;

N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide;

N^2-(isopropylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(phenylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(cyclopentylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

isopropyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

isopropyl (*S*)-3,3-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-ylcarbamate;

cyclopentyl (*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

N^2-(2,2-dimethylpropanoyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(3-chloro-4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(pyridin-3-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(thiophen-2-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethoxy)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(thien-2-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-chloro-4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

N^2-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(pyridin-3-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-cyanophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-methoxyphenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[3,5-bis(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-methyl-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(2-chloro-4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

N^2-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(1-naphthylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-norvalinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[4-bromo-3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-*N*^{2}-methyl-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3,4-dichlorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-*N*^{2}-methyl-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-*tert*-butylphenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-*N*^{2}-methyl-L-norvalinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-(1,1'-biphenyl-4-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-*N*^{2}-methyl-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3,4-dimethoxyphenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-*N*^{2}-methyl-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-cyanophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-*N*^{2}-methyl-L-norvalinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-(2-furylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-*N*^{2}-methyl-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(2,3-dichlorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-*N*^{2}-methyl-L-norvalinamide;

N^2-methyl-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)benzyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-methyl-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[2-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-bromophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-*N*^{2}-methyl-L-norvalinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-*N*^{2}-methyl-L-norvalinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-5-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-*N*^{2}-methyl-L-norvalinamide;

N^2-methyl-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzoyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*-isopropyl-3-(trifluoromethyl)benzenesulfonamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide;

N-isopropyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide;

N-[(3a*R*,4*S*,6a*S*)-2-(*N*-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide;

N-cyclopropyl-*N*-[(3a*S**,4*S**,6a*R**)-[2-(*N*-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide; and

4-fluoro-*N*-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzamide.

Compounds of the present application may exist as stereoisomers wherein, asymmetric or chiral centers are present. These stereoisomers are "*R*" or "*S*" depending on the configuration of substituents around the chiral carbon atom. The terms "*R*" and "*S*" used herein are configurations as defined in IUPAC 1974 Recommendations for Section E, Fundamental Stereochemistry, Pure Appl. Chem., 1976, 45: 13-30.

On occasion, the relative stereochemistry of an enantiomeric pair is known, however, the absolute configuration is not known. In that circumstance, the relative stereochemistry descriptor terms "*R**" and "*S**" are used. The terms "*R**" and "*S**" used herein are defined in Eliel, E. L.; Wilen, S. H. Stereochemistry of Organic Compounds; John Wiley & Sons, Inc.: New York, 1994; pp 119-120 and 1206. In a particular enantiomeric pair, the relative descriptors are reversed to indicate that this pair of enantiomers is of unknown absolute stereochemistry.

The present application contemplates various stereoisomers and mixtures thereof and these are specifically included within the scope of this application. Stereoisomers include enantiomers and diastereomers, and mixtures of enantiomers or diastereomers. Individual stereoisomers of compounds of the present application may be prepared synthetically from commercially available starting materials which contain asymmetric or chiral centers or by preparation of racemic mixtures followed by resolution which is well known to those of ordinary skill in the art. These methods of resolution are exemplified by (1) attachment of a mixture of enantiomers to a chiral auxiliary, separation of the resulting mixture of diastereomers by recrystallization or chromatography and liberation of the optically pure product from the auxiliary or (2) direct separation of the mixture of optical enantiomers on chiral chromatographic columns.

Geometric isomers may exist in the present compounds. The invention contemplates the various geometric isomers and mixtures thereof resulting from the disposition of substituents around a carbon-carbon double bond, a carbon-nitrogen double bond, a cycloalkyl group, or a heterocycle group. Substituents around a carbon-carbon double bond or a carbon-nitrogen bond are designated as being of *Z* or *E* configuration and substituents around a cycloalkyl or a heterocycle are designated as being of *cis* or *trans* configuration.

Within the present invention it is to be understood that compounds disclosed herein may exhibit the phenomenon of tautomerism.

Thus, the formulae drawings within this specification can represent only one of the possible tautomeric or stereoisomeric forms. It is to be understood that the invention encompasses any tautomeric or stereoisomeric form, and mixtures thereof, and is not to be limited merely to any one tautomeric or stereoisomeric form utilized within the naming of the compounds or formulae drawings.

Compounds of this invention can exist in an isotopic form containing one or more atoms having an atomic mass or mass number different from the atomic mass or mass number most abundantly found in nature. Isotopes of atoms such as hydrogen, carbon, phosphorous, sulfur fluorine, chlorine, and iodine include, but are not limited to ^{2}H, ^{3}H, ^{11}C, ^{14}C, ^{32}P, ^{35}S, ^{18}F, ^{36}Cl, and ^{125}I, respectively. Compounds that contain other isotopes of these and/or other atoms are within the scope of this invention. Compounds containing tritium (^{3}H) and ^{14}C radioisotopes are preferred in general for their ease in preparation and detectability for radiolabeled compounds. Isotopically labeled compounds of this invention can be prepared by the general methods well known to persons having ordinary skill in the art. Such Isotopically labeled compounds can be conveniently prepared by carrying out the procedures disclosed in the Examples and Schemes below by substituting a readily available isotopically labeled reagent for a non-isotopically labeled reagent.

c. Biological Data

Abbreviations which have been used in the descriptions of Biological Data that follow are: EDTA for ethylenediaminetetraacetic acid; FBS for fetal bovine serum; FLIPR for fluorometric imaging plate reader; HBSS for Hank's balanced salt solution; HEPES for 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid; i.p. for intraperitoneal; MEM for minimum essential medium; MEM NEAA for minimum essential medium non-essential amino acid; p.o. for per orem (by mouth).

(i) In Vitro Methods--Assessment of calcium channel activity using FLIPR:

IMR32 cells endogenously expressing human $Ca_v2.2$ were assayed for Ca^{2+} influx using a no-wash calcium indicator dye (Calcium 4 dye: Molecular Probes) and FLIPR technology (Lubin, M. L.; Reitz, T. L.; Todd, M. J.; Flores, C. M.; Qin, N.; Xin, H. A nonadherent cell-based HTS assay for N-type calcium channel using calcium 3 dye. Assay and Drug Development Technologies 2006, 4(6), 689-694.). The IMR32 cells were maintained in MEM media containing 10% (v/v) FBS, 1% (v/v) antibiotic/antimitotic, 1% (v/v) sodium pyruvate and 1% (v/v) MEM NEAA. Following dissociation in 0.05% (v/v) trypsin/EDTA, cells were seeded into black 1 x 96-well plates (Corning Cellbind) at a density of 1-1.2 x 10^5 cells/well and incubated in the maintenance media above for 48 hours at 37 °C. Immediately prior to performing the assay the media was removed and cells were loaded for 1.5 hours with 1 x Calcium 4 dye prepared in HBSS (137 mM NaCl, 5.4 mM KCl, 0.25 mM Na_2HPO_4, 0.44 mM KH_2PO_4, 1.3 mM $CaCl_2$, 1mM $MgSO_4$, 4.2 mM $NaHCO_3$) containing HEPES pH 7.4 at room temperature. After dye loading and a subsequent 3 minute or 60 minute pre-incubation with compounds (full log dilutions from 10 μM to 0.1 nM) in the presence of 1.3 mM $CaCl_2$ and 2 μM nifedipine to block endogenous L-type channels, the external Ca^{2+} concentration was increased to 5 mM $CaCl_2$ and the cells concomitantly depolarized with 80 mM KCl to assay channel activity. To determine the IC_{50} values, the percent inhibition of the compound at each concentration was determined relative to the activity in the absence of inhibitor, and data was fitted using non-linear regression sigmoidal dose response curve analysis with GraphPad Prism®.

Example	IC_{50} (μM) or percent inhibition (* indicates 3 minute incubation, otherwise 60 minute)	Example	IC_{50} (μM) or percent inhibition (* indicates 3 minute incubation, otherwise 60 minute)
1	3.5*	271	3.41
2	4.2*	272	5.14
3	91% @ 10 μM	273	0.18
4	3.5*	274	1.38
5	3.8*	275	0.92
6	2.2*	276	0.38
7	1.8*	277	0.72
8	1.1	278	0.34

9	1.8*	**280**	5.04
10	1.3*	**281**	4.18
11	4	**282**	5.24
13	23	**283**	8.69
14	3.8	**284**	3.71
15	15.7	**285**	0.48
16	9.8	**286**	0.38
17	1.6	**287**	3.09
18	2.7	**288**	10.36
19	25% @ 10 μM *	**289**	9.74
20	1.8	**290**	7.80
21	10.1*	**291**	4.40
22	14.7*	**292**	3.91
23	2.5	**293**	4.82
24	2.9*	**294**	7.81
25	3.7*	**295**	2.97
26	17.3*	**296**	2.14
27	9.7*	**297**	7.88
28	13.9*	**298**	9.00
29	5.6*	**299**	3.68
30	1.8	**300**	1.54
31	1.6	**302**	1.14
32	1.4	**303**	3.11
33	7.4	**304**	3.78
34	1.5	**305**	3.51
35	3.3	**306**	0.50
36	44% @ 10 μM*	**307**	1.54
37	15% @ 10 μM*	**308**	1.93
38	27% @ 10 μM*	**309**	1.74
39	92% @ 10 μM*	**310**	0.68
40	3.6*	**311**	2.05
41	56% @ 10 μM*	**312**	1.59

43	1.5	**313**	2.10
44	1.7*	**314**	2.15
46	3.1*	**315**	5.36
47	15.6*	**316**	2.02
48	10.5*	**317**	0.90
49	4.6*	**318**	1.07
50	5.0*	**319**	1.21
51	15.2*	**320**	0.70
52	3.4	**321**	0.44
53	8.6	**322**	0.70
54	0.5	**323**	0.20
55	0.8	**324**	0.69
56	1	**325**	0.25
57	0.3	**326**	1.46
58	1.4	**327**	1.83
59	0.5	**328**	1.38
60	1.5	**329**	2.60
61	1.5	**330**	1.11
62	1.6	**331**	0.75
63	0.6	**332**	0.48
64	1.3	**333**	0.57
65	4.5	**334**	0.69
66	0.9	**335**	0.83
67	1.3	**336**	0.48
68	1.7	**337**	0.78
69	1.7	**338**	0.23
70	1.9	**339**	1.11
71	1.2	**340**	1.03
72	3.2	**341**	2.01
73	3.3	**342**	2.17
74	11.2*	**343**	1.01
75	0.5	**344**	0.99

76	5.7	**345**	4.32
77	9.4	**349**	17.65
78	0.4	**358**	9.00
79	0.9	**361**	24.74
80	1.7	**364**	8.12
81	1.1	**366**	5.28
82	1.5	**367**	7.00
83	2.6*	**368**	12.42
84	5.8% @ 10 μM*	**370**	6.02
85	3.6	**371**	8.89
86	1.6	**373**	7.58
87	3.1	**374**	5.36
88	1.2	**375**	8.22
89	2	**376**	10.63
90	83% @ 10 μM*	**377**	13.37
91	1.8	**379**	8.59
92	2	**380**	9.73
93	3.3	**382**	14.42
94	2.3	**383**	0.80
95	1	**384**	1.14
96	2.4*	**385**	1.85
97	5.3*	**386**	1.62
98	4.9*	**387**	5.88
99	4.8*	**388**	4.53
100	4.2*	**389**	1.48
101	4.7*	**390**	2.46
102	2.8	**391**	1.46
103	31*	**392**	0.95
104	79% @ 10 μM*	**393**	1.08
105	1.5	**394**	0.98
106	5.8*	**395**	2.12
107	1.1	**396**	3.55

108	11.3*	**397**	1.45
109	9.0*	**398**	3.25
110	2.0*	**399**	15.29
111	2.2*	**400**	6.86
112	2.8*	**401**	2.96
113	3.1*	**402**	2.06
114	2.8*	**403**	8.66
115	1.2	**404**	1.02
116	1.2	**405**	3.84
117	0.9	**406**	3.69
118	1	**407**	5.43
119	1.1	**408**	5.11
120	3.4	**409**	5.02
121	14.3	**410**	1.80
122	0.6	**411**	4.22
123	0.6	**412**	4.72
124	0.7	**413**	0.78
125	2.8	**414**	0.90
126	1	**415**	2.97
127	1.5	**416**	1.33
128	1	**417**	1.16
129	2.9	**418**	0.82
130	0.8	**419**	0.80
131	0.7	**420**	5.70
132	1.1	**421**	2.56
133	0.7	**422**	7.83
134	1.2	**423**	6.46
135	0.9	**424**	3.11
136	1.1	**425**	3.21
137	0.6	**426**	1.79
138	0.8	**427**	6.45
139	1	**428**	2.31

140	0.6	**429**	0.96
141	0.6	**430**	1.75
142	0.9	**431**	0.58
143	0.6	**432**	1.67
144	1	**433**	1.26
145	1.2	**434**	2.70
146	0.8	**435**	2.32
147	0.5	**436**	1.77
148	0.8	**437**	2.43
149	0.6	**438**	5.70
150	0.5	**439**	1.43
151	0.7	**440**	3.19
152	0.8	**441**	0.37
153	0.4	**442**	7.18
154	1.3	**443**	7.68
155	0.7	**444**	2.11
156	0.8	**445**	7.96
157	2.1	**446**	4.96
158	3.5	**447**	2.71
159	5.6	**448**	12.35
160	3.8	**449**	4.06
161	3.9	**450**	9.25
162	3.9	**451**	0.80
163	4.6	**452**	9.12
164	1.6	**453**	4.23
165	33.3	**454**	2.03
166	2.7	**455**	3.03
167	1.2	**456**	5.33
168	12.9	**457**	3.07
169	0.9	**458**	3.08
170	4.6	**459**	1.62
171	6.2	**460**	2.69

172	2	**461**	1.88
173	1.8	**462**	2.96
174	1	**463**	2.03
175	1.5	**466**	2.33
176	0.9	**467**	3.49
177	2.6	**468**	2.25
178	1	**469**	2.24
179	0.9	**470**	1.03
180	1.8	**471**	0.65
181	0.9	**472**	1.27
182	1.5	**473**	2.66
183	1.4	**474**	1.74
184	1.5	**475**	1.84
185	0.9	**476**	1.31
186	0.6	**477**	1.88
187	1.2	**478**	0.75
188	0.8	**479**	0.25
189	1	**480**	1.31
190	1.3	**481**	2.28
191	0.5	**482**	1.97
192	2.3	**483**	0.49
193	0.6	**484**	0.97
194	1.4	**485**	1.50
195	22.1	**486**	1.21
196	3.2	**487**	0.56
197	69.7	**488**	7.43
198	40.4	**489**	9.76
199	2.2	**490**	3.12
200	1	**491**	0.26
201	5.2	**492**	2.00
202	0.8	**493**	5.08
203	1.6	**496**	0.53

204	1.3	**497**	0.57
205	3.4	**498**	1.58
206	>100	**499**	2.70
207	>100	**500**	1.70
208	>100	**501**	0.82
209	>100	**502**	0.97
210	76% @ 10 μM*	**503**	0.89
211	3.8	**504**	0.91
212	4.1	**505**	2.24
213	60% @ 10 μM*	**506**	1.72
215	2	**507**	0.87
216	85% @ 10 μM*	**508**	8.60
217	1.3	**509**	4.56
218	56% @ 10 μM*	**510**	1.68
219	63% @ 10 μM*	**511**	2.12
220	>9	**512**	0.47
221	3.93	**513**	2.15
222	2.05	**515**	3.17
223	2.06	**516**	2.99
224	4.64	**517**	4.45
225	9.38	**518**	0.81
226	4.06	**519**	5.14
227	3.17	**520**	12.82
228	2.09	**521**	9.60
229	13.10	**522**	2.90
231	6.14	**523**	4.43
232	3.60	**524**	2.07
233	2.81	**525**	1.39
234	7.40	**526**	2.77
235	14.23	**527**	2.29
237	1.88	**528**	7.23
238	5.73	**529**	0.96

239	3.31	**530**	7.63
240	2.67	**531**	3.49
241	2.09	**532**	3.16
242	7.92	**533**	9.69
243	8.59	**534**	6.38
244	9.10	**536**	8.38
245	8.08	**537**	11.32
246	8.39	**538**	3.76
247	3.62	**539**	4.39
248	1.67	**540**	1.67
252	0.64	**541**	2.57
253	0.36	**542**	2.36
254	0.72	**543**	3.21
255	0.55	**544**	2.15
256	1.38	**546**	6.32
257	0.70	**548**	1.05
258	0.85	**549**	2.74
259	1.14	**550**	2.57
260	1.11	**551**	2.49
261	1.26	**552**	0.78
262	1.80	**553**	1.94
264	0.28	**554**	10.32
265	2.62	**555**	2.51
266	0.87	**556**	2.58
267	14.06	**557**	1.14
268	0.73	**558**	4.88
269	1.90	**559**	1.68
270	0.77	**560**	1.45

(ii) In Vivo Data-- Capsaicin induced secondary mechanical hyperalgesia model:

Sprague Dawley rats were briefly restrained, and capsaicin was administered at 10 μg in 10 μL of vehicle by intraplantar injection into the center of the right hind paw. Secondary mechanical hyperalgesia (SMH) was measured at the heel away from the site of injection 180

minutes following capsaicin exposure. Compounds and gabapentin (positive control), were administered p.o. 60 minutes before testing (2 hours after capsaicin) or i.p. 30 minutes before testing (2.5 hours after capsaicin). SMH was measured using calibrated von Frey filaments (Stoelting, Woodale, IL). Following the 1 hour habituation in the testing room, rats were moved to individual plexiglass chambers that sit on top of a wire mesh to allow for access for stimulation of the plantar surface of the hind paws. Rats were allowed to acclimate to the new chambers for 15 minutes before the onset of testing. The paw withdrawal threshold was determined by increasing and decreasing stimulus intensity (force: g) and calculated using Dixon's up-down method (Chaplan, S. R.; Bach, F. W.; Pogrel, J. W.; Chung, J. M.; Yaksh, T. L.; Quantitative assessment of tactile allodynia in the rat paw. J. Neuroscience Methods 1994, 53(1), 55-63.). The filaments (maximum force of 15.0 g) were held in place for 8 seconds or until there was a withdrawal response from the mechanical stimulation.

Example	% inhibition @ 30 mg/kg p.o.	Example	% inhibition @ 30 mg/kg p.o.
54	38	**405**	32
75	85	**415**	52
156	67	**461**	43
157	57	**478**	57
165	92	**479**	40
170	57	**480**	64
172	85	**488**	55
183	78	**489**	47
220	76	**560**	42
280	38		

d. Methods of Using the Compounds

One embodiment of the present invention provides a method of treating pain in a subject in need thereof. The method comprises administering to the subject, including a mammal, such as a human, a therapeutically suitable amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof. Conditions related to pain include acute pain, chronic pain, neuropathic pain, inflammatory pain, visceral pain, cancer pain, allodynia, fibromyalgia, sciatica, back pain, and headache pain including migraine, or combinations thereof. Preferably, the method comprises administering to the mammal a therapeutically

effective amount of any of the compounds as described herein, or a pharmaceutically acceptable salt thereof. In certain embodiments, the method comprises administering to the mammal a therapeutically effective amount of any of the compounds as described herein, or a pharmaceutically acceptable salt thereof, in combination with one or more of the following: nonsteroidal anti-inflammatory drug (NSAID), opioid analgesic, barbiturate, benzodiazapine, histamine antagonist, sedative, skeletal muscle relaxant, transient receptor potential ion channel antagonist, α-adrenergic, tricyclic antidepressant, anticonvulsant, tachykinin antagonist, muscarinic antagonist, cyclooxygenase-2 selective inhibitor, neuroleptic, vanilloid receptor agonist, vanilloid receptor antagonist, β-adrenergic, local anesthetic, corticosteroid, 5-HT receptor agonist, 5-HT receptor antagonist, 5-HT_{2A} receptor antagonist, cholinergic analgesic, $\alpha_2\delta$ ligand such as gabapentin or pregabalin, cannabinoid receptor ligand, metabotropic glutamate subtype 1 receptor antagonist, serotonin reuptake inhibitor, norepinephrine reuptake inhibitor, dual serotonin-noradrenaline reuptake inhibitor, Rho kinase inhibitor, inducible nitric oxide synthase inhibitor, acetylcholinesterase inhibitor, prostaglandin E_2 subtype 4 antagonist, leukotriene B4 antagonist, 5-lipoxygenase inhibitor, sodium channel blocker, 5-HT3 antagonist, N-methyl-D-aspartic acid receptor antagonist, and phosphodiesterase V inhibitor.

Yet another embodiment of the present invention relates to a method for providing a method for treating disorders of the central nervous system including stroke, epilepsy, manic depression, bipolar disorders, depression, anxiety, schizophrenia, migraine, and psychoses; neural degenerative disorders including Alzheimer's disease, AIDS related dementia, Parkinson's disease, neuropathy caused by head injury, and dementia caused by cerebrovascular disorders; disorders of the lower urinary tract including overactive bladder, prostatis, prostadynia, interstitial cystitis, and benign prostatic hyperplasia; disorders caused by psychogenic stress including bronchial asthma, unstable angina, and hypersensitive colon inflammation; cardiovascular disorders including hypertension, atherosclerosis, heart failure, and cardiac arrhythmias; drug addiction withdrawal symptoms, including ethanol addiction withdrawal symptoms; skin disorders including pruritis and allergic dermatitis, inflammatory bowel disease; cancer; diabetes; and infertility and sexual dysfunction in a mammal in need of such treatment. This method comprises administering to the mammal (including human) a therapeutically effective amount of a compound of the invention or a pharmaceutically acceptable salt thereof.

Calcium channel blockers have been associated with a slightly greater decreased risk of stroke compared to other types of antihypertensive agents (Angeli, F.; et al. Calcium channel blockade to prevent stroke in hypertension. American Journal of Hypertension 2004, 17(9), 817-822). The enhanced effect did not correlate with differences in systolic blood pressure and the mechanism of action remains unknown. However, calcium channel blockers have been associated with blockade of central neuronal calcium influx and subsequent ischemic injury in two rodent models (Barone, F. C.; et al. SB 201823-A antagonizes calcium currents in central neurons and reduces the effects of focal ischemia in rats and mice. Stroke 1995, 26, 1683-1690.). In another model of global ischemia, a calcium channel blocker offered neuroprotection although not permanently (Colbourne, F.; et al. Continuing postischemic neuronal death in CA1: Influence of ischemia duration and cytoprotective doses of NBQX and SNX-111 in rats. Stroke 1999, 30(3), 662-668.). Additionally, diminished progression of carotid atherosclerosis has been observed with calcium channel blocker use (Zanchetti, A.; et al. Calcium antagonist lacidipine slows down progression of asymptomatic carotid atherosclerosis. Principal results of the European lacidipine study on atherosclerosis (ELSA), a randomized, double-blind, long-term trial. Circulation 2002, 106, r47-r52.).

An increase in intracellular calcium concentration has been correlated with seizure activity (Heinemann, U.; et al. Extracellular free calcium and potassium during paroxysmal activity in the cerebral cortex of the cat. Exp. Brain Res. 1977, 27, 237-243.). Several studies have indicated that calcium channel blockers produce anticonvulsant activity (Vezzani, A.; et al. Effects of various calcium channel blockers on three different models of limbic seizures in rats. Neuropharmacology 1988, 27(5), 451-458. Otoom, S.; et al. Nifedipine inhibits picrotoxin-induced seizure activity: further evidence on the involvement of L-type calcium channel blockers in epilepsy. Fundamental & Clinical Pharmacology 2006, 20, 115-119.).

Calcium channel blockers have been evaluated in the treatment of bipolar disorders and manic depression for decades. There are suggestions that the calcium channel subtype has influence on efficacy of these disorders (Gitlin, M. Treatment-resistant bipolar disorder. Molecular Psychiatry 2006, 11, 227-240. Levy, N. A.; Janicak, P. G. Bipolar Disorders 2000, 2, 108-119.).

Calcium channel blockers have also been associated with the treatment of anxiety and depression (Saade, S.; et al. The L-type calcium channel blocker nimodipine mitigates

"learned helplessness" in rats. Pharmacology, Biochemistry and Behavior 2003, 74, 269-278.).

Antischizophrenic drugs have been found to be calcium channel antagonists (Gould, R. J.; et al. Antischizophrenic drugs of the diphenylbutylpiperidine type act as calcium channel antagonists. Proc. Natl. Acad. Sci. USA 1983, 80, 5122-5125.). Other calcium channel blockers have been suggested for the treatment of schizophrenia (Tort, A. B. L.; et al. Atypical antipsychotic profile of flunarizine in animal models. Psychopharmacology 2005, 177, 344-348.).

Migraines are treated with calcium channel blockers (Arulmoshi, D. K.; et al. Migraine: Current concepts and emerging therapies. Vascular Pharmacology 2005, 43, 176-187. Gladstone, J. P.; et al. Current and emerging treatment options for migraine and other primary headache disorders. Expert Rev. Neurotherapeutics 2003, 3(6), 845-872.).

Disorders of the lower urinary tract including overactive bladder, prostatis, prostadynia, interstitial cystitis, and benign prostatic hyperplasia can be treated with calcium channel blockers (Fraser, M. O.; et al. US20050148587, 2005).

Ethanol withdrawal syndrome is decreased with calcium channel blockers (Little, H. J.; et al. Calcium channel antagonists decrease the ethanol withdrawal syndrome. Life Sciences 1986, 39, 2059-2065.).

Several cardiac disorders are treated with calcium channel blockers. Atherosclerosis may be reduced by a decrease in free radical-mediated damage as a result of influence on the biophysical properties of membranes (Mason, R. P.; et al. Antioxidant and cytoprotective activities of the calcium channel blocker mibefradil. Biochemical Pharmacology 1998, 55, 1843-1852.). Hypertension and angina are both successfully treated with calcium channel blockers (Croom, K. F.; et al. Modified-release nifedipine: A review of the use of modified-release formulations in the treatment of hypertension and angina pectoris. Drugs 2006, 66(4), 497-528.).

There is data suggesting that calcium channel blockers inhibit the proliferation of cancer cells (Gray, L. S.; et al.. International Publication No. WO200059882, 2000.).

Calcium channels have been suggested as a target for the treatment of diabetes (Bhattacharjee, A.; et al. T-Type calcium channels facilitate insulin secretion by enhancing general excitability in the insulin-secreting β-cell line, INS-1. Endocrinology 1997, 138(9), 3735-3740.).

Ion channels including calcium channels play an important role in sperm physiology and fertilization (Darszon, A.; et al. Ion channels in sperm physiology. Physiological Reviews 1999, 79(2), 481-510).

Calcium channel blockers modulate inflammation (Bilici, D.; et al. Protective effect of T-type calcium channel blocker in histamine-induced paw inflammation in rat. Pharmacological Research 2001, 44(6), 527-531.).

Increased calcium levels in neurones has been implicated in Alzheimer's disease. Two suggested mechanisms of increased calcium influx are that β-amyloid may form calcium permeable channels (Bhatia, R.; et al. Fresh and globular amyloid beta protein (1-42) induces rapid cellular degeneration: evidence for AβP channel-mediated cellular toxicity. FASEB J. 2000, 14(9), 1233-1243.) or a G-protein-coupled receptor may be activated by β-amyloid (Lorton, D. β-Amyloid induced IL-1 β release from an activated human monocyte cell line is calcium- and G-protein-dependent. Mech. Ageing Dev. 1997, 94(1-3), 199-211.).

Neurodegenerative diseases, including Parkinson's and Alzheimer's diseases can be modulated by calcium channel blockers (Rodnitzky, R. L. Can calcium antagonists provide a neuroprotective effect in Parkinson's disease. Drugs 1999, 57(6), 845-849. Vagnucci, A. H., Jr.; et al. Alzheimer's disease and angiogenesis. The Lancet 2003, 361(9357), 605-608. Veng, L. M.; et al. Age-related working memory impairment is correlated with increases in the L-type calcium channel protein α_{1D} ($Ca_v1.3$) in area CA1 of the hippocampus and both are ameliorated by chronic nimodipine treatment. Molecular Brain Research 2203, 110, 193-202. Geldenhuys, W. J.; et al. Structure-activity relationships of pentacycloundecylamines at the N-methyl-D-aspartate receptor. Bioorganic and Medicinal Chemistry 2007, 15, 1525-1532. Cavalli, A.; et al. Multi-target-directed ligands to combat neurodegenerative diseases. J. Med. Chem. 2008, 51(3), 347-372.)

Actual dosage levels of active ingredients in the pharmaceutical compositions of this invention can be varied so as to obtain an amount of the active compound(s) that is effective to achieve the desired therapeutic response for a particular patient, compositions and mode of administration. The selected dosage level will depend upon the activity of the particular compound, the route of administration, the severity of the condition being treated and the condition and prior medical history of the patient being treated. However, it is within the skill of the art to start doses of the compound at levels lower than required to achieve the desired therapeutic effect and to gradually increase the dosage until the desired effect is achieved.

Compounds of the invention can also be administered as a pharmaceutical composition comprising the compounds of interest in combination with one or more pharmaceutically acceptable carriers. The phrase "therapeutically effective amount" of the compound of the invention means a sufficient amount of the compound to treat disorders, at a reasonable benefit/risk ratio applicable to any medical treatment. It will be understood, however, that the total daily usage of the compounds and compositions of the invention will be decided by the attending physician within the scope of sound medical judgment. The specific therapeutically effective dose level for any particular patient will depend upon a variety of factors including the disorder being treated and the severity of the disorder; activity of the specific compound employed; the specific composition employed; the age, body weight, general health, sex and diet of the patient; the time of administration, route of administration, and rate of excretion of the specific compound employed; the duration of the treatment; drugs used in combination or coincidental with the specific compound employed; and like factors well-known in the medical arts. For example, it is well within the skill of the art to start doses of the compound at levels lower than required to achieve the desired therapeutic effect and to gradually increase the dosage until the desired effect is achieved.

The total daily dose of the compounds of this invention administered to a human or other animal range from about 0.01 mg/kg body weight to about 100 mg/kg body weight. More preferable doses can be in the range of from about 0.01 mg/kg body weight to about 30 mg/kg body weight. If desired, the effective daily dose can be divided into multiple doses for purposes of administration. Consequently, single dose compositions may contain such amounts or submultiples thereof to make up the daily dose.

e. Pharmaceutical Compositions

The present invention further provides pharmaceutical compositions that comprise compounds of the present invention or a pharmaceutically acceptable salt or solvate thereof. The pharmaceutical compositions comprise compounds of the present invention that may be formulated together with one or more non-toxic pharmaceutically acceptable carriers.

Another aspect of the present invention is a pharmaceutical composition comprising compounds of the invention, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable carriers, alone or in combination with one or more nonsteroidal anti-inflammatory drugs (NSAID), opioid analgesics, barbiturates, benzodiazepines,

histamine antagonists, sedatives, skeletal muscle relaxants, transient receptor potential ion channel antagonists, α-adrenergics, tricyclic antidepressants, anticonvulsants, tachykinin antagonists, muscarinic antagonists, cyclooxygenase-2 selective inhibitors, neuroleptics, vanilloid receptor agonists, vanilloid receptor antagonists, β-adrenergics, local anesthetics, corticosteroids, 5-HT receptor agonists, 5-HT receptor antagonists, 5-HT_{2A} receptor antagonists, cholinergic analgesics, $\alpha_2\delta$ ligands such as gabapentin or pregabalin, cannabinoid receptor ligands, metabotropic glutamate subtype 1 receptor antagonists, serotonin reuptake inhibitors, norepinephrine reuptake inhibitors, dual serotonin-noradrenaline reuptake inhibitors, Rho kinase inhibitors, inducible nitric oxide synthase inhibitors, acetylcholinesterase inhibitors, prostaglandin E_2 subtype 4 antagonists, leukotriene B4 antagonists, 5-lipoxygenase inhibitors, sodium channel blockers, 5-HT3 antagonists, N-methyl-D-aspartic acid receptor antagonists, and phosphodiesterase V inhibitors.

The pharmaceutical compositions of this invention can be administered to humans and other mammals orally, rectally, parenterally, intracisternally, intravaginally, intraperitoneally, topically (as by powders, ointments or drops), bucally or as an oral or nasal spray. The term "parenterally" as used herein, refers to modes of administration which include intravenous, intramuscular, intraperitoneal, intrasternal, subcutaneous and intraarticular injection and infusion.

The term "pharmaceutically acceptable carrier" as used herein, means a non-toxic, inert solid, semi-solid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type. Some examples of materials which can serve as pharmaceutically acceptable carriers are sugars such as, but not limited to, lactose, glucose and sucrose; starches such as, but not limited to, corn starch and potato starch; cellulose and its derivatives such as, but not limited to, sodium carboxymethyl cellulose, ethyl cellulose and cellulose acetate; powdered tragacanth; malt; gelatin; talc; excipients such as, but not limited to, cocoa butter and suppository waxes; oils such as, but not limited to, peanut oil, cottonseed oil, safflower oil, sesame oil, olive oil, corn oil and soybean oil; glycols; such a propylene glycol; esters such as, but not limited to, ethyl oleate and ethyl laurate; agar; buffering agents such as, but not limited to, magnesium hydroxide and aluminum hydroxide; alginic acid; pyrogen-free water; isotonic saline; Ringer's solution; ethyl alcohol, and phosphate buffer solutions, as well as other non-toxic compatible lubricants such as, but not limited to, sodium lauryl sulfate and magnesium stearate, as well as coloring agents, releasing agents, coating agents, sweetening,

flavoring and perfuming agents, preservatives and antioxidants can also be present in the composition, according to the judgment of the formulator.

Pharmaceutical compositions of this invention for parenteral injection comprise pharmaceutically acceptable sterile aqueous or nonaqueous solutions, dispersions, suspensions or emulsions as well as sterile powders for reconstitution into sterile injectable solutions or dispersions just prior to use. Examples of suitable aqueous and nonaqueous carriers, diluents, solvents or vehicles include water, ethanol, polyols (such as glycerol, propylene glycol, polyethylene glycol and the like), vegetable oils (such as olive oil), injectable organic esters (such as ethyl oleate) and suitable mixtures thereof. Proper fluidity can be maintained, for example, by the use of coating materials such as lecithin, by the maintenance of the required particle size in the case of dispersions and by the use of surfactants.

These compositions may also contain adjuvants such as preservatives, wetting agents, emulsifying agents and dispersing agents. Prevention of the action of microorganisms can be ensured by the inclusion of various antibacterial and antifungal agents, for example, paraben, chlorobutanol, phenol sorbic acid and the like. It may also be desirable to include isotonic agents such as sugars, sodium chloride and the like. Prolonged absorption of the injectable pharmaceutical form can be brought about by the inclusion of agents which delay absorption such as aluminum monostearate and gelatin.

In some cases, in order to prolong the effect of the drug, it is desirable to slow the absorption of the drug from subcutaneous or intramuscular injection. This can be accomplished by the use of a liquid suspension of crystalline or amorphous material with poor water solubility. The rate of absorption of the drug then depends upon its rate of dissolution which, in turn, may depend upon crystal size and crystalline form. Alternatively, delayed absorption of a parenterally administered drug form is accomplished by dissolving or suspending the drug in an oil vehicle.

Injectable depot forms are made by forming microencapsule matrices of the drug in biodegradable polymers such as polylactide-polyglycolide. Depending upon the ratio of drug to polymer and the nature of the particular polymer employed, the rate of drug release can be controlled. Examples of other biodegradable polymers include poly(orthoesters) and poly(anhydrides). Depot injectable formulations are also prepared by entrapping the drug in liposomes or microemulsions which are compatible with body tissues.

The injectable formulations can be sterilized, for example, by filtration through a bacterial-retaining filter or by incorporating sterilizing agents in the form of sterile solid

compositions which can be dissolved or dispersed in sterile water or other sterile injectable medium just prior to use.

Solid dosage forms for oral administration include capsules, tablets, pills, powders and granules. In such solid dosage forms, the active compound may be mixed with at least one inert, pharmaceutically acceptable excipient or carrier, such as sodium citrate or dicalcium phosphate and/or a) fillers or extenders such as starches, lactose, sucrose, glucose, mannitol and silicic acid; b) binders such as carboxymethylcellulose, alginates, gelatin, polyvinylpyrrolidone, sucrose and acacia; c) humectants such as glycerol; d) disintegrating agents such as agar-agar, calcium carbonate, potato or tapioca starch, alginic acid, certain silicates and sodium carbonate; e) solution retarding agents such as paraffin; f) absorption accelerators such as quaternary ammonium compounds; g) wetting agents such as cetyl alcohol and glycerol monostearate; h) absorbents such as kaolin and bentonite clay and i) lubricants such as talc, calcium stearate, magnesium stearate, solid polyethylene glycols, sodium lauryl sulfate and mixtures thereof. In the case of capsules, tablets and pills, the dosage form may also comprise buffering agents.

Solid compositions of a similar type may also be employed as fillers in soft and hard-filled gelatin capsules using such carriers as lactose or milk sugar as well as high molecular weight polyethylene glycols and the like.

The solid dosage forms of tablets, dragees, capsules, pills and granules can be prepared with coatings and shells such as enteric coatings and other coatings well-known in the pharmaceutical formulating art. They may optionally contain opacifying agents and may also be of a composition such that they release the active ingredient(s) only, or preferentially, in a certain part of the intestinal tract, optionally, in a delayed manner. Examples of embedding compositions which can be used include polymeric substances and waxes.

The active compounds can also be in micro-encapsulated form, if appropriate, with one or more of the above-mentioned carriers.

Liquid dosage forms for oral administration include pharmaceutically acceptable emulsions, solutions, suspensions, syrups and elixirs. In addition to the active compounds, the liquid dosage forms may contain inert diluents commonly used in the art such as, for example, water or other solvents, solubilizing agents and emulsifiers such as ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1,3-butylene glycol, dimethyl formamide, oils (in particular, cottonseed, groundnut, corn, germ, olive, castor and sesame oils), glycerol, tetrahydrofurfuryl alcohol, polyethylene glycols and fatty acid esters of sorbitan and mixtures thereof.

Besides inert diluents, the oral compositions may also include adjuvants such as wetting agents, emulsifying and suspending agents, sweetening, flavoring and perfuming agents.

Suspensions, in addition to the active compounds, may contain suspending agents as, for example, ethoxylated isostearyl alcohols, polyoxyethylene sorbitol and sorbitan esters, microcrystalline cellulose, aluminum metahydroxide, bentonite, agar-agar, tragacanth and mixtures thereof.

Compositions for rectal or vaginal administration are preferably suppositories which can be prepared by mixing the compounds of this invention with suitable non-irritating carriers or carriers such as cocoa butter, polyethylene glycol or a suppository wax which are solid at room temperature but liquid at body temperature and therefore melt in the rectum or vaginal cavity and release the active compound.

Compounds of the present invention can also be administered in the form of liposomes. As is known in the art, liposomes are generally derived from phospholipids or other lipid substances. Liposomes are formed by mono- or multi-lamellar hydrated liquid crystals which are dispersed in an aqueous medium. Any non-toxic, physiologically acceptable and metabolizable lipid capable of forming liposomes can be used. The present compositions in liposome form can contain, in addition to a compound of the present invention, stabilizers, preservatives, excipients and the like. The preferred lipids are natural and synthetic phospholipids and phosphatidyl cholines (lecithins) used separately or together.

Methods to form liposomes are known in the art. See, for example, Prescott, Ed., Methods in Cell Biology, Volume XIV, Academic Press, New York, N.Y. (1976), p. 33 et seq.

Dosage forms for topical administration of a compound of this invention include powders, sprays, ointments and inhalants. The active compound may be mixed under sterile conditions with a pharmaceutically acceptable carrier and any needed preservatives, buffers or propellants which may be required. Ophthalmic formulations, eye ointments, powders and solutions are also contemplated as being within the scope of this invention.

The compounds of the present invention can be used in the form of pharmaceutically acceptable salts derived from inorganic or organic acids. The phrase "pharmaceutically acceptable salt" means those salts which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response and the like and are commensurate with a reasonable benefit/risk ratio.

Pharmaceutically acceptable salts are well known in the art. For example, S. M. Berge et al. describe pharmaceutically acceptable salts in detail in (J. Pharmaceutical Sciences, 1977, 66: 1 et seq). The salts can be prepared in situ during the final isolation and purification of the compounds of the invention or separately by reacting a free base function with a suitable organic acid. Representative acid addition salts include, but are not limited to acetate, adipate, alginate, citrate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, camphorate, camphorsulfonate, digluconate, glycerophosphate, hemisulfate, heptanoate, hexanoate, fumarate, hydrochloride, hydrobromide, hydroiodide, 2-hydroxyethansulfonate (isothionate), lactate, malate, maleate, methanesulfonate, nicotinate, 2-naphthalenesulfonate, oxalate, palmitoate, pectinate, persulfate, 3-phenylpropionate, picrate, pivalate, propionate, succinate, tartrate, thiocyanate, phosphate, glutamate, bicarbonate, p-toluenesulfonate and undecanoate. Also, the basic nitrogen-containing groups can be quaternized with such agents as lower alkyl halides such as, but not limited to, methyl, ethyl, propyl, and butyl chlorides, bromides and iodides; dialkyl sulfates like dimethyl, diethyl, dibutyl and diamyl sulfates; long chain halides such as, but not limited to, decyl, lauryl, myristyl and stearyl chlorides, bromides and iodides; arylalkyl halides like benzyl and phenethyl bromides and others. Water or oil-soluble or dispersible products are thereby obtained. Examples of acids which can be employed to form pharmaceutically acceptable acid addition salts include such inorganic acids as hydrochloric acid, hydrobromic acid, sulfuric acid, and phosphoric acid and such organic acids as acetic acid, fumaric acid, maleic acid, 4-methylbenzenesulfonic acid, succinic acid and citric acid.

Basic addition salts can be prepared in situ during the final isolation and purification of compounds of this invention by reacting a carboxylic acid-containing moiety with a suitable base such as, but not limited to, the hydroxide, carbonate or bicarbonate of a pharmaceutically acceptable metal cation or with ammonia or an organic primary, secondary or tertiary amine. Pharmaceutically acceptable salts include, but are not limited to, cations based on alkali metals or alkaline earth metals such as, but not limited to, lithium, sodium, potassium, calcium, magnesium and aluminum salts and the like and nontoxic quaternary ammonia and amine cations including ammonium, tetramethylammonium, tetraethylammonium, methylamine, dimethylamine, trimethylamine, triethylamine, diethylamine, ethylamine and the like. Other representative organic amines useful for the formation of base addition salts include ethylenediamine, ethanolamine, diethanolamine, piperidine, piperazine and the like.

The term "pharmaceutically acceptable prodrug" or "prodrug" as used herein, represents those prodrugs of the compounds of the present invention which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response, and the like, commensurate with a reasonable benefit/risk ratio, and effective for their intended use.

The present invention contemplates compounds of the invention formed by synthetic means or formed by in vivo biotransformation of a prodrug.

The compounds of the invention can exist in unsolvated as well as solvated forms, including hydrated forms, such as hemi-hydrates. In general, the solvated forms, with pharmaceutically acceptable solvents such as water and ethanol among others are equivalent to the unsolvated forms for the purposes of the invention.

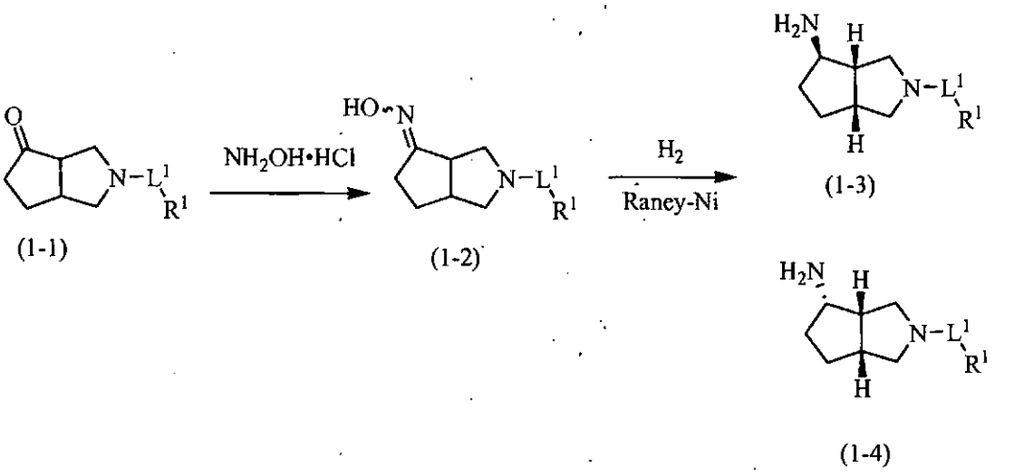
f. General Synthesis

This invention is intended to encompass compounds of the invention when prepared by synthetic processes or by metabolic processes. Preparation of the compounds by metabolic processes includes those occurring in the human or animal body (*in vivo*) or processes occurring *in vitro*.

The compounds of the invention may be prepared by a variety of processes well known for the preparation of compounds of this class. For example, the compounds of the invention wherein the groups L^1, L^2, R^1, R^2, R^3,R^4, R^5, R^6, R^e, R^f, R^g, R^h, n, q, and G^1, have the meanings as set forth in the Summary of the Invention section unless otherwise noted, can be synthesized as shown in Schemes 1-20.

Abbreviations which have been used in the descriptions of the Schemes and the Examples that follow are: Ac for acetyl; $AlMe_3$ for trimethylaluminum; Boc for *t*-butoxy carbonyl; Boc_2O for di-*tert*-butyl dicarbonate; Bu for butyl; Et for ethyl, EtOH for ethanol; DMF or *N,N*-dimethylformamide; DMSO for dimethyl sulfoxide; lcms for liquid chromatography/mass spec; MeOH for methanol; MsCl for methanesulfonyl chloride; NEt_3 for triethylamine; OAc for acetate; Ph for phenyl; PPh_3 for triphenylphosphine; PS-cyanoborohydride for polymer-supported cyanoborohydride; psi for pounds per square inch; tBu for *tert*-butyl; THF for tetrahydrofuran, and tlc for thin layer chromatography.

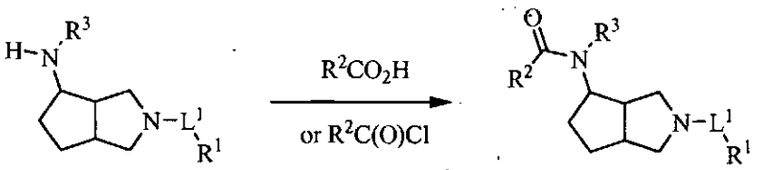
Scheme 1



(1-1) (1-2) (1-3) (1-4)

Compounds of formula (1-3) and (1-4), wherein L^L and R^1 are as defined in the Summary of the Invention, may be prepared as illustrated in Scheme 1. Compounds of formula (1-1) can be treated with hydroxylamine hydrochloride in the presence of a base such as sodium carbonate, sodium bicarbonate, or sodium acetate in a solvent such as water or aqueous methanol and optionally heated to furnish oximes of formula (1-2). Oximes of formula (1-2) can then be reduced in the presence of hydrogen (30 psi) in the presence of Raney®-nickel in a solvent such as 20% ammonia in methanol at ambient temperature over 1 to 24 hours to provide a diastereomeric mixture of amines, compounds of formulas (1-3) and (1-4). The diastereomeric amines can be separated by techniques know to one skilled in the art such as chromatography.

Scheme 2



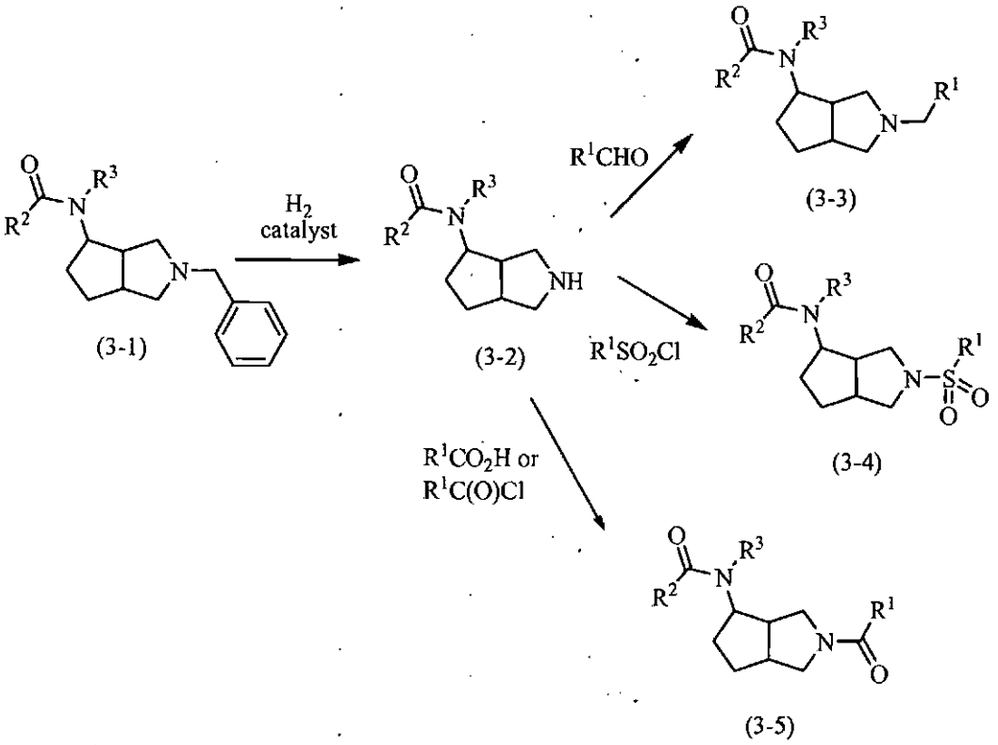
(2-1) (2-2)

Compounds of formula (2-2) which are representative of compounds of formula (I), wherein L^1, R^1, R^2 and R^3 are as described in the Summary of the Invention, are prepared by reacting compounds of formula (2-1) with carboxylic acids of formula R^2CO_2H under amide bond coupling conditions. Examples of conditions known to generate amides from a mixture of a carboxylic acid and an amine include but are not limited to adding a coupling reagent such as but not limited to *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide (EDC or EDCI), 1,3-dicyclohexylcarbodiimide (DCC), bis(2-oxo-3-oxazolidinyl)phosphinic chloride

(BOPCl), O-(7-azabenzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (HATU), O-benzotriazol-1-yl-*N,N,N',N'*-tetramethyluronium tetrafluoroborate (TBTU),and 2-(1*H*-benzo[*d*][1,2,3]triazol-1-yl)-1,1,3,3-tetramethylisouronium hexafluorophosphate(V) (HBTU). The coupling reagents may be added as a solid, a solution or as the reagent bound to a solid support resin. In addition to the coupling reagents, auxiliary-coupling reagents may facilitate the coupling reaction. Auxiliary coupling reagents that are often used in the coupling reactions include but are not limited to (dimethylamino)pyridine (DMAP), 1-hydroxy-7-azabenzotriazole (HOAT) and 1-hydroxybenzotriazole (HOBT). The reaction may be carried out optionally in the presence of a base such as triethylamine or diisopropylethylamine. The coupling reaction may be carried out in solvents such as but not limited to tetrahydrofuran, *N,N*-dimethylformamide, dichloromethane, and ethyl acetate. The reaction may be conducted at ambient or elevated temperatures.

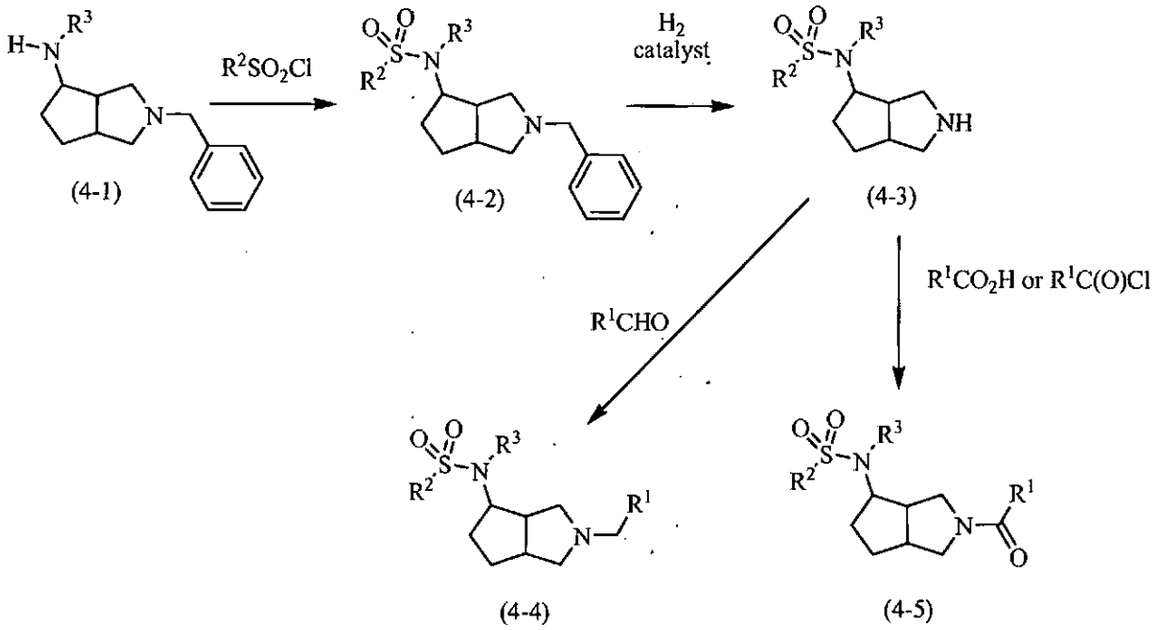
Alternatively, compounds of formula (2-2) may be prepared from compounds of formula (2-1) by reacting with an acid chloride of formula $R^2C(O)Cl$. Compounds of formula (2-1), may be treated $R_2C(O)Cl$ in a solvent such as dichloromethane in the presence of an amine such as triethylamine or diisopropylethylamine at room temperature over 1 to 24 hours to afford compounds of formula (2-2).

Scheme 3



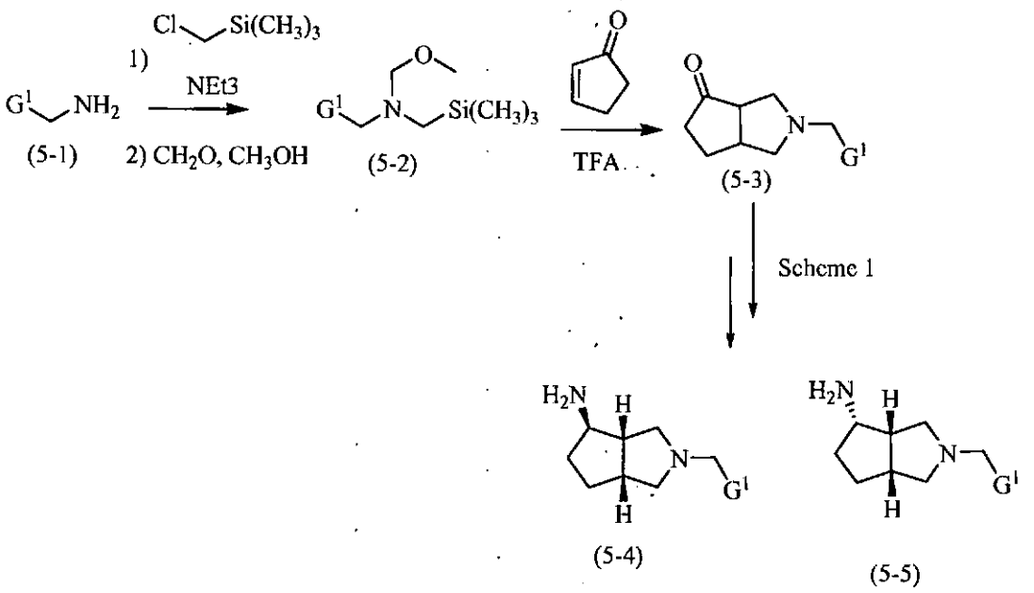
As illustrated in Scheme 3, compounds of formulas (3-3), (3-4), and (3-5) which are representative of compounds of formula (I), and wherein R^1, R^2 and R^3 are as defined in the Summary of the Invention, can be obtained from compounds of formula (3-1). Compounds of formula (3-1) can be converted to compounds of formula (3-2) by treatment with hydrogen (15-60 psi) in the presence of a catalyst such as palladium hydroxide on carbon or palladium on carbon in a solvent such as methanol or ethanol at ambient temperature over 3-36 hours. Compounds of formula (3-2) can then be reductively aminated with aldehydes of formula R^1CHO in the presence of a reducing agent such as PS-cyanoborohydride, sodium cyanoborohydride, or sodium triacetoxyborohydride and acetic acid in a solvent such as methanol or dichloromethane at room temperature over 4-24 hours to supply compounds of formula (3-3). Alternatively, compounds of formula (3-2) can be reacted with a sulfonyl chloride of formula R^1SO_2Cl in the presence of a base such as triethylamine or diisopropylamine optionally in the presence of (dimethylamino)pyridine in a solvent such as dichloromethane at ambient temperature over 4-24 hours to supply compounds of formula (3-4). Compounds of formula (3-5) can also be prepared from compounds of formula (3-2). Compounds of formula (3-2) can be treated with a carboxylic acid of formula R^1CO_2H or and acid chloride of formula $R^1C(O)Cl$ under the amide bond forming conditions described in Scheme 2 to give compounds of formula (3-5).

Scheme 4



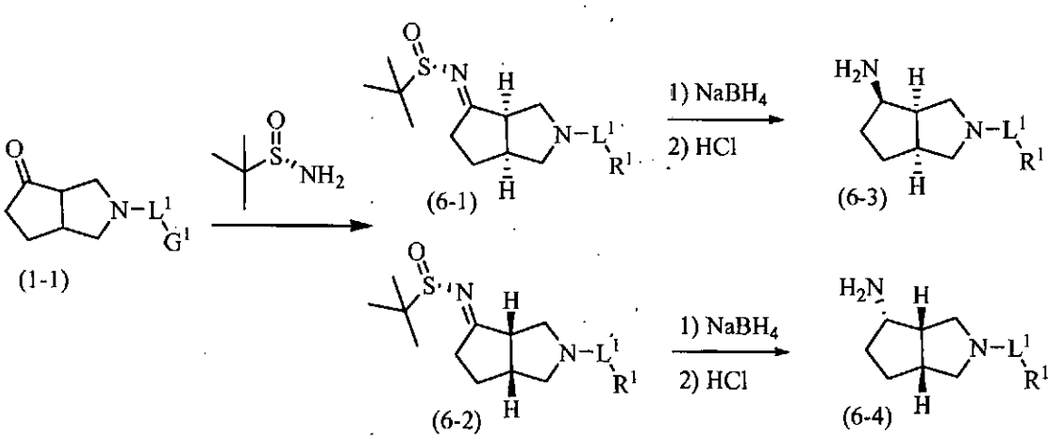
As illustrated in Scheme 4, compounds of formulas (4-2), (4-3), (4-4) and (4-5) which are representative of compounds of formula (I), wherein R^1, R^2 and R^3 are as defined in the Summary of the Invention, can be obtained from compounds of formula (4-1). Accordingly, compounds of formula (4-1) can be treated with sulfonyl chlorides of formula R_2SO_2Cl using the conditions described in Scheme 3 to give compounds of formula (4-2). The benzyl group can be reductively cleaved with hydrogen and a palladium catalyst as described in Scheme 3 to deliver compounds of formula (4-3). Compounds of formula (4-3) can be reductively alkylated with aldehydes of formula R^1CHO under the reaction conditions described in Scheme 3 to give compounds of formula (4-4). The secondary amine of compounds of formula (4-3) can be coupled with a carboxylic acid or acid chloride with the conditions described in Scheme 2 to give amides of formula (4-5).

Scheme 5



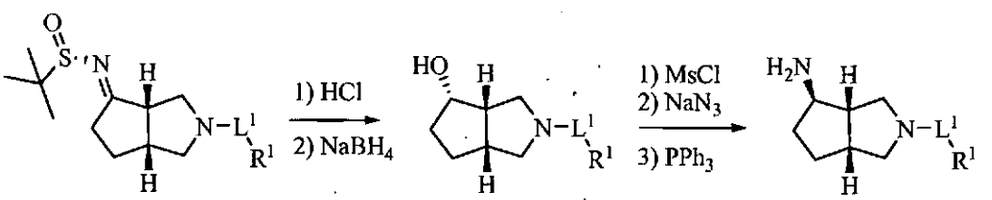
Compounds of formula (5-4) and (5-5), wherein G^1 is aryl or heteroaryl and unsubstituted or substituted as described in the Summary of the Invention, can be prepared from compounds of formula (5-1) as described in Scheme 5. Compounds of formula (5-1) can be combined with chloromethyltrimethylsilane and triethylamine and refluxed for 8-24 hours. The intermediate can then be reacted with formaldehyde in the presence of potassium carbonate and in methanol to give compounds of formula (5-2). Compounds of formula (5-2) can be reacted with cyclopent-2-enone at room temperature in the presence of trifluoroacetic acid in a solvent such as dichloromethane to give compounds of formula (5-3). Compounds of formula (5-3) can be transformed to compounds of formulas (5-4) and (5-5) upon treatment first with hydroxylamine hydrochloride and subsequently with hydrogen in the presence of Raney®-nickel as described in Scheme 1.

Scheme 6



Chiral compounds of formulas (6-3) and (6-4), wherein L^1 and R^1 are as defined in the Summary of the Invention, can be synthesized as described in Scheme 6. To this end, compounds of formula (1-1) can be treated with a chiral sulfinamide such as (*S*)-2-methylpropane-2-sulfinamide in the presence of titanium tetraethoxide in a solvent such as tetrahydrofuran and heated to 30-65 °C for 4 to 24 hours to give the diastereomeric compounds (6-1) and (6-2). The chiral diastereomers can be chromatographically separated and then treated individually in the following sequence. Chiral compounds of formula (6-1) can be reduced with sodium borohydride in methanol at -78 °C with gradual warming to room temperature over 8 to 20 hours. Subsequent hydrolysis with hydrochloric acid in methanol delivers chiral compounds of formula (6-3). In similar fashion, chiral compounds of formula (6-2) can be converted to chiral compounds of formula (6-4).

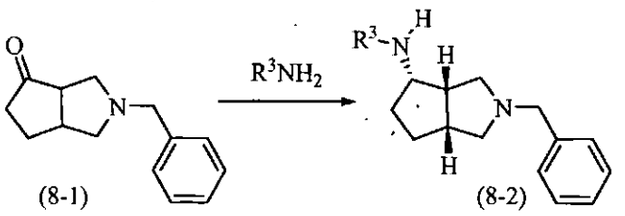
Scheme 7



(6-2) (7-1) (7-2)

As illustrated in Scheme 7, chiral compounds of formulas (7-2), wherein L^1 and R^1 are as defined in the Summary of the Invention, can be obtained from chiral compounds of formula (6-2). Chiral compounds of formula (6-2) can be hydrolyzed with hydrochloric acid in tetrahydrofuran at room temperature over 1-8 hours. Subsequent reduction with sodium borohydride in methanol at -40 °C to room temperature over 8-24 hours supplies chiral alcohols (7-1). Alcohols (7-1) can be transformed to chiral amines (7-2) in a three-step process. Compounds of formula (7-1) can be treated with methanesulfonyl chloride in the presence of triethylamine in dichloromethane at ambient temperature for 10 minutes to 2 hours. The sulfonates can then be displaced with inversion with sodium azide in heated *N,N*-dimethylacetamide over 8-24 hours. The derived azides can finally be reduced with triphenylphosphine in a heated mixture of water and tetrahydrofuran to give chiral compounds of formula (7-2).

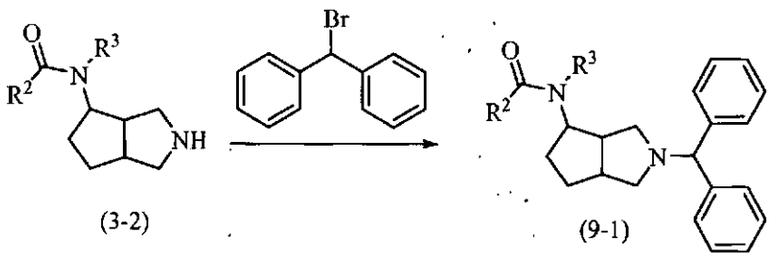
Scheme 8



(8-1) (8-2)

As described in Scheme 8, compounds of formula (8-1) can be converted to compounds of formula (8-2) wherein R^3 is alkyl, haloalkyl, cycloalkyl, or cycloalkylalkyl. Compounds of formula (8-1) can be treated with amines of formula R^3NH_2 in the presence of PS-cyanoborohydride, sodium cyanoborohydride, or triacetoxy borohydride and acetic acid in dichloromethane at ambient temperature for 1-6 hours to give compounds of formula (8-2). Compounds of formula (8-2) can be used in Scheme 4 in place of compounds of formula (4-1).

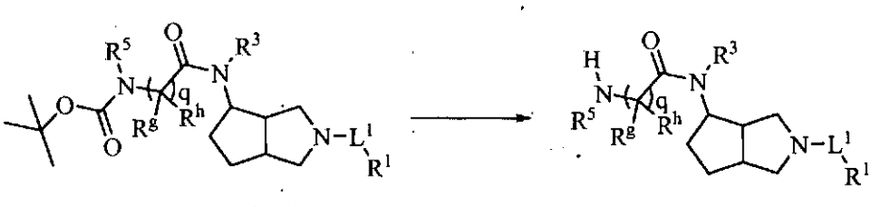
Scheme 9



(3-2) (9-1)

As illustrated in Scheme 9, compounds of formula (9-1), wherein R^2 and R^3 are as defined in the Summary of the Invention, can be obtained from compounds of formula (3-2). Compounds of formula (3-2) can be reacted with (bromomethylene)dibenzene in the presence of potassium iodide, and sodium carbonate in methyl ethyl ketone heated to 90 °C for 6 to 24 hours to give compounds of formula (9-1) which are representative of compounds of formula (I).

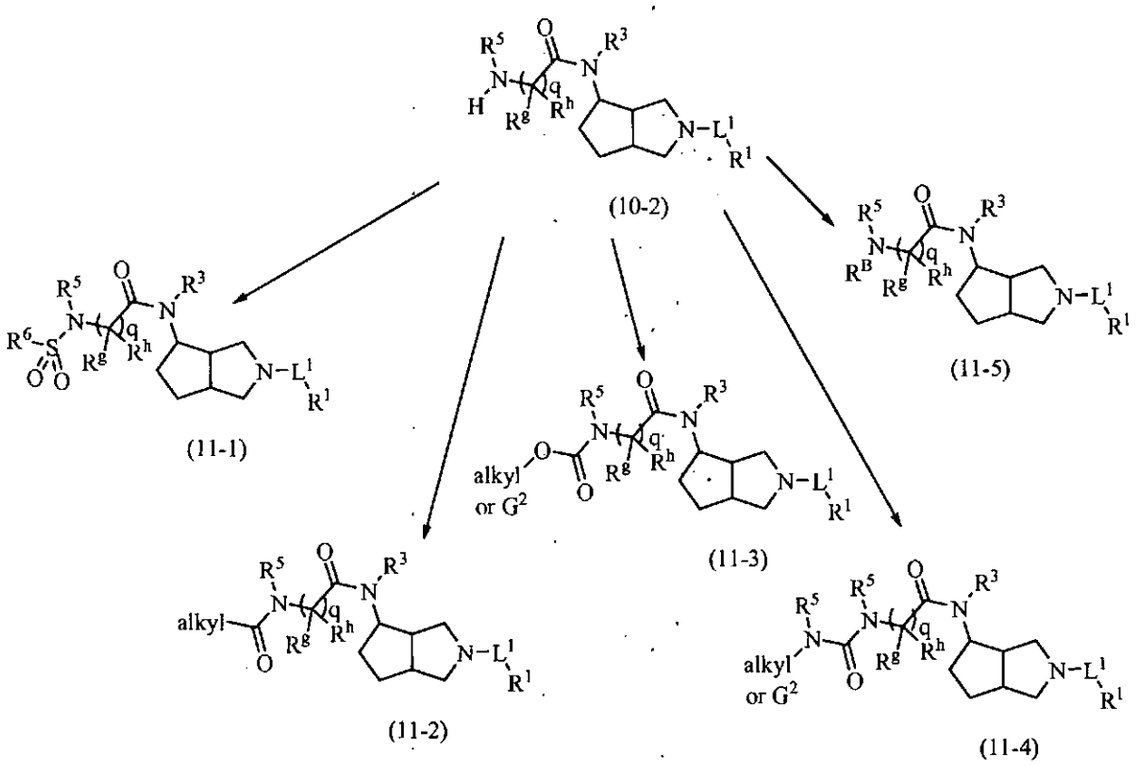
Scheme 10



(10-1) (10-2)

As illustrated in Scheme 10, compounds of formula (10-2) which are representative of compounds of formula (I) and wherein L^1, R^1, R^3, R^5, R^g, R^h, and q are as defined in the Summary of the Invention can be obtained from compounds of formula (10-1). Compounds of formula (10-1) can be treated with an acid such as hydrochloric acid or trifluoroacetic acid at room temperature in a solvent such as ether, dioxane, or dichloromethane for 2-24 hours to supply compounds of formula (10-2).

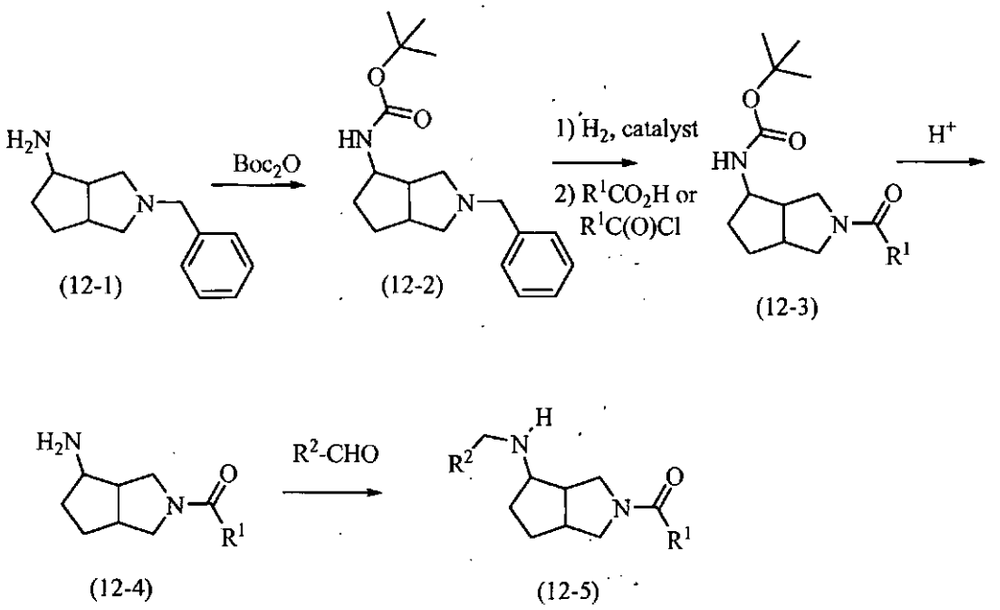
Scheme 11



As illustrated in Scheme 11, compounds of formula (11-1), (11-2), (11-3), (11-4), and (11-5) which are representative of compounds of formula (I) and wherein L^1, R^1, R^3, R^5, R^g, R^h, q, and G^2 are as defined in the Summary of the Invention can be obtained from compounds of formula (10-2). Compounds of formula (10-2) can be treated with a sulfonyl chloride of formula R^6SO_2Cl in dichloromethane in the presence of diisopropylethylamine at room temperature for 2-24 hours to provide compounds of formula (11-1). Similarly, compounds of formula (11-2) can be obtained upon treatment of compounds of formula (10-2) with an anhydride or acid chloride in dichloromethane at ambient temperature in the presence of diisopropylethylamine over 2-24 hours. Compounds of formula (11-3) are obtained from compounds of formula (10-2) upon treatment with a carbonochloridate in the presence of diisopropylethylamine in dichloromethane at room temperature over 2-24 hours.

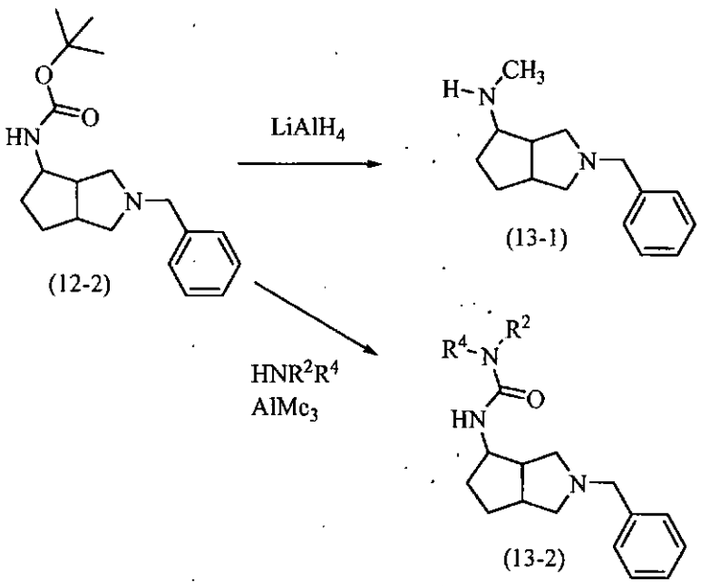
In like manner, compounds of formula (11-4) are made from compounds of formula (10-2) by reacting with an isocyanate in dichloromethane at room temperature over 2-24 hours. Compounds of formula (11-5), wherein R^B is alkyl, arylalkyl, cycloalkyl, cycloalkylalkyl, or heteroarylalkyl can be prepared either by alkylation or reductive amination of compounds of formula (10-2) using methodology known to one skilled in the art.

Scheme 12



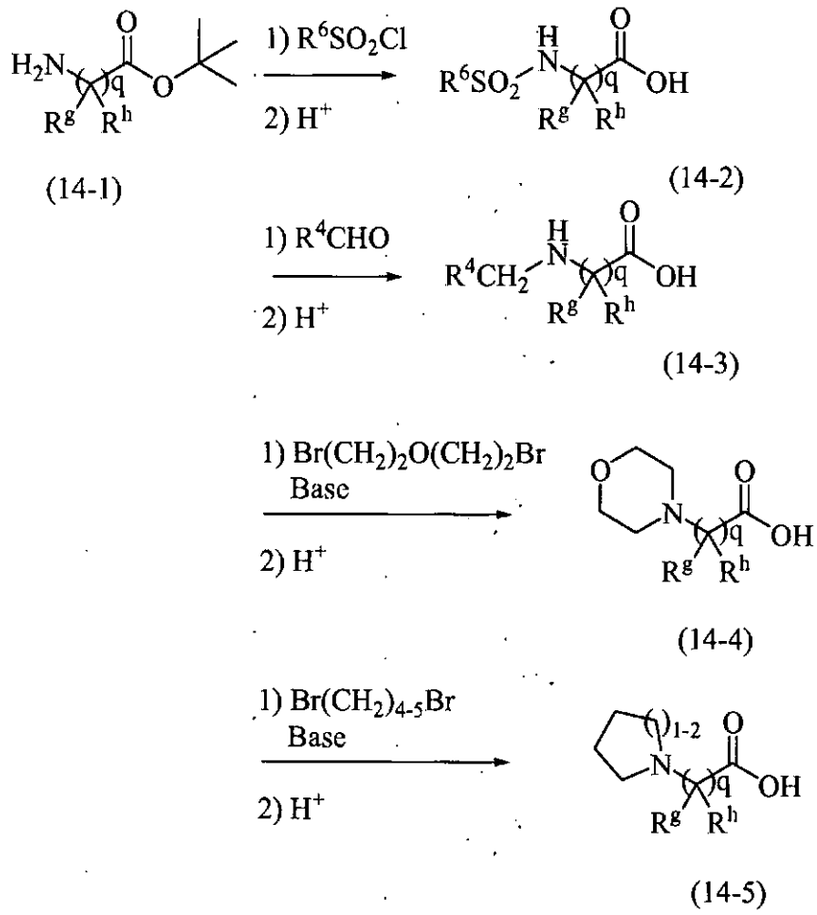
As illustrated in Scheme 12, compounds of formula (12-5) which are representative of compounds of formula (I) and wherein R^1 and R^2 are as defined in the Summary of the Invention can be obtained from compound of formula (12-1). Compound (12-1) can reacted with di-*tert*-butyl dicarbonate in the presence of (dimethylamino)pyridine in a solvent such as dichloromethane or dioxane at room temperature for 20 minutes to 4 hours to provide compound of formula (12-2). The benzyl group of compound of formula (12-2) can be removed with hydrogen in the presence of a palladium catalyst as described and then coupled with a carboxylic acid or acid chloride as described in the methods of Scheme 3 to provide compounds of formula (12-3). Removal of the *tert*-butoxy carbonyl group from compounds of formula (12-3) with the acid conditions described in Scheme 10 supplies compounds of formula (12-4). Compounds of formula (12-4) can be reductively aminated with aldehydes of formula R^2-CHO using the conditions described in Scheme 3 to give compounds of formula (12-5).

Scheme 13



As illustrated in Scheme 13, compounds of formula (13-2) which are representative of compounds of formula (I), wherein R^2 and R^4 are as defined in the Summary of the Invention, and compound of formula (13-1) can be obtained from compound of formula (12-2). Compound or formula (12-2) can be treated with lithium aluminum hydride in tetrahydrofuran initially at room temperature and then heated to reflux to afforded compound of formula (13-1). Compound of formula (13-1) can be used in the methods described in Schemes 2 and 4. Compound of formula (12-2) can be treated with an amine in the presence of trimethylaluminum in toluene initially at 0 °C and then at 90 °C for 6 to 24 hours to provide urea compounds of formula (13-2).

Scheme 14

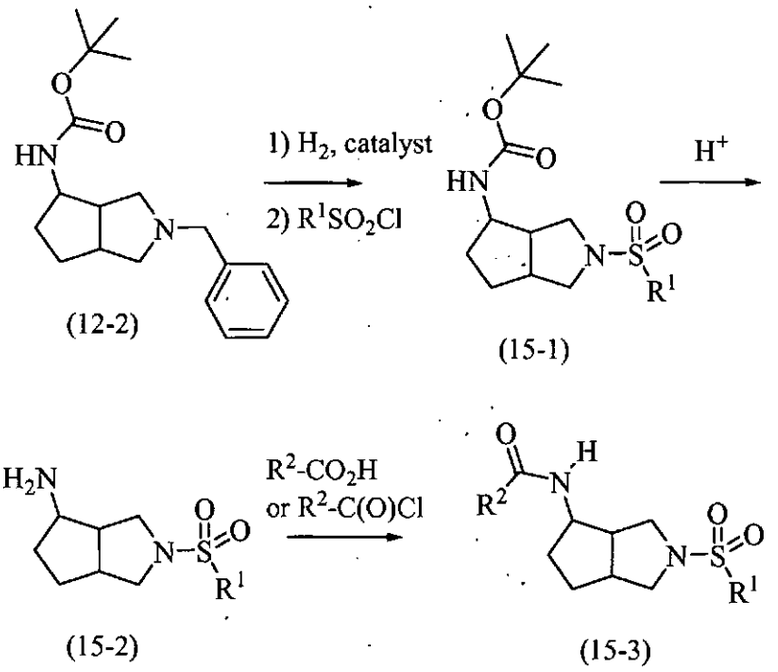


(14-1) (14-2) (14-3) (14-4) (14-5)

As shown in Scheme 14, compounds of formulas (14-2), (14-3), (14-4), and (14-5), wherein R^4, R^6, R^g, R^h, and q are as defined in the Summary of the Invention can be obtained from compounds of formula (14-1). Compounds of formula (14-1) can be treated with a sulfonyl chloride of formula R^6SO_2Cl in the presence of a base such as triethylamine or diisopropylethylamine in a solvent such as dichloromethane. Subsequent removal of the *t*-butyl group under acidic conditions deliver compounds of formula (14-2). Compounds of formula (14-1) can also be reductively aminated with an aldehyde of formula R^4CHO and a reductant such as sodium cyanoborohydride, polymer supported cyanoborohydride resin, or sodium triacetoxyborohydride optionally in the presence of an acid such as acetic acid in solvents such as dichloromethane or methanol. Acidic removal of the *t*-butyl group supplies compounds of formula (14-3). Compounds of formula (14-1) can also be dialkylated with dibromo compounds. Accordingly, alkylation of (14-1) with 1-bromo-2-(2-bromoethoxy)ethane in heated acetonitrile in the presence of a base followed by acid catalyzed *t*-butyl removal delivers compounds of formula (14-4). Alkylation with 1,4-dibromobutane or 1,5-dibromopentane under similar conditions followed by acid catalyzed *t*-

butyl removal delivers compounds of formula (14-5). Compounds of formulas (14-2), (14-3), (14-4), and (14-5) can be used in Schemes 2, 3, 4 and 12.

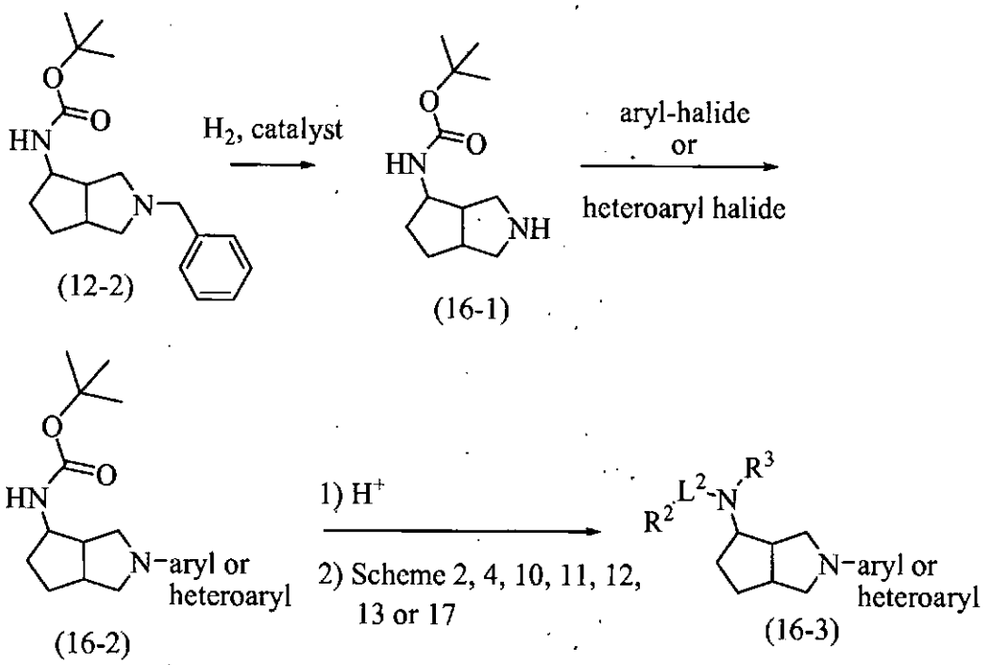
Scheme 15



(12-2) (15-1) (15-2) (15-3)

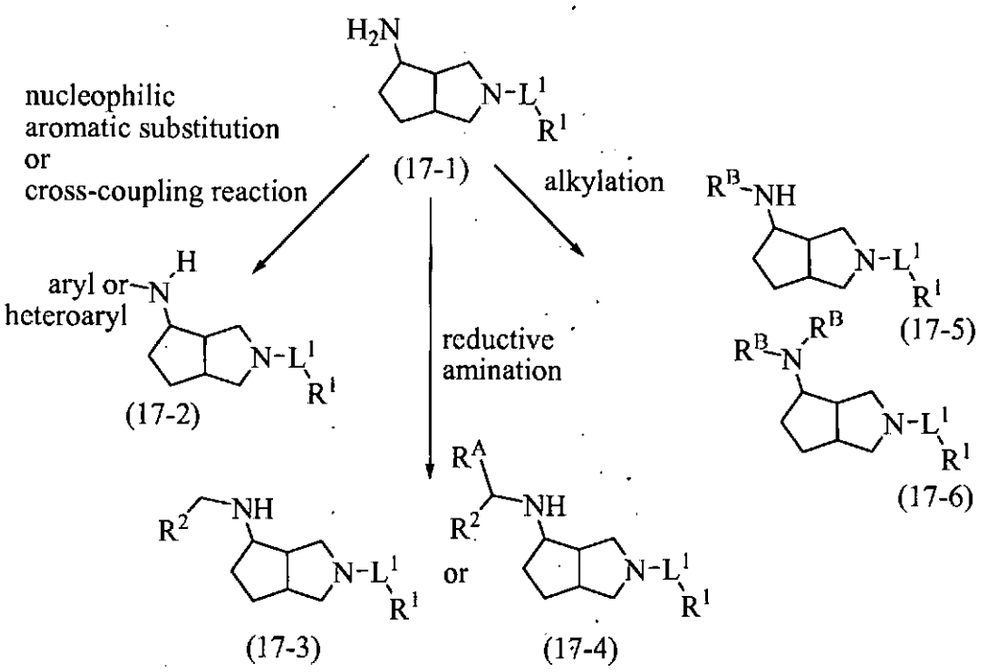
As illustrated in Scheme 15, compounds of formula (15-3) which are representative of compounds of formula (I) and wherein R^1 and R^2 are as defined in the Summary of the Invention can be obtained from compound of formula (12-2). The benzyl group of compound of formula (12-2) can be removed with hydrogen in the presence of a palladium catalyst as described in Scheme 3 and then coupled with a sulfonyl chloride of formula R^1SO_2Cl as described in the methods of Scheme 3 to provide compounds of formula (15-1). Removal of the *tert*-butoxy carbonyl group from compounds of formula (15-1) with the acid conditions described in Scheme 10 supplies compounds of formula (15-2). Compounds of formula (15-2) can be coupled with carboxylic acids of formula R^2-CO_2H or acid chlorides of formula R^2-C(O)Cl under the reaction conditions described in Scheme 2 to give compounds of formula (15-3).

Scheme 16



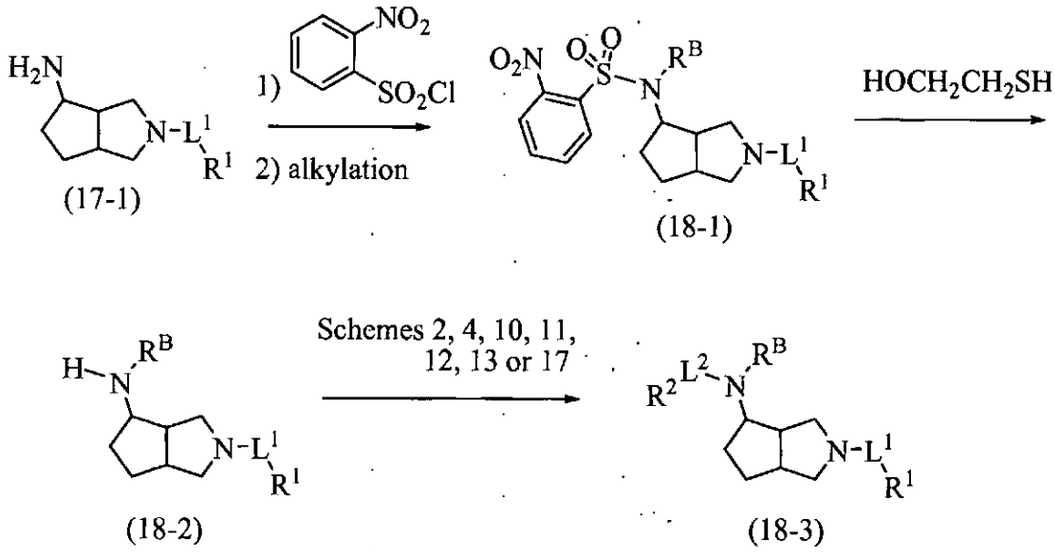
As illustrated in Scheme 17, compounds of formulas (16-3) which are representative of compounds of formula (I), wherein L^2, R^1, R^2 and R^3 are as defined in the Summary of the Invention, can be obtained from compounds of formula (12-2). Compounds of formula (12-2) can be converted to compounds of formula (16-1) by treatment with hydrogen (15-60 psi) in the presence of a catalyst such as palladium hydroxide on carbon or palladium on carbon in a solvent such as methanol or ethanol at ambient temperature over 3-36 hours. Compounds of formula (16-1) can then be reacted with an aryl halide or heteroaryl halide suitable for a nucleophilic aromatic substitution reaction to furnish compounds of formula (16-2). For example, a compound of formula (16-1) can be heated in a solvent such as ethanol in the presence of a base and heteroaryl bromide to supply compounds of formula (16-2). Compounds of formula (16-2) can then be deprotected under acidic conditions and further functionalized as described in but not limited to Schemes 2, 4, 10, 11, 12, 13 or 17 to give compounds of formula (16-3).

Scheme 17



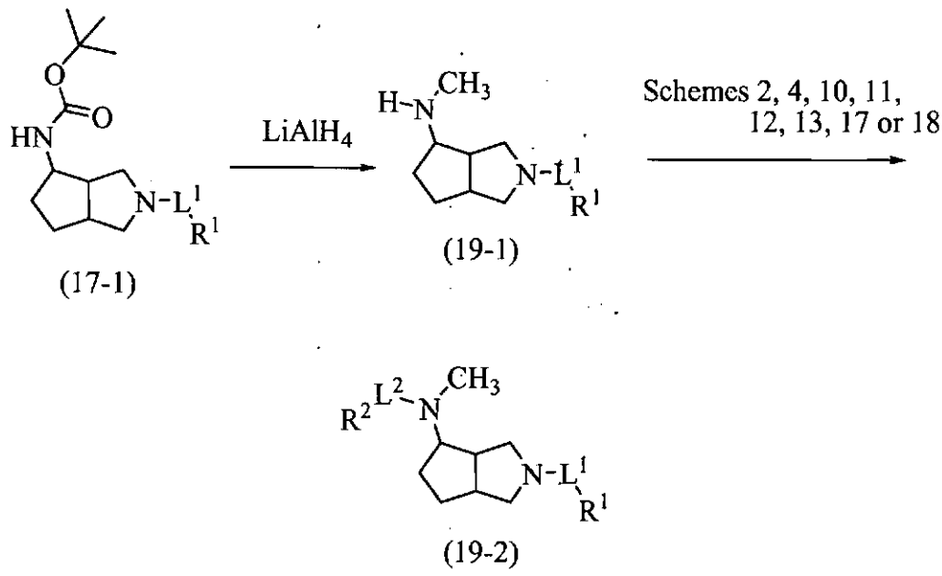
As illustrated in Scheme 17, compounds of formula (17-1) can be transformed into compounds of formulas (17-2), (17-3), (17-4), (17-5), and (17-6) which are representative of compounds of formula (I), wherein L^1, R^1, and R^2 are as defined in the Summary of the Invention. Compounds of formula (17-1) can be converted to compounds of formula (17-2) through either a nucleophilic aromatic substitution reaction under conditions described in Scheme 16 or under cross-coupling reaction conditions known to one skilled in the art. Compounds of formula (17-1) can also be reductively aminated with an aldehyde to give compounds of formula (17-3) or a ketone to give compounds of formula (17-4), wherein R^A is alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, or heteroarylalkyl. Alternatively, in compounds of formula (17-4), R^A and R^2 together with the atom to which they are attached may be joined to form a cyclic group. Reductive amination conditions are described in but not limited to those in Schemes 3, 4, 8, 12, and 14. Compounds of formula (17-1) can be mono-alkylated to give compounds of formula (17-5) or di-alkylated to give compounds of formula (17-6). Compounds of formula (17-1) can be treated with an alkyl-, arylalkyl-, cycloalkyl-, cycloalkylalkyl-, or heteroarylalkyl-halide or sulfonate optionally in the presence of a base in an optionally heated solvent such as tetrahydrofuran or *N,N*-dimethylformamide to give compounds of formula (17-5), wherein R^B is alkyl, arylalkyl, cycloalkyl, cycloalkylalkyl, or heteroarylalkyl. Excess alkylating agent leads to compounds of formula (17-6).

Scheme 18



As illustrated in Scheme 18, compounds of formula (17-1) can be converted to compounds of formulas (18-1), (18-2), and (18-3) which are representative of compounds of formula (I), wherein, L^1, L^2, R^1, and R^2 are as defined in the Summary of the Invention and R^B is alkyl, arylalkyl, cycloalkyl, cycloalkylalkyl, or heteroarylalkyl. Compounds of formula (17-1) can be reacted with 2-nitrobenzene-1-sulfonyl chloride in the presence of a base. The resultant sulfonamide can then be alkylated under conditions known to one skilled in the art to give compounds of formula (18-1). Treatment with 2-mercaptoethanol in the presence of a base in a solvent such as *N*,*N*-dimethylformamide gives compounds of formula (18-2). Compounds of formula (18-2) can be reacted as described in Schemes 2, 4, 10, 11, 12, 13, or 17 to give compounds of formula (18-3).

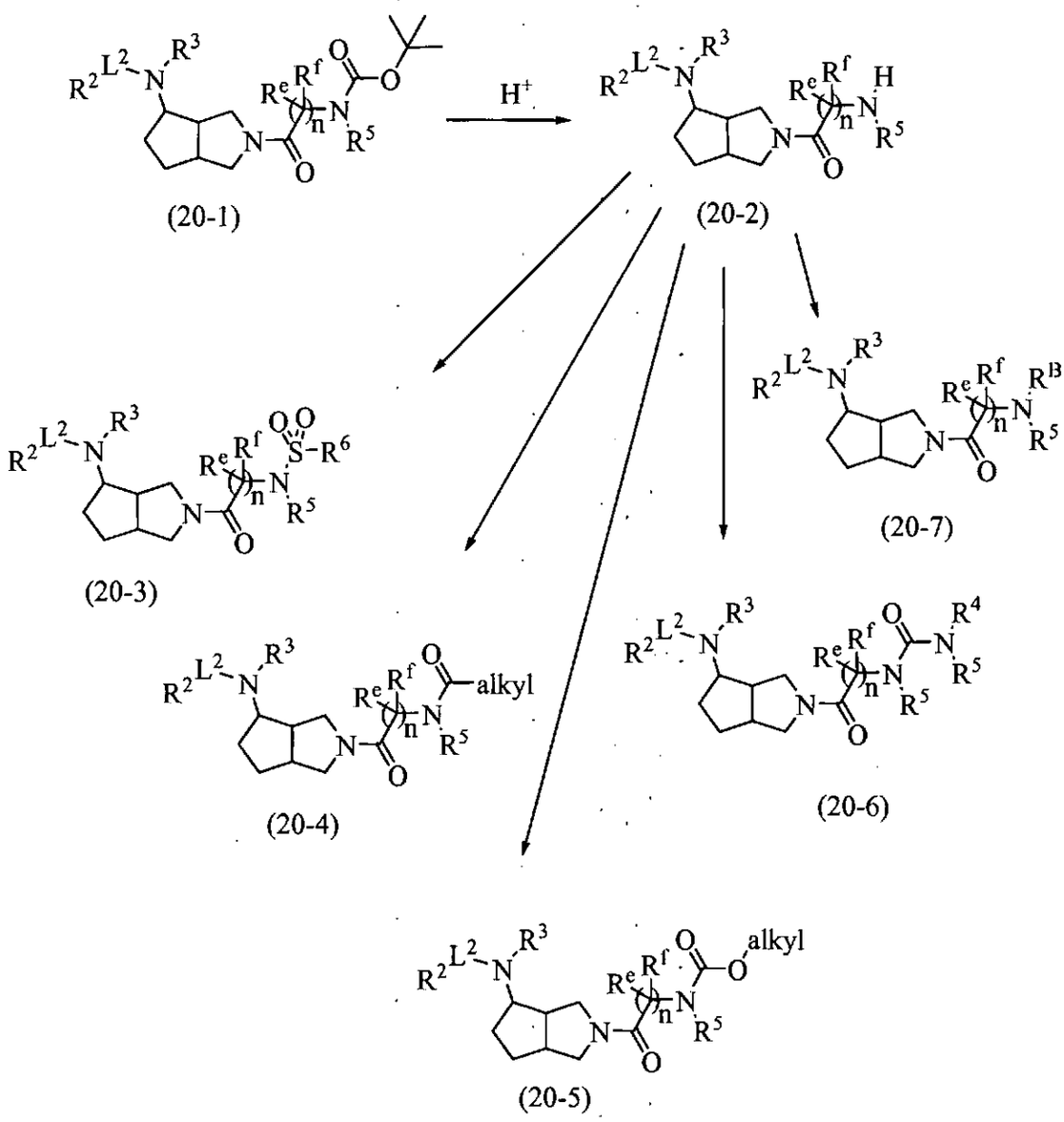
Scheme 19



(17-1) (19-1) (19-2)

As illustrated in Scheme 19, compounds of formula (19-2) which are representative of compounds of formula (I), wherein L^1, L^2, R^1 and R^2 are as defined in the Summary of the Invention, can be obtained from compound of formula (17-1). Compound or formula (17-1) can be treated with lithium aluminum hydride in tetrahydrofuran initially at room temperature and then heated to reflux to afforded compound of formula (19-1). Compound of formula (19-1) can be used in the methods described in Schemes 2, 4, 10, 11, 12, 13, 17 or 18 to give compounds of formula (19-2).

Scheme 20



As illustrated in Scheme 20, compounds of formula (20-3), (20-4), (20-5), (20-6) and (20-7) which are representative of compounds of formula (I) and wherein L^2, R^2, R^3, R^4, R^5, R^6, R^e, R^f, and n are as defined in the Summary of the Invention can be obtained from compounds of formula (20-2). Compounds of formula (20-2) are obtained from compounds of formula (20-1) upon treatment with an acid such as trifluoroacetic acid in dichloromethane or hydrochloric acid in dioxane. Compounds of formula (20-2) can be treated with a sulfonyl chloride of formula R^6SO_2Cl in dichloromethane in the presence of diisopropylethylamine at room temperature for 2-24 hours to provide compounds of formula (20-3). Similarly, compounds of formula (20-4) can be obtained upon treatment of compounds of formula (20-2) with an anhydride or acid chloride in dichloromethane at ambient temperature in the

presence of diisopropylethylamine over 2-24 hours. Compounds of formula (20-5) are obtained from compounds of formula (20-2) upon treatment with a carbonochloridate in the presence of diisopropylethylamine in dichloromethane at room temperature over 2-24 hours. In like manner, compounds of formula (20-6) are made from compounds of formula (20-2) by reacting with an isocyanate in dichloromethane at room temperature over 2-24 hours. Compounds of formula (20-7), wherein R^B is alkyl, arylalkyl, cycloalkyl, cycloalkylalkyl, or heteroarylalkyl can be prepared either by alkylation or reductive amination of compounds of formula (20-2) using methodology known to one skilled in the art.

It will be appreciated that the synthetic schemes and specific examples as illustrated in the Examples section are illustrative and are not to be read as limiting the scope of the invention as it is defined in the appended claims. All alternatives, modifications, and equivalents of the synthetic methods and specific examples are included within the scope of the claims.

Optimum reaction conditions and reaction times for each individual step may vary depending on the particular reactants employed and substituents present in the reactants used. Unless otherwise specified, solvents, temperatures and other reaction conditions may be readily selected by one of ordinary skill in the art. Specific procedures are provided in the Examples section. Reactions may be worked up in the conventional manner, e.g. by eliminating the solvent from the residue and further purified according to methodologies generally known in the art such as, but not limited to, crystallization, distillation, extraction, trituration and chromatography. Unless otherwise described, the starting materials and reagents are either commercially available or may be prepared by one skilled in the art from commercially available materials using methods described in the chemical literature.

Routine experimentations, including appropriate manipulation of the reaction conditions, reagents and sequence of the synthetic route, protection of any chemical functionality that may not be compatible with the reaction conditions, and deprotection at a suitable point in the reaction sequence of the method are included in the scope of the invention. Suitable protecting groups and the methods for protecting and deprotecting different substituents using such suitable protecting groups are well known to those skilled in the art; examples of which may be found in T. Greene and P. Wuts, Protecting Groups in Chemical Synthesis (3rd ed.), John Wiley & Sons, NY (1999), which is incorporated herein by reference in its entirety. Synthesis of the compounds of the invention may be

accomplished by methods analogous to those described in the synthetic schemes described hereinabove and in specific examples.

Starting materials, if not commercially available, may be prepared by procedures selected from standard organic chemical techniques, techniques that are analogous to the synthesis of known, structurally similar compounds, or techniques that are analogous to the above described schemes or the procedures described in the synthetic examples section.

When an optically active form of a compound of the invention is required, it may be obtained by carrying out one of the procedures described herein using an optically active starting material (prepared, for example, by asymmetric induction of a suitable reaction step), or by resolution of a mixture of the stereoisomers of the compound or intermediates using a standard procedure (such as chromatographic separation, recrystallization or enzymatic resolution).

Similarly, when a pure geometric isomer of a compound of the invention is required, it may be obtained by carrying out one of the above procedures using a pure geometric isomer as a starting material, or by resolution of a mixture of the geometric isomers of the compound or intermediates using a standard procedure such as chromatographic separation.

g. Examples

Example 1 and Example 2

***N*-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclopentanecarboxamide (Example 1) and *N*-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclopentanecarboxamide (Example 2)**

1-Hydroxybenzotriazole (33 mg, 0.24 mmol) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide (43 μL, 0.24 mmol) were added to a solution of 1-phenylcyclopentanecarboxylic acid (46 mg, 0.24 mmol) in dichloromethane (2 mL). The reaction was stirred at room temperature for 10 minutes, then (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine (52 mg, 0.24 mmol) was added and the reaction stirred at room temperature overnight. The reaction was quenched with water, and extracted with dichloromethane, then purified by silica gel chromatography using 1-10% methanol (2 *N* ammonia)/chloroform as eluent to give the title compounds.

Example 1: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.52 – 7.28 (m, 9H), 7.25 (d, J = 7.7, 1H), 4.43 – 4.34 (m, 1H), 3.56 (d, J = 12.9, 1H), 3.17 (d, J = 12.9, 1H), 2.83 – 2.67 (m, 2H), 2.59 – 2.50 (m, 1H), 2.50 – 2.44 (m, 1H), 2.35 – 2.29 (m, 2H), 2.04 – 1.87 (m, 4H), 1.84 – 1.54 (m, 6H), 1.43 – 1.26 (m, 1H), 1.04 – 0.94 (m, 1H); MS (ESI+) *m/z* 389 $(M+H)^+$.

Example 2: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.52 – 7.47 (m, 2H), 7.41 (d, J = 7.4, 2H), 7.38 – 7.29 (m, 4H), 7.25 (q, J = 7.3, 2H), 4.36 (m, 1H), 3.57 (d, J = 13.2, 1H), 3.40 (d, J = 13.2, 1H), 2.78 (m, 3H), 2.33 (m, 3H), 2.27 (d, J = 8.7, 1H), 2.21 – 2.13 (m, 1H), 1.99 (dt, J = 5.8, 11.7, 3H), 1.87 – 1.75 (m, 2H), 1.71 – 1.60 (m, 3H), 1.44 (ddd, J = 7.7, 12.1, 14.5, 1H), 1.31 (m, 1H); MS (ESI+) *m/z* 389 $(M+H)^+$.

Example 3 and Example 4

***N*-[(3a*R**,4*R**,6a*S**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclohexyl-2-phenylacetamide (Example 3) and *N*-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclohexyl-2-phenylacetamide (Example 4)**

The title compounds were prepared by substituting 2-cyclohexyl-2-phenylacetic acid for 1-phenylcyclopentanecarboxylic acid in the procedure that describes the preparation of Examples 1 and 2.

Example 3: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.10 (s, 1H), 7.67 (d, J = 7.2, 1H), 7.44 (dd, J = 5.7, 12.3, 3H), 7.40 – 7.35 (m, 3H), 7.33 (t, J = 7.4, 1H), 7.27 (dd, J = 7.6, 16.2, 1H), 4.43 – 4.37 (m, 0.5H), 4.36 – 4.29 (m, 0.5H), 3.56 (d, J = 12.6, 0.5H), 3.42 (t, J = 11.7, 1H), 3.26 (dd, J = 6.6, 11.7, 1H), 3.14 (d, J = 10.5, 0.5H), 2.80 (d, J = 8.3, 1H), 2.63 (d, J = 6.9, 0.5H), 2.24 – 2.13 (m, 1.5H), 2.02 (d, J = 12.5, 0.5H), 1.91 (d, J = 7.0, 1H), 1.74 – 1.59 (m, 2.5H), 1.58 – 1.34 (m, 4H), 1.33 – 1.19 (m, 1.5H), 1.18 – 0.99 (m, 3H), 0.87 (d, J = 14.3, 0.5H), 0.81 – 0.68 (m, 1H); MS (ESI+) *m/z* 417 $(M+H)^+$.

Example 4: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.65 – 8.56 (m, 1H), 7.66 (dd, J = 3.1, 7.3, 2H), 7.43 (d, J = 7.4, 1H), 7.39 – 7.30 (m, 5H), 7.27 (dd, J = 5.0, 7.6, 2H), 4.35 (s, 1H), 3.59 (d, J = 13.1, 0.5H), 3.52 (d, J = 13.2, 0.5H), 3.44 (d, J = 13.1, 0.5H), 3.33 (dd, J = 8.2, 11.7, 1.5H), 2.89 (dd, J = 3.1, 9.1, 0.5H), 2.63 – 2.54 (m, 1H), 2.53 – 2.45 (m, 1H), 2.36 (m, 2H), 2.28 (t, J = 8.0, 1H), 2.22 (t, J = 7.0, 2H), 2.16 (dd, J = 6.0, 12.2, 1H), 1.92 (dd, J = 6.1, 12.2, 0.5H), 1.84 (dd, J = 7.5, 12.6, 0.5H), 1.71 (dd, J = 6.2, 12.8, 2H), 1.44 (dd, J = 20.6, 55.0, 4H), 1.29 (m, 1.5H), 1.18 (m, 1H), 1.06 (m, 2H), 0.70 (m, 1H); MS (ESI+) *m/z* 389 $(M+H)^+$.

Example 5 and Example 6

***N*-[(3a*R**,4*R**,6a*S**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide (Example 5) and *N*-[(3a*R**,4*S**,6a*S**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide (Example 6)**

The title compounds were prepared by substituting 3-methyl-2-phenylbutanoic acid for 1-phenylcyclopentanecarboxylic acid in the procedure that describes the preparation of Examples 1 and 2.

Example 5: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.13 – 8.03 (m, 1H), 7.65 (d, J = 7.2, 1H), 7.55 (d, J = 7.3, 1H), 7.44 (d, J = 4.3, 2H), 7.41 (d, J = 7.0, 1H), 7.36 (t, J = 6.9, 3H), 7.28 (ddd, J = 7.3, 14.7, 17.5, 2H), 4.40 (dd, J = 6.7, 13.3, 0.5H), 4.35 – 4.27 (m, 0.5H), 3.55 (d, J = 12.7, 0.5H), 3.40 (dd, J = 4.5, 12.8, 1H), 3.26 (d, J = 12.9, 0.5H), 3.16 (d, J = 10.5, 0.5H), 3.05 (d, J = 10.5, 0.5H), 2.78 (dd, J = 8.1, 15.8, 1H), 2.69 – 2.54 (m, 1.5H), 2.43 – 2.26 (m, 3H), 2.23 – 2.13 (m, 1H), 1.94 – 1.82 (m, 1H), 1.73 – 1.57 (m, 1.5H), 1.50 (dt, J = 7.1, 15.0, 0.5H), 1.38 (td, J = 6.4, 12.2, 0.5H), 1.27 (m, 0.5H), 1.19 (d, J = 6.4, 1.5H), 1.11 (dd, J = 5.7, 12.0, 0.5H), 1.03 (d, J = 6.5, 1.5H), 0.73 (dd, J = 6.7, 10.7, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Example 6: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.56 (d, J = 12.9, 1H), 7.67 – 7.61 (m, 2H), 7.43 (d, J = 7.1, 1H), 7.39 – 7.31 (m, 5H), 7.29 – 7.24 (m, 2H), 4.40 – 4.28 (m, 1H), 3.60 (d, J = 13.1, 0.5H), 3.52 (d, J = 13.1, 0.5H), 3.44 (d, J = 13.2, 0.5H), 3.33 (d, J = 13.2, 0.5H), 3.22 (d, J = 10.4, 1H), 2.89 (dd, J = 3.0, 9.1, 0.5H), 2.64 (m, 1H), 2.55 (m 1H), 2.51 – 2.44 (m, 1H), 2.36 (s, 1H), 2.28 (t, J = 8.3, 1H), 2.24 – 2.10 (m, 2H), 1.95 – 1.87 (m, 0.5H), 1.81 (d, J = 8.1, 0.5H), 1.77 – 1.62 (m, 1H), 1.36 (m, 1.5H), 1.20 (dt, J = 5.3, 10.6, 3H), 0.70 (dd, J = 1.6, 6.7, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Example 7 and Example 8

***N*-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclopentyl-2-phenylacetamide (Example 7) and *N*-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclopentyl-2-phenylacetamide (Example 8)**

The title compounds were prepared by substituting 2-cyclopentyl-2-phenylacetic acid for 1-phenylcyclopentanecarboxylic acid in the procedure that describes the preparation of Examples 1 and 2.

Example 7: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.06 (dd, J = 6.8, 23.5, 1H), 7.67 (d, J = 7.2, 1H), 7.46 – 7.39 (m, 3H), 7.40 – 7.29 (m, 4H), 7.29 – 7.22 (m, 1H), 4.45 – 4.37 (m, 0.5H), 4.35 – 4.27 (m, 0.5H), 3.54 (d, J = 12.7, 0.5H), 3.42 (dd, J = 4.0, 12.8, 1H), 3.34 – 3.19 (m, 1.5H), 2.97 – 2.77 (m, 2.5H), 2.63 (d, J = 7.2, 0.5H), 2.46– 2.27 (m, 3H), 2.26 – 2.05 (m, 1.5H), 2.03 – 1.84 (m, 1.5H), 1.71 (dt, J = 7.0, 14.1, 0.5H), 1.65 – 1.36 (m, 8H), 1.33 – 1.22 (m, 0.5H), 1.20 – 0.98 (m, 2H); MS (ESI+) *m/z* 403 $(M+H)^+$.

Example 8: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.60 – 8.49 (m, 1H), 7.67 (dd, J = 2.3, 7.6, 2H), 7.44 (d, J = 7.2, 1H), 7.36 (dt, J = 5.0, 7.6, 5H), 7.26 (t, J = 6.9, 2H), 4.36 (m, 1H), 3.61 (d, J = 13.1, 0.5H), 3.52 (d, J = 13.1, 0.5H), 3.45 (d, J = 13.2, 0.5H), 3.36 (dd, J = 12.0, 16.0, 1.5H), 2.95 – 2.83 (m, 1.5H), 2.63 – 2.55 (m, 1H), 2.53 – 2.46 (m, 1H), 2.38 (s, 1H), 2.29 (dd, J = 7.0, 12.8, 1.5H), 2.22 (dd, J = 6.1, 12.3, 1H), 2.18– 2.504 (m, 1.5H), 1.94 (dd, J = 6.1, 12.2, 0.5H), 1.84 (dd, J = 7.5, 12.7, 0.5H), 1.79 – 1.66 (m, 1H), 1.65 – 1.24 (m, 8.5H), 1.09 – 0.92 (m, 1H); MS (ESI+) *m/z* 403 $(M+H)^+$.

Example 9 and Example 10

***N*-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclohexanecarboxamide (Example 9) and *N*-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclohexanecarboxamide (Example 10)**

The title compounds were prepared by substituting 1-phenylcyclohexanecarboxylic acid for 1-phenylcyclopentanecarboxylic acid in the procedure that describes the preparation of Examples 1 and 2.

Example 9: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.57 – 7.54 (m, 2H), 7.45 (t, J = 7.3, 2H), 7.37 (dd, J = 7.6, 15.3, 5H), 7.29 (d, J = 6.9, 1H), 7.25 (t, J = 7.3, 1H), 4.41 (m, 1H), 3.59 (d, J = 12.9, 1H), 3.18 (d, J = 12.9, 1H), 2.52 (dd, J = 8.9, 17.6, 4H), 2.34 (dd, J = 8.5, 15.2, 2H), 2.01 – 1.92 (m, 2H), 1.91 – 1.80 (m, 2H), 1.79 – 1.68 (m, 3H), 1.61 (d, J = 25.2, 4H), 1.43 – 1.33 (m, 1H), 1.27 (d, J = 8.7, 1H), 1.04 – 0.93 (m, 1H); MS (ESI+) *m/z* 403 $(M+H)^+$.

Example 10: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.60 (s, 1H), 7.42 (d, J = 7.2, 2H), 7.36 (t, J = 6.7, 4H), 7.27 (d, J = 7.5, 2H), 4.42 (m, 1H), 3.58 (d, J = 13.2, 1H), 3.40 (d, J = 13.1, 1H), 2.81 (d, J = 8.1, 1H), 2.68 (m, 2H), 1.41 – 2.24 (m, 4H), 2.18 (m, 1H), 2.00 (m, 1H), 1.80 (m, 4H), 1.73 – 1.54 (m, 4H), 1.52 – 1.39 (m, 1H), 1.36 – 1.18 (m, 2H); MS (ESI+) *m/z* 403 $(M+H)^+$.

Example 11

N-[(3aS*,4S*,6aR*)-2-benzyloctahydrocyclopenta[c]pyrrol-4-yl]-2,2-dicyclohexylacetamide

(3aS*,6aR*)-2-Benzyloctahydrocyclopenta[c]pyrrol-4-amine (500 mg, 2.311 mmol), 2,2-dicyclohexylacetic acid (570 mg, 2.54 mmol), and 1-hydroxybenzotriazole (389 mg, 2.54 mmol) were combined in dichloromethane (20 mL). The reaction was stirred at room temperature for 10 minutes, then *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide (0.449 mL, 2.54 mmol) was added dropwise. The reaction was stirred at room temperature for 20 hours, and then the reaction was quenched with 10 mL of water. The reaction was extracted with 2×20 mL of dichloromethane, the solvent was removed in vacuo, and the crude material was chromatographed over a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-40) eluting with 30-50% ethyl acetate/hexanes to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.60 (d, J = 5.1, 1H), 7.45 – 7.38 (m, 4H), 7.35 (m, 1H), 4.49 – 4.41 (m, 1H), 3.57 (d, J = 12.6, 1H), 3.37 (d, J = 12.5, 1H), 2.76 (d, J = 9.6, 1H), 2.69 (dd, J = 7.9, 15.7, 1H), 2.50 (d, J = 9.1, 1H), 2.48 – 2.41 (m, 1H), 2.28 (t, J = 8.2, 1H), 2.15 – 2.08 (m, 1H), 1.99 – 1.06 (m, 26H), 1.04 – 0.92 (m, 1H); MS (ESI+) *m/z* 423 $(M+H)^+$.

Example 12 and Example 13

(2S)-2-(3-benzoylphenyl)-N-[(3aS*,4S*,6aR*)-2-benzyloctahydrocyclopenta[c]pyrrol-4-yl]propanamide (Example 12) and

(2S)-2-(3-benzoylphenyl)-N-[(3aS*,4R*,6aR*)-2-benzyloctahydrocyclopenta[c]pyrrol-4-yl]propanamide (Example 13)

The title compounds were prepared by substituting (*S*)-2-(3-benzoylphenyl)propanoic acid for 1-phenylcyclopentanecarboxylic acid in the procedure that describes the preparation of Examples 1 and 2.

Example 12: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.28 (d, J = 6.9, 0.5H), 8.21 (d, J = 7.1, 0.5H), 8.13 (d, J = 15.9, 1H), 7.92 – 7.82 (m, 2H), 7.75 (t, J = 9.1, 2H), 7.56 – 7.52 (m, 1H), 7.50 – 7.25 (m, 8H), 4.49 – 4.32 (m, 1H), 3.90 (q, J = 7.1, 0.5H), 3.81 (t, J = 7.0, 0.5H), 3.45 (q, J = 12.8, 1.5H), 3.25 (d, J = 13.0, 0.5H), 2.75 (d, J = 9.2, 1.5H), 2.49 (dd, J = 2.9, 9.5, 0.5H), 2.44 – 2.31 (m, 1.5H), 2.24 (dt, J = 7.7, 16.5, 1.5H), 2.14 (d, J = 9.6, 0.5H), 2.09 – 2.01 (m, 0.5H), 1.90 – 1.71 (m, 1H), 1.66 – 1.44 (m, 5H), 1.20 (dd, J = 5.4, 28.1, 1H); MS (ESI+) *m/z* 453 $(M+H)^+$.

Example 13: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.67 (d, J = 7.1, 1H), 8.10 (s, 1H), 7.91 – 7.86 (m, 2H), 7.83 (d, J = 7.7, 1H), 7.74 (d, J = 7.6, 1H), 7.56 – 7.51 (m, 1H), 7.47 –

7.32 (m, 7H), 7.30 – 7.24 (m, 1H), 4.47 – 4.29 (m, 1H), 3.93 (q, *J* = 6.9, 1H), 3.56 (t, *J* = 12.3, 1H), 3.44 (d, *J* = 13.1, 0.5H), 3.37 (d, *J* = 13.1, 0.5H), 2.81 (dd, *J* = 3.0, 9.1, 0.5H), 2.72 (d, *J* = 7.0, 0.5H), 2.53 (m, 0.5H), 2.49 – 2.39 (m, 2H), 2.37 – 2.32 (m, 0.5H), 2.31 – 2.18 (m, 2H), 2.12 (dd, *J* = 6.0, 12.1, 0.5H), 2.03 (dd, *J* = 6.0, 12.2, 0.5H), 1.86 – 1.71 (m, 1H), 1.63 (t, *J* = 9.9, 3H), 1.57 – 1.47 (m, 1H), 1.40 – 1.27 (m, 1H); MS (ESI+) *m/z* 453 $(M+H)^+$.

Example 14

***N*-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide**

Step A: 2-Benzylhexahydrocyclopenta[*c*]pyrrol-4(5*H*)-one (16.28 g, 76 mmol), titanium tetraethoxide (28.5 mL, 137 mmol), and (*S*)-2-methylpropane-2-sulfinamide (10.452 g, 86 mmol) were combined in tetrahydrofuran (200 mL). The reaction was heated at 60 °C overnight. The reaction was then reduced in volume to about half and poured into 150 mL of saturated aqueous ammonium chloride. The precipitate was collected by filtration and washed with ethyl acetate. The filtrate was poured into a separatory funnel and the organic layer was removed. The aqueous layer was extracted with ethyl acetate (3×100 mL). The organic washes were combined and washed with brine, dried (Na_2SO_4) and concentrated. The crude material was chromatographed using silica gel cartridge (Analogix®, Burlington, Wisconsin, RS65-400) eluting with 5-100% ethyl acetate/hexanes to give (*S*,*E*)-*N*-((3a*R*,6a*S*)-2-benzylhexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)-2-methylpropane-2-sulfinamide and (*S*,*E*)-*N*-((3a*S*,6a*R*)-2-benzylhexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)-2-methylpropane-2-sulfinamide.

Step B: A mixture of (*S*,*E*)-*N*-((3a*S*,6a*R*)-2-benzylhexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)-2-methylpropane-2-sulfinamide (0.940 g, 2.95 mmol) from Step A in methanol (20 mL) was cooled to -78 °C in a dry ice/acetone bath. Sodium borohydride (0.335 g, 8.85 mmol) was added, and the reaction was allowed to warm to room temperature overnight. The reaction was quenched with saturated aqueous ammonium chloride, diluted with water, and extracted with 3×100 mL of ethyl acetate. The extracts were dried (Na_2SO_4) and filtered. The solvent was removed in vacuo, and the crude material was chromatographed using a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-40) with 5-50% acetone/hexanes to give (*S*)-*N*-((3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-2-methylpropane-2-sulfinamide: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.37 – 7.11 (m, 5H), 4.85 (d, *J* = 7.0, 1H), 3.90 – 3.71 (m, 2H), 3.28 (d, *J* = 13.0, 1H), 3.09 (d, *J* = 9.8, 1H), 2.72 – 2.50 (m, 2H), 2.46 (d, *J* = 9.6, 1H), 2.32 – 2.12

(m, 2H), 1.82 (td, J = 5.5, 12.7, 1H), 1.68 – 1.60 (m, J = 10.6, 2H), 1.35 – 1.24 (m, 1H), 1.20 (s, J = 5.5, 9H).

Step C: (*S*)-*N*-((3a*S*,4*S*,6a*R*)-2-Benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-2-methylpropane-2-sulfinamide (855 mg, 2.67 mmol) from Step B and 2 *N* HCl (10 mL, 40.0 mmol) were combined in methanol (10 mL). After 30 minutes, the solvent was removed and the crude material was purified on a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-25) loading with 10% methanol(2 *N* ammonia)/dichloromethane solution and eluting with 2-10% methanol (2 *N* ammonia)/dichloromethane to give (3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.44 (d, J = 7.4, 2H), 7.36 (t, J = 7.5, 2H), 7.28 (t, J = 7.3, 1H), 3.52 (q, J = 13.0, 2H), 3.29 (q, J = 7.3, 1H), 2.84 (dd, J = 3.7, 9.3, 1H), 2.55 – 2.43 (m, 3H), 2.37 – 2.30 (m, 1H), 2.24 (d, J = 5.3, 1H), 1.74 – 1.64 (m, 2H), 1.62 – 1.53 (m, 1H), 1.34 (dd, J = 5.0, 10.1, 1H).

Step D: 3-Methyl-2-phenylbutanoic acid (1.049 mmol), 1-hydroxybenzotriazole hydrate (1.049 mmol), and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide (185 µL, 1.049 mmol) were combined in dichloromethane (4 mL). The mixture was stirred at room temperature for 10 minutes, then (3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine (1.049 mmol) from Step C was added in 2 mL of dichloromethane. The reaction was stirred at room temperature for 3.5 hours, and then quenched with 0.5 mL of water. The organic layer was separated and chromatographed using a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-12) eluting with 1-10% methanol(ammonia)/dichloromethane to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.08 (dd, J = 7.2, 14.4, 1H), 7.64 (dd, J = 7.5, 14.5, 1H), 7.56 – 7.52 (m, 1H), 7.43 (d, J = 4.4, 2H), 7.42 – 7.40 (m, 1H), 7.38 – 7.22 (m, 5H), 4.40 (dt, J = 7.2, 14.3, 0.5H), 4.35 – 4.28 (m, 0.5H), 3.55 (d, J = 12.7, 0.5H), 3.40 (dd, J = 4.5, 12.8, 1H), 3.26 (d, J = 12.9, 0.5H), 3.15 (d, J = 10.5, 0.5H), 3.05 (d, J = 10.5, 0.5H), 2.83 – 2.74 (m, 1H), 2.70 – 2.55 (m, 1.5H), 2.43 – 2.26 (m, 3H), 2.23 – 2.13 (m, 1H), 1.94 – 1.83 (m, 1H), 1.74 – 1.57 (m, 1.5H), 1.50 (dt, J = 7.1, 15.3, 0.5H), 1.37 (td, J = 6.5, 12.1, 0.5H), 1.31 – 1.23 (m, 0.5H), 1.18 (d, J = 6.5, 1.5H), 1.10 (dt, J = 6.5, 11.5, 0.5H), 1.03 (d, J = 6.5, 1.5H), 0.73 (dd, J = 6.7, 10.7, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Example 15

***N*-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide**

The title compound was prepared by substituting 2,2-dicyclohexylacetic acid for 3-methyl-2-phenylbutanoic acid in the procedure used to prepare Example 14: ^{1}H NMR (500

MHz, pyridine-d_5) δ ppm 7.44 – 7.38 (m, 4H), 7.37 – 7.32 (m, 1H), 4.49 – 4.38 (m, 1H), 3.57 (d, J = 12.6, 1H), 3.37 (d, J = 12.5, 1H), 2.77 (dd, J = 1.7, 9.6, 1H), 2.68 (td, J = 2.0, 9.3, 1H), 2.51 (dd, J = 1.9, 9.0, 1H), 2.45 (dd, J = 7.1, 15.9, 1H), 2.30 – 2.25 (m, 1H), 2.11 (dd, J = 7.1, 9.6, 1H), 1.98 – 1.83 (m, 3H), 1.83 – 1.58 (m, 12H), 1.57 – 1.51 (m, 1H), 1.48 (d, J = 13.0, 1H), 1.44 – 1.37 (m, 1H), 1.36 – 1.09 (m, 9H), 1.04 – 0.94 (m, 1H); MS (ESI+) *m/z* 423 $(M+H)^+$.

Example 16

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide

Step A: (*S,E*)-*N*-((3a*S*,6a*R*)-2-Benzylhexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)-2-methylpropane-2-sulfinamide (2.67 g, 8.38 mmol) from Example 14 Step A and 2.0 *N* aqueous HCl (18.86 mL, 37.7 mmol) were combined in tetrahydrofuran (25 mL). The reaction was stirred at room temperature for 2 hours and the tetrahydrofuran was removed in vacuo and the remaining aqueous portion was made slightly basic with aqueous sodium bicarbonate solution. The aqueous layer was extracted with 3×200 mL of dichloromethane. The combined organic layers were separated, and the solvent was removed in vacuo. The crude material was purified on a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS25-25) eluting with ethyl acetate/hexanes to give (3a*S*,6a*R*)-2-benzylhexahydrocyclopenta[*c*]pyrrol-4(5*H*)-one: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.35 – 7.16 (m, 5H), 3.61 (d, J = 13.1, 1H), 3.48 (d, J = 13.1, 1H), 3.02 (dd, J = 1.8, 9.1, 1H), 2.96 – 2.82 (m, 1H), 2.71 – 2.56 (m, 2H), 2.43 (dt, J = 8.2, 17.4, 3H), 2.34 – 2.21 (m, 1H), 2.12 (ddd, J = 8.3, 13.0, 16.9, 1H), 1.79 (dddd, J = 4.2, 6.4, 9.2, 13.2, 1H).

Step B: A mixture of (3a*S*,6a*R*)-2-benzylhexahydrocyclopenta[*c*]pyrrol-4(5*H*)-one (1.462 g, 6.79 mmol) from Step A in methanol (20mL) was cooled in an dry ice/acetone bath to -40 °C. Sodium borohydride (0.514 g, 13.58 mmol) was added in portions over 5 minutes. The reaction allowed to warm to room temperature overnight, then it was quenched with saturated aqueous ammonium chloride, diluted with water, and extracted with 3×150 mL of ethyl acetate. The combined extracts were dried (Na_2SO_4) and the solvent was removed in vacuo to give (3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ol: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.38 – 7.16 (m, 5H), 4.21 – 4.04 (m, 1H), 3.66 (d, J = 12.8, 1H), 3.51 (d, J = 12.8, 1H), 3.07 (d, J = 9.3, 1H), 2.65 – 2.53 (m, J = 11.8, 2H), 2.52 – 2.43 (m, 1H), 2.18 – 2.07 (m, J = 7.5, 16.3, 2H), 2.05 – 1.94 (m, J = 8.7, 12.6, 1H), 1.84 – 1.74 (m, J = 6.2, 1H), 1.49 – 1.34 (m, 3H).

Step C: (3a*S*,4*S*,6a*R*)-2-Benzyloctahydrocyclopenta[*c*]pyrrol-4-ol (1.476 g, 6.79 mmol) from Step B and triethylamine (1.420 mL, 10.19 mmol) were combined in dichloromethane (30 mL). Methanesulfonyl chloride (0.635 mL, 8.15 mmol) was added as a solution in 20mL of dichloromethane dropwise via addition funnel. The reaction was stirred at room temperature for 30 minutes and concentrated. The crude material was absorbed onto silica gel and chromatographed on a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS25-25) eluting with 20-100% ethyl acetate/hexanes to give (3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl methanesulfonate: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.35 – 7.27 (m, 4H), 7.27 – 7.20 (m, 1H), 4.96 (ddd, *J* = 6.1, 7.6, 9.1, 1H), 3.71 – 3.44 (m, 1H), 2.94 (s, *J* = 13.5, 3H), 2.85 (ddd, *J* = 4.9, 8.1, 16.0, 1H), 2.75 – 2.68 (m, 2H), 2.67 – 2.55 (m, 1H), 2.54 – 2.44 (m, 1H), 2.31 (dd, *J* = 4.1, 8.7, 1H), 2.20 – 2.04 (m, 1H), 1.97 (dtd, *J* = 3.4, 6.2, 9.6, 1H), 1.79 – 1.63 (m, 1H), 1.61 – 1.49 (m, 2H).

Step D: (3a*S*,4*S*,6a*R*)-2-Benzyloctahydrocyclopenta[*c*]pyrrol-4-yl methanesulfonate (1.686 g, 5.71 mmol) from Step C and sodium azide (0.557 g, 8.56 mmol) were combined in *N*,*N*-dimethylacetamide (10 mL). The reaction was heated at 90 °C for 15 hours. The reaction was cooled and diluted with 200 mL of ethyl acetate and then quenched with 30mL water. The organic layer was removed and washed with 2×20 mL of water, then 20 mL of brine. The solvent was removed in vacuo to give (3a*S*,4*R*,6a*R*)-4-azido-2-benzyloctahydrocyclopenta[*c*]pyrrole: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.36 – 7.27 (m, 4H), 7.22 (dd, *J* = 2.9, 5.8, 1H), 3.72 – 3.61 (m, 1H), 3.54 (s, 2H), 2.76 – 2.60 (m, 1H), 2.55 – 2.40 (m, 4H), 2.35 (dd, *J* = 3.5, 9.1, 1H), 2.07 – 1.86 (m, 2H), 1.72 – 1.60 (m, 1H), 1.49 – 1.38 (m, 1H).

Step E: Triphenylphosphine (4.49 g, 17.13 mmol) and water (1.234 mL, 68.5 mmol) were added successively to a mixture of (3a*S*,4*R*,6a*R*)-4-azido-2-benzyloctahydrocyclopenta[*c*]pyrrole (1.384 g, 5.71 mmol) in tetrahydrofuran (30 mL). The reaction was refluxed at 80 °C for 2 hours. The crude material was adsorbed onto silica gel and applied to a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-40) and eluted with 1-10% methanol (2 *N* ammonia)/chloroform to give (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.45 (d, *J* = 7.4, 2H), 7.38 (t, *J* = 7.5, 2H), 7.29 (t, *J* = 7.3, 1H), 3.52 (s, 2H), 3.14 (dd, *J* = 5.7, 10.7, 1H), 2.62 – 2.55 (m, 1H), 2.52 (dd, *J* = 3.2, 9.0, 1H), 2.38 – 2.29 (m, 3H), 2.20 – 2.13 (m, 1H), 2.01 – 1.84 (m, 2H), 1.40 – 1.29 (m, 2H).

Step F: (*S*)-2-Phenylbutanoic acid (41.7 mg, 0.254 mmol), 1-hydroxybenzotriazole (38.9 mg, 0.254 mmol), and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide (0.045 mL,

0.254 mmol) were combined in dichloromethane (1 mL). The reaction was stirred at room temperature for 10 minutes, and then (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine (50 mg, 0.231 mmol) from Step E was added in 0.5 mL of dichloromethane. The reaction was stirred at room temperature for 20 hours, and then quenched with 0.5 mL of water. The organic layer was separated. The crude material was chromatographed using a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-4) eluting with 1-10% methanol(ammonia)/dichloromethane to give the title compound: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.47 (d, J = 7.0, 1H), 7.59 (m, 2H), 7.42 (d, J = 7.1, 2H), 7.34 (dd, J = 7.6, 16.5, 4H), 7.25 (dt, J = 5.0, 10.1, 2H), 4.45 – 4.29 (m, 1H), 3.62 – 3.51 (m, 2H), 3.44 (d, J = 13.2, 1H), 2.85 (dd, J = 2.7, 9.0, 1H), 2.58 – 2.50 (m, 1H), 2.50 – 2.42 (m, 2H), 2.40 – 2.31 (m, 1H), 2.31 – 2.22 (m, 2H), 1.97 (dq, J = 6.1, 12.1, 1H), 1.85 (td, J = 6.9, 13.6, 1H), 1.74 (dt, J = 6.4, 14.3, 1H), 1.46 (dt, J = 7.1, 19.2, 1H), 1.31 (dt, J = 6.2, 20.5, 1H), 0.96 (dd, J = 5.5, 9.1, 3H); MS (ESI+) *m/z* 363 $(M+H)^+$.

Example 17

***N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclopentyl-2-phenylacetamide**

The title compound was prepared by substituting 2-cyclopentyl-2-phenylacetic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.61 (dd, J = 7.4, 10.6, 1H), 7.69 (dd, J = 1.5, 8.1, 2H), 7.44 (d, J = 7.3, 1H), 7.36 (dt, J = 7.2, 15.3, 5H), 7.30 – 7.25 (m, 2H), 4.42 – 4.29 (m, 1H), 3.61 (d, J = 13.1, 0.5H), 3.52 (d, J = 13.2, 0.5H), 3.43 (dd, J = 12.0, 18.8, 1.5H), 3.34 (d, J = 13.2, 0.5H), 2.96 – 2.83 (m, 1.5H), 2.55 (dt, J = 15.9, 16.3, 2H), 2.41 (t, J = 18.3, 1H), 2.31 (d, J = 9.0, 0.5H), 2.28 (d, J = 6.3, 1H), 2.23 (d, J = 5.0, 1H), 2.20 – 2.04 (m, 1.5H), 1.94 (dt, J = 7.1, 12.1, 0.5H), 1.89 – 1.81 (m, 0.5H), 1.80 – 1.67 (m, 1H), 1.65 – 1.26 (m, 7H), 1.05 – 0.94 (m, 1H); MS (ESI+) *m/z* 403 $(M+H)^+$.

Example 18

***N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 3-methyl-2-phenylbutanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.64 (dd, J = 7.3, 11.3, 1H), 7.66 (dd, J = 2.4, 7.5, 2H), 7.43 (d, J = 7.5, 1H), 7.40 – 7.30 (m, 5H), 7.29 – 7.23 (m, 2H), 4.40 – 4.28 (m, 1H), 3.60 (d, J =

13.2, 0.5H), 3.52 (d, J = 13.1, 0.5H), 3.44 (d, J = 13.1, 0.5H), 3.33 (d, J = 13.1, 0.5H), 3.25 (d, J = 10.5, 1H), 2.88 (dd, J = 3.1, 9.1, 0.5H), 2.66 (s, 1H), 2.60 – 2.56 (m, 0.5H), 2.55 – 2.46 (m, 1.5H), 2.39 (t, J = 18.7, 1H), 2.28 (t, J = 8.0, 1.5H), 2.22 (d, J = 5.1, 1H), 2.18 – 2.09 (m, 0.5H), 1.91 (dd, J = 6.0, 12.0, 0.5H), 1.84 (dd, J = 7.1, 13.4, 0.5H), 1.72 (ddd, J = 6.5, 12.3, 25.1, 1H), 1.49 – 1.40 (m, 0.5H), 1.33 (ddd, J = 13.3, 19.9, 32.3, 1H), 1.20 (dd, J = 5.0, 6.4, 3H), 0.70 (dd, J = 1.7, 6.7, 3H); MS (ESI+) m/z 377 $(M+H)^+$.

Example 19

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylpropanamide

The title compound was prepared by substituting (*S*)-2-phenylpropanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.41 (d, J = 6.8, 1H), 7.54 (d, J = 7.0, 2H), 7.41 (t, J = 9.7, 2H), 7.38 – 7.30 (m, 4H), 7.26 (dd, J = 5.3, 16.7, 2H), 4.43 – 4.32 (m, 1H), 3.84 (q, J = 7.0, 1H), 3.56 (t, J = 12.3, 1H), 3.40 (dd, J = 13.1, 33.2, 1H), 2.81 (dd, J = 2.9, 9.0, 1H), 2.51 (m, 1H), 2.48 – 2.36 (m, 2H), 2.33 – 2.17 (m, 2H), 2.14 (s, 3H, OAc), 2.00 (dq, J = 6.1, 12.1, 1H), 1.73 (dt, J = 6.3, 14.2, 1H), 1.60 (d, J = 7.0, 3H), 1.47 (dt, J = 7.1, 14.8, 1H), 1.39 – 1.24 (m, 1H); MS (ESI+) m/z 349 $(M+H)^+$.

Example 20

***N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide**

The title compound was prepared by substituting 2,2-dicyclohexylacetic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.12 (d, J = 7.2, 1H), 7.45 (d, J = 7.4, 2H), 7.36 (t, J = 7.5, 2H), 7.27 (t, J = 7.3, 1H), 4.52 – 4.43 (m, 1H), 3.63 (d, J = 13.1, 1H), 3.48 (d, J = 13.1, 1H), 2.89 (dd, J = 2.7, 8.9, 1H), 2.65 – 2.50 (m, 3H), 2.35 (d, J = 4.5, 2H), 2.18 – 2.10 (m, 1H), 2.03 (t, J = 7.4, 1H), 1.96 (d, J = 13.0, 2H), 1.87 (dt, J = 7.4, 13.9, 3H), 1.80 (d, J = 12.6, 2H), 1.76 – 1.64 (m, 5H), 1.60 (d, J = 10.7, 2H), 1.51 – 1.38 (m, 3H), 1.30 – 1.05 (m, 8H); MS (ESI+) m/z 423 $(M+H)^+$.

Example 21

***N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-propylpentanamide**

The title compound was prepared by substituting 2-propylpentanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500

MHz, pyridine-d_5) δ ppm 8.36 (d, J = 7.2, 1H), 7.43 (d, J = 7.4, 2H), 7.36 (t, J = 7.5, 2H), 7.27 (t, J = 7.3, 1H), 4.56 – 4.38 (m, 1H), 3.60 (d, J = 11.8, 1H), 3.45 (d, J = 13.1, 1H), 2.85 (dd, J = 2.8, 9.0, 1H), 2.61 – 2.50 (m, 2H), 2.50 – 2.45 (m, 1H), 2.39 – 2.25 (m, 3H), 2.20 – 2.09 (m, 1H), 1.93 – 1.79 (m, 3H), 1.66 (dd, J = 7.7, 12.2, 1H), 1.53 – 1.29 (m, 7H), 0.87 (td, J = 3.1, 7.2, 6H); MS (ESI+) *m/z* 343 $(M+H)^+$.

Example 22

***N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]cycloheptanecarboxamide**

The title compound was prepared by substituting cycloheptanecarboxylic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.08 (d, J = 7.2, 1H), 7.44 (d, J = 7.4, 2H), 7.36 (t, J = 7.6, 2H), 7.27 (t, J = 7.3, 1H), 4.50 – 4.34 (m, 1H), 3.60 (d, J = 13.7, 1H), 3.44 (d, J = 13.1, 1H), 2.83 (d, J = 9.0, 1H), 2.54 (s, 2H), 2.49 – 2.41 (m, 2H), 2.33 (d, J = 6.8, 1H), 2.30 – 2.25 (m, 1H), 2.19 – 2.10 (m, 1H), 2.01 – 1.81 (m, 5H), 1.74 – 1.58 (m, 3H), 1.47 – 1.37 (m, 5H), 1.31 (s, 2H); MS (ESI+) *m/z* 341 $(M+H)^+$.

Example 23

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(4-isobutylphenyl)propanamide

The title compound was prepared by substituting (*S*)-2-(3-isobutylphenyl)propanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37 (d, J = 7.2, 1H), 7.49 (d, J = 8.0, 2H), 7.42 (d, J = 7.5, 2H), 7.36 (t, J = 7.5, 2H), 7.27 (t, J = 7.3, 1H), 7.14 (d, J = 8.0, 2H), 4.43 – 4.31 (m, 1H), 3.84 (q, J = 7.0, 1H), 3.58 (d, J = 13.1, 1H), 3.44 (d, J = 13.1, 1H), 2.82 (dd, J = 2.8, 9.1, 1H), 2.55 – 2.48 (m, 1H), 2.48 – 2.42 (m, 2H), 2.39 (d, J = 7.2, 2H), 2.31 – 2.21 (m, 2H), 2.00 (dt, J = 6.0, 12.1, 1H), 1.83 – 1.69 (m, 2H), 1.63 (d, J = 7.0, 3H), 1.48 (dt, J = 7.0, 19.1, 1H), 1.36 – 1.25 (m, 1H), 0.86 – 0.77 (m, 6H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Example 24

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclohexanecarboxamide

The title compound was prepared by substituting 1-phenylcyclohexanecarboxylic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.73 (d, J = 7.8, 1H), 7.63 – 7.59 (m, 1H), 7.41 (d, J =

7.3, 2H), 7.39 – 7.31 (m, 4H), 7.29 – 7.23 (m, 3H), 4.45 – 4.35 (m, 1H), 3.58 (d, J = 13.2, 1H), 3.40 (d, J = 13.2, 1H), 2.80 (d, J = 7.7, 1H), 2.69 – 2.59 (m, 2H), 2.41 – 2.31 (m, 3H), 2.28 (d, J = 8.6, 1H), 2.20 – 2.13 (m, 1H), 2.00 (td, J = 5.7, 11.7, 1H), 1.87 – 1.75 (m, 4H), 1.74 – 1.54 (m, J = 9.1, 18.8, 38.4, 4H), 1.46 (dt, J = 7.8, 14.8, 1H), 1.36 – 1.19 (m, 2H); MS (ESI+) *m/z* 403 $(M+H)^+$.

Example 25

***N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,3-diphenylpropanamide**

The title compound was prepared by substituting 2,3-diphenylpropanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.52 (dd, J = 7.3, 13.3, 1H), 7.65 (d, J = 7.4, 2H), 7.44 (d, J = 7.1, 1H), 7.41 – 7.29 (m, 8H), 7.26 (dt, J = 4.8, 10.9, 4H), 4.35 – 4.22 (m, 1H), 3.96 (dt, J = 5.0, 10.0, 1H), 3.77 (ddd, J = 3.7, 10.1, 13.5, 1H), 3.52 (dt, J = 13.2, 18.8, 1.5H), 3.33 (d, J = 13.1, 0.5H), 3.05 (dt, J = 4.7, 13.0, 1H), 2.77 (d, J = 8.9, 0.5H), 2.56 (d, J = 6.2, 0.5H), 2.38 – 2.23 (m, 3H), 2.23 – 2.17 (m, J = 8.7, 1H), 1.94 (ddd, J = 5.7, 11.8, 23.8, 1H), 1.72 – 1.57 (m, J = 6.0, 1H), 1.51 – 1.19 (m, 3H); MS (ESI+) *m/z* 425 $(M+H)^+$.

Example 26

***N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-methyl-3-phenylpropanamide**

The title compound was prepared by substituting 2-methyl-3-phenylpropanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.12 (dd, J = 7.0, 21.5, 1H), 7.47 – 7.22 (m, 10H), 4.43 – 4.29 (m, 1H), 3.58 (dd, J = 6.6, 13.2, 1H), 3.45 (dd, J = 13.2, 21.2, 1H), 3.20 (ddd, J = 4.6, 10.8, 15.0, 1H), 2.81 – 2.66 (m, 3H), 2.48 – 2.19 (m, 5H), 2.04 (ddt, J = 6.0, 12.1, 24.4, 1H), 1.82 – 1.63 (m, 1H), 1.47 (ddd, J = 7.1, 15.9, 18.8, 1H), 1.39 – 1.30 (m, 1H), 1.28 (d, J = 6.3, 3H); MS (ESI+) *m/z* 363 $(M+H)^+$.

Example 27

***N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-methyl-2-phenylpropanamide**

The title compound was prepared by substituting 2-methyl-2-phenylpropanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.44 (dd, J = 7.9, 16.1, 4H), 7.31 (ddd, J = 7.7, 14.5,

22.6, 6H), 7.12 – 7.03 (m, 1H), 4.46 – 4.36 (m, 1H), 3.58 (d, J = 13.2, 1H), 3.43 (d, J = 13.2, 1H), 2.84 (d, J = 6.5, 1H), 2.39 – 2.26 (m, J = 6.9, 20.1, 4H), 2.23 – 2.14 (m, J = 6.7, 1H), 2.04 (dd, J = 5.8, 11.8, 1H), 1.67 (s, 7H), 1.54 – 1.40 (m, 1H), 1.38 – 1.24 (m, 1H); MS (ESI+) m/z 363 $(M+H)^+$.

Example 28

***N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclopropanecarboxamide**

The title compound was prepared by substituting 1-phenylcyclopropanecarboxylic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.42 (dd, J = 7.2, 16.3, 4H), 7.33 (dt, J = 7.6, 17.1, 4H), 7.25 (dd, J = 5.8, 13.1, 2H), 6.27 (d, J = 7.5, 1H), 4.41 – 4.24 (m, J = 5.8, 1H), 3.56 (d, J = 13.2, 1H), 3.40 (d, J = 13.2, 1H), 2.87 – 2.74 (m, 1H), 2.37 – 2.19 (m, 4H), 2.12 (t, J = 8.0, 1H), 2.03 – 1.94 (m, 1H), 1.75 (dd, J = 3.5, 6.6, 2H), 1.68 – 1.58 (m, J = 8.7, 16.8, 1H), 1.37 – 1.23 (m, 2H), 1.01 (dd, J = 3.5, 6.6, 2H); MS (ESI+) m/z 361 $(M+H)^+$.

Example 29

2-benzyl-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethylbutanamide

The title compound was prepared by substituting 2-benzyl-3,3-dimethylbutanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.08 (dd, J = 7.4, 13.5, 1H), 7.46 (d, J = 7.3, 1H), 7.44 – 7.32 (m, 5H), 7.32 – 7.23 (m, 4H), 4.33 (s, 1H), 3.58 (dd, J = 13.2, 16.9, 1H), 3.50 (d, J = 13.1, 0.5H), 3.40 (d, J = 13.1, 0.5H), 3.25 (q, J = 11.9, 1H), 2.80 – 2.66 (m, 2H), 2.45 (d, J = 6.9, 1H), 2.41 – 2.23 (m, 3.5H), 2.20 (t, J = 8.3, 0.5H), 2.16 – 2.09 (m, 0.5H), 2.06 (dd, J = 5.8, 11.6, 0.5H), 1.89 (dd, J = 5.8, 11.8, 0.5H), 1.75 (s, 0.5H), 1.61 (s, 0.5H), 1.47 (s, 0.5H), 1.38 – 1.20 (m, 2H), 1.16 (s, 9H); MS (ESI+) m/z 405 $(M+H)^+$.

Example 30

***N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethyl-2-phenylbutanamide**

The title compound was prepared by substituting 3,3-dimethyl-2-phenylbutanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.57 – 8.49 (m, 1H), 7.73 (dd, J = 3.3, 5.3, 2H), 7.44 (d,

J = 7.1, 1H), 7.41 – 7.24 (m, 7H), 4.41 – 4.29 (m, J = 6.9, 13.0, 1H), 3.62 (d, J = 13.2, 0.5H), 3.53 (d, J = 13.1, 0.5H), 3.43 (s, 0.5H), 3.35 (d, J = 13.1, 0.5H), 2.90 (dd, J = 3.1, 8.9, 1H), 2.63 – 2.46 (m, 2H), 2.44 – 2.37 (m, 0.5H), 2.36 – 2.30 (m, J = 8.3, 1H), 2.28 (d, J = 5.3, 1H), 2.23 (d, J = 5.5, 1H), 2.15 (dt, J = 6.2, 12.5, 0.5H), 1.91 (dt, J = 6.1, 12.2, 0.5H), 1.88 – 1.79 (m, 0.5H), 1.77 – 1.66 (m, 1H), 1.46 – 1.35 (m, 1H), 1.34 – 1.23 (m, 1H), 1.15 (s, 4.5H), 1.14 (s, 4.5H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Example 31 and Example 32

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethyl-2-phenylbutanamide (Example 31) and

(2*R*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethyl-2-phenylbutanamide (Example 32)

The material from example 30 was subjected to separation by chiral supercritical fluid chromatography on a ChiralCel® OD-H column (21×250 mm, 5 μm, Chiral Technologies, Inc.), 5-50% methanol:CO_2 (100 bar), at 40 mL/minute over 10 minutes to give the title compounds.

Example 31: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.50 (d, J = 7.1, 1H), 7.74 – 7.70 (m, 1H), 7.44 (d, J = 7.2, 2H), 7.40 – 7.24 (m, J = 8.0, 15.4, 18.2, 7H), 4.43 – 4.31 (m, 1H), 3.63 (d, J = 13.1, 1H), 3.49 – 3.41 (m, J = 6.6, 2H), 2.91 (dd, J = 3.0, 8.9, 1H), 2.63 – 2.43 (m, 3H), 2.28 (d, J = 5.3, 2H), 1.92 (dq, J = 6.1, 12.1, 1H), 1.78 – 1.68 (m, 1H), 1.41 (dt, J = 7.0, 18.9, 1H), 1.30 (dt, J = 6.4, 14.5, 1H), 1.14 (s, 9H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Example 32: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.52 (d, J = 7.0, 1H), 7.72 (d, J = 7.0, 2H), 7.41 – 7.24 (m, J = 7.2, 21.5, 29.9, 8H), 4.41 – 4.25 (m, 1H), 3.53 (d, J = 13.1, 1H), 3.45 (s, 1H), 3.35 (d, J = 13.1, 1H), 2.57 (d, J = 5.7, 1H), 2.45 – 2.36 (m, 1H), 2.31 (dd, J = 5.1, 10.5, 2H), 2.25 – 2.20 (m, 2H), 2.15 (td, J = 6.4, 12.4, 1H), 1.83 (td, J = 6.8, 14.8, 1H), 1.69 (td, J = 6.7, 13.4, 1H), 1.38 (td, J = 6.7, 12.4, 1H), 1.14 (s, 9H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Example 33

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide

Step A: (3a*R*,4*S*,6a*S*)-2-Benzyloctahydrocyclopenta[*c*]pyrrol-4-amine was prepared according to the procedure described in Example 16 Steps A-E substituting (*S,E*)-*N*-((3a*R*,6a*S*)-2-benzylhexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)-2-methylpropane-2-sulfinamide from Step A in Example 14 for (*S,E*)-*N*-((3a*S*,6a*R*)-2-benzylhexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)-2-methylpropane-2-sulfinamide in Step

A of Example 16 to give (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.34 – 7.28 (m, 4H), 7.25 – 7.18 (m, 1H), 3.54 (s, 2H), 3.09 (dd, *J* = 4.8, 10.9, 1H), 2.75 – 2.58 (m, 1H), 2.48 (dd, *J* = 8.6, 16.5, 2H), 2.40 (dd, *J* = 3.9, 9.3, 1H), 2.30 (dd, *J* = 3.9, 9.0, 1H), 2.21 – 2.09 (m, 1H), 2.01 – 1.84 (m, *J* = 6.9, 12.0, 2H), 1.47 – 1.25 (m, 4H).

Step B: The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.55 (d, *J* = 4.5, 1H), 7.59 (s, *J* = 5.1, 1H), 7.39 (d, *J* = 7.2, 2H), 7.34 (dd, *J* = 7.7, 16.5, 4H), 7.25 (dd, *J* = 7.6, 16.2, 3H), 4.43 – 4.33 (m, 1H), 3.59 – 3.50 (m, 2H), 3.36 (d, *J* = 13.1, 1H), 2.69 – 2.61 (m, 1H), 2.43 – 2.28 (m, 4H), 2.28 – 2.23 (m, 1H), 2.22 – 2.18 (m, 1H), 2.13 (dq, *J* = 6.3, 12.3, 1H), 1.89 – 1.77 (m, 2H), 1.65 (td, *J* = 7.0, 14.2, 1H), 1.40 – 1.32 (m, 1H), 0.97 (t, *J* = 7.3, 3H); MS (ESI+) *m/z* 363 $(M+H)^+$.

Example 34

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclopentyl-2-phenylacetamide

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and substituting 2-cyclopentyl-2-phenylacetic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.54 (d, *J* = 14.7, 1H), 7.66 (dd, *J* = 2.5, 7.5, 2H), 7.43 (d, *J* = 7.4, 1H), 7.40 – 7.31 (m, 5H), 7.26 (t, *J* = 6.9, 2H), 4.41 – 4.30 (m, 1H), 3.61 (d, *J* = 13.1, 0.5H), 3.52 (d, *J* = 13.1, 0.5H), 3.45 (d, *J* = 13.2, 0.5H), 3.36 (app. t, *J* = 12.7, 1.5H), 2.89 (d, *J* = 9.0, 1H), 2.61 – 2.55 (m, 1H), 2.53 – 2.46 (m, 1H), 2.44 – 2.33 (m, 1H), 2.29 (dd, *J* = 7.3, 12.8, 1.5H), 2.22 (t, *J* = 4.9, 1H), 2.19 – 2.04 (m, 1.5H), 1.98 – 1.89 (m, 0.5H), 1.88 – 1.80 (m, 0.5H), 1.79 – 1.65 (m, 1H), 1.65 – 1.25 (m, 8H), 1.05 – 0.95 (m, 1H); MS (ESI+) *m/z* 403 $(M+H)^+$.

Example 35

***N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and substituting 3-methyl-2-phenylbutanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.64 – 8.49 (m, *J* = 20.1, 1H), 7.67 – 7.61 (m, 2H), 7.43 (d, *J* = 7.0, 1H), 7.39 – 7.30 (m, 5H), 7.29 – 7.24 (m, 2H), 4.41 – 4.27 (m, 1H), 3.60 (d, *J* = 13.1, 0.5H), 3.52 (d, *J* = 13.1, 0.5H), 3.44 (d, *J* = 13.2, 0.5H), 3.33 (d, *J* = 13.2, 0.5H), 3.23 (d, *J* = 10.5, 1H), 2.89 (dd, *J* = 3.0, 9.1, 0.5H), 2.69 – 2.60 (m, *J* = 10.0, 1H), 2.59 – 2.53 (m, *J* = 3.0, 9.0, 1H), 2.52 – 2.44 (m, 1H), 2.44 – 2.33 (m, 1H), 2.30 – 2.25 (m, *J* = 6.4, 10.0, 1.5H), 2.25 – 2.20 (m, 1H), 2.14 (dd, *J* = 5.9, 12.3, 0.5H), 1.91 (dd, *J* = 6.1, 12.1, 0.5H), 1.86 – 1.79 (m, *J* = 4.7, 0.5H), 1.78 – 1.64 (m, 1H), 1.47 – 1.24 (m, *J* = 30.2, 37.0, 1.5H), 1.20 (dd, *J* = 4.9, 6.4, 3H), 0.70 (dd, *J* = 1.6, 6.7, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Example 36

(2*R*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and substituting (*R*)-2-phenylbutanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.38 – 7.21 (m, 10H), 5.29 (d, *J* = 6.9, 1H), 4.04 – 3.90 (m, 1H), 3.65 (d, *J* = 12.9, 1H), 3.52 (d, *J* = 12.9, 1H), 3.15 (t, *J* = 7.6, 1H), 2.68 (t, *J* = 8.6, 1H), 2.64 – 2.48 (m, *J* = 8.5, 3H), 2.30 – 2.22 (m, *J* = 3.7, 8.3, 1.5H), 2.14 (ddd, *J* = 7.4, 13.9, 19.9, 1.5H), 1.93 (dt, *J* = 6.2, 12.5, 1H), 1.84 – 1.62 (m, *J* = 7.6, 14.5, 20.6, 2H), 1.45 – 1.27 (m, 2H), 0.95 – 0.80 (m, 4H); MS (ESI+) *m/z* 363 $(M+H)^+$.

Example 37

(2*R*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylpropanamide

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and substituting (*R*)-2-phenylpropanoic acid for

(*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.37 – 7.26 (m, *J* = 5.5, 7.5, 8H), 7.25 – 7.18 (m, 2H), 5.19 (d, *J* = 5.9, 1H), 4.06 – 3.89 (m, 1H), 3.59 (d, *J* = 13.0, 1H), 3.48 (ddd, *J* = 7.6, 13.7, 21.0, 2H), 2.60 – 2.46 (m, 3H), 2.43 – 2.33 (m, *J* = 7.0, 14.4, 1H), 2.26 (dd, *J* = 3.8, 9.0, 1H), 2.20 – 2.07 (m, *J* = 34.2, 1H), 2.03 – 1.93 (m, 1H), 1.49 (d, *J* = 7.2, 3H), 1.44 – 1.22 (m, 3H); MS (ESI+) *m/z* 349 $(M+H)^+$.

Example 38

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylpropanamide

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and substituting (*S*)-2-phenylpropanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.38 – 7.26 (m, 8H), 7.25 – 7.20 (m, 2H), 5.20 (d, *J* = 6.7, 1H), 4.03 – 3.91 (m, 1H), 3.60 (d, *J* = 13.0, 1H), 3.52 – 3.43 (m, 2H), 2.54 (dd, *J* = 5.7, 13.8, 2H), 2.43 (dd, *J* = 7.1, 16.0, 1H), 2.29 – 2.23 (m, 1H), 2.22 – 2.08 (m, 2H), 1.98 (ddd, *J* = 5.8, 11.9, 15.7, 1H), 1.74 – 1.60 (m, 1H), 1.50 (t, *J* = 6.4, 3H), 1.44 – 1.30 (m, 2H); MS (ESI+) *m/z* 349 $(M+H)^+$.

Example 39

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(4-isobutylphenyl)propanamide

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and substituting (*S*)-2-(4-isobutylphenyl)propanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.28 (d, *J* = 4.4, 3H), 7.25 – 7.18 (m, 1H), 7.15 (dd, *J* = 2.3, 8.2, 2H), 7.09 (dd, *J* = 1.8, 8.2, 2H), 5.17 (d, *J* = 7.2, 1H), 4.03 – 3.89 (m, 1H), 3.58 (d, *J* = 13.0, 1H), 3.51 – 3.41 (m, 2H), 2.55 – 2.48 (m, 3H), 2.45 (d, *J* = 7.2, 2H), 2.39 (dd, *J* = 7.3, 9.0, 1H), 2.27 – 2.20 (m, 1H), 2.19 – 2.06 (m, 1H), 2.05 – 1.91 (m, 1H), 1.85 (dt, *J* = 6.8, 13.5, 1H), 1.72 – 1.61 (m, 2H), 1.48 (d, *J* = 7.2, 3H), 1.44 – 1.28 (m, 2H), 0.89 (d, *J* = 6.6, 6H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Example 40

***N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide**

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and substituting 2,2-dicyclohexylacetic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.32 – 7.27 (m, *J* = 6.3, 4H), 7.24 – 7.18 (m, 1H), 5.22 (d, *J* = 6.9, 1H), 4.11 – 3.99 (m, 1H), 3.62 (d, *J* = 13.0, 1H), 3.46 (d, *J* = 13.0, 1H), 2.67 – 2.58 (m, 2H), 2.54 (dd, *J* = 4.2, 9.4, 1H), 2.51 – 2.43 (m, 1H), 2.31 (dt, *J* = 4.0, 7.6, 1H), 2.25 (dd, *J* = 4.2, 9.0, 1H), 2.08 – 1.99 (m, 1H), 1.87 – 1.76 (m, 1H), 1.67 (dd, *J* = 15.7, 26.7, 10H), 1.55 (s, 3H), 1.50 – 1.38 (m, 2H), 1.31 – 1.02 (m, 8H), 1.00 – 0.85 (m, 2H); MS (ESI+) *m/z* 423 $(M+H)^+$.

Example 41

***N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclopropyl-2-phenylacetamide**

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and substituting 2-cyclopropyl-2-phenylacetic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.36 – 7.26 (m, 8H), 7.25 – 7.18 (m, 2H), 5.57 – 5.40 (m, 1H), 4.08 – 3.97 (m, 1H), 3.60 (dd, *J* = 5.8, 13.0, 1H), 3.46 (dd, *J* = 3.0, 13.0, 1H), 2.65 (d, *J* = 9.5, 1H), 2.62 – 2.50 (m, 2H), 2.46 – 2.38 (m, 1H), 2.30 – 2.18 (m, 2H), 2.03 (ddd, *J* = 6.0, 12.1, 18.9, 1H), 1.80 – 1.69 (m, 1H), 1.49 – 1.30 (m, 4H), 0.71 (ddd, *J* = 5.7, 9.1, 10.4, 1H), 0.60 – 0.51 (m, 1H), 0.38 (td, *J* = 4.7, 9.0, 1H), 0.19 (dq, *J* = 4.7, 9.4, 1H); MS (ESI+) *m/z* 375 $(M+H)^+$.

Example 42

***N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclobutyl-2-phenylacetamide**

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and substituting 2-cyclobutyl-2-phenylacetic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16:

^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.51 (t, J = 6.2, 1H), 7.61 (d, J = 7.7, 2H), 7.43 (dd, J = 7.3, 16.6, 2H), 7.38 – 7.30 (m, 4H), 7.30 – 7.23 (m, 2H), 4.42 – 4.31 (m, 1H), 3.67 (d, J = 10.7, 1H), 3.59 (dd, J = 13.1, 28.6, 1H), 3.43 (dd, J = 13.0, 35.2, 1H), 3.34 – 3.23 (m, 1H), 2.85 (d, J = 7.5, 0.5H), 2.67 (d, J = 7.1, 0.5H), 2.61 – 2.47 (m, J = 9.6, 29.9, 1.5H), 2.46 – 2.33 (m, 1.5H), 2.28 (d, J = 17.6, 3H), 2.12 (dt, J = 4.5, 12.2, 0.5H), 2.03 – 1.91 (m, 1.5H), 1.87 – 1.55 (m, J = 7.8, 17.0, 28.7, 5H), 1.47 (dt, J = 7.8, 14.5, 0.5H), 1.42 – 1.26 (m, J = 16.4, 37.6, 1.5H); MS (ESI+) *m/z* 389 $(M+H)^+$.

Example 43

***N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(4-chlorophenyl)-3-methylbutanamide**

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and substituting 2-(4-chlorophenyl)-3-methylbutanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.69 (s, 1H), 7.54 (dd, J = 2.9, 8.4, 2H), 7.47 (d, J = 7.5, 1H), 7.42 (d, J = 7.3, 1H), 7.38 – 7.31 (m, 4H), 7.28 (t, J = 7.5, 1H), 4.36 (s, 1H), 3.66 (d, J = 13.1, 0.5H), 3.58 (d, J = 13.1, 0.5H), 3.51 (d, J = 13.1, 0.5H), 3.42 (d, J = 13.1, 0.5H), 3.19 (d, J = 10.4, 1H), 2.94 (d, J = 5.0, 0.5H), 2.66 (d, J = 5.0, 0.5H), 2.62 – 2.49 (m, 2.5H), 2.40 (m, 1.5H), 2.34 (m, 1H), 2.31 – 2.25 (m, 1H), 2.14 (dt, J = 6.2, 12.3, 0.5H), 2.01 – 1.91 (m, J = 4.7, 13.4, 0.5H), 1.87 – 1.62 (m, 1.5H), 1.52 – 1.43 (m, 0.5H), 1.42 – 1.33 (m, J = 10.3, 30.3, 1H), 1.17 (t, J = 5.9, 3H), 0.67 (dd, J = 2.2, 6.7, 3H); MS (ESI+) *m/z* 411 $(M+H)^+$.

Example 44

***N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-ethyl-2-phenylpentanamide**

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and substituting 3-ethyl-2-phenylpentanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.69 – 8.62 (m, 1H), 7.65 (s, 2H), 7.45 (s, 1H), 7.41 (d, J = 7.8, 1H), 7.38 – 7.31 (m, 4H), 7.27 (d, J = 7.0, 2H), 4.34 (dd, J = 5.5, 10.8, 1H), 3.68 – 3.62 (m, 0.5H), 3.60 – 3.47 (m, 2H), 3.45 – 3.32 (m, 0.5H), 2.97 – 2.86 (m, 0.5H), 2.67 –

2.21 (m, 5H), 2.19 – 2.08 (m, 0.5H), 1.94 – 1.55 (m, 4H), 1.48 – 1.38 (m, 2H), 1.12 – 1.00 (m, 1H), 0.97 (q, J = 7.5, 3H), 0.93 – 0.84 (m, 1.5H), 0.83 – 0.74 (m, 0.5H), 0.61 (t, J = 6.6, 3H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Example 45

***N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(4-hydroxyphenyl)-3-methylbutanamide**

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and 2-(4-hydroxyphenyl)-3-methylbutanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.53 – 8.46 (m, 1H), 7.56 (d, J = 2.8, 1H), 7.43 (d, J = 7.2, 1H), 7.36 (dt, J = 7.5, 18.2, 4H), 7.26 (q, J = 7.1, 1H), 7.16 (dd, J = 3.0, 8.6, 2H), 4.44 – 4.32 (m, 1H), 3.60 (d, J = 13.1, 0.5H), 3.53 (d, J = 13.1, 0.5H), 3.44 (d, J = 13.2, 0.5H), 3.33 (d, J = 13.1, 0.5H), 3.18 (d, J = 10.4, 1H), 2.90 (dd, J = 3.0, 9.1, 0.5H), 2.66 (s, 1H), 2.58 (d, J = 8.8, 1H), 2.49 (t, J = 10.5, 1H), 2.44 – 2.35 (m, J = 10.0, 1H), 2.33 – 2.11 (m, 2H), 1.99 – 1.89 (m, 0.5H), 1.88 – 1.63 (m, 1.5H), 1.53 – 1.42 (m, 0.5H), 1.41 – 1.24 (m, 2H), 1.22 (dd, J = 4.4, 6.3, 3H), 0.97 – 0.82 (m, J = 21.9, 35.1, 1H), 0.79 (d, J = 6.7, 3H); MS (ESI+) *m/z* 393 $(M+H)^+$.

Example 46

***N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclohexanecarboxamide**

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and 1-phenylcyclohexanecarboxylic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.73 (d, J = 8.2, 1H), 7.59 (s, 1H), 7.41 (d, J = 7.4, 2H), 7.36 (td, J = 2.7, 7.6, 4H), 7.26 (dd, J = 6.0, 8.7, 2H), 4.45 – 4.33 (m, 1H), 3.58 (d, J = 13.2, 1H), 3.40 (d, J = 13.2, 1H), 2.81 (d, J = 7.3, 1H), 2.68 – 2.59 (m, J = 10.2, 2H), 2.41 – 2.31 (m, J = 6.2, 14.8, 3H), 2.28 (d, J = 8.8, 1H), 2.20 – 2.13 (m, 1H), 1.99 (dt, J = 7.4, 14.8, 1H), 1.88 – 1.75 (m, J = 9.0, 4H), 1.74 – 1.53 (m, J = 8.8, 36.2, 4H), 1.50 – 1.40 (m, 1H), 1.36 – 1.20 (m, 2H); MS (ESI+) *m/z* 403 $(M+H)^+$.

Example 47

***N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-methyl-2-phenylpropanamide**

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and 2-methyl-2-phenylpropanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.49 – 7.38 (m, 4H), 7.31 (ddd, *J* = 7.3, 14.4, 22.5, 5H), 7.08 (d, *J* = 7.3, 1H), 4.46 – 4.35 (m, 1H), 3.58 (d, *J* = 13.2, 1H), 3.43 (d, *J* = 13.2, 1H), 2.84 (d, *J* = 6.7, 1H), 2.36 (d, *J* = 4.8, 3H), 2.31 (d, *J* = 9.6, 1H), 2.21 – 2.13 (m, 1H), 2.04 (td, *J* = 5.9, 11.7, 1H), 1.70 (dd, *J* = 6.7, 12.3, 1H), 1.67 (s, 6H), 1.53 – 1.41 (m, 1H), 1.38 – 1.26 (m, 1H); MS (ESI+) *m/z* 363 $(M+H)^+$.

Example 48

***N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclopropanecarboxamide**

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and 1-phenylcyclopropanecarboxylic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.46 – 7.37 (m, 4H), 7.33 (dt, *J* = 7.5, 11.5, 4H), 7.28 – 7.22 (m, 2H), 6.22 (d, *J* = 7.3, 1H), 4.31 (dd, *J* = 6.7, 12.7, 1H), 3.56 (d, *J* = 13.2, 1H), 3.40 (d, *J* = 13.2, 1H), 2.81 (dd, *J* = 2.1, 8.9, 1H), 2.39 – 2.18 (m, *J* = 7.3, 12.5, 18.1, 4H), 2.13 (dd, *J* = 7.3, 8.9, 1H), 1.99 (dt, *J* = 5.6, 11.0, 1H), 1.75 (q, *J* = 3.6, 2H), 1.67 – 1.58 (m, *J* = 8.3, 16.6, 1H), 1.38 – 1.22 (m, 2H), 1.01 (q, *J* = 3.6, 2H); MS (ESI+) *m/z* 361 $(M+H)^+$.

Example 49

2-benzyl-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethylbutanamide

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and 2-benzyl-3,3-dimethylbutanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.08 (dd, *J* = 7.4, 13.6, 1H), 7.46 (d, *J* = 7.3, 1H), 7.44 – 7.40 (m,

1H), 7.38 (dd, J = 7.6, 15.7, 2H), 7.34 (d, J = 4.3, 2H), 7.31 – 7.23 (m, 4H), 4.36 – 4.29 (m, 1H), 3.59 (d, J = 13.1, 0.5H), 3.53 (dd, J = 13.2, 32.6, 1H), 3.40 (d, J = 13.1, 0.5H), 3.25 (q, J = 12.0, 1H), 2.79 – 2.67 (m, 2H), 2.48 – 2.42 (m, J = 7.0, 1H), 2.41 – 2.23 (m, 3.5H), 2.20 (t, J = 8.3, 0.5H), 2.12 (d, J = 6.7, 0.5H), 2.06 (dd, J = 5.9, 11.7, 0.5H), 1.88 (dd, J = 5.8, 11.7, 0.5H), 1.74 (dd, J = 9.4, 16.4, 0.5H), 1.60 (dd, J = 7.0, 13.2, 0.5H), 1.51 – 1.42 (m, 0.5H), 1.37 – 1.21 (m, 2H), 1.15 (s, 9H); MS (ESI+) m/z 405 $(M+H)^+$.

Example 50

***N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,3-diphenylpropanamide**

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and 2,3-diphenylpropanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.53 (dd, J = 7.3, 13.7, 1H), 7.66 (d, J = 7.4, 2H), 7.44 (d, J = 7.1, 1H), 7.41 – 7.22 (m, 12H), 4.36 – 4.23 (m, J = 7.5, 14.9, 1H), 3.97 (dt, J = 4.9, 9.9, 1H), 3.77 (ddd, J = 3.7, 10.1, 13.5, 1H), 3.52 (dt, J = 13.1, 18.6, 1H), 3.33 (d, J = 13.1, 0.5H), 3.05 (dt, J = 4.7, 13.0, 1H), 2.77 (dd, J = 2.6, 9.0, 0.5H), 2.55 (d, J = 6.3, 0.5H), 2.38 – 2.24 (m, 3H), 2.21 (d, J = 9.2, 1.5H), 2.03 – 1.86 (m, 1.5H), 1.72 – 1.56 (m, 1H), 1.52 – 1.20 (m, 2.5H); MS (ESI+) m/z 425 $(M+H)^+$.

Example 51

***N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-methyl-3-phenylpropanamide**

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and 2-methyl-3-phenylpropanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.13 (dd, J = 7.0, 21.3, 1H), 7.40 (ddd, J = 7.5, 15.5, 25.3, 4H), 7.31 – 7.22 (m, 6H), 4.42 – 4.27 (m, 1H), 3.58 (dd, J = 6.6, 13.1, 1H), 3.45 (dd, J = 13.1, 21.0, 1H), 3.25 – 3.15 (m, 1H), 2.81 – 2.67 (m, 3H), 2.49 – 2.19 (m, 5H), 2.04 (ddd, J = 6.0, 12.1, 24.6, 1H), 1.82 – 1.64 (m, 1H), 1.57 – 1.40 (m, 1H), 1.40 – 1.30 (m, 1H), 1.28 (d, J = 6.4, 3H); MS (ESI+) m/z 363 $(M+H)^+$.

Example 52

***N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethyl-2-phenylbutanamide**

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and 3,3-dimethyl-2-phenylbutanoic acid for (*S*)-2-phenylbutanoic acid in Step F of the procedure used to prepare Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.53 (dd, J = 7.4, 10.9, 1H), 7.73 (dd, J = 3.3, 5.3, 2H), 7.44 (d, J = 7.0, 1H), 7.41 – 7.24 (m, 7H), 4.41 – 4.30 (m, 1H), 3.62 (d, J = 13.1, 0.5H), 3.53 (d, J = 13.1, 0.5H), 3.45 (d, J = 15.0, 0.5H), 3.35 (d, J = 13.1, 0.5H), 2.90 (dd, J = 3.1, 8.9, 0.5H), 2.63 – 2.45 (m, 2.5H), 2.44 – 2.36 (m, 0.5H), 2.31 (d, J = 6.5, 1H), 2.28 (d, J = 5.3, 1H), 2.23 (d, J = 5.8, 1H), 2.15 (dd, J = 5.9, 12.3, 0.5H), 1.92 (dd, J = 6.1, 12.2, 0.5H), 1.84 (dd, J = 8.1, 12.6, 0.5H), 1.72 (ddd, J = 6.5, 12.5, 18.9, 1H), 1.46 – 1.25 (m, 2H), 1.14 (d, J = 1.8, 9H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Example 53

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide

N-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide (2.65 g, 6.27 mmol) from Example 15 and methanol 60 mL were added to 20% palladium hydroxide on carbon, (wet, 0.530 g, 3.77 mmol) in a 250 mL pressure bottle. The reaction was stirred for 16 hours under hydrogen (30 psi) at room temperature. The mixture was filtered through a nylon membrane and the solvent removed in vacuo. The crude material was chromatographed on a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS25-25) eluting with 1-10% methanol (2 *N* ammonia)/dichloromethane to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.97 (d, J = 7.1, 1H), 4.57 (dt, J = 7.0, 13.8, 1H), 3.03 (dd, J = 3.2, 10.1, 1H), 2.89 (dd, J = 7.8, 9.7, 1H), 2.78 (dd, J = 7.4, 10.1, 1H), 2.71 (ddd, J = 3.2, 7.5, 16.7, 1H), 2.58 (dd, J = 3.2, 9.8, 1H), 2.50 – 2.39 (m, J = 8.3, 1H), 1.98 – 1.89 (m, 3H), 1.89 – 1.80 (m, 3H), 1.79 – 1.67 (m, J = 6.4, 14.9, 7H), 1.66 – 1.56 (m, 3H), 1.49 – 1.36 (m, 2H), 1.36 – 1.28 (m, 1H), 1.28 – 1.02 (m, 8H); MS (ESI+) *m/z* 333 $(M+H)^+$.

Example 54

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide

2,2-Dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide (154 mg, 0.463 mmol) from Example 53 and 3-(trifluoromethyl)benzaldehyde (0.062 mL, 0.463 mmol) were combined in dichloromethane (5 mL), and then 2 mL of acetic acid was added. The reaction was stirred at room temperature for 20 minutes, and then PS-cyanoborohydride (396 mg, 0.926 mmol) was added. The reaction was stirred at room temperature overnight, then filtered and the resin was washed with dichloromethane. The solvent was removed in vacuo, and the crude material was purified using a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-25) eluting with 1-10% methanol (2 *N* ammonia)/dichloromethane to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.73 (s, 1H), 7.66 (d, *J* = 7.7, 1H), 7.56 (s, 1H), 7.50 (t, *J* = 7.7, 1H), 4.51 – 4.43 (m, 1H), 3.55 (d, *J* = 12.9, 1H), 3.46 (d, *J* = 12.9, 1H), 2.75 (d, *J* = 8.6, 2H), 2.52 – 2.41 (m, *J* = 8.5, 19.1, 2H), 2.34 – 2.29 (m, 1H), 2.20 (dd, *J* = 7.7, 9.8, 1H), 2.14 (s, 3H, OAc), 1.96 – 1.54 (m, 15H), 1.49 – 1.05 (m, 12H), 1.03 – 0.93 (m, *J* = 11.7, 21.1, 1H); MS (ESI+) *m/z* 491 $(M+H)^+$.

Example 55

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(2-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide

The title compound was prepared by substituting 2-fluorobenzaldehyde for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.55 (s, 1H), 7.36 (dt, *J* = 6.6, 24.8, 2H), 7.20 – 7.15 (m, 2H), 4.44 (s, 1H), 3.68 (d, *J* = 12.6, 1H), 3.44 (d, *J* = 12.6, 1H), 2.77 (d, *J* = 9.6, 1H), 2.64 (dd, *J* = 7.5, 15.0, 1H), 2.53 (d, *J* = 9.0, 1H), 2.49 – 2.40 (m, 1H), 2.29 (t, *J* = 8.3, 1H), 2.16 – 2.09 (m, 1H), 1.98 – 1.64 (m, 12H), 1.61 (d, *J* = 11.4, 2H), 1.55 – 1.37 (m, *J* = 13.8, 20.5, 31.3, 3H), 1.34 – 1.08 (m, 9H), 1.00 (dd, *J* = 13.4, 22.1, 1H); MS (ESI+) *m/z* 441 $(M+H)^+$.

Example 56

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide

The title compound was prepared by substituting 4-fluorobenzaldehyde for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.54

(d, J = 6.0, 1H), 7.40 – 7.29 (m, 2H), 7.18 (d, J = 8.7, 2H), 4.53 – 4.38 (m, 1H), 3.55 (d, J = 12.5, 1H), 3.29 (d, J = 12.6, 1H), 2.72 (dd, J = 8.6, 17.7, 2H), 2.56 – 2.39 (m, 2H), 2.29 (t, J = 8.3, 1H), 2.10 (t, J = 8.1, 1H), 1.98 – 1.07 (m, 26H), 0.99 (dd, J = 10.2, 22.0, 1H); MS (ESI+) m/z 441 $(M+H)^+$.

Example 57

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[4-fluoro-3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide

The title compound was prepared by substituting 4-fluoro-3-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.69 (d, J = 6.9, 1H), 7.56 – 7.54 (m, 1H), 7.36 – 7.28 (m, 1H), 4.52 – 4.42 (m, 1H), 3.53 (d, J = 12.9, 1H), 3.39 (d, J = 12.9, 1H), 2.85 – 2.68 (m, 2H), 2.53 – 2.41 (m, 2H), 2.34 (t, J = 8.3, 1H), 2.24 – 2.16 (m, 1H), 1.96 – 1.56 (m, 16H), 1.49 (d, J = 12.4, 1H), 1.44 – 1.05 (m, 10H), 1.05 – 0.94 (m, 1H); MS (ESI+) m/z 509 $(M+H)^+$.

Example 58

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-fluoro-4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide

The title compound was prepared by substituting 3-fluoro-4-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.62 (d, J = 7.5, 2H), 7.32 (d, J = 11.8, 1H), 7.25 (d, J = 8.0, 1H), 4.51 – 4.40 (m, 1H), 3.54 (d, J = 13.5, 1H), 3.42 (d, J = 13.5, 1H), 2.84 (dd, J = 7.5, 16.5, 1H), 2.76 (dd, J = 2.6, 9.5, 1H), 2.56 – 2.47 (m, 1H), 2.44 (dd, J = 2.6, 8.8, 1H), 2.40 – 2.34 (m, 1H), 2.23 (dd, J = 7.7, 9.3, 1H), 1.97 – 1.52 (m, 16H), 1.45 – 0.97 (m, J = 14.9, 40.1, 72.1, 11H); MS (ESI+) m/z 509 $(M+H)^+$.

Example 59

***N*-{(3a*S*,4*S*,6a*R*)-2-[3,5-bis(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide**

The title compound was prepared by substituting 3,5-bis(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.10 (s, 1H), 7.97 (s, 2H), 4.53 – 4.44 (m, 1H), 3.64 – 3.55 (m, 2H), 2.85 – 2.75 (m, 2H), 2.55 – 2.46 (m, 1H), 2.45 – 2.35 (m, 2H), 2.31 (t, J = 8.3,

1H), 1.95 – 1.55 (m, 15H), 1.48 (d, J = 12.6, 1H), 1.44 – 0.92 (m, 12H); MS (ESI+) *m/z* 559 $(M+H)^+$.

Example 60

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[2-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide

The title compound was prepared by substituting 2-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.74 (d, J = 7.8, 1H), 7.64 (d, J = 7.7, 1H), 7.55 (d, J = 7.6, 1H), 7.43 (dd, J = 7.0, 13.9, 2H), 4.51 – 4.43 (m, 1H), 3.82 (d, J = 13.7, 1H), 3.54 (d, J = 13.7, 1H), 2.81 – 2.70 (m, 2H), 2.53 – 2.43 (m, 2H), 2.35 (t, J = 8.1, 1H), 2.23 – 2.17 (m, 1H), 1.95 – 1.68 (m, 10H), 1.67 – 1.52 (m, 5H), 1.46 – 1.04 (m, 11H), 0.97 – 0.86 (m, 1H); MS (ESI+) *m/z* 491 $(M+H)^+$.

Example 61

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-methylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide

The title compound was prepared by substituting 3-methylbenzaldehyde for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.53 (d, J = 5.8, 1H), 7.32 (t, J = 7.5, 1H), 7.24 – 7.22 (m, 1H), 7.20 – 7.14 (m, 2H), 4.50 – 4.42 (m, 1H), 3.57 (d, J = 12.4, 1H), 3.34 (d, J = 12.3, 1H), 2.78 (d, J = 9.4, 1H), 2.66 (dd, J = 7.5, 15.1, 1H), 2.55 (d, J = 8.8, 1H), 2.50 – 2.42 (m, 1H), 2.33 (s, 3H), 2.31 – 2.24 (m, 1H), 2.14 – 2.07 (m, 1H), 1.98 – 1.57 (m, 13H), 1.53 (ddd, J = 6.4, 11.9, 18.4, 1H), 1.42 (t, J = 10.0, 2H), 1.38 – 1.08 (m, 10H), 1.02 – 0.92 (m, 1H); MS (ESI+) *m/z* 437 $(M+H)^+$.

Example 62

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(4-methylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide

The title compound was prepared by substituting 4-methylbenzaldehyde for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.54 (d, J = 7.8, 1H), 7.30 (d, J = 7.7, 2H), 7.21 – 7.18 (m, 2H), 4.49 – 4.42 (m, 1H), 3.58 (d, J = 12.3, 1H), 3.31 (d, J = 12.4, 1H), 2.77 (d, J = 9.5, 1H), 2.66 (dd, J = 8.3, 15.9, 1H), 2.54 (d, J = 8.8, 1H), 2.50 – 2.41 (m, 1H), 2.32 (s, 3H), 2.30 – 2.23 (m, 2H), 2.11 – 2.03 (m, 1H), 1.99 – 1.58 (m, 13H), 1.57 – 1.08 (m, 12H), 1.03 – 0.90 (m, 1H); MS (ESI+) *m/z* 437 $(M+H)^+$.

Example 63

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethoxy)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide

The title compound was prepared by substituting 3-(trifluoromethoxy)benzaldehyde for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.60 (d, J = 7.3, 1H), 7.42 (t, J = 7.9, 1H), 7.37 (s, 1H), 7.30 (dd, J = 7.9, 16.8, 2H), 4.51 – 4.44 (m, 1H), 3.50 (d, J = 13.0, 1H), 3.45 (d, J = 13.0, 1H), 2.80 – 2.72 (m, J = 4.8, 16.2, 2H), 2.51 – 2.42 (m, J = 8.7, 2H), 2.29 (t, J = 8.3, 1H), 2.20 (dd, J = 7.2, 9.2, 1H), 1.96 – 1.89 (m, 2H), 1.89 – 1.78 (m, 4H), 1.77 – 1.65 (m, 5H), 1.64 – 1.51 (m, 4H), 1.42 (dd, J = 9.4, 23.0, 1H), 1.36 – 1.09 (m, 10H), 1.08 – 0.98 (m, 1H); MS (ESI+) *m/z* 507 $(M+H)^+$.

Example 64

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide

The title compound was prepared by substituting 3-fluorobenzaldehyde for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.36 (dd, J = 7.8, 13.9, 1H), 7.19 – 7.11 (m, 3H), 4.49 – 4.42 (m, 1H), 3.55 (d, J = 12.8, 1H), 3.34 (d, J = 12.8, 1H), 2.78 – 2.69 (m, J = 8.0, 15.6, 2H), 2.51 – 2.43 (m, J = 10.6, 2H), 2.29 (t, J = 8.4, 1H), 2.13 (dd, J = 7.2, 9.5, 1H), 1.97 – 1.77 (m, 7H), 1.77 – 1.64 (m, 5H), 1.63 – 1.47 (m, 4H), 1.42 (ddd, J = 3.0, 12.2, 23.0, 1H), 1.33 (dd, J = 9.7, 23.2, 1H), 1.29 – 1.08 (m, 8H), 1.02 (dd, J = 11.8, 22.6, 1H); MS (ESI+) *m/z* 441 $(M+H)^+$.

Example 65

***N*-{(3a*S*,4*S*,6a*R*)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide**

The title compound was prepared by substituting 3,3-bis(4-fluorophenyl)propanal for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.77 (d, J = 7.3, 1H), 7.39 – 7.31 (m, 4H), 7.20 – 7.13 (m, 4H), 4.58 – 4.50 (m, 1H), 4.13 (d, J = 7.5, 1H), 2.85 (dd, J = 2.2, 9.4, 1H), 2.74 (dd, J = 7.2, 14.4, 1H), 2.47 (d, J = 7.4, 2H), 2.38 – 2.26 (m, 4H), 2.22 (t, J = 8.6, 1H), 2.12 (dd, J = 7.4, 9.3, 1H), 1.98 – 1.90 (m, 4H), 1.90 – 1.82 (m, 2H), 1.82 – 1.76 (m, J = 8.6, 2H), 1.76 – 1.66 (m, 5H), 1.65 – 1.57 (m, 3H), 1.47 – 1.33 (m, 3H), 1.30 – 1.18 (m, 4H), 1.18 – 1.03 (m, 4H); MS (ESI+) *m/z* 563 $(M+H)^+$.

Example 66

***N*-{(3a*S*,4*S*,6a*R*)-2-[6,6-bis(4-fluorophenyl)hexyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide**

The title compound was prepared by substituting 6,6-bis(4-fluorophenyl)hexanal for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.80 (d, J = 6.7, 1H), 7.35 (ddd, J = 2.1, 5.4, 7.9, 4H), 7.16 (td, J = 3.1, 8.8, 4H), 4.56 – 4.47 (m, 1H), 3.99 (t, J = 7.8, 1H), 2.82 (d, J = 9.3, 1H), 2.65 (d, J = 7.7, 1H), 2.49 (dd, J = 8.5, 19.2, 2H), 2.30 (d, J = 31.9, 2H), 2.16 – 2.01 (m, 4H), 1.99 – 1.68 (m, 11H), 1.67 – 1.57 (m, 2H), 1.57 – 1.04 (m, 14H); MS (ESI+) *m/z* 605 $(M+H)^+$.

Example 67

***N*-{(3a*S*,4*S*,6a*R*)-2-[3-(3-chlorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide**

The title compound was prepared by substituting 3-(3-chlorophenyl)propanal for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.87 (s, 1H), 7.31 (d, J = 13.4, 2H), 7.27 (t, J = 7.6, 1H), 7.13 (d, J = 7.3, 1H), 4.57 – 4.49 (m, 1H), 2.86 (d, J = 8.6, 1H), 2.74 (dd, J = 7.3, 14.6, 1H), 2.62 (dd, J = 7.0, 15.3, 2H), 2.53 – 2.45 (m, J = 6.7, 2H), 2.39 – 2.32 (m, J = 6.1, 2H), 2.23 (t, J = 8.0, 1H), 2.01 – 1.68 (m, 16H), 1.65 – 1.56 (m, 3H), 1.48 – 1.33 (m, 3H), 1.32 – 1.18 (m, 4H), 1.17 – 1.04 (m, J = 12.5, 25.1, 4H); MS (ESI+) *m/z* 485 $(M+H)^+$.

Example 68

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(3-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide

The title compound was prepared by substituting 3-(3-fluorophenyl)propanal for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.81 (d, J = 3.1, 1H), 7.31 (dd, J = 7.3, 14.5, 1H), 7.10 – 7.02 (m, J = 11.5, 3H), 4.60 – 4.46 (m, 1H), 2.85 (d, J = 8.2, 1H), 2.76 – 2.59 (m, 3H), 2.55 – 2.43 (m, 2H), 2.41 – 2.28 (m, 2H), 2.25 – 2.16 (m, 1H), 2.15 – 2.06 (m, 1H), 2.00 – 1.90 (m, 4H), 1.89 – 1.67 (m, J = 37.4, 11H), 1.67 – 1.54 (m, 3H), 1.49 – 1.33 (m, 3H), 1.30 – 1.18 (m, J = 10.6, 4H), 1.17 – 1.05 (m, 4H); MS (ESI+) *m/z* 469 $(M+H)^+$.

Example 69

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-phenylpropyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide

The title compound was prepared by substituting 3-phenylpropanal for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.83 (d, J = 5.1, 1H), 7.38 (t, J = 7.6, 2H), 7.28 (d, J = 7.4, 3H), 4.57 – 4.48 (m, 1H), 2.85 (d, J = 8.7, 1H), 2.75 – 2.61 (m, 3H), 2.48 (dd, J = 8.7, 19.0, 2H), 2.35 (dd, J = 7.0, 17.3, 2H), 2.17 (t, J = 7.8, 1H), 2.12 – 2.07 (m, 1H), 1.93 (dd, J = 8.6, 14.2, 4H), 1.89 – 1.75 (m, 7H), 1.71 (d, J = 10.9, 4H), 1.65 – 1.53 (m, J = 6.0, 14.1, 3H), 1.49 – 1.32 (m, 3H), 1.30 – 1.18 (m, 4H), 1.17 – 1.04 (m, J = 9.5, 21.4, 4H); MS (ESI+) *m/z* 451 $(M+H)^+$.

Example 70

2,2-dicyclohexyl-*N*-((3a*S*,4*S*,6a*R*)-2-{3-[4-(trifluoromethyl)phenyl]propyl}octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide

The title compound was prepared by substituting 3-(4-(trifluoromethyl)phenyl)propanal for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.82 (d, J = 7.1, 1H), 7.67 (d, J = 8.1, 2H), 7.36 (d, J = 8.1, 2H), 4.57 – 4.50 (m, 1H), 2.85 (d, J = 9.5, 1H), 2.70 (tt, J = 7.0, 14.1, 3H), 2.49 (d, J = 7.5, 2H), 2.35 (t, J = 6.4, 2H), 2.22 (t, J = 8.5, 1H), 2.16 – 2.09 (m, 1H), 1.98 – 1.89 (m, 4H), 1.89 – 1.74 (m, 7H), 1.70 (d, J = 8.5, 4H), 1.60 (dd, J = 4.9, 12.1, 3H), 1.41 (dt, J = 9.0, 20.3, 3H), 1.30 – 1.17 (m, 4H), 1.10 (dt, J = 10.4, 12.0, 4H); MS (ESI+) *m/z* 519 $(M+H)^+$.

Example 71

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide

The title compound was prepared by substituting 3-(4-fluorophenyl)propanal for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.94 – 7.77 (m, 1H), 7.25 – 7.20 (m, 2H), 7.14 (t, J = 8.7, 2H), 4.61 – 4.47 (m, 1H), 2.93 – 2.80 (m, 1H), 2.79 – 2.69 (m, 1H), 2.62 (dd, J = 7.6, 15.5, 2H), 2.55 – 2.44 (m, 2H), 2.43 – 2.29 (m, 2H), 2.27 – 2.08 (m, 2H), 2.02 – 1.90 (m, 4H), 1.89 – 1.75 (m, 7H), 1.70 (d, J = 11.2, 4H), 1.60 (d, J = 6.9, 3H), 1.49 – 1.32 (m, 3H), 1.30 – 1.17 (m, 4H), 1.12 (dd, J = 12.0, 24.1, 4H); MS (ESI+) *m/z* 469 $(M+H)^+$.

Example 72

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(pyridin-4-ylmethyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide

The title compound was prepared by substituting isonicotinaldehyde for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.76 (d, J = 5.7, 2H), 7.75 – 7.69 (m, 1H), 7.31 (d, J = 5.5, 2H), 4.48 (dd, J = 6.9, 13.1, 1H), 3.47 (d, J = 13.5, 1H), 3.39 (d, J = 13.5, 1H), 2.87 – 2.75 (m, J = 9.2, 21.0, 2H), 2.53 – 2.45 (m, 1H), 2.43 (d, J = 9.0, 1H), 2.34 (t, J = 8.3, 1H), 2.26 – 2.20 (m, 1H), 1.97 – 1.87 (m, 4H), 1.87 – 1.76 (m, 4H), 1.75 – 1.64 (m, J = 6.5, 12.2, 17.6, 5H), 1.63 – 1.56 (m, J = 13.2, 3H), 1.43 (dd, J = 10.1, 22.9, 1H), 1.35 (dd, J = 5.6, 12.1, 1H), 1.30 – 1.18 (m, J = 12.4, 24.4, 4H), 1.17 – 1.08 (m, J = 10.1, 19.2, 4H), 1.09 – 0.99 (m, 1H); MS (ESI+) m/z 424 $(M+H)^+$.

Example 73

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(pyridin-3-ylmethyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide

The title compound was prepared by substituting nicotinaldehyde for 3-(trifluoromethyl)benzaldehyde in Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.80 (d, J = 1.7, 1H), 7.64 (d, J = 6.4, 2H), 7.30 (dd, J = 4.8, 7.7, 1H), 4.49 – 4.41 (m, 1H), 3.54 (d, J = 12.9, 1H), 3.35 (d, J = 12.8, 1H), 2.80 – 2.71 (m, J = 7.7, 2H), 2.51 – 2.42 (m, J = 8.7, 2H), 2.31 (t, J = 8.3, 1H), 2.16 (t, J = 8.8, 1H), 1.91 (dd, J = 6.4, 11.9, 2H), 1.86 – 1.64 (m, 10H), 1.57 (dd, J = 11.4, 24.2, 4H), 1.42 (d, J = 12.8, 1H), 1.35 – 1.08 (m, 10H), 1.03 (d, J = 14.0, 1H); MS (ESI+) m/z 424 $(M+H)^+$.

Example 74

2,2-dicyclohexyl-*N*-[(3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide

The title compound was prepared by substituting *N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide from Example 20 for *N*-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide in Example 53: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 5.31 (d, J = 7.5, 1H), 3.97 – 3.82 (m, 1H), 3.09 – 2.85 (m, 3H), 2.66 (dd, J = 3.7, 12.5, 2H), 2.40 – 2.26 (m, 1H), 2.10 – 1.80 (m, 6H), 1.79 – 1.53 (m, 11H), 1.52 – 1.30 (m, J = 21.5, 31.0, 2H), 1.29 – 1.03 (m, 7H), 0.93 (dd, J = 11.9, 23.1, 2H); MS (ESI+) m/z 333 $(M+H)^+$.

Example 75

2,2-dicyclohexyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide

The title compound was prepared by substituting 2,2-dicyclohexyl-*N*-[(3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide from Example 74 for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.07 (d, J = 7.2, 1H), 7.75 (s, 1H), 7.63 – 7.54 (m, 2H), 7.43 (t, J = 7.8, 1H), 4.51 – 4.42 (m, 1H), 3.61 (d, J = 13.6, 1H), 3.46 (d, J = 13.5, 1H), 2.87 (dd, J = 2.4, 8.9, 1H), 2.64 – 2.52 (m, 2H), 2.52 – 2.46 (m, 1H), 2.30 (s, 2H), 2.18 – 2.08 (m, 1H), 2.03 (t, J = 7.3, 1H), 1.99 – 1.76 (m, 7H), 1.75 – 1.55 (m, 7H), 1.51 – 1.35 (m, 3H), 1.31 – 1.03 (m, 8H); MS (ESI+) *m/z* 491 $(M+H)^+$.

Example 76

2,2-dicyclohexyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide

The title compound was prepared by substituting 3-fluoro-4-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde and 2,2-dicyclohexyl-*N*-[(3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide from Example 74 for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.16 (d, J = 7.3, 1H), 7.59 (d, J = 10.3, 1H), 7.33 (d, J = 11.7, 1H), 7.28 (d, J = 8.0, 1H), 4.52 – 4.44 (m, 1H), 3.56 (d, J = 14.2, 1H), 3.45 (d, J = 14.2, 1H), 2.92 (dd, J = 1.8, 8.9, 1H), 2.63 – 2.52 (m, J = 11.3, 2H), 2.43 (dd, J = 6.9, 8.8, 1H), 2.34 (dd, J = 2.0, 9.0, 1H), 2.29 – 2.23 (m, 1H), 2.13 (dq, J = 5.9, 11.8, 1H), 2.04 (t, J = 7.4, 1H), 2.00 – 1.84 (m, 5H), 1.80 (d, J = 12.4, 2H), 1.76 – 1.56 (m, 7H), 1.46 (dd, J = 10.4, 23.5, 3H), 1.30 – 1.18 (m, 4H), 1.17 – 1.05 (m, 4H); MS (ESI+) *m/z* 509 $(M+H)^+$.

Example 77

***N*-{(3a*S*,4*R*,6a*R*)-2-[3,5-bis(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide**

The title compound was prepared by substituting 3,5-bis(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde and 2,2-dicyclohexyl-*N*-[(3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide from Example 74 for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure

described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.16 (d, J = 7.1, 1H), 7.99 (s, 3H), 4.50 – 4.42 (m, 1H), 3.69 (d, J = 13.9, 1H), 3.54 (d, J = 13.9, 1H), 2.92 (dd, J = 2.7, 9.0, 1H), 2.65 – 2.56 (m, J = 10.2, 15.6, 2H), 2.55 – 2.50 (m, 1H), 2.31 (d, J = 4.2, 2H), 2.10 (dq, J = 5.9, 11.8, 1H), 2.03 (t, J = 7.4, 1H), 1.99 – 1.83 (m, 5H), 1.80 (d, J = 12.4, 2H), 1.75 – 1.64 (m, J = 12.4, 18.4, 5H), 1.63 – 1.56 (m, J = 8.7, 2H), 1.44 (td, J = 7.6, 21.0, 3H), 1.31 – 1.16 (m, 4H), 1.16 – 1.04 (m, 4H); MS (ESI+) *m/z* 559 $(M+H)^+$.

Example 78

_N_-{(3a_S_,4_R_,6a_R_)-2-[6,6-bis(4-fluorophenyl)hexyl]octahydrocyclopenta[_c_]pyrrol-4-yl}-2,2-dicyclohexylacetamide

The title compound was prepared by substituting 6,6-bis(4-fluorophenyl)hexanal for 3-(trifluoromethyl)benzaldehyde and 2,2-dicyclohexyl-_N_-[(3a_S_,4_R_,6a_R_)-octahydrocyclopenta[_c_]pyrrol-4-yl]acetamide from Example 74 for 2,2-dicyclohexyl-_N_-[(3a_S_,4_S_,6a_R_)-octahydrocyclopenta[_c_]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.14 (d, J = 7.3, 1H), 7.33 (dd, J = 5.6, 8.5, 4H), 7.14 (t, J = 8.7, 4H), 4.52 – 4.44 (m, 1H), 3.96 (t, J = 7.8, 1H), 2.94 (d, J = 8.8, 1H), 2.58 (s, 2H), 2.42 (d, J = 8.1, 2H), 2.31 (d, J = 22.9, 3H), 2.17 – 2.09 (m, 1H), 2.08 – 1.85 (m, 8H), 1.85 – 1.77 (m, 2H), 1.76 – 1.64 (m, 5H), 1.61 (d, J = 12.0, 2H), 1.52 – 1.42 (m, 5H), 1.41 – 1.34 (m, 2H), 1.31 – 1.19 (m, 5H), 1.18 – 1.07 (m, 5H); MS (ESI+) *m/z* 605 $(M+H)^+$.

Example 79

2,2-dicyclohexyl-_N_-[(3a_S_,4_R_,6a_R_)-2-(3,3-diphenylpropyl)octahydrocyclopenta[_c_]pyrrol-4-yl]acetamide

The title compound was prepared by substituting 3,3-diphenylpropanal for 3-(trifluoromethyl)benzaldehyde and 2,2-dicyclohexyl-_N_-[(3a_S_,4_R_,6a_R_)-octahydrocyclopenta[_c_]pyrrol-4-yl]acetamide from Example 74 for 2,2-dicyclohexyl-_N_-[(3a_S_,4_S_,6a_R_)-octahydrocyclopenta[_c_]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.10 (d, J = 7.7, 1H), 7.45 (d, J = 7.3, 2H), 7.42 (d, J = 7.1, 3H), 7.38 – 7.30 (m, 5H), 4.56 – 4.48 (m, 1H), 4.27 (t, J = 7.5, 1H), 2.92 – 2.86 (m, 1H), 2.59 – 2.48 (m, J = 6.7, 14.0, 2H), 2.38 – 2.26 (m, 5H), 2.21 – 2.12 (m, 2H), 2.05 (t, J = 7.4, 1H), 1.97 (dd, J = 8.3, 17.0, 2H), 1.94 – 1.85 (m, 4H), 1.81 (d, J = 11.8, 2H), 1.72 (d, J = 13.2, 4H), 1.66 (dd, J = 7.4, 11.8, 1H), 1.61 (d, J = 12.6, 2H), 1.48 (ddd, J = 3.4, 12.8, 15.5, 3H), 1.30 – 1.19 (m, 4H), 1.19 – 1.06 (m, 4H); MS (ESI+) *m/z* 527 $(M+H)^+$.

Example 80

***N*-{(3a*S*,4*R*,6a*R*)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide**

The title compound was prepared by substituting 3,3-bis(4-fluorophenyl)propanal for 3-(trifluoromethyl)benzaldehyde and 2,2-dicyclohexyl-*N*-[(3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide from Example 74 for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.13 (s, 1H), 7.41 (dd, J = 5.5, 8.7, 2H), 7.35 (dd, J = 5.1, 13.8, 3H), 7.14 (dt, J = 8.8, 14.7, 4H), 4.60 – 4.51 (m, J = 21.3, 1H), 4.30 (t, J = 7.7, 1H), 2.95 (d, J = 8.9, 1H), 2.57 – 2.51 (m, 2H), 2.40 (d, J = 8.7, 1H), 2.30 (d, J = 7.0, 3H), 2.26 – 2.12 (m, 4H), 2.05 (t, J = 7.4, 1H), 2.02 – 1.94 (m, J = 12.5, 2H), 1.94 – 1.85 (m, J = 6.7, 18.0, 2H), 1.82 (d, J = 11.7, 2H), 1.72 (d, J = 11.8, 4H), 1.67 – 1.57 (m, J = 10.6, 16.3, 3H), 1.48 (qd, J = 3.3, 12.7, 3H), 1.25 (dd, J = 15.5, 28.8, 4H), 1.13 (t, J = 18.3, 4H); MS (ESI+) *m/z* 563 $(M+H)^+$.

Example 81

***N*-{(3a*S*,4*R*,6a*R*)-2-[4,4-bis(4-fluorophenyl)butyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide**

The title compound was prepared by substituting 4;4-bis(4-fluorophenyl)butanal for 3-(trifluoromethyl)benzaldehyde and 2,2-dicyclohexyl-*N*-[(3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide from Example 74 for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.12 (d, J = 7.5, 1H), 7.36 (ddd, J = 5.5, 8.6, 16.2, 4H), 7.17 (t, J = 8.8, 2H), 7.11 (t, J = 8.8, 2H), 4.52 – 4.45 (m, 1H), 3.99 (t, J = 7.9, 1H), 2.91 (d, J = 9.1, 1H), 2.59 – 2.50 (m, 2H), 2.36 (t, J = 7.1, 3H), 2.24 – 2.16 (m, J = 6.6, 13.0, 2H), 2.14 – 2.02 (m, J = 9.6, 17.5, 3H), 2.02 – 1.86 (m, J = 9.2, 27.4, 5H), 1.81 (t, J = 10.7, 2H), 1.73 (d, J = 9.6, 4H), 1.68 – 1.57 (m, J = 13.6, 3H), 1.53 – 1.37 (m, 6H), 1.31 – 1.19 (m, J = 11.2, 23.8, 4H), 1.18 – 1.07 (m, J = 10.5, 22.1, 4H); MS (ESI+) *m/z* 577 $(M+H)^+$.

Example 82

3-methyl-2-phenyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide

Step A: 3-Methyl-*N*-[(3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide was prepared by substituting *N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide from Example 18 for *N*-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide in the procedure described for Example 53: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.31 (dd, *J* = 1.5, 6.6, 2H), 5.50 – 5.38 (m, *J* = 3.8, 9.7, 1H), 3.84 (dd, *J* = 4.1, 13.5, 1H), 2.92 (ddd, *J* = 10.1, 15.8, 20.7, 3H), 2.76 (dt, *J* = 3.7, 11.5, 2H), 2.65 – 2.53 (m, *J* = 7.9, 12.1, 3H), 2.47 – 2.25 (m, *J* = 9.8, 17.7, 31.5, 2H), 2.20 – 2.07 (m, *J* = 9.3, 17.5, 1H), 2.05 – 1.80 (m, 2H), 1.53 – 1.39 (m, 1H), 1.27 (s, 2H), 1.03 (dd, *J* = 3.4, 6.5, 3H), 0.70 (d, *J* = 6.7, 3H); MS (ESI+) *m/z* 287 $(M+H)^+$.

Step B: The title compound was prepared by substituting 3-methyl-*N*-[(3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.60 (t, *J* = 7.9, 1H), 7.73 (d, *J* = 26.6, 1H), 7.63 (dd, *J* = 2.0, 7.5, 1H), 7.57 – 7.52 (m, 2H), 7.43 (dd, *J* = 7.7, 17.9, 1H), 7.33 (td, *J* = 4.1, 7.5, 2H), 7.26 (dt, *J* = 3.6, 7.2, 1H), 4.38 – 4.28 (m, 1H), 3.60 (d, *J* = 13.6, 0.5H), 3.52 (d, *J* = 13.5, 0.5H), 3.46 (d, *J* = 13.6, 0.5H), 3.35 (d, *J* = 13.5, 0.5H), 3.22 (dd, *J* = 1.4, 10.4, 1H), 2.90 (dd, *J* = 3.0, 9.1, 0.5H), 2.70 – 2.60 (m, *J* = 5.3, 11.8, 1H), 2.59 – 2.53 (m, 1H), 2.52 – 2.46 (m, 1H), 2.44 – 2.32 (m, 1H), 2.28 (d, *J* = 9.1, 0.5H), 2.25 (d, *J* = 5.1, 1H), 2.20 (dd, *J* = 2.4, 4.7, 1H), 2.13 – 2.07 (m, 1.5H), 1.92 – 1.80 (m, 1H), 1.75 (dt, *J* = 6.3, 18.8, 0.5H), 1.71 – 1.64 (m, 0.5H), 1.47 – 1.39 (m, 0.5H), 1.39 – 1.32 (m, 0.5H), 1.32 – 1.24 (m, *J* = 4.2, 16.6, 0.5H), 1.20 (dd, *J* = 4.3, 6.4, 3H), 0.70 (d, *J* = 6.7, 3H); MS (ESI+) *m/z* 445 $(M+H)^+$.

Example 83

N-[(3a*R*,4*S*,6a*S*)-2-(cyclohexylmethyl)octahydrocyclopenta[c]pyrrol-4-yl]-3-methyl-2-phenylbutanamide

Step A: 3-Methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide was prepared by substituting *N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide from Example 35 for *N*-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide

in Example 53: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.61 (d, J = 6.9, 1H), 7.65 (dd, J = 4.6, 6.9, 2H), 7.34 (t, J = 7.5, 2H), 7.26 (t, J = 7.3, 1H), 4.24 (tt, J = 6.2, 12.6, 1H), 3.23 (d, J = 10.4, 1H), 3.19 (dd, J = 2.7, 10.8, 0.5H), 2.99 (dd, J = 7.2, 10.9, 0.5H), 2.84 – 2.72 (m, 2H), 2.70 – 2.61 (m, 1H), 2.58 (dd, J = 2.8, 10.7, 0.5H), 2.53 (dd, J = 3.3, 10.5, 1H), 2.49 – 2.44 (m, 0.5H), 2.43 – 2.35 (m, J = 10.5, 0.5H), 2.35 – 2.28 (m, J = 12.5, 0.5H), 2.06 (dq, J = 6.1, 12.2, 0.5H), 1.91 – 1.72 (m, 1.5H), 1.66 (dt, J = 7.2, 19.4, 0.5H), 1.42 (dd, J = 7.9, 19.3, 0.5H), 1.30 – 1.13 (m, 4 H), 0.71 (d, J = 6.7, 3H); MS (ESI+) m/z 287 $(M+H)^+$.

Step B: The title compound was prepared by substituting cyclohexanecarbaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.57 (dd, J = 7.0, 10.9, 1H), 7.64 (dd, J = 4.9, 7.0, 2H), 7.34 (t, J = 7.6, 2H), 7.25 (t, J = 7.4, 1H), 4.37 – 4.28 (m, 1H), 3.23 (d, J = 10.4, 1H), 2.85 (dd, J = 2.8, 9.0, 0.5H), 2.70 – 2.60 (m, 1H), 2.59 – 2.53 (m, J = 4.6, 11.8, 0.5H), 2.51 (dd, J = 3.1, 9.1, 1H), 2.44 – 2.38 (m, 1H), 2.37 – 2.32 (m, 0.5H), 2.31 – 2.28 (m, 0.5H), 2.27 – 2.08 (m, 3.5H), 2.08 – 1.99 (m, 1H), 1.93 – 1.73 (m, 3.5H), 1.73 – 1.54 (m, 3.5H), 1.47 – 1.27 (m, 2.5H), 1.22 (dd, J = 6.5, 10.5, 3H), 1.19 – 1.06 (m, 3H), 0.90 – 0.75 (m, 2H), 0.71 (dd, J = 2.2, 6.7, 3H); MS (ESI+) m/z 383 $(M+H)^+$.

Example 84

3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-2-methyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide

The title compound was prepared by substituting formaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.55 (t, J = 5.4, 1H), 7.65 (t, J = 6.5, 2H), 7.34 (ddd, J = 3.7, 7.6, 10.9, 2H), 7.29 – 7.25 (m, 1H), 4.42 – 4.28 (m, 1H), 3.22 (d, J = 10.5, 1H), 2.91 (dd, J = 2.2, 9.0, 0.5H), 2.65 (dt, J = 6.7, 17.3, 1H), 2.53 (dd, J = 2.5, 9.2, 1H), 2.46 (dd, J = 4.4, 10.2, 0.5H), 2.42 – 2.35 (m, 0.5H), 2.30 (d, J = 8.8, 1.5H), 2.25 (dd, J = 2.8, 9.0, 0.5H), 2.19 (s, 1.5H), 2.16 – 2.05 (m, 3.5H), 1.85 (td, J = 6.2, 12.0, 1H), 1.75 (dd, J = 6.6, 13.8, 0.5H), 1.63 (dt, J = 7.0, 15.3, 0.5H), 1.39 (dt, J = 8.1, 14.4, 1H), 1.31 (dt, J = 2.9, 9.4, 0.5H), 1.22 (dd, J = 6.5, 11.7, 3H), 0.71 (dd, J = 2.9, 6.7, 3H); MS (ESI+) m/z 301 $(M+H)^+$.

Example 85

***N*-[(3a*R*,4*S*,6a*S*)-2-(2-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 2-fluorobenzaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.66 – 8.58 (m, 1H), 7.63 (dd, J = 3.1, 7.4, 2H), 7.53 (t, J = 7.4, 1H), 7.33 (td, J = 2.2, 7.6, 2H), 7.28 – 7.22 (m, J = 7.4, 9.9, 2H), 7.17 – 7.06 (m, J = 8.2, 14.8, 26.9, 2H), 4.34 (dd, J = 6.0, 11.5, 1H), 3.75 (d, J = 13.6, 0.5H), 3.71 – 3.62 (m, 1H), 3.57 (d, J = 13.6, 0.5H), 3.22 (dd, J = 2.2, 10.4, 1H), 3.00 (d, J = 6.7, 0.5H), 2.69 – 2.48 (m, J = 23.7, 34.8, 3H), 2.47 – 2.28 (m, 3.5H), 2.17 – 2.07 (m, 0.5H), 1.93 – 1.78 (m, J = 6.7, 12.4, 20.1, 1H), 1.78 – 1.62 (m, 1H), 1.49 – 1.27 (m, J = 10.3, 19.5, 26.3, 1.5H), 1.20 (dd, J = 2.9, 6.4, 3H), 0.70 (dd, J = 1.4, 6.6, 3H); MS (ESI+) *m/z* 395 $(M+H)^+$.

Example 86

***N*-[(3a*R*,4*S*,6a*S*)-2-(3-chlorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 3-chlorobenzaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.62 (t, J = 6.5, 1H), 7.64 (dd, J = 4.3, 7.0, 2H), 7.51 (s, 0.5H), 7.46 (s, 0.5H), 7.33 (td, J = 2.5, 7.5, 3H), 7.30 – 7.28 (m, 1H), 7.28 – 7.23 (m, 2H), 4.37 – 4.28 (m, 1H), 3.60 (d, J = 13.4, 0.5H), 3.51 (d, J = 13.4, 0.5H), 3.45 (d, J = 13.4, 0.5H), 3.33 (d, J = 13.4, 0.5H), 3.22 (dd, J = 2.2, 10.4, 1H), 2.93 (d, J = 6.3, 0.5H), 2.69 – 2.48 (m, 3H), 2.31 (dddd, J = 8.9, 13.2, 14.5, 20.2, 3H), 2.16 – 2.05 (m, 1H), 1.92 – 1.79 (m, 1H), 1.78 – 1.62 (m, 1H), 1.49 – 1.40 (m, 0.5H), 1.37 (dd, J = 5.8, 12.6, 0.5H), 1.30 (dd, J = 7.2, 13.5, 0.5H), 1.20 (dd, J = 3.0, 6.5, 3H), 0.70 (dd, J = 1.5, 6.7, 3H); MS (ESI+) *m/z* 411 $(M+H)^+$.

Example 87

***N*-[(3a*R*,4*S*,6a*S*)-2-(3-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 3-fluorobenzaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.61 (t, *J* = 8.0, 1H), 7.64 (dd, *J* = 4.1, 7.0, 2H), 7.37 – 7.16 (m, 5H), 7.13 (d, *J* = 7.6, 1H), 7.04 (s, 1H), 4.33 (dd, *J* = 5.7, 12.4, 1H), 3.57 (d, *J* = 13.5, 0.5H), 3.48 (d, *J* = 13.4, 0.5H), 3.42 (d, *J* = 13.5, 0.5H), 3.30 (d, *J* = 13.5, 0.5H), 3.23 (d, *J* = 10.5, 1H), 2.90 (dd, *J* = 2.9, 9.1, 0.5H), 2.70 – 2.61 (m, 1H), 2.59 – 2.53 (m, 1H), 2.53 – 2.45 (m, 1H), 2.44 – 2.31 (m, *J* = 18.5, 1H), 2.27 (t, *J* = 7.7, 1H), 2.19 (dd, *J* = 6.3, 13.0, 1H), 2.12 (dd, *J* = 6.0, 12.3, 0.5H), 1.93 – 1.80 (m, *J* = 6.9, 12.4, 20.6, 1H), 1.79 – 1.64 (m, 1H), 1.47 – 1.24 (m, 2H), 1.20 (dd, *J* = 3.1, 6.4, 3H), 0.70 (d, *J* = 6.7, 3H); MS (ESI+) *m/z* 395 $(M+H)^+$.

Example 88

3-methyl-2-phenyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide

The title compound was prepared by substituting 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.60 (t, *J* = 7.6, 1H), 7.76 (s, 0.5H), 7.71 (s, 0.5H), 7.64 (d, *J* = 7.8, 2H), 7.57 – 7.53 (m, *J* = 7.1, 2H), 7.43 (dd, *J* = 7.8, 17.8, 1H), 7.36 – 7.30 (m, 2H), 7.28 – 7.23 (m, 1H), 4.33 (dd, *J* = 5.8, 12.3, 1H), 3.61 (d, *J* = 13.6, 0.5H), 3.53 (d, *J* = 13.5, 0.5H), 3.47 (d, *J* = 13.5, 0.5H), 3.36 (d, *J* = 13.5, 0.5H), 3.22 (dd, *J* = 1.5, 10.4, 1H), 2.91 (dd, *J* = 3.0, 9.0, 0.5H), 2.69 – 2.59 (m, 1H), 2.55 (dd, *J* = 3.0, 9.0, 1H), 2.52 – 2.47 (m, 1H), 2.44 – 2.32 (m, *J* = 10.5, 32.1, 1H), 2.29 (d, *J* = 8.9, 0.5H), 2.26 (d, *J* = 5.2, 1H), 2.22 – 2.18 (m, 1H), 2.16 – 2.06 (m, 0.5H), 1.92 – 1.79 (m, 1H), 1.79 – 1.63 (m, 1H), 1.48 – 1.25 (m, 1.5H), 1.20 (dd, *J* = 4.5, 6.4, 3H), 0.70 (d, *J* = 5.8, 3H); MS (ESI+) *m/z* 445 $(M+H)^+$.

Example 89

***N*-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 4-fluorobenzaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.61 (t, *J* = 7.2, 1H), 7.64 (dd, *J* = 2.4, 7.5, 2H), 7.39 (dd, *J* = 5.8, 8.2, 1H), 7.33 (dt, *J* = 5.8, 11.6, 3H), 7.28 – 7.23 (m, 1H), 7.11 (dd, *J* = 8.8, 19.1, 2H), 4.34 (dd, *J* = 5.8, 12.6, 1H), 3.56 (d, *J* = 13.3, 0.5H), 3.45 (dd, *J* = 13.3, 16.8, 1H), 3.31 (d, *J* = 13.1, 0.5H), 3.22 (dd, *J* = 2.3, 10.5, 1H), 2.92 (d, *J* = 6.5, 0.5H), 2.69 – 2.60 (m, 1H), 2.57 (d, *J* = 6.6, 1H), 2.51 (d, *J* = 8.4, 1H), 2.46 – 2.33 (m, 1H), 2.29 (d, *J* = 4.4, 1H), 2.22 (d, *J* = 6.5, 1H), 2.14 (dq, *J* = 6.2, 12.2, 0.5H), 1.95 – 1.80 (m, *J* = 7.1, 12.4, 20.7, 1H), 1.79 – 1.72 (m, 0.5H), 1.71 – 1.64 (m, 1H), 1.48 – 1.23 (m, 1.5H), 1.20 (t, *J* = 6.1, 3H), 0.70 (dd, *J* = 2.1, 6.7, 3H); MS (ESI+) *m/z* 395 $(M+H)^+$.

Example 90

***N*-[(3a*R*,4*S*,6a*S*)-2-(3-methoxybenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 3-methoxybenzaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.61 – 8.54 (m, 1H), 7.63 (d, *J* = 7.6, 2H), 7.36 – 7.24 (m, *J* = 5.6, 12.0, 20.6, 4H), 7.17 (s, 0.5H), 7.11 (s, 0.5H), 7.06 (d, *J* = 7.8, 0.5H), 7.00 (d, *J* = 7.5, 0.5H), 6.95 – 6.88 (m, 1H), 4.42 – 4.29 (m, 1H), 3.72 (s, 1.5H), 3.70 (s, 1.5H), 3.60 (d, *J* = 13.3, 0.5H), 3.52 (d, *J* = 13.2, 0.5H), 3.48 (d, *J* = 13.3, 0.5H), 3.36 (d, *J* = 13.2, 0.5H), 3.23 – 3.19 (m, 1H), 2.93 (dd, *J* = 2.7, 9.0, 0.5H), 2.68 – 2.61 (m, 1H), 2.58 (dd, *J* = 3.0, 8.9, 1H), 2.52 – 2.46 (m, 1H), 2.45 – 2.20 (m, 3H), 2.18 – 2.11 (m, 1H), 1.91 (dd, *J* = 6.0, 12.0, 0.5H), 1.87 – 1.80 (m, 0.5H), 1.78 – 1.64 (m, 1H), 1.48 – 1.26 (m, *J* = 28.4, 35.4, 1.5H), 1.20 (t, *J* = 6.7, 3H), 0.70 (dd, *J* = 2.8, 6.7, 3H); MS (ESI+) *m/z* 407 $(M+H)^+$.

Example 91

3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(3-methylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide

The title compound was prepared by substituting 3-methylbenzaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.62 – 8.50 (m, 1H), 7.64 (d, *J* = 7.5, 2H), 7.33 (td, *J* = 3.7, 7.5, 2H), 7.29 – 7.23 (m, *J* = 5.5, 11.0, 3H), 7.18 (s, 1H), 7.07 (d, *J* = 7.0, 1H), 4.42 – 4.29 (m, 1H), 3.60 (d, *J* = 13.1, 0.5H), 3.51 (d, *J* = 13.0, 0.5H), 3.45 (d, *J* = 13.1, 0.5H), 3.33 (d, *J* = 13.0, 0.5H), 3.22 (d, *J* = 10.4, 1H), 2.90 (dd, *J* = 2.9, 8.9, 0.5H), 2.64 (tt, *J* = 6.8, 13.6, 1H), 2.59 – 2.46 (m, *J* = 5.3, 12.0, 23.8, 2H), 2.44 – 2.34 (m, 1H), 2.30 (d, *J* = 5.3, 1H), 2.28 – 2.23 (m, *J* = 8.0, 4H), 2.13 (dt, *J* = 6.3, 12.4, 1H), 1.94 – 1.78 (m, 1H), 1.78 – 1.64 (m, 1H), 1.48 – 1.25 (m, 1.5H), 1.20 (t, *J* = 6.1, 3H), 0.70 (dd, *J* = 1.9, 6.7, 3H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Example 92

3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(2-methylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide

The title compound was prepared by substituting 2-methylbenzaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.57 – 8.51 (m, 1H), 7.63 (dd, *J* = 3.5, 7.1, 2H), 7.43 – 7.36 (m, 1H), 7.36 – 7.30 (m, 3H), 7.25 (dd, *J* = 6.9, 9.6, 2H), 7.20 – 7.13 (m, *J* = 10.0, 2H), 4.31 (dd, *J* = 5.5, 11.3, 1H), 3.57 (d, *J* = 13.1, 0.5H), 3.48 (d, *J* = 13.0, 0.5H), 3.39 (d, *J* = 13.0, 0.5H), 3.29 (d, *J* = 13.0, 0.5H), 3.21 (d, *J* = 10.3, 1H), 2.92 (dd, *J* = 2.8, 9.0, 0.5H), 2.68 – 2.60 (m, 1H), 2.60 – 2.53 (m, 1H), 2.51 – 2.45 (m, 1H), 2.35 (s, 1.5H), 2.30 (s, 1.5H), 2.28 – 2.17 (m, 2H), 2.15 – 2.06 (m, 1H), 1.84 (ddd, *J* = 6.8, 12.4, 20.0, 1H), 1.76 – 1.62 (m, 1H), 1.42 (dt, *J* = 7.2, 19.2, 0.5H), 1.33 (dt, *J* = 7.0, 12.5, 0.5H), 1.29 – 1.22 (m, 0.5H), 1.20 (d, *J* = 6.5, 3H), 0.70 (d, *J* = 6.7, 3H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Example 93

***N*-[(3a*R*,4*S*,6a*S*)-2-(2,6-dimethylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 2,6-dimethylbenzaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.54 – 8.50 (m, *J* = 6.7, 1H), 7.65 – 7.60 (m, 2H), 7.32 (t, *J* = 7.1, 2H), 7.28 – 7.23 (m, 1H), 7.11 (dd, *J* = 6.2, 14.3, 1H), 7.04 (t, *J* = 8.3, 2H), 4.27 – 4.19 (m, 1H), 3.57 (d, *J* = 12.5, 0.5H), 3.44 (dd, *J* = 12.5, 15.5, 1H), 3.34 (d, *J* = 12.5, 0.5H), 3.20 (d, *J* = 10.4, 1H), 2.92 (d, *J* = 5.9, 0.5H), 2.68 – 2.58 (m, *J* = 10.2, 18.3, 1H), 2.55 – 2.51 (m, *J* = 4.5, 1H), 2.48 – 2.42 (m, 0.5H), 2.39 (s, 3H), 2.34 (s, 3H), 2.32 – 2.18 (m, 3H), 2.07 (td, *J* = 6.6, 12.6, 0.5H), 1.87 – 1.73 (m, 1H), 1.72 – 1.62 (m, 1H), 1.33 (dd, *J* = 19.1, 78.6, 2.5H), 1.19 (dd, *J* = 4.9, 6.3, 3H), 0.69 (d, *J* = 6.6, 3H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Example 94

***N*-[(3a*R*,4*S*,6a*S*)-2-(2-methoxybenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 2-methoxybenzaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.50 (t, *J* = 7.3, 1H), 7.62 (d, *J* = 7.3, 2H), 7.55 (d, *J* = 7.8, 1H), 7.32 (dq, *J* = 3.8, 11.6, 2H), 7.25 (dd, *J* = 3.6, 7.5, 2H), 7.04 (dt, *J* = 7.4, 11.4, 1H), 6.89 (t, *J* = 8.3, 1H), 4.43 – 4.31 (m, 1H), 3.80 – 3.57 (m, 5H), 3.21 (d, *J* = 10.4, 1H), 2.99 (d, *J* = 6.2, 0.5H), 2.61 (ddd, *J* = 4.5, 12.6, 15.9, 2.5H), 2.52 – 2.45 (m, 0.5H), 2.45 – 2.31 (m, 3.5H), 2.19 – 2.09 (m, 0.5H), 2.00 – 1.80 (m, 1H), 1.72 (ddd, *J* = 6.5, 12.3, 19.3, 1H), 1.47 – 1.25 (m, 2.5H), 1.20 (dd, *J* = 3.0, 6.4, 3H), 0.70 (d, *J* = 6.7, 3H); MS (ESI+) *m/z* 407 $(M+H)^+$.

Example 95

***N*-[(3a*R*,4*S*,6a*S*)-2-(4-*tert*-butylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 4-*tert*-butylbenzaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-

4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.57 (dd, *J* = 6.7, 11.0, 1H), 7.63 (dd, *J* = 3.4, 7.1, 2H), 7.44 – 7.30 (m, 6H), 7.25 (t, *J* = 7.4, 1H), 4.36 (tt, *J* = 6.3, 12.6, 1H), 3.63 (d, *J* = 13.1, 0.5H), 3.55 (d, *J* = 13.0, 0.5H), 3.46 (d, *J* = 13.0, 0.5H), 3.35 (d, *J* = 13.0, 0.5H), 3.21 (d, *J* = 10.4, 1H), 2.90 (dd, *J* = 2.7, 8.7, 0.5H), 2.65 (dt, *J* = 6.6, 16.9, 1H), 2.58 – 2.44 (m, 2H), 2.44 – 2.34 (m, 1H), 2.32 (d, *J* = 8.6, 0.5H), 2.30 (d, *J* = 5.2, 1H), 2.24 (d, *J* = 5.0, 1H), 2.19 – 2.12 (m, 1H), 1.92 (dq, *J* = 6.1, 12.1, 0.5H), 1.82 (td, *J* = 7.3, 14.3, 0.5H), 1.70 (dq, *J* = 8.1, 14.7, 1H), 1.48 – 1.30 (m, *J* = 22.3, 41.1, 1H), 1.27 (s, *J* = 1.6, 9H), 1.20 (dd, *J* = 3.5, 6.4, 3H), 0.70 (d, *J* = 6.4, 3H); MS (ESI+) *m/z* 433 $(M+H)^+$.

Example 96

***N*-[(3a*R*,4*S*,6a*S*)-2-(4-methoxybenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 4-methoxybenzaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.57 (dd, *J* = 8.3, 10.9, 1H), 7.63 (dd, *J* = 2.8, 7.4, 2H), 7.39 – 7.28 (m, 4H), 7.28 – 7.23 (m, 1H), 6.98 (dd, *J* = 8.7, 10.2, 2H), 4.41 – 4.30 (m, 1H), 3.68 (s, 3H), 3.57 (d, *J* = 12.9, 0.5H), 3.48 (d, *J* = 12.9, 0.5H), 3.42 (d, *J* = 12.9, 0.5H), 3.31 (d, *J* = 12.8, 0.5H), 3.21 (d, *J* = 10.4, 1H), 2.90 (dd, *J* = 2.8, 8.9, 0.5H), 2.69 – 2.59 (m, 1H), 2.56 (dd, *J* = 2.9, 9.0, 1H), 2.53 – 2.46 (m, 1H), 2.45 – 2.33 (m, 1H), 2.32 – 2.26 (m, *J* = 10.0, 1H), 2.24 (t, *J* = 5.2, 1H), 2.15 (dt, *J* = 6.3, 12.3, 0.5H), 1.96 – 1.88 (m, 0.5H), 1.88 – 1.79 (m, 0.5H), 1.79 – 1.65 (m, 1H), 1.48 – 1.24 (m, *J* = 19.9, 48.8, 3H), 1.20 (dd, *J* = 4.3, 6.4, 3H), 0.70 (dd, *J* = 2.0, 6.7, 2H); MS (ESI+) *m/z* 407 $(M+H)^+$.

Example 97

***N*-[(3a*R*,4*S*,6a*S*)-2-(3-cyanobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 3-formylbenzonitrile for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H

NMR (500 MHz, pyridine-d_5) δ ppm 8.60 (t, J = 7.1, 1H), 7.63 (d, J = 5.9, 2H), 7.56 – 7.50 (m, 2H), 7.39 – 7.30 (m, 3H), 7.29 – 7.23 (m, J = 8.9, 13.2, 2H), 4.32 (dd, J = 5.7, 11.2, 1H), 3.53 (d, J = 13.6, 0.5H), 3.44 (d, J = 13.5, 0.5H), 3.40 (d, J = 13.6, 0.5H), 3.28 (d, J = 13.6, 0.5H), 3.21 (dd, J = 1.3, 10.4, 1H), 2.90 (dd, J = 2.8, 9.1, 0.5H), 2.64 (qd, J = 6.6, 13.2, 1H), 2.59 – 2.47 (m, 1H), 2.46 – 2.37 (m, 1H), 2.37 – 2.30 (m, 0.5H), 2.26 – 2.20 (m, 1H), 2.19 – 2.13 (m, 1H), 2.10 (dt, J = 6.2, 12.3, 0.5H), 1.89 – 1.79 (m, 1H), 1.75 (dt, J = 6.1, 20.0, 0.5H), 1.66 (dt, J = 7.0, 19.3, 0.5H), 1.47 – 1.38 (m, 0.5H), 1.38 – 1.23 (m, 2H), 1.20 (dd, J = 3.6, 6.4, 3H), 0.70 (d, J = 6.7, 3H); MS (ESI+) *m/z* 402 $(M+H)^+$.

Example 98

3-methyl-2-phenyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide

The title compound was prepared by substituting 4-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.62 (t, J = 7.8, 1H), 7.64 (dd, J = 7.0, 11.8, 4H), 7.51 (d, J = 8.0, 1H), 7.46 (d, J = 7.9, 1H), 7.33 (dd, J = 7.4, 12.1, 2H), 7.29 – 7.24 (m, 1H), 4.40 – 4.30 (m, 1H), 3.58 (d, J = 13.7, 0.5H), 3.48 (t, J = 13.8, 1H), 3.35 (d, J = 13.7, 0.5H), 3.23 (dd, J = 1.4, 10.4, 1H), 2.92 (dd, J = 2.7, 9.0, 0.5H), 2.69 – 2.60 (m, 1H), 2.57 (dd, J = 2.7, 9.1, 1H), 2.54 – 2.47 (m, 0.5H), 2.47 – 2.39 (m, 1H), 2.39 – 2.32 (m, 0.5H), 2.31 – 2.20 (m, 2H), 2.19 – 2.11 (m, 1H), 1.95 – 1.82 (m, J = 6.4, 37.0, 1H), 1.77 (dt, J = 6.4, 13.8, 0.5H), 1.69 (dt, J = 6.9, 19.1, 0.5H), 1.50 – 1.25 (m, J = 34.6, 62.0, 1.5H), 1.21 (t, J = 6.4, 3H), 0.70 (d, J = 5.1, 3H); MS (ESI+) *m/z* 445 $(M+H)^+$.

Example 99

3-methyl-2-phenyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[2-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide

The title compound was prepared by substituting 2-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.61 (d, J = 6.0, 1H), 7.93 (d, J = 7.6, 0.5H), 7.85 (d, J = 7.8, 0.5H), 7.63 (t, J = 5.8, 3H), 7.53 (dd, J = 7.9, 16.0,

1H), 7.38 – 7.23 (m, 5H), 4.36 (dd, J = 5.7, 13.2, 1H), 3.76 (q, J = 14.5, 1H), 3.66 (q, J = 15.0, 1H), 3.23 (dd, J = 2.2, 10.5, 1H), 3.03 (dd, J = 2.2, 9.0, 0.5H), 2.69 – 2.60 (m, J = 5.6, 17.6, 1H), 2.59 – 2.47 (m, 1H), 2.47 – 2.40 (m, J = 10.2, 17.4, 1H), 2.39 – 2.12 (m, 3H), 1.96 – 1.82 (m, 1H), 1.78 (dt, J = 6.2, 20.1, 0.5H), 1.68 (dt, J = 7.2, 13.8, 0.5H), 1.48 – 1.24 (m, 1.5H), 1.20 (t, J = 6.7, 3H), 0.70 (dd, J = 1.7, 6.7, 3H); MS (ESI+) *m/z* 445 $(M+H)^+$.

Example 100

***N*-{(3a*R*,4*S*,6a*S*)-2-[4-fluoro-3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 4-fluoro-3-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.63 (t, J = 7.0, 1H), 7.69 (d, J = 6.3, 1H), 7.64 (d, J = 7.6, 2H), 7.55 – 7.49 (m, 1H), 7.33 (dd, J = 7.2, 13.6, 2H), 7.25 (dd, J = 7.6, 15.5, 2H), 4.33 (dd, J = 5.7, 11.4, 1H), 3.54 (d, J = 13.5, 0.5H), 3.44 (t, J = 14.0, 1H), 3.31 (d, J = 13.4, 0.5H), 3.22 (d, J = 10.4, 1H), 2.91 (dd, J = 2.6, 9.0, 0.5H), 2.69 – 2.60 (m, J = 7.5, 13.7, 1H), 2.55 (dd, J = 3.1, 9.1, 1H), 2.53 – 2.39 (m, 2H), 2.38 – 2.32 (m, J = 8.0, 0.5H), 2.29 – 2.21 (m, 1H), 2.19 (d, J = 4.0, 1H), 2.12 (dd, J = 6.1, 12.1, 0.5H), 1.91 – 1.81 (m, J = 10.9, 16.7, 1H), 1.77 (dt, J = 6.3, 19.8, 0.5H), 1.68 (td, J = 7.0, 14.0, 0.5H), 1.44 (dt, J = 7.6, 14.7, 0.5H), 1.40 – 1.25 (m, 1H), 1.20 (t, J = 5.7, 3H), 0.70 (d, J = 6.4, 3H); MS (ESI+) *m/z* 463 $(M+H)^+$.

Example 101

***N*-{(3a*R*,4*S*,6a*S*)-2-[3-fluoro-4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 3-fluoro-4-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.63 (t, J = 6.6, 1H), 7.64 (dd, J = 3.0, 7.5, 2H), 7.37 – 7.30 (m, 3H), 7.30 – 7.23 (m, 3H), 4.38 – 4.30 (m, 1H), 3.56 (d, J = 14.1, 0.5H), 3.46 (t, J = 13.4, 1H), 3.33 (d, J = 14.1, 0.5H), 3.23 (d, J = 10.4, 1H), 2.94 (dd, J = 2.5, 9.0, 0.5H), 2.65 (dt, J = 6.2, 10.9, 1H), 2.58 (dd, J = 2.8, 9.2,

1H), 2.54 – 2.48 (m, 0.5H), 2.47 – 2.39 (m, 1H), 2.39 – 2.32 (m, 0.5H), 2.28 (dd, J = 2.7, 8.9, 0.5H), 2.26 – 2.20 (m, 1H), 2.19 – 2.09 (m, 1H), 1.87 (ddd, J = 6.4, 12.3, 18.7, 1H), 1.78 (dt, J = 6.2, 19.6, 0.5H), 1.68 (dt, J = 7.5, 14.6, 0.5H), 1.49 – 1.24 (m, 2H), 1.21 (dd, J = 4.3, 6.2, 3H), 0.70 (d, J = 6.7, 3H); MS (ESI+) *m/z* 463 $(M+H)^+$.

Example 102

3-methyl-2-phenyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(thien-2-ylmethyl)octahydrocyclopenta[*c*]pyrrol-4-yl]butanamide

The title compound was prepared by substituting thiophene-2-carbaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.62 – 8.53 (m, 1H), 7.63 (dd, J = 4.4, 7.0, 2H), 7.33 (t, J = 7.6, 3H), 7.28 – 7.23 (m, 1H), 6.98 (dd, J = 4.8, 9.3, 1H), 6.94 (d, J = 3.0, 1H), 4.33 (dd, J = 7.7, 13.5, 1H), 3.77 (d, J = 13.7, 0.5H), 3.68 (dd, J = 4.6, 13.7, 1H), 3.57 (d, J = 13.7, 0.5H), 3.21 (d, J = 10.4, 1H), 2.94 (d, J = 8.5, 0.5H), 2.69 – 2.44 (m, 3H), 2.44 – 2.28 (m, 3H), 2.28 – 2.22 (m, 0.5H), 2.18 – 2.09 (m, 0.5H), 1.90 (td, J = 6.1, 12.1, 0.5H), 1.86 – 1.79 (m, 0.5H), 1.78 – 1.63 (m, 1H), 1.47 – 1.35 (m, 1H), 1.32 (dd, J = 7.1, 13.2, 0.5H), 1.20 (dd, J = 2.0, 6.4, 3H), 0.70 (d, J = 6.7, 3H); MS (ESI+) *m/z* 383 $(M+H)^+$.

Example 103

3-methyl-2-phenyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(pyridin-4-ylmethyl)octahydrocyclopenta[*c*]pyrrol-4-yl]butanamide

The title compound was prepared by substituting isonicotinaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.70 (d, J = 5.9, 2H), 8.62 (s, 1H), 7.64 (dd, J = 3.0, 7.5, 2H), 7.36 – 7.30 (m, 2H), 7.25 (dd, J = 7.0, 12.4, 3H), 4.39 – 4.30 (m, 1H), 3.51 (d, J = 14.2, 0.5H), 3.41 (dd, J = 11.5, 14.2, 1H), 3.28 (d, J = 14.3, 0.5H), 3.23 (dd, J = 1.8, 10.5, 1H), 2.94 (dd, J = 2.6, 9.2, 0.5H), 2.69 – 2.60 (m, 1H), 2.57 (dd, J = 2.9, 9.2, 1H), 2.52 – 2.46 (m, 0.5H), 2.42 (dd, J = 7.2, 8.8, 1H), 2.38 – 2.31 (m, 0.5H), 2.28 (dd, J = 2.7, 9.0, 0.5H), 2.24 – 2.18 (m, 1H), 2.17 – 2.11 (m, 1H), 1.95 – 1.82 (m, 1H), 1.77 (dt, J = 5.8, 12.3, 0.5H), 1.73 –

1.64 (m, 0.5H), 1.49 – 1.25 (m, 2H), 1.23 – 1.17 (m, 3H), 0.70 (d, *J* = 6.5, 3H); MS (ESI+) *m/z* 378 $(M+H)^+$.

Example 104

3-methyl-2-phenyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(2-phenylethyl)octahydrocyclopenta[*c*]pyrrol-4-yl]butanamide

The title compound was prepared by substituting 2-phenylacetaldehyde for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.57 (dd, *J* = 5.2, 12.0, 1H), 7.65 (t, *J* = 7.1, 2H), 7.38 – 7.23 (m, 8H), 4.40 – 4.29 (m, 1H), 3.23 (d, *J* = 10.5, 1H), 3.00 (dd, *J* = 2.6, 9.0, 0.5H), 2.80 (t, *J* = 7.8, 1H), 2.75 – 2.70 (m, 1H), 2.70 – 2.61 (m, 1H), 2.61 – 2.52 (m, 1H), 2.52 – 2.46 (m, 1H), 2.43 (dd, *J* = 7.6, 8.7, 0.5H), 2.38 (dd, *J* = 2.7, 8.8, 1H), 2.34 (dd, *J* = 2.7, 8.5, 1H), 2.26 (d, *J* = 8.3, 0.5H), 2.24 – 2.18 (m, 1H), 2.12 (td, *J* = 6.4, 12.4, 0.5H), 1.91 – 1.82 (m, 1H), 1.76 (dt, *J* = 6.2, 18.7, 0.5H), 1.70 – 1.61 (m, 0.5H), 1.46 – 1.26 (m, 2H), 1.23 (dd, *J* = 6.5, 13.5, 3H), 0.97 – 0.83 (m, 1H), 0.71 (dd, *J* = 2.7, 6.7, 3H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Example 105

3-methyl-2-phenyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(3-phenylpropyl)octahydrocyclopenta[*c*]pyrrol-4-yl]butanamide

The title compound was prepared by substituting 3-phenylpropanal for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.60 (t, *J* = 6.8, 1H), 7.69 – 7.63 (m, 2H), 7.39 – 7.22 (m, 8H), 4.41 – 4.31 (m, 1H), 3.25 (d, *J* = 10.4, 1H), 2.95 (dd, *J* = 2.5, 8.9, 0.5H), 2.68 (td, *J* = 2.7, 7.2, 2H), 2.65 – 2.60 (m, 1H), 2.58 (dd, *J* = 2.8, 9.2, 0.5H), 2.56 – 2.52 (m, 0.5H), 2.51 – 2.46 (m, 0.5H), 2.44 – 2.38 (m, 0.5H), 2.37 – 2.26 (m, 3H), 2.23 (t, *J* = 7.2, 1H), 2.18 (d, *J* = 7.3, 0.5H), 2.13 (t, *J* = 8.8, 1.5H), 1.88 (dd, *J* = 6.1, 12.1, 1H), 1.79 (dd, *J* = 7.2, 14.5, 1.5H), 1.74 – 1.64 (m, 1.5H), 1.48 – 1.37 (m, 1H), 1.37 – 1.28 (m, 0.5H), 1.23 (dd, *J* = 6.5, 12.2, 3H), 0.71 (dd, *J* = 3.0, 6.7, 3H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Example 106

***N*-{(3a*R*,4*S*,6a*S*)-2-[3-(4-*tert*-butylphenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 3-(4-*tert*-butylphenyl)propanal for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.57 (t, J = 8.5, 1H), 7.65 (t, J = 6.6, 2H), 7.40 (dd, J = 5.4, 8.0, 2H), 7.34 (t, J = 7.4, 2H), 7.30 – 7.23 (m, 3H), 4.37 (dt, J = 6.1, 11.1, 1H), 3.23 (d, J = 10.4, 1H), 2.96 (dd, J = 1.9, 8.9, 0.5H), 2.67 (ddd, J = 6.7, 11.6, 23.3, 2H), 2.59 (dd, J = 2.6, 9.3, 0.5H), 2.57 – 2.51 (m, 0.5H), 2.50 – 2.44 (m, 0.5H), 2.43 – 2.38 (m, 0.5H), 2.35 (t, J = 8.1, 2H), 2.29 (dd, J = 2.6, 8.8, 0.5H), 2.25 (t, J = 7.1, 1H), 2.19 (d, J = 7.2, 0.5H), 2.17 – 2.11 (m, 1H), 1.92 – 1.85 (m, 1H), 1.81 (dt, J = 7.7, 15.5, 1H), 1.74 (dt, J = 7.9, 15.9, 1H), 1.69 – 1.63 (m, 0.5H), 1.46 – 1.31 (m, 2H), 1.28 (s, 9H), 1.23 (dd, J = 6.5, 13.4, 3H), 0.94 – 0.84 (m, 2H), 0.71 (dd, J = 3.2, 6.6, 3H); MS (ESI+) *m/z* 461 $(M+H)^+$.

Example 107

***N*-{(3a*R*,4*S*,6a*S*)-2-[6,6-bis(4-fluorophenyl)hexyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 6,6-bis(4-fluorophenyl)hexanal for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.59 (t, J = 6.4, 1H), 7.65 (dd, J = 4.9, 6.9, 2H), 7.33 (dd, J = 6.8, 11.6, 6H), 7.25 (dd, J = 6.5, 8.2, 1H), 7.14 (dd, J = 1.4, 8.7, 4H), 4.40 – 4.30 (m, 1H), 3.97 (q, J = 7.7, 1H), 3.23 (d, J = 10.4, 1H), 2.96 (d, J = 6.8, 0.5H), 2.71 – 2.61 (m, 1H), 2.59 (dd, J = 2.5, 9.0, 0.5H), 2.56 – 2.46 (m, 1H), 2.40 (dd, J = 8.4, 16.1, 1H), 2.37 – 2.33 (m, 1H), 2.30 (dd, J = 4.4, 8.1, 1H), 2.20 (t, J = 6.2, 2H), 2.17 – 2.10 (m, 1H), 2.01 (ddd, J = 7.8, 11.6, 15.5, 2H), 1.88 (dq, J = 6.0, 11.8, 1H), 1.78 (dt, J = 6.3, 20.2, 0.5H), 1.67 (td, J = 7.1, 14.5, 0.5H), 1.49 – 1.30 (m, 6H), 1.29 – 1.25 (m, 2H), 1.22 (dd, J = 6.5, 11.0, 3H), 0.71 (dd, J = 3.2, 6.7, 3H); MS (ESI+) *m/z* 559 $(M+H)^+$.

Example 108

3-methyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(2-methylphenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2-phenylbutanamide

The title compound was prepared by substituting 3-*o*-tolylpropanal for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.57 (dd, *J* = 7.2, 14.2, 1H), 7.68 – 7.62 (m, 2H), 7.34 (t, *J* = 7.5, 2H), 7.29 – 7.23 (m, 2H), 7.23 – 7.22 (m, 1H), 7.17 (dd, *J* = 2.6, 3.9, 2H), 4.42 – 4.31 (m, 1H), 3.23 (d, *J* = 10.4, 1H), 2.98 (dd, *J* = 2.3, 8.8, 0.5H), 2.69 – 2.64 (m, 2H), 2.64 – 2.59 (m, 2H), 2.58 – 2.51 (m, 0.5H), 2.51 – 2.45 (m, 0.5H), 2.45 – 2.39 (m, 0.5H), 2.39 – 2.34 (m, 2H), 2.32 (dd, *J* = 2.7, 8.9, 1H), 2.28 (s, 1.5H), 2.25 (s, 1.5H), 2.19 (d, *J* = 8.1, 0.5H), 2.17 – 2.11 (m, 1.5H), 1.93 – 1.85 (m, 1H), 1.84 – 1.77 (m, 0.5H), 1.73 (dd, *J* = 7.6, 15.1, 1H), 1.66 (dt, *J* = 7.4, 9.4, 1.5H), 1.43 (dt, *J* = 7.5, 13.8, 1H), 1.38 – 1.30 (m, 1H), 1.23 (dd, *J* = 6.5, 12.1, 3H), 0.71 (dd, *J* = 2.8, 6.7, 3H); MS (ESI+) *m/z* 419 $(M+H)^+$.

Example 109

***N*-{(3a*R*,4*S*,6a*S*)-2-[3-(3-chlorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 3-(3-chlorophenyl)propanal for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.60 (d, *J* = 4.6, 1H), 7.66 (dd, *J* = 4.3, 7.0, 2H), 7.35 (dd, *J* = 10.9, 18.3, 3H), 7.29 – 7.23 (m, 3H), 7.16 (d, *J* = 6.8, 0.5H), 7.12 (d, *J* = 7.0, 0.5H), 4.41 – 4.31 (m, 1H), 3.24 (d, *J* = 10.4, 1H), 2.98 (d, *J* = 8.9, 0.5H), 2.72 – 2.62 (m, 2H), 2.62 – 2.55 (m, 2H), 2.55 – 2.51 (m, 0.5H), 2.50 – 2.45 (m, 0.5H), 2.43 – 2.37 (m, 0.5H), 2.31 (ddd, *J* = 2.6, 7.2, 12.1, 3H), 2.23 – 2.16 (m, 1H), 2.15 – 2.09 (m, 1H), 1.91 – 1.84 (m, 1H), 1.80 (td, *J* = 6.3, 12.5, 1H), 1.72 (dd, *J* = 7.5, 14.5, 1H), 1.69 – 1.61 (m, 1H), 1.46 – 1.37 (m, 1H), 1.37 – 1.28 (m, 1H), 1.23 (dd, *J* = 6.5, 13.3, 3H), 0.71 (dd, *J* = 3.9, 6.7, 3H); MS (ESI+) *m/z* 439 $(M+H)^+$.

Example 110

3-methyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(3-methylphenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2-phenylbutanamide

The title compound was prepared by substituting 3-*m*-tolylpropanal for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.57 (dd, J = 7.1, 13.5, 1H), 7.65 (dd, J = 4.8, 7.0, 2H), 7.34 (t, J = 7.5, 2H), 7.29 – 7.22 (m, 2H), 7.12 (d, J = 5.9, 1H), 7.09 (d, J = 7.1, 1H), 7.06 – 7.02 (m, 1H), 4.42 – 4.31 (m, 1H), 3.24 (d, J = 10.4, 1H), 2.97 (d, J = 6.8, 0.5H), 2.71 – 2.58 (m, 4H), 2.56 – 2.44 (m, 1H), 2.43 – 2.38 (m, 0.5H), 2.35 (t, J = 6.6, 3H), 2.29 (s, 1.5H), 2.27 (s, 1.5H), 2.27 – 2.23 (m, 1H), 2.17 – 2.11 (m, 1.5H), 1.89 (dt, J = 6.1, 11.8, 1H), 1.79 (dd, J = 7.4, 14.7, 1.5H), 1.72 (dt, J = 7.6, 15.1, 1H), 1.66 (dd, J = 5.9, 13.1, 0.5H), 1.42 (dt, J = 7.5, 12.0, 1H), 1.37 – 1.30 (m, 0.5H), 1.23 (dd, J = 6.5, 11.7, 3H), 0.71 (dd, J = 3.0, 6.6, 3H); MS (ESI+) *m/z* 419 $(M+H)^+$.

Example 111

3-methyl-2-phenyl-*N*-((3a*R*,4*S*,6a*S*)-2-{3-[3-(trifluoromethyl)phenyl]propyl}octahydrocyclopenta[*c*]pyrrol-4-yl)butanamide

The title compound was prepared by substituting 3-(3-(trifluoromethyl)phenyl)propanal for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.61 (d, J = 6.4, 1H), 7.69 – 7.62 (m, 3H), 7.53 (d, J = 6.5, 1H), 7.46 (t, J = 7.8, 1H), 7.42 (d, J = 5.5, 1H), 7.34 (t, J = 7.5, 2H), 7.26 (t, J = 7.3, 1H), 4.37 (tt, J = 6.4, 12.7, 1H), 3.24 (d, J = 10.5, 1H), 3.00 (dd, J = 1.9, 8.9, 0.5H), 2.78 – 2.63 (m, 3H), 2.61 (dd, J = 2.3, 9.1, 0.5H), 2.57 – 2.45 (m, 1H), 2.40 (dd, J = 7.1, 14.3, 0.5H), 2.37 – 2.26 (m, 3H), 2.24 – 2.07 (m, 3H), 1.93 – 1.83 (m, 1H), 1.83 – 1.71 (m, 2H), 1.71 – 1.63 (m, 1H), 1.48 – 1.37 (m, 1H), 1.37 – 1.30 (m, 0.5H), 1.23 (dd, J = 6.5, 13.6, 3H), 0.72 (dd, J = 4.4, 6.6, 3H); MS (ESI+) *m/z* 473 $(M+H)^+$.

Example 112

***N*-{(3a*R*,4*S*,6a*S*)-2-[3-(3-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 3-(3-fluorophenyl)propanal for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.52 (s, 1H), 7.69 – 7.61 (m, 2H), 7.33 (t, *J* = 7.5, 2H), 7.27 (ddd, *J* = 3.5, 7.6, 10.6, 2H), 7.14 – 6.95 (m, 3H), 4.43 – 4.29 (m, 1H), 3.23 (d, *J* = 10.4, 1H), 2.97 (dd, *J* = 2.2, 8.8, 0.5H), 2.72 – 2.58 (m, 3H), 2.57 – 2.44 (m, 1H), 2.44 – 2.38 (m, 0.5H), 2.36 – 2.26 (m, 3H), 2.25 – 2.16 (m, 1H), 2.16 – 2.09 (m, 1H), 1.93 – 1.83 (m, 1H), 1.77 (dt, *J* = 7.2, 14.6, 1.5H), 1.72 – 1.63 (m, 1.5H), 1.47 – 1.27 (m, 2H), 1.22 (dd, *J* = 6.5, 10.4, 3H), 0.94 – 0.83 (m, 1H), 0.71 (dd, *J* = 2.7, 6.7, 3H); MS (ESI+) *m/z* 423 $(M+H)^+$.

Example 113

3-methyl-2-phenyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(4-phenylbutyl)octahydrocyclopenta[*c*]pyrrol-4-yl]butanamide

The title compound was prepared by substituting 4-phenylbutanal for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.58 (dd, *J* = 9.0, 16.5, 1H), 7.66 (t, *J* = 6.4, 2H), 7.34 (t, *J* = 5.6, 4H), 7.29 – 7.22 (m, 4H), 4.39 – 4.29 (m, 1H), 3.24 (d, *J* = 10.4, 1H), 2.91 (dd, *J* = 2.4, 9.0, 0.5H), 2.66 (ddd, *J* = 6.5, 10.6, 13.1, 1H), 2.57 (ddd, *J* = 5.3, 12.3, 17.7, 3H), 2.51 – 2.45 (m, 1H), 2.43 – 2.29 (m, 3H), 2.26 (dd, *J* = 3.0, 8.8, 0.5H), 2.24 – 2.08 (m, 2H), 1.91 – 1.83 (m, 1H), 1.81 – 1.72 (m, 1H), 1.71 – 1.58 (m, 2H), 1.49 (dt, *J* = 7.8, 15.9, 1H), 1.41 (dt, *J* = 6.9, 17.2, 2H), 1.31 (ddd, *J* = 6.7, 13.2, 20.5, 1H), 1.23 (dd, *J* = 6.5, 13.0, 3H), 0.71 (dd, *J* = 2.6, 6.6, 3H); MS (ESI+) *m/z* 419 $(M+H)^+$.

Example 114

***N*-{(3a*R*,4*S*,6a*S*)-2-[3-(3-chloro-5-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 3-(3-chloro-5-fluorophenyl)propanal for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-

octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.61 (d, *J* = 7.4, 1H), 7.66 (dd, *J* = 3.2, 7.5, 2H), 7.35 (dd, *J* = 7.5, 15.0, 2H), 7.25 (dd, *J* = 6.1, 13.7, 2H), 7.12 (d, *J* = 7.5, 1H), 7.06 – 6.95 (m, 1H), 4.43 – 4.31 (m, 1H), 3.24 (d, *J* = 10.4, 1H), 3.01 (dd, *J* = 1.3, 8.7, 0.5H), 2.73 – 2.64 (m, 1H), 2.62 (dd, *J* = 6.0, 9.0, 1H), 2.59 – 2.54 (m, 1H), 2.53 – 2.45 (m, 1H), 2.43 – 2.38 (m, 0.5H), 2.37 – 2.25 (m, 3H), 2.24 – 2.06 (m, 3H), 1.93 – 1.76 (m, 2H), 1.75 – 1.58 (m, 2H), 1.47 – 1.28 (m, 2H), 1.23 (dd, *J* = 6.5, 14.4, 3H), 0.72 (dd, *J* = 5.0, 6.2, 3H); MS (ESI+) *m/z* 457 $(M+H)^+$.

Example 115

3-methyl-2-phenyl-*N*-((3a*R*,4*S*,6a*S*)-2-{3-[4-(trifluoromethyl)phenyl]propyl}octahydrocyclopenta[*c*]pyrrol-4-yl)butanamide

The title compound was prepared by substituting 3-(4-(trifluoromethyl)phenyl)propanal for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.69 – 7.62 (m, 4H), 7.39 (d, *J* = 8.0, 1H), 7.37 – 7.32 (m, 3H), 7.26 (t, *J* = 7.3, 1H), 4.41 – 4.33 (m, 1H), 3.25 (d, *J* = 10.5, 1H), 3.00 (dd, *J* = 2.2, 9.0, 0.5H), 2.76 – 2.59 (m, 3H), 2.56 – 2.46 (m, 1H), 2.44 – 2.39 (m, 0.5H), 2.37 (dd, *J* = 2.1, 8.9, 0.5H), 2.31 (dt, *J* = 5.8, 14.1, 2H), 2.23 – 2.07 (m, 3H), 1.94 – 1.71 (m, 2.5H), 1.67 (ddd, *J* = 5.6, 7.9, 11.8, 1H), 1.47 – 1.28 (m, 2H), 1.23 (dd, *J* = 6.5, 13.1, 3H), 0.89 (dt, *J* = 7.2, 24.8, 1H), 0.72 (dd, *J* = 3.7, 6.7, 3H); MS (ESI+) *m/z* 473 $(M+H)^+$.

Example 116

***N*-[(3a*R*,4*S*,6a*S*)-2-(3,3-diphenylpropyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 3,3-diphenylpropanal for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.59 (dd, *J* = 2.9, 7.0, 1H), 7.65 (d, *J* = 8.1, 2H), 7.46 (d, *J* = 7.2, 1H), 7.44 – 7.37 (m, 4H), 7.33 (tt, *J* = 3.7, 7.7, 6H), 7.28 – 7.24 (m, 1H), 7.23 –

7.18 (m, 1H), 4.44 – 4.34 (m, 1H), 4.28 (d, J = 7.2, 1H), 4.20 (dd, J = 5.4, 9.1, 1H), 3.24 (d, J = 10.4, 1H), 2.93 (dd, J = 2.4, 9.0, 0.5H), 2.71 – 2.61 (m, 1H), 2.56 (dd, J = 2.7, 9.2, 0.5H), 2.54 – 2.50 (m, 0.5H), 2.50 – 2.43 (m, 0.5H), 2.43 – 2.36 (m, 0.5H), 2.35 – 2.28 (m, 3H), 2.24 (tt, J = 5.1, 10.0, 2H), 2.18 – 2.07 (m, 2H), 1.94 – 1.83 (m, 1H), 1.82 – 1.74 (m, 0.5H), 1.68 (td, J = 7.0, 14.3, 0.5H), 1.47 – 1.37 (m, 1H), 1.37 – 1.29 (m, 0.5H), 1.22 (dd, J = 4.6, 6.4, 3H), 0.71 (dd, J = 1.7, 6.7, 3H); MS (ESI+) m/z 481 $(M+H)^+$.

Example 117

N-{(3aR,4S,6aS)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[c]pyrrol-4-yl}-3-methyl-2-phenylbutanamide

The title compound was prepared by substituting 3,3-bis(4-fluorophenyl)propanal for 3-(trifluoromethyl)benzaldehyde and 3-methyl-N-[(3aR,4S,6aS)-octahydrocyclopenta[c]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-N-[(3aS,4S,6aR)-octahydrocyclopenta[c]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.62 (d, J = 5.3, 1H), 7.65 (d, J = 7.3, 2H), 7.42 (dd, J = 5.6, 8.6, 1H), 7.39 – 7.29 (m, 5H), 7.26 (td, J = 5.3, 7.2, 1H), 7.19 – 7.09 (m, 4H), 4.47 – 4.37 (m, 1H), 4.29 (t, J = 7.7, 0.5H), 4.21 (t, J = 7.6, 0.5H), 3.24 (d, J = 10.4, 1H), 3.02 (dd, J = 1.2, 8.9, 0.5H), 2.71 – 2.60 (m, 1H), 2.57 – 2.46 (m, 1H), 2.44 – 2.30 (m, 3H), 2.27 – 2.20 (m, 2H), 2.19 – 2.09 (m, 4H), 1.90 (dq, J = 6.0, 17.7, 1H), 1.81 (dq, J = 6.2, 18.7, 0.5H), 1.67 (ddd, J = 7.6, 12.3, 14.8, 0.5H), 1.48 – 1.38 (m, 1H), 1.38 – 1.30 (m, 0.5H), 1.22 (dd, J = 2.5, 6.5, 3H), 0.71 (dd, J = 1.4, 6.7, 3H); MS (ESI+) m/z 517 $(M+H)^+$.

Example 118

N-{(3aR,4S,6aS)-2-[4,4-bis(4-fluorophenyl)butyl]octahydrocyclopenta[c]pyrrol-4-yl}-3-methyl-2-phenylbutanamide

The title compound was prepared by substituting 4,4-bis(4-fluorophenyl)butanal for 3-(trifluoromethyl)benzaldehyde and 3-methyl-N-[(3aR,4S,6aS)-octahydrocyclopenta[c]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-N-[(3aS,4S,6aR)-octahydrocyclopenta[c]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.61 (d, J = 7.0, 1H), 7.66 (dd, J = 5.3, 7.0, 2H), 7.44 – 7.31 (m, 6H), 7.26 (t, J = 7.4, 1H), 7.19 – 7.08 (m, 4H), 4.41 – 4.30 (m, 1H), 4.03 – 3.92 (m, 1H), 3.24 (d, J = 10.4, 1H), 2.95 (dd, J = 2.3, 8.9, 0.5H), 2.67 (ddd, J = 6.6, 13.3, 17.1, 1H), 2.56 (dd, J = 2.8, 9.1, 0.5H), 2.54 – 2.43 (m, 1H), 2.42 –

2.30 (m, 2H), 2.29 – 2.20 (m, 2.5H), 2.19 – 2.02 (m, 4H), 1.90 – 1.72 (m, 1.5H), 1.65 (dt, *J* = 7.1, 19.2, 0.5H), 1.52 – 1.34 (m, 3H), 1.34 – 1.26 (m, 0.5H), 1.23 (dd, *J* = 6.5, 15.3, 3H), 0.71 (dd, *J* = 5.0, 6.5, 3H); MS (ESI+) *m/z* 531 $(M+H)^+$.

Example 119

***N*-{(3a*R*,4*S*,6a*S*)-2-[5,5-bis(4-fluorophenyl)pentyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide**

The title compound was prepared by substituting 5,5-bis(4-fluorophenyl)pentanal for 3-(trifluoromethyl)benzaldehyde and 3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.61 (s, 1H), 7.66 (dd, *J* = 4.3, 7.3, 2H), 7.37 – 7.30 (m, 5H), 7.25 (dd, *J* = 5.6, 13.1, 2H), 7.19 – 7.11 (m, 4H), 4.38 – 4.29 (m, 1H), 3.96 (dd, *J* = 7.9, 18.0, 1H), 3.25 (d, *J* = 10.5, 1H), 2.96 (d, *J* = 10.4, 0.5H), 2.72 – 2.62 (m, 1H), 2.62 – 2.57 (m, .50H), 2.56 – 2.51 (m, 0.5H), 2.50 – 2.45 (m, 0.5H), 2.43 – 2.36 (m, 1H), 2.36 – 2.31 (m, 1H), 2.30 – 2.26 (m, 1H), 2.23 – 2.06 (m, 3H), 2.07 – 1.96 (m, 2H), 1.86 (dt, *J* = 6.0, 12.2, 1H), 1.81 – 1.72 (m, 1H), 1.66 (dt, *J* = 7.0, 19.1, 1H), 1.56 – 1.49 (m, 1H), 1.48 – 1.40 (m, 1H), 1.38 – 1.26 (m, 3H), 1.23 (dd, *J* = 6.5, 9.7, 3H), 0.71 (dd, *J* = 2.5, 6.7, 3H); MS (ESI+) *m/z* 545 $(M+H)^+$.

Example 120

***N*-[(3a*S*,4*S*,6aR)-2-benzhydryloctahydrocyclopenta[c]pyrrol-4-yl]-2,2-dicyclohexylacetamide**

Potassium iodide (12.48 mg, 0.075 mmol) and sodium carbonate (80 mg, 0.752 mmol) were combined with methyl ethyl ketone (5mL) and then 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide (200 mg, 0.601 mmol) from Example 53 was added followed by the addition of (bromomethylene)dibenzene (124 mg, 0.501 mmol). The reaction was heated overnight at 90 °C. The reaction mixture was concentrated with a stream of nitrogen and then purified by silica gel chromatography eluting with 2-10% methanol (2 *N* ammonia)/dichloromethane to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.74 (dd, *J* = 6.7, 15.4, 1H), 7.61 (t, *J* = 6.7, 3H), 7.35 (t, *J* = 7.6, 4H), 7.28 – 7.23 (m, 3H), 4.42 (dt, *J* = 7.4, 14.4, 1H), 4.16 (s, 1H), 2.96 (qd, *J* = 4.2, 8.0, 1H), 2.63 (dd, *J* = 4.1, 9.8, 1H), 2.57 – 2.48 (m, 1H), 2.42 (dt, *J* = 9.4, 14.6, 2H), 2.33 (dd, *J* = 3.7, 9.3, 1H), 2.09 – 1.90 (m, 3H), 1.90 – 1.80 (m, 3H), 1.79 – 1.70 (m, 4H), 1.69 – 1.55

(m, 6H), 1.46 (d, J = 14.7, 1H), 1.39 (s, 1H), 1.33 – 1.00 (m, 8H), 1.00 – 0.89 (m, 1H); MS (ESI+) m/z 499 $(M+H)^+$.

Example 121

N-[(3aS,4R,6aR)-2-benzhydryloctahydrocyclopenta[c]pyrrol-4-yl]-2,2-dicyclohexylacetamide

The title compound was prepared by substituting 2,2-dicyclohexyl-N-[(3aS,4R,6aR)-octahydrocyclopenta[c]pyrrol-4-yl]acetamide from Example 74 for 2,2-dicyclohexyl-N-[(3aS,4S,6aR)-octahydrocyclopenta[c]pyrrol-4-yl]acetamide in the procedure described for Example 120: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.11 (d, J = 7.2, 1H), 7.64 (d, J = 7.1, 2H), 7.32 (t, J = 7.6, 4H), 7.20 – 7.15 (m, 4H), 4.55 – 4.48 (m, 1H), 4.21 (s, 1H), 2.81 (dd, J = 2.9, 9.4, 1H), 2.63 – 2.57 (m, 1H), 2.57 – 2.51 (m, 1H), 2.41 (dd, J = 7.0, 9.2, 1H), 2.36 – 2.24 (m, 3H), 2.01 (t, J = 7.4, 1H), 1.99 – 1.90 (m, 3H), 1.86 (ddd, J = 3.3, 8.1, 15.4, 2H), 1.82 – 1.76 (m, 2H), 1.70 (ddd, J = 8.9, 13.9, 15.3, 5H), 1.63 – 1.55 (m, 2H), 1.51 – 1.37 (m, 3H), 1.28 – 1.01 (m, 8H); MS (ESI+) m/z 499 $(M+H)^+$.

Example 122

3-methyl-2-phenyl-N-{(3aS*,4S*,6aR*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[c]pyrrol-4-yl}butanamide

Step A: (3-(Trifluoromethyl)phenyl)methanamine (25 g, 143 mmol), (chloromethyl)trimethylsilane (19.92 mL, 143 mmol), and triethylamine (23.87 mL, 171 mmol) were combined neat and the resultant mixture was refluxed overnight. The reaction was cooled to room temperature and 150 mL of heptane was added. The HCl salts were removed by filtration and washed with heptane. The solvent was removed by placing under house vacuum and then high vacuum. N-(3-(Trifluoromethyl)benzyl)-1-(trimethylsilyl)methanamine was isolated by vacuum distillation (bp 70-90 °C/3.2 torr): ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.59 (s, 1H), 7.53 – 7.38 (m, 3H), 3.86 (s, 2H), 2.04 (s, 2H), 1.34 (s, 1H), 0.06 (s, 9H).

Step B: Formaldehyde (4.08 g, 50.2 mmol) and methanol (2.032 mL, 50.2 mmol) were combined, and the mixture was cooled to 0 °C (ice bath). N-(3-(trifluoromethyl)benzyl)-1-(trimethylsilyl)methanamine (10.94 g, 41.9 mmol) was added dropwise via addition funnel over 30 minutes. Potassium carbonate (4.63 g, 33.5 mmol) was added, and the reaction stirred at 0 °C for 2 additional hours. The reaction product was decanted from the potassium carbonate, treated with more potassium carbonate, and decanted

again. The potassium carbonate solids were washed several times with ether, and these washes were added to the product solution. The solvent was removed in vacuo to give 1-methoxy-*N*-(3-(trifluoromethyl)benzyl)-*N*-((trimethylsilyl)methyl)methanamine which was used directly in the next step.

Step C: Cyclopent-2-enone (3.31 g, 40.4 mmol) and trifluoroacetic acid (0.031 mL, 0.404 mmol) were combined in dichloromethane (40 mL). 1-Methoxy-*N*-(3-(trifluoromethyl)benzyl)-*N*-((trimethylsilyl)methyl)methanamine (12.33 g, 40.4 mmol) from Step B was added as a solution in 10 mL of dichloromethane dropwise via addition funnel over 45 minutes at room temperature under nitrogen. The reaction was quenched with aqueous sodium bicarbonate and extracted with 2×100 mL of dichloromethane. The organic washes were combined and washed with brine. The solvent was removed in vacuo to give 2-(3-(trifluoromethyl)benzyl)hexahydrocyclopenta[*c*]pyrrol-4(5*H*)-one: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.54 – 7.34 (m, 4H), 3.66 (d, *J* = 13.4, 1H), 3.52 (d, *J* = 13.4, 1H), 3.04 (dd, *J* = 1.8, 8.9, 1H), 2.91 (ddd, *J* = 2.8, 7.4, 11.7, 1H), 2.72 – 2.65 (m, 1H), 2.62 (d, *J* = 8.9, 1H), 2.52 – 2.23 (m, 4H), 2.15 (ddd, *J* = 8.1, 12.9, 17.1, 1H), 1.85 – 1.70 (m, 1H).

Step D: Hydroxylamine hydrochloride (3.47 g, 50.0 mmol) and sodium acetate (4.27 g, 52.0 mmol) were dissolved in 15 mL of water and added to a solution of 2-(3-(trifluoromethyl)benzyl)hexahydrocyclopenta[*c*]pyrrol-4(5*H*)-one (11.33 g, 40 mmol) from Step C in ethanol (80 mL). The reaction was brought to reflux for 5 minutes and allowed to cool to 70 °C. After 1 hour, the reaction mixture was cooled, and the solvent was removed in vacuo to give (*E*)-2-(3-(trifluoromethyl)benzyl)hexahydrocyclopenta[*c*]pyrrol-4(5*H*)-one oxime which was used without additional purification in the next step.

Step E: (*E*)-2-(3-(Trifluoromethyl)benzyl)hexahydrocyclopenta[*c*]pyrrol-4(5*H*)-one oxime (11.9 g, 39.9 mmol) from Step D in 20% ammonia-methanol (115 mL) was added to methanol-washed Raney®-nickel, (water-wet, 38.52 g, 295 mmol) in a 500 mL pressure bottle. The vessel was pressurized with hydrogen (30 psi), and the mixture was shaken for 16 hours at ambient temperature. The mixture was filtered through a nylon membrane, the solvent was removed in vacuo, and the crude material was adsorbed onto silica gel. Silica gel chromatography using a cartridge (Analogix®, Burlington, Wisconsin, SF65-400) eluting with 1-10% methanol (2 *N* ammonia)/dichloromethane gave the following diastereomers. (3a*S**,4*R**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine: ^{1}H NMR (300 MHz, pyridine-d_5) δ ppm 7.58 (s, 1H), 7.50 (t, *J* = 6.7, 2H), 7.45 – 7.37 (m, 1H), 3.59 (s, 2H), 3.26 (dt, *J* = 6.3, 12.6, 1H), 2.67 – 2.50 (m, 4H), 2.38 (dd, *J* = 6.6, 8.4, 1H), 2.31 – 2.20 (m, 1H), 1.79 – 1.62 (m, 2H), 1.60 – 1.33 (m, 4H); and

(3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine: ^{1}H NMR (300 MHz, pyridine-d_5) δ ppm 7.58 (s, 1H), 7.50 (t, *J* = 7.2, 2H), 7.45 – 7.37 (m, 1H), 3.59 (s, 2H), 3.09 (dd, *J* = 4.9, 11.4, 1H), 2.77 – 2.57 (m, *J* = 3.9, 1H), 2.52 – 2.38 (m, 3H), 2.34 (dd, *J* = 3.7, 9.0, 1H), 2.22 – 2.09 (m, 1H), 2.03 – 1.85 (m, *J* = 4.7, 7.0, 10.8, 2H), 1.42 – 1.21 (m, 4H).

Step F: The title compound was prepared by substituting 3-methyl-2-phenylbutanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in Example 1: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.23 (d, *J* = 6.9, 0.5H), 8.13 (d, *J* = 7.1, 0.5H), 7.73 (s, 0.5H), 7.67 (s, 0.5H), 7.63 (dd, *J* = 6.7, 8.0, 2H), 7.56 – 7.53 (m, 1H), 7.50 (t, *J* = 8.5, 2H), 7.38 – 7.22 (m, 3H), 4.45 – 4.38 (m, 0.5H), 4.33 – 4.26 (m, 0.5H), 3.50 (s, 1H), 3.44 (d, *J* = 13.4, 0.5H), 3.21 (d, *J* = 13.4, 0.5H), 3.17 (d, *J* = 10.5, 0.5H), 3.10 (d, *J* = 10.5, 0.5H), 2.91 (qd, *J* = 3.4, 7.9, 0.5H), 2.79 (dd, *J* = 3.4, 9.5, 0.5H), 2.74 – 2.56 (m, 1.5H), 2.47 – 2.31 (m, 2.5H), 2.27 (dd, *J* = 3.1, 8.9, 0.5H), 2.21 (d, *J* = 2.7, 0.5H), 1.98 – 1.93 (m, 0.5H), 1.89 – 1.79 (m, 0.5H), 1.74 – 1.56 (m, 1.5H), 1.53 – 1.46 (m, 0.5H), 1.46 – 1.39 (m, 0.5H), 1.30 – 1.23 (m, 1H), 1.19 (d, *J* = 6.5, 1.5H), 1.17 – 1.11 (m, 0.5H), 1.08 (d, *J* = 6.5, 1.5H), 0.72 (dd, *J* = 6.7, 9.6, 3H); MS (ESI+) *m/z* 445 $(M+H)^+$.

Example 123

3,3-dimethyl-2-phenyl-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[c]pyrrol-4-yl}butanamide

The title compound was prepared by substituting 3,3-dimethyl-2-phenylbutanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 1: ^{1}H *N*MR (500 MHz, pyridine-d_5) δ ppm 8.32 (d, *J* = 6.7, 0.5H), 8.13 (d, *J* = 7.1, 0.5H), 7.74 – 7.70 (m, 1H), 7.69 – 7.66 (m, 1H), 7.61 (t, *J* = 8.6, 3H), 7.48 – 7.43 (m, 1H), 7.37 – 7.24 (m, 3H), 4.48 – 4.39 (m, 0.5H), 4.36 – 4.28 (m, 0.5H), 3.51 (q, *J* = 13.1, 0.5H), 3.41 (d, *J* = 17.1, 1H), 3.35 (d, *J* = 13.3, 0.5H), 3.13 (d, *J* = 13.4, 0.5H), 2.98 (qd, *J* = 4.0, 8.2, 0.5H), 2.81 (dd, *J* = 3.9, 9.5, 0.5H), 2.74 (ddd, *J* = 3.4, 7.8, 16.6, 0.5H), 2.49 – 2.37 (m, 2H), 2.31 (dd, *J* = 3.4, 9.6, 0.5H), 2.24 – 2.15 (m, 2H), 2.01 – 1.94 (m, 0.5H), 1.84 (ddd, *J* = 8.1, 11.7, 14.5, 0.5H), 1.73 – 1.65 (m, 1H), 1.64 – 1.56 (m, 0.5H), 1.52 – 1.38 (m, 1H), 1.27 (dt, *J* = 5.6, 12.2, 1H), 1.16 (s, 4.5H), 1.11 (s, 4.5H); MS (ESI+) *m/z* 459 $(M+H)^+$.

Example 124

2,2-dicyclohexyl-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide**

The title compound was prepared by substituting 2,2-dicyclohexylacetic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 1: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.73 (s, 1H), 7.65 (d, J = 7.6, 1H), 7.57 – 7.44 (m, 3H), 4.46 (dt, J = 6.4, 12.6, 1H), 3.55 (d, J = 12.9, 1H), 3.47 (d, J = 12.8, 1H), 2.75 (d, J = 8.1, 2H), 2.53 – 2.39 (m, 2H), 2.32 (t, J = 8.2, 1H), 2.21 (t, J = 8.3, 1H), 1.97 – 1.53 (m, 15H), 1.50 – 1.04 (m, 11H), 0.98 (dd, J = 11.3, 23.1, 1H); MS (ESI+) *m/z* 491 $(M+H)^+$.

Example 125

2-ethyl-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide**

The title compound was prepared by substituting 2-ethylbutanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 1: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.90 (d, J = 6.7, 1H), 7.71 (s, 1H), 7.61 (d, J = 7.7, 1H), 7.54 (d, J = 7.7, 1H), 7.46 (t, J = 7.7, 1H), 4.51 – 4.43 (m, 1H), 3.49 (s, 2H), 2.83 (ddd, J = 2.9, 7.8, 16.8, 1H), 2.75 (dd, J = 2.9, 9.5, 1H), 2.52 – 2.43 (m, 1H), 2.37 (dd, J = 2.9, 9.1, 1H), 2.35 – 2.30 (m, 1H), 2.25 (dd, J = 7.6, 9.4, 1H), 2.01 (tt, J = 4.8, 9.5, 1H), 1.89 (dt, J = 7.3, 11.6, 1H), 1.77 (ddt, J = 7.5, 9.3, 15.2, 2H), 1.70 – 1.60 (m, 2H), 1.51 – 1.37 (m, 2H), 1.34 – 1.26 (m, 1H), 0.95 (t, J = 7.4, 3H), 0.83 (t, J = 7.4, 3H); MS (ESI+) *m/z* 383 $(M+H)^+$.

Example 126

2-propyl-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}pentanamide**

The title compound was prepared by substituting 2-propylpentanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-

(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 1: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.94 (d, *J* = 6.9, 1H), 7.72 (s, 1H), 7.62 (d, *J* = 7.7, 1H), 7.56 (d, *J* = 7.7, 1H), 7.47 (t, *J* = 7.7, 1H), 4.48 (dt, *J* = 7.3, 14.6, 1H), 3.52 (d, *J* = 13.0, 1H), 3.48 (d, *J* = 13.0, 1H), 2.84 (ddd, *J* = 3.0, 7.7, 16.7, 1H), 2.74 (dd, *J* = 3.1, 9.5, 1H), 2.52 – 2.45 (m, 1H), 2.38 – 2.34 (m, 2H), 2.27 (dd, *J* = 7.6, 9.5, 1H), 2.22 (td, *J* = 4.6, 9.5, 1H), 1.90 (dt, *J* = 7.3, 11.5, 1H), 1.84 – 1.75 (m, 2H), 1.73 – 1.61 (m, 2H), 1.48 – 1.27 (m, 6H), 1.20 – 1.08 (m, 1H), 0.88 (t, *J* = 7.0, 3H), 0.83 (t, *J* = 7.1, 3H); MS (ESI+) *m/z* 411 $(M+H)^+$.

Example 127

***N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}cyclohexanecarboxamide**

The title compound was prepared by substituting cyclohexanecarboxylic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 1: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.74 (d, *J* = 6.1, 1H), 7.71 (s, 1H), 7.62 (d, *J* = 7.7, 1H), 7.57 (d, *J* = 9.2, 1H), 7.47 (t, *J* = 7.7, 1H), 4.48 – 4.41 (m, 1H), 3.53 (d, *J* = 13.2, 1H), 3.47 (d, *J* = 13.2, 1H), 2.84 (ddd, *J* = 2.8, 7.9, 10.3, 1H), 2.75 (dd, *J* = 2.8, 9.5, 1H), 2.51 – 2.43 (m, 1H), 2.37 (dd, *J* = 2.8, 9.1, 1H), 2.34 – 2.29 (m, 1H), 2.27 – 2.19 (m, 2H), 1.94 – 1.83 (m, 2H), 1.80 (d, *J* = 12.9, 1H), 1.73 – 1.60 (m, 6H), 1.57 – 1.51 (m, 1H), 1.35 – 1.27 (m, 1H), 1.22 – 1.10 (m, 3H); MS (ESI+) *m/z* 395 $(M+H)^+$.

Example 128

***N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}cycloheptanecarboxamide**

The title compound was prepared by substituting cycloheptanecarboxylic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 1: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.79 (d, *J* = 6.9, 1H), 7.71 (s, 1H), 7.62 (d, *J* = 7.7, 1H), 7.56 (s, 1H), 7.47 (t, *J* = 7.7, 1H), 4.48 – 4.40 (m, 1H), 3.54 (d, *J* = 13.2, 1H), 3.46 (d, *J* = 13.2, 1H), 2.86 (ddd, *J* = 3.0, 7.8, 16.6, 1H), 2.76 (dd, *J* = 3.0, 9.5, 1H), 2.51

– 2.39 (m, 2H), 2.37 – 2.30 (m, 2H), 2.26 (dd, J = 7.5, 9.4, 1H), 2.00 – 1.80 (m, 5H), 1.75 – 1.60 (m, 4H), 1.49 – 1.41 (m, 4H), 1.33 (ddt, J = 7.2, 8.9, 12.1, 3H); MS (ESI+) *m/z* 409 $(M+H)^+$.

Example 129

***N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}cyclopentanecarboxamide**

The title compound was prepared by substituting cyclopentanecarboxylic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 1: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.82 (d, J = 6.9, 1H), 7.71 (s, 1H), 7.61 (d, J = 7.7, 1H), 7.55 (d, J = 7.7, 1H), 7.46 (t, J = 7.7, 1H), 4.48 – 4.41 (m, 1H), 4.07 (q, J = 7.1, 1H), 2.82 (ddd, J = 2.9, 7.8, 16.7, 1H), 2.72 (dd, J = 2.9, 9.5, 1H), 2.66 (p, J = 7.9, 1H), 2.50 – 2.42 (m, 1H), 2.37 (dd, J = 2.9, 9.0, 1H), 2.34 – 2.29 (m, 1H), 2.21 (dd, J = 7.5, 9.4, 1H), 2.03 (dt, J = 7.0, 15.3, 1H), 1.86 (dddd, J = 7.4, 12.3, 20.5, 23.4, 3H), 1.75 – 1.60 (m, 5H), 1.53 – 1.41 (m, 2H), 1.30 (td, J = 4.7, 11.1, 1H), 1.11 (t, J = 7.1, 1H); MS (ESI+) *m/z* 381 $(M+H)^+$.

Example 130

6,6-bis(4-fluorophenyl)-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}hexanamide**

The title compound was prepared by substituting 6,6-bis(4-fluorophenyl)hexanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 1: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.99 (d, J = 7.1, 1H), 7.69 (s, 1H), 7.58 (s, 1H), 7.54 (d, J = 7.6, 1H), 7.42 (dd, J = 6.9, 14.5, 1H), 7.26 (dd, J = 5.5, 8.6, 4H), 7.14 – 7.08 (m, 4H), 4.51 – 4.41 (m, 1H), 3.91 (t, J = 7.8, 1H), 3.47 (d, J = 2.3, 2H), 2.84 (qd, J = 3.0, 8.0, 1H), 2.69 (dd, J = 3.1, 9.5, 1H), 2.53 – 2.43 (m, 1H), 2.38 – 2.20 (m, 5H), 1.99 (dd, J = 7.8, 15.6, 2H), 1.89 – 1.78 (m, 3H), 1.70 – 1.59 (m, 2H), 1.37 – 1.25 (m, 3H); MS (ESI+) *m/z* 571 $(M+H)^+$.

Example 131

3,3-diphenyl-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}propanamide**

The title compound was prepared by substituting 3,3-diphenylpropanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 1: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.10 (d, J = 7.0, 1H), 7.72 (s, 1H), 7.62 (d, J = 7.8, 1H), 7.48 (t, J = 7.7, 1H), 7.39 (dd, J = 2.6, 7.5, 5H), 7.26 (dt, J = 7.6, 15.1, 5H), 7.17 (dd, J = 6.2, 13.5, 2H), 4.38 – 4.27 (m, 1H), 3.54 (d, J = 13.4, 1H), 3.38 (d, J = 13.4, 1H), 3.15 – 3.09 (m, 2H), 2.75 (qd, J = 3.6, 7.9, 1H), 2.44 – 2.35 (m, 2H), 2.32 (t, J = 8.3, 1H), 2.20 (dd, J = 3.3, 8.9, 1H), 2.08 (dd, J = 7.8, 9.5, 1H), 1.70 (t, J = 7.9, 1H), 1.58 – 1.46 (m, 2H), 1.18 – 1.10 (m, 1H); MS (ESI+) *m/z* 493 $(M+H)^+$.

Example 132

5,5-bis(4-fluorophenyl)-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}pentanamide**

The title compound was prepared by substituting 5,5-bis(4-fluorophenyl)pentanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 1: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.06 (d, J = 7.0, 1H), 7.70 (s, 1H), 7.60 (d, J = 8.0, 1H), 7.54 (d, J = 7.7, 1H), 7.44 (t, J = 7.7, 1H), 7.26 (dd, J = 5.6, 8.4, 4H), 7.08 (td, J = 1.2, 8.8, 4H), 4.51 – 4.42 (m, 1H), 3.96 (t, J = 7.8, 1H), 2.86 (qd, J = 3.2, 7.9, 1H), 2.69 (dd, J = 3.2, 9.5, 1H), 2.52 – 2.43 (m, 1H), 2.43 – 2.29 (m, 5H), 2.24 (dd, J = 7.7, 9.4, 1H), 2.15 – 2.06 (m, 3H), 1.85 (dt, J = 9.9, 17.8, 1H), 1.76 (dt, J = 7.3, 15.3, 2H), 1.70 – 1.59 (m, 2H), 1.33 – 1.26 (m, 1H); MS (ESI+) *m/z* 557 $(M+H)^+$.

Example 133

3,3-bis(4-fluorophenyl)-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}propanamide**

The title compound was prepared by substituting 3,3-bis(4-fluorophenyl)propanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for

(3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 1: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.13 (d, *J* = 7.0, 1H), 7.71 (s, 1H), 7.61 (d, *J* = 7.7, 1H), 7.56 (s, 1H), 7.47 (t, *J* = 7.7, 1H), 7.32 (ddd, *J* = 3.7, 5.4, 8.8, 4H), 7.11 – 7.02 (m, 4H), 4.94 (d, *J* = 8.0, 1H), 4.39 – 4.25 (m, 1H), 3.52 (d, *J* = 13.4, 1H), 3.41 (d, *J* = 13.4, 1H), 3.06 (d, *J* = 7.9, 2H), 2.76 (qd, *J* = 3.4, 7.9, 1H), 2.43 (dd, *J* = 3.3, 9.5, 2H), 2.31 (t, *J* = 8.3, 1H), 2.23 (dd, *J* = 3.1, 9.0, 1H), 2.10 (dd, *J* = 7.8, 9.4, 1H), 1.76 – 1.67 (m, 1H), 1.59 – 1.49 (m, 2H), 1.22 – 1.11 (m, 1H); MS (ESI+) *m/z* 529 $(M+H)^+$.

Example 134

4,4-bis(4-fluorophenyl)-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[c]pyrrol-4-yl}butanamide**

The title compound was prepared by substituting 4,4-bis(4-fluorophenyl)butanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 1: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.16 (d, *J* = 6.9, 1H), 7.66 (s, 1H), 7.58 (s, 1H), 7.50 (d, *J* = 7.7, 1H), 7.38 (t, *J* = 7.7, 1H), 7.28 (dd, *J* = 5.5, 7.3, 4H), 7.10 – 7.02 (m, 4H), 4.49 (dt, *J* = 7.6, 14.7, 1H), 4.10 (t, *J* = 7.9, 1H), 3.50 (d, *J* = 13.4, 1H), 3.42 (d, *J* = 13.4, 1H), 2.92 (qd, *J* = 3.6, 7.9, 1H), 2.67 (dd, *J* = 3.5, 9.5, 1H), 2.55 (dd, *J* = 7.2, 15.0, 2H), 2.52 – 2.46 (m, 1H), 2.40 (t, *J* = 8.3, 1H), 2.36 – 2.24 (m, 4H), 1.91 – 1.82 (m, 1H), 1.71 (td, *J* = 5.8, 11.3, 1H), 1.67 – 1.60 (m, 1H), 1.35 – 1.27 (m, 1H); MS (ESI+) *m/z* 543 $(M+H)^+$.

Example 135

2,2-diphenyl-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide**

The title compound was prepared by substituting 2,2-diphenylacetic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 1: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.50 (s, 1H), 7.71 (d, *J* = 7.5, 2H), 7.63 (d, *J* = 7.2, 2H), 7.45 (d, *J* = 7.4, 2H), 7.39 – 7.28 (m, 5H), 7.25 (dd, *J* = 5.8, 8.9, 3H), 4.51 – 4.42 (m, 1H), 3.44 (d, *J* = 13.3, 1H), 3.25 (d, *J* = 13.3, 1H), 2.85 (qd, *J* = 3.2, 7.9, 1H), 2.59 (dd, *J* = 3.4, 9.5, 1H), 2.47 – 2.37 (m, 1H), 2.26 (t, *J* = 8.3, 1H), 2.21 – 2.13 (m, 2H), 1.85 – 1.76 (m, 1H), 1.67 – 1.52 (m, 3H), 1.27 – 1.18 (m, 1H); MS (ESI+) *m/z* 479 $(M+H)^+$.

Example 136

2,2-bis(4-fluorophenyl)-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide**

The title compound was prepared by substituting 2,2-bis(4-fluorophenyl)acetic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 1: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.68 (d, J = 7.0, 1H), 7.64 (s, 1H), 7.60 (t, J = 6.4, 1H), 7.57 – 7.54 (m, 2H), 7.52 – 7.43 (m, 4H), 7.17 – 7.07 (m, 4H), 4.48 – 4.41 (m, 1H), 3.46 (d, J = 13.3, 1H), 3.30 (d, J = 13.3, 1H), 2.90 (qd, J = 3.5, 8.0, 1H), 2.59 (dd, J = 3.5, 9.5, 1H), 2.50 – 2.42 (m, 1H), 2.32 (t, J = 8.3, 1H), 2.25 – 2.19 (m, 3H), 1.87 – 1.77 (m, 1H), 1.66 (td, J = 5.7, 11.4, 1H), 1.62 – 1.54 (m, 1H), 1.29 – 1.20 (m, 1H); MS (ESI+) *m/z* 515 $(M+H)^+$.

Example 137

N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*R,4*R**,6a*S**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-L-leucine for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in Example the procedure described for Example 1: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.50 (d, J = 7.1, 0.5H), 8.46 (d, J = 6.8, 0.5H), 8.03 (dd, J = 8.2, 17.0, 1H), 7.74 (s, 1H), 7.71 (d, J = 7.7, 0.5H), 7.61 (d, J = 6.5, 0.5H), 7.47 (t, J = 7.7, 1H), 4.67 (dd, J = 8.2, 14.1, 0.5H), 4.61 (dd, J = 8.1, 14.7, 0.5H), 4.53 – 4.39 (m, 1H), 3.81 (d, J = 13.1, 0.5H), 3.70 (d, J = 13.3, 0.5H), 3.44 (d, J = 13.3, 0.5H), 3.29 (d, J = 13.2, 0.5H), 2.93 – 2.86 (m, 1H), 2.85 – 2.74 (m, 1H), 2.46 (d, J = 4.1, 1H), 2.39 – 2.21 (m, 3H), 1.96 – 1.76 (m, 5H), 1.73 – 1.55 (m, 2H), 1.50 (s, 4.5H), 1.50 (s, 4.5H), 1.34 – 1.23 (m, 1H), 0.91 – 0.82 (m, 6H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Example 138

N^2-(tert-butyloxycarbonyl)-N^1-{(3a*S,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-D-leucine for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 1: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.50 (d, J = 7.0, 0.5H), 8.46 (d, J = 6.8, 0.5H), 8.03 (dd, J = 8.1, 17.2, 1H), 7.74 (s, 1H), 7.71 (d, J = 7.7, 1H), 7.61 (d, J = 5.8, 1H), 7.48 (t, J = 7.7, 1H), 4.67 (dd, J = 8.3, 14.3, 0.5H), 4.61 (dd, J = 7.9, 14.5, 0.5H), 4.47 (ddd, J = 7.0, 13.9, 17.8, 1H), 3.81 (d, J = 13.1, 0.5H), 3.70 (d, J = 13.1, 0.5H), 3.44 (d, J = 13.3, 0.5H), 3.29 (d, J = 13.2, 0.5H), 2.89 (t, J = 13.2, 1H), 2.85 – 2.75 (m, 1H), 2.51 – 2.42 (m, 1H), 2.39 – 2.30 (m, 1H), 2.28 (dd, J = 6.1, 15.3, 2H), 1.97 – 1.77 (m, 4H), 1.73 – 1.55 (m, 2H), 1.50 (s, 4.5H), 1.50 (s, 4.5H), 1.34 – 1.22 (m, 1H), 0.91 – 0.81 (m, 6H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Example 139

N^2-(tert-butyloxycarbonyl)-N^2-methyl-N^1-{(3a*S,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-D-leucine for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 1: ^{1}H NMR (300 MHz, pyridine-d_5) δ ppm 7.76 (d, J = 15.9, 2H), 7.57 (s, 3H), 7.54 – 7.43 (m, 1H), 7.42 – 7.36 (m, 0.5H), 7.34 – 7.21 (m, 1H), 4.86 (t, J = 9.6, 0.5H), 4.48 – 4.35 (m, 0.5H), 3.71 (d, J = 13.3, 0.5H), 3.52 (d, J = 13.4, 0.5H), 3.40 (d, J = 13.2, 0.5H), 2.98 (s, 1.5H), 2.97 (s, 1.5H), 2.77 (ddd, J = 2.0, 7.2, 9.8, 2H), 2.57 – 2.46 (m, 1H), 2.43 (dd, J = 2.9, 9.2, 0.5H), 2.36 (dd, J = 2.3, 6.4, 0.5H), 2.34 – 2.22 (m, 2H), 1.93 (dddd, J = 2.0, 6.2, 8.1, 14.3, 1H), 1.85 – 1.59 (m, 4H), 1.52 (s, 4.5H), 1.50 (s, 4.5H), 1.39 – 1.28 (m, 1H), 0.96 – 0.89 (m, 6H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Example 140

6,6-bis(4-fluorophenyl)-*N*-{(3a*S,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}hexanamide**

The title compound was prepared by substituting 6,6-bis(4-fluorophenyl)hexanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*R**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 2: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.31 (d, J = 7.3, 1H), 7.77 (s, 1H), 7.61 (t, J = 7.4, 1H), 7.57 (d, J = 7.2, 1H), 7.45 (t, J = 7.7, 1H), 7.25 (dd, J = 5.6, 8.2, 4H), 7.10 (t, J = 8.7, 4H), 4.46 – 4.37 (m, 1H), 3.90 (t, J = 7.8, 1H), 3.61 (d, J = 13.5, 1H), 3.47 (d, J = 13.5, 1H), 2.85 – 2.79 (m, 1H), 2.49 (d, J = 16.3, 2H), 2.47 – 2.41 (m, 1H), 2.30 (ddd, J = 8.1, 15.0, 20.0, 4H), 2.15 – 2.06 (m, 1H), 1.98 (dd, J = 7.8, 15.5, 2H), 1.90 – 1.79 (m, 3H), 1.60 (dt, J = 7.4, 19.3, 1H), 1.44 – 1.36 (m, 1H), 1.32 (dq, J = 7.8, 15.3, 2H); MS (ESI+) *m/z* 571 $(M+H)^+$.

Example 141

3,3-diphenyl-*N*-{(3a*S,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}propanamide**

The title compound was prepared by substituting 3,3-diphenylpropanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*R**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 2: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.28 (d, J = 7.4, 1H), 7.74 (s, 1H), 7.45 (t, J = 7.7, 1H), 7.38 (dd, J = 1.8, 7.4, 4H), 7.28 (dt, J = 7.6, 9.4, 4H), 7.20 – 7.17 (m, 4H), 5.00 (t, J = 7.8, 1H), 4.34 – 4.26 (m, 1H), 3.56 (d, J = 13.5, 1H), 3.43 (d, J = 13.5, 1H), 3.14 (d, J = 7.9, 2H), 2.65 (dd, J = 2.1, 8.3, 1H), 2.45 – 2.36 (m, 1H), 2.36 – 2.28 (m, 2H), 2.26 – 2.19 (m, 2H), 1.98 – 1.89 (m, 1H), 1.72 (ddd, J = 6.3, 12.5, 14.5, 1H), 1.43 (dt, J = 7.4, 14.1, 1H), 1.34 – 1.25 (m, 1H); MS (ESI+) *m/z* 493 $(M+H)^+$.

Example 142

5,5-bis(4-fluorophenyl)-*N*-{(3a*S,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}pentanamide**

The title compound was prepared by substituting 5,5-bis(4-fluorophenyl)pentanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*R**,6a*R**)-2-(3-

(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 2: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.36 (d, *J* = 7.2, 1H), 7.75 (s, 1H), 7.62 – 7.54 (m, 2H), 7.44 (t, *J* = 7.7, 1H), 7.24 (dt, *J* = 5.7, 11.3, 4H), 7.07 (t, *J* = 8.7, 4H), 4.47 – 4.39 (m, 1H), 3.96 (t, *J* = 7.8, 1H), 3.59 (d, *J* = 13.5, 1H), 3.46 (d, *J* = 13.5, 1H), 2.84 (d, *J* = 9.0, 1H), 2.51 (s, 2H), 2.42 (dd, *J* = 7.0, 14.2, 3H), 2.30 (d, *J* = 7.1, 1H), 2.27 – 2.22 (m, 1H), 2.15 – 2.06 (m, 3H), 1.85 (dd, *J* = 6.2, 13.9, 1H), 1.78 (dt, *J* = 7.4, 15.1, 2H), 1.60 (dt, *J* = 7.6, 14.6, 1H), 1.43 – 1.34 (m, 1H); MS (ESI+) *m/z* 557 $(M+H)^+$.

Example 143

3,3-bis(4-fluorophenyl)-*N*-{(3a*S,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}propanamide**

The title compound was prepared by substituting 3,3-bis(4-fluorophenyl)propanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*R**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 2: : ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.36 (d, *J* = 7.4, 1H), 7.74 (s, 1H), 7.62 – 7.56 (m, 2H), 7.45 (t, *J* = 7.7, 1H), 7.32 (ddd, *J* = 2.0, 5.4, 7.8, 4H), 7.07 (dt, *J* = 8.7, 11.2, 4H), 4.36 – 4.26 (m, 1H), 3.56 (d, *J* = 13.5, 1H), 3.45 (d, *J* = 13.5, 1H), 3.09 (d, *J* = 7.9, 2H), 2.70 – 2.63 (m, 1H), 2.47 – 2.37 (m, 1H), 2.33 (t, *J* = 6.7, 3H), 2.26 (dd, *J* = 3.0, 9.0, 1H), 2.24 – 2.18 (m, 1H), 1.96 (tt, *J* = 6.0, 11.8, 1H), 1.79 – 1.70 (m, 1H), 1.44 (dt, *J* = 7.6, 14.4, 1H), 1.35 – 1.26 (m, 1H); MS (ESI+) *m/z* 529 $(M+H)^+$.

Example 144

4,4-bis(4-fluorophenyl)-*N*-{(3a*S,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide**

The title compound was prepared by substituting 4,4-bis(4-fluorophenyl)butanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*R**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 2: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.39 (d, *J* = 7.2, 1H), 7.77 (s, 1H), 7.62 (d, *J* = 7.9, 2H), 7.45 (t, *J* = 7.7, 1H), 7.25 (dd, *J* = 5.5, 7.3, 4H), 7.05 (t, *J* = 8.7, 4H), 4.50 – 4.40 (m, 1H), 4.08 (t, *J* = 7.9, 1H), 3.61 (d, *J* = 13.5, 1H), 3.49 (d, *J* = 13.5, 1H), 2.87 (dd, *J* = 1.4, 8.8, 1H), 2.56 (dd, *J* = 7.7, 15.3, 4H), 2.48 (d, *J* = 8.8, 1H), 2.31 (dd, *J* = 8.0, 15.4, 4H),

2.13 (dq, J = 6.0, 12.0, 1H), 1.87 (td, J = 6.3, 12.5, 1H), 1.62 (dt, J = 7.4, 14.3, 1H), 1.41 (dd, J = 11.7, 20.8, 1H); MS (ESI+) m/z 543 $(M+H)^+$.

Example 145

2,2-diphenyl-*N*-{(3a*S,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide**

The title compound was prepared by substituting 2,2-diphenylacetic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*R**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 2: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.94 (d, J = 6.8, 1H), 7.74 (s, 2H), 7.64 (d, J = 7.8, 4H), 7.47 – 7.40 (m, 1H), 7.38 – 7.29 (m, 5H), 7.28 – 7.23 (m, 3H), 4.45 – 4.37 (m, 1H), 3.57 (d, J = 13.5, 1H), 3.42 (d, J = 13.5, 1H), 2.76 (dd, J = 3.0, 9.1, 1H), 2.54 – 2.47 (m, 1H), 2.47 – 2.42 (m, 1H), 2.39 (dd, J = 7.3, 9.0, 1H), 2.23 (d, J = 3.0, 2H), 2.06 (dq, J = 6.2, 12.2, 1H), 1.83 – 1.74 (m, 1H), 1.59 (dt, J = 6.9, 14.5, 1H), 1.33 (dt, J = 6.3, 19.6, 1H); MS (ESI+) m/z 479 $(M+H)^+$.

Example 146

2,2-bis(4-fluorophenyl)-*N*-{(3a*S,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide**

The title compound was prepared by substituting 2,2-bis(4-fluorophenyl)acetic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*R**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 2: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.07 (d, J = 7.1, 1H), 7.74 (s, 1H), 7.59 (s, 1H), 7.56 (d, J = 5.3, 5H), 7.44 (t, J = 7.7, 1H), 7.12 (q, J = 8.6, 4H), 5.23 (s, 1H), 4.45 – 4.36 (m, 1H), 3.57 (d, J = 13.5, 1H), 3.44 (d, J = 13.5, 1H), 2.78 (dd, J = 2.9, 9.1, 1H), 2.56 – 2.49 (m, 1H), 2.49 – 2.44 (m, 1H), 2.41 (dd, J = 7.3, 8.9, 1H), 2.27 – 2.22 (m, 2H), 2.07 (dq, J = 6.1, 12.1, 1H), 1.86 – 1.76 (m, 1H), 1.60 (td, J = 7.2, 14.6, 1H), 1.35 (td, J = 6.3, 12.6, 1H); MS (ESI+) m/z 515 $(M+H)^+$.

Example 147

3,3-dimethyl-2-phenyl-*N*-{(3a*S,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide**

The title compound was prepared by substituting 3,3-dimethyl-2-phenylbutanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*R**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 2: ^{1}H NMR (400 MHz,) δ ppm 8.47 (t, *J* = 6.7, 1H), 7.77 (s, 0.5H), 7.71 (d, *J* = 7.3, 2H), 7.60 (d, *J* = 7.7, 0.5H), 7.54 (s, 1H), 7.43 (dd, *J* = 8.1, 16.6, 1H), 7.35 – 7.24 (m, 4H), 4.39 – 4.29 (m, 1H), 3.62 (d, *J* = 13.6, 0.5H), 3.53 (d, *J* = 13.5, 0.5H), 3.47 (d, *J* = 13.6, 0.5H), 3.44 (s, 1H), 3.38 (d, *J* = 13.5, 0.5H), 2.92 (dd, *J* = 2.9, 9.0, 0.5H), 2.62 – 2.54 (m, 1H), 2.54 – 2.46 (m, 1H), 2.46 – 2.36 (m, 0.5H), 2.32 (dd, *J* = 9.1, 12.0, 1H), 2.27 (d, *J* = 5.2, 1H), 2.21 (d, *J* = 5.6, 1H), 2.17 – 2.07 (m, 0.5H), 1.86 (ddd, *J* = 6.4, 13.3, 21.3, 1H), 1.71 (tdd, *J* = 6.4, 13.0, 19.3, 1H), 1.36 (ddt, *J* = 8.2, 14.4, 20.6, 1.5H), 1.14 (d, *J* = 1.3, 9H); MS (ESI+) *m/z* 459 $(M+H)^+$.

Example 148

N^2-(tert-butyloxycarbonyl)-N^1-{(3a*S,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-L-leucine for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*R**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 2: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.66 (dd, *J* = 7.6, 11.3, 1H), 7.98 (d, *J* = 6.0, 1H), 7.74 (d, *J* = 7.5, 1H), 7.58 (d, *J* = 21.6, 2H), 7.44 (t, *J* = 7.8, 1H), 4.74 – 4.66 (m, 1H), 4.45 – 4.36 (m, 1H), 3.58 (t, *J* = 13.6, 1H), 3.43 (dd, *J* = 13.6, 20.1, 1H), 2.81 (s, 0.5H), 2.73 (s, 0.5H), 2.57 (s, 0.5H), 2.47 (d, *J* = 9.1, 2H), 2.34 (s, 0.5H), 2.26 (d, *J* = 6.7, 1H), 2.24 – 2.20 (m, 0.5H), 2.11 (s, 1H), 2.07 – 1.99 (m, 0.5H), 1.87 (s, 4H), 1.71 – 1.62 (m, 0.5H), 1.61 – 1.55 (m, 0.5H), 1.50 (d, *J* = 2.8, 9H), 1.40 (s, 1H), 0.87 (d, *J* = 5.8, 3H), 0.84 (d, *J* = 5.5, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Example 149

N^2-(tert-butyloxycarbonyl)-N^1-{(3a*S,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-D-leucine for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*R**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 2: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.66 (dd, *J* = 7.4, 11.1, 1H), 7.97 (d, *J* = 6.0, 1H), 7.74 (d, *J* = 7.6, 1H), 7.57 (d, *J* = 10.9, 2H), 7.44 (dd, *J* = 5.9, 13.6, 1H), 4.74 – 4.66 (m, 1H), 4.41 (dd, *J* = 6.2, 11.5, 1H), 3.58 (t, *J* = 13.4, 1H), 3.43 (dd, *J* = 13.6, 19.7, 1H), 2.82 (dd, *J* = 2.4, 9.0, 0.5H), 2.74 (d, *J* = 8.7, 0.5H), 2.62 – 2.54 (m, 0.5H), 2.54 – 2.43 (m, 2H), 2.37 – 2.32 (m, 0.5H), 2.27 (d, *J* = 6.7, 1H), 2.24 – 2.19 (m, 0.5H), 2.16 – 2.08 (m, 0.5H), 2.06 – 1.99 (m, 0.5H), 1.94 – 1.78 (m, 4.5H), 1.66 (dt, *J* = 7.2, 19.6, 0.5H), 1.62 – 1.56 (m, 0.5H), 1.50 (d, *J* = 2.9, 9H), 1.43 – 1.31 (m, 1H), 0.86 (dd, *J* = 5.7, 13.5, 6H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Example 150

N^2-(tert-butyloxycarbonyl)-N^2-methyl-N^1-{(3a*S,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-D-leucine for 1-phenylcyclopentanecarboxylic acid and (3a*S**,4*R**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described for Example 2: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.31 (s, 1H), 7.75 (s, 1H), 7.57 (d, *J* = 11.6, 2H), 7.44 (t, *J* = 7.7, 1H), 5.18 – 5.09 (m, 0.5H), 4.84 – 4.73 (m, 0.5H), 4.44 – 4.32 (m, 1H), 3.59 (d, *J* = 13.5, 1H), 3.47 (d, *J* = 13.6, 1H), 3.07 (d, *J* = 25.1, 2.5H), 2.83 (d, *J* = 8.5, 0.5H), 2.79 – 2.72 (m, 0.5H), 2.55 – 2.44 (m, 2H), 2.44 – 2.39 (m, 1H), 2.37 – 2.33 (m, 0.5H), 2.29 (d, *J* = 7.4, 1H), 2.23 (dd, *J* = 7.9, 15.2, 1H), 2.08 (dt, *J* = 5.2, 11.8, 1H), 1.88 – 1.78 (m, 3H), 1.64 – 1.51 (m, 2H), 1.46 (s, 9H), 1.41 – 1.33 (m, 1H), 0.88 (d, *J* = 6.4, 3H), 0.84 (d, *J* = 6.5, 3H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Example 151

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(tert-butyloxycarbonyl)-N^2-methyl-L-leucinamide

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-leucine for 1-phenylcyclopentanecarboxylic acid in the procedure described for Example 2: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.28 (d, J = 6.6, 1H), 7.41 (s, 2H), 7.38 – 7.34 (m, 2H), 7.27 (t, J = 7.3, 1H), 5.16 – 5.11 (m, 0.5H), 4.82 – 4.74 (m, 0.5H), 4.44 – 4.33 (m, 1H), 3.57 (s, 1H), 3.46 – 3.38 (m, 1H), 3.07 (d, J = 26.9, 3H), 2.89 – 2.82 (m, 0.5H), 2.80 – 2.73 (m, 1H), 2.50 – 2.43 (m, 2H), 2.40 – 2.29 (m, 2H), 2.24 – 2.19 (m, 1H), 2.10 (dq, J = 5.8, 11.6, 1H), 1.92 – 1.87 (m, 0.5H), 1.83 (dd, J = 5.2, 9.3, 2H), 1.64 – 1.51 (m, 2H), 1.46 (s, 9H), 1.42 – 1.35 (m, 1H), 0.88 (d, J = 6.3, 3H), 0.84 (d, J = 6.6, 3H); MS (ESI+) *m/z* 444 $(M+H)^+$.

Example 152

2,2-dicyclohexyl-2-hydroxy-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide

Step A: (3a*S*,4*S*,6a*R*)-2-(3-(Trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine was prepared according to the procedure described in Example 14 Step A-C. Substituting 2-(3-(trifluoromethyl)benzyl)hexahydrocyclopenta[*c*]pyrrol-4(5*H*)-one from Steps A-C in Example 122 for 2-benzylhexahydrocyclopenta[*c*]pyrrol-4(5*H*)-one in Step A of Example 14 gave (*S*,*E*)-2-methyl-*N*-((3a*R*,6a*S*)-2-(3-(trifluoromethyl)benzyl)hexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)propane-2-sulfinamide and (*S*,*E*)-2-methyl-*N*-((3a*S*,6a*R*)-2-(3-(trifluoromethyl)benzyl)hexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)propane-2-sulfinamide. (*S*,*E*)-2-Methyl-*N*-((3a*S*,6a*R*)-2-(3-(trifluoromethyl)benzyl)hexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)propane-2-sulfinamide was used as described in Example 14 Steps B-C to give (3a*S*,4*S*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.72 (s, 1H), 7.59 (d, J = 12.2, 1H), 7.54 (d, J = 7.7, 1H), 7.39 (t, J = 7.7, 1H), 3.71 – 3.66 (m, 1H), 3.64 (d, J = 13.3, 1H), 3.49 (d, J = 13.3, 1H), 3.22 (dd, J = 3.7, 9.9, 1H), 2.77 (qd, J = 3.8, 7.9, 1H), 2.49 (dd, J = 8.9, 16.7, 2H), 2.39 (t, J = 8.3, 1H), 2.29 (dd, J = 3.4, 9.0, 1H), 2.10 (ddd, J = 6.1, 9.7, 15.6, 1H), 1.90 (td, J = 5.9, 12.0, 1H), 1.69 – 1.60 (m, 1H), 1.42 (dt, J = 5.6, 12.2, 1H); MS (ESI+) *m/z* 284 $(M+H)^+$.

Step B: The title compound was prepared by substituting 2,2-dicyclohexyl-2-hydroxyacetic acid for 3-methyl-2-phenylbutanoic acid and (3a*S*,4*S*,6a*R*)-2-(3-

(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A for (3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Step D of Example 14: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.45 (br s, 1H), 7.85 (s, 1H), 7.75 (d, *J* = 7.4, 1H), 7.54 (d, *J* = 7.6, 1H), 7.36 (dd, *J* = 5.4, 13.2, 1H), 5.93 (br s, 1H), 4.64 – 4.57 (m, 1H), 3.85 (d, *J* = 13.2, 1H), 3.29 (d, *J* = 13.2, 1H), 2.92 (d, *J* = 9.5, 1H), 2.66 (dd, *J* = 7.4, 15.2, 1H), 2.49 – 2.41 (m, 1H), 2.39 (d, *J* = 9.1, 1H), 2.24 – 2.01 (m, 5H), 1.96 – 1.83 (m, 4H), 1.83 – 1.70 (m, 6H), 1.63 (t, *J* = 13.2, 2H), 1.58 – 1.49 (m, 1H), 1.45 – 1.08 (m, 10H); MS (ESI+) *m/z* 507 $(M+H)^+$.

Example 153

N^2-(tert-butyloxycarbonyl)-N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-leucine for 3-methyl-2-phenylbutanoic acid and (3a*S*,4*S*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from 152 Step A for (3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Step D of Example 14: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.01 (s, 1H), 7.83 (s, 1H), 7.76 (s, 1H), 7.64 (d, *J* = 7.7, 2H), 5.12 – 5.04 (m, 1H), 4.42 (s, 1H), 3.61 (s, 1H), 3.52 (s, 1H), 3.12 – 2.97 (m, 3H), 2.78 (s, 1H), 2.72 (d, *J* = 9.5, 1H), 2.50 – 2.41 (m, 1H), 2.37 (d, *J* = 7.3, 1H), 2.32 – 2.16 (m, 2H), 1.98 – 1.72 (m, 3H), 1.64 (dt, *J* = 6.8, 14.9, 1H), 1.60 – 1.53 (m, 2H), 1.50 (s, 9H), 1.33 – 1.20 (m, 1H), 0.89 (d, *J* = 6.5, 6H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Example 154

2,2-dicyclohexyl-2-hydroxy-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide

Step A: (3a*S*,4*R*,6a*R*)-2-(3-(Trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine was prepared according to the procedure described in Example 16 Steps A-E substituting (*S*,*E*)-2-methyl-*N*-((3a*S*,6a*R*)-2-(3-(trifluoromethyl)benzyl)hexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)propane-2-sulfinamide from Step A in Example 152 for (*S*,*E*)-*N*-((3a*S*,6a*R*)-2-benzylhexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)-2-methylpropane-2-sulfinamide in Step A-E of Example 16 to give (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.78 (s, 1H), 7.59 (d, *J* = 6.0, 2H), 7.45 (t, *J* = 7.7, 1H), 4.94 (br s, 2H), 3.53 (s, 2H), 3.13 (dd, *J* = 5.1, 11.6, 1H), 2.63 – 2.54 (m, 1H), 2.49 (dd, *J* = 3.3,

9.0, 1H), 2.35 (dd, J = 7.5, 9.0, 1H), 2.32 (d, J = 5.9, 2H), 2.21 – 2.13 (m, 1H), 1.96 (dt, J = 6.0, 8.7, 1H), 1.88 (td, J = 3.9, 9.7, 1H), 1.38 – 1.29 (m, 2H); MS (ESI+) m/z 284 $(M+H)^+$.

Step B: The title compound was prepared by substituting (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and 2,2-dicyclohexyl-2-hydroxyacetic acid for (*S*)-2-phenylbutanoic acid in the procedure described in Step F of Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.75 (s, 1H), 7.70 (d, J = 7.8, 1H), 7.63 – 7.54 (m, 1H), 7.44 (t, J = 7.7, 1H), 6.25 – 6.09 (m, 1H), 4.45 – 4.37 (m, 1H), 3.61 (d, J = 13.5, 1H), 3.44 (d, J = 13.5, 1H), 2.91 (dd, J = 2.1, 9.0, 1H), 2.58 – 2.46 (m, 1H), 2.40 (dd, J = 7.1, 8.8, 1H), 2.33 (dd, J = 2.3, 8.9, 1H), 2.22 (dd, J = 7.0, 8.7, 1H), 2.19 – 2.04 (m, 5H), 1.94 – 1.82 (m, 4H), 1.82 – 1.71 (m, 4H), 1.63 (s, 3H), 1.58 – 1.46 (m, 1H), 1.37 (s, 4H), 1.25 (s, 7H); MS (ESI+) m/z 507 $(M+H)^+$.

Example 155

N^2-(tert-butyloxycarbonyl)-N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 154 Step A for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-leucine for (*S*)-2-phenylbutanoic acid in the procedure described in Step F of Example 16: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.30 (s, 1H), 7.74 (s, 1H), 7.57 (d, J = 9.4, 2H), 7.44 (t, J = 7.7, 1H), 5.21 – 5.04 (m, 1H), 4.37 (s, 1H), 3.58 (d, J = 12.2, 1H), 3.44 (d, J = 13.8, 1H), 3.07 (d, J = 25.6, 3H), 2.77 (d, J = 8.6, 1H), 2.47 (s, 2H), 2.41 – 2.32 (m, 1H), 2.29 (d, J = 7.2, 1H), 2.25 – 2.18 (m, 1H), 2.08 (dq, J = 5.8, 11.7, 1H), 1.83 (dd, J = 5.4, 9.0, 3H), 1.64 – 1.52 (m, 2H), 1.46 (s, 9H), 1.41 – 1.32 (m, 1H), 0.88 (d, J = 6.3, 3H), 0.84 (d, J = 6.5, 3H); MS (ESI+) m/z 512 $(M+H)^+$.

Example 156

2,2-dicyclohexyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide

Step A: (3a*R*,4*S*,6a*S*)-2-(3-(Trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine was prepared according to the procedure described in Example 16 Step A-E substituting (*S*,*E*)-2-methyl-*N*-((3a*R*,6a*S*)-2-(3-(trifluoromethyl)benzyl)hexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)propane-2-sulfinamide

from Example 152 Step A for (*S*,*E*)-*N*-((3a*S*,6a*R*)-2-benzylhexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)-2-methylpropane-2-sulfinamide prepared in Step A of Example 14 to give (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.78 (s, 1H), 7.59 (d, *J* = 11.1, 2H), 7.45 (t, *J* = 7.7, 1H), 4.94 (br s, 2H), 3.14 (dd, *J* = 5.2, 11.5, 1H), 2.58 (tt, *J* = 5.1, 10.1, 1H), 2.49 (dd, *J* = 3.3, 9.0, 1H), 2.35 (dd, *J* = 7.5, 9.0, 1H), 2.31 (d, *J* = 5.8, 2H), 2.21 – 2.14 (m, 1H), 2.01 – 1.91 (m, 1H), 1.88 (td, *J* = 4.2, 9.9, 1H), 1.38 – 1.29 (m, 2H).

Step B: The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A for (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and 2,2-dicyclohexylacetic acid for (*S*)-2-phenylbutanoic acid in the procedure described for Example 16 Step F: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.13 (d, *J* = 7.2, 1H), 7.76 (s, 1H), 7.63 – 7.53 (m, 2H), 7.44 (t, *J* = 7.9, 1H), 4.51 – 4.43 (m, 1H), 3.61 (d, *J* = 13.5, 1H), 3.46 (d, *J* = 13.5, 1H), 2.88 (dd, *J* = 2.8, 9.0, 1H), 2.63 – 2.52 (m, 2H), 2.49 (dd, *J* = 7.1, 8.9, 1H), 2.32 – 2.27 (m, 2H), 2.13 (dq, *J* = 6.1, 11.9, 1H), 2.03 (t, *J* = 7.4, 1H), 1.96 (d, *J* = 13.0, 2H), 1.92 – 1.83 (m, 3H), 1.80 (d, *J* = 12.2, 2H), 1.75 – 1.68 (m, 4H), 1.67 – 1.63 (m, 1H), 1.63 – 1.57 (m, 2H), 1.50 – 1.37 (m, 3H), 1.30 – 1.18 (m, 4H), 1.12 (dtd, *J* = 2.7, 12.5, 24.6, 4H); MS (ESI+) *m/z* 491 $(M+H)^+$.

Example 157

2,2-dicyclohexyl-*N*-{(3a*R*,4*R*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide

Step A: (3a*R*,4*R*,6a*S*)-2-(3-(Trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine was prepared according to the procedure described in Example 14 Steps B-C substituting (*S*,*E*)-2-methyl-*N*-((3a*R*,6a*S*)-2-(3-(trifluoromethyl)benzyl)hexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)propane-2-sulfinamide from Example 152 Step A for (*S*,*E*)-*N*-((3a*S*,6a*R*)-2-benzylhexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)-2-methylpropane-2-sulfinamide prepared in Step A of Example 14 to give (3a*R*,4*R*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.78 (s, 1H), 7.59 (d, *J* = 11.1, 2H), 7.45 (t, *J* = 7.7, 1H), 4.94 (br s, 2H), 3.14 (dd, *J* = 5.2, 11.5, 1H), 2.58 (tt, *J* = 5.1, 10.1, 1H), 2.49 (dd, *J* = 3.3, 9.0, 1H), 2.35 (dd, *J* = 7.5, 9.0, 1H), 2.31 (d, *J* = 5.8, 2H), 2.21 – 2.14 (m, 1H), 2.00 – 1.92 (m, 1H), 1.88 (td, *J* = 4.2, 9.9, 1H), 1.39 – 1.29 (m, 2H); MS (ESI+) *m/z* 284 $(M+H)^+$.

Step B: The title compound was prepared by substituting 2,2-dicyclohexylacetic acid for 3-methyl-2-phenylbutanoic acid in and (3a*R*,4*R*,6a*S*)-2-(3-

(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A for (3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Step D of Example 14: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.73 (s, 1H), 7.66 (d, J = 7.7, 1H), 7.55 (d, J = 7.3, 2H), 7.50 (t, J = 7.7, 1H), 4.50 – 4.43 (m, 1H), 3.54 (d, J = 12.9, 1H), 3.46 (d, J = 12.9, 1H), 2.74 (td, J = 2.6, 10.5, 2H), 2.51 – 2.42 (m, 2H), 2.31 (t, J = 8.3, 1H), 2.20 (dd, J = 7.8, 9.8, 1H), 1.94 – 1.54 (m, 15H), 1.46 (d, J = 13.0, 1H), 1.40 (d, J = 14.4, 1H), 1.35 – 1.07 (m, 9H), 0.98 (qd, J = 3.0, 12.3, 1H); MS (ESI+) *m/z* 491 $(M+H)^+$.

Example 158

N^1-{(3a*S,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide**

N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide (140 mg, 0.281 mmol) from Example 137 and 2 *N* HCl (2.5 mL, 5.00 mmol) were combined in ether, and the reaction was stirred at room temperature overnight. The solids were collected and dried to give the title compound as the hydrochloride salt: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.59 (s, 0.5H), 8.48 (s, 0.5H), 7.89 (s, 0.5H), 7.83 (s, 0.5H), 7.69 (t, J = 6.8, 1H), 7.60 (d, J = 7.8, 1H), 7.50 – 7.44 (m, 1H), 4.96 (br s, 2H), 4.57 – 4.48 (m, 1H), 3.73 (d, J = 13.2, 0.5H), 3.67 (s, 1H), 3.64 (d, J = 13.2, 1H), 3.39 (d, J = 13.1, 0.5H), 3.35 (d, J = 13.2, 0.5H), 2.81 – 2.70 (m, 2H), 2.45 (dd, J = 7.5, 15.3, 1H), 2.39 – 2.31 (m, 1H), 2.27 – 2.14 (m, 2H), 1.95 – 1.79 (m, 2.5H), 1.72 – 1.56 (m, 2H), 1.53 – 1.46 (m, 0.5H), 1.33 – 1.23 (m, 1.5H), 0.90 (dt, J = 6.2, 14.1, 6H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Example 159

N^1-{(3a*R,4*R**,6a*S**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide**

The title compound was prepared by substituting N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide from Example 138 for N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide in the procedure described for Example 158: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.67 (d, J = 7.4, 0.5H), 8.57 (d, J = 7.6, 0.5H), 7.88 (s, 0.5H), 7.81 (s, 0.5H), 7.68 (d, J = 7.3, 1H), 7.61 (s, 1H), 7.48 (dd, J = 7.3, 14.5, 1H), 4.56 – 4.47 (m, 1H), 3.79 – 3.70 (m, 1H), 3.65 (d, J = 13.2, 0.5H), 3.38 (t, J = 13.5, 1H), 2.82 – 2.71 (m, 2H), 2.50 – 2.42 (m, 1H), 2.38 – 2.31 (m, 1H), 2.27 –

2.16 (m, 2H), 2.08 (dt, J = 6.8, 19.9, 0.5H), 1.96 – 1.88 (m, 1.5H), 1.88 – 1.80 (m, 1H), 1.70 – 1.59 (m, 2H), 1.58 – 1.52 (m, 0.5H), 1.42 – 1.20 (m, 4H), 0.90 (dt, J = 6.1, 13.2, 6H); MS (ESI+) m/z 398 $(M+H)^+$.

Example 160

N^2-methyl-N^1-{(3a*S,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide**

The title compound was prepared by substituting N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide from Example 139 for N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide in the procedure described for Example 158: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.52 (s, 0.5H), 8.29 (s, 0.5H), 7.92 (s, 0.5H), 7.79 (s, 0.5H), 7.69 (dd, J = 7.6, 18.7, 1H), 7.62 (d, J = 7.6, 1H), 7.48 (dd, J = 7.8, 18.2, 1H), 4.59 – 4.48 (m, 1H), 3.82 (d, J = 13.2, 0.5H), 3.63 (d, J = 13.1, 0.5H), 3.42 (d, J = 13.1, 0.5H), 3.31 – 3.18 (m, 1H), 2.81 (dd, J = 1.9, 9.4, 0.5H), 2.74 (dd, J = 8.5, 18.2, 1H), 2.50 – 2.43 (m, 1H), 2.41 (s, 1.5H), 2.40 (s, 1.5H), 2.33 (dd, J = 1.9, 9.0, 0.5H), 2.25 (dd, J = 7.3, 9.4, 0.5H), 2.21 – 2.03 (m, 1.5H), 1.92 – 1.81 (m, 2H), 1.80 – 1.48 (m, 4H), 1.42 – 1.21 (m, 3.5H), 0.94 (d, J = 6.6, 1.5H), 0.93 (d, J = 6.6, 1.5H), 0.90 (d, J = 6.6, 1.5H), 0.87 (d, J = 6.6, 1.5H); MS (ESI+) m/z 412 $(M+H)^+$.

Example 161

N^1-{(3a*S,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide**

The title compound was prepared by substituting N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 148 for N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide in the procedure described for Example 158: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.33 (s, 1H), 7.76 (s, 1H), 7.63 – 7.58 (m, 2H), 7.45 (d, J = 4.3, 1H), 4.40 (dd, J = 6.5, 12.5, 1H), 3.63 – 3.53 (m, 1H), 3.46 (dd, J = 6.1, 13.6, 1H), 2.82 – 2.73 (m, 1H), 2.69 – 2.51 (m, 2H), 2.48 – 2.38 (m, 1H), 2.33 (dd, J = 8.8, 16.3, 1H), 2.24 (dd, J = 7.6, 16.5, 1H), 2.16 – 1.88 (m, 5H), 1.85 (dt, J = 7.8, 15.2, 0.5H), 1.76 – 1.62 (m, 1H), 1.39 (qd, J = 6.6, 14.9, 1.5H), 1.31 – 1.20 (m, 2H), 0.95 (d, J = 6.0, 3H), 0.91 (dd, J = 3.2, 5.6, 3H); MS (ESI+) m/z 398 $(M+H)^+$.

Example 162

N^1-{(3a*S,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide**

The title compound was prepared by substituting N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide from Example 149 for N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide in the procedure described for Example 158: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.31 (s, 1H), 7.75 (s, 1H), 7.62 – 7.53 (m, 2H), 7.44 (dd, *J* = 7.4, 15.0, 1H), 4.44 – 4.35 (m, 1H), 3.60 (d, *J* = 13.5, 2H), 3.46 (dd, *J* = 5.5, 13.5, 1H), 2.87 – 2.79 (m, 1H), 2.57 – 2.43 (m, 2H), 2.42 – 2.37 (m, 1H), 2.32 (dt, *J* = 3.0, 8.8, 1H), 2.27 – 2.20 (m, 1H), 2.08 (td, *J* = 6.0, 12.2, 1H), 1.96 – 1.80 (m, 3H), 1.61 – 1.50 (m, 2H), 1.44 – 1.35 (m, 1H), 1.30 – 1.19 (m, 2H), 0.90 (d, *J* = 6.2, 3H), 0.85 (d, *J* = 6.2, 3H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Example 163

N^2-methyl-N^1-{(3a*S,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide**

The title compound was prepared by substituting N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide from Example 150 for N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide in the procedure described for Example 158: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.32 (d, *J* = 6.0, 1H), 7.76 (s, 1H), 7.61 (d, *J* = 7.6, 1H), 7.55 (d, *J* = 14.8, 1H), 7.45 (t, *J* = 7.7, 1H), 4.47 – 4.40 (m, 1H), 3.61 (d, *J* = 13.5, 1H), 3.47 (dd, *J* = 3.1, 13.6, 1H), 3.30 (t, *J* = 6.7, 1H), 2.86 (d, *J* = 8.9, 1H), 2.59 – 2.51 (m, 1H), 2.46 (d, *J* = 2.5, 3H), 2.42 (dd, *J* = 8.5, 15.4, 1H), 2.35 – 2.30 (m, 1H), 2.28 – 2.23 (m, 1H), 2.14 – 2.05 (m, 1H), 1.93 – 1.82 (m, 2H), 1.74 (ddd, *J* = 4.0, 9.7, 13.7, 1H), 1.62 (dt, *J* = 7.4, 15.4, 1H), 1.40 (dt, *J* = 14.2, 15.7, 1H), 1.3 – 1.22 (m, 3H), 0.91 (dt, *J* = 3.0, 6.0, 3H), 0.85 (d, *J* = 6.7, 3H); MS (ESI+) *m/z* 412 $(M+H)^+$.

Example 164

N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-

L-leucinamide from Example 153 for N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide in the procedure described for Example 158: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.56 (d, J = 7.4, 1H), 7.91 (s, 1H), 7.67 (d, J = 7.6, 1H), 7.61 (d, J = 7.8, 1H), 7.47 (t, J = 7.7, 1H), 4.54 (dt, J = 6.6, 13.2, 1H), 3.81 (d, J = 13.2, 1H), 3.32 (dd, J = 6.0, 7.9, 1H), 3.28 (d, J = 13.2, 1H), 2.81 (d, J = 9.5, 1H), 2.78 – 2.71 (m, 1H), 2.48 – 2.44 (m, 1H), 2.42 (s, 3H), 2.33 (d, J = 9.1, 1H), 2.26 (dd, J = 7.4, 9.3, 1H), 2.16 – 2.11 (m, 1H), 1.91 – 1.83 (m, 2H), 1.82 – 1.75 (m, 1H), 1.65 (ddq, J = 6.3, 12.1, 18.8, 3H), 1.26 (td, J = 6.2, 12.7, 1H), 0.95 (d, J = 6.5, 3H), 0.90 (d, J = 6.6, 3H); MS (ESI+) *m/z* 412 $(M+H)^+$.

Example 165

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide

The title compound was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide in the procedure described for Example 158: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.35 (d, J = 6.9, 1H), 7.44 (d, J = 7.4, 2H), 7.37 (t, J = 7.6, 2H), 7.27 (t, J = 7.3, 1H), 4.50 – 4.42 (m, 1H), 3.61 (d, J = 13.1, 1H), 3.45 (d, J = 13.2, 1H), 3.33 (t, J = 7.0, 1H), 2.87 (d, J = 8.7, 1H), 2.56 – 2.50 (m, 1H), 2.47 (s, 3H), 2.43 (dd, J = 5.5, 14.6, 1H), 2.37 (d, J = 8.7, 1H), 2.29 – 2.23 (m, 1H), 2.17 – 2.04 (m, 1H), 1.94 – 1.82 (m, 2H), 1.79 – 1.73 (m, 1H), 1.68 – 1.57 (m, 1H), 1.41 (dd, J = 7.2, 13.5, 1H), 1.27 (s, 2H), 0.92 (d, J = 6.6, 3H), 0.85 (d, J = 6.6, 3H); MS (ESI+) *m/z* 344 $(M+H)^+$.

Example 166

N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[c]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 155 for N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide in the procedure described for Example 158: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.09 – 7.97 (m, 1H), 7.76 (s, 1H), 7.63 – 7.61 (m, 1H), 7.45 (d, J = 7.6, 1H), 7.42 (d, J = 7.6, 1H), 4.49 – 4.40 (m, 1H), 3.60 (d, J = 12.4, 1H), 3.47 (d, J = 13.6, 1H), 2.87 (d, J = 7.6, 1H), 2.59 (d, J = 9.4, 4H),

2.43 (dt, J = 7.2, 9.1, 1H), 2.34 (dd, J = 1.7, 8.9, 1H), 2.28 – 2.23 (m, 1H), 2.16 – 2.03 (m, 2H), 1.98 – 1.77 (m, 3H), 1.70 – 1.61 (m, 1H), 1.46 – 1.33 (m, 1H), 1.32 – 1.21 (m, 2H), 0.93 (d, J = 6.4, 3H), 0.86 (d, J = 6.4, 3H); MS (ESI+) m/z 412 $(M+H)^+$.

Example 167

N^2-methyl-N^2-(methylsulfonyl)-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

To N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 164 (122 mg, 0.296 mmol) in dichloromethane (0.5 mL) was added *N,N*-diisopropylethylamine (78 μL, 0.445 mmol) followed by methanesulfonyl chloride (25.4 μL, 0.326 mmol), and the reaction mixture was stirred at room temperature overnight. The reaction was reduced in volume and loaded onto a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-12). The title compound was eluted with a gradient of 0% to 5% methanol (2 *N* ammonia)/dichloromethane over 20 minutes: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.59 (d, J = 6.7, 1H), 7.73 (s, 1H), 7.66 (d, J = 7.6, 1H), 7.62 (d, J = 7.8, 1H), 7.51 (t, J = 7.7, 1H), 4.78 (dd, J = 6.2, 9.5, 1H), 4.41 – 4.33 (m, 1H), 3.67 (d, J = 13.3, 1H), 3.16 (s, 3H), 3.15 (s, 3H), 2.90 (qd, J = 3.3, 7.9, 1H), 2.75 (dd, J = 3.3, 9.6, 1H), 2.53 – 2.44 (m, 1H), 2.38 – 2.29 (m, 3H), 1.89 – 1.70 (m, 4H), 1.70 – 1.58 (m, 3H), 1.36 – 1.26 (m, 1H), 0.83 (d, J = 6.6, 3H), 0.81 (d, J = 6.5, 3H); MS (ESI+) m/z 490 $(M+H)^+$.

Example 168

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-N^2-(methylsulfonyl)-L-leucinamide

The title compound was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide from Example 165 for N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide in the procedure described in Example 167: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.97 (d, J = 7.0, 1H), 7.43 (d, J = 7.3, 2H), 7.37 (d, J = 7.3, 2H), 7.30 – 7.25 (m, 1H), 4.78 (dd, J = 5.1, 10.2, 1H), 4.42 – 4.35 (m, 1H), 3.58 (d, J = 13.1, 1H), 3.46 (d, J = 13.2, 1H), 3.21 (s, 3H), 3.12 (s, 3H), 2.83 (d, J = 8.7, 1H), 2.55 – 2.47 (m, 2H), 2.36 (dd, J = 8.1, 14.7, 2H), 2.26 – 2.22 (m, 1H), 2.13 (dt, J = 5.9, 11.7, 1H), 1.93 – 1.82 (m, 2H), 1.70 – 1.61 (m, 2H), 1.44 – 1.36 (m, 1H), 0.82 (d, J = 6.2, 3H), 0.73 (d, J = 5.9, 3H); MS (ESI+) m/z 422 $(M+H)^+$.

Example 169

N^2-methyl-N^2-(methylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 166 for N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide in the procedure described in Example 167: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.98 (d, J = 7.4, 1H), 7.77 (s, 1H), 7.62 – 7.58 (m, 2H), 7.45 (t, J = 7.7, 1H), 4.78 (dd, J = 5.0, 10.2, 1H), 4.41 – 4.33 (m, 1H), 3.59 (d, J = 13.5, 1H), 3.48 (d, J = 13.6, 1H), 3.21 (s, 3H), 3.12 (s, 3H), 2.84 (d, J = 7.4, 1H), 2.51 (t, J = 5.4, 2H), 2.37 (dd, J = 6.9, 8.9, 1H), 2.32 (d, J = 7.1, 1H), 2.23 (dd, J = 6.8, 8.9, 1H), 2.11 (dd, J = 5.8, 11.8, 1H), 1.93 – 1.82 (m, 2H), 1.70 – 1.61 (m, 3H), 1.44 – 1.35 (m, 1H), 0.82 (d, J = 6.2, 3H), 0.73 (d, J = 6.0, 3H); MS (ESI+) *m/z* 490 $(M+H)^+$.

Example 170

N^2-(methylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

Step A: *N*-(*tert*-Butoxycarbonyl)-L-leucine (180 mg, 0.778 mmol), hydroxybenzotriazole (119 mg, 0.778 mmol), and (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine (201 mg, 0.707 mmol) from Example 154 Step A were combined in dichloromethane (1 mL). After 20 minutes, *N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide (0.138 mL, 0.778 mmol) was added and the reaction stirred at room temperature for 24 hours. The reaction was quenched with water, and the layers were separated. The aqueous layer extracted with 1 mL of dichloromethane. The combined organic layers were applied to a silica gel cartridge (Analogix®, Burlington, Wisconsin, R*S*15-24) and eluted with 1-10% methanol (2 *N* ammonia)/dichloromethane to give N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.66 (d, J = 7.1, 1H), 7.97 (d, J = 8.5, 1H), 7.73 (s, 1H), 7.56 (s, 2H), 7.44 (t, J = 7.7, 1H), 4.70 (dd, J = 5.9, 11.0, 1H), 4.40 (br s, 1H), 3.56 (d, J = 13.5, 1H), 3.41 (d, J = 13.5, 1H), 2.74 (d, J = 8.9, 1H), 2.48 (s, 2H), 2.37 – 2.31 (m, 1H), 2.27 (d, J = 8.4, 1H), 2.24 – 2.19 (m, 1H), 2.12 (dq, J = 6.0, 12.0, 1H), 1.91 – 1.81 (m, 4H), 1.66 (td, J =

7.4, 14.7, 1H), 1.50 (s, 9H), 1.43 – 1.35 (m, 1H), 0.87 (d, J = 5.9, 3H), 0.84 (d, J = 5.6, 3H); MS (ESI+) m/z 498 $(M+H)^+$.

Step B: N^2-(*tert*-Butyloxycarbonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Step A (0.731 g, 1.469 mmol) in ethanol (5 mL) was treated with HCl (4 *N* in dioxane, 10.0 mL, 40.0 mmol). The reaction was stirred at room temperature for 2 hours and the solvent removed in vacuo. The reaction was quenched with saturated aqueous sodium bicarbonate and extracted with 3×50 mL of dichloromethane. The solvent was removed in vacuo to give N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.27 (d, J = 7.6, 1H), 7.75 (s, 1H), 7.63 – 7.54 (m, 2H), 7.44 (dd, J = 6.9, 14.6, 1H), 4.44 – 4.33 (m, 1H), 3.62 – 3.53 (m, 2H), 3.45 (d, J = 13.5, 1H), 2.84 (dd, J = 2.5, 8.9, 1H), 2.52 (dd, J = 7.2, 14.0, 1H), 2.50 – 2.43 (m, 1H), 2.42 – 2.37 (m, 1H), 2.32 (dd, J = 2.8, 9.0, 1H), 2.23 (dd, J = 7.2, 8.8, 1H), 2.09 (td, J = 6.0, 12.0, 2H), 1.94 – 1.81 (m, 4H), 1.61 – 1.50 (m, 2H), 1.39 (ddt, J = 6.3, 8.7, 12.6, 1H), 0.90 (d, J = 6.4, 3H), 0.84 (d, J = 6.3, 3H); MS (ESI+) m/z 398 $(M+H)^+$.

Step C: The title compound was prepared by substituting N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Step B for N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide in the procedure described in Example 167: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.41 (d, J = 9.4, 1H), 9.22 (d, J = 7.3, 1H), 7.76 (s, 1H), 7.59 (d, J = 14.0, 2H), 7.43 (dd, J = 6.2, 13.9, 1H), 4.47 (tt, J = 6.3, 12.5, 2H), 3.59 (d, J = 13.5, 1H), 3.48 (d, J = 13.6, 1H), 3.17 (s, 3H), 2.87 (dd, J = 2.3, 9.1, 1H), 2.59 – 2.50 (m, 2H), 2.38 (dd, J = 7.0, 9.0, 1H), 2.34 (dd, J = 2.3, 9.0, 1H), 2.24 (dd, J = 6.9, 8.8, 1H), 2.20 – 2.12 (m, 1H), 1.99 (dq, J = 6.7, 20.2, 1H), 1.89 (ddd, J = 6.0, 10.8, 15.0, 2H), 1.80 – 1.66 (m, 2H), 1.43 (ddd, J = 6.3, 10.7, 12.2, 1H), 0.82 (d, J = 6.7, 3H), 0.79 (d, J = 6.6, 3H); MS (ESI+) m/z 476 $(M+H)^+$.

Example 171

N^2-(methylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-D-leucine for *N*-(*tert*-butoxycarbonyl)-L-leucine in the procedure described in Step A and then following the procedures described in Steps B and C of Example 170: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.42 (d, J = 9.3, 1H), 9.22 (d, J = 7.3, 1H), 7.78 (s, 1H), 7.61 (d, J = 7.7, 2H), 7.44 (dd, J = 8.7, 16.4, 1H), 4.51 – 4.41 (m, 2H), 3.62 (d, J = 13.5, 1H), 3.49 (d, J =

13.6, 1H), 3.19 (s, 3H), 2.87 (dd, J = 2.8, 9.1, 1H), 2.66 – 2.60 (m, 1H), 2.55 (dd, J = 9.0, 15.6, 1H), 2.49 (dd, J = 7.3, 9.0, 1H), 2.33 (dd, J = 3.0, 9.0, 1H), 2.30 – 2.25 (m, 1H), 2.12 (dq, J = 5.8, 11.9, 1H), 1.98 (td, J = 6.7, 13.5, 1H), 1.93 – 1.83 (m, 2H), 1.77 (ddd, J = 5.6, 8.5, 13.8, 1H), 1.63 (dt, J = 7.5, 19.4, 1H), 1.45 – 1.36 (m, 1H), 0.82 (d, J = 6.7, 3H), 0.78 (d, J = 6.5, 3H); MS (ESI+) m/z 476 $(M+H)^+$.

Example 172

N^2-(cyclopropylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting cyclopropanesulfonyl chloride for methanesulfonyl chloride and N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 170 Step B for N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide in the procedure described in Example 167: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.34 (d, J = 9.4, 1H), 9.03 (d, J = 7.2, 1H), 7.76 (s, 1H), 7.60 (d, J = 10.5, 2H), 7.44 (dd, J = 6.1, 13.8, 1H), 4.45 (dd, J = 6.4, 11.7, 2H), 3.57 (d, J = 13.5, 1H), 3.49 (d, J = 13.5, 1H), 2.84 (dd, J = 2.4, 9.1, 1H), 2.80 – 2.73 (m, 1H), 2.61 – 2.50 (m, 2H), 2.38 (dd, J = 7.0, 8.9, 1H), 2.34 (dd, J = 2.5, 9.0, 1H), 2.28 – 2.23 (m, 1H), 2.18 (td, J = 5.8, 11.9, 1H), 2.04 (dt, J = 6.9, 20.3, 1H), 1.91 (ddd, J = 4.1, 7.2, 14.3, 2H), 1.77 (ddd, J = 5.3, 8.7, 13.8, 1H), 1.73 – 1.65 (m, 1H), 1.44 (ddd, J = 6.1, 12.3, 18.6, 1H), 1.33 (td, J = 4.7, 11.0, 1H), 1.22 – 1.16 (m, 1H), 0.91 (ddd, J = 4.5, 8.5, 11.2, 1H), 0.88 – 0.85 (m, 1H), 0.84 (d, J = 6.7, 3H), 0.82 (d, J = 6.6, 3H); MS (ESI+) m/z 502 $(M+H)^+$.

Example 173

N^2-(isobutylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting 2-methylpropane-1-sulfonyl chloride for methanesulfonyl chloride and N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 170 Step B for N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide in the procedure described in Example 167: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.34 (d, J = 9.3, 1H), 9.20 (d, J = 7.4, 1H), 7.77 (s, 1H), 7.62 (d, J = 7.6, 1H), 7.60 – 7.55 (m, 1H), 7.45 (t, J = 7.7,

1H), 4.52 – 4.43 (m, 2H), 3.61 (d, J = 13.5, 1H), 3.52 (d, J = 13.6, 1H), 3.19 – 3.16 (m, 2H), 2.91 (dd, J = 2.0, 9.0, 1H), 2.63 – 2.46 (m, 3H), 2.42 (dd, J = 6.8, 8.9, 1H), 2.37 (dd, J = 2.1, 9.0, 1H), 2.27 (dd, J = 6.9, 8.8, 1H), 2.18 (td, J = 5.8, 11.7, 1H), 2.01 (tt, J = 6.7, 13.4, 1H), 1.96 – 1.85 (m, 2H), 1.73 (tdd, J = 6.3, 10.3, 14.9, 2H), 1.45 (ddt, J = 6.2, 9.0, 12.2, 1H), 1.08 (d, J = 6.7, 3H), 1.04 (d, J = 6.7, 3H), 0.81 (app t, J = 7.0, 6H); MS (ESI+) m/z 518 $(M+H)^+$.

Example 174

N^2-(cyclopropylsulfonyl)-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

Step A: N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide was prepared as described in the procedures in Example 170 Steps A-B by substituting (3a*S*,4*S*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from 152 Step A for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.57 - 8.51 (m, 1H), 7.90 (bs, 1H), 7.71 - 7.65 (m, 1H), 7.47 (t, J = 7.7, 1H), 4.57 - 4.49 (m, 1H), 3.73 (d, J = 13.1, 1H), 3.66 - 3.59 (m, 1H), 3.35 (d, J = 13.1, 1H), 2.80 (dd, J = 2.6, 9.4, 1H), 2.78 - 2.69 (m, 1H), 2.49 - 2.40 (m, 1H), 2.35 (dd, J = 2.5, 9.0, 1H), 2.24 - 1.79 (m, 7H), 1.73 - 1.50 (m, 3H), 1.47 - 1.21 (m, 2H), 0.95 - 0.85 (m, 6H).

Step B: To N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Step A (80 mg, 0.184 mmol) in dichloromethane (0.5 mL) was added triethylamine (0.064 mL, 0.461 mmol) followed by cyclopropanesulfonyl chloride (38.9 mg, 0.277 mmol) in a solution of 300 μL dichloromethane and the reaction mixture was stirred at room temperature overnight. The reaction was reduced in volume and loaded onto a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-12). The title compound was eluted with a gradient of 20% to 100% ethyl acetate/hexanes over 20 minutes to give N^2-(cyclopropylsulfonyl)-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.34 (d, J = 9.0, 1H), 8.84 (d, J = 6.8, 1H), 7.73 (s, 1H), 7.64 (d, J = 7.5, 1H), 7.59 (d, J = 12.3, 1H), 7.43 (dd, J = 6.6, 14.3, 1H), 4.53 – 4.42 (m, 2H), 3.76 (d, J = 13.2, 1H), 3.41 (d, J = 13.2, 1H), 2.99 (qd, J = 4.2, 8.0, 1H), 2.90 (dd, J = 3.6, 9.5, 1H), 2.82 – 2.74 (m, 1H), 2.57 – 2.48 (m, 1H), 2.40 (dd, J = 8.5, 19.8, 2H), 2.30 (dd, J = 3.4, 9.2, 1H), 2.02 (td, J = 6.5, 13.7, 1H), 1.94 – 1.85 (m, 2H), 1.85 – 1.78

(m, 1H), 1.71 (td, J = 6.2, 11.6, 1H), 1.67 – 1.58 (m, 1H), 1.40 – 1.28 (m, 2H), 1.22 (dt, J = 4.7, 10.8, 1H), 0.93 (ddd, J = 6.6, 12.3, 14.0, 2H), 0.87 (d, J = 6.5, 3H), 0.84 (d, J = 6.7, 3H); MS (ESI+) m/z 502 $(M+H)^+$.

Example 175

N^2-acetyl-N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

To N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide (123 mg, 0.299 mmol) from Example 164 in dichloromethane (0.5 mL) was added *N*,*N*-diisopropylethylamine (78 µL, 0.448 mmol) followed by acetic anhydride (33.9 µL, 0.359 mmol), and the reaction mixture was stirred at room temperature overnight. The reaction was reduced in volume and loaded onto a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-12), and the product was eluted with a gradient of 0% to 5% methanol (2 *N* ammonia)/dichloromethane over 20 minutes. The solvent was removed in vacuo to supply the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.10 (d, J = 7.1, 1H), 7.81 (d, J = 7.5, 1H), 7.76 (s, 1H), 7.63 (d, J = 7.8, 1H), 7.56 (d, J = 7.7, 1H), 5.54 (dd, J = 6.5, 9.2, 1H), 4.41 (dt, J = 7.3, 14.5, 1H), 3.62 (d, J = 13.2, 1H), 3.49 (d, J = 13.2, 1H), 3.01 (s, 3H), 2.84 – 2.77 (m, 1H), 2.73 (dd, J = 2.8, 9.5, 1H), 2.48 – 2.41 (m, 1H), 2.34 (dd, J = 2.8, 9.0, 1H), 2.25 (dt, J = 7.7, 17.0, 2H), 2.09 (s, 3H), 1.85 (ddd, J = 5.6, 9.9, 13.2, 1H), 1.81 – 1.70 (m, 2H), 1.66 – 1.46 (m, 3H), 1.30 – 1.23 (m, 1H), 0.87 (d, J = 2.7, 3H), 0.85 (d, J = 2.6, 3H); MS (ESI+) m/z 454 $(M+H)^+$.

Example 176

N^2-(2,2-dimethylpropanoyl)-N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

To N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide (38.9 mg, 0.095 mmol) from Example 166 in dichloromethane (0.5 mL) was added *N*,*N*-diisopropylethylamine (24.77 µL, 0.142 mmol) followed by pivaloyl chloride (12.79 µL, 0.104 mmol), and the resultant reaction mixture was stirred at room temperature overnight. The reaction was reduced in volume and loaded onto a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-4). The title compound was eluted with a gradient of 0% to 100% ethyl acetate/hexanes over 15 minutes: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.81 (d, J =

7.4, 1H), 7.74 (s, 1H), 7.60 – 7.55 (m, 2H), 7.43 (dd, J = 6.6, 14.3, 1H), 5.45 (dd, J = 7.0, 8.7, 1H), 4.35 – 4.29 (m, 1H), 3.57 (d, J = 13.5, 1H), 3.44 (d, J = 13.5, 1H), 3.13 (s, 3H), 2.73 (dd, J = 2.6, 8.9, 1H), 2.53 – 2.45 (m, 1H), 2.41 (ddd, J = 2.7, 8.3, 12.0, 1H), 2.37 – 2.32 (m, 1H), 2.29 (dd, J = 3.0, 9.0, 1H), 2.26 – 2.21 (m, 1H), 2.05 (dq, J = 6.0, 12.0, 1H), 1.86 – 1.80 (m, 3H), 1.55 (ddd, J = 6.9, 12.8, 19.6, 2H), 1.41 – 1.31 (m, 1H), 1.30 (s, 9H), 0.88 (d, J = 6.7, 3H), 0.82 (d, J = 6.6, 3H); MS (ESI+) m/z 496 $(M+H)^+$.

Example 177

N^2-(2,2-dimethylpropanoyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared as described in Example 176 substituting N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 170 Step B for N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.77 (d, J = 7.3, 1H), 7.86 (d, J = 8.4, 1H), 7.73 (s, 1H), 7.60 – 7.55 (m, J = 10.6, 2H), 7.45 (t, J = 7.7, 1H), 4.42 – 4.35 (m, 1H), 3.55 (d, J = 13.5, 1H), 3.41 (d, J = 13.5, 1H), 2.71 (d, J = 9.0, 1H), 2.50 (s, 2H), 2.34 (dd, J = 6.9, 8.9, 1H), 2.29 – 2.20 (m, 2H), 2.12 (dq, J = 6.1, 12.3, 1H), 1.94 – 1.74 (m, 5H), 1.66 (dt, J = 7.1, 19.3, 1H), 1.39 (d, J = 6.9, 1H), 1.33 (s, 9H), 0.84 (d, J = 6.1, 3H), 0.82 (d, J = 6.1, 3H); MS (ESI+) m/z 482 $(M+H)^+$.

Example 178

isobutyl (*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate

The title compound was prepared by substituting isobutyl carbonochloridate for methanesulfonyl chloride and N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 170 Step B for N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide in the procedure described in Example 167: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.83 (d, J = 6.8, 1H), 8.42 (d, J = 8.5, 1H), 7.73 (s, 1H), 7.65 – 7.53 (m, 2H), 7.46 – 7.40 (m, 1H), 4.77 (dd, J = 7.5, 15.2, 1H), 4.48 – 4.39 (m, 1H), 4.01 (dd, J = 6.7, 10.3, 1H), 3.92 (dd, J = 6.7, 10.4, 1H), 3.56 (d, J = 13.4, 1H), 3.40 (d, J = 13.5, 1H), 2.77 (d, J = 7.0, 1H), 2.57 – 2.45 (m, 2H), 2.38 – 2.32 (m, 1H), 2.30 – 2.24 (m, 1H), 2.23 – 2.19 (m, 1H), 2.14 (td, J = 5.9, 11.9, 1H), 1.95 –

1.79 (m, 5H), 1.73 – 1.63 (m, 1H), 1.45 – 1.34 (m, 1H), 0.87 (d, J = 5.9, 3H), 0.84 (d, J = 5.8, 3H), 0.82 (d, J = 4.3, 3H), 0.80 (d, J = 4.3, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Example 179

cyclopentyl (*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate

The title compound was prepared by substituting cyclopentyl carbonochloridate for methanesulfonyl chloride and N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 170 Step B for N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide in the procedure describe in Example 167: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.82 (d, J = 7.0, 1H), 8.26 (d, J = 8.6, 1H), 7.73 (s, 1H), 7.62 – 7.53 (m, 2H), 7.43 (t, J = 7.8, 1H), 5.32 – 5.24 (m, 1H), 4.77 (dd, J = 7.0, 15.0, 1H), 4.47 – 4.36 (m, 1H), 3.56 (d, J = 13.4, 1H), 3.40 (d, J = 13.6, 1H), 2.76 (d, J = 9.0, 1H), 2.55 – 2.46 (m, 2H), 2.38 – 2.31 (m, 1H), 2.27 (d, J = 7.2, 1H), 2.21 (t, J = 7.9, 1H), 2.13 (dq, J = 6.2, 12.5, 1H), 1.94 – 1.83 (m, 4H), 1.77 (dd, J = 6.9, 12.4, 2H), 1.73 – 1.64 (m, 3H), 1.58 (dt, J = 8.0, 14.7, 2H), 1.39 (td, J = 9.0, 14.1, 3H), 0.87 (d, J = 5.9, 3H), 0.84 (d, J = 5.3, 3H); MS (ESI+) *m/z* 510 $(M+H)^+$.

Example 180

N^2-[(tert-butylamino)carbonyl]-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

To N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide (113 mg, 0.284 mmol) from Example 170 Step B in dichloromethane (0.5 mL) was added 2-isocyanato-2-methylpropane (35.1 μL, 0.313 mmol) and the reaction mixture was stirred at room temperature overnight. The reaction was reduced in volume and loaded onto a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-12). The title compound was eluted with a gradient of 0% to 10% methanol (2 *N* ammonia)/dichloromethane over 20 minutes: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.74 (d, J = 8.3, 1H), 7.73 (s, 1H), 7.57 (d, J = 9.5, 2H), 7.44 (t, J = 7.7, 1H), 6.56 (d, J = 8.6, 1H), 6.33 (s, 1H), 4.88 (td, J = 5.6, 8.9, 1H), 4.41 – 4.33 (m, 1H), 3.56 (d, J = 13.5, 1H), 3.41 (d, J = 13.6, 1H), 2.71 (dd, J = 1.7, 9.2, 1H), 2.55 – 2.45 (m, 2H), 2.35 (dd, J = 6.9, 8.9, 1H), 2.29 – 2.20 (m, 2H), 2.11 (dq, J = 6.1, 12.1, 1H), 1.92 – 1.77 (m, 3H), 1.73 – 1.64 (m, 2H), 1.44 (s,

9H), 1.43 – 1.35 (m, 1H), 0.85 (d, J = 3.3, 3H), 0.84 (d, J = 3.2, 3H); MS (ESI+) m/z 497 $(M+H)^+$.

Example 181

N^2-[(cyclopentylamino)carbonyl]-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting isocyanatocyclopentane for 2-isocyanato-2-methylpropane as described in the procedure in Example 180: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.84 (d, J = 7.2, 1H), 7.73 (s, 1H), 7.64 – 7.53 (m, 2H), 7.44 (t, J = 9.1, 2H), 6.60 (d, J = 7.4, 1H), 6.57 (d, J = 8.8, 1H), 4.42 – 4.36 (m, 2H), 3.56 (d, J = 13.7, 1H), 3.40 (d, J = 13.6, 1H), 2.73 (dd, J = 1.9, 9.3, 1H), 2.53 – 2.49 (m, 2H), 2.34 (dd, J = 7.0, 9.0, 1H), 2.26 (dd, J = 1.8, 8.9, 1H), 2.24 – 2.20 (m, 1H), 2.16 – 2.09 (m, 1H), 1.90 (tdd, J = 5.7, 12.5, 18.4, 4H), 1.80 (ddd, J = 5.7, 7.9, 13.6, 1H), 1.76 – 1.65 (m, 2H), 1.51 (dt, J = 6.3, 14.9, 3H), 1.41 (tt, J = 7.2, 11.8, 4H), 0.85 (d, J = 6.5, 6H); MS (ESI+) m/z 509 $(M+H)^+$.

Example 182

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

Step A: N^1-[(3a*S*,4*R*,6a*R*)-Octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for *N*-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide in Example 53.

Step B: To N^1-[(3a*S*,4*R*,6a*R*)-Octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Step A (220 mg, 0.622 mmol) in dichloromethane (5.0 mL) was added triethylamine (0.130 mL, 0.934 mmol) followed by 3-(trifluoromethyl)benzene-1-sulfonyl chloride (0.110 ml, 0.685 mmol) and the reaction mixture was stirred at room temperature overnight. The reaction was reduced in volume and loaded onto a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-24). The title compound was eluted with a gradient of 0% to 10% methanol (2 *N* ammonia)/dichloromethane over 20 minutes to give N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.32 (bs, 1H), 8.18 – 8.13 (m, 1H), 8.02 – 7.95 (m, 1H), 7.90 – 7.84 (m, 1H), 7.68 (t, J = 7.9, 1H), 4.17 – 4.09 (m, 1H), 3.77

– 3.69 (m, 1H), 3.20 – 3.11 (m, 2H), 3.05 – 2.97 (m, 4H), 2.53 – 2.47 (m, 2H), 1.98 – 1.88 (m, 1H), 1.87 – 1.71 (m, 3H), 1.62 – 1.48 (m, 3H), 1.46 (s, 9H), 1.32 – 1.22 (m, 1H), 0.87 (dd, J = 6.6, 15.5, 6H).

Step C: The title compound was prepared by substituting N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide for N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide in the procedure described in Example 158: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.38 (s, 1H), 8.30 (d, J = 6.8, 1H), 8.20 (d, J = 7.8, 1H), 7.91 (d, J = 8.0, 1H), 7.72 (t, J = 7.8, 1H), 4.31 – 4.24 (m, 1H), 3.87 (dd, J = 2.2, 10.0, 1H), 3.21 – 3.17 (m, 2H), 3.15 (dd, J = 7.4, 9.9, 1H), 2.95 (dd, J = 7.2, 9.6, 1H), 2.60 – 2.49 (m, 2H), 2.38 (s, 3H), 2.00 – 1.92 (m, 2H), 1.91 – 1.80 (m, 2H), 1.68 (ddd, J = 5.8, 7.9, 13.6, 1H), 1.60 – 1.52 (m, 2H), 1.29 (ddd, J = 6.4, 12.8, 16.2, 1H), 0.89 (d, J = 6.6, 3H), 0.84 (d, J = 6.6, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 183

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared as described in Example 182 substituting 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in Step B: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.30 (d, J = 7.1, 1H), 8.14 (d, J = 8.2, 2H), 7.90 (d, J = 8.3, 2H), 4.30 – 4.23 (m, 1H), 3.86 (dd, J = 2.6, 10.0, 1H), 3.22 – 3.13 (m, 3H), 2.97 (dd, J = 7.3, 9.6, 1H), 2.61 – 2.50 (m, 2H), 2.39 (s, 3H), 2.00 – 1.92 (m, 2H), 1.91 – 1.80 (m, 2H), 1.68 (ddd, J = 5.9, 7.9, 13.7, 1H), 1.61 – 1.52 (m, 2H), 1.30 (ddt, J = 6.7, 9.9, 13.4, 1H), 0.90 (d, J = 6.6, 3H), 0.84 (d, J = 6.6, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 184

N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

Step A: N^1-[(3a*S*,4*R*,6a*R*)-2-Benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-L-leucinamide was prepared by substituting *N*-(*tert*-butoxycarbonyl)-L-leucine for (S)-2-phenylbutanoic acid in the procedure described in Example 16 Step F: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.64 (d, J = 7.1, 1H), 7.97 (d, J = 8.5, 1H), 7.41 (d, J = 7.3, 2H), 7.36 (t, J = 7.5, 2H), 7.27 (t, J = 7.3, 1H), 4.71 (s, 1H), 4.41 (s, 1H), 3.56 (d, J =

13.1, 1H), 3.39 (d, J = 13.1, 1H), 2.74 (d, J = 8.9, 1H), 2.48 (s, 2H), 2.39 - 2.19 (m, 3H), 2.14 (td, J = 6.3, 12.4, 1H), 2.00 - 1.78 (m, 4H), 1.73 - 1.55 (m, 1H), 1.50 (s, 9H), 1.39 (d, J = 7.0, 1H), 0.86 (dd, J = 5.8, 13.4, 6H).

Step B: The title compound was prepared as described with the procedures in Example 182 Steps A-C substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-L-leucinamide from Step A for N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37 (s, 1H), 8.33 (d, J = 6.9, 1H), 8.18 (d, J = 7.9, 1H), 7.91 (d, J = 7.8, 1H), 7.72 (t, J = 7.9, 1H), 4.27 – 4.19 (m, 1H), 3.84 (dd, J = 2.5, 9.9, 1H), 3.55 (dd, J = 4.4, 9.3, 1H), 3.17 (dd, J = 2.7, 9.7, 1H), 3.07 (dd, J = 7.6, 9.8, 1H), 2.91 (dd, J = 7.3, 9.6, 1H), 2.55 – 2.45 (m, 2H), 2.09 (s, 1H), 1.97 – 1.78 (m, 5H), 1.52 (ddd, J = 4.5, 9.5, 18.5, 2H), 1.27 (ddt, J = 6.7, 9.6, 13.2, 1H), 0.89 (d, J = 6.4, 3H), 0.83 (d, J = 6.3, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Example 185 and Example 186

3-(trifluoromethyl)-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide (Example 185) and**

3-(trifluoromethyl)-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide (Example 186)**

To (3a*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 122 Step E (200 mg, 0.703 mmol) in dichloromethane (2 mL) was added triethylamine (0.147 mL, 1.055 mmol) followed by 3-(trifluoromethyl)benzene-1-sulfonyl chloride (0.124 mL, 0.774 mmol), and the reaction mixture was stirred at room temperature overnight. The reaction was quenched with water and extracted with dichloromethane. The organics were reduced in volume and loaded onto a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-24). The title compounds were eluted with a gradient of 0% to 10% methanol (2 *N* ammonia)/dichloromethane over 20 minutes.

Example 185: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.42 (s, 1H), 8.27 (d, J = 7.9, 1H), 7.82 (d, J = 7.8, 1H), 7.64 (s, 1H), 7.61 (d, J = 7.8, 1H), 7.57 (d, J = 8.2, 2H), 7.50 (d, J = 7.7, 1H), 7.40 (t, J = 7.7, 1H), 3.91 – 3.84 (m, 1H), 3.47 (d, J = 13.4, 1H), 3.37 (d, J = 13.4, 1H), 2.78 (dd, J = 4.3, 9.6, 1H), 2.69 (dd, J = 4.4, 7.7, 1H), 2.47 – 2.39 (m, 2H), 2.22 (dt, J = 8.0,

12.6, 2H), 1.89 (qd, J = 7.1, 11.0, 1H), 1.65 (dtd, J = 2.9, 6.2, 8.9, 1H), 1.57 – 1.47 (m, 1H), 1.34 – 1.26 (m, 1H); MS (ESI+) *m/z* 493 $(M+H)^+$.

Example 186: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.51 (d, J = 7.3, 1H), 8.43 (s, 1H), 8.30 (d, J = 7.9, 1H), 7.81 (d, J = 7.7, 1H), 7.72 (s, 1H), 7.60 (dd, J = 3.2, 7.9, 2H), 7.55 (d, J = 7.7, 1H), 7.46 (t, J = 7.7, 1H), 3.82 – 3.74 (m, 1H), 3.54 – 3.44 (m, 2H), 2.61 (dd, J = 1.9, 9.2, 1H), 2.57 – 2.44 (m, 2H), 2.33 (dd, J = 2.0, 9.0, 1H), 2.18 (ddd, J = 6.8, 9.0, 12.7, 2H), 1.96 (td, J = 5.9, 11.8, 1H), 1.89 – 1.79 (m, 1H), 1.64 – 1.54 (m, 1H), 1.29 (ddt, J = 6.4, 10.0, 12.6, 1H); MS (ESI+) *m/z* 493 $(M+H)^+$.

Example 187

3-(trifluoromethyl)-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide

The title compound was prepared by substituting (3a*S*,4*S*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 152 Step A for (3a*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 185: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.26 (s, 1H), 8.41 (s, 1H), 8.27 (d, J = 7.9, 1H), 7.82 (d, J = 7.8, 1H), 7.62 (d, J = 7.9, 1H), 7.57 (d, J = 9.8, 2H), 7.50 (d, J = 7.7, 1H), 7.40 (t, J = 7.7, 1H), 3.87 (dd, J = 7.1, 16.1, 1H), 3.48 (d, J = 13.4, 1H), 3.38 (d, J = 13.4, 1H), 2.77 (dd, J = 4.3, 9.6, 1H), 2.73 – 2.65 (m, 1H), 2.47 – 2.41 (m, 2H), 2.26 – 2.19 (m, 2H), 1.89 (qd, J = 7.1, 10.9, 1H), 1.65 (dtd, J = 2.9, 6.2, 8.9, 1H), 1.52 (dq, J = 8.3, 12.8, 1H), 1.34 – 1.26 (m, 1H); MS (ESI+) *m/z* 493 $(M+H)^+$.

Example 188

3-(trifluoromethyl)-*N*-{(3a*R*,4*R*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide

The title compound was prepared by substituting (3a*R*,4*R*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 157 Step A for (3a*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 185: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.27 (s, 1H), 8.42 (s, 1H), 8.27 (d, J = 7.9, 1H), 7.82 (d, J = 7.8, 1H), 7.64 (s, 1H), 7.62 (d, J = 7.9, 1H), 7.57 (d, J = 9.2, 1H), 7.50 (d, J = 7.6, 1H), 7.40 (t, J = 7.7, 1H), 3.87 (dd, J = 7.1, 16.2, 1H), 3.47 (d, J = 13.4, 1H), 3.37 (d, J = 13.4, 1H), 2.77 (dd, J = 4.3, 9.6, 1H), 2.73 – 2.66 (m, 1H), 2.47 – 2.41 (m, 2H), 2.26 – 2.19 (m, 2H), 1.89 (qd, J = 7.1, 11.0, 1H), 1.65 (dtd, J = 2.9, 6.2, 8.9, 1H), 1.52 (dq, J = 8.4, 12.9, 1H), 1.33 – 1.26 (m, 1H); MS (ESI+) *m/z* 493 $(M+H)^+$.

Example 189

3-(trifluoromethyl)-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide

The title compound was prepared by substituting (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 154 Step A for (3a*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 185: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.51 (d, J = 6.7, 1H), 8.43 (s, 1H), 8.30 (d, J = 7.8, 1H), 7.81 (d, J = 7.9, 1H), 7.72 (s, 1H), 7.62 – 7.52 (m, 3H), 7.45 (t, J = 7.6, 1H), 3.82 – 3.74 (m, 1H), 3.54 – 3.44 (m, 2H), 2.61 (d, J = 9.4, 1H), 2.57 – 2.44 (m, 2H), 2.33 (dd, J = 1.9, 9.0, 1H), 2.18 (ddd, J = 6.9, 9.0, 13.4, 2H), 1.96 (ddd, J = 5.1, 11.0, 16.3, 1H), 1.84 (dt, J = 7.5, 12.3, 1H), 1.58 (dt, J = 9.3, 12.1, 1H), 1.35 – 1.25 (m, 1H); MS (ESI+) *m/z* 493 $(M+H)^+$.

Example 190

***N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide**

The title compound was prepared by substituting (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Example 16 Step E for (3a*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 185: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.49 (d, J = 7.0, 1H), 8.43 (s, 1H), 8.29 (d, J = 7.9, 1H), 7.81 (d, J = 7.8, 1H), 7.60 (d, J = 8.0, 1H), 7.38 (d, J = 4.7, 4H), 7.33 – 7.27 (m, 1H), 3.84 – 3.75 (m, 1H), 3.47 (q, J = 13.1, 2H), 2.61 (dd, J = 2.0, 9.2, 1H), 2.56 – 2.43 (m, 2H), 2.35 (dd, J = 2.0, 9.0, 1H), 2.21 – 2.12 (m, 2H), 1.99 (td, J = 5.9, 11.7, 1H), 1.87 – 1.77 (m, 1H), 1.64 – 1.53 (m, 1H), 1.29 (ddt, J = 6.4, 10.0, 12.6, 1H); MS (ESI+) *m/z* 425 $(M+H)^+$.

Example 191

***N*-{(3a*S*,4*R*,6a*R*)-2-[6,6-bis(4-fluorophenyl)hexyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-(trifluoromethyl)benzenesulfonamide**

Step A: *N*-((3a*S*,4*R*,6a*R*)-Octahydrocyclopenta[*c*]pyrrol-4-yl)-3-(trifluoromethyl)benzenesulfonamide was prepared by substituting *N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide from

Example 190 for *N*-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide in the procedure described in Example 53.

Step B: The title compound was prepared by substituting 6,6-bis(4-fluorophenyl)hexanal for 3-(trifluoromethyl)benzaldehyde and *N*-((3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl)-3-(trifluoromethyl)benzenesulfonamide from Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.53 (d, J = 6.8, 1H), 8.46 (s, 1H), 8.33 (d, J = 7.9, 1H), 7.82 (d, J = 7.8, 1H), 7.63 (t, J = 7.8, 1H), 7.36 – 7.31 (m, 4H), 7.15 (t, J = 8.7, 4H), 3.97 (t, J = 7.8, 1H), 3.83 – 3.74 (m, 1H), 2.66 (d, J = 9.4, 1H), 2.56 – 2.43 (m, 2H), 2.39 (d, J = 8.5, 1H), 2.24 (dt, J = 5.8, 12.0, 2H), 2.10 – 2.04 (m, 2H), 2.04 – 1.99 (m, 2H), 1.99 – 1.91 (m, 1H), 1.87 (dt, J = 6.8, 11.4, 1H), 1.62 – 1.52 (m, 1H), 1.34 (ddd, J = 6.9, 17.6, 29.2, 7H); MS (ESI+) *m/z* 607 $(M+H)^+$.

Example 192

***N*-{(3a*S*,4*R*,6a*R*)-2-[3,5-bis(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-(trifluoromethyl)benzenesulfonamide**

The title compound was prepared by substituting 3,5-bis(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde and *N*-((3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl)-3-(trifluoromethyl)benzenesulfonamide from Example 191 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.53 (d, J = 7.4, 1H), 8.42 (s, 1H), 8.30 (d, J = 7.9, 1H), 8.03 (s, 1H), 7.96 (s, 2H), 7.81 (d, J = 7.8, 1H), 7.60 (t, J = 7.9, 1H), 3.82 – 3.74 (m, 1H), 3.59 (s, 2H), 2.68 – 2.64 (m, 1H), 2.59 – 2.49 (m, 2H), 2.38 – 2.33 (m, 1H), 2.23 (dt, J = 5.9, 8.9, 2H), 1.97 – 1.81 (m, 2H), 1.59 (ddd, J = 8.2, 11.8, 13.0, 1H), 1.35 – 1.24 (m, 1H); MS (ESI+) *m/z* 561 $(M+H)^+$.

Example 193

***N*-{(3a*S*,4*R*,6a*R*)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-(trifluoromethyl)benzenesulfonamide**

The title compound was prepared by substituting 3,3-bis(4-fluorophenyl)propanal for 3-(trifluoromethyl)benzaldehyde and *N*-((3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl)-3-(trifluoromethyl)benzenesulfonamide from Example 191 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.56 (d, J = 7.4, 1H), 8.46 (s, 1H), 8.35

(d, J = 7.9, 1H), 7.80 (d, J = 7.8, 1H), 7.61 (d, J = 7.8, 1H), 7.37 (dd, J = 5.6, 8.4, 2H), 7.34 – 7.30 (m, 2H), 7.16 (dt, J = 8.7, 12.8, 4H), 4.19 (t, J = 7.7, 1H), 3.87 – 3.78 (m, 1H), 2.69 (d, J = 9.1, 1H), 2.55 – 2.44 (m, 2H), 2.39 (d, J = 8.7, 1H), 2.28 – 2.24 (m, 2H), 2.17 (dd, J = 7.8, 15.3, 2H), 2.06 (dd, J = 9.2, 16.3, 2H), 1.98 (dt, J = 5.7, 16.5, 1H), 1.89 (dd, J = 12.0, 19.0, 1H), 1.64 – 1.53 (m, 1H), 1.38 – 1.23 (m, 1H); MS (ESI+) m/z 565 $(M+H)^+$.

Example 194

***N*-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-(trifluoromethyl)benzenesulfonamide**

The title compound was prepared by substituting 3-fluoro-4-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde and *N*-((3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl)-3-(trifluoromethyl)benzenesulfonamide from Example 191 Step A for 2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide in the procedure described for Example 54: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.56 (d, J = 6.8, 1H), 8.44 (s, 1H), 8.33 (d, J = 7.9, 1H), 7.82 (d, J = 7.6, 1H), 7.65 – 7.59 (m, 2H), 7.29 (d, J = 11.8, 1H), 7.21 (s, 1H), 3.81 – 3.74 (m, 1H), 3.46 (s, 2H), 2.64 (d, J = 9.3, 1H), 2.55 (ddd, J = 8.5, 13.8, 27.5, 2H), 2.35 (d, J = 8.7, 1H), 2.17 (dd, J = 7.9, 15.7, 2H), 1.99 (dt, J = 5.9, 16.5, 1H), 1.87 (dt, J = 7.3, 12.1, 1H), 1.60 (dt, J = 8.3, 10.0, 1H), 1.35 – 1.26 (m, 1H); MS (ESI+) m/z 510 $(M+H)^+$.

Example 195

***N*-[(3a*S*,4*S*,6a*R*)-2-(4-hydroxybutyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide**

Step A: *N*-((3a*S*,4*S*,6a*R*)-2-Benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-3-(trifluoromethyl)benzenesulfonamide was prepared by substituting (3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Example 14 Step C for (3a*S**,6a*R**)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 185.

Step B: *N*-((3a*S*,4*S*,6a*R*)-2-Benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-3-(trifluoromethyl)benzenesulfonamide (0.4237 g, 0.998 mmol) from Step A in tetrahydrofuran (10 mL) was added to 20% palladium hydroxide on carbon (wet, 0.085 g, 0.603 mmol) in a 50 mL pressure bottle under nitrogen. The reaction mixture was then placed under a hydrogen atmosphere (30 psi) and shaken at 50 °C for 18 hours. The mixture was filtered through a nylon membrane and the solvent was removed in vacuo. The crude material was

purified by silica gel chromatography using 1-10% methanol (2 *N* ammonia)/dichloromethane supplied the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.50 (s, 1H), 8.38 (d, *J* = 7.9, 1H), 7.85 (d, *J* = 7.8, 1H), 7.68 (t, *J* = 7.8, 1H), 3.89 (dd, *J* = 8.4, 14.2, 1H), 3.82 (t, *J* = 6.2, 2H), 2.82 (dd, *J* = 3.3, 9.7, 1H), 2.62 (qd, *J* = 3.4, 7.9, 1H), 2.42 – 2.36 (m, 1H), 2.32 (d, *J* = 4.5, 2H), 2.26 (dd, *J* = 6.8, 11.7, 2H), 2.10 (t, *J* = 8.7, 1H), 1.91 – 1.82 (m, 1H), 1.74 – 1.67 (m, 2H), 1.64 – 1.49 (m, 5H), 1.32 (dd, *J* = 6.1, 9.6, 1H); MS (ESI+) *m/z* 407 $(M+H)^+$.

Example 196

(3a*S,4*S**,6a*R**)-*N*,*N*-dicyclopropyl-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-amine**

(3a*S**,4*S**,6a*R**)-2-(3-(Trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine (228 mg, 0.802 mmol) from Example 122 Step E and (1-ethoxycyclopropoxy)trimethylsilane (140 mg, 0.802 mmol) were combined in dichloromethane (1.5 mL) and 5 mL of acetic acid was added. The reaction was stirred at room temperature for 20 minutes, and then PS-cyanoborohydride (343 mg, 0.802 mmol) was added. The reaction was heated to 40 °C overnight. Silica gel chromatography eluting with 1-10% methanol (2 *N* ammonia)/dichloromethane to gave the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.58 (s, 1H), 7.48 (d, *J* = 7.6, 2H), 7.42 (d, *J* = 7.6, 1H), 3.64 (d, *J* = 13.6, 1H), 3.51 (d, *J* = 13.6, 1H), 2.94 – 2.82 (m, 3H), 2.80 – 2.71 (m, 2H), 2.55 (dd, *J* = 5.4, 9.4, 3H), 2.41 (t, *J* = 8.3, 1H), 2.16 (dd, *J* = 4.7, 8.7, 1H), 1.97 – 1.70 (m, 7H), 1.70 – 1.59 (m, 3H), 1.40 (dd, *J* = 6.7, 12.6, 1H); MS (ESI+) *m/z* 365 $(M+H)^+$.

Example 197 and Example 198

(3a*S,4*R**,6a*R**)-2-benzyl-*N*-cyclopropyloctahydrocyclopenta[*c*]pyrrol-4-amine (Example 197) and**

(3a*S,4*S**,6a*R**)-2-benzyl-*N*-cyclopropyloctahydrocyclopenta[*c*]pyrrol-4-amine (Example 198)**

2-Benzylhexahydrocyclopenta[*c*]pyrrol-4(5*H*)-one (0.578 g, 2.68 mmol), cyclopropylamine (0.189 mL, 2.68 mmol), and acetic acid (10 mL) were combined in dichloromethane (20 mL). PS-Cyanoborohydride (1.147 g, 2.68 mmol) was added. The reaction was stirred at room temperature for 2 hours, then filtered and the resin was washed with dichloromethane. The solvent was removed in vacuo, and the crude material was

applied to a silica gel column and was eluted with 1-10% methanol(2 *N* ammonia)/dichloromethane to give the title compounds.

(3a*S**,4*R**,6a*R**)-2-benzyl-*N*-cyclopropyloctahydrocyclopenta[*c*]pyrrol-4-amine (Example 197): ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.34 – 7.29 (m, 2H), 7.28 – 7.20 (m, 2H), 3.56 (s, 2H), 3.14 (ddd, *J* = 5.7, 7.3, 10.5, 1H), 2.84 (t, *J* = 8.4, 1H), 2.77 – 2.55 (m, 3H), 2.41 (dd, *J* = 6.2, 9.4, 1H), 2.14 – 2.02 (m, 2H), 1.83 – 1.72 (m, 2H), 1.63 – 1.47 (m, 3H), 1.46 – 1.35 (m, 1H), 0.40 (tdd, *J* = 1.3, 3.0, 4.7, 2H), 0.31 (ddd, *J* = 2.8, 4.3, 6.2, 2H); MS (ESI+) *m/z* 256 $(M+H)^+$.

(3a*S**,4*S**,6a*R**)-2-benzyl-*N*-cyclopropyloctahydrocyclopenta[*c*]pyrrol-4-amine (Example 198): ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.34 – 7.29 (m, 4H), 7.29 – 7.20 (m, 1H), 3.66 – 3.50 (m, 2H), 3.04 – 2.92 (m, 1H), 2.63 (s, 1H), 2.54 – 2.50 (m, 2H), 2.48 – 2.40 (m, 1H), 2.34 (dd, *J* = 3.8, 9.0, 1H), 2.26 (dt, *J* = 5.0, 16.3, 1H), 2.13 – 2.04 (m, 2H), 2.03 – 1.82 (m, 2H), 1.46 – 1.35 (m, 2H), 0.46 – 0.38 (m, 2H), 0.36 – 0.30 (m, 2H); MS (ESI+) *m/z* 256 $(M+H)^+$.

Example 199

***N*-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*-cyclopropyl-3-(trifluoromethyl)benzenesulfonamide**

(3a*S**,4*S**,6a*R**)-2-Benzyl-*N*-cyclopropyloctahydrocyclopenta[*c*]pyrrol-4-amine (382 mg, 1.490 mmol) from Example 198, triethylamine (312 μL, 2.235 mmol), and 3-(trifluoromethyl)benzene-1-sulfonyl chloride (262 μL, 1.639 mmol) were combined in tetrahydrofuran (7 mL). A catalytic amount of (dimethylamino)pyridine was added, and the reaction mixture was stirred at room temperature overnight. The solvent was reduced in volume, and the crude material applied to silica gel and eluted with 20% to 100% ethyl acetate/hexanes to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.46 (s, 1H), 8.31 (d, *J* = 7.9, 1H), 7.93 (d, *J* = 7.8, 1H), 7.74 (t, *J* = 7.9, 1H), 7.41 (d, *J* = 7.2, 2H), 7.36 (t, *J* = 7.4, 2H), 7.29 (t, *J* = 7.2, 1H), 3.97 (ddd, *J* = 6.1, 7.7, 13.5, 1H), 3.54 – 3.45 (m, 2H), 3.17 (dt, *J* = 5.9, 11.8, 1H), 2.82 (dd, *J* = 3.6, 9.7, 1H), 2.55 (t, *J* = 8.2, 1H), 2.51 – 2.43 (m, 2H), 2.36 – 2.22 (m, 2H), 1.88 – 1.82 (m, 1H), 1.57 (dt, *J* = 5.9, 11.6, 1H), 1.43 – 1.32 (m, 3H), 1.05 – 0.98 (m, 1H), 0.80 (ddd, *J* = 6.9, 9.8, 12.4, 1H), 0.73 – 0.65 (m, 1H); MS (ESI+) *m/z* 465 $(M+H)^+$.

Example 200

***N*-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*-cyclopropyl-3-(trifluoromethyl)benzenesulfonamide**

The title compound was prepared by substituting (3a*S**,4*R**,6a*R**)-2-benzyl-*N*-cyclopropyloctahydrocyclopenta[*c*]pyrrol-4-amine from Example 197 for (3a*S**,4*S**,6a*R**)-2-benzyl-*N*-cyclopropyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 199: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.45 (s, 1H), 8.29 (d, *J* = 7.8, 1H), 7.92 (d, *J* = 7.8, 1H), 7.69 (t, *J* = 7.9, 1H), 7.49 (d, *J* = 7.4, 2H), 7.41 (t, *J* = 7.6, 2H), 7.31 (t, *J* = 7.3, 1H), 4.41 (dd, *J* = 7.7, 17.3, 1H), 3.63 (d, *J* = 13.2, 1H), 3.53 (d, *J* = 13.2, 1H), 2.87 (d, *J* = 8.9, 1H), 2.70 (dd, *J* = 8.2, 15.9, 1H), 2.49 (d, *J* = 8.9, 1H), 2.46 – 2.37 (m, 1H), 2.16 – 2.07 (m, 2H), 1.99 – 1.94 (m, 1H), 1.84 – 1.77 (m, 1H), 1.73 – 1.65 (m, 1H), 1.65 – 1.57 (m, 1H), 1.35 – 1.25 (m, 1H), 1.18 (ddd, *J* = 5.1, 6.9, 10.5, 1H), 0.99 (dq, *J* = 4.7, 6.7, 1H), 0.81 – 0.74 (m, 1H), 0.69 (ddd, *J* = 6.9, 10.8, 11.8, 1H); MS (ESI+) *m/z* 465 $(M+H)^+$.

Example 201

***N*-cyclopropyl-*N*-[(3a*S**,4*S**,6a*R**)-octahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide**

(3a*S**,4*S**,6a*R**)-2-benzyl-*N*-cyclopropyloctahydrocyclopenta[*c*]pyrrol-4-amine (0.308 g, 0.663mmol) from Example 199 and methanol (2mL) were added to 20% palladium hydroxide on carbon (wet, 4 mg) in a 50 mL pressure bottle. The reaction was stirred for 16 hours under hydrogen (30 psi) at room temperature. The mixture was filtered through a nylon membrane and the solvent removed in vacuo. The crude material was chromatographed on a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS15-24) eluting with 1-10% methanol (2 *N* ammonia)/dichloromethane to give the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 8.14 (s, 1H), 8.07 (d, *J* = 7.9, 1H), 7.87 (d, *J* = 7.9, 1H), 7.70 (t, *J* = 7.8, 1H), 3.80 – 3.69 (m, 1H), 3.25 (dd, *J* = 7.8, 10.7, 1H), 3.06 – 2.88 (m, 2H), 2.79 – 2.71 (m, 1H), 2.63 – 2.51 (m, 1H), 2.46 (dd, *J* = 5.9, 10.8, 1H), 2.05 (qd, *J* = 7.0, 12.1, 1H), 1.79 (ddd, *J* = 3.9, 6.8, 10.7, 1H), 1.72 – 1.63 (m, 2H), 1.56 (dd, *J* = 4.8, 6.1, 1H), 1.48 (td, *J* = 6.9, 12.8, 1H), 1.31 (ddd, *J* = 2.7, 5.5, 8.8, 1H), 0.92 – 0.70 (m, 3H); MS (ESI+) *m/z* 375 $(M+H)^+$.

Example 202

***N*-{(3a*S**,4*S**,6a*R**)-2-[6,6-bis(4-fluorophenyl)hexyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-*N*-cyclopropyl-3-(trifluoromethyl)benzenesulfonamide**

N-Cyclopropyl-*N*-[(3a*S**,4*S**,6a*R**)-octahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide from Example 201 (140mg, 0.374 mmol) and 6,6-bis(4-fluorophenyl)hexanal (108 mg, 0.374 mmol) were combined in dichloromethane (2 mL) and then acetic acid (1 mL) was added. The reaction was stirred at room temperature for 20 minutes, then PS-cyanoborohydride (306 mg, 0.748 mmol) was added. The reaction was stirred at room temperature overnight, then filtered and the resin washed with dichloromethane. The solvent was removed in vacuo and the crude material purified using a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-12) eluting with 1-10% methanol (2 *N* ammonia)/dichloromethane to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.50 (s, 1H), 8.36 (d, *J* = 7.9, 1H), 7.95 (d, *J* = 7.9, 1H), 7.76 (dd, *J* = 6.4, 14.2, 1H), 7.33 (dd, *J* = 5.6, 8.3, 4H), 7.18 – 7.11 (m, 4H), 3.96 (dd, *J* = 8.0, 16.3, 2H), 3.18 – 3.10 (m, 1H), 2.82 (dd, *J* = 3.5, 9.5, 1H), 2.50 – 2.44 (m, 2H), 2.39 (t, *J* = 8.0, 1H), 2.31 – 2.21 (m, 4H), 2.03 (dd, *J* = 7.8, 15.3, 2H), 1.91 (dt, *J* = 3.5, 10.4, 1H), 1.59 (dt, *J* = 5.6, 11.5, 1H), 1.51 (dd, *J* = 10.6, 16.2, 1H), 1.46 – 1.33 (m, 6H), 1.28 (dd, *J* = 7.4, 15.1, 2H), 1.08 (td, *J* = 5.0, 10.5, 1H), 0.84 (dt, *J* = 6.9, 12.6, 1H), 0.75 – 0.66 (m, 1H); MS (ESI+) *m/z* 647 $(M+H)^+$.

Example 203

***N*-{(3a*S**,4*S**,6a*R**)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-*N*-cyclopropyl-3-(trifluoromethyl)benzenesulfonamide**

The title compound was prepared by substituting 3,3-bis(4-fluorophenyl)propanal for 6,6-bis(4-fluorophenyl)hexanal in the procedure described for Example 202: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.49 (s, 1H), 8.35 (d, *J* = 7.9, 1H), 7.94 (d, *J* = 7.8, 1H), 7.77 (t, *J* = 7.9, 1H), 7.34 (ddd, *J* = 2.1, 5.5, 8.4, 4H), 7.14 (td, *J* = 2.2, 8.8, 4H), 4.16 (t, *J* = 7.3, 1H), 3.97 – 3.90 (m, 1H), 3.24 – 3.15 (m, 1H), 2.77 (dd, *J* = 4.1, 9.1, 1H), 2.54 (t, *J* = 8.1, 1H), 2.47 (dd, *J* = 7.1, 15.3, 2H), 2.32 – 2.20 (m, 6H), 1.91 (dt, *J* = 3.5, 10.5, 1H), 1.63 (dt, *J* = 5.8, 11.6, 1H), 1.52 – 1.36 (m, 3H), 1.03 (dt, *J* = 4.5, 10.6, 1H), 0.83 (dt, *J* = 6.8, 12.6, 1H), 0.78 – 0.70 (m, 1H); MS (ESI+) *m/z* 605 $(M+H)^+$.

Example 204

***N*-cyclopropyl-3-(trifluoromethyl)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide**

The title compound was prepared by substituting 3-(trifluoromethyl)benzaldehyde for 6,6-bis(4-fluorophenyl)hexanal in the procedure described for Example 202: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.46 (s, 1H), 8.32 (d, J = 7.9, 1H), 7.93 (d, J = 7.8, 1H), 7.76 – 7.72 (m, 2H), 7.52 (d, J = 7.7, 1H), 7.44 (t, J = 7.7, 1H), 4.00 – 3.93 (m, 1H), 3.50 (d, J = 13.2, 1H), 3.43 (d, J = 13.2, 1H), 3.15 (qd, J = 3.8, 7.8, 1H), 2.78 (dd, J = 3.8, 9.7, 1H), 2.52 – 2.43 (m, 2H), 2.39 (dd, J = 8.0, 9.5, 1H), 2.32 – 2.22 (m, 2H), 1.90 – 1.82 (m, 1H), 1.59 (dt, J = 5.9, 11.5, 1H), 1.48 – 1.32 (m, 4H), 0.99 – 0.93 (m, 1H), 0.81 (ddd, J = 6.9, 9.8, 12.4, 1H), 0.75 – 0.67 (m, 1H); MS (ESI+) *m/z* 533 $(M+H)^+$.

Example 205

2,2-dicyclohexyl-*N*-((3a*S*,4*S*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide

2,2-Dicyclohexyl-*N*-((3a*S*,4*S*,6a*R*)-octahydrocyclopenta[c]pyrrol-4-yl)acetamide from Example 53 (101 mg, 0.304 mmol), triethylamine (0.042 mL, 0.304 mmol), and 3-(trifluoromethyl)benzene-1-sulfonyl chloride (0.049 mL, 0.304 mmol) were combined in dichloromethane (2 mL). A catalytic amount of *N,N*-dimethylaminopyridine was added. The reaction was stirred at room temperature for 1 hour and lcms showed product, and tlc showed no more starting material. The reaction was quenched with aqueous sodium bicarbonate and the aqueous layer was separated. The organic layers was concentrated to give a precipitate. The precipitate was washed with water and ether and dried under a stream of nitrogen to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.49 (d, J = 6.3, 1H), 8.34 (s, 1H), 8.19 (d, J = 7.9, 1H), 7.93 (d, J = 7.8, 1H), 7.73 (t, J = 7.8, 1H), 4.46 – 4.38 (m, 1H), 3.73 (dd, J = 3.4, 9.3, 1H), 3.17 (dd, J = 2.8, 9.7, 1H), 3.07 (ddd, J = 6.4, 12.0, 23.6, 3H), 2.49 (dd, J = 8.0, 15.9, 1H), 2.12 (t, J = 7.2, 1H), 2.02 – 1.77 (m, 8H), 1.73 (dd, J = 5.3, 9.0, 4H), 1.68 – 1.58 (m, 3H), 1.52 (ddd, J = 3.2, 12.5, 14.7, 1H), 1.43 (ddd, J = 3.1, 12.6, 15.0, 1H), 1.37 – 1.03 (m, 9H); MS (ESI+) *m/z* 541 $(M+H)^+$.

Example 206

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[(2-phenylethyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide

The title compound was prepared by substituting 2-phenylethanesulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 205: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.35 (d, J = 7.0, 1H), 7.33 – 7.25 (m, 4H), 4.60 – 4.51 (m, 1H), 3.79 (dd, J = 4.8, 10.2, 1H), 3.56 – 3.39 (m, 4H), 3.27 (t, J = 8.3, 2H), 3.24 – 3.16 (m, 2H), 2.66 – 2.57 (m, 1H), 2.09 (t, J = 7.4, 1H), 2.00 – 1.76 (m, 9H), 1.72 (d, J = 12.9, 4H), 1.67 – 1.64 (m, 1H), 1.59 (t, J = 13.7, 2H), 1.54 – 1.36 (m, 3H), 1.30 – 1.18 (m, 4H), 1.18 – 1.06 (m, 4H); MS (ESI+) *m/z* 501 $(M+H)^+$.

Example 207

2,2-dicyclohexyl-*N*-((3a*S*,4*S*,6a*R*)-2-{[2-(1-naphthyl)ethyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide

The title compound was prepared by substituting 2-(naphthalen-1-yl)ethanesulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 205: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37 (d, J = 6.8, 1H), 8.13 (d, J = 9.0, 1H), 7.97 – 7.94 (m, 1H), 7.85 (d, J = 8.2, 1H), 7.53 (p, J = 6.9, 2H), 7.46 – 7.40 (m, 1H), 7.36 (t, J = 7.9, 1H), 4.60 – 4.49 (m, 1H), 3.81 (dd, J = 4.8, 10.2, 1H), 3.75 (t, J = 8.3, 2H), 3.57 – 3.46 (m, 4H), 3.27 – 3.16 (m, 2H), 2.67 – 2.59 (m, 1H), 2.09 (t, J = 7.3, 1H), 1.95 (t, J = 13.3, 2H), 1.89 – 1.76 (m, 5H), 1.72 (d, J = 12.2, 4H), 1.66 (dd, J = 5.1, 7.2, 1H), 1.60 (t, J = 10.5, 2H), 1.46 (dt, J = 10.8, 20.4, 3H), 1.29 – 1.18 (m, 4H), 1.18 – 1.03 (m, 5H); MS (ESI+) *m/z* 551 $(M+H)^+$.

Example 208

2,2-dicyclohexyl-*N*-((3a*S*,4*S*,6a*R*)-2-{[3-(trifluoromethyl)benzyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide

The title compound was prepared by substituting (3-(trifluoromethyl)phenyl)methanesulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 205: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.32 (d, J = 6.7, 1H), 7.96 (s, 1H), 7.81 (d, J = 7.7, 1H), 7.64 (d, J = 7.7, 1H), 7.46 (t, J = 7.7, 1H), 4.69 (q, J = 13.5, 2H), 4.58 – 4.49 (m, 1H), 3.81 (dd, J = 4.9, 10.4, 1H), 3.52 (dd, J = 6.3, 13.7, 2H), 3.26 (dd, J = 3.1, 9.9, 1H), 3.23 – 3.15 (m, 1H), 2.65 – 2.58 (m, 1H), 2.06 (t, J = 7.3, 1H), 1.93 (d, J = 13.8, 2H), 1.82 (dt, J = 9.9, 14.4, 6H), 1.71 (t, J = 10.2, 4H), 1.67 (dd,

J = 7.0, 11.0, 1H), 1.60 (d, *J* = 9.5, 2H), 1.51 – 1.35 (m, 3H), 1.29 – 1.02 (m, 8H); MS (ESI+) *m/z* 555 $(M+H)^+$.

Example 209

2,2-dicyclohexyl-*N*-((3a*S*,4*S*,6a*R*)-2-{[2-(4-fluorophenyl)ethyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide

The title compound was prepared by substituting 2-(4-fluorophenyl)ethanesulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 205: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37 (d, *J* = 6.8, 1H), 7.18 (dd, *J* = 5.6, 8.5, 2H), 7.09 (t, *J* = 8.7, 2H), 4.60 – 4.49 (m, 1H), 3.80 (dd, *J* = 4.9, 10.3, 1H), 3.57 – 3.39 (m, 4H), 3.27 – 3.16 (m, 4H), 2.67 – 2.59 (m, 1H), 2.09 (t, *J* = 7.3, 1H), 1.99 – 1.77 (m, 8H), 1.72 (d, *J* = 12.4, 4H), 1.66 (dd, *J* = 3.0, 8.1, 1H), 1.59 (t, *J* = 14.2, 2H), 1.46 (ddd, *J* = 7.9, 16.4, 33.2, 3H), 1.24 (ddd, *J* = 3.2, 12.7, 25.7, 4H), 1.18 – 1.03 (m, 4H); MS (ESI+) *m/z* 519 $(M+H)^+$.

Examples 210 and Example 211

(2*S*)-2-phenyl-*N*-{(3a*R*,4*R*,6a*S*)-2-[(1*S*)-1-phenylethyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide (Example 210) and

(2*S*)-2-phenyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[(1*S*)-1-phenylethyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide (Example 211)

Step A: (3a*R*,6a*S*)-2-((*S*)-1-Phenylethyl)hexahydrocyclopenta[c]pyrrol-4(5*H*)-one and (3a*S*,6a*R*)-2-((*S*)-1-phenylethyl)hexahydrocyclopenta[c]pyrrol-4(5*H*)-one were prepared as described in the procedure described in Example 122 Step C substituting *S*(-)-*N*-methoxymethyl-*N*-(trifluorosilyl)methyl-1-phenylethyl amine for 1-methoxy-*N*-(3-(trifluoromethyl)benzyl)-*N*-((trimethylsilyl)methyl)methanamine.

(3a*R*,6a*S*)-2-((*S*)-1-phenylethyl)hexahydrocyclopenta[c]pyrrol-4(5*H*)-one: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.34 – 7.16 (m, 5H), 3.23 (d, *J* = 8.9, 1H), 3.12 (q, *J* = 6.6, 1H), 2.80 (dt, *J* = 7.5, 14.9, 1H), 2.60 (t, *J* = 8.6, 1H), 2.48 (dd, *J* = 2.0, 9.5, 1H), 2.44 – 2.20 (m, 5H), 2.08 (ddd, *J* = 8.2, 13.0, 17.0, 1H), 1.72 (ddd, *J* = 6.7, 10.1, 17.4, 1H), 1.31 (d, *J* = 6.6, 3H); MS (ESI+) *m/z* 230 $(M+H)^+$.

(3a*S*,6a*R*)-2-((*S*)-1-phenylethyl)hexahydrocyclopenta[c]pyrrol-4(5*H*)-one: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.39 – 7.13 (m, 5H), 3.15 (dd, *J* = 6.5, 13.1, 1H), 2.88 (dd, *J* = 7.1, 13.7, 1H), 2.76 (t, *J* = 9.0, 3H), 2.54 (dd, *J* = 9.9, 18.1, 2H), 2.45 – 2.35 (m, 2H), 2.34 – 2.26 (m,

1H), 2.13 (ddd, J = 6.5, 10.8, 17.2, 1H), 1.91 – 1.77 (m, 1H), 1.33 (d, J = 6.2, 3H); MS (ESI+) m/z 230 $(M+H)^+$.

Step B: (3a*R*,6a*S*)-2-((*S*)-1-Phenylethyl)octahydrocyclopenta[*c*]pyrrol-4-amine was prepared as described in Example 122 Step D-E substituting (3a*R*,6a*S*)-2-((*S*)-1-phenylethyl)hexahydrocyclopenta[c]pyrrol-4(5*H*)-one from Step A for 2-(3-(trifluoromethyl)benzyl)hexahydrocyclopenta[*c*]pyrrol-4(5*H*)-one: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.47 – 7.09 (m, 5H), 3.12 (dd, J = 6.1, 12.5, 1H), 2.75 (br s, 2H), 2.48 (d, J = 6.5, 3H), 2.33 – 2.20 (m, 1H), 2.11 – 1.95 (m, 1H), 1.94 – 1.73 (m, 2H), 1.73 – 1.54 (m, 2H), 1.43 (s, 3H), 1.35 (d, J = 6.3, 3H); MS (ESI+) m/z 231 $(M+H)^+$.

Step C: The title compounds were prepared by substituting (*S*)-2-phenylbutanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*R*,6a*S*)-2-((*S*)-1-phenylethyl)octahydrocyclopenta[*c*]pyrrol-4-amine for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Examples 1 and 2.

Example 210: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 11.04 (d, J = 6.9, 1H), 10.39 (d, J = 7.2, 2H), 10.16 (q, J = 8.0, 4H), 10.13 – 10.04 (m, 4H), 7.19 (dt, J = 7.1, 14.1, 1H), 6.36 (dd, J = 6.3, 8.7, 1H), 5.82 (q, J = 6.5, 1H), 5.69 (dd, J = 2.5, 9.4, 1H), 5.56 (qd, J = 2.7, 7.7, 1H), 5.22 – 5.07 (m, 2H), 4.99 – 4.92 (m, 2H), 4.90 (dd, J = 2.7, 9.2, 1H), 4.65 (td, J = 6.8, 13.6, 1H), 4.55 (dt, J = 7.1, 11.8, 1H), 4.32 – 4.20 (m, 2H), 4.11 (d, J = 6.5, 3H), 3.86 – 3.80 (m, 1H), 3.75 (t, J = 7.3, 3H); MS (ESI+) m/z 377 $(M+H)^+$.

Example 211: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 11.35 (d, J = 7.1, 1H), 10.40 (d, J = 7.1, 2H), 10.13 (dt, J = 7.6, 15.2, 6H), 10.04 (dt, J = 4.6, 14.8, 2H), 7.22 – 7.14 (m, 1H), 6.36 (dd, J = 6.3, 8.8, 1H), 5.78 (q, J = 6.5, 1H), 5.55 (d, J = 8.8, 1H), 5.22 – 5.09 (m, 3H), 5.04 – 4.98 (m, 1H), 4.92 (dd, J = 8.9, 15.9, 3H), 4.70 – 4.60 (m, 1H), 4.59 – 4.52 (m, 1H), 4.42 (dt, J = 6.9, 19.0, 1H), 4.10 (dd, J = 6.6, 18.3, 1H), 4.01 (d, J = 6.5, 3H), 3.75 (t, J = 7.3, 3H); MS (ESI+) m/z 377 $(M+H)^+$.

Example 212 and Example 213

(2*S*)-2-phenyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[(1*S*)-1-phenylethyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide (Example 212) and

(2*S*)-2-phenyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[(1*S*)-1-phenylethyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide (Example 213)

Step A: (3a*S*,6a*R*)-2-((*S*)-1-phenylethyl)octahydrocyclopenta[*c*]pyrrol-4-amine was prepared as described in Example 122 Steps D-E substituting (3a*S*,6a*R*)-2-((*S*)-1-

phenylethyl)hexahydrocyclopenta[*c*]pyrrol-4(5*H*)-one from Example 210 Step A for 2-(3-(trifluoromethyl)benzyl)hexahydrocyclopenta[*c*]pyrrol-4(5*H*)-one: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.47 – 7.09 (m, 5H), 3.12 (dd, *J* = 6.1, 12.5, 1H), 2.75 (br s, 2H), 2.48 (d, *J* = 6.5, 3H), 2.33 – 2.20 (m, 1H), 2.11 – 1.95 (m, 1H), 1.94 – 1.73 (m, 2H), 1.73 – 1.54 (m, 2H), 1.43 (br s, 2H), 1.35 (d, *J* = 6.3, 3H); MS (ESI+) *m/z* 231 $(M+H)^+$.

Step B: The title compounds were prepared by substituting (*S*)-2-phenylbutanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*S*,6a*R*)-2-((*S*)-1-phenylethyl)octahydrocyclopenta[*c*]pyrrol-4-amine for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Examples 1 and 2.

Example 212: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 10.86 (d, *J* = 6.3, 1H), 10.31 (d, *J* = 7.3, 2H), 10.18 – 10.07 (m, 7H), 10.04 (t, *J* = 7.3, 1H), 7.12 (dt, *J* = 7.2, 14.6, 1H), 6.31 (dd, *J* = 6.4, 8.6, 1H), 5.77 (q, *J* = 6.6, 1H), 5.61 – 5.53 (m, 1H), 5.21 – 5.08 (m, 3H), 4.99 (dd, *J* = 4.6, 9.8, 1H), 4.94 (dd, *J* = 8.3, 16.1, 2H), 4.70 – 4.60 (m, 2H), 4.46 (dt, *J* = 5.8, 16.8, 1H), 4.41 – 4.33 (m, 1H), 4.13 – 4.06 (m, 1H), 4.01 (d, *J* = 6.6, 3H), 3.75 (t, *J* = 7.3, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Example 213: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.50 (d, *J* = 7.1, 1H), 7.56 (s, 1H), 7.45 (d, *J* = 7.3, 2H), 7.34 (dt, *J* = 7.6, 16.7, 4H), 7.25 (dd, *J* = 7.3, 13.4, 3H), 4.37 – 4.30 (m, 1H), 3.52 (dd, *J* = 6.2, 8.8, 1H), 3.11 (q, *J* = 6.5, 1H), 2.60 (dd, *J* = 2.3, 8.1, 1H), 2.56 – 2.44 (m, 3H), 2.37 – 2.27 (m, 3H), 2.04 – 1.96 (m, 1H), 1.85 – 1.74 (m, 2H), 1.49 (dq, *J* = 6.8, 13.3, 1H), 1.38 – 1.32 (m, 1H), 1.29 (d, *J* = 6.6, 3H), 0.92 (t, *J* = 7.3, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Example 214

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*,3-dimethyl-2-phenylbutanamide

Step A: Di-*tert*-butyl dicarbonate (0.429 mL, 1.849 mmol), (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine (200 mg, 0.925 mmol) from Example 33 Step A, and (dimethylamino)pyridine (22.59 mg, 0.185 mmol) were combined in dichloromethane (5mL). The reaction mixture was stirred at room temperature for 30 minutes. The crude material was purified on a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-4) eluting with ethyl acetate/hexanes to give *tert*-butyl (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylcarbamate: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7.39 – 7.12 (m, 5H), 4.47 (s, 1H), 3.74 (s, 1H), 3.61 (s, 1H), 3.52 (s, 1H), 2.55 (t, *J* = 31.6, 4H),

2.31 (s, 2H), 2.03 (d, J = 6.1, 1H), 1.83 (d, J = 8.0, 1H), 1.58 (s, 1H), 1.43 (s, 9H), 0.98 – 0.79 (m, 1H); MS (ESI+) m/z 317 $(M+H)^+$.

Step B: *tert*-Butyl (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylcarbamate (59 mg, 0.187mmol) from Step A was treated with lithium aluminum hydride (0.374 mmol) in tetrahydrofuran (0.5 mL). The reaction was stirred at room temperature for 1 hour and then heated to reflux for 2 hours. The reaction was cooled to room temperature and quenched with dropwise addition of saturated aqueous sodium sulfate (50 µL) to give a precipitate. The precipitate was washed with tetrahydrofuran, and then the solvent was removed to give (3a*R*,4*S*,6a*S*)-2-benzyl-*N*-methyloctahydrocyclopenta[*c*]pyrrol-4-amine: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.34 – 7.28 (m, 4H), 7.25 – 7.19 (m, 1H), 3.60 – 3.51 (m, 2H), 2.76 (q, J = 5.6, 1H), 2.64 (d, J = 15.7, 1H), 2.58 – 2.53 (m, 1H), 2.51 – 2.46 (m, 1H), 2.40 – 2.35 (m, 4H), 2.31 – 2.22 (m, 2H), 1.98 – 1.85 (m, 2H), 1.39 (dt, J = 5.7, 10.6, 3H); MS (ESI+) m/z 231 $(M+H)^+$.

Step C: The title compound was prepared by substituting 3-methyl-2-phenylbutanoic acid for 1-phenylcyclopentanecarboxylic acid and (3a*R*,4*S*,6a*S*)-2-benzyl-*N*-methyloctahydrocyclopenta[*c*]pyrrol-4-amine for (3a*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 2: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.59 – 7.41 (m, 5H), 7.39 – 7.16 (m, 5H), 3.64 (d, J = 13.2, 1H), 3.50 (d, J = 9.5, 1H), 2.69 – 2.52 (m, 2H), 2.50 – 2.33 (m, 3H), 2.25 – 2.15 (m, 1H), 2.05 (dd, J = 6.3, 9.2, 1H), 1.88 – 1.67 (m, 2H), 1.34 (dd, J = 13.4, 19.6, 3H), 1.08 (d, J = 6.4, 3H), 1.03 – 0.95 (m, 1H), 0.79 – 0.66 (m, 6H); MS (ESI+) m/z 391 $(M+H)^+$.

Example 215

N-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*,3-dimethyl-2-phenylbutanamide

The title compound was prepared as described in Example 214 substituting (3a*R**,4*S**,6a*S**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine (International Publication No. WO2006/012396) for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in Example 214 Step A: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.61 – 7.41 (m, 5H), 7.26 (dd, J = 15.4, 37.9, 5H), 3.65 (d, J = 13.2, 1H), 3.54 (dd, J = 7.6, 19.9, 2H), 2.70 – 2.53 (m, 2H), 2.50 – 2.36 (m, 2H), 2.25 – 2.15 (m, 1H), 2.07 (s, 1H), 1.87 – 1.66 (m, 2H), 1.43 – 1.26 (m, 3H), 1.19 (d, J = 6.4, 2H), 1.08 (d, J = 6.5, 2H), 1.01 (d, J = 6.4, 1H), 0.79 – 0.63 (m, 5H); MS (ESI+) m/z 391 $(M+H)^+$.

Example 216

(3a*R,4*S**,6a*S**)-*N*-benzyl-2-(3-methyl-2-phenylbutanoyl)octahydrocyclopenta[*c*]pyrrol-4-amine**

Step A: *tert*-Butyl (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylcarbamate was prepared as described in Example 214 Step A substituting (3a*R**,4*S**,6a*S**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine (International Publication No. WO2006/012396) for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine: MS (ESI+) *m/z* 317 $(M+H)^+$.

Step B: *tert*-Butyl (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylcarbamate (100 mg, 0.316 mmol) from Step A and ammonium formate (100 mg, 1.580 mmol) were combined in ethanol. The reaction was deoxygenated at low temperature, and palladium on carbon (3.36 mg, 0.032 mmol) was added. The reaction was heated to reflux under nitrogen. After 3 hours, tlc and lcms showed mostly starting material. Degussa's catalyst and 5 equivalents more ammonium formate were added and the reaction mixture was refluxed under nitrogen overnight. More ammonium formate and Degussa's catalyst were added and the reaction heated to 90 °C. After 2 hours, tlc and lcms show no remaining starting material. The reaction was filtered through diatomaceous earth containing carbonate functionalized silica gel (Silicycle, Quebec, Canada) with methanol. Solvent removal in vacuo gave *tert*-butyl (3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate: MS (ESI+) *m/z* 226 $(M+H)^+$.

Step C: 3-Methyl-2-phenylbutanoic acid (63 mg, 0.353 mmol), 1-hydroxybenzotriazole (54.1 mg, 0.353 mmol), and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide (0.063 mL, 0.353 mmol) were combined in dichloromethane (5 mL). The reaction was stirred at room temperature for 20 minutes, and then *tert*-butyl (3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate (80 mg, 0.353 mmol) from Step B was added. After 30 minutes, the reaction was quenched with water and extracted with dichloromethane. The combined extracts were concentrated, and the crude material purified using 10-100% ethyl acetate/hexanes to give *tert*-butyl (3a*R*,4*S*,6a*S*)-2-(3-methyl-2-phenylbutanoyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate: MS (ESI+) *m/z* 387 $(M+H)^+$.

Step D: *tert*-Butyl (3a*R*,4*S*,6a*S*)-2-(3-methyl-2-phenylbutanoyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate (39 mg, 0.101 mmol) from Step C was combined with 4 *M* HCl in dioxane (5 mL, 20.00 mmol) in ether (5 mL). After about 2 hours, the solvent was removed in vacuo to give 1-((3a*R*,4*S*,6a*S*)-4-

aminohexahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)-3-methyl-2-phenylbutan-1-one hydrochloric acid salt which was used in the next step without additional purification: MS (ESI+) *m/z* 287 $(M+H)^+$.

Step E: 1-((3a*R*,4*S*,6a*S*)-4-aminohexahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)-3-methyl-2-phenylbutan-1-one hydrochloric acid salt (49 mg, 0.152 mmol) and benzaldehyde (0.023 mL, 0.228 mmol) were combined in dichloromethane (1.5 mL). Acetic acid (1.5 mL) was added. The reaction was stirred at room temperature for 30 minutes, then PS-cyanoborohydride (64.9 mg, 0.152 mmol) was added. After 72 hours, lcms of the reaction showed no more starting material. The reaction mixture was filtered, and the solvent was removed under a stream of nitrogen. The crude material was purified using a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-4) eluting with 1-10% methanol (2 *N* ammonia)/dichloromethane to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.69 – 7.60 (m, 2H), 7.54 – 7.44 (m, 2H), 7.44 – 7.34 (m, 5H), 7.29 (tdd, *J* = 4.8, 7.8, 13.0, 2H), 3.90 – 3.36 (m, 4H), 3.29 (dd, *J* = 3.8, 10.6, 0.5H), 2.99 (dd, *J* = 5.7, 11.4, 0.5H), 2.93 (dd, *J* = 6.0, 11.3, 0.5H), 2.75 – 2.63 (m, 1H), 2.59 – 2.48 (m, 1H), 2.46 – 2.31 (m, 1H), 2.25 (dt, *J* = 4.1, 8.7, 0.5H), 1.97 (dt, *J* = 9.3, 11.6, 1H), 1.93 – 1.85 (m, 0.5H), 1.84 – 1.74 (m, 1H), 1.65 – 1.55 (m, 0.5H), 1.51 – 1.35 (m, 1H), 1.33 – 1.21 (m, 1H), 1.18 – 1.10 (m, 3H), 1.01 (td, *J* = 7.7, 13.1, 0.5H), 0.87 (dt, *J* = 6.6, 12.9, 0.5H), 0.75 (t, *J* = 7.2, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Example 217

2,2-dicyclohexyl-*N*-[(3a*S*,4*R*,6a*R*)-2-(*N*,*N*-dimethyl-D-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide

Step A: *N*-(*tert*-Butoxycarbonyl)-D-leucine (72.7 mg, 0.314 mmol), 2,2-dicyclohexyl-*N*-[(3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide (95 mg, 0.286 mmol) from Example 74, and hydroxybenzotriazole (48.1 mg, 0.314 mmol) were combined in dichloromethane (10 mL). After 20 minutes, *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide (0.056 mL, 0.314 mmol) was added, and the reaction mixture was stirred at room temperature for 18 hours. The reaction was quenched with water. The separated organic layer was reduced in volume, and the crude material was applied to a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-12) and eluted first with 10% to 100% ethyl acetate/hexanes and then with 1-10% methanol (2 *N* ammonia)/dichloromethane to give *tert*-butyl (*R*)-1-((3a*S*,4*R*,6a*R*)-4-(2,2-dicyclohexylacetamido)hexahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)-4-methyl-1-oxopentan-2-ylcarbamate: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm

8.26 (dd, J = 7.2, 24.0, 1H), 7.91 (d, J = 8.6, 1H), 4.48 – 4.36 (m, 1H), 4.12 – 3.96 (m, 1H), 3.87 (dd, J = 7.4, 10.3, 1H), 3.70 (ddd, J = 8.0, 14.4, 23.7, 1H), 3.40 (dd, J = 5.7, 12.3, 1H), 2.77 (s, 1H), 2.58 (d, J = 6.1, 1H), 2.08 (s, 1H), 2.01 (dd, J = 5.6, 10.4, 2H), 1.96 – 1.55 (m, 17H), 1.54 – 1.50 (m, 9H), 1.49 – 1.37 (m, 2H), 1.19 (qdd, J = 12.3, 22.3, 24.7, 11H), 1.00 (t, J = 6.6, 3H), 0.88 (d, J = 6.6, 1H).

Step B: *tert*-Butyl (*R*)-1-((3a*S*,4*R*,6a*R*)-4-(2,2-dicyclohexylacetamido)hexahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)-4-methyl-1-oxopentan-2-ylcarbamate (185 mg, 0.339 mmol) from Step A, and 2 *N* HCl in ether (2.5 mL, 5.00 mmol) were combined in ether (1 mL). The reaction mixture was stirred at room temperature overnight. The solids were collected and dried to give *N*-((3a*S*,4*R*,6a*R*)-2-((*R*)-2-amino-4-methylpentanoyl)octahydrocyclopenta[*c*]pyrrol-4-yl)-2,2-dicyclohexylacetamide: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.34 – 8.24 (m, 1H), 4.92 (br s, 2H), 4.46 – 4.31 (m, 1H), 4.07 (d, J = 9.2, 0.5H), 3.91 – 3.81 (m, 1.5H), 3.77 (dd, J = 8.8, 12.1, 1H), 3.72 – 3.64 (m, 0.5H), 3.59 – 3.53 (m, 0.5H), 3.45 (dd, J = 5.2, 12.2, 0.5H), 3.32 (d, J = 6.5, 0.5H), 2.82 – 2.69 (m, 1H), 2.63 (dd, J = 8.4, 14.5, 0.5H), 2.54 (dd, J = 8.0, 16.4, 0.5H), 2.21 – 2.06 (m, 2H), 2.02 (q, J = 7.6, 1H), 1.99 – 1.55 (m, 15H), 1.50 – 1.38 (m, 3H), 1.37 – 1.12 (m, 9H), 1.09 (d, J = 6.5, 3H), 1.01 (d, J = 6.6, 2H), 0.96 (d, J = 6.4, 1H), 0.91 (d, J = 6.6, 1H). MS (ESI+) *m/z* 466 $(M+H)^+$.

Step C: To *N*-((3a*S*,4*R*,6a*R*)-2-((*R*)-2-amino-4-methylpentanoyl)octahydrocyclopenta[*c*]pyrrol-4-yl)-2,2-dicyclohexylacetamide (0.133 g, 0.298 mmol) from Step B was added formaldehyde (0.228 mL, 2.98 mmol) in dichloromethane (0.5 mL). Acetic acid (0.5 mL) was added. The reaction was stirred at room temperature for 30 minutes, PS-cyanoborohydride (0.255 g, 0.597 mmol) was then added, and the reaction mixture was stirred at room temperature overnight. The reaction was filtered, and the solvent was removed in vacuo. The crude material was purified on silica gel chromatography on a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-12) eluting with 1-10% methanol (2 *N* ammonia)/dichloromethane to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.29 (dd, J = 7.1, 15.9, 1H), 4.46 – 4.35 (m, 1H), 4.09 – 3.99 (m, 1H), 3.92 – 3.80 (m, 1H), 3.70 (dd, J = 8.6, 12.4, 1H), 3.66 – 3.58 (m, 2H), 3.45 (dd, J = 4.8, 9.1, 0.5H), 2.78 – 2.64 (m, 1H), 2.63 – 2.53 (m, 1H), 2.42 (s, 3H), 2.38 (s, 3H), 2.23 – 2.14 (m, 0.5H), 2.13 – 1.99 (m, 2H), 1.99 – 1.82 (m, 5H), 1.82 – 1.63 (m, 8H), 1.60 (d, J = 14.0, 1H), 1.57 – 1.51 (m, 1H), 1.45 (ddd, J = 8.6, 18.8, 29.3, 3H), 1.36 – 1.05 (m, 9H), 1.01 (d, J = 6.6, 3H), 0.91 (dd, J = 6.6, 19.9, 3H); MS (ESI+) *m/z* 474 $(M+H)^+$.

Example 218

***N*-[(3a*R*,4*S*,6a*S*)-2-benzoyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide**

3-Methyl-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide from Example 83 Step A (25 mg, 0.087 mmol), triethylamine (0.018 mL, 0.131 mmol), and benzoyl chloride (10.12 μL, 0.087 mmol) were combined in dichloromethane (5 mL). After 5 minutes, tlc shows no more starting material. The crude reaction mixture was concentrated and applied to a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-4) eluting with 1-10% methanol(2 *N* ammonia)/dichloromethane to give the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.49 – 7.42 (m, 2H), 7.41 – 7.35 (m, 3H), 7.33 – 7.27 (m, 3H), 5.43 (d, *J* = 6.7, 1H), 3.97 (m, 1H), 3.74 (m, 2H), 3.56 (m, 2H), 3.39 (m, 1H), 2.74 (m, 2H), 2.48 (m, 1H), 2.38 (m, 2H), 2.07 (dd, *J* = 4.6, 10.8, 1H), 1.94 (m, 1H), 1.52 – 1.31 (m, 2H), 1.01 (d, *J* = 6.3, 3H), 0.68 (d, *J* = 6.6, 3H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Example 219

***N'*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*-isopropyl-*N*-phenylurea**

2 *M* Trimethylaluminum in toluene (0.198mL, 0.395 mmol) was added dropwise to *N*-isopropylaniline (0.068 mL, 0.474 mmol) in toluene (2 mL) at 0 °C. The reaction was warmed to room temperature and stirred for 1 hour. The aluminum amide solution was then added dropwise to a solution of *tert*-butyl (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylcarbamate from Example 214 Step A (50 mg, 0.158 mmol) in 1 mL of toluene at 0 °C. The reaction was heated at 90 °C overnight, and then the reaction was quenched with 1 mL of 5% aqueous sodium hydroxide. The separated toluene layer was applied directly to a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS-4) eluting with 1-10% methanol (2 *N* ammonia)/dichloromethane to give the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.40 (ddd, *J* = 1.8, 3.2, 5.7, 3H), 7.29 (d, *J* = 4.4, 4H), 7.24 – 7.18 (m, 1H), 7.14 (t, *J* = 2.0, 1H), 7.13 – 7.10 (m, 1H), 4.87 (dt, *J* = 6.8, 13.6, 1H), 3.94 – 3.84 (m, 1H), 3.74 (d, *J* = 7.1, 1H), 3.60 (d, *J* = 13.0, 1H), 3.44 (d, *J* = 13.0, 1H), 2.53 (t, *J* = 5.5, 2H), 2.48 – 2.40 (m, 1H), 2.40 – 2.33 (m, 1H), 2.22 (dd, *J* = 3.7, 8.8, 1H), 2.07 (ddd, *J* = 5.1, 9.2, 11.7, 1H), 1.95 (td, *J* = 6.0, 12.0, 1H), 1.63 – 1.52 (m, 1H), 1.40 – 1.30 (m, 1H), 1.29 – 1.17 (m, 1H), 1.05 (d, *J* = 3.2, 3H), 1.02 (d, *J* = 3.2, 3H); MS (ESI+) *m/z* 378 $(M+H)^+$.

Example 220

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide

Step A: (*S*)-*tert*-Butyl 2-amino-4-methylpentanoate hydrochloride (0.516 g, 2.306 mmol) were dissolved in dichloromethane (15 mL) and triethylamine (1.061 mL, 7.61 mmol) was added. 3-Chloropropane-1-sulfonyl chloride (0.337 mL, 2.77 mmol) was added dropwise, and the reaction mixture was stirred at room temperature overnight. The solvent was removed in vacuo, and the crude material was taken up in ether, filtered, and concentrated to give (*S*)-*tert*-butyl 2-(3-chloropropylsulfonamido)-4-methylpentanoate: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 4.70 (d, J = 9.7, 1H), 4.02 - 3.91 (m, 1H), 3.77 - 3.60 (m, 2H), 3.25 - 2.96 (m, 3H), 2.31 (tdd, J = 2.2, 6.6, 9.2, 2H), 1.83 (dq, J = 6.5, 13.0, 1H), 1.58 - 1.53 (m, 8H), 1.38 (t, J = 7.3, 1H), 0.96 (dd, J = 2.1, 6.6, 6H); MS (ESI+) *m/z* 345 $(M+NH_4)^+$.

Step B: (S)-*tert*-Butyl 2-(3-chloropropylsulfonamido)-4-methylpentanoate (0.756 g, 2.306 mmol) from Step A was dissolved in tetrahydrofuran and potassium *tert*-butoxide (0.517 g, 4.61 mmol) was added. The reaction was stirred at room temperature overnight. The solvent was removed in vacuo, and the crude material was partitioned between ether and water. The ether layer was separated, washed with brine, dried (Na_2SO_4), and concentrated in vacuo to supply *tert*-butyl (2*S*)-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanoate: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 4.17 - 4.05 (m, 1H), 3.68 (dd, J = 7.9, 16.6, 1H), 3.40 - 3.28 (m, 1H), 3.21 - 3.09 (m, 2H), 2.39 (td, J = 5.3, 13.6, 2H), 1.68 (m, 3H), 1.47 (s, 9H), 0.97 (dd, J = 3.2, 6.2, 6H).

Step C: *tert*-Butyl (2*S*)-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanoate (0.656 g, 2.251 mmol) from Step B was combined with HCl (4 *N* in dioxane, 5 mL, 20.00 mmol). The reaction mixture was stirred at room temperature for 24 hours, then the solvent removed in vacuo to furnish (2*S*)-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanoic acid: MS (DCI+) *m/z* 253 $(M+NH_4)^+$.

Step D: (2*S*)-2-(1,1-Dioxidoisothiazolidin-2-yl)-4-methylpentanoic acid (359 mg, 1.526 mmol) was combined with triethylamine (0.387 mL, 2.77 mmol) in dichloromethane (10 mL). 1-Hydroxybenzotriazole (234 mg, 1.526 mmol) and *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide (0.270 mL, 1.526 mmol) were added, and the reaction mixture was stirred for 15 minutes. Then (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine (300 mg, 1.387 mmol) from Example 16 Step E was added, and the reaction mixture was stirred at room temperature for 24 hours. The reaction was quenched with 10 mL of aqueous sodium bicarbonate and extracted with 3x20 mL of dichloromethane. The solvent was

removed in vacuo. The crude material was applied to a silica gel cartridge (Analogix®, Burlington, Wisconsin, RS15-24) and eluted with 1-10% methanol (2 *N* ammonia)/dichloromethane to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.76 (d, J = 6.9, 1H), 7.46 - 7.39 (m, 2H), 7.40 - 7.33 (m, 2H), 7.26 (dd, J = 9.9, 17.2, 1H), 4.52 (t, J = 7.7, 1H), 4.44 - 4.34 (m, 1H), 3.93 (dt, J = 7.0, 14.5, 1H), 3.57 (dd, J = 5.4, 13.1, 1H), 3.49 - 3.36 (m, 2H), 3.30 - 3.20 (m, 2H), 2.83 - 2.74 (m, 1H), 2.62 - 2.45 (m, 2H), 2.44 - 2.37 (m, 1H), 2.33 - 2.17 (m, 4H), 2.11 (qd, J = 6.5, 12.5, 1H), 1.92 - 1.78 (m, 3H), 1.77 - 1.59 (m, 2H), 1.45 - 1.32 (m, 1H), 0.88 (d, J = 6.6, 3H), 0.83 (dd, J = 2.5, 6.5, 3H); MS (ESI+) *m/z* 434 $(M+H)^+$.

Example 221

***tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-ylcarbamate**

N-(*tert*-Butoxycarbonyl)-L-leucine (0.374 g, 1.617 mmol), 1-hydroxybenzotriazole hydrate (0.248 g, 1.617 mmol), and (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 33 (0.318g, 1.470 mmol) were combined in dichloromethane (3.0 mL). After 20 minutes, N^1-((ethylimino)methylene)-N^3,N^3-dimethylpropane-1,3-diamine (0.286 mL, 1.617 mmol) was added, and the reaction was stirred at room temperature overnight. The reaction was quenched with water and extracted with of dichloromethane (2×2mL), and the extracts were applied directly to a 25 g silica gel cartridge and purified with a gradient of 5-40% acetone/hexanes over 30 minutes to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.61-8.64 (m, 1H), 7.96-7.99 (m, 1H), 7.42-7.44 (m, 2H), 7.36 (t, J = 7.4 Hz, 2H), 7.28 (d, J = 7.3 Hz, 1H), 4.65-4.73 (m, 1H), 4.37-4.45 (m, 1H), 3.59 (d, J = 13.1 Hz, 1H), 3.43 (d, J = 13.1 Hz, 1H), 2.81-2.84 (m, 1H), 2.55-2.58 (m, 1H), 2.44-2.54 (m, 2H), 2.24-2.36 (m, 2H), 2.02-2.13 (m, 1H), 1.78-1.94 (m, 4H), 1.53-1.66 (m, 1H), 1.50 (s, 9H), 1.26-1.43 (m, 1H), 0.87 (d, J = 5.5 Hz, 3H), 0.83-0.85 (m, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Example 222

***tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-leucine for *N*-(*tert*-butoxycarbonyl)-L-leucine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.23-8.32 (m, 1H), 7.42-7.44 (m, 2H), 7.36 (t, J =

7.5 Hz, 2H), 7.27 (t, J = 7.4 Hz, 1H), 5.02 (m, 0.7H), 4.69 (m, 0.3H), 4.37-4.43 (m, 1H), 3.58 (d, J = 13.1 Hz, 1H), 3.45 (d, J = 13.1 Hz, 1H), 3.04-3.11 (m, 3H), 2.82-2.91 (m, 1H), 2.40-2.52 (m, 3H), 2.31-2.34 (m, 1H), 2.21-2.25 (m, 1H), 1.99-2.14 (m, 1H), 1.77-1.94 (m, 3H), 1.51-1.62 (m, 2H), 1.47 (s, 9H), 1.34-1.37 (m, 1H), 0.88 (d, J = 6.4 Hz, 3H), 0.85 (d, J = 6.4 Hz, 3H); MS (ESI+) m/z 444 $(M+H)^+$.

Example 223

***tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(ethyl)carbamate**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-ethyl-L-leucine for *N*-(*tert*-butoxycarbonyl)-L-leucine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.11-8.14 (m, 1H), 7.42-7.44 (m, 2H), 7.36 (t, J = 7.4 Hz, 2H), 7.27 (t, J = 7.3 Hz, 1H), 4.36-4.41 (m, 1H), 3.59 (d, J = 13.1 Hz, 1H), 3.43-3.47 (m, 3H), 2.80-2.85 (m, 1H), 2.47-2.51 (m, 2H), 2.39-2.43 (m, 1H), 2.33-2.35 (m, 1H), 2.22-2.25 (m, 1H), 2.05-2.13 (m, 1H), 1.94-2.04 (m, 1H), 1.81-1.84 (m, 1H), 1.72-1.78 (m, 1H), 1.52-1.61 (m, 1H), 1.46-1.49 (m, 9H), 1.34-1.41 (m, 2H), 1.17-1.33 (m, 3H), 0.89-0.91 (m, 6H); MS (ESI+) m/z 458 $(M+H)^+$.

Example 224

***tert*-butyl (2*S*,3*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-isoleucine for *N*-(*tert*-butoxycarbonyl)-L-leucine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.43 (d, J = 8.7 Hz, 1H), 7.43 (s, 1H), 7.37 (t, J = 7.4 Hz, 2H), 7.25-7.30 (m, 1H), 4.68-4.72 (m, 1H), 4.34-4.44 (m, 1H), 3.61 (d, J = 13.1 Hz, 1H), 3.46 (d, J = 13.1 Hz, 1H), 3.22-3.26 (m, 1H), 3.13-3.14 (m, 2H), 2.87-2.90 (m, 1H), 2.46-2.54 (m, 3H), 2.25-2.35 (m, 3H), 2.00-2.12 (m, 1H), 1.82 (dq, J = 12.7, 6.3 Hz, 1H), 1.52-1.63 (m, 1H), 1.48-1.50 (m, 9H), 1.32-1.43 (m, 3H), 0.96-1.10 (m, 4H), 0.78-0.86 (m, 3H); MS (ESI+) m/z 444 $(M+H)^+$.

Example 225

***tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3,3-dimethyl-1-oxobutan-2-ylcarbamate**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-*tert*-leucine for *N*-(*tert*-butoxycarbonyl)-L-leucine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.71 (m, 1H), 7.70 (d, J = 9.6 Hz, 1H), 7.43-7.45 (m, 2H), 7.37 (t, J = 7.5 Hz, 2H), 7.26-7.30 (m, 1H), 4.61 (d, J = 9.7 Hz, 1H), 4.39-4.45 (m, 1H), 3.63 (d, J = 13.1 Hz, 1H), 3.44 (d, J = 13.1 Hz, 1H), 2.86 (dd, J = 9.0, 2.9 Hz, 1H), 2.57-2.63 (m, 1H), 2.45-2.55 (m, 2H), 2.26-2.33 (m, 2H), 2.00 (dd, J = 12.1, 6.1 Hz, 1H), 1.77-1.84 (m, 1H), 1.48-1.56 (m, 1H), 1.48 (s, 9H), 1.25-1.38 (m, 1H), 1.18 (s, 9H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Example 226

***tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-ylcarbamate**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-L-neopentylglycine for *N*-(*tert*-butoxycarbonyl)-L-leucine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.54-8.57 (m, 1H), 8.10-8.13 (m, 1H), 7.41-7.45 (m, 2H), 7.36 (t, J = 7.4 Hz, 2H), 7.25-7.29 (m, 1H), 4.72-4.76 (m, 1H), 4.38-4.42 (m, 1H), 3.59 (d, J = 13.1 Hz, 1H), 3.43 (d, J = 13.1 Hz, 1H), 2.84 (dd, J = 9.0, 2.9 Hz, 1H), 2.53-2.60 (m, 1H), 2.46-2.53 (m, 1H), 2.42-2.46 (m, 1H), 2.29-2.32 (m, 1H), 2.22-2.27 (m, 1H), 2.16 (dd, J = 14.1, 4.8 Hz, 1H), 2.01-2.07 (m, 1H), 1.77-1.87 (m, 2H), 1.54-1.62 (m, 1H), 1.50 (s, 9H), 1.31-1.41 (m, 1H), 0.98 (s, 9H); MS (ESI+) *m/z* 444 $(M+H)^+$.

Example 227

***tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxohexan-2-yl(methyl)carbamate**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-norleucine for *N*-(*tert*-butoxycarbonyl)-L-leucine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.21-8.24 (m, 1H), 7.42-7.44 (m, 2H), 7.36 (t, J = 7.4 Hz, 2H), 7.24-7.31 (m, 1H), 5.02 (m, 0.7H), 4.66 (m, 0.3H), 4.34-4.47 (m, 1H), 3.59 (d, J = 13.1 Hz, 1H), 3.45 (d, J = 13.1 Hz, 1H), 3.05-3.10 (m, 3H), 2.82-2.85 (m, 1H), 2.45-2.50 (m, 2H), 2.37-2.45 (m, 1H), 2.31-2.37 (m, 1H), 2.24 (t, J = 7.5 Hz, 1H), 2.05-2.12 (m,

2H), 1.79-1.84 (m, 2H), 1.53-1.62 (m, 1H), 1.47 (s, 9H), 1.34-1.38 (m, 1H), 1.21-1.29 (m, 4H), 0.75-0.81 (m, 3H); MS (ESI+) *m/z* 444 $(M+H)^+$.

Example 228

N-[(3aR,4S,6aS)-2-benzyloctahydrocyclopenta[c]pyrrol-4-yl]-2,2-bis(4-fluorophenyl)acetamide

The title compound was prepared by substituting 2,2-bis(4-fluorophenyl)acetic acid for *N*-(*tert*-butoxycarbonyl)-L-leucine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.04 (d, *J* = 7.0, 1H), 7.57 – 7.52 (m, 4H), 7.42 (d, *J* = 7.1, 2H), 7.36 (t, *J* = 7.5, 2H), 7.27 (t, *J* = 7.3, 1H), 7.12 (dt, *J* = 15.8, 8.0, 4H), 5.23 (s, 1H), 4.45 – 4.37 (m, 1H), 3.57 (d, *J* = 13.1, 1H), 3.43 (d, *J* = 13.1, 1H), 2.78 (dd, *J* = 9.1, 2.9, 1H), 2.54 – 2.47 (m, 1H), 2.47 – 2.43 (m, 1H), 2.40 (dd, *J* = 8.9, 7.3, 1H), 2.29 (dd, *J* = 9.0, 3.0, 1H), 2.27 – 2.21 (m, 1H), 2.10 (dq, *J* = 12.2, 6.2, 1H), 1.84 – 1.75 (m, 1H), 1.60 (td, *J* = 14.6, 7.3, 1H), 1.41 – 1.31 (m, 1H); MS (ESI+) *m/z* 447 $(M+H)^+$.

Example 229

N-[(3aR,4S,6aS)-2-benzyloctahydrocyclopenta[c]pyrrol-4-yl]-2-isopropyl-3-methylbutanamide

The title compound was prepared by substituting 2-isopropyl-3-methylbutanoic acid for *N*-(*tert*-butoxycarbonyl)-L-leucine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.18 (d, *J* = 7.5, 1H), 7.44 (d, *J* = 7.5, 2H), 7.37 (t, *J* = 7.6, 2H), 7.27 (t, *J* = 7.3, 1H), 4.52 – 4.37 (m, 1H), 3.62 (d, *J* = 13.2, 1H), 3.44 (d, *J* = 13.1, 1H), 2.83 (dd, *J* = 9.0, 2.8, 1H), 2.62 – 2.51 (m, 2H), 2.48 (dd, *J* = 8.8, 7.1, 1H), 2.34 – 2.26 (m, 2H), 2.17 – 2.05 (m, 3H), 1.92 – 1.81 (m, 2H), 1.64 (dt, *J* = 19.2, 7.1, 1H), 1.44 – 1.34 (m, 1H), 1.13 (dd, *J* = 6.6, 3.9, 6H), 0.98 (d, *J* = 6.8, 6H); MS (ESI+) *m/z* 343 $(M+H)^+$.

Example 230

N-[(3aR,4S,6aS)-2-benzyloctahydrocyclopenta[c]pyrrol-4-yl]-3-methylbutanamide

The title compound was prepared by substituting 3-methylbutanoic acid for *N*-(*tert*-butoxycarbonyl)-L-leucine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.36 (d, *J* = 7.8, 1H), 7.44 (d, *J* = 7.6, 2H), 7.37 (t, *J* = 7.5, 2H), 7.28 (t, *J* = 7.2, 1H), 4.48 – 4.40 (m, 1H), 3.60 (d, *J* = 13.1, 1H), 3.45 (d, *J* = 13.2, 1H), 2.82 (dd, *J* = 9.0, 2.2, 1H), 2.59 – 2.50 (m, 2H), 2.50 – 2.43 (m, 1H), 2.31 (tt, *J* = 19.8, 7.9, 3H), 2.23 (d, *J*

= 7.3, 2H), 2.17 – 2.08 (m, 1H), 1.87 (dd, *J* = 13.1, 6.7, 1H), 1.68 – 1.58 (m, 1H), 1.46 – 1.34 (m, 1H), 0.95 (d, *J* = 6.6, 5H); MS (ESI+) *m/z* 343 $(M+H)^+$.

Example 231

tert-butyl (2*S*)-2-({[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]amino}carbonyl)piperidine-1-carboxylate

The title compound was prepared by substituting (*S*)-1-(*tert*-butoxycarbonyl)piperidine-2-carboxylic acid for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step E of Example 16 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5, temperature 90 °C) δ ppm 7.35-7.39 (m, 2H), 7.30 (t, *J* = 7.5 Hz, 2H), 7.21 (t, *J* = 7.2 Hz, 2H), 4.86-4.88 (m, 1H), 4.25-4.30 (m, 1H), 4.08-4.12 (m, 1H), 3.58 (d, *J* = 13.2 Hz, 1H), 3.47 (d, *J* = 13.1 Hz, 1H), 3.29 (td, *J* = 12.8, 3.1 Hz, 1H), 2.80 (d, *J* = 6.1 Hz, 1H), 2.49-2.56 (m, 1H), 2.42-2.47 (m, 2H), 2.36 (dd, *J* = 9.0, 3.2 Hz, 1H), 2.32 (d, *J* = 7.7 Hz, 1H), 2.22-2.26 (m, 1H), 2.03-2.11 (m, 1H), 1.79-1.93 (m, 1H), 1.49-1.68 (m, 5H), 1.48 (s, 9H), 1.32-1.44 (m, 2H); MS (ESI+) *m/z* 428 $(M+H)^+$.

Example 232

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxobutan-2-yl(methyl)carbamate

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)- *N*-methyl-L-valine for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step E of Example 16 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (501 MHz, pyridine-d_5, temperature 90 °C) δ ppm 7.35-7.39 (m, 3H), 7.29 (t, *J* = 7.5 Hz, 2H), 7.21 (t, *J* = 7.3 Hz, 1H), 4.30-4.38 (m, 1H), 4.20-4.29 (m, 1H), 3.56 (d, *J* = 13.0 Hz, 1H), 3.47 (d, *J* = 13.2 Hz, 1H), 3.00-3.02 (m, 3H), 2.76 (d, *J* = 6.5 Hz, 1H), 2.48-2.55 (m, 1H), 2.33-2.47 (m, 4H), 2.28-2.32 (m, 1H), 2.04-2.12 (m, 1H), 1.81-1.88 (m, 1H), 1.49-1.59 (m, 1H), 1.46 (s, 9H), 1.36-1.45 (m, 1H), 1.00 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.7 Hz, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Example 233

***tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-norvaline for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step E of Example 16 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5, temperature 90 °C) δ ppm 7.36-7.38 (m, 2H), 7.28-7.31 (m, 3H), 7.21 (t, *J* = 7.2 Hz, 1H), 4.70-4.79 (m, 1H), 4.23-4.29 (m, 1H), 3.57 (d, *J* = 13.2 Hz, 1H), 3.47 (d, *J* = 13.2 Hz, 1H), 2.95 (s, 3H), 2.77-2.81 (m, 1H), 2.48-2.52 (m, 1H), 2.39-2.46 (m, 2H), 2.36 (dd, *J* = 9.0, 2.9 Hz, 1H), 2.30 (t, *J* = 8.0 Hz, 1H), 2.07 (dq, *J* = 12.1, 6.1 Hz, 1H), 1.92-2.03 (m, 1H), 1.72-1.86 (m, 2H), 1.50-1.59 (m, 1H), 1.47 (s, 9H), 1.36-1.44 (m, 1H), 1.25-1.35 (m, 2H), 0.86 (t, *J* = 7.3 Hz, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Example 234

***tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3,3-dimethyl-1-oxobutan-2-ylcarbamate**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-L-*tert*-leucine for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step E of Example 16 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.71 (m, 1H), 7.69 (d, *J* = 9.6 Hz, 1H), 7.39-7.42 (m, 2H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.25-7.29 (m, 1H), 4.61 (d, *J* = 9.7 Hz, 1H), 4.32-4.42 (m, 1H), 3.53-3.56 (m, 1H), 3.37-3.40 (m, 1H), 2.63-2.66 (m, 1H), 2.41-2.51 (m, 2H), 2.27-2.33 (m, 2H), 2.20-2.25 (m, 1H), 2.11-2.19 (m, 1H), 1.80-1.91 (m, 1H), 1.61-1.73 (m, 1H), 1.48 (s, 9H), 1.35-1.44 (m, 1H), 1.18 (s, 9H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Example 235

***N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-isopropyl-3-methylbutanamide**

The title compound was prepared by substituting 2-isopropyl-3-methylbutanoic acid for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step E of Example 16 for (3a*R*,4*S*,6a*S*)-2-

benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.18 (d, J = 7.1, 1H), 7.44 (d, J = 7.3, 2H), 7.36 (t, J = 7.6, 2H), 7.27 (t, J = 7.3, 1H), 4.51 – 4.37 (m, 1H), 3.61 (d, J = 13.1, 1H), 3.44 (d, J = 13.2, 1H), 2.83 (dd, J = 9.0, 2.8, 1H), 2.61 – 2.51 (m, 2H), 2.48 (dd, J = 8.8, 7.2, 1H), 2.35 – 2.24 (m, 2H), 2.16 – 2.06 (m, 3H), 1.93 – 1.81 (m, 2H), 1.64 (dt, J = 14.6, 7.1, 1H), 1.44 – 1.35 (m, 1H), 1.13 (dd, J = 6.6, 3.9, 6H), 0.98 (d, J = 6.7, 6H); MS (ESI+) *m/z* 343 $(M+H)^+$.

Example 236

***N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methylbutanamide**

The title compound was prepared by substituting 3-methylbutanoic acid for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step E of Example 16 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.30 – 8.17 (m, 1H), 7.43 (dd, J = 11.2, 4.2, 2H), 7.37 (t, J = 7.5, 2H), 7.27 (t, J = 7.3, 1H), 4.49 – 4.39 (m, 1H), 3.60 (d, J = 13.1, 1H), 3.45 (d, J = 13.1, 1H), 2.89 – 2.78 (m, 1H), 2.55 – 2.49 (m, 2H), 2.45 (dd, J = 10.4, 5.3, 1H), 2.36 – 2.24 (m, 3H), 2.21 (d, J = 7.1, 2H), 2.17 – 2.08 (m, 1H), 1.90 – 1.79 (m, 1H), 1.62 (ddd, J = 15.1, 12.3, 7.2, 1H), 1.40 (dtd, J = 9.2, 8.2, 6.1, 1H), 0.95 (d, J = 6.6, 6H); MS (ESI+) *m/z* 301 $(M+H)^+$.

Example 237

2-cyclohexyl-2-hydroxy-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide

The title compound was prepared by substituting 2-cyclohexyl-2-hydroxyacetic acid for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*S*,6a*R*)-2-(3-trifluoromethyl)benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 152 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.59 (d, J = 7.9, 0.5H), 8.40 – 8.33 (m, 0.5H), 7.97 (s, 0.5H), 7.77 (dd, J = 42.9, 9.6, 1.5H), 7.48 – 7.39 (m, 1.5H), 7.29 (d, J = 5.3, 0.5H), 4.67 – 4.57 (m, 1H), 4.37 (t, J = 3.8, 1H), 3.80 (dd, J = 21.0, 13.1, 1H), 3.27 (dd, J = 64.7, 13.0, 1H), 2.86 (dd, J = 13.0, 4.7, 1H), 2.73 – 2.61 (m, 1H), 2.50 – 2.40 (m, 1H), 2.36 (d, J = 9.1, 1H), 2.28 – 2.08 (m, 3H), 2.03 (dd, J = 14.3, 6.2, 0.5H), 2.00 – 1.93 (m, 0.5H), 1.92 – 1.88 (m, 0.5H), 1.86 – 1.45 (m, 9.5H), 1.35 – 1.06 (m, 4H); MS (ESI+) *m/z* 425$(M+H)^+$.

Example 238

***tert*-butyl (*S*)-1-((3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-norvaline for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step C of Example 14 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (501 MHz, pyridine-d_5, temperature 90 °C) δ ppm 7.44-7.45 (bs, 2H), 7.35-7.40 (m, 2H), 7.30-7.37 (m, 1H), 7.25-7.29 (m, 1H), 4.70-4.75 (bs, 1H), 4.37-4.43 (m, 1H), 3.56 (d, *J* = 12.9 Hz, 1H), 3.52 (d, *J* = 12.8 Hz, 1H), 2.95 (s, 3H), 2.71 (d, *J* = 8.9 Hz, 1H), 2.62-2.68 (m, 1H), 2.44-2.48 (m, 2H), 2.25 (t, *J* = 8.5 Hz, 1H), 2.14 (t, *J* = 8.3 Hz, 1H), 1.91-1.99 (m, 1H), 1.66-1.80 (m, 3H), 1.56-1.63 (m, 1H), 1.50 (s, 9H), 1.26-1.38 (m, 3H), 0.88 (t, *J* = 7.4 Hz, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Example 239

***tert*-butyl (*S*)-1-((3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-leucine for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step C of Example 14 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (501 MHz, pyridine-d_5, temperature 90 °C) δ ppm 7.44-7.49 (m, 2H), 7.36-7.40 (m, 2H), 7.32-7.39 (m, 1H), 7.27 (t, *J* = 7.4 Hz, 1H), 4.82-4.89 (m, 1H), 4.37-4.43 (m, 1H), 3.63 (d, *J* = 13.2 Hz, 1H), 3.50 (d, *J* = 13.0 Hz, 1H), 2.94 (s, 3H), 2.73 (dd, *J* = 9.7, 1.8 Hz, 1H), 2.64-2.70 (m, 1H), 2.44-2.47 (m, 2H), 2.22-2.28 (m, 1H), 2.15-2.19 (m, 1H), 1.88 (ddd, *J* = 14.1, 8.2, 6.0 Hz, 1H), 1.64-1.81 (m, 3H), 1.55-1.65 (m, 2H), 1.50 (s, 9H), 1.28-1.38 (m, 1H), 0.90-0.93 (m, 6H); MS (ESI+) *m/z* 444 $(M+H)^+$.

Example 240

***tert*-butyl (*S*)-1-((3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate**

Step A: (3a*R*,4*R*,6a*S*)-2-Benzyloctahydrocyclopenta[*c*]pyrrol-4-amine was prepared according to the procedure described in Example 14 Steps B-C substituting (*S*,*E*)-*N*-((3a*R*,6a*S*)-2-benzylhexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)-2-methylpropane-2-sulfinamide from Example 14 Step A for (*S*,*E*)-*N*-((3a*S*,6a*R*)-2-benzylhexahydrocyclopenta[*c*]pyrrol-4(5*H*)-ylidene)-2-methylpropane-2-sulfinamide prepared in Step A of Example 14 to give (3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.44 (d, *J* = 7.4, 2H), 7.36 (t, *J* = 7.5, 2H), 7.28 (t, *J* = 7.3, 1H), 3.52 (q, *J* = 13.0, 2H), 3.29 (q, *J* = 7.3, 1H), 2.84 (dd, *J* = 3.7, 9.3, 1H), 2.55 – 2.43 (m, 3H), 2.37 – 2.30 (m, 1H), 2.24 (d, *J* = 5.3, 1H), 1.74 – 1.64 (m, 2H), 1.62 – 1.53 (m, 1H), 1.34 (dd, *J* = 5.0, 10.1, 1H).

Step B: The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-norvaline for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.40 (d, *J* = 7.4, 2H), 7.34 (t, *J* = 7.5, 2H), 7.25 (t, *J* = 7.3, 1H), 4.79 – 4.68 (m, 1H), 4.44 – 4.32 (m, 1H), 3.82 (d, *J* = 13.2, 1H), 3.36 (d, *J* = 13.0, 1H), 2.94 (s, 3H), 2.80 – 2.65 (m, 2H), 2.46 (s, 1H), 2.35 (dd, *J* = 9.2, 2.7, 1H), 2.31 – 2.25 (m, 2H), 1.99 (dt, *J* = 14.0, 7.0, 1H), 1.83 – 1.72 (m, 2H), 1.70 – 1.56 (m, 2H), 1.49 (d, *J* = 4.5, 1H), 1.48 (s, 9H), 1.41 – 1.23 (m, 3H), 0.89 (t, *J* = 7.4, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Example 241

***tert*-butyl (*S*)-1-((3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-leucine for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 240 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 7.40-7.43 (m, 2H), 7.31-7.37 (m, 3H), 7.23-7.30 (m, 1H), 4.82-4.89 (m, 1H), 4.35-4.42 (m, 1H), 3.35 (d, *J* = 12.9 Hz, 1H), 2.95 (s, 3H), 2.68-2.78 (m, 2H), 2.42-2.50 (m, 1H), 2.26-2.36 (m, 3H), 1.89 (ddd, *J* = 14.1, 8.2, 5.9

Hz, 1H), 1.71-1.82 (m, 2H), 1.60-1.70 (m, 3H), 1.48-1.51 (m, 1H), 1.48 (s, 9H), 1.22-1.35 (m, 1H), 0.88-0.98 (m, 6H); MS (ESI+) *m/z* 444 $(M+H)^+$.

Example 242

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(methylsulfonyl)-L-leucinamide

Step A: (*S*)-*tert*-Butyl 2-amino-4-methylpentanoate hydrochloride (1.53 g, 6.84 mmol) was dissolved in dichloromethane and triethylamine (3.15 mL, 22.57 mmol). Methanesulfonyl chloride (0.638 mL, 8.21 mmol) was added dropwise, and the reaction stirred at room temperature for 1 hour. The reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with dichloromethane (3×50mL). The solvent was removed in vacuo to give (*S*)-*tert*-butyl 4-methyl-2-(methylsulfonamido)pentanoate: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 4.71 (d, *J* = 9.7, 1H), 3.98 (td, *J* = 9.5, 5.5, 1H), 2.92 (s, 3H), 1.84 (dt, *J* = 13.1, 6.6, 1H), 1.54 (s, 9H), 1.44-1.48 br s, 1H), 0.96 (dd, *J* = 6.6, 2.4, 6H); MS (ESI-) *m/z* 264$(M-H)^-$. (*S*)-*tert*-Butyl 4-methyl-2-(methylsulfonamido)pentanoate was dissolved in 10 mL of 4 *N* HCl in dioxane and stirred at room temperature overnight. The solvent was removed under a stream of nitrogen and under high vacuum to give (*S*)-4-methyl-2-(methylsulfonamido)pentanoic acid: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 4.86 (d, *J* = 9.6, 1H), 4.17 (td, *J* = 9.6, 4.8, 1H), 3.18 – 3.07 (m, 1H), 2.99 (s, 3H), 1.96 – 1.80 (m, 1H), 1.64 (dddd, *J* = 23.4, 13.9, 9.1, 5.0, 2H), 1.40 (t, *J* = 7.3, 1H), 0.98 (dd, *J* = 6.6, 3.3, 6H).

Step B: The title compound was prepared by substituting (*S*)-4-methyl-2-(methylsulfonamido)pentanoic acid from Step A for *N*-(*tert*-butoxycarbonyl)-L-leucine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.41 (d, *J* = 9.4, 1H), 9.21 (d, *J* = 7.3, 1H), 7.45 (d, *J* = 7.2, 2H), 7.37 (t, *J* = 7.5, 2H), 7.29 (t, *J* = 7.3, 1H), 4.53 – 4.42 (m, 2H), 3.62 (d, *J* = 13.1, 1H), 3.47 (d, *J* = 13.1, 1H), 3.19 (s, 3H), 2.87 (dd, *J* = 9.1, 2.9, 1H), 2.66 – 2.58 (m, 1H), 2.57 – 2.45 (m, 2H), 2.35 (dd, *J* = 9.0, 3.0, 1H), 2.31 – 2.25 (m, 1H), 2.14 (dq, *J* = 12.0, 6.0, 1H), 1.99 (dq, *J* = 13.2, 6.5, 1H), 1.93 – 1.82 (m, 2H), 1.77 (ddd, *J* = 13.8, 8.5, 5.6, 1H), 1.63 (dt, *J* = 19.3, 7.2, 1H), 1.46 – 1.35 (m, 1H), 0.82 (d, *J* = 6.7, 3H), 0.79 (d, *J* = 6.5, 3H); MS (ESI+) *m/z* 408 $(M+H)^+$.

Example 243

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(methylsulfonyl)-L-leucinamide

The title compound was prepared by substituting (*S*)-4-methyl-2-(methylsulfonamido)pentanoic acid from Step A of Example 242 for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step E of Example 16 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.40 (d, J = 9.4, 1H), 9.21 (d, J = 7.2, 1H), 7.43 (d, J = 7.5, 2H), 7.36 (t, J = 7.6, 2H), 7.27 (t, J = 7.3, 1H), 4.52 – 4.38 (m, 2H), 3.57 (d, J = 13.1, 1H), 3.47 (d, J = 13.1, 1H), 3.17 (s, 3H), 2.85 (dd, J = 9.1, 2.2, 1H), 2.59 – 2.48 (m, 2H), 2.37 (dd, J = 9.0, 6.8, 2H), 2.25 (dd, J = 8.7, 7.1, 1H), 2.19 (dq, J = 11.9, 5.9, 1H), 1.99 (dq, J = 13.1, 6.5, 1H), 1.94 – 1.84 (m, 2H), 1.80 – 1.66 (m, 2H), 1.44 (ddd, J = 18.9, 12.5, 6.2, 1H), 0.82 (d, J = 6.7, 3H), 0.79 (d, J = 6.5, 3H). ; MS (ESI+) *m/z* 408 $(M+H)^+$.

Example 244

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-neopentyl-L-leucinamide

Step A: (*S*)-*tert*-Butyl 2-amino-4-methylpentanoate hydrochloride (1.022 g, 4.57 mmol) and pivalaldehyde (0.502 mL, 4.57 mmol) were combined in dichloromethane (25 mL). Acetic acid (1.0 mL) was added. The reaction was stirred at room temperature for 5 minutes, then PS-cyanoborohydride (3.90 g, 9.14 mmol) was added. The reaction was stirred at room temperature overnight, then filtered and the solvent was removed in vacuo. The crude material was diluted with dichloromethane and basified using saturated aqueous sodium bicarbonate to give (*S*)-*tert*-butyl 4-methyl-2-(neopentylamino)pentanoate: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 3.04 (t, J = 7.4, 1H), 2.40 (d, J = 11.1, 1H), 2.09 (d, J = 11.1, 1H), 1.86 – 1.70 (m, 1H), 1.46 (s, 10H), 1.40 (t, J = 7.2, 3H), 0.95 – 0.89 (m, 6H), 0.89 (s, 9H). (*S*)-*tert*-butyl 4-methyl-2-(neopentylamino)pentanoate was dissolved in 10 mL of 4 *N* HCl in dioxane and stirred at room temperature overnight. The solvent was removed under a stream of nitrogen and under high vacuum to give (*S*)-4-methyl-2-(neopentylamino)pentanoic acid: ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.89 – 8.37 (m, 1H), 8.34 – 8.03 (m, 1H), 3.82 (t, J = 6.5, 1H), 2.88 (d, J = 12.3, 1H), 2.62 (d, J = 12.2, 1H), 1.83 – 1.67 (m, 2H), 1.67 – 1.56 (m, 1H), 1.00 (s, 9H), 0.97 – 0.88 (m, 6H).

Step B: The title compound was prepared by substituting (*S*)-4-methyl-2-(neopentylamino)pentanoic acid from Step A for *N*-(*tert*-butoxycarbonyl)-L-leucine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.06-8.08 (m, 1H), 7.43-7.46 (m, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.28 (t, *J* = 7.3 Hz, 1H), 4.39-4.46 (m, 1H), 3.61 (d, *J* = 13.1 Hz, 1H), 3.46 (d, *J* = 13.1 Hz, 1H), 3.27 (dd, *J* = 8.5, 5.6 Hz, 1H), 2.84 (dd, *J* = 8.7, 2.5 Hz, 1H), 2.49-2.61 (m, 2H), 2.43-2.49 (m, 2H), 2.36 (dd, *J* = 9.1, 2.9 Hz, 1H), 2.32-2.36 (m, 1H), 2.30 (dd, *J* = 8.8, 7.0 Hz, 1H), 2.15 (dq, *J* = 12.1, 6.1 Hz, 1H), 1.80-1.96 (m, 2H), 1.55-1.76 (m, 4H), 1.39-1.46 (m, 1H), 0.94 (s, 9H), 0.93 (d, *J* = 6.8 Hz, 3H), 0.87 (d, *J* = 6.5 Hz, 3H); MS (ESI+) *m/z* 400 $(M+H)^+$.

Example 245

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-neopentyl-L-leucinamide

The title compound was prepared by substituting (*S*)-4-methyl-2-(neopentylamino)pentanoic acid from Step A of Example 244 for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine of Step E from Example 16 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.07-8.09 (m, 1H), 7.43-7.45 (m, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.28 (t, *J* = 7.3 Hz, 1H), 4.43 (p, *J* = 6.2 Hz, 1H), 3.60 (d, *J* = 13.1 Hz, 1H), 3.45 (d, *J* = 13.1 Hz, 1H), 3.26 (dd, *J* = 8.6, 5.6 Hz, 1H), 2.86 (dd, *J* = 8.9, 2.6 Hz, 1H), 2.47-2.60 (m, 2H), 2.42-2.47 (m, 2H), 2.36 (dd, *J* = 9.1, 3.0 Hz, 1H), 2.29-2.35 (m, 1H), 2.29 (dd, *J* = 8.7, 7.3 Hz, 1H), 2.14 (dq, *J* = 12.1, 6.0 Hz, 1H), 1.81-1.95 (m, 2H), 1.52-1.76 (m, 4H), 1.44 (dq, *J* = 13.2, 6.6 Hz, 1H), 0.94 (s, 9H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.5 Hz, 3H); MS (ESI+) *m/z* 400 $(M+H)^+$.

Example 246

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-neopentyl-L-norvalinamide

Step A: (*S*)-2-(Neopentylamino)pentanoic acid hydrochloride was prepared by substituting (*S*)-*tert*-butyl 2-amino pentanoate for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate in the procedure described in Step A of Example 244: ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8.49 (ddd, *J* = 34.9, 23.2, 14.1, 2H), 3.84 (dd, *J* = 8.0, 5.2, 1H), 2.86 (d, *J* = 12.3, 1H),

2.66 (d, J = 12.3, 1H), 1.99 – 1.73 (m, 2H), 1.58 – 1.42 (m, 1H), 1.41 – 1.26 (m, 1H), 1.00 (s, 9H), 0.92 (t, J = 7.3, 3H); MS (ESI+) m/z 188 $(M+H)^+$.

Step B: The title compound was prepared by substituting (*S*)-2-(neopentylamino)pentanoic acid from Step A for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step E of Example 16 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.00-8.03 (m, 1H), 7.43-7.45 (m, 2H), 7.37 (t, J = 7.5 Hz, 2H), 7.28 (t, J = 7.3 Hz, 1H), 4.40-4.45 (m, 1H), 3.60 (d, J = 13.1 Hz, 1H), 3.45 (d, J = 13.1 Hz, 1H), 3.20 (t, J = 6.5 Hz, 1H), 2.85 (dd, J = 8.8, 2.6 Hz, 1H), 2.52-2.60 (m, 1H), 2.46-2.52 (m, 1H), 2.38-2.46 (m, 2H), 2.31-2.38 (m, 2H), 2.28 (dd, J = 8.8, 7.3 Hz, 1H), 2.13 (dq, J = 12.1, 6.0 Hz, 1H), 1.79-1.92 (m, 2H), 1.71-1.80 (m, 1H), 1.65-1.73 (m, 1H), 1.57-1.65 (m, 1H), 1.39-1.57 (m, 3H), 0.93 (s, 9H), 0.86 (t, J = 7.3 Hz, 3H); MS (ESI-) m/z 384 $(M-H)^-$.

Example 247

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate

Step A: (*S*)-2-(*tert*-Butoxycarbonylamino)-4,4-dimethylpentanoic acid (50 mg, 0.204 mmol) and iodomethane (0.102 mL, 1.631 mmol) were dissolved in tetrahydrofuran (2 mL) at 0 °C and sodium hydride (24.46 mg, 0.611 mmol) was added. The reaction was stirred at 0 °C for a half hour and at room temperature overnight. The reaction was cooled to 0 °C and ethyl acetate (1 mL) was added followed by dropwise quenching with water (2 mL). The solvent was removed in vacuo and the crude material was partitioned between ether and water. The ether layer was separated. The aqueous layer was acidified to pH~5 using 1 *N* citric acid and extracted with ethyl acetate. The organic layer was washed with 1 *N* sodium thiosulfate and brine, dried (Na_2SO_4) and concentrated in vacuo. The compound was purified using a 4 g silica gel cartridge with a gradient of 0-3% methanol/dichloromethane over 20 minutes to give (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4,4-dimethylpentanoic acid: ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 12.63 (s, 1H), 4.57 (ddd, J = 74.4, 9.5, 3.1, 1H), 2.69 (s, 3H), 1.83 – 1.53 (m, 2H), 1.39 (s, 9H), 0.89 (s, 9H); MS (DSI+) m/z 260$(M+H)^+$.

Step B: The title compound was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4,4-dimethylpentanoic acid from Step A for *N*-(*tert*-butoxycarbonyl)-L-leucine in the procedure described in Example 221: ^{1}H NMR (400 MHz,

pyridine-d_5, temperature 90 °C) δ ppm 7.35-7.38 (m, 2H), 7.29 (t, J = 7.5 Hz, 2H), 7.20 (t, J = 7.3 Hz, 1H), 6.98-7.02 (m, 1H), 4.85-4.90 (m, 1H), 4.20-4.26 (m, 1H), 3.56 (d, J = 13.2 Hz, 1H), 3.48 (d, J = 13.2 Hz, 1H), 2.92 (s, 3H), 2.79 (d, J = 6.5 Hz, 1H), 2.51-2.55 (m, 1H), 2.39-2.47 (m, 2H), 2.37 (dd, J = 9.0, 3.1 Hz, 1H), 2.32 (dd, J = 8.9, 7.2 Hz, 1H), 2.19 (dd, J = 14.3, 5.6 Hz, 1H), 2.00-2.08 (m, 1H), 1.77-1.86 (m, 1H), 1.62 (dd, J = 14.3, 6.9 Hz, 1H), 1.50-1.56 (m, 1H), 1.48 (s, 9H), 1.35-1.47 (m, 1H), 0.95 (s, 9H); MS (DSI+) *m/z* 458(M+H)$^+$.

Example 248

***tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4,4-dimethylpentanoic acid from Step A of Example 247 for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step E of Example 16 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.41-7.43 (m, 2H), 7.36 (t, J = 7.5 Hz, 2H), 7.25-7.29 (m, 1H), 5.14 (m, 0.7H), 4.79 (m, 0.2H), 4.35 (dd, J = 5.6, 2.9 Hz, 1H), 3.56-3.60 (m, 1H), 3.40-3.44 (m, 1H), 3.02-3.09 (m, 3H), 2.76-2.84 (m, 1H), 2.42-2.51 (m, 2H), 2.31-2.40 (m, 2H), 2.17-2.24 (m, 2H), 2.06-2.15 (m, 1H), 1.79-1.83 (m, 1H), 1.62-1.70 (m, 1H), 1.51-1.63 (m, 2H), 1.47 (s, 9H), 1.32-1.42 (m, 1H), 0.94 (s, 9H); MS (ESI+) *m/z* 458 (M+H)$^+$.

Example 249

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-morpholin-4-ylpentanamide

Step A: (*S*)-*tert*-Butyl 2-amino-4-methylpentanoate (1.0042 g, 5.36 mmol), potassium carbonate (2.446 g, 17.69 mmol), and 1-bromo-2-(2-bromoethoxy)ethane (1.368 g, 5.90 mmol) were combined in acetonitrile (30 mL). The reaction was heated at 80 °C overnight. The reaction was cooled and filtered and the solvent removed in vacuo. The crude material was purified by silica gel chromatography using 5-50% ethyl acetate/hexanes to give (*S*)-*tert*-butyl 4-methyl-2-morpholinopentanoate: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 3.76 - 3.58 (m, 4H), 3.11 (dd, J = 6.9, 8.1, 1H), 2.74 - 2.53 (m, 4H), 1.71 - 1.55 (m, 2H), 1.51 - 1.34 (m, 10H), 0.92 (dd, J = 6.6, 7.3, 6H). (*S*)-*tert*-Butyl 4-methyl-2-morpholinopentanoate (0.637 g, 2.475 mmol) and 4 *N* hydrochloric acid in dioxane (5 mL) were combined. The

reaction mixture was stirred at ambient temperature for 24 hours, then the solvent removed in vacuo to give (*S*)-4-methyl-2-morpholinopentanoic acid hydrochloride: MS (DCI+) *m/z* 202(M+H)$^+$.

Step B: (*S*)-4-Methyl-2-morpholinopentanoic acid hydrochloride (363 mg, 1.526 mmol) and triethylamine (0.387 mL, 2.77 mmol) were combined in dichloromethane (10 mL). 1-Hydroxybenzotriazole hydrate (234 mg, 1.526 mmol) and N^1-((ethylimino)methylene)-N^3,N^3-dimethylpropane-1,3-diamine (0.270 mL, 1.526 mmol) were added, and the reaction was stirred for 15 minutes. Then (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine (300 mg, 1.387 mmol) from Example 16 Step E was added, and the reaction mixture was stirred at ambient temperature for 24 hours. The reaction was quenched with aqueous sodium bicarbonate and extracted with dichloromethane. The solvent was removed in vacuo and the crude material was purified by silica gel chromatography using 1-10% methanol (2 *N* ammonia)/dichloromethane to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.27 (d, *J* = 7.3, 1H), 7.44 (d, *J* = 7.4, 2H), 7.37 (t, *J* = 7.5, 2H), 7.27 (dd, *J* = 9.8, 17.3, 1H), 4.51 - 4.39 (m, 1H), 3.74 (t, *J* = 4.5, 4H), 3.62 (d, *J* = 13.1, 1H), 3.45 (d, *J* = 13.1, 1H), 3.29 - 3.21 (m, 1H), 2.87 (dd, *J* = 2.4, 9.0, 1H), 2.79 (dt, *J* = 4.5, 9.3, 2H), 2.75 - 2.68 (m, 2H), 2.55 (d, *J* = 14.8, 2H), 2.49 - 2.43 (m, 1H), 2.35 (dd, *J* = 2.6, 8.9, 1H), 2.32 - 2.26 (m, 1H), 2.11 (dq, *J* = 6.1, 12.1, 1H), 1.86 (dd, *J* = 6.6, 12.2, 3H), 1.67 - 1.55 (m, 2H), 1.41 (dt, *J* = 6.2, 20.1, 1H), 0.94 (dd, *J* = 6.2, 11.1, 6H); MS (ESI+) *m/z* 400(M+H)$^+$.

Example 250

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-pyrrolidin-1-ylpentanamide

The title compound was prepared by substituting 1,4-dibromobutane for 1-bromo-2-(2-bromoethoxy)ethane in Step A of Example 249: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.98 - 7.93 (m, 1H), 7.47 - 7.41 (m, 2H), 7.36 (t, *J* = 7.4, 2H), 7.31 - 7.24 (m, 1H), 4.45 (t, *J* = 5.2, 1H), 3.61 (d, *J* = 13.1, 1H), 3.45 (d, *J* = 13.1, 1H), 3.16 (dd, *J* = 5.1, 9.3, 1H), 2.87 (d, *J* = 7.9, 1H), 2.73 - 2.65 (m, 2H), 2.66 - 2.52 (m, 4H), 2.44 (dd, *J* = 6.2, 8.9, 1H), 2.36 (dd, *J* = 2.1, 9.0, 1H), 2.30 - 2.23 (m, 1H), 2.12 (dq, *J* = 6.0, 11.9, 1H), 1.95 - 1.78 (m, 3H), 1.66 - 1.54 (m, 6H), 1.47 - 1.36 (m, 1H), 1.00 (d, *J* = 6.4, 3H), 0.91 (d, *J* = 6.4, 3H); MS (ESI+) *m/z* 384(M+H)$^+$.

Example 251

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-piperidin-1-ylpentanamide

The title compound was prepared by substituting 1,5-dibromopentane for 1-bromo-2-(2-bromoethoxy)ethane in Step A of Example 249: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.09 (d, J = 7.5, 1H), 7.44 (d, J = 7.3, 2H), 7.36 (d, J = 7.7, 2H), 7.28 (t, J = 7.3, 1H), 4.46 – 4.36 (m, 1H), 3.61 (d, J = 13.1, 1H), 3.45 (d, J = 13.1, 1H), 3.21 (dd, J = 8.1, 5.4, 1H), 2.85 (d, J = 8.8, 1H), 2.70 – 2.50 (m, 6H), 2.49 – 2.44 (m, 1H), 2.32 (dt, J = 27.0, 7.9, 2H), 2.11 (dq, J = 12.1, 6.1, 1H), 1.95 – 1.79 (m, 3H), 1.63 – 1.47 (m, 6H), 1.45 – 1.32 (m, 3H), 0.94 (d, J = 5.8, 6H); MS (ESI+) *m/z* 398(M+H)$^+$.

Example 252

N^2-neopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

Step A: (3a*R*,4*S*,6a*S*)-2-Benzyloctahydrocyclopenta[*c*]pyrrol-4-amine (0.83 g, 3.84 mmol) from Step A of Example 33 was dissolved in anhydrous dichloromethane (5 mL) under nitrogen and triethylamine (0.588 mL, 4.22 mmol) was added followed by di-*tert*-butyl dicarbonate (1.010 mL, 4.22 mmol). The reaction was stirred at 25 °C for 1 hour. Thin-layer chromatography (SiO_2, 5% methanol/dichloromethane) showed complete reaction. The volatiles were removed in vacuo, and the crude material was purified using a 24 g silica gel cartridge eluting with a gradient of 1-5% methanol (2 *N* ammonia)/dichloromethane over 20 minutes to give *tert*-butyl (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylcarbamate: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.54 (d, J = 6.3, 1H), 7.43 (d, J = 7.3, 2H), 7.36 (t, J = 7.4, 2H), 7.27 (t, J = 7.2, 1H), 4.12 (q, J = 12.1, 1H), 3.59 (d, J = 12.9, 1H), 3.43 (d, J = 13.0, 1H), 2.78 (s, 1H), 2.59 – 2.49 (m, 2H), 2.49 – 2.41 (m, 1H), 2.37 – 2.25 (m, 2H), 2.16 – 2.05 (m, 1H), 1.88 (td, J = 13.1, 6.1, 1H), 1.65 (td, J = 14.8, 7.3, 1H), 1.52 (s, 9H), 1.43 – 1.35 (m, 1H); MS (ESI+) *m/z* 317(M+H)$^+$.

Step B: *tert*-Butyl (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylcarbamate (1.06 g, 3.35 mmol) from Step A and ethanol (20 mL) were added to 20% $Pd(OH)_2$ on carbon, wet (212.0 mg, 1.51 mmol) in a 250 mL stainless steel pressure bottle. The reaction mixture was stirred for 16 hours under 30 psi hydrogen at room temperature. The mixture was filtered through a nylon membrane and the solvent was removed in vacuo to give *tert*-butyl (3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 4.02-3.99 (m, 1H), 3.03 (d, J = 10.4, 1H), 2.98 – 2.89 (m, 1H), 2.84

(dd, J = 10.1, 6.4, 1H), 2.61-2.50 (m, 3H), 2.06 – 1.98 (m, 1H), 1.91 (td, J = 12.9, 6.7, 1H), 1.63 (dt, J = 19.5, 7.6, 1H), 1.53 (s, 9H), 1.29-1.23 (m, 1H); MS (ESI+) *m/z* 227(M+H)$^+$.

Step C: *tert*-Butyl (3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate (0.71 g, 3.14 mmol) from Step B, triethylamine (0.656 mL, 4.71 mmol), and 3-(trifluoromethyl)benzene-1-sulfonyl chloride (0.552 mL, 3.45 mmol) were combined in dichloromethane (10.0 mL). The reaction was stirred at room temperature for 16 hours and quenched with saturated aqueous $NaHCO_3$. The organic layer was separated and concentrated in vacuo. The resultant crude material was applied to a SF-25-60g cartridge (Analogix®, Burlington, Wisconsin) and purified with a gradient of 0-2% methanol/dichloromethane over 20 minutes to give *tert*-butyl (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.30 (s, 1H), 8.14 (d, J = 7.8, 1H), 7.84 (d, J = 7.8, 1H), 7.65 (t, J = 7.8, 1H), 6.83 – 6.71 (m, 1H), 3.88 – 3.76 (m, 1H), 3.61 (dd, J = 10.1, 3.3, 1H), 3.24 (dd, J = 9.8, 8.1, 1H), 3.12 (d, J = 5.6, 2H), 2.64 – 2.44 (m, 2H), 1.99 – 1.78 (m, 2H), 1.55 (tt, J = 12.4, 7.7, 1H), 1.48 (s, 9H), 1.38 – 1.20 (m, 1H); MS (ESI-) *m/z* 433(M-H)$^-$.

Step D: *tert*-Butyl (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate (0.814 g, 1.874 mmol) from Step C and HCl (26.2 mL, 52.5 mmol, 2 *M* in ether) in ethanol (3 mL) were combined. The reaction was stirred at room temperature overnight and then the volatiles were removed. The compound was purified using a 24 g silica gel cartridge with a gradient of 1-10% methanol (2 *N* ammonia)/dichloromethane over 20 minutes to give (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37 (s, 1H), 8.21 (d, J = 7.9, 1H), 7.93 (d, J = 7.9, 1H), 7.75 (t, J = 7.9, 1H), 3.41 (dd, J = 9.8, 2.8, 1H), 3.13 (dd, J = 9.7, 3.1, 1H), 3.03 – 2.98 (m, 1H), 2.97 – 2.89 (m, 2H), 2.56 – 2.45 (m, 1H), 2.14 (tdd, J = 8.7, 5.9, 2.9, 1H), 1.5-2.0 (m, 2H)1.95 – 1.85 (m, 1H), 1.79 – 1.69 (m, 1H), 1.32 – 1.15 (m, 2H); MS (ESI+) *m/z* 335(M+H)$^+$.

Step E: The title compound was prepared by substituting (*S*)-4-methyl-2-(neopentylamino)pentanoic acid from Step A of Example 244 for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step D for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.38 (s, 1H), 8.19-8.22 (m, 2H), 7.90-7.93 (m, 1H), 7.72 (t, J = 7.8 Hz, 1H), 4.21-4.29 (m, 1H), 3.87 (dd, J = 9.9, 2.6 Hz, 1H), 3.25

(dd, J = 8.6, 5.6 Hz, 1H), 3.15-3.21 (m, 2H), 2.97 (dd, J = 9.6, 7.0 Hz, 1H), 2.43-2.60 (m, 3H), 2.28-2.32 (m, 1H), 1.79-2.01 (m, 3H), 1.67-1.78 (m, 1H), 1.69 (ddd, J = 13.6, 7.9, 5.7 Hz, 1H), 1.51-1.60 (m, 2H), 1.32 (ddt, J = 9.3, 12.8, 6.4 Hz, 1H), 0.93 (d, J = 6.6 Hz, 3H), 0.93 (s, 9H), 0.86 (d, J = 6.5 Hz, 3H); MS (ESI+) m/z 518 $(M+H)^+$.

Example 253

N^2-neopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

The title compound was prepared by substituting (*S*)-2-(Neopentylamino)pentanoic acid from Step A of Example 246 for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step D of Example 252 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.38-8.39 (bs, 1H), 8.19-8.21 (m, 1H), 8.13-8.16 (m, 1H), 7.90-7.93 (m, 1H), 7.72 (t, J = 7.8 Hz, 1H), 4.21-4.28 (m, 1H), 3.87 (dd, J = 9.9, 2.8 Hz, 1H), 3.15-3.21 (m, 3H), 2.97 (dd, J = 9.6, 7.3 Hz, 1H), 2.45-2.59 (m, 2H), 2.40 (d, J = 11.2 Hz, 1H), 2.31 (d, J = 11.2 Hz, 1H), 1.93-2.00 (m, 1H), 1.76-1.89 (m, 2H), 1.61-1.93 (m, 1H), 1.61-1.70 (m, 1H), 1.41-1.58 (m, 3H), 1.31 (ddt, J = 9.4, 13.0, 6.5 Hz, 1H), 0.92 (s, 9H), 0.86 (t, J = 7.3 Hz, 3H); MS (ESI+) m/z 504 $(M+H)^+$.

Example 254

N^2-neopentyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

Step A: (3a*S*,4*R*,6a*R*)-2-(3-(Trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine was prepared by substituting (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step E of Example 16 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in Step A of Example 252 and following steps B-D in Example 252: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37 (s, 1H), 8.20 (d, J = 7.9, 1H), 7.93 (d, J = 7.8, 1H), 7.74 (t, J = 7.8, 1H), 3.40 (dd, J = 9.8, 2.8, 1H), 3.13 (dd, J = 9.7, 3.1, 1H), 3.00 (dd, J = 12.9, 5.7, 1H), 2.93 (ddd, J = 12.0, 9.7, 7.9, 2H), 2.52 (qd, J = 8.6, 4.3, 1H), 2.17 – 2.09 (m, 1H), 1.94 – 1.84 (m, 1H), 1.78 – 1.69 (m, 1H), 1.67 – 1.33 (m, 2H), 1.30 – 1.15 (m, 2H); MS (ESI+) m/z 335$(M+H)^+$.

Step B: The title compound was prepared by substituting (*S*)-4-methyl-2-(neopentylamino)pentanoic acid from Step A of Example 244 for *N*-(*tert*-butoxycarbonyl)-L-

leucine and (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37-8.38 (bs, 1H), 8.15-8.19 (m, 2H), 7.90-7.92 (m, 1H), 7.71 (t, J = 7.8 Hz, 1H), 4.22-4.28 (m, 1H), 3.88 (dd, J = 9.9, 2.8 Hz, 1H), 3.23 (dd, J = 8.5, 5.7 Hz, 1H), 3.19 (dd, J = 9.7, 2.8 Hz, 1H), 3.15 (dd, J = 9.9, 7.6 Hz, 1H), 2.96 (dd, J = 9.6, 7.2 Hz, 1H), 2.50-2.59 (m, 2H), 2.41-2.44 (m, 1H), 2.32 (d, J = 11.2 Hz, 1H), 1.92-2.01 (m, 1H), 1.82-1.92 (m, 2H), 1.60-1.78 (m, 1H), 1.69 (ddd, J = 13.5, 7.8, 5.7 Hz, 1H), 1.50-1.59 (m, 2H), 1.32 (ddt, J = 9.4, 13.0, 6.5 Hz, 1H), 0.92 (s, 9H), 0.92 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.5 Hz, 3H); MS (ESI+) *m/z* 518 $(M+H)^+$.

Example 255

N^2-neopentyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

The title compound was prepared by substituting (*S*)-2-(neopentylamino)pentanoic acid from Step A of Example 246 for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 254 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37-8.38 (bs, 1H), 8.18 (d, J = 7.9 Hz, 1H), 8.09-8.11 (m, 1H), 7.90-7.92 (m, 1H), 7.71 (t, J = 7.8 Hz, 1H), 4.20-4.27 (m, 1H), 3.88 (dd, J = 9.9, 2.8 Hz, 1H), 3.20 (dd, J = 6.6, 3.1 Hz, 1H), 3.16-3.20 (m, 1H), 3.14 (dd, J = 9.9, 7.8 Hz, 1H), 2.96 (dd, J = 9.6, 7.3 Hz, 1H), 2.46-2.61 (m, 2H), 2.38 (d, J = 11.3 Hz, 1H), 2.33 (d, J = 11.3 Hz, 1H), 1.92-1.99 (m, 1H), 1.83-1.90 (m, 1H), 1.76-1.83 (m, 1H), 1.66-1.87 (m, 1H), 1.61-1.70 (m, 1H), 1.38-1.58 (m, 3H), 1.26-1.37 (m, 1H), 0.92 (s, 9H), 0.85 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 504 $(M+H)^+$.

Example 256

N^2-neopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

Step A: (3a*R*,4*S*,6a*S*)-2-(4-(Trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine was prepared by substituting 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in Step C of Example 252 and following the procedure of Step D in

Example 252: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.15 (d, J = 8.2, 2H), 7.92 (d, J = 8.3, 2H), 3.40 (dd, J = 9.8, 2.9, 1H), 3.13 (dd, J = 9.7, 3.2, 1H), 3.06 – 2.93 (m, 3H), 2.54 (s, 1H), 2.21 – 2.12 (m, 1H), 1.93 – 1.85 (m, 1H), 1.78 – 1.69 (m, 1H), 1.67 – 1.33 (m, 2H),1.33 – 1.15 (m, 2H); MS (ESI+) *m/z* 335(M+H)$^+$.

Step B: The title compound was prepared by substituting (*S*)-4-methyl-2-(neopentylamino)pentanoic acid from Step A of Example 244 for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.20-8.23 (m, 1H), 8.13-8.16 (m, 2H), 7.89-7.92 (m, 2H), 4.21-4.29 (m, 1H), 3.86 (dd, J = 9.9, 2.8 Hz, 1H), 3.22-3.28 (m, 1H), 3.15-3.22 (m, 2H), 2.99 (dd, J = 9.6, 7.0 Hz, 1H), 2.50-2.62 (m, 2H), 2.43-2.47 (m, 1H), 2.28-2.32 (m, 1H), 1.92-2.02 (m, 1H), 1.80-1.92 (m, 2H), 1.64-1.76 (m, 1H), 1.69 (ddd, J = 13.5, 7.7, 5.8 Hz, 1H), 1.50-1.61 (m, 2H), 1.25-1.40 (m, 1H), 0.93 (d, J = 6.8 Hz, 3H), 0.93 (s, 9H), 0.86 (d, J = 6.5 Hz, 3H); MS (ESI+) *m/z* 518 (M+H)$^+$.

Example 257

N^2-neopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

The title compound was prepared by substituting (*S*)-2-(neopentylamino)pentanoic acid from Step A of Example 246 for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 256 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37-8.38 (bs, 1H), 8.13-8.18 (m, 3H), 7.89-7.91 (m, 2H), 4.21-4.28 (m, 1H), 3.86 (dd, J = 9.9, 2.9 Hz, 1H), 3.16-3.22 (m, 3H), 2.98 (dd, J = 9.6, 7.3 Hz, 1H), 2.47-2.61 (m, 2H), 2.41 (d, J = 11.2 Hz, 1H), 2.32 (d, J = 11.2 Hz, 1H), 1.93-2.00 (m, 1H), 1.78-1.88 (m, 2H), 1.63-1.70 (m, 1H), 1.41-1.58 (m, 3H), 1.28-1.36 (m, 1H), 0.93 (s, 9H), 0.86 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 504 (M+H)$^+$.

Example 258

***N*-(*tert*-butoxycarbonyl)-*N*-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-phenylalanine for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 256 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.09-8.12 (m, 2H), 7.83-7.86 (m, 2H), 7.52-7.59 (bs, 1H), 7.28-7.32 (m, 2H), 7.23-7.28 (m, 2H), 7.15-7.21 (m, 1H), 4.95-5.12 (m, 1H), 4.09 (p, J = 6.9 Hz, 1H), 3.62 (dd, J = 10.4, 3.4 Hz, 1H), 3.48 (dd, J = 14.0, 7.0 Hz, 1H), 3.26 (dd, J = 10.1, 7.9 Hz, 1H), 3.10-3.18 (m, 1H), 3.04-3.13 (m, 1H), 2.97 (s, 3H), 2.46-2.57 (m, 1H), 2.36-2.46 (m, 1H), 1.86-1.96 (m, 1H), 1.74-1.83 (m, 1H), 1.44-1.55 (m, 1H), 1.42-1.46 (m, 1H), 1.38 (s, 9H), 1.21-1.32 (m, 1H); MS (ESI+) *m/z* 596 $(M+H)^+$.

Example 259

***tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-norvaline for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 256 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.06-8.09 (m, 2H), 7.79-7.82 (m, 2H), 7.40 (d, J = 3.1 Hz, 1H), 4.66-4.76 (m, 1H), 4.07 (p, J = 6.8 Hz, 1H), 3.65 (dd, J = 10.2, 3.4 Hz, 1H), 3.28 (dd, J = 10.2, 7.7 Hz, 1H), 3.06-3.17 (m, 2H), 2.93 (s, 3H), 2.53-2.62 (m, 1H), 2.45-2.53 (m, 1H), 1.93-2.02 (m, 1H), 1.86-1.95 (m, 1H), 1.70-1.85 (m, 2H), 1.47-1.57 (m, 1H), 1.45 (s, 9H), 1.27-1.37 (m, 2H), 1.22-1.32 (m, 1H), 0.86 (t, J = 7.4 Hz, 3H); MS (ESI+) *m/z* 548 $(M+H)^+$.

Example 260

N^2-neopentyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

Step A: (3a*S*,4*R*,6a*R*)-2-(4-(Trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine was prepared by following the procedures described in Example 252 Steps A-D substituting (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step E of Example 16 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in Step A of Example 252 and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Step C of Example 252: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.15 (d, J = 8.2, 2H), 7.92 (d, J = 8.3, 2H), 3.40 (dd, J = 9.8, 2.9, 1H), 3.13 (dd, J = 9.7, 3.2, 1H), 3.06 – 2.93 (m, 3H), 2.54 (s, 1H), 2.21 – 2.12 (m, 1H), 1.93 – 1.85 (m, 1H), 1.78 – 1.69 (m, 1H), 1.67 – 1.33 (m, 2H),1.33 – 1.15 (m, 2H); MS (ESI+) *m/z* 335(M+H)$^+$.

Step B: The title compound was prepared by substituting (*S*)-2-(neopentylamino)pentanoic acid from Step A of Example 246 for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.09-8.14 (m, 3H), 7.88-7.91 (m, 2H), 4.20-4.26 (m, 1H), 3.88 (dd, J = 9.9, 2.9 Hz, 1H), 3.13-3.21 (m, 3H), 2.98 (dd, J = 9.6, 7.4 Hz, 1H), 2.49-2.64 (m, 2H), 2.38 (d, J = 11.2 Hz, 1H), 2.33 (d, J = 11.2 Hz, 1H), 1.91-1.99 (m, 1H), 1.76-1.90 (m, 2H), 1.66-1.95 (m, 1H), 1.62-1.71 (m, 1H), 1.41-1.58 (m, 3H), 1.33 (ddt, J = 9.5, 13.0, 6.5 Hz, 1H), 0.92 (s, 9H), 0.86 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 504 (M+H)$^+$.

Example 261

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-neopentyl-L-leucinamide

Step A: (3a*R*,4*S*,6a*S*)-2-(4-Fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine was prepared by substituting 4-fluorobenzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in Step C of Example 252 and following Step D in Example 252: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.05 – 7.96 (m, 2H), 7.38 – 7.31

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(m, 2H), 3.34 (dd, J = 9.8, 3.0, 1H), 3.08 (dd, J = 9.7, 3.3, 1H), 3.05 – 2.98 (m, 1H), 2.97 – 2.89 (m, 2H), 2.59 – 2.49 (m, 1H), 2.20 – 2.10 (m, 1H), 1.95 – 1.85 (m, 1H), 1.79 – 1.69 (m, 1H), 1.67 – 1.33 (m, 2H) 1.31 – 1.15 (m, 2H); MS (ESI+) *m/z* 285(M+H)$^+$.

Step B: The title compound was prepared by substituting (*S*)-4-methyl-2-(neopentylamino)pentanoic acid from Step A of Example 244 for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.21-8.23 (m, 1H), 7.99-8.02 (m, 2H), 7.32 (t, J = 8.5 Hz, 2H), 4.23-4.29 (m, 1H), 3.78 (dd, J = 9.9, 2.9 Hz, 1H), 3.26 (dd, J = 8.5, 5.7 Hz, 1H), 3.12-3.18 (m, 2H), 2.96 (dd, J = 9.6, 7.1 Hz, 1H), 2.51-2.60 (m, 2H), 2.44-2.47 (m, 1H), 2.29-2.32 (m, 1H), 1.93-2.01 (m, 1H), 1.81-1.93 (m, 2H), 1.67-1.79 (m, 1H), 1.70 (ddd, J = 13.5, 7.8, 5.7 Hz, 1H), 1.53-1.60 (m, 2H), 1.23-1.36 (m, 1H), 0.93 (d, J = 6.7 Hz, 3H), 0.93 (s, 9H), 0.87 (d, J = 6.5 Hz, 3H); MS (ESI+) *m/z* 468 (M+H)$^+$.

Example 262

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(5-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate

Step A: *tert*-Butyl (3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate from Step B of Example 252 (250 mg, 1.105 mmol), 2-bromo-5-(trifluoromethyl)pyridine (250 mg, 1.105 mmol), and triethylamine (0.462 mL, 3.31 mmol) were combined in ethanol (0.6 mL). The reaction was heated at 81 °C for 16 hours. To the reaction mixture was added 50% water/ethanol (5 mL), and the precipitate was collected by filtration. This crude material was purified using a 12 g silica gel cartridge with a gradient of 0-1.5% methanol (2 *N* ammonia)/dichloromethane over 20 minutes to give *tert*-butyl (3a*R*,4*S*,6a*S*)-2-(5-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.62 (s, 1H), 7.76 (d, J = 6.4, 1H), 7.68 (d, J = 8.6, 1H), 6.38 (d, J = 8.8, 1H), 4.10 (s, 1H), 3.73 (d, J = 10.4, 1H), 3.65 (s, 1H), 3.61 – 3.53 (m, 1H), 3.32 (d, J = 10.1, 1H), 2.82 – 2.71 (m, 2H), 2.15 (td, J = 12.6, 6.8, 1H), 1.97 (dt, J = 13.1, 6.4, 1H), 1.74 (dq, J = 15.6, 7.9, 1H), 1.54 (s, 9H), 1.45 – 1.34 (m, 1H); MS(DCI+) *m/z* 372(M+H)$^+$.

Step B: *tert*-Butyl (3a*R*,4*S*,6a*S*)-2-(5-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate (282 mg, 0.759 mmol) from Step A was combined with 4 *N* HCl in 1,4-dioxane (2.5 mL, 9.87 mmol). The reaction was stirred at

room temperature overnight and then the volatiles were removed in vacuo. The compound was purified using a 12 g silica gel cartridge eluting with a gradient of 0-7.5% methanol (2 *N* ammonia)/dichloromethane over 20 minutes to give (3a*R*,4*S*,6a*S*)-2-(5-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-amine: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.64 (s, 1H), 7.69 (dd, *J* = 8.9, 2.5, 1H), 6.38 (d, *J* = 8.9, 1H), 4.95 (s, 2H), 3.56 (dd, *J* = 23.7, 14.1, 3H), 3.25 (d, *J* = 6.2, 1H), 3.11 (q, *J* = 6.0, 1H), 2.83 – 2.68 (m, 1H), 2.35 (ddd, *J* = 13.1, 7.9, 5.3, 1H), 2.02 (dtd, *J* = 13.5, 8.3, 5.5, 1H), 1.92 (ddd, *J* = 18.3, 7.4, 5.6, 1H), 1.46 – 1.30 (m, 2H); MS (ESI+) *m/z* 272(M+H)$^+$.

Step C: The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-L-neopentylglycine for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(5-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step B for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.52 (s, 1H), 7.81 (d, *J* = 5.8, 1H), 7.60 (dd, *J* = 8.9, 2.5, 1H), 7.07 (d, *J* = 7.0, 1H), 6.35 (d, *J* = 8.9, 1H), 4.53 (td, *J* = 8.3, 4.7, 1H), 4.30 – 4.18 (m, 1H), 3.72 (dd, *J* = 11.3, 3.5, 1H), 3.65 (dd, *J* = 11.3, 7.6, 1H), 3.57 (dd, *J* = 11.1, 7.8, 1H), 3.31 (dd, *J* = 11.2, 3.9, 1H), 2.80 – 2.67 (m, 2H), 2.10 (ddd, *J* = 19.9, 13.5, 5.8, 2H), 1.93 (td, *J* = 13.1, 7.7, 1H), 1.74 (dd, *J* = 14.3, 8.0, 1H), 1.64 (dq, *J* = 12.9, 7.8, 1H), 1.50 (s, 9H), 1.44 – 1.33 (m, 1H), 1.00 (s, 9H); MS (ESI+) *m/z* 499(M+H)$^+$.

Example 263

isopropyl (*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(5-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate

Step A: (*S*)-2-Aminopentanoic acid (1.874 g, 16mmol) was dissolved in dioxane (16 mL) and 16 mL of 1 *N* NaOH at 0 °C. 1 *M* Isopropyl carbonochloridate in toluene (16.00 mL, 16.00 mmol) was added simultaneously with 16 mL of 1 *N* NaOH dropwise using addition funnels. The reaction was stirred at 0 °C for 3 hours and allowed to warm to room temperature overnight to give a biphasic solution pH 8-9. The solvent was reduced in volume. The aqueous layer was washed with ether, acidified with 1 *M* $KHSO_4$, and extracted with ethyl acetate to give (*S*)-2-(isopropoxycarbonylamino)pentanoic acid: ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 12.43 (s, 1H), 7.25 (d, *J* = 8.0, 1H), 4.73 (hept, *J* = 6.3, 1H), 3.89 (td, *J* = 8.6, 5.2, 1H), 1.68 – 1.46 (m, 2H), 1.41 – 1.22 (m, 2H), 1.16 (d, *J* = 6.2, 6H), 0.85 (t, *J* = 7.3, 3H); MS (DCI+) *m/z* 204(M+H)$^+$

Step B: The title compound was prepared by substituting (*S*)-2-(isopropoxycarbonylamino)pentanoic acid from Step A for *N*-(*tert*-butoxycarbonyl)-L-

leucine and (3a*R*,4*S*,6a*S*)-2-(5-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step B of Example 262 for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.52 (d, *J* = 1.0, 1H), 7.94 (dd, *J* = 4.3, 2.4, 1H), 7.60 (dd, *J* = 8.9, 2.5, 1H), 7.07 (d, *J* = 7.0, 1H),6.35 (d, *J* = 8.9, 1H), 5.03 (dt, *J* = 12.5, 6.2, 1H), 4.49 (dd, *J* = 13.9, 8.0, 1H), 4.35 – 4.19 (m, 1H), 3.73 (dd, *J* = 11.3, 3.6, 1H), 3.66 (dd, *J* = 11.3, 7.6, 1H), 3.57 (dd, *J* = 11.0, 8.0, 1H), 3.32 (dd, *J* = 11.2, 3.9, 1H), 2.81 – 2.66 (m, 2H), 2.10 (dt, *J* = 12.4, 7.0, 1H), 2.04 – 1.88 (m, 2H), 1.86 – 1.75 (m, 1H), 1.72 – 1.60 (m, 1H), 1.57 – 1.46 (m, 2H), 1.45 – 1.33 (m, 1H), 1.21 (d, *J* = 6.2, 3H), 1.18 (d, *J* = 6.2, 3H), 0.87 (t, *J* = 7.4, 3H). ;MS (ESI+) *m/z* 457(M+H)$^+$.

Example 264

***tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(6-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate**

Step A: (3a*R*,4*S*,6a*S*)-2-(6-(Trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-amine was prepared as described for Example 262 Steps A-B substituting 2-bromo-6-(trifluoromethyl)pyridine for 2-bromo-5-(trifluoromethyl)pyridine in Step A of Example 262: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.53 (t, *J* = 7.9, 1H), 6.98 (d, *J* = 7.2, 1H), 6.51 (d, *J* = 8.6, 1H), 3.49 (dd, *J* = 20.2, 8.4, 3H), 3.19 (dd, *J* = 10.7, 4.8, 1H), 3.08 (q, *J* = 6.0, 1H), 2.78 – 2.69 (m, 1H), 2.32 (td, *J* = 12.2, 5.8, 1H), 2.04 – 1.95 (m, 1H), 1.89 (dt, *J* = 12.7, 5.7, 1H), 1.80 – 1.49 (m, 2H), 1.44 – 1.36 (m, 1H), 1.35 – 1.27 (m, 1H); MS (ESI+) *m/z* 272(M+H)$^+$.

Step B: The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-L-neopentylglycine for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(6-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.78 (s, 1H), 7.45 (s, 1H), 7.05 (s, 1H), 6.91 (d, *J* = 7.3, 1H), 6.47 (d, *J* = 8.6, 1H), 4.53 (td, *J* = 8.3, 4.7, 1H), 4.28 – 4.19 (m, 1H), 3.67 – 3.56 (m, 2H), 3.52 (dd, *J* = 10.9, 7.9, 1H), 3.27 (dd, *J* = 11.0, 3.7, 1H), 2.76 – 2.66 (m, 2H), 2.13 (dd, *J* = 14.3, 4.6, 1H), 2.06 (dt, *J* = 12.8, 6.4, 1H), 1.91 (td, *J* = 13.3, 7.9, 1H), 1.73 (dd, *J* = 14.3, 8.0, 1H), 1.62 (dq, *J* = 15.1, 7.7, 1H), 1.50 (s, 9H), 1.37 (qd, *J* = 7.9, 4.9, 1H), 1.00 (s, 9H). ;MS (ESI+) *m/z* 499(M+H)$^+$.

Example 265

***tert*-butyl (*S*)-4,4-dimethyl-1-((3a*R*,4*S*,6a*S*)-2-(2-(methylsulfonyl)pyrimidin-5-yl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-ylcarbamate**

Step A: (3a*R*,4*S*,6a*S*)-2-(2-(Methylsulfonyl)pyrimidin-5-yl)octahydrocyclopenta[*c*]pyrrol-4-amine was prepared as described in Example 262 Steps A-B substituting 5-bromo-2-(methylsulfonyl)pyrimidine for 2-bromo-5-(trifluoromethyl)pyridine in Step A of Example 262: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.48 (s, 2H), 4.96 (s, 3H), 3.71 (dd, *J* = 11.6, 8.6, 1H), 3.66 (d, *J* = 6.1, 2H), 3.41 (dd, *J* = 11.7, 4.9, 1H), 3.11 (q, *J* = 6.0, 1H), 2.80 – 2.71 (m, 1H), 2.37 – 2.30 (m, 1H), 2.00 (ddd, *J* = 21.4, 10.5, 6.5, 1H), 1.90 (td, *J* = 12.5, 5.6, 1H), 1.82 – 1.51 (m, 2H), 1.44 – 1.29 (m, 2H); MS (ESI+) *m/z* 283(M+H)$^+$.

Step B: The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-L-neopentylglycine for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(2-(methylsulfonyl)pyrimidin-5-yl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.34 (s, 2H), 7.79 (ddd, *J* = 3.5, 1.7, 0.7, 1H), 7.10 – 6.93 (m, 1H), 4.52 (td, *J* = 8.2, 4.7, 1H), 4.27 (qd, *J* = 7.1, 5.4, 1H), 3.90 (d, *J* = 11.1, 3H), 3.85 (dd, *J* = 8.1, 3.9, 1H), 3.77 (dd, *J* = 12.1, 7.6, 1H), 3.67 (dd, *J* = 11.8, 7.9, 1H), 3.42 (dd, *J* = 11.8, 4.1, 1H), 2.79 – 2.63 (m, 2H), 2.16 – 2.02 (m, 2H), 1.97 – 1.83 (m, 1H), 1.72 (dd, *J* = 14.3, 8.0, 1H), 1.68 – 1.56 (m, 1H), 1.49 (s, 9H), 1.44 – 1.30 (m, 1H), 0.99 (s, 9H); MS (ESI+) *m/z* 510(M+H)$^+$.

Example 266

(*S*)-*tert*-butyl 2-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamoyl)pyrrolidine-1-carboxylate

(*S*)-1-(*tert*-Butoxycarbonyl)pyrrolidine-2-carboxylic acid (53.1 mg, 0.247 mmol), and 2-(3*H*-[1,2,3]triazolo[4,5-*b*]pyridin-3-yl)-1,1,3,3-tetramethylisouronium hexafluorophosphate(V) (94 mg, 0.247 mmol) were combined in dichloromethane (2 mL). After 10 minutes, (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine (75 mg, 0.224 mmol) from Step A of Example 254 was added. After stirring for 10 more minutes, *N*-ethyl-*N*-isopropylpropan-2-amine (0.098 mL, 0.561 mmol) was added and the reaction mixture was stirred at room temperature overnight. The reaction was quenched with saturated $NaHCO_3$

solution, extracted with 2 mL of dichloromethane, washed with 0.1 *N* HCl, and concentrated in vacuo. The crude material was purified using a 12 g silica gel cartridge with a gradient of 1-5% methanol (2 *N* ammonia)/dichloromethane over 20 minutes to give the title compound: ^{1}H NMR (501 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.29-8.30 (bs, 1H), 8.13 (d, *J* = 7.9 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.66-7.72 (m, 1H), 7.64 (t, *J* = 7.9 Hz, 1H), 4.29-4.32 (m, 1H), 4.06-4.10 (m, 1H), 3.68-3.71 (m, 1H), 3.46-3.51 (m, 1H), 3.34-3.42 (m, 1H), 3.26 (dd, *J* = 9.9, 7.4 Hz, 1H), 3.06-3.17 (m, 2H), 2.55-2.57 (m, 2H), 2.09 (d, *J* = 3.0 Hz, 1H), 1.88-1.98 (m, 3H), 1.80-1.88 (m, 1H), 1.59-1.68 (m, 1H), 1.55 (dd, *J* = 13.2, 8.7 Hz, 1H), 1.50 (s, 9H), 1.25-1.37 (m, 1H); MS (ESI+) *m/z* 532 $(M+H)^+$.

Example 267

***tert*-butyl (1*R*)-1-isopropyl-3-oxo-3-[((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]propylcarbamate**

The title compound was prepared by substituting (*R*)-3-(*tert*-butoxycarbonylamino)-4-methylpentanoic acid for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid in the procedure described in Example 266: ^{1}H NMR (501 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.29-8.31 (bs, 1H), 8.14 (d, *J* = 7.8 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.76-7.80 (bs, 1H), 7.65 (t, *J* = 7.9 Hz, 1H), 6.53-6.62 (m, 1H), 4.08-4.15 (m, 1H), 4.02-4.08 (m, 1H), 3.67 (dd, *J* = 10.1, 3.2 Hz, 1H), 3.28 (dd, *J* = 9.9, 7.9 Hz, 1H), 3.08-3.16 (m, 2H), 2.46-2.59 (m, 4H), 1.87-1.98 (m, 2H), 1.79-1.87 (m, 1H), 1.50-1.62 (m, 1H), 1.48 (s, 9H), 1.24-1.36 (m, 1H), 0.89-0.93 (m, 6H); MS (ESI+) *m/z* 548 $(M+H)^+$.

Example 268

***tert*-butyl (2*S*)-2-{[((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]carbonyl}piperidine-1-carboxylate**

The title compound was prepared by substituting (*S*)-1-(*tert*-butoxycarbonyl)piperidine-2-carboxylic acid for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid in the procedure described in Example 266: ^{1}H NMR (501 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.29-8.30 (bs, 1H), 8.14 (d, *J* = 7.8 Hz, 1H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.64 (t, *J* = 7.9 Hz, 1H), 7.39-7.43 (bs, 1H), 4.82-4.84 (m, 1H), 4.04-4.12 (m, 2H), 3.68 (dd, *J* = 10.1, 3.3 Hz, 1H), 3.28-3.32 (m, 1H), 3.23-3.28 (m, 1H), 3.08-3.16 (m, 2H), 2.48-

2.58 (m, 2H), 2.16-2.21 (m, 1H), 1.89-1.96 (m, 1H), 1.78-1.85 (m, 1H), 1.49-1.63 (m, 5H), 1.47 (s, 9H), 1.32-1.39 (m, 1H), 1.23-1.32 (m, 1H); MS (ESI+) *m/z* 544 $(M+H)^+$.

Example 269

_N_-(*tert*-butoxycarbonyl)-_N_-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-L-phenylalanine for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step D of Example 252 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (500 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.28-8.32 (m, 1H), 8.11-8.17 (m, 1H), 7.82-7.93 (m, 2H), 7.63-7.69 (m, 1H), 7.21-7.29 (m, 4H), 7.16-7.21 (m, 1H), 7.07-7.15 (m, 1H), 4.65-4.70 (m, 1H), 4.0 (m, 1H), 3.52-3.62 (m, 1H), 3.26-3.31 (m, 1H), 3.12-3.21 (m, 2H), 3.03-3.11 (m, 2H), 2.42-2.48 (m, 1H), 2.31-2.36 (m, 1H), 1.81-1.88 (m, 1H), 1.69-1.77 (m, 1H), 1.37-1.48 (m, 1H), 1.42 (s, 9H), 1.16-1.26 (m, 1H); MS (ESI+) *m/z* 599 $(M+H)^+$.

Example 270

_N_-(*tert*-butoxycarbonyl)-_N_-methyl-_N_-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-phenylalanine for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step D of Example 252 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.65 – 8.52 (m, 1H), 8.38 (s, 1H), 8.22 (d, J = 7.8, 1H), 7.93 (d, J = 7.8, 1H), 7.75 (t, J = 7.8, 1H), 7.39 – 7.23 (m, 5H), 5.40 – 5.29 (m, 1H), 4.30 – 4.14 (m, 1H), 3.84 – 3.72 (m, 1H), 3.65 – 3.45 (m, 1H), 3.13 (d, J = 5.4, 2H), 3.06 (s, 3H), 3.03 (dd, J = 9.7, 7.6, 1H), 2.89 (dd, J = 9.5, 7.5, 1H), 2.41 (dd,

J = 13.4, 6.1, 1H), 2.39 – 2.30 (m, 1H), 1.95-1.80 (m, 1H), 1.74 (s, 1H), 1.55 – 1.40 (m, 1H), 1.36 (s, 5H), 1.25 (s, 4H), 1.22 – 1.15 (m, 1H); MS (ESI+) *m/z* 596 $(M+H)^+$.

Example 271

(*S*)-*tert*-butyl 2-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamoyl)pyrrolidine-1-carboxylate

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step D of Example 252 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.42-8.59 (m, 1H), 8.36-8.38 (bs, 1H), 8.16-8.22 (m, 1H), 7.92 (d, J = 7.3 Hz, 1H), 7.74 (t, J = 7.5 Hz, 1H), 4.31-4.55 (m, 1H), 4.09-4.31 (m, 1H), 3.73-3.90 (m, 1H), 3.48-3.68 (m, 1H), 3.27-3.48 (m, 1H), 3.06-3.25 (m, 2H), 2.85-3.03 (m, 1H), 2.42-2.65 (m, 2H), 1.72-2.22 (m, 5H), 1.60-1.72 (m, 1H), 1.53-1.57 (bs, 5H), 1.49-1.54 (bs, 4H), 1.4 (m, 1H), 1.13-1.26 (m, 1H); MS (ESI+) *m/z* 532 $(M+H)^+$,549 $(M+NH_4)^+$.

Example 272

***tert*-butyl (1*R*)-1-isopropyl-3-oxo-3-[((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]propylcarbamate**

The title compound was prepared by substituting (*R*)-3-(*tert*-butoxycarbonylamino)-4-methylpentanoic acid for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step D of Example 252 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (500 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.30-8.31 (bs, 1H), 8.14 (d, J = 7.8 Hz, 1H), 7.84 (d, J = 7.6 Hz, 1H), 7.76-7.85 (bs, 1H), 7.66 (t, J = 7.8 Hz, 1H), 6.50-6.69 (bs, 1H), 4.08-4.16 (m, 1H), 3.64-3.72 (m, 1H), 3.24-3.33 (m, 1H), 3.12 (d, J = 5.2 Hz, 2H), 2.42-2.63 (m, 4H), 1.89-2.00 (m, 2H), 1.79-1.89 (m, 1H), 1.49-1.63 (m, 1H), 1.48 (s, 9H), 1.23-1.33 (m, 2H), 0.88-0.95 (m, 6H); MS (ESI+) *m/z* 570 $(M+Na)^+$.

Example 273

***tert*-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-valine for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step D of Example 252 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (500 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.30-8.32 (bs, 1H), 8.14 (d, J = 7.8 Hz, 1H), 7.84 (d, J = 7.8 Hz, 1H), 7.64 (t, J = 7.8 Hz, 1H), 7.58-7.69 (bs, 1H), 4.32 (d, J = 9.5 Hz, 1H), 4.03-4.12 (m, 1H), 3.68 (dd, J = 10.2, 3.3 Hz, 1H), 3.27-3.31 (m, 1H), 3.08-3.16 (m, 2H), 3.00 (s, 3H), 2.53-2.61 (m, 1H), 2.46-2.53 (m, 1H), 2.33-2.43 (m, 1H), 1.85-1.93 (m, 1H), 1.77-1.85 (m, 1H), 1.47-1.54 (m, 1H), 1.45 (s, 9H), 1.21-1.30 (m, 1H), 0.97 (d, J = 6.5 Hz, 3H), 0.86 (d, J = 6.7 Hz, 3H); MS (ESI+) *m/z* 570 $(M+Na)^+$.

Example 274

***tert*-butyl (2*S*)-2-{[((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]carbonyl}piperidine-1-carboxylate**

The title compound was prepared by substituting (*S*)-1-(*tert*-butoxycarbonyl)piperidine-2-carboxylic acid for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step D of Example 252D for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37-8.38 (bs, 1H), 8.32 (d, J = 5.2 Hz, 1H), 8.19 (d, J = 7.9 Hz, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.71 (t, J = 7.8 Hz, 1H), 4.07-4.23 (m, 2H), 3.84 (dd, J = 9.9, 2.2 Hz, 1H), 3.46 (td, J = 12.9, 2.8 Hz, 1H), 3.16 (d, J = 9.2 Hz, 1H), 3.12 (dd, J = 9.5, 7.6 Hz, 1H), 2.90-2.94 (m, 1H), 2.41-2.57 (bs, 2H), 2.24-2.29 (m, 1H), 1.75-1.97 (m, 2H), 1.53-1.65 (m, 3H), 1.49-1.55 (m, 2H), 1.48 (s, 9H), 1.42-1.51 (m, 1H), 1.29-1.39 (m, 1H), 1.17-1.29 (m, 1H); MS (ESI+) *m/z* 563 $(M+H)^+$.

Example 275

***tert*-butyl (3*S*)-3-{[((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]carbonyl}-3,4-dihydroisoquinoline-2(1*H*)-carboxylate**

The title compound was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step D of Example 252 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (500 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.26-8.27 (bs, 1H), 8.08-8.10 (m, 1H), 7.81-7.84 (m, 1H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.29-7.36 (m, 1H), 7.12-7.14 (m, 2H), 7.08-7.11 (m, 2H), 4.83-5.02 (m, 1H), 4.78 (d, *J* = 15.6 Hz, 1H), 4.67 (d, *J* = 15.6 Hz, 1H), 3.90-3.97 (m, 1H), 3.52 (dd, *J* = 10.1, 3.3 Hz, 1H), 3.30 (dd, *J* = 15.3, 4.8 Hz, 1H), 3.14 (dd, *J* = 9.9, 7.8 Hz, 1H), 3.11 (dd, *J* = 15.4, 6.3 Hz, 1H), 3.04-3.08 (m, 2H), 2.45-2.53 (m, 1H), 2.38-2.45 (m, 1H), 1.64-1.75 (m, 2H), 1.50 (s, 9H), 1.35-1.46 (m, 1H), 1.15-1.25 (m, 1H); MS (ESI+) *m/z* 594 $(M+H)^+$,611 $(M+NH_4)^+$.

Example 276

***tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-L-neopentylglycine for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step D of Example 252D for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (500 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.29-8.30 (bs, 1H), 8.14 (d, *J* = 7.9 Hz, 1H), 7.83 (d, *J* = 7.9 Hz, 1H), 7.79-7.87 (bs, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 7.05-7.18 (bs, 1H), 4.46-4.51 (m, 1H), 4.06-4.14 (m, 1H), 3.67 (dd, *J* = 10.2, 2.8 Hz, 1H), 3.27 (dd, *J* = 10.1, 7.6 Hz, 1H), 3.07-3.15 (m, 2H), 2.50-2.59 (m, 2H), 2.08 (dd,

J = 14.2, 4.6 Hz, 1H), 1.85-1.92 (m, 1H), 1.77-1.85 (m, 1H), 1.70 (dd, J = 14.2, 8.0 Hz, 1H), 1.48-1.54 (m, 1H), 1.47 (s, 9H), 1.21-1.30 (m, 1H), 0.96 (s, 9H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Example 277

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)hexan-2-yl)carbamate

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-norleucine for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step D of Example 252 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.44 (d, J = 6.9 Hz, 1H), 8.36-8.38 (bs, 1H), 8.19 (d, J = 7.9 Hz, 1H), 7.91 (d, J = 7.6 Hz, 1H), 7.72 (t, J = 7.8 Hz, 1H), 5.0 (m, 0.7H), 4.6 (m, 0.3H), 4.18-4.24 (m, 1H), 3.83-3.86 (m, 1H), 3.13-3.19 (m, 1H), 3.08-3.13 (m, 1H), 2.97-3.10 (bs, 3H), 2.91 (dd, J = 9.4, 7.4 Hz, 1H), 2.44-2.59 (m, 2H), 1.98-2.19 (m, 1H), 1.84-1.98 (m, 1H), 1.72-1.85 (m, 2H), 1.47-1.60 (m, 1H), 1.44-1.46 (m, 9H), 1.22-1.34 (m, 1H), 1.15-1.34 (m, 4H), 0.76-0.81 (m, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$,579 $(M+NH_4)^+$.

Example 278

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-norvaline for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step D of Example 252 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (500 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.30-8.31 (bs, 1H), 8.14 (d, J = 7.9 Hz, 1H), 7.84 (d, J = 7.8 Hz, 1H), 7.64 (t, J = 7.8 Hz, 1H), 7.49 (d, J = 5.6 Hz, 1H), 4.72-4.73 (m, 1H), 4.04-4.11 (m, 1H), 3.67 (dd, J = 10.1, 3.3 Hz, 1H), 3.26 (dd, J = 10.1, 7.7 Hz, 1H), 3.10-3.13 (m, 2H), 2.93 (s, 3H), 2.46-2.59 (m, 2H), 1.86-2.01

(m, 2H), 1.71-1.84 (m, 2H), 1.46-1.58 (m, 1H), 1.45 (s, 9H), 1.29-1.36 (m, 2H), 1.22-1.30 (m, 1H), 0.86 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 548 $(M+H)^+$.

Example 279

isopropyl (*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate

The title compound was prepared by substituting (*S*)-2-(isopropoxycarbonylamino)pentanoic acid from Step A of Example 263 for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 256 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (501 MHz, pyridine-d_5) δ ppm 8.08 (d, J = 8.2, 2H), 7.96 (d, J = 4.8, 1H), 7.82 (d, J = 8.3, 2H), 7.18 (d, J = 4.5, 2H), 5.01 (hept, J = 6.2, 1H), 4.45 (dd, J = 14.0, 7.7, 1H), 4.11 (dt, J = 13.0, 6.7, 1H), 3.67 (dd, J = 10.2, 3.0, 1H), 3.30 (dd, J = 10.2, 7.6, 1H), 3.16 – 3.07 (m, 2H), 2.57 (h, J = 9.3, 2H), 1.99 – 1.85 (m, 2H), 1.86 – 1.72 (m, 2H), 1.58 – 1.50 (m, 1H), 1.45 (ddd, J = 20.8, 11.7, 7.2, 2H), 1.26 (ddd, J = 13.1, 10.9, 6.6, 1H), 1.19 (d, J = 6.2, 3H), 1.16 (d, J = 6.2, 3H), 0.84 (t, J = 7.4, 3H); MS (ESI+) *m/z* 520 $(M+H)^+$.

Example 280

isopropyl (*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate

The title compound was prepared by substituting N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide from Example 382 for (*S*)-tert-butyl 2-amino-4-methylpentanoate and isopropyl carbonochloridate for methanesulfonyl chloride in the procedure described in Example 242: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.22 – 8.15 (m, 1H), 7.65 (d, J = 8.0, 2H), 7.51 (d, J = 7.9, 2H), 7.39 – 7.34 (m, 1H), 5.11 – 5.02 (m, 1H), 4.74 – 4.64 (m, 1H), 4.48 – 4.40 (m, 1H), 3.57 (d, J = 13.7, 1H), 3.46 (d, J = 13.6, 1H), 2.90 – 2.82 (m, 1H), 2.62 – 2.49 (m, 2H), 2.44 – 2.38 (m, 1H), 2.34 – 2.28 (m, 1H), 2.24 (dd, J = 9.7, 6.3, 1H), 2.10 – 2.00 (m, 2H), 1.92 – 1.81 (m, 2H), 1.65 – 1.57 (m, 1H), 1.55 – 1.45 (m, 2H), 1.42 – 1.33 (m, 1H), 1.22 (d, J = 6.2, 3H), 1.15 (d, J = 6.2, 3H), 0.81 (t, J = 7.4, 3H); MS (ESI+) *m/z* 470 $(M+H)^+$.

Example 281

(3a*S*,4*R*,6a*R*)-*N*-neopentyl-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine

(3a*S*,4*R*,6a*R*)-2-(3-(Trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine (100 mg, 0.299 mmol) from Step A of Example 254 and pivalaldehyde (0.043 mL, 0.389 mmol) were combined in dichloromethane (1 mL). Acetic acid (0.3 mL) was added. The reaction was stirred at room temperature for 20 minutes, then PS-cyanoborohydride (147 mg, 0.359 mmol) was added. The reaction was stirred at room temperature for 72 hours, then filtered. The reaction mixture was washed with 1 *N* $NaHCO_3$ and concentrate in vacuo. The crude material was purified using a 12 g silica gel cartridge with a gradient of 0-4% methanol (2 *N* ammonia)/dichloromethane to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.40-8.41 (bs, 1H), 8.22-8.25 (m, 1H), 7.92-7.95 (m, 1H), 7.75 (t, *J* = 7.8 Hz, 1H), 3.42 (dd, *J* = 9.8, 3.1 Hz, 1H), 3.17 (dd, *J* = 9.6, 3.1 Hz, 1H), 3.06-3.10 (m, 1H), 2.96 (dd, *J* = 9.6, 7.7 Hz, 1H), 2.74-2.77 (m, 1H), 2.48-2.53 (m, 1H), 2.30 (d, *J* = 11.3 Hz, 1H), 2.22-2.27 (m, 1H), 2.22 (d, *J* = 7.9 Hz, 1H), 1.78-1.92 (m, 2H), 1.18-1.31 (m, 3H), 0.90 (s, 9H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Example 282

(3a*R*,4*S*,6a*S*)-*N*-neopentyl-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step D of Example 252 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.40-8.41 (bs, 1H), 8.22-8.25 (m, 1H), 7.92-7.95 (m, 1H), 7.75 (t, *J* = 7.9 Hz, 1H), 3.42 (dd, *J* = 9.8, 3.1 Hz, 1H), 3.17 (dd, *J* = 9.6, 3.0 Hz, 1H), 3.05-3.09 (m, 1H), 2.96 (dd, *J* = 9.6, 7.7 Hz, 1H), 2.73-2.77 (m, 1H), 2.48-2.53 (m, 1H), 2.30 (d, *J* = 11.3 Hz, 1H), 2.22-2.27 (m, 1H), 2.21 (d, *J* = 11.0 Hz, 1H), 1.78-1.93 (m, 2H), 1.18-1.32 (m, 3H), 0.90 (s, 9H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Example 283

(3a*R*,4*S*,6a*S*)-*N*-isopropyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A of Example 256 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.14-8.22 (m, 2H), 7.91-7.98 (m, 2H), 3.40 (dd, J = 9.7, 3.0 Hz, 1H), 3.16 (dd, J = 9.6, 3.3 Hz, 1H), 3.06 (dd, J = 9.7, 7.8 Hz, 1H), 2.99 (dd, J = 9.6, 7.7 Hz, 1H), 2.85-2.90 (m, 1H), 2.74 (hept, J = 6.2 Hz, 1H), 2.46-2.53 (m, 1H), 2.14-2.25 (m, 1H), 1.80-1.91 (m, 2H), 1.07-1.43 (m, 3H), 1.00 (d, J = 6.2 Hz, 3H), 0.96 (d, J = 6.1 Hz, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Example 284

(3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}-*N*-isopropyloctahydrocyclopenta[*c*]pyrrol-4-amine

Step A: *tert*-Butyl (3a*R*,4*S*,6a*S*)-2-(2-chloro-4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate was prepared by substituting 2-chloro-4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in Step C of Example 252: ^{1}H NMR (500 MHz, pyridine-d_5) δ 8.33 (d, J = 8.0, 1H), 8.00 (s, 1H), 7.77 – 7.68 (m, 2H), 4.04 – 3.96 (m, 1H), 3.83 (d, J = 9.5, 1H), 3.48 (dd, J = 10.2, 7.5, 1H), 3.41 – 3.29 (m, 2H), 2.72 – 2.59 (m, 2H), 2.02 (td, J = 12.0, 6.4, 1H), 1.90 (qd, J = 7.1, 4.5, 1H), 1.64 (ddd, J = 16.1, 12.4, 8.8, 1H), 1.50 (s, 9H), 1.41 – 1.32 (m, 1H) ;MS (ESI+) *m/z* 486$(M+NH_4)^+$.

Step B: (3a*R*,4*S*,6a*S*)-2-{[2-Chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[c]pyrrol-4-amine was prepared by substituting *tert*-butyl (3a*R*,4*S*,6a*S*)-2-(2-chloro-4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate from Step A for *tert*-butyl (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate in the procedure described in Step D of Example 252: ^{1}H NMR (500 MHz, pyridine-d_5) δ 8.34 (d, J = 8.2, 1H), 8.01 (s, 1H), 7.75 (d, J = 8.3, 1H), 3.55 (dd, J = 10.1, 3.1, 1H), 3.38 – 3.31 (m, 2H), 3.28 (dd, J = 9.9, 3.7, 1H), 3.10 (q, J = 6.1, 1H), 2.70 – 2.60 (m, 1H), 2.31 – 2.22 (m,

1H), 1.93 (ddd, J = 11.1, 8.2, 5.7, 1H), 1.87 – 1.76 (m, 1H), 1.74 – 1.49 (m, 2H), 1.37 – 1.24 (m, 2H); MS (ESI+) m/z 369$(M+H)^+$.

Step C: The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine from Step A for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37 (d, J = 8.2 Hz, 1H), 8.03 (d, J = 1.7 Hz, 1H), 7.77 (d, J = 9.0 Hz, 1H), 3.56 (dd, J = 10.0, 3.1 Hz, 1H), 3.41 (dd, J = 10.1, 7.8 Hz, 1H), 3.31-3.38 (m, 2H), 2.97 (q, J = 6.3 Hz, 1H), 2.78 (hept, J = 6.2 Hz, 1H), 2.58-2.63 (m, 1H), 2.30-2.35 (m, 1H), 1.87-1.96 (m, 2H), 1.05-1.67 (m, 1H), 1.21-1.37 (m, 2H), 1.01 (d, J = 6.2 Hz, 3H), 0.98 (d, J = 6.1 Hz, 3H); MS (ESI+) m/z 411 $(M+H)^+$.

Example 285

(3a*S*,4*R*,6a*R*)-*N*-(4-fluorobenzyl)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine

The title compound was prepared by substituting 4-fluorobenzaldehyde for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.39-8.40 (bs, 1H), 8.23 (d, J = 7.9 Hz, 1H), 7.94 (d, J = 7.9 Hz, 1H), 7.76 (t, J = 7.8 Hz, 1H), 7.41 (dd, J = 8.3, 5.5 Hz, 2H), 7.11-7.15 (m, 2H), 3.71 (d, J = 13.2 Hz, 1H), 3.67 (d, J = 13.2 Hz, 1H), 3.39 (dd, J = 9.8, 3.1 Hz, 1H), 3.16 (dd, J = 9.6, 3.0 Hz, 1H), 3.06 (dd, J = 9.8, 8.0 Hz, 1H), 2.96 (dd, J = 9.6, 7.6 Hz, 1H), 2.83-2.88 (m, 1H), 2.47-2.56 (m, 1H), 2.30-2.36 (m, 1H), 1.92-2.09 (m, 1H), 1.87-1.94 (m, 1H), 1.80-1.88 (m, 1H), 1.29-1.37 (m, 1H), 1.20-1.29 (m, 1H); MS (ESI+) m/z 443 $(M+H)^+$.

Example 286

(3a*R*,4*S*,6a*S*)-*N*-(4-fluorobenzyl)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step D of Example 252 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and 4-fluorobenzaldehyde for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.39-8.40 (bs, 1H), 8.22-8.24 (m, 1H), 7.93-7.95 (m, 1H), 7.75

(t, J = 7.8 Hz, 1H), 7.41 (dd, J = 8.3, 5.5 Hz, 2H), 7.13 (t, J = 8.7 Hz, 2H), 3.71 (d, J = 13.3 Hz, 1H), 3.67 (d, J = 13.2 Hz, 1H), 3.39 (dd, J = 9.8, 3.1 Hz, 1H), 3.16 (dd, J = 9.6, 3.0 Hz, 1H), 3.06 (dd, J = 9.8, 8.0 Hz, 1H), 2.96 (dd, J = 9.6, 7.6 Hz, 1H), 2.85 (q, J = 6.1 Hz, 1H), 2.47-2.56 (m, 1H), 2.30-2.35 (m, 1H), 1.93-2.07 (m, 1H), 1.87-1.94 (m, 1H), 1.79-1.87 (m, 1H), 1.29-1.38 (m, 1H), 1.20-1.29 (m, 1H); MS (ESI+) *m/z* 443 $(M+H)^+$.

Example 287

(3a*R*,4*S*,6a*S*)-*N*-(4-fluorobenzyl)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-amine

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine (0.83 g, 3.84 mmol) from Step A of Example 33 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and 4-fluorobenzaldehyde for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.79-7.80 (bs, 1H), 7.58-7.61 (m, 1H), 7.60 (s, 1H), 7.44-7.49 (m, 1H), 7.39-7.44 (m, 2H), 7.12 (t, J = 8.6 Hz, 2H), 3.71-3.79 (m, 2H), 3.55-3.56 (bs, 2H), 2.96 (q, J = 5.1 Hz, 1H), 2.57-2.63 (m, 1H), 2.51 (dd, J = 8.8, 3.2 Hz, 1H), 2.39-2.43 (m, 1H), 2.31-2.39 (m, 3H), 1.91-1.98 (m, 2H), 1.72-1.93 (m, 1H), 1.34-1.48 (m, 2H); MS (ESI+) *m/z* 393 $(M+H)^+$.

Example 288

(3a*R*,4*S*,6a*S*)-*N*-ethyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine

(3a*R*,4*S*,6a*S*)-2-(4-(Trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine (120 mg, 0.359 mmol) from Step A of Example 256, iodoethane (0.287 mL, 3.59 mmol), and triethylamine (0.750 mL, 5.38 mmol) were in tetrahydrofuran (1 mL). The reaction was stirred at 65 °C for 3 days, and then the solvent was removed in vacuo. The residue was diluted with dichloromethane (5 mL), and addition of saturated aqueous sodium bicarbonate gave the products as a solid. This material was purified using a 12 g silica gel cartridge with a gradient of 0-5% methanol (2 *N* ammonia)/dichloromethane over 20 minutes to give two products. The second product was further purified on 4×0.25 mm preparative thin-layer chromatography plate eluting with 6% methanol (2 *N* ammonia)/dichloromethane to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.17-8.19 (m, 2H), 7.93-7.95 (m, 2H), 3.38 (dd, J = 9.8, 3.1 Hz, 1H), 3.15 (dd, J = 9.6, 3.2 Hz, 1H), 3.06 (dd, J = 9.8,

8.0 Hz, 1H), 2.96 (dd, J = 9.6, 7.7 Hz, 1H), 2.78 (q, J = 6.1 Hz, 1H), 2.44-2.58 (m, 4H), 2.25-2.33 (m, 1H), 1.85-1.92 (m, 1H), 1.75-1.85 (m, 1H), 1.16-1.34 (m, 2H), 1.05 (t, J = 7.1 Hz, 3H); MS (ESI+) *m/z* 363 $(M+H)^+$.

Example 289

(3a*R*,4*S*,6a*S*)-*N*,*N*-diethyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine

The first product from Example 288 was purified on a 2×0.25 mm preparative thin-layer chromatography plate eluting with acetone to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.18-8.20 (m, 2H), 7.94-7.97 (m, 2H), 3.43 (dd, J = 9.6, 2.6 Hz, 1H), 3.22 (dd, J = 9.5, 2.6 Hz, 1H), 2.98 (dd, J = 9.6, 7.8 Hz, 1H), 2.88 (dd, J = 9.5, 7.4 Hz, 1H), 2.70-2.75 (m, 1H), 2.30-2.50 (m, 5H), 2.22-2.29 (m, 1H), 1.75-1.81 (m, 1H), 1.62-1.68 (m, 1H), 1.25-1.34 (m, 1H), 1.16-1.25 (m, 1H), 0.92 (t, J = 7.0 Hz, 6H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Example 290

(3a*R*,4*S*,6a*S*)-*N*-propyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine

The title compound was prepared by substituting 1-iodopropane for iodoethane in the procedure described in Example 288: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.17-8.19 (m, 2H), 7.93-7.95 (m, 2H), 3.39 (dd, J = 9.8, 3.1 Hz, 1H), 3.16 (dd, J = 9.6, 3.2 Hz, 1H), 3.07 (dd, J = 9.8, 8.0 Hz, 1H), 2.98 (dd, J = 9.6, 7.7 Hz, 1H), 2.77 (q, J = 5.9 Hz, 1H), 2.50-2.58 (m, 1H), 2.39-2.51 (m, 2H), 2.24-2.30 (m, 1H), 1.77-1.92 (m, 2H), 1.36-1.50 (m, 2H), 1.16-1.57 (m, 1H), 1.19-1.34 (m, 2H), 0.88 (t, J = 7.4 Hz, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Example 291

(3a*R*,4*S*,6a*S*)-*N*,*N*-dipropyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine

The title compound was prepared as described in Example 290 following the procedures described in Examples 288 and 289: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.18-8.20 (m, 2H), 7.93-7.95 (m, 2H), 3.48 (dd, J = 9.5, 2.3 Hz, 1H), 3.23 (dd, J = 9.5, 2.8 Hz, 1H), 2.99 (dd, J = 9.4, 7.7 Hz, 1H), 2.92 (dd, J = 9.3, 7.8 Hz, 1H), 2.74-2.80 (m, 1H),

2.37-2.48 (m, 1H), 2.19-2.35 (m, 5H), 1.78-1.84 (m, 1H), 1.61-1.66 (m, 1H), 1.16-1.39 (m, 6H), 0.84 (t, J = 7.3 Hz, 6H); MS (ESI+) *m/z* 419 $(M+H)^+$.

Example 292

(3a*R*,4*S*,6a*S*)-*N*-(cyclopropylmethyl)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine

The title compound was prepared by substituting (bromomethyl)cyclopropane for iodoethane in the procedure described in Example 288: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.17-8.19 (m, 2H), 7.93-7.95 (m, 2H), 3.38 (dd, J = 9.8, 3.2 Hz, 1H), 3.16 (dd, J = 9.6, 3.2 Hz, 1H), 3.07 (dd, J = 9.8, 8.0 Hz, 1H), 2.98 (dd, J = 9.6, 7.6 Hz, 1H), 2.79-2.84 (m, 1H), 2.51-2.58 (m, 1H), 2.36-2.50 (m, 2H), 2.26-2.32 (m, 1H), 1.85-1.93 (m, 1H), 1.78-1.85 (m, 1H), 1.35-1.78 (m, 1H), 1.22-1.33 (m, 2H), 0.89-0.98 (m, 1H), 0.36-0.44 (m, 2H), 0.11-0.13 (m, 2H); MS (ESI+) *m/z* 389 $(M+H)^+$.

Example 293

(3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}-*N*-ethyloctahydrocyclopenta[*c*]pyrrol-4-amine

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[c]pyrrol-4-amine from Step B of Example 284 for (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 288: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37 (d, J = 8.2 Hz, 1H), 8.03 (s, 1H), 7.78 (dd, J = 8.3, 1.7 Hz, 1H), 3.54 (dd, J = 10.0, 3.5 Hz, 1H), 3.43 (dd, J = 10.0, 8.0 Hz, 1H), 3.27-3.36 (m, 2H), 2.86 (q, J = 5.9 Hz, 1H), 2.59-2.65 (m, 1H), 2.47-2.58 (m, 2H), 2.35-2.41 (m, 1H), 1.82-1.95 (m, 2H), 1.04-1.73 (m, 1H), 1.25-1.40 (m, 2H), 1.05 (t, J = 7.1 Hz, 3H); MS (ESI+) *m/z* 397 $(M+H)^+$.

Example 294

(3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}-*N*,*N*-diethyloctahydrocyclopenta[*c*]pyrrol-4-amine

The title compound was prepared as described in Example 293 following the procedures described in Examples 288 and 289: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.38 (d, J = 8.2 Hz, 1H), 8.04 (d, J = 1.7 Hz, 1H), 7.77-7.79 (m, 1H), 3.57 (dd, J = 9.9, 2.7

Hz, 1H), 3.34-3.41 (m, 2H), 3.29 (dd, J = 9.9, 7.3 Hz, 1H), 2.81-2.87 (m, 1H), 2.33-2.57 (m, 6H), 1.80-1.86 (m, 1H), 1.68-1.74 (m, 1H), 1.22-1.43 (m, 2H), 0.94 (t, J = 7.1 Hz, 6H); MS (ESI+) m/z 442 $(M+NH_4)^+$.

Example 295

(3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}-*N*-[5-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-amine

(3a*R*,4*S*,6a*S*)-2-{[2-Chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[c]pyrrol-4-amine (70 mg, 0.190 mmol) from Step B of Example 284, 2-bromo-5-(trifluoromethyl)pyridine (42.9 mg, 0.190 mmol), and triethylamine (0.079 mL, 0.569 mmol) were combined in ethanol (0.6 mL). The reaction was heated at 86 °C for 5 days and the solvent was evaporated in vacuo. The resultant material was purified using a 12 g silica gel cartridge with a gradient of 0-0.8% methanol (2 *N* ammonia)/dichloromethane over 20 minutes to give crude product. It was further purified by loading it onto 2×0.25 mm preparative thin-layer chromatography plate and eluted with 30% acetone/hexanes to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.50-8.52 (bs, 1H), 8.40 (d, J = 8.2 Hz, 1H), 8.03 (s, 1H), 7.96-7.98 (m, 1H), 7.75-7.78 (m, 1H), 7.54-7.59 (m, 1H), 6.59 (d, J = 8.8 Hz, 1H), 4.30-4.42 (m, 1H), 3.89 (dd, J = 10.2, 2.7 Hz, 1H), 3.57 (dd, J = 10.2, 7.0 Hz, 1H), 3.43 (dd, J = 9.9, 6.7 Hz, 1H), 3.39 (dd, J = 10.0, 2.9 Hz, 1H), 2.68 (d, J = 3.5 Hz, 2H), 2.13-2.20 (m, 1H), 1.90-1.97 (m, 1H), 1.59-1.66 (m, 1H), 1.40-1.48 (m, 1H); MS (ESI+) m/z 514 $(M+H)^+$.

Example 296

***tert*-butyl (*S*)-1-(ethyl((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4,4-dimethylpentanoic acid from Step A of Example 247 for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-*N*-ethyl-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 288 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.11 (d, J = 8.3, 2H), 7.83 (d, J = 8.4, 2H), 5.44 – 4.96 (m, 2H), 4.20 – 3.97 (m, 1H), 3.57 –

3.39 (m, 2H), 3.38 – 3.23 (m, 2H), 3.19 (d, J = 4.1, 2H), 2.89 (s, 3H), 2.85 – 2.73 (m, 1H), 2.72 – 2.59 (m, 1H), 2.25 – 2.08 (m, 1H), 1.97 – 1.73 (m, 3H), 1.52 (s, 9H), 1.35 – 1.21 (m, 1H), 1.17 (t, J = 7.0, 3H), 0.97 (s, 9H); MS (ESI+) m/z 604(M+H)$^+$.

Example 297

***tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-(propyl((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)pentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4,4-dimethylpentanoic acid from Step A of Example 247 for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-*N*-propyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine from Example 290 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.11 (d, J = 8.2, 2H), 7.83 (d, J = 8.4, 2H), 5.37 – 5.09 (m, 1H), 4.15 – 3.99 (m, 1H), 3.54 (dd, J = 10.1, 3.2, 1H), 3.48 – 3.35 (m, 1H), 3.29 (dt, J = 9.1, 8.7, 1H), 3.18 (dd, J = 9.1, 4.5, 3H), 2.90 (s, 3H), 2.86 – 2.77 (m, 1H), 2.74 – 2.64 (m, 1H), 2.24 – 2.09 (m, 1H), 1.96 – 1.86 (m, 2H), 1.85 – 1.75 (m, 1H), 1.59 (dt, J = 15.2, 7.5, 3H), 1.52 (s, 9H), 1.34 – 1.22 (m, 1H), 0.98 (s, 9H), 0.90 (t, J = 7.3, 3H); MS (ESI+) m/z 618(M+H)$^+$.

Example 298

***tert*-butyl (*S*)-1-((cyclopropylmethyl)((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4,4-dimethylpentanoic acid from Step A of Example 247 for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-*N*-(cyclopropylmethyl)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine from Example 292 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.11 (d, J = 8.2, 2H), 7.83 (d, J = 8.3, 2H), 5.39 – 5.07 (m, 1H), 4.12 – 3.95 (m, 1H), 3.58 (dd, J = 9.9, 3.4, 1H), 3.44 – 3.24 (m, 3H), 3.20 (d, J = 4.7, 2H), 3.11 – 2.96 (m, 1H), 2.88 (s, 3H), 2.80 – 2.65 (m, 1H), 2.32 – 2.16 (m, 1H), 2.13 – 2.00 (m, 1H), 1.99 – 1.90 (m, 1H), 1.90 – 1.80 (m, 1H), 1.51

(m, 10H), 1.31 (ddd, J = 20.7, 12.5, 7.9, 1H), 1.03 – 0.92 (m, 10H), 0.55 (tt, J = 14.1, 7.5, 2H), 0.47 – 0.36 (m, 1H), 0.32 – 0.22 (m, 1H); MS (ESI+) m/z 630$(M+H)^+$.

Example 299

2-nitro-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)benzenesulfonamide

(3a*R*,4*S*,6a*S*)-2-(4-(Trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine (300 mg, 0.897 mmol) from Step A of Example 256 and triethylamine (0.313 mL, 2.243 mmol) were combined in dichloromethane (20 mL). 2-Nitrobenzene-1-sulfonyl chloride (258 mg, 1.166 mmol) in dichloromethane (5 mL) was added dropwise. The reaction mixture was stirred at room temperature for 16 hours. The reaction was quenched with water, and the organic layer was separated and concentrated. The resulted crude material was triturated with 50% diethyl ether/hexane, collected by filtration, washed with water then hexane to yield a solid. The crude solid was purified using a 12 g silica gel cartridge with a gradient of 10-100% ethyl acetate/hexane over 20 minutes to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.69 (s, 1H), 8.31 (dd, J = 6.0, 3.3, 1H), 8.12 (d, J = 8.2, 2H), 7.92 (dd, J = 8.6, 2.1, 3H), 7.67 (dd, J = 5.9, 3.3, 2H), 4.94 (s, 2H), 3.84 (dd, J = 15.0, 6.2, 1H), 3.58 (dd, J = 10.0, 2.4, 1H), 3.17 (dd, J = 9.7, 2.7, 1H), 2.94 (dd, J = 10.0, 7.7, 1H), 2.87 (dd, J = 9.6, 7.7, 1H), 2.71 (td, J = 9.3, 2.4, 1H), 2.60 – 2.50 (m, 1H), 1.94 – 1.80 (m, 2H), 1.71 – 1.58 (m, 1H), 1.23 (tt, J = 10.5, 6.5, 1H); MS (ESI+) m/z 518$(M+H)^+$.

Example 300

***N*-methyl-2-nitro-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)benzenesulfonamide**

2-Nitro-*N*-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)benzenesulfonamide (250 mg, 0.481 mmol) from Example 299 and dimethyl sulfate (0.138 mL, 1.444 mmol) were combined in *N,N*-dimethylformamide (3 mL) at 0 °C and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.145 mL, 0.962 mmol) was added dropwise. The reaction mixture was stirred for 0.5 hours, water was added, and the precipitate was collected by filtration. The resultant crude material was purified using a 12 g silica gel cartridge eluting with a gradient of 0-60% ethyl

acetate/hexane over 20 minutes to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.15 (dd, J = 12.1, 4.7, 3H), 7.94 (d, J = 8.3, 2H), 7.88 (dd, J = 7.7, 1.3, 1H), 7.68 (dtd, J = 19.1, 7.5, 1.3, 2H), 4.29 (dt, J = 10.8, 7.0, 1H), 3.63 (dd, J = 9.9, 1.5, 1H), 3.21 (dd, J = 9.7, 2.3, 1H), 2.90 (s, 3H), 2.89 – 2.81 (m, 2H), 2.58 – 2.39 (m, 2H), 1.83 – 1.72 (m, 1H), 1.68 – 1.58 (m, 1H), 1.50 (qd, J = 11.8, 7.3, 1H), 1.21 (ddd, J = 19.4, 12.4, 7.1, 1H); MS (ESI+) *m/z* 551(M+NH_4)$^+$.

Example 301

(3a*R*,4*S*,6a*S*)-*N*-methyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine

2-Mercaptoethanol (0.056 mL, 0.793 mmol) was added dropwise to a mixture of *N*-methyl-2-nitro-*N*-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)benzenesulfonamide (235 mg, 0.440 mmol) from Example 300 and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.166 mL, 1.101 mmol) in *N*,*N*-dimethylformamide (1mL) at room temperature. The reaction mixture was stirred for 30 minutes, and 1 *N* NaHCO3 solution was added, The mixture was extracted with dichloromethane, and the separated the organic layer was concentrated. The resultant crude material was purified using a SF15-12g cartridge (Analogix®, Burlington, Wisconsin) with a gradient of 0-5.5% methanol (2 *N* NH_3)/dichloromethane over 20 minutes to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.17 (d, J = 8.1, 2H), 7.94 (d, J = 8.2, 2H), 4.93 – 4.86 (m, 1H), 3.34 (dd, J = 9.8, 3.3, 1H), 3.14 (dd, J = 9.7, 3.2, 1H), 3.06 (dd, J = 9.7, 8.2, 1H), 2.65 (q, J = 5.7, 1H), 2.57 – 2.46 (m, 1H), 2.29 (s, 3H), 2.25 (ddd, J = 8.6, 5.0, 2.5, 1H), 1.86 (ddd, J = 12.0, 8.6, 6.1, 1H), 1.80 – 1.72 (m, 1H), 1.61 – 1.32 (m, 1H), 1.32 – 1.19 (m, 2H); MS (ESI+) *m/z* 349(M+H)$^+$.

Example 302

***tert*-butyl (*S*)-4,4-dimethyl-1-(methyl((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4,4-dimethylpentanoic acid from Step A of Example 247 for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-*N*-methyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine from Example 301 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-

amine in the procedure described in Example 266: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.11 (d, J = 8.2, 2H), 7.83 (d, J = 8.3, 2H), 5.37 – 5.10 (m, 1H), 4.73 – 4.53 (m, 1H), 3.57 (d, J = 9.1, 1H), 3.24 (dd, J = 16.5, 7.2, 2H), 3.16 (dd, J = 9.9, 3.4, 1H), 2.94 (s, 3H), 2.88 (s, 3H), 2.64 – 2.51 (m, 2H), 2.25 – 2.09 (m, 1H), 1.89 – 1.78 (m, 1H), 1.77 – 1.54 (m, 3H), 1.52 (s, 9H), 1.26 (dt, J = 17.5, 7.1, 1H), 0.96 (s, 9H); MS (ESI+) m/z 590(M+H)$^+$.

Example 303

(2*S*)-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}pentanamide

Step A: (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-Benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide (265 mg, 0.611 mmol) from Example 220 Step D and ethanol (20 mL) were added to 20% $Pd(OH)_2$ on carbon, wet (53.0 mg, 0.377 mmol) in a 50 mL pressure bottle and stirred for 48 hours under 30 psi hydrogen at 50 °C. The mixture was filtered through a nylon membrane and the solvent removed in vacuo to give (2*S*)-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methyl-*N*-[(3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]pentanamide: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.89 (dd, J = 6.6, 18.9, 1H), 4.55 - 4.50 (m, 1H), 4.42 - 4.31 (m, 1H), 3.99 - 3.91 (m, 1H), 3.44 - 3.39 (m, 1H), 3.34 (dd, J = 2.8, 11.4, 0.5H), 3.29 - 3.25 (m, 2H), 3.21 (dd, J = 5.4, 13.2, 1H), 3.13 (dd, J = 7.7, 11.2, 0.5H), 2.99 (td, J = 7.5, 10.8, 1H), 2.79 (dd, J = 3.3, 10.9, 0.5H), 2.73 (dd, J = 3.3, 10.9, 0.5H), 2.69 - 2.55 (m, 2H), 2.31 - 2.16 (m, 2H), 2.12 - 2.00 (m, 1H), 1.94 - 1.78 (m, 4H), 1.69 (dddd, J = 5.2, 11.0, 16.7, 19.8, 2H), 1.49 - 1.29 (m, 1H), 0.88 (t, J = 6.5, 3H), 0.83 (t, J = 6.4, 3H); MS (ESI+) m/z 344(M+H)$^+$

Step B: (2*S*)-2-(1,1-Dioxidoisothiazolidin-2-yl)-4-methyl-*N*-[(3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]pentanamide (204 mg, 0.594 mmol) and 3-(trifluoromethyl)benzaldehyde (0.158 mL, 1.188 mmol) were dissolved in dichloromethane (3 mL). Acetic acid (1 mL) was added. The reaction was stirred at ambient temperature for 20 min, then PS-cyanoborohydride (487 mg, 1.188 mmol) was added. The reaction was stirred at room temperature overnight, then filtered, and the solvent was removed in vacuo. The crude material was purified by silica gel chromatography using 1-10% methanol (2 *N* ammonia)/dichloromethane to the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.79 (d, J = 7.0, 1H), 7.75 (d, J = 10.3, 1H), 7.61 - 7.54 (m, 2H), 7.44 (t, J = 7.7, 1H), 4.52 (dd, J = 6.6, 8.9, 1H), 4.38 (dq, J = 6.4, 12.6, 1H), 3.94 (dd, J = 7.3, 16.2, 1H), 3.57 (dd, J = 9.1, 13.5, 1H), 3.50 - 3.37 (m, 2H), 3.31 - 3.19 (m, 2H), 2.79 (ddd, J = 3.0, 9.1, 19.0, 1H), 2.62 - 2.54 (m, 1H), 2.54 - 2.45 (m, 1H), 2.43 - 2.36 (m, 1H), 2.31 - 2.16 (m, 4H), 2.13 - 2.03

(m, 1H), 1.94 - 1.78 (m, 3H), 1.77 - 1.59 (m, 2H), 1.39 (dt, J = 6.5, 19.8, 1H), 0.88 (d, J = 6.6, 3H), 0.82 (dd, J = 2.3, 6.5, 3H); MS (ESI+) m/z 502$(M+H)^+$.

Example 304

2-isopropyl-3-methyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide

The title compound was prepared by substituting *N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-isopropyl-3-methylbutanamide from Example 235 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide in the procedures described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.12-8.14 (m, 1H), 7.75-7.76 (bs, 1H), 7.55-7.63 (m, 2H), 7.44 (t, J = 7.8 Hz, 1H), 4.42-4.48 (m, 1H), 3.62 (d, J = 13.5 Hz, 1H), 3.46 (d, J = 13.5 Hz, 1H), 2.86 (dd, J = 9.0, 2.4 Hz, 1H), 2.50-2.57 (m, 2H), 2.44-2.49 (m, 1H), 2.25-2.31 (m, 2H), 2.06-2.15 (m, 3H), 1.83-1.90 (m, 2H), 1.58-1.65 (m, 1H), 1.35-1.42 (m, 1H), 1.14 (d, J = 6.7 Hz, 3H), 1.13 (d, J = 6.6 Hz, 3H), 0.98 (d, J = 6.8 Hz, 6H); MS (ESI+) m/z 411 $(M+H)^+$.

Example 305

2-isopropyl-3-methyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide

The title compound was prepared by substituting *N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-isopropyl-3-methylbutanamide from Example 229 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide in the procedures described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.12-8.14 (m, 1H), 7.75-7.77 (bs, 1H), 7.58-7.63 (m, 1H), 7.42-7.47 (m, 1H), 4.42-4.48 (m, 1H), 3.62 (d, J = 13.5 Hz, 1H), 3.46 (d, J = 13.5 Hz, 1H), 2.85 (dd, J = 8.9, 2.5 Hz, 1H), 2.50-2.58 (m, 2H), 2.45-2.49 (m, 1H), 2.28 (d, J = 6.6 Hz, 2H), 2.06-2.16 (m, 4H), 1.84-1.90 (m, 2H), 1.58-1.66 (m, 1H), 1.35-1.42 (m, 1H), 1.14 (d, J = 6.6 Hz, 3H), 1.13 (d, J = 6.6 Hz, 3H), 0.98 (d, J = 6.8 Hz, 6H); MS (ESI-) m/z 409 (M-H)-.

Example 306

***tert*-butyl (*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-ylcarbamate from Example 221 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide in the procedures described in Example 303: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.64 (d, J = 7.2 Hz, 1H), 7.96-7.99 (m, 1H), 7.72-7.77 (m, 1H), 7.55-7.63 (m, 2H), 7.44 (t, J = 7.7 Hz, 1H), 4.66-4.75 (m, 1H), 4.35-4.44 (m, 1H), 3.59 (d, J = 13.5 Hz, 1H), 3.46 (d, J = 13.6 Hz, 1H), 2.81-2.84 (m, 1H), 2.44-2.59 (m, 3H), 2.22-2.31 (m, 2H), 2.14 (s, 3H, OAc), 1.96-2.07 (m, 1H), 1.79-1.91 (m, 4H), 1.55-1.70 (m, 1H), 1.50 (s, 9H), 1.27-1.41 (m, 1H), 0.82-0.89 (m, 6H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Example 307

***tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Example 222 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide in the procedures described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.27-8.34 (m, 1H), 7.75-7.76 (bs, 1H), 7.52-7.63 (m, 2H), 7.42-7.47 (m, 1H), 5.1 (m, 0.7H), 4.7 (0.3H), 4.35-4.41 (m, 1H), 3.59 (d, J = 13.5 Hz, 1H), 3.45-3.49 (m, 1H), 3.04-3.13 (m, 3H), 2.82-2.85 (m, 1H), 2.42-2.54 (m, 3H), 2.22-2.31 (m, 2H), 1.98-2.11 (m, 1H), 1.80-2.11 (m, 1H), 1.79-1.87 (m, 2H), 1.53-1.62 (m, 2H), 1.46-1.48 (m, 9H), 1.33-1.38 (m, 1H), 0.88 (d, J = 6.4 Hz, 3H), 0.85 (d, J = 6.6 Hz, 3H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Example 308

***tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Example 222 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide and 4-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde in the procedures described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.31-8.36 (bs, 1H), 7.64-7.66 (m, 2H), 7.50-7.53 (m, 2H), 5.1 (m, 0.7H) 4.7 (0.3H), 4.38-4.43 (m, 1H), 3.57 (d, J = 13.7 Hz, 1H), 3.45-3.49 (m, 1H), 3.04-3.12 (m, 3H), 2.84-2.87 (m, 1H), 2.51-2.56 (m, 2H), 2.35-2.42 (m, 1H), 2.30-2.35 (m, 1H), 2.20-2.24 (m, 1H), 2.05-2.10 (m, 1H), 1.81-1.93 (m, 3H), 1.55-1.61 (m, 2H), 1.46-1.48 (m, 9H), 1.35-1.40 (m, 1H), 0.88 (d, J = 6.3 Hz, 3H), 0.85 (d, J = 6.6 Hz, 3H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Example 309

***tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Example 222 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide and 4-fluorobenzaldehyde for 3-(trifluoromethyl)benzaldehyde in the procedures described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.30-8.32 (m, 1H), 7.35-7.38 (m, 2H), 7.12 (t, J = 8.6 Hz, 2H), 5.1 (m, 0.7H) 4.7 (0.3H), 4.37-4.41 (m, 1H), 3.50 (d, J = 13.1 Hz, 1H), 3.40 (d, J = 13.1 Hz, 1H), 3.04-3.11 (m, 3H), 2.81-2.84 (m, 1H), 2.47-2.53 (m, 2H), 2.29-2.39 (m, 2H), 2.19-2.23 (m, 1H), 2.02-2.11 (m, 1H), 1.79-1.94 (m, 3H), 1.53-1.62 (m, 2H), 1.46-1.48 (m, 9H), 1.34-1.39 (m, 1H), 0.89 (d, J = 6.4 Hz, 3H), 0.85 (d, J = 6.6 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 310

***tert*-butyl ethyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(ethyl)carbamate from Example 223 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide in the procedures described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.14-8.17 (m, 1H), 7.74-7.77 (m, 1H), 7.55-7.61 (m, 2H), 7.41-7.46 (m, 1H), 5.1 (m, 0.7H) 4.7 (0.3H), 4.32-4.42 (m, 1H), 3.59 (d, J = 13.4 Hz, 1H), 3.38-3.53 (m, 3H), 2.78-2.87 (m, 1H), 2.44-2.54 (m, 2H), 2.36-2.44 (m, 1H), 2.28-2.35 (m, 1H), 2.20-2.27 (m, 1H), 2.01-2.13 (m, 1H), 1.91-2.01 (m, 1H), 1.79-1.88 (m, 1H), 1.71-1.79 (m, 1H), 1.62-1.71 (m, 1H), 1.53-1.62 (m, 1H), 1.48 (s, 9H), 1.33-1.42 (m, 1H), 1.17-1.33 (m, 3H), 0.83-0.97 (m, 6H); MS (ESI+) *m/z* 526 $(M+H)^+$.

Example 311

***tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(3-fluoro-4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide and 3-fluoro-4-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde in the procedures described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.33-8.42 (m, 1H), 7.31-7.35 (m, 1H), 7.24-7.29 (m, 1H), 5.1 (m, 0.7H) 4.7 (0.3H), 4.35-4.42 (m, 1H), 3.51-3.56 (m, 1H), 3.41-3.45 (m, 1H), 3.04-3.12 (m, 3H), 2.77-2.97 (m, 1H), 2.47-2.52 (m, 2H), 2.29-2.35 (m, 2H), 2.19-2.22 (m, 1H), 2.06-2.15 (m, 1H), 1.83-1.89 (m, 3H), 1.53-1.66 (m, 2H), 1.47 (s, 9H), 1.32-1.41 (m, 2H), 0.88-0.90 (m, 3H), 0.85 (d, J = 6.6 Hz, 3H); MS (ESI+) *m/z* 530 $(M+H)^+$.

Example 312

***tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluoro-3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide and 4-fluoro-3-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde in the procedures described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.32-8.39 (m, 1H), 7.62-7.75 (m, 1H), 7.20-7.27 (m, 2H), 5.1 (m, 0.7H) 4.7 (0.3H), 4.29-4.47 (m, 1H), 3.49-3.54 (m, 1H), 3.38-3.43 (m, 1H), 3.04-3.12 (m, 3H), 2.74-2.89 (m, 1H), 2.47-2.51 (m, 2H), 2.19-2.38 (m, 3H), 2.05-2.15 (m, 1H), 1.84 (dd, *J* = 9.0, 5.2 Hz, 3H), 1.54-1.65 (m, 2H), 1.46 (s, 9H), 1.26-1.42 (m, 1H), 0.89 (d, *J* = 6.4 Hz, 3H), 0.85 (d, *J* = 6.6 Hz, 3H); MS (ESI+) *m/z* 530 $(M+H)^+$.

Example 313

***tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

Step A: *tert*-Butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-norvaline for *N*-(*tert*-butoxycarbonyl)-L-leucine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.26 – 8.15 (m, 1H), 7.43 (d, *J* = 7.4, 2H), 7.36 (t, *J* = 7.5, 2H), 7.27 (t, *J* = 7.3, 1H), 5.07 – 5.00 (m, 1H), 4.72 – 4.58 (m, 1H), 4.46 – 4.31 (m, 1H), 3.59 (d, *J* = 13.1, 1H), 3.44 (d, *J* = 13.1, 1H), 3.12 – 2.99 (m, 3H), 2.83 (d, *J* = 8.9, 1H), 2.53 – 2.44 (m, 2H), 2.44 – 2.37 (m, 1H), 2.33 (d, *J* = 7.9, 1H), 2.26 – 2.19 (m, 1H), 2.14 – 1.95 (m, 2H), 1.79 (ddt, *J* = 7.1, 5.2, 4.2, 2H), 1.62 – 1.51 (m, 1H), 1.46 (s, 9H), 1.40 – 1.24 (m, 2H), 0.83 (t, *J* = 6.7, 3H); MS (ESI+) *m/z* 430$(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-

yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide in the procedures described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.24-8.26 (m, 1H), 7.75-7.76 (bs, 1H), 7.54-7.62 (m, 2H), 7.44 (t, J = 7.7 Hz, 1H), 5.1 (m, 0.7H), 4.7 (0.3H), 4.33-4.44 (m, 1H), 3.59 (d, J = 13.5 Hz, 1H), 3.45-3.48 (m, 1H), 3.02-3.10 (m, 3H), 2.82-2.85 (m, 1H), 2.46-2.54 (m, 2H), 2.40-2.43 (m, 1H), 2.28-2.32 (m, 1H), 2.21-2.25 (m, 1H), 1.99-2.04 (m, 2H), 1.76-1.86 (m, 2H), 1.48-1.63 (m, 1H), 1.46 (s, 9H), 1.20-1.41 (m, 3H), 0.80-0.86 (m, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Example 314

***tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A of Example 313 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide and 4-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde in the procedures described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.25-8.29 (bs, 1H), 7.64-7.66 (m, 2H), 7.50-7.52 (m, 2H), 5.1 (m, 0.7H), 4.7 (0.3H), 4.37-4.43 (m, 1H), 3.55-3.59 (m, 1H), 3.45-3.48 (m, 1H), 3.02-3.11 (m, 3H), 2.84-2.87 (m, 1H), 2.45-2.54 (m, 2H), 2.30-2.39 (m, 2H), 2.20-2.23 (m, 1H), 2.02-2.15 (m, 2H), 1.77-1.87 (m, 2H), 1.52-1.59 (m, 1H), 1.46-1.47 (m, 9H), 1.28-1.39 (m, 3H), 0.81-0.85 (m, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Example 315

***tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A of Example 313 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide and 4-fluorobenzaldehyde for 3-(trifluoromethyl)benzaldehyde in the procedures described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.23-8.27 (m, 1H), 7.34-7.38 (m, 2H), 7.12 (t, J = 8.5 Hz, 2H), 5.1 (m, 0.7H), 4.7 (0.3H), 4.33-4.45 (m, 1H), 3.50 (d, J = 13.1 Hz, 1H), 3.38-3.41 (m, 1H), 3.02-

3.11 (m, 3H), 2.81-2.84 (m, 1H), 2.44-2.53 (m, 2H), 2.29-2.39 (m, 2H), 2.19-2.23 (m, 1H), 2.02-2.04 (m, 2H), 1.81-1.84 (m, 2H), 1.55-1.59 (m, 1H), 1.46-1.47 (m, 9H), 1.28-1.38 (m, 3H), 0.81-0.85 (m, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Example 316

***tert*-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxobutan-2-yl(methyl)carbamate from Example 232 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide in the procedures described in Example 303: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 7.69-7.70 (bs, 1H), 7.49-7.57 (m, 2H), 7.32-7.41 (m, 2H), 4.31-4.35 (m, 1H), 4.19-4.29 (m, 1H), 3.57 (d, *J* = 13.5 Hz, 1H), 3.50 (d, *J* = 13.6 Hz, 1H), 3.00 (s, 3H), 2.76 (d, *J* = 6.4 Hz, 1H), 2.50-2.56 (m, 1H), 2.38-2.46 (m, 3H), 2.28-2.37 (m, 2H), 2.06 (dq, *J* = 12.2, 6.1 Hz, 1H), 1.82-1.90 (m, 1H), 1.52-1.62 (m, 1H), 1.46 (s, 9H), 1.35-1.44 (m, 1H), 1.00 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.7 Hz, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Example 317

***tert*-butyl methyl((*S*)-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate from Example 233 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide and 4-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde in the procedures described in Example 303: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 7.58-7.61 (m, 2H), 7.45-7.48 (m, 2H), 7.18-7.28 (m, 1H), 4.70-4.75 (m, 1H), 4.22-4.30 (m, 1H), 3.48-3.59 (m, 2H), 2.94 (s, 3H), 2.78-2.81 (m, 1H), 2.52-2.57 (m, 1H), 2.34-2.47 (m, 3H), 2.27-2.32 (m, 1H), 2.04-2.12 (m, 1H), 1.93-2.03 (m, 1H), 1.82-1.91 (m, 1H), 1.71-1.81 (m, 1H), 1.49-1.67 (m, 1H), 1.46-1.47 (m, 9H), 1.37-1.46 (m, 1H), 1.26-1.36 (m, 2H), 0.87 (t, *J* = 7.4 Hz, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Example 318

***tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate from Example 233 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide and 4-fluorobenzaldehyde for 3-(trifluoromethyl)benzaldehyde in the procedures described in Example 303: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 7.28-7.32 (m, 2H), 7.16-7.21 (m, 1H), 7.02 (t, *J* = 8.6 Hz, 2H), 4.69-4.77 (m, 1H), 4.21-4.28 (m, 1H), 3.49 (d, *J* = 13.2 Hz, 1H), 3.43 (d, *J* = 13.2 Hz, 1H), 2.94 (s, 3H), 2.76-2.78 (m, 1H), 2.48-2.55 (m, 1H), 2.33-2.46 (m, 3H), 2.25-2.32 (m, 1H), 2.04-2.14 (m, 1H), 1.94-2.03 (m, 1H), 1.82-1.91 (m, 1H), 1.70-1.81 (m, 1H), 1.49-1.58 (m, 1H), 1.46-1.48 (m, 9H), 1.37-1.44 (m, 1H), 1.28-1.36 (m, 2H), 0.87 (t, *J* = 7.4 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Example 319

(2*S*)-4-methyl-2-morpholin-4-yl-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide

Step A: (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-Benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide (0.400 g, 1.001 mmol) from Step B of Example 249 and ethanol (40 mL) were added to 20% $Pd(OH)_2$ on carbon, wet (0.080 g, 0.570 mmol) in a 250 mL stainless steel pressure bottle and stirred for 16 hours under 30 psi hydrogen at 55 °C. The mixture was filtered through a nylon membrane and the solvent removed in vacuo to give (*S*)-4-methyl-2-morpholino-*N*-((3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.46 (d, *J* = 6.9, 1H), 4.46 - 4.38 (m, 1H), 3.74 (s, 4H), 3.45 (dd, *J* = 2.0, 11.3, 1H), 3.31 - 3.21 (m, 2H), 3.10 (dd, *J* = 7.0, 11.0, 1H), 2.89 (dd, *J* = 2.3, 11.0, 1H), 2.83 - 2.77 (m, 2H), 2.76 - 2.67 (m, 4H), 2.09 (td, *J* = 6.0, 11.8, 1H), 1.95 - 1.87 (m, 1H), 1.84 (dq, *J* = 6.0, 9.7, 2H), 1.71 - 1.57 (m, 2H), 1.49 (ddt, *J* = 6.3, 9.1, 12.5, 1H), 0.94 (dd, *J* = 6.3, 11.2, 6H); MS (ESI+) *m/z* 310$(M+H)^+$

Step B: (*S*)-4-Methyl-2-morpholino-*N*-((3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide (191mg, 0.617 mmol), triethylamine (0.129 mL, 0.926 mmol), and 3-(trifluoromethyl)benzene-1-sulfonyl chloride (0.109 mL, 0.679 mmol) were combined in

dichloromethane (0.5 mL). The reaction was stirred at room temperature for 3 hours. The crude material was purified by silica gel chromatography using 1-10% methanol (2 *N* ammonia)/dichloromethane to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.44 (d, *J* = 6.2, 1H), 8.38 (s, 1H), 8.19 (d, *J* = 7.9, 1H), 7.92 (d, *J* = 7.8, 1H), 7.72 (t, *J* = 7.9, 1H), 4.27 - 4.20 (m, 1H), 3.90 (dd, *J* = 2.3, 10.0, 1H), 3.76 - 3.67 (m, 4H), 3.20 (ddd, *J* = 3.9, 9.4, 10.9, 3H), 2.97 (dd, *J* = 7.1, 9.6, 1H), 2.78 - 2.72 (m, 2H), 2.72 - 2.67 (m, 2H), 2.62 - 2.53 (m, 2H), 1.94 (dt, *J* = 6.2, 12.1, 1H), 1.89 - 1.77 (m, 3H), 1.64 - 1.54 (m, 2H), 1.30 (ddt, *J* = 6.5, 9.3, 12.8, 1H), 0.92 (d, *J* = 4.4, 3H), 0.91 (d, *J* = 4.4, 3H); MS (ESI+) *m/z* 518(M+H)$^+$.

Example 320

(2*S*)-4-methyl-2-pyrrolidin-1-yl-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide

The title compound was prepared by substituting (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-pyrrolidin-1-ylpentanamide from Example 250 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide in the procedures described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37-8.39 (m, 1H), 8.17-8.20 (m, 1H), 8.12-8.15 (m, 1H), 7.89-7.92 (m, 1H), 7.71 (t, *J* = 7.8 Hz, 1H), 4.23-4.29 (m, 1H), 3.86 (dd, *J* = 9.9, 2.4 Hz, 1H), 3.16-3.20 (m, 2H), 3.13-3.15 (m, 1H), 2.97 (dd, *J* = 9.6, 6.8 Hz, 1H), 2.65-2.69 (m, 2H), 2.55-2.61 (m, 4H), 1.90-2.00 (m, 1H), 1.76-1.90 (m, 3H), 1.54-1.62 (m, 6H), 1.25-1.34 (m, 1H), 0.98 (d, *J* = 6.3 Hz, 3H), 0.91 (d, *J* = 6.3 Hz, 3H); MS (ESI+) *m/z* 502 (M+H)$^+$.

Example 321

(2*S*)-4-methyl-2-piperidin-1-yl-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide

The title compound was prepared by substituting (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-piperidin-1-ylpentanamide from Example 251 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide in the procedures described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.38-8.39 (bs, 1H), 8.18-8.20 (m, 2H), 7.90-7.92 (m, 1H), 7.71 (t, *J* = 7.8 Hz, 1H), 4.20-4.26 (m, 1H), 3.87 (dd, *J* = 9.9, 2.1 Hz, 1H), 3.16-3.20 (m, 3H), 2.97 (dd, *J* =

9.5, 6.3 Hz, 1H), 2.56-2.64 (m, 6H), 1.80-1.97 (m, 4H), 1.46-1.59 (m, 6H), 1.23-1.37 (m, 3H), 0.93 (d, J = 6.6 Hz, 3H), 0.92 (d, J = 6.7 Hz, 3H); MS (ESI+) m/z 516 $(M+H)^+$.

Example 322

tert-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Example 222 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide in the procedures described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.48-8.50 (m, 1H), 8.36-8.37 (bs, 1H), 8.19 (d, J = 7.9 Hz, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.72 (t, J = 7.8 Hz, 1H), 5.13 (m, 0.7H), 4.78 (m, 0.3H), 4.15-4.29 (m, 1H), 3.84 (dd, J = 9.9, 2.1 Hz, 1H), 3.13-3.16 (m, 1H), 3.02-3.12 (m, 4H), 2.91 (dd, J = 9.6, 6.9 Hz, 1H), 2.48-2.52 (m, 2H), 1.74-1.90 (m, 4H), 1.49-1.67 (m, 2H), 1.44-1.46 (m, 9H), 1.16-1.29 (m, 1H), 0.89 (d, J = 6.4 Hz, 3H), 0.84 (d, J = 6.4 Hz, 3H); MS (ESI+) m/z 562 $(M+H)^+$.

Example 323

tert-butyl ethyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(ethyl)carbamate from Example 223 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide in the procedures described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37-8.40 (m, 2H), 8.19 (d, J = 7.9 Hz, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.72 (t, J = 7.9 Hz, 1H), 5.0 (m, 0.7H), 4.7 (m, 0.3H), 4.16-4.27 (m, 1H), 3.83-3.86 (m, 1H), 3.43-3.49 (m, 2H), 3.09-3.18 (m, 2H), 2.90-2.94 (m, 1H), 2.43-2.58 (m, 2H), 1.90-2.02 (m, 2H), 1.71-1.84 (m, 2H), 1.62-1.67 (m, 1H), 1.34-1.59 (m, 10H), 1.21-1.31 (m, 4H), 0.88-0.91 (m, 6H); MS (ESI+) m/z 576 $(M+H)^+$.

Example 324

***tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

The title compound was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (501 MHz, pyridine-d_5, temperature 60 °C) δ ppm 8.08-8.11 (m, 2H), 7.99-8.03 (bs, 1H), 7.84-7.87 (m, 2H), 4.95 (m, 0.7H), 4.4 (m, 0.3H), 4.11-4.17 (m, 1H), 3.70-3.74 (m, 1H), 3.15-3.21 (m, 1H), 3.13 (dd, J = 9.8, 2.8 Hz, 1H), 3.03 (dd, J = 9.7, 7.3 Hz, 1H), 3.00 (s, 3H), 2.50-2.54 (m, 2H), 1.89-1.97 (m, 1H), 1.72-1.89 (m, 3H), 1.50-1.61 (m, 2H), 1.45 (s, 9H), 1.28 (ddt, J = 9.5, 12.9, 6.5 Hz, 1H), 0.89 (d, J = 6.8 Hz, 3H), 0.85 (d, J = 6.5 Hz, 3H); MS (DCI+) *m/z* 562 $(M+H)^+$,579 $(M+NH_4)^+$.

Example 325

***tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

The title compound was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide in the procedures described in Example 319: ^{1}H NMR (501 MHz, pyridine-d_5, temperature 60 °C) δ ppm 8.32-8.33 (bs, 1H), 8.15 (d, J = 8.1 Hz, 1H), 7.97-8.01 (m, 1H), 7.87 (d, J = 7.7 Hz, 1H), 7.68 (t, J = 7.9 Hz, 1H), 4.95 (m, 0.7H), 4.4 (m, 0.3H), 4.11-4.15 (m, 1H), 3.71-3.75 (m, 1H), 3.12-3.18 (m, 2H), 3.00-3.04 (m, 1H), 2.99 (s, 3H), 2.48-2.52 (m, 2H), 1.90-1.96 (m, 1H), 1.73-1.86 (m, 3H), 1.50-1.60 (m, 2H), 1.46 (s, 9H), 1.24-1.30 (m, 1H), 0.88 (d, J = 6.6 Hz, 3H), 0.85 (d, J = 6.5 Hz, 3H); MS (ESI+) *m/z* 579 $(M+NH_4)^+$.

Example 326

***tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-fluorobenzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.51-8.58 (m, 1H), 7.97-7.99 (m, 2H), 7.29-7.35 (m, 2H), 5.13 (m, 0.7H), 4.8 (m, 0.3H), 4.20-4.23 (m, 1H), 3.70-3.81 (m, 1H), 3.00-3.11 (m, 5H), 2.86-2.91 (m, 1H), 2.42-2.53 (m, 2H), 1.75-1.96 (m, 4H), 1.49-1.62 (m, 2H), 1.41-1.50 (bs, 9H), 1.23-1.39 (m, 1H), 0.81-0.88 (m, 6H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Example 327

***tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluoro-3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-fluoro-3-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (501 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.28 (dd, *J* = 6.6, 2.3 Hz, 1H), 8.16-8.20 (m, 1H), 7.54-7.59 (m, 1H), 7.44 (t, *J* = 9.4 Hz, 1H), 4.79-4.84 (m, 1H), 4.08 (p, *J* = 6.9 Hz, 1H), 3.67 (dd, *J* = 10.1, 3.3 Hz, 1H), 3.25 (dd, *J* = 10.1, 7.7 Hz, 1H), 3.09-3.17 (m, 2H), 2.94 (s, 3H), 2.53-2.61 (m, 1H), 2.46-2.53 (m, 1H), 1.91-1.98 (m, 1H), 1.79-1.87 (m, 2H), 1.73 (ddd, *J* = 14.1, 9.1, 5.1 Hz, 1H), 1.56-1.64 (m, 1H), 1.48-1.56 (m, 1H), 1.46 (s, 9H), 1.26-1.33 (m, 1H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H); MS (ESI+) *m/z* 580 $(M+H)^+$.

Example 328

***tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*R*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate from Example 240 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.04-8.07 (m, 2H), 7.80-7.83 (m, 2H), 7.54-7.57 (m, 1H), 4.79 (dd, J = 9.4, 6.0 Hz, 1H), 4.29 (dq, J = 9.8, 7.0 Hz, 1H), 3.49 (dd, J = 10.3, 4.7 Hz, 1H), 3.21 (dd, J = 9.9, 7.8 Hz, 1H), 3.07-3.13 (m, 2H), 3.01 (s, 3H), 2.92-3.01 (m, 1H), 2.46-2.54 (m, 1H), 1.95-2.07 (m, 1H), 1.75-1.85 (m, 1H), 1.68-1.77 (m, 1H), 1.55-1.66 (m, 2H), 1.54 (s, 9H), 1.25-1.39 (m, 3H), 0.87 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 548 $(M+H)^+$.

Example 329

***tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*R*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Example 241 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.04-8.07 (m, 2H), 7.80-7.83 (m, 2H), 7.54-7.61 (m, 1H), 4.90 (dd, J = 9.2, 6.0 Hz, 1H), 4.26-4.34 (m, 1H), 3.49 (dd, J = 10.3, 4.7 Hz, 1H), 3.21 (dd, J = 9.9, 7.8 Hz, 1H), 3.06-3.14 (m, 2H), 3.02 (s, 3H), 2.94-3.01 (m, 1H), 2.47-2.55 (m, 1H), 1.87 (ddd, J = 14.2, 8.5, 5.6 Hz, 1H), 1.69-1.83 (m, 2H), 1.57-1.67 (m, 3H), 1.54 (s, 9H), 1.27-1.39 (m, 1H), 0.90 (d, J = 6.9 Hz, 3H), 0.89 (d, J = 6.9 Hz, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Example 330

***tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate from Example 233 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-fluorobenzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 7.90-7.97 (m, 2H), 7.38-7.48 (bs, 1H), 7.18-7.24 (m, 2H), 7.18-7.23 (m, 1H), 4.65-4.75 (m, 1H), 4.03-4.13 (m, 1H), 3.58 (dd, *J* = 10.1, 3.4 Hz, 1H), 3.22 (dd, *J* = 10.1, 7.8 Hz, 1H), 3.03-3.13 (m, 2H), 2.94 (s, 3H), 2.51-2.60 (m, 1H), 2.43-2.51 (m, 1H), 1.89-2.01 (m, 2H), 1.80-1.86 (m, 1H), 1.69-1.81 (m, 1H), 1.47-1.62 (m, 1H), 1.45 (s, 9H), 1.23-1.38 (m, 3H), 0.86 (t, *J* = 7.3 Hz, 2H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Example 331

***tert*-butyl methyl((*S*)-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate from Example 233 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.05-8.08 (m, 2H), 7.79-7.83 (m, 2H), 7.43-7.48 (bs, 1H), 4.68-4.72 (m, 1H), 4.01-4.11 (m, 1H), 3.65 (dd, *J* = 10.2, 3.3 Hz, 1H), 3.26 (dd, *J* = 10.1, 7.7 Hz, 1H), 3.07-3.18 (m, 2H), 2.94 (s, 3H), 2.45-2.58 (m, 2H), 1.89-2.00 (m, 2H), 1.70-1.86 (m, 2H), 1.46-1.57 (m, 1H), 1.45 (s, 9H), 1.31 (dt, *J* = 15.2, 7.6 Hz, 2H), 1.23-1.37 (m, 1H), 0.85 (t, *J* = 7.3 Hz, 3H); MS (ESI+) *m/z* 565 $(M+NH_4)^+$.

Example 332

***tert*-butyl methyl((2*S*,3*S*)-3-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

The title compound was prepared by substituting *tert*-butyl (2*S*,3*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxopentan-2-yl(methyl)carbamate from Example 224 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide in the procedures described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.66 (d, J = 6.0 Hz, 1H), 8.39-8.40 (m, 1H), 8.21 (d, J = 7.9 Hz, 1H), 7.92 (d, J = 7.6 Hz, 1H), 7.72 (t, J = 7.9 Hz, 1H), 4.67 (d, J = 11.1 Hz, 1H), 4.15-4.25 (m, 1H), 4.15-4.23 (m, 1H), 3.89 (d, J = 9.9 Hz, 1H), 3.09-3.26 (m, 5H), 2.88-3.08 (m, 1H), 2.46-2.55 (m, 2H), 2.17-2.31 (m, 1H), 1.74-1.94 (m, 2H), 1.42-1.55 (m, 1H), 1.48 (s, 9H), 1.18-1.30 (m, 1H), 1.00-1.12 (m, 1H), 0.94 (d, J = 6.3 Hz, 3H), 0.80 (t, J = 7.0 Hz, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Example 333

***tert*-butyl methyl((2*S*,3*S*)-3-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

The title compound was prepared by substituting *tert*-butyl (2*S*,3*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxopentan-2-yl(methyl)carbamate from Example 224 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.68 (d, J = 6.3 Hz, 1H), 8.12-8.17 (m, 2H), 7.87-7.95 (m, 2H), 4.68 (d, J = 11.0 Hz, 1H), 4.16-4.24 (m, 1H), 3.87 (d, J = 9.8 Hz, 1H), 3.09-3.24 (m, 5H), 2.89-3.08 (m, 1H), 2.50-2.58 (m, 2H), 2.22-2.27 (m, 1H), 1.77-1.85 (m, 2H), 1.51-1.66 (m, 1H), 1.48 (s, 9H), 1.34-1.49 (m, 1H), 1.19-1.31 (m, 1H), 0.98-1.13 (m, 1H), 0.95 (d, J = 6.1 Hz, 3H), 0.80 (t, J = 6.9 Hz, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Example 334

***tert*-butyl methyl((2*S*,3*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

Step A: *tert*-Butyl (2*S*,3*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxopentan-2-yl(methyl)carbamate was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-isoleucine for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Example 16 Step E for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.43 (d, J = 6.4, 1H), 7.41 (d, J = 7.2, 2H), 7.36 (t, J = 7.5, 2H), 7.27 (t, J = 7.2, 1H), 4.70 (d, J = 11.1, 1H), 4.36 (d, J = 4.4, 2H), 3.56 (d, J = 13.0, 1H), 3.40 (d, J = 13.1, 1H), 3.24 (s, 1H), 3.13 (s, 3H), 2.72 (d, J = 8.6, 1H), 2.47 (s, 2H), 2.37 – 2.18 (m, 4H), 2.13 (dd, J = 11.7, 5.6, 1H), 1.91 – 1.76 (m, 1H), 1.65 (dd, J = 11.4, 6.8, 1H), 1.48 (s, 9H), 1.11 – 0.95 (m, 4H), 0.80 (t, J = 7.1, 3H); MS (ESI+) *m/z* 444 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (2*S*,3*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxopentan-2-yl(methyl)carbamate from Step A for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide in the procedures described in Example 319: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.68 (d, J = 7.2 Hz, 1H), 8.35-8.40 (m, 1H), 8.15 (d, J = 7.8 Hz, 1H), 7.91 (d, J = 7.6 Hz, 1H), 7.72 (t, J = 7.8 Hz, 1H), 4.68 (d, J = 11.3 Hz, 1H), 4.13-4.25 (m, 1H), 3.74-3.88 (m, 1H), 3.15-3.25 (m, 1H), 3.11-3.16 (bs, 3H), 2.95-3.05 (m, 1H), 2.83-2.94 (m, 1H), 2.38-2.61 (m, 2H), 2.17-2.32 (m, 1H), 1.88-2.03 (m, 1H), 1.76-1.88 (m, 1H), 1.52-1.66 (m, 1H), 1.44-1.53 (bs, 9H), 1.33-1.46 (m, 1H), 1.21-1.33 (m, 1H), 0.96-1.12 (m, 1H), 0.94 (d, J = 6.4 Hz, 3H), 0.79 (t, J = 7.2 Hz, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Example 335

***tert*-butyl methyl((2*S*,3*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

The title compound was prepared by substituting *tert*-butyl (2*S*,3*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxopentan-2-

yl(methyl)carbamate from Step A of Example 334 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.66-8.72 (m, 1H), 8.05-8.13 (m, 2H), 7.88-7.91 (m, 2H), 4.69 (d, *J* = 11.3 Hz, 1H), 4.15-4.22 (m, 1H), 3.73-3.87 (m, 1H), 3.16-3.23 (m, 1H), 3.11-3.18 (bs, 3H), 3.00 (t, *J* = 8.3 Hz, 1H), 2.90 (t, *J* = 8.4 Hz, 1H), 2.42-2.56 (m, 2H), 2.21-2.28 (m, 1H), 1.88-2.03 (m, 1H), 1.73-1.88 (m, 1H), 1.52-1.66 (m, 1H), 1.48 (s, 9H), 1.34-1.46 (m, 1H), 1.21-1.34 (m, 1H), 0.98-1.13 (m, 1H), 0.94 (d, *J* = 6.3 Hz, 3H), 0.76-0.81 (m, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Example 336

***tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate from Example 247 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide in the procedures described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.36-8.38 (bs, 1H), 8.30-8.37 (m, 1H), 8.19 (d, *J* = 7.8 Hz, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 7.72 (t, *J* = 7.8 Hz, 1H), 5.4 (m, 0.7H), 4.7 (m, 0.3H), 4.16-4.20 (m, 1H), 3.86 (d, *J* = 9.8 Hz, 1H), 3.13-3.18 (m, 1H), 3.08-3.13 (m, 1H), 2.96-3.08 (bs, 3H), 2.90-2.93 (m, 1H), 2.41-2.56 (m, 2H), 2.13-2.37 (m, 1H), 1.81-1.92 (m, 1H), 1.72-1.81 (m, 1H), 1.60-1.72 (m, 1H), 1.47-1.60 (m, 1H), 1.41-1.50 (bs, 9H), 1.19-1.33 (m, 1H), 0.87-0.99 (bs, 9H); MS (ESI+) *m/z* 576 $(M+H)^+$,593 $(M+NH_4)^+$.

Example 337

***tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate from Example 247 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-

benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.35-8.38 (m, 1H), 8.12-8.15 (m, 2H), 7.89-7.91 (m, 2H), 5.11-5.19 (m, 1H), 4.15-4.19 (m, 1H), 3.83-3.86 (m, 1H), 3.13-3.17 (m, 1H), 3.09-3.14 (m, 1H), 2.97-3.09 (bs, 3H), 2.92-2.96 (m, 1H), 2.43-2.57 (m, 2H), 2.15-2.38 (m, 1H), 1.81-1.91 (m, 1H), 1.72-1.81 (m, 1H), 1.61-1.72 (m, 1H), 1.48-1.60 (m, 1H), 1.40-1.51 (bs, 9H), 1.20-1.36 (m, 1H), 0.89-0.99 (bs, 9H); MS (ESI+) *m/z* 576 $(M+H)^+$.

Example 338

***tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate from Example 248 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide in the procedures described in Example 319: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.29-8.30 (bs, 1H), 8.13 (d; J = 7.9 Hz, 1H), 7.83 (d, J = 8.6 Hz, 1H), 7.64 (t, J = 7.8 Hz, 1H), 7.29 (d, J = 3.9 Hz, 1H), 4.82-4.87 (bs, 1H), 4.05 (p, J = 6.7 Hz, 1H), 3.63 (dd, J = 10.2, 3.3 Hz, 1H), 3.25 (dd, J = 10.1, 7.8 Hz, 1H), 3.07-3.17 (m, 2H), 2.91 (s, 3H), 2.51-2.59 (m, 1H), 2.43-2.50 (m, 1H), 2.15 (dd, J = 14.3, 5.6 Hz, 1H), 1.92 (dq, J = 12.2, 6.1 Hz, 1H), 1.77-1.85 (m, 1H), 1.61 (dd, J = 14.3, 7.2 Hz, 1H), 1.47-1.55 (m, 1H), 1.46 (s, 9H), 1.23-1.36 (m, 1H), 0.93 (s, 9H); MS (ESI+) *m/z* 576 $(M+H)^+$.

Example 339

***tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate from Example 248 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-

(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.05-8.08 (m, 2H), 7.79-7.82 (m, 2H), 7.28-7.32 (m, 1H), 4.79-4.91 (m, 1H), 4.05 (p, J = 6.7 Hz, 1H), 3.62 (dd, J = 10.2, 3.4 Hz, 1H), 3.26 (dd, J = 10.2, 7.8 Hz, 1H), 3.09-3.17 (m, 2H), 2.92 (s, 3H), 2.51-2.62 (m, 1H), 2.43-2.51 (m, 1H), 2.15 (dd, J = 14.3, 5.6 Hz, 1H), 1.88-1.98 (m, 1H), 1.76-1.86 (m, 1H), 1.62 (dd, J = 14.3, 7.0 Hz, 1H), 1.47-1.56 (m, 1H), 1.46 (s, 9H), 1.29 (ddt, J = 9.0, 13.0, 6.5 Hz, 1H), 0.94 (s, 9H); MS (ESI+) *m/z* 576 $(M+H)^+$.

Example 340

***tert*-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxobutan-2-yl(methyl)carbamate from Example 232 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide in the procedures described in Example 319: ^{1}H NMR (501 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.29-8.30 (bs, 1H), 8.13 (d, J = 7.8 Hz, 1H), 7.83 (d, J = 7.7 Hz, 1H), 7.64 (t, J = 7.8 Hz, 1H), 7.59-7.68 (m, 1H), 4.32 (d, J = 10.4 Hz, 1H), 4.07 (p, J = 6.6 Hz, 1H), 3.64 (dd, J = 10.2, 3.3 Hz, 1H), 3.23 (t, J = 9.0 Hz, 1H), 3.07-3.15 (m, 2H), 3.00 (s, 3H), 2.49-2.59 (m, 1H), 2.42-2.49 (m, 1H), 2.31-2.42 (m, 1H), 1.90-1.97 (m, 1H), 1.79-1.86 (m, 1H), 1.47-1.59 (m, 1H), 1.45 (s, 9H), 1.24-1.33 (m, 1H), 0.97 (d, J = 6.5 Hz, 3H), 0.86 (d, J = 6.7 Hz, 3H); MS (ESI+) *m/z* 548 $(M+H)^+$.

Example 341

***tert*-butyl (*S*)-3,3-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-ylcarbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3,3-dimethyl-1-oxobutan-2-ylcarbamate from Example 225 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-

(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.86 (d, J = 6.7 Hz, 1H), 8.11-8.18 (m, 2H), 7.89-7.92 (m, 2H), 7.71 (d, J = 9.5 Hz, 1H), 4.56 (d, J = 9.8 Hz, 1H), 4.20 (p, J = 6.4 Hz, 1H), 3.79 (dd, J = 10.0, 3.0 Hz, 1H), 3.24 (dd, J = 9.9, 7.7 Hz, 1H), 3.14 (d, J = 3.2 Hz, 1H), 3.02 (dd, J = 9.7, 7.3 Hz, 1H), 2.55-2.65 (m, 2H), 1.76-1.84 (m, 2H), 1.44-1.56 (m, 1H), 1.48 (s, 9H), 1.19-1.27 (m, 1H), 1.16 (s, 9H); MS (ESI+) *m/z* 548 $(M+H)^+$,565 $(M+NH_4)^+$.

Example 342

***tert*-butyl (*S*)-3,3-dimethyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-ylcarbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3,3-dimethyl-1-oxobutan-2-ylcarbamate from Example 234 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.89 (d, J = 7.4, 1H), 8.10 (d, J = 8.1, 2H), 7.90 (d, J = 8.3, 2H), 7.73 (s, 1H), 4.55 (d, J = 9.8, 1H), 4.27 – 4.16 (m, 1H), 3.70 (dd, J = 9.8, 2.2, 1H), 3.14 (dd, J = 9.8, 2.5, 1H), 2.98 – 2.92 (m, 1H), 2.91 – 2.85 (m, 1H), 2.53 – 2.39 (m, 2H), 1.99 (td, J = 11.5, 5.7, 1H), 1.83 (td, J = 12.4, 7.2, 1H), 1.60 (dt, J = 12.3, 8.2, 1H), 1.48 (s, 9H), 1.34 – 1.25 (m, 1H), 1.15 (s, 9H); MS (ESI+) *m/z* 548 $(M+H)^+$, 565 $(M+NH_4)^+$.

Example 343

***tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)hexan-2-yl)carbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxohexan-2-yl(methyl)carbamate from Example 227 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.06-8.09 (m, 2H), 7.79-7.82 (m, 2H), 7.40 (d, J = 5.6 Hz, 1H), 4.68-4.72 (m, 1H), 4.07 (p, J = 6.8 Hz, 1H), 3.65 (dd, J = 10.2,

3.4 Hz, 1H), 3.28 (dd, J = 10.2, 7.7 Hz, 1H), 3.09-3.17 (m, 2H), 2.94 (s, 3H), 2.54-2.59 (m, 1H), 2.47-2.53 (m, 1H), 1.97-2.07 (m, 1H), 1.87-1.96 (m, 1H), 1.72-1.86 (m, 2H), 1.47-1.56 (m, 1H), 1.46 (s, 9H), 1.23-1.35 (m, 1H), 1.27-1.30 (m, 4H), 0.80-0.84 (m, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$,579 $(M+NH_4)^+$,620 $(M+CH_3CN+NH_4)^+$.

Example 344

***tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-ylcarbamate from Example 226 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.06-8.08 (m, 1H), 8.06 (d, J = 0.9 Hz, 1H), 7.79-7.82 (m, 2H), 7.73-7.77 (m, 1H), 7.00-7.05 (m, 1H), 4.47 (td, J = 8.2, 4.7 Hz, 1H), 4.04-4.11 (m, 1H), 3.65 (dd, J = 10.2, 3.0 Hz, 1H), 3.29 (dd, J = 10.2, 7.3 Hz, 1H), 3.15 (dd, J = 10.0, 6.9 Hz, 1H), 3.11 (dd, J = 9.9, 3.4 Hz, 1H), 2.51-2.59 (m, 2H), 2.08 (dd, J = 14.2, 4.6 Hz, 1H), 1.84-1.93 (m, 1H), 1.75-1.83 (m, 1H), 1.69 (dd, J = 14.2, 8.0 Hz, 1H), 1.48-1.56 (m, 1H), 1.47 (s, 9H), 1.22-1.33 (m, 1H), 0.96 (s, 9H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Example 345

(2*S*)-4-methyl-2-pyrrolidin-1-yl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzoyl]octahydrocyclopenta[*c*]pyrrol-4-yl}pentanamide

The title compound was prepared by substituting (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-pyrrolidin-1-ylpentanamide from Example 250 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 3-(trifluoromethyl)benzoyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.41 – 8.17 (m, 1H), 8.14 – 8.05 (m, 1H), 8.01 – 7.78 (m, 1H), 7.76 – 7.66 (m, 1H), 7.53 (t, J = 7.6, 1H), 4.51 – 4.29 (m, 1H), 4.20 – 4.00 (m, 1H), 3.89 (ddd, J = 12.0, 6.6, 1.5, 1H), 3.74 (tdd, J = 8.3, 5.2, 2.8, 1H), 3.67 – 3.45 (m, 1H), 3.32 –

3.13 (m, 2H), 2.87 – 2.57 (m, 6H), 2.23 – 2.02 (m, 1H), 1.96 – 1.78 (m, 2H), 1.73 – 1.55 (m, 6H), 1.47 – 1.24 (m, 1H), 1.04 – 0.79 (m, 6H); MS (ESI+) *m/z* 466 $(M+H)^+$.

Example 346

(2*S*)-4-methyl-*N*-[(3a*S*,4*R*,6a*R*)-2-(methylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-2-pyrrolidin-1-ylpentanamide

The title compound was prepared by substituting (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-pyrrolidin-1-ylpentanamide from Example 250 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and methanesulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.24-8.26 (m, 1H), 4.35 (p, *J* = 6.8 Hz, 1H), 3.79 (dd, *J* = 9.9, 2.6 Hz, 1H), 3.50 (dd, *J* = 9.9, 7.0 Hz, 1H), 3.35 (dd, *J* = 9.6, 7.0 Hz, 1H), 3.17-3.21 (m, 2H), 3.04 (s, 3H), 2.67-2.75 (m, 4H), 2.60-2.63 (m, 2H), 1.99-2.07 (m, 1H), 1.78-1.95 (m, 3H), 1.58-1.68 (m, 6H), 1.32-1.39 (m, 1H), 0.99 (d, *J* = 6.2 Hz, 3H), 0.92 (d, *J* = 6.3 Hz, 3H); MS (ESI+) *m/z* 372 $(M+H)^+$.

Example 347

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-(cyclopropylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-pyrrolidin-1-ylpentanamide

The title compound was prepared by substituting (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-pyrrolidin-1-ylpentanamide from Example 250 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and cyclopropanesulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedures described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.14 (d, *J* = 7.3 Hz, 1H), 4.33-4.40 (m, 1H), 3.82 (dd, *J* = 9.9, 2.6 Hz, 1H), 3.57 (dd, *J* = 9.9, 7.0 Hz, 1H), 3.41 (dd, *J* = 9.6, 7.0 Hz, 1H), 3.22 (dd, *J* = 9.6, 3.2 Hz, 1H), 3.16 (dd, *J* = 9.2, 5.1 Hz, 1H), 2.60-2.70 (m, 7H), 2.04 (dq, *J* = 11.9, 5.9 Hz, 1H), 1.79-1.97 (m, 3H), 1.56-1.67 (m, 6H), 1.33-1.40 (m, 1H), 1.16-1.23 (m, 2H), 0.99 (d, *J* = 6.3 Hz, 3H), 0.92 (d, *J* = 6.4 Hz, 3H), 0.86-0.92 (m, 2H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Example 348

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide

tert-Butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate (60 mg, 0.135 mmol) from Example 222 was combined with 4 *N* hydrogen chloride in 1,4-dioxane (0.698 mL, 2.79 mmol). The reaction was stirred at room temperature for 16 hours and then concentrated. The material was purified using a 12 g silica gel cartridge with a gradient of 1-10% methanol (2 *N* ammonia)/dichloromethane over 20 minutes to give the title compound: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.16-8.19 (m, 1H), 7.44-7.46 (m, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.28 (t, *J* = 7.3 Hz, 1H), 4.42-4.48 (m, 1H), 3.61 (d, *J* = 13.1 Hz, 1H), 3.46 (d, *J* = 13.1 Hz, 1H), 3.22 (dd, *J* = 8.2, 5.8 Hz, 1H), 2.87 (d, *J* = 10.3 Hz, 1H), 2.51-2.61 (m, 2H), 2.44 (dd, *J* = 8.8, 7.1 Hz, 1H), 2.43 (s, 3H), 2.37 (dd, *J* = 9.0, 2.0 Hz, 1H), 2.25-2.29 (m, 1H), 2.09-2.17 (m, 1H), 1.95-2.07 (m, 1H), 1.82-1.95 (m, 2H), 1.72 (ddd, *J* = 13.5, 7.8, 5.8 Hz, 1H), 1.55-1.64 (m, 2H), 1.38-1.45 (m, 1H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 3H); MS (ESI+) *m/z* 344 $(M+H)^+$.

Example 349

***tert*-butyl methyl((*S*)-4-methyl-1-((3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl)carbamate**

The title compound was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(tert-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide in the procedure described in Example 319 Step A: ^{1}H NMR (500 MHz, pyridine-d_5) δ 8.47 – 8.30 (m, 1H), 5.15 (dd, *J* = 6.4, 5.1, 1H), 4.82 – 4.77 (m, 1H), 4.40 – 4.21 (m, 1H), 3.25 – 3.04 (m, 4H), 3.03 – 2.92 (m, 1H), 2.88 (dd, *J* = 10.8, 7.1, 1H), 2.69 (d, *J* = 10.2, 1H), 2.56 – 2.44 (m, 2H), 2.04 (td, *J* = 11.6, 5.8, 1H), 1.93 – 1.78 (m, 3H), 1.64 – 1.53 (m, 2H), 1.47 (s, 9H), 1.34 (ddt, *J* = 11.0, 7.1, 5.5, 1H), 0.89 (d, *J* = 6.3, 3H), 0.85 (d, *J* = 6.5, 3H); MS (ESI+) *m/z* 354 $(M+H)^+$.

Example 350

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]piperidine-2-carboxamide

The title compound was prepared by substituting *tert*-butyl (2*S*)-2-({[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]amino}carbonyl)piperidine-1-carboxylate from Example 231 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.67-7.70 (m, 1H), 7.42-7.44 (m, 2H), 7.36 (t, J = 7.5 Hz, 2H), 7.27 (t, J = 7.3 Hz, 1H), 4.34-4.40 (m, 1H), 3.59 (d, J = 13.1 Hz, 1H), 3.41 (d, J = 13.1 Hz, 1H), 3.32 (dd, J = 10.3, 3.2 Hz, 1H), 2.99-3.02 (m, 1H), 2.83 (dd, J = 8.9, 2.5 Hz, 1H), 2.54-2.61 (m, 1H), 2.46-2.54 (m, 1H), 2.40-2.58 (m, 1H), 2.39-2.47 (m, 1H), 2.33-2.39 (m, 2H), 2.21 (dd, J = 8.9, 7.2 Hz, 1H), 2.02-2.10 (m, 2H), 1.77-1.84 (m, 1H), 1.64-1.74 (m, 1H), 1.47-1.64 (m, 2H), 1.34-1.45 (m, 2H), 1.25-1.34 (m, 2H); MS (ESI+) *m/z* 328 $(M+H)^+$.

Example 351

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-valinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxobutan-2-yl(methyl)carbamate from Example 232 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.10-8.12 (m, 1H), 7.43-7.45 (m, 2H), 7.37 (t, J = 7.5 Hz, 2H), 7.28 (t, J = 7.3 Hz, 1H), 4.44-4.50 (m, 1H), 3.62 (d, J = 13.1 Hz, 1H), 3.44 (d, J = 13.1 Hz, 1H), 2.85-2.90 (m, 2H), 2.47-2.57 (m, 2H), 2.43 (dd, J = 8.8, 7.0 Hz, 1H), 2.40 (s, 3H), 2.36 (dd, J = 8.9, 2.7 Hz, 1H), 2.26 (dd, J = 8.9, 6.8 Hz, 1H), 2.07-2.16 (m, 2H), 1.91-2.06 (m, 1H), 1.81-1.89 (m, 1H), 1.59 (dq, J = 12.1, 7.6 Hz, 1H), 1.38-1.45 (m, 1H), 1.06 (d, J = 6.9 Hz, 3H), 1.05 (d, J = 6.9 Hz, 3H); MS (ESI+) *m/z* 330 $(M+H)^+$.

Example 352

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate from Example 233 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.11-8.14 (m, 1H), 7.43-7.45 (m, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.28 (t, *J* = 7.3 Hz, 1H), 4.42-4.48 (m, 1H), 3.61 (d, *J* = 13.1 Hz, 1H), 3.44 (d, *J* = 13.1 Hz, 1H), 3.16 (t, *J* = 6.5 Hz, 1H), 2.86 (dd, *J* = 8.9, 2.6 Hz, 1H), 2.47-2.57 (m, 2H), 2.42 (dd, *J* = 8.9, 7.2 Hz, 1H), 2.40 (s, 3H), 2.36 (dd, *J* = 8.9, 2.7 Hz, 1H), 2.26 (dd, *J* = 8.9, 7.0 Hz, 1H), 2.12 (dq, *J* = 11.9, 6.0 Hz, 2H), 1.77-1.89 (m, 2H), 1.65-1.73 (m, 1H), 1.54-1.64 (m, 1H), 1.37-1.54 (m, 3H), 0.84 (t, *J* = 7.3 Hz, 3H); MS (ESI+) *m/z* 330 $(M+H)^+$.

Example 353

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-isoleucinamide

The title compound was prepared by substituting *tert*-butyl (2*S*,3*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxopentan-2-yl(methyl)carbamate from Example 224 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.10-8.14 (m, 1H), 7.44-7.46 (m, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.26-7.30 (m, 1H), 4.42-4.50 (m, 1H), 3.61 (d, *J* = 13.1 Hz, 1H), 3.46 (d, *J* = 13.1 Hz, 1H), 2.97 (d, *J* = 6.0 Hz, 1H), 2.87 (d, *J* = 10.2 Hz, 1H), 2.50-2.57 (m, 2H), 2.41-2.45 (m, 1H), 2.41 (s, 3H), 2.35-2.39 (m, 1H), 2.24-2.29 (m, 1H), 2.07-2.16 (m, 1H), 1.89-2.09 (m, 1H), 1.73-1.92 (m, 3H), 1.55-1.68 (m, 1H), 1.26-1.46 (m, 2H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.86 (t, *J* = 7.4 Hz, 3H); MS (ESI+) *m/z* 344 $(M+H)^+$.

Example 354

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-isoleucinamide

The title compound was prepared by substituting *tert*-butyl (2*S*,3*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxopentan-2-yl(methyl)carbamate from Step A of Example 334 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.11-8.14 (m, 1H), 7.43-7.46 (m, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.25-7.30 (m, 1H), 4.44-4.51 (m, 1H), 3.62 (d, *J* = 13.1 Hz, 1H), 3.44 (d, *J* = 13.1 Hz, 1H), 2.96 (d, *J* = 6.0 Hz, 1H), 2.87 (dd, *J* = 8.9, 2.1 Hz, 1H), 2.47-2.61 (m, 2H), 2.43 (dd, *J* = 8.8, 7.0 Hz, 1H), 2.40 (s, 3H), 2.36 (dd, *J* = 8.9, 2.4 Hz, 1H), 2.26 (dd, *J* = 8.9, 6.6 Hz, 1H), 2.07-2.16 (m, 1H), 1.88-2.02 (m, 1H), 1.73-1.91 (m, 3H), 1.60 (dq, *J* = 12.1, 7.5 Hz, 1H), 1.25-1.46 (m, 2H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.86 (t, *J* = 7.4 Hz, 3H); MS (ESI+) *m/z* 344 $(M+H)^+$.

Example 355

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2,4-dimethyl-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate from Example 247 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.21-8.24 (m, 1H), 7.43-7.46 (m, 2H), 7.37 (t, *J* = 7.4 Hz, 2H), 7.24-7.30 (m, 1H), 4.42-4.47 (m, 1H), 3.61 (d, *J* = 13.0 Hz, 1H), 3.46 (d, *J* = 13.1 Hz, 1H), 3.19-3.22 (m, 1H), 2.88 (d, *J* = 10.0 Hz, 1H), 2.52 (d, *J* = 4.7 Hz, 2H), 2.40-2.46 (m, 1H), 2.41 (s, 3H), 2.37 (dd, *J* = 9.0, 2.4 Hz, 1H), 2.26 (dd, *J* = 8.7, 6.2 Hz, 1H), 2.07-2.18 (m, 1H), 1.93 (dd, *J* = 14.1, 5.1 Hz, 1H), 1.80-1.89 (m, 1H), 1.58-1.82 (m, 1H), 1.55-1.65 (m, 1H), 1.51 (dd, *J* = 14.0, 6.6 Hz, 1H), 1.34-1.46 (m, 1H), 0.98 (s, 9H); MS (ESI+) *m/z* 358 $(M+H)^+$.

Example 356

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-L-valinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3,3-dimethyl-1-oxobutan-2-ylcarbamate from Example 234 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.09-8.12 (m, 1H), 7.42-7.44 (m, 2H), 7.37 (t, J = 7.3 Hz, 2H), 7.25-7.32 (m, 1H), 4.38-4.44 (m, 1H), 3.58 (d, J = 13.0 Hz, 1H), 3.44 (d, J = 13.1 Hz, 1H), 3.26 (s, 1H), 2.78 (dd, J = 8.9, 2.5 Hz, 1H), 2.44-2.52 (m, 2H), 2.38-2.42 (m, 1H), 2.33 (dd, J = 9.0, 2.7 Hz, 1H), 2.23-2.27 (m, 1H), 2.07-2.16 (m, 2H), 1.91-2.26 (m, 1H), 1.80-1.88 (m, 1H), 1.55-1.62 (m, 1H), 1.36-1.43 (m, 1H), 1.14 (s, 9H); MS (ESI+) *m/z* 330 $(M+H)^+$.

Example 357

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-L-valinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3,3-dimethyl-1-oxobutan-2-ylcarbamate from Example 225 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.07-8.10 (m, 1H), 7.43-7.45 (m, 2H), 7.37 (t, J = 7.4 Hz, 2H), 7.25-7.31 (m, 1H), 4.42 (t, J = 5.0 Hz, 1H), 3.61 (d, J = 13.1 Hz, 1H), 3.44 (d, J = 13.1 Hz, 1H), 3.26 (s, 1H), 2.84-2.87 (m, 1H), 2.44-2.55 (m, 2H), 2.41-2.44 (m, 1H), 2.33-2.36 (m, 1H), 2.24-2.27 (m, 1H), 1.96-2.20 (m, 1H), 2.03-2.12 (m, 2H), 1.79-1.86 (m, 1H), 1.51-1.59 (m, 1H), 1.35-1.41 (m, 1H), 1.14 (s, 9H); MS (ESI+) *m/z* 330 $(M+H)^+$.

Example 358

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2,4-dimethyl-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate from Example 248 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-

yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.21-8.24 (m, 1H), 7.43-7.45 (m, 2H), 7.37 (t, J = 7.4 Hz, 2H), 7.27 (t, J = 7.3 Hz, 1H), 4.42-4.48 (m, 1H), 3.61 (d, J = 13.1 Hz, 1H), 3.45 (d, J = 13.1 Hz, 1H), 3.19 (t, J = 5.8 Hz, 1H), 2.88 (d, J = 10.3 Hz, 1H), 2.50-2.55 (m, 2H), 2.42 (dd, J = 9.0, 7.1 Hz, 1H), 2.40 (s, 3H), 2.36 (dd, J = 8.6, 2.6 Hz, 1H), 2.23-2.27 (m, 1H), 2.12 (dq, J = 11.9, 5.9 Hz, 1H), 1.93 (dd, J = 14.0, 5.2 Hz, 1H), 1.80-1.90 (m, 2H), 1.68-1.93 (m, 1H), 1.55-1.64 (m, 1H), 1.51 (dd, J = 14.0, 6.6 Hz, 1H), 1.36-1.45 (m, 1H), 0.98 (s, 9H); MS (ESI+) *m/z* 358 $(M+H)^+$.

Example 359

N^1-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate from Example 238 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37-8.42 (m, 1H), 7.51-7.53 (m, 2H), 7.36-7.41 (m, 2H), 7.31 (t, J = 7.4 Hz, 1H), 4.52-4.57 (m, 1H), 3.73 (d, J = 12.7 Hz, 1H), 3.30 (d, J = 12.8 Hz, 1H), 3.19 (t, J = 6.2 Hz, 1H), 2.77-2.82 (m, 1H), 2.67-2.73 (m, 1H), 2.39-2.47 (m, 3H), 2.40 (s, 3H), 2.18 (dd, J = 9.5, 7.1 Hz, 1H), 2.07-2.15 (m, 1H), 1.85-1.91 (m, 1H), 1.79-1.83 (m, 1H), 1.63-1.78 (m, 2H), 1.54-1.62 (m, 1H), 1.42-1.52 (m, 2H), 1.23-1.31 (m, 1H), 0.86 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 330 $(M+H)^+$.

Example 360

N^1-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Example 239 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.47 (d, J = 7.3 Hz, 1H), 7.51-7.53 (m, 2H), 7.39 (t, J = 7.5 Hz, 2H), 7.31 (t, J = 7.3 Hz, 1H), 4.52-4.58 (m, 1H), 3.77 (d, J = 12.8 Hz, 1H), 3.29 (d, J = 12.8 Hz, 1H), 3.27 (dd, J = 8.2, 5.7 Hz, 1H), 2.82 (dd, J = 9.5, 2.3 Hz, 1H), 2.71-2.76 (m, 1H), 2.42-2.49

(m, 1H), 2.41 (s, 3H), 2.37-2.42 (m, 1H), 2.22 (dd, J = 9.4, 7.2 Hz, 1H), 2.15 (t, J = 8.3 Hz, 1H), 1.83-1.96 (m, 2H), 1.72-1.80 (m, 1H), 1.54-1.72 (m, 3H), 1.28 (dq, J = 12.9, 6.4 Hz, 1H), 0.92 (d, J = 6.6 Hz, 3H), 0.90 (d, J = 6.6 Hz, 3H); MS (ESI+) *m/z* 344 $(M+H)^+$.

Example 361

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-ylcarbamate from Example 226 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.27-8.30 (m, 1H), 7.43-7.45 (m, 2H), 7.37 (t, J = 7.4 Hz, 2H), 7.25-7.29 (m, 1H), 4.36-4.42 (m, 1H), 3.58-3.61 (m, 2H), 3.45 (d, J = 13.1 Hz, 1H), 2.86 (dd, J = 9.0, 2.4 Hz, 1H), 2.45-2.54 (m, 2H), 2.39 (dd, J = 9.0, 7.2 Hz, 1H), 2.36 (dd, J = 9.1, 2.5 Hz, 1H), 2.24 (dd, J = 8.8, 6.9 Hz, 1H), 2.18 (dd, J = 14.0, 4.3 Hz, 1H), 2.01-2.23 (m, 2H), 2.07-2.14 (m, 1H), 1.79-1.87 (m, 1H), 1.56 (dq, J = 12.0, 7.7 Hz, 1H), 1.44 (dd, J = 14.0, 7.5 Hz, 1H), 1.35-1.44 (m, 1H), 0.98 (s, 9H); MS (ESI+) *m/z* 344 $(M+H)^+$.

Example 362

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norleucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxohexan-2-yl(methyl)carbamate from Example 227 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.07-8.10 (m, 1H), 7.43-7.46 (m, 2H), 7.37 (t, J = 7.5 Hz, 2H), 7.28 (t, J = 7.4 Hz, 1H), 4.42-4.47 (m, 1H), 3.61 (d, J = 13.1 Hz, 1H), 3.46 (d, J = 13.1 Hz, 1H), 3.15 (t, J = 6.5 Hz, 1H), 2.87 (dd, J = 9.0, 2.5 Hz, 1H), 2.47-2.58 (m, 2H), 2.40-2.44 (m, 1H), 2.41 (s, 3H), 2.37 (dd, J = 8.9, 2.6 Hz, 1H), 2.26 (dd, J = 8.9, 6.8 Hz, 1H), 2.08-2.17 (m, 1H), 1.93-2.16 (m, 1H), 1.80-1.89 (m, 2H), 1.67-1.75 (m, 1H), 1.59 (dq, J = 12.0, 7.6 Hz, 1H), 1.38-1.50 (m, 3H), 1.20-1.28 (m, 2H), 0.81 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 344 $(M+H)^+$.

Example 363

N^1-[(3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate from Example 240 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.26 (d, J = 7.8 Hz, 1H), 7.50-7.52 (m, 2H), 7.39 (t, J = 7.5 Hz, 2H), 7.32 (t, J = 7.3 Hz, 1H), 4.51-4.57 (m, 1H), 3.57 (d, J = 12.7 Hz, 1H), 3.42 (d, J = 12.7 Hz, 1H), 3.13-3.16 (m, 1H), 2.75-2.78 (m, 1H), 2.63-2.70 (m, 1H), 2.45-2.49 (m, 1H), 2.39-2.47 (m, 1H), 2.39 (s, 3H), 2.14 (dd, J = 8.9, 7.6 Hz, 1H), 2.09 (dd, J = 9.5, 7.2 Hz, 1H), 1.82-2.27 (m, 1H), 1.83-1.91 (m, 1H), 1.63-1.81 (m, 3H), 1.54-1.63 (m, 1H), 1.39-1.54 (m, 2H), 1.25-1.33 (m, 1H), 0.86 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 330 $(M+H)^+$.

Example 364

N^1-[(3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Example 241 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.24-8.27 (m, 1H), 7.50-7.52 (m, 2H), 7.40 (t, J = 7.5 Hz, 2H), 7.32 (t, J = 7.4 Hz, 1H), 4.50-4.56 (m, 1H), 3.54 (d, J = 12.7 Hz, 1H), 3.45 (d, J = 12.7 Hz, 1H), 3.20 (dd, J = 8.2, 5.7 Hz, 1H), 2.76-2.78 (m, 1H), 2.64-2.71 (m, 1H), 2.46-2.49 (m, 1H), 2.41-2.47 (m, 1H), 2.39 (s, 3H), 2.16 (t, J = 8.2 Hz, 1H), 2.06-2.12 (m, 1H), 1.78-2.09 (m, 1H), 1.82-1.93 (m, 2H), 1.63-1.76 (m, 2H), 1.55-1.63 (m, 1H), 1.48-1.56 (m, 1H), 1.25-1.35 (m, 1H), 0.93 (d, J = 6.5 Hz, 3H), 0.88 (d, J = 6.6 Hz, 3H); MS (ESI+) *m/z* 344 $(M+H)^+$.

Example 365

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A of Example 313 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.08-8.10 (m, 1H), 7.43-7.46 (m, 2H), 7.37 (t, J = 7.4 Hz, 2H), 7.28 (t, J = 7.3 Hz, 1H), 4.41-4.46 (m, 1H), 3.61 (d, J = 13.1 Hz, 1H), 3.45 (d, J = 13.1 Hz, 1H), 3.15 (t, J = 6.5 Hz, 1H), 2.86 (dd, J = 9.0, 2.5 Hz, 1H), 2.47-2.57 (m, 2H), 2.40-2.44 (m, 1H), 2.40 (s, 3H), 2.37 (dd, J = 9.0, 2.3 Hz, 1H), 2.24-2.27 (m, 1H), 2.07-2.16 (m, 1H), 1.90-2.10 (m, 1H), 1.77-1.88 (m, 2H), 1.63-1.73 (m, 1H), 1.54-1.63 (m, 1H), 1.36-1.53 (m, 3H), 0.84 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 330 $(M+H)^+$.

Example 366

N^2-ethyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting *tert*-butyl ethyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 310 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.23-8.26 (m, 1H), 7.76-7.77 (bs, 1H), 7.55-7.63 (m, 2H), 7.45 (t, J = 7.7 Hz, 1H), 4.41-4.45 (m, 1H), 3.61 (d, J = 13.5 Hz, 1H), 3.48 (d, J = 13.5 Hz, 1H), 3.33 (dd, J = 8.2, 5.8 Hz, 1H), 2.86 (dd, J = 9.0, 2.3 Hz, 1H), 2.70-2.78 (m, 1H), 2.60-2.64 (m, 1H), 2.53-2.55 (m, 2H), 2.43-2.47 (m, 1H), 2.33 (dd, J = 9.0, 2.4 Hz, 1H), 2.28 (dd, J = 8.8, 6.3 Hz, 1H), 2.08-2.12 (m, 1H), 1.80-2.05 (m, 1H), 1.82-1.95 (m, 2H), 1.72 (ddd, J = 13.5, 7.8, 5.8 Hz, 1H), 1.56-1.63 (m, 2H), 1.39-1.45 (m, 1H), 1.08 (t, J = 7.1 Hz, 3H), 0.92 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.5 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 367

N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-valinamide

Step A: *tert*-Butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxobutan-2-yl(methyl)carbamate from Example 232 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide and 4-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde in the procedures described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.59 (d, J = 8.0, 2H), 7.46 (d, J = 7.9, 2H), 4.35 (d, J = 9.6, 1H), 4.30 – 4.23 (m, 1H), 3.55 (d, J = 13.7, 1H), 3.48 (d, J = 13.7, 1H), 3.01 (s, 3H), 2.77 (dd, J = 8.9, 2.1, 1H), 2.57 – 2.48 (m, 1H), 2.42 (ddd, J = 10.7, 9.3, 6.0, 2H), 2.36 (dd, J = 14.0, 5.7, 2H), 2.30 – 2.25 (m, 1H), 2.12 – 2.03 (m, 2H), 1.87 (td, J = 12.9, 6.3, 1H), 1.57 (dt, J = 14.8, 7.9, 1H), 1.45 (s, 9H), 1.43 – 1.35 (m, 1H), 1.01 (d, J = 6.5, 3H), 0.87 (d, J = 6.7, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.13-8.16 (m, 1H), 7.65-7.67 (m, 2H), 7.51-7.54 (m, 2H), 4.45-4.51 (m, 1H), 3.60 (d, J = 13.7 Hz, 1H), 3.47 (d, J = 13.7 Hz, 1H), 2.90 (d, J = 13.1 Hz, 1H), 2.88-2.90 (m, 1H), 2.48-2.59 (m, 2H), 2.40 (s, 3H), 2.33-2.40 (m, 2H), 2.24 (dd, J = 8.9, 7.0 Hz, 1H), 2.08-2.16 (m, 2H), 1.94-2.10 (m, 1H), 1.85-1.93 (m, 1H), 1.60 (dq, J = 12.0, 7.7 Hz, 1H), 1.43 (ddt, J = 8.9, 12.4, 6.2 Hz, 1H), 1.06 (t, J = 6.9 Hz, 6H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Example 368

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]piperidine-2-carboxamide

Step A: *tert*-Butyl (2*S*)-2-({[(3a*S*,4*R*,6a*R*)-2-(4-flurobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]amino}carbonyl)piperidine-1-carboxylate was

prepared by substituting *tert*-butyl (2*S*)-2-({[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]amino}carbonyl)piperidine-1-carboxylate from Example 231 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide and 4-fluorobenzaldehyde for 3-(trifluoromethyl)benzaldehyde in the procedures described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.37 (d, J = 7.2, 2H), 7.30 (t, J = 7.5, 2H), 7.21 (t, J = 7.3, 2H), 4.87 (d, J = 3.9, 1H), 4.32 – 4.23 (m, 1H), 4.10 (d, J = 12.8, 1H), 3.58 (d, J = 13.2, 1H), 3.47 (d, J = 13.2, 1H), 3.29 (td, J = 12.8, 2.9, 1H), 2.83 – 2.76 (m, 1H), 2.52 (td, J = 8.1, 3.4, 1H), 2.48 – 2.41 (m, 2H), 2.36 (dd, J = 9.0, 3.1, 1H), 2.33 – 2.28 (m, 1H), 2.24 (dd, J = 11.7, 1.6, 1H), 2.07 (dq, J = 12.2, 6.1, 1H), 1.87 – 1.78 (m, 1H), 1.69 – 1.59 (m, 1H), 1.59 – 1.49 (m, 3H), 1.48 (s, 9H), 1.45 – 1.29 (m, 3H); MS (ESI+) *m/z* 428 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-Butyl (2*S*)-2-({[(3a*S*,4*R*,6a*R*)-2-(4-flurobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]amino}carbonyl)piperidine-1-carboxylate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.68-7.70 (m, 1H), 7.35 (dd, J = 8.3, 5.6 Hz, 2H), 7.10-7.14 (m, 2H), 4.34-4.40 (m, 1H), 3.51 (d, J = 13.1 Hz, 1H), 3.36 (d, J = 13.1 Hz, 1H), 3.32 (dd, J = 10.4, 3.2 Hz, 1H), 2.98-3.02 (m, 1H), 2.82 (dd, J = 9.0, 2.6 Hz, 1H), 2.54-2.61 (m, 1H), 2.48-2.54 (m, 1H), 2.39-2.46 (m, 1H), 2.33-2.45 (m, 1H), 2.29-2.35 (m, 2H), 2.16-2.22 (m, 1H), 2.01-2.10 (m, 2H), 1.78-1.87 (m, 1H), 1.65-1.74 (m, 1H), 1.56-1.64 (m, 1H), 1.47-1.56 (m, 1H), 1.34-1.44 (m, 2H), 1.26-1.34 (m, 2H); MS (ESI+) *m/z* 346 $(M+H)^+$.

Example 369

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-valinamide

Step A: *tert*-Butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxobutan-2-yl(methyl)carbamate from Example 232 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide and 4-fluorobenzaldehyde for 3-(trifluoromethyl)benzaldehyde in the procedures described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.43 (s,

1H), 7.30 (dd, J = 8.3, 5.7, 2H), 7.03 (t, J = 8.8, 2H), 4.35 (d, J = 9.5, 1H), 4.25 (s, 1H), 3.49 (d, J = 13.2, 1H), 3.41 (d, J = 13.2, 1H), 3.01 (s, 3H), 2.75 (dd, J = 8.9, 2.3, 1H), 2.57 – 2.48 (m, 1H), 2.45 – 2.31 (m, 4H), 2.27 (dd, J = 8.8, 7.4, 1H), 2.11 – 2.03 (m, 1H), 1.85 (dt, J = 20.7, 6.5, 1H), 1.56 (dt, J = 15.2, 7.3, 1H), 1.46 (s, 9H), 1.43 – 1.35 (m, 1H), 1.01 (d, J = 6.5, 3H), 0.87 (d, J = 6.7, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.11-8.14 (m, 1H), 7.37 (dd, J = 8.3, 5.6 Hz, 2H), 7.11-7.15 (m, 2H), 4.43-4.49 (m, 1H), 3.54 (d, J = 13.1 Hz, 1H), 3.39 (d, J = 13.1 Hz, 1H), 2.90 (d, J = 5.8 Hz, 1H), 2.86 (dd, J = 9.0, 2.6 Hz, 1H), 2.47-2.56 (m, 2H), 2.40 (s, 3H), 2.38 (dd, J = 9.0, 7.0 Hz, 1H), 2.34 (dd, J = 9.0, 2.6 Hz, 1H), 2.23 (dd, J = 8.9, 7.0 Hz, 1H), 2.07-2.16 (m, 2H), 1.93-2.04 (m, 1H), 1.83-1.92 (m, 1H), 1.59 (dq, J = 12.1, 7.7 Hz, 1H), 1.41 (ddt, J = 8.9, 12.4, 6.2 Hz, 1H), 1.06 (t, J = 6.8 Hz, 6H); MS (ESI+) *m/z* 348 $(M+H)^+$.

Example 370

(2*S*)-*N*-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}piperidine-2-carboxamide

Step A: *tert*-Butyl (2*S*)-2-({[(3a*S*,4*R*,6a*R*)-2-(4-(trifluromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]amino}carbonyl)piperidine-1-carboxylate was prepared by substituting *tert*-butyl (2*S*)-2-({[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]amino}carbonyl)piperidine-1-carboxylate from Example 231 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide and 4-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde in the procedures described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.59 (d, J = 8.1, 2H), 7.47 (d, J = 8.0, 2H), 7.27 – 7.20 (m, 1H), 4.87 (d, J = 3.7, 1H), 4.32 – 4.23 (m, 1H), 3.57 (d, J = 13.7, 1H), 3.49 (d, J = 13.8, 1H), 3.29 (td, J = 12.8, 3.0, 1H), 2.81 (dd, J = 8.7, 2.0, 1H), 2.59 – 2.50 (m, 1H), 2.46 (ddd, J = 12.1, 7.0, 2.8, 1H), 2.43 – 2.38 (m, 1H), 2.36 (dd, J = 9.0, 2.9, 1H), 2.32 – 2.27 (m, 1H), 2.27 – 2.20 (m, 1H), 2.11 – 2.03 (m, 2H), 1.86 (ddd, J = 12.7, 8.1, 6.3, 1H), 1.70 – 1.60 (m, 1H), 1.59 – 1.49 (m, 4H), 1.47 (s, 9H), 1.45 – 1.29 (m, 2H); MS (ESI+) *m/z* 496 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (2*S*)-2-({[(3a*S*,4*R*,6a*R*)-2-(4-(trifluromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]amino}carbonyl)piperidine-1-carboxylate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.71 (d, J = 7.5 Hz, 1H), 7.64-7.66 (m, 2H), 7.49-7.52 (m, 2H), 4.36-4.41 (m, 1H), 3.57 (d, J = 13.7 Hz, 1H), 3.43 (d, J = 13.7 Hz, 1H), 3.33 (dd, J = 10.3, 3.2 Hz, 1H), 2.98-3.03 (m, 1H), 2.85 (dd, J = 9.0, 2.5 Hz, 1H), 2.50-2.60 (m, 2H), 2.36-2.58 (m, 1H), 2.41-2.46 (m, 1H), 2.34 (d, J = 7.6 Hz, 1H), 2.31-2.33 (m, 1H), 2.20 (dd, J = 8.9, 7.2 Hz, 1H), 2.02-2.10 (m, 2H), 1.81-1.88 (m, 1H), 1.66-1.71 (m, 1H), 1.50-1.63 (m, 2H), 1.35-1.42 (m, 2H), 1.24-1.34 (m, 2H); MS (ESI+) *m/z* 396 $(M+H)^+$.

Example 371

N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 317 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.14-8.17 (m, 1H), 7.64-7.67 (m, 2H), 7.51-7.54 (m, 2H), 4.43-4.49 (m, 1H), 3.59 (d, J = 13.7 Hz, 1H), 3.47 (d, J = 13.7 Hz, 1H), 3.16 (t, J = 6.5 Hz, 1H), 2.88 (dd, J = 9.0, 2.6 Hz, 1H), 2.44-2.58 (m, 2H), 2.40 (s, 3H), 2.34-2.39 (m, 2H), 2.24 (t, J = 8.0 Hz, 1H), 2.12 (dq, J = 11.8, 5.9 Hz, 1H), 1.95-2.18 (m, 1H), 1.85-1.93 (m, 1H), 1.76-1.85 (m, 1H), 1.66-1.73 (m, 1H), 1.56-1.64 (m, 1H), 1.39-1.53 (m, 3H), 0.84 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Example 372

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate from Example 318 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-

4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.12-8.15 (m, 1H), 7.35-7.39 (m, 2H), 7.11-7.15 (m, 2H), 4.41-4.47 (m, 1H), 3.53 (d, J = 13.1 Hz, 1H), 3.39 (d, J = 13.1 Hz, 1H), 3.16 (t, J = 6.5 Hz, 1H), 2.85 (dd, J = 9.0, 2.6 Hz, 1H), 2.46-2.59 (m, 2H), 2.40 (s, 3H), 2.38 (dd, J = 8.9, 6.8 Hz, 1H), 2.34 (dd, J = 8.9, 2.8 Hz, 1H), 2.23 (dd, J = 8.9, 7.1 Hz, 1H), 2.07-2.16 (m, 1H), 1.91-2.12 (m, 1H), 1.84-1.91 (m, 1H), 1.76-1.83 (m, 1H), 1.66-1.73 (m, 1H), 1.54-1.63 (m, 1H), 1.36-1.54 (m, 3H), 0.84 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 348 $(M+H)^+$.

Example 373

N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-valinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate from Example 316 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.13 (d, J = 7.6, 1H), 7.76 (s, 1H), 7.61 (d, J = 7.6, 1H), 7.56 (s, 1H), 7.45 (t, J = 7.7, 1H), 4.52 – 4.36 (m, 1H), 3.62 (d, J = 13.6, 1H), 3.46 (d, J = 13.6, 1H), 2.92 – 2.79 (m, 2H), 2.59 – 2.46 (m, 2H), 2.43 (d, J = 8.8, 1H), 2.40 (s, 3H), 2.33 (dd, J = 9.0, 2.5, 1H), 2.28 – 2.22 (m, 1H), 2.15 – 2.05 (m, 2H), 2.04 – 1.93 (m, 1H), 1.86 (td, J = 12.9, 6.4, 1H), 1.59 (dt, J = 14.9, 7.7, 1H), 1.44 – 1.36 (m, 1H), 1.05 (t, J = 7.0, 6H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Example 374

N^1-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(3-fluoro-4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Example 311 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.20-8.22 (m, 1H), 7.58-7.61 (m, 1H), 7.32-7.36 (m, 1H), 7.27-7.29 (m,

1H), 4.43-4.48 (m, 1H), 3.55-3.62 (m, 1H), 3.45 (d, J = 14.1 Hz, 1H), 3.22 (dd, J = 8.2, 5.8 Hz, 1H), 2.91 (dd, J = 9.0, 2.5 Hz, 1H), 2.48-2.60 (m, 2H), 2.42 (s, 3H), 2.35-2.39 (m, 2H), 2.23 (dd, J = 8.9, 7.1 Hz, 1H), 2.07-2.16 (m, 1H), 1.91-2.11 (m, 1H), 1.84-1.95 (m, 2H), 1.71 (ddd, J = 13.5, 7.8, 5.8 Hz, 1H), 1.56-1.65 (m, 2H), 1.39-1.46 (m, 1H), 0.91 (d, J = 6.6 Hz, 3H), 0.85 (d, J = 6.5 Hz, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Example 375

N^1-{(3a*S*,4*R*,6a*R*)-2-[4-fluoro-3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluoro-3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Example 312 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.18-8.21 (m, 1H), 7.68-7.71 (m, 1H), 7.57-7.60 (m, 1H), 7.22-7.28 (m, 1H), 4.42-4.46 (m, 1H), 3.55 (d, J = 13.5 Hz, 1H), 3.43 (d, J = 13.4 Hz, 1H), 3.21 (dd, J = 8.2, 5.8 Hz, 1H), 2.88 (dd, J = 9.0, 2.6 Hz, 1H), 2.48-2.60 (m, 2H), 2.42 (s, 3H), 2.37-2.42 (m, 1H), 2.34 (dd, J = 8.8, 2.4 Hz, 1H), 2.21-2.28 (m, 1H), 2.06-2.14 (m, 1H), 1.90-2.08 (m, 1H), 1.83-1.94 (m, 2H), 1.71 (ddd, J = 13.5, 7.8, 5.8 Hz, 1H), 1.55-1.64 (m, 2H), 1.38-1.45 (m, 1H), 0.91 (d, J = 6.5 Hz, 3H), 0.85 (d, J = 6.5 Hz, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Example 376

N^2-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 313 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.09-8.12 (m, 1H), 7.76-7.77 (bs, 1H), 7.60-7.63 (m, 1H), 7.55-7.58 (m, 1H), 7.45 (t, J = 7.7 Hz, 1H), 4.40-4.44 (m, 1H), 3.61 (d, J = 13.5 Hz, 1H), 3.47 (d, J = 13.5 Hz, 1H), 3.15 (t, J = 6.5 Hz, 1H), 2.87 (dd, J = 9.0, 2.6 Hz, 1H), 2.47-2.57 (m, 2H), 2.40-2.44 (m, 1H), 2.40 (s, 3H), 2.33 (dd, J = 9.0, 2.7 Hz, 1H), 2.23-2.27 (m, 1H), 2.05-2.12 (m, 1H),

1.93-2.10 (m, 1H), 1.83-1.90 (m, 1H), 1.76-1.83 (m, 1H), 1.64-1.73 (m, 1H), 1.54-1.63 (m, 1H), 1.36-1.53 (m, 3H), 0.84 (t, J = 7.3 Hz, 3H); MS (ESI+) m/z 398 $(M+H)^+$.

Example 377

N^2-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 314 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.12-8.15 (m, 1H), 7.64-7.67 (m, 2H), 7.51-7.54 (m, 2H), 4.42-4.47 (m, 1H), 3.57-3.61 (m, 1H), 3.48 (d, J = 13.7 Hz, 1H), 3.16 (t, J = 6.5 Hz, 1H), 2.89 (dd, J = 9.0, 2.5 Hz, 1H), 2.48-2.58 (m, 2H), 2.41 (s, 3H), 2.34-2.41 (m, 2H), 2.24 (dd, J = 8.9, 7.0 Hz, 1H), 2.03-2.18 (m, 1H), 1.94-2.26 (m, 1H), 1.77-1.95 (m, 2H), 1.66-1.73 (m, 1H), 1.55-1.64 (m, 1H), 1.38-1.55 (m, 3H), 0.84 (t, J = 7.3 Hz, 3H); MS (ESI+) m/z 398 $(M+H)^+$.

Example 378

N^1-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate from Example 315 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.12-8.15 (m, 1H), 7.64-7.67 (m, 2H), 7.51-7.54 (m, 2H), 4.42-4.47 (m, 1H), 3.57-3.61 (m, 1H), 3.48 (d, J = 13.7 Hz, 1H), 3.16 (t, J = 6.5 Hz, 1H), 2.89 (dd, J = 9.0, 2.5 Hz, 1H), 2.48-2.58 (m, 2H), 2.41 (s, 3H), 2.34-2.41 (m, 2H), 2.24 (dd, J = 8.9, 7.0 Hz, 1H), 2.03-2.18 (m, 1H), 1.94-2.26 (m, 1H), 1.77-1.95 (m, 2H), 1.66-1.73 (m, 1H), 1.55-1.64 (m, 1H), 1.38-1.55 (m, 3H), 0.84 (t, J = 7.3 Hz, 3H); MS (ESI+) m/z 398 $(M+H)^+$.

Example 379

N^2-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 307 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.18-8.20 (m, 1H), 7.76-7.77 (bs, 1H), 7.60-7.64 (m, 1H), 7.54-7.59 (m, 1H), 7.45 (t, J = 7.7 Hz, 1H), 4.40-4.47 (m, 1H), 3.61 (d, J = 13.5 Hz, 1H), 3.47 (d, J = 13.5 Hz, 1H), 3.22 (dd, J = 8.2, 5.8 Hz, 1H), 2.87 (d, J = 10.4 Hz, 1H), 2.49-2.57 (m, 2H), 2.40-2.46 (m, 1H), 2.42 (s, 3H), 2.33 (dd, J = 8.9, 2.5 Hz, 1H), 2.26 (dd, J = 8.9, 6.5 Hz, 1H), 2.01-2.16 (m, 1H), 1.92-2.12 (m, 1H), 1.83-1.97 (m, 2H), 1.71 (ddd, J = 13.5, 7.7, 5.8 Hz, 1H), 1.55-1.64 (m, 2H), 1.37-1.44 (m, 1H), 0.91 (d, J = 6.6 Hz, 3H), 0.85 (d, J = 6.5 Hz, 3H); MS (ESI+) *m/z* 412 $(M+H)^+$.

Example 380

N^2-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 308 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.19-8.22 (m, 1H), 7.64-7.67 (m, 2H), 7.51-7.54 (m, 2H), 4.43-4.48 (m, 1H), 3.59 (d, J = 13.7 Hz, 1H), 3.48 (d, J = 13.7 Hz, 1H), 3.23 (dd, J = 8.2, 5.8 Hz, 1H), 2.90 (dd, J = 9.0, 2.4 Hz, 1H), 2.49-2.58 (m, 2H), 2.43 (s, 3H), 2.38-2.42 (m, 1H), 2.37 (dd, J = 19.2, 2.5 Hz, 1H), 2.24 (dd, J = 8.9, 6.8 Hz, 1H), 2.09-2.17 (m, 1H), 1.95-2.13 (m, 1H), 1.83-1.97 (m, 2H), 1.72 (ddd, J = 13.5, 7.8, 5.8 Hz, 1H), 1.56-1.65 (m, 2H), 1.39-1.46 (m, 1H), 0.91 (d, J = 6.6 Hz, 3H), 0.85 (d, J = 6.5 Hz, 3H); MS (ESI+) *m/z* 412 $(M+H)^+$.

Example 381

N^1-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Example 309 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.17-8.20 (m, 1H), 7.37 (dd, *J* = 8.2, 5.6 Hz, 2H), 7.11-7.15 (m, 2H), 4.41-4.47 (m, 1H), 3.52 (d, *J* = 13.1 Hz, 1H), 3.40 (d, *J* = 13.1 Hz, 1H), 3.22 (dd, *J* = 8.2, 5.8 Hz, 1H), 2.86 (dd, *J* = 9.0, 2.4 Hz, 1H), 2.46-2.57 (m, 2H), 2.42 (s, 3H), 2.34-2.41 (m, 2H), 2.24 (dd, *J* = 8.9, 6.7 Hz, 1H), 2.05-2.18 (m, 1H), 1.98-2.11 (m, 1H), 1.83-1.97 (m, 2H), 1.71 (ddd, *J* = 13.5, 7.8, 5.8 Hz, 1H), 1.55-1.64 (m, 2H), 1.41 (ddt, *J* = 8.9, 12.3, 6.2 Hz, 1H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.85 (d, *J* = 6.6 Hz, 3H); MS (ESI+) *m/z* 362 $(M+H)^+$.

Example 382

N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide

Step A: *tert*-Butyl ((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting *N*-(*tert*-butoxycarbonyl)-L-norvaline for *N*-(*tert*-butoxycarbonyl)-L-leucine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.61 – 8.53 (m, 1H), 7.92 (d, *J* = 8.2, 1H), 7.43 (d, *J* = 7.4, 2H), 7.35 (d, *J* = 7.6, 2H), 7.27 (t, *J* = 7.2, 1H), 4.64 (dd, *J* = 14.4, 7.8, 1H), 4.47 – 4.35 (m, 1H), 3.59 (d, *J* = 13.1, 1H), 3.43 (d, *J* = 13.2, 1H), 2.83 (dd, *J* = 4.7, 4.1, 1H), 2.60 – 2.48 (m, 2H), 2.47 – 2.40 (m, 1H), 2.32 (dd, *J* = 5.0, 3.9, 1H), 2.27 – 2.20 (m, 1H), 2.11 – 1.97 (m, 2H), 1.91 – 1.76 (m, 2H), 1.63 – 1.42 (m, 12H), 1.40 – 1.29 (m, 1H), 0.81 (t, *J* = 7.3, 3H); MS (ESI+) *m/z* 416 $(M+H)^+$.

Step B: *tert*-Butyl-((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting *tert*-butyl ((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide and 4-(trifluoromethyl)benzaldehyde for 3-

(trifluoromethyl)benzaldehyde in the procedures described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.60 (d, J = 7.0, 1H), 7.93 (d, J = 8.3, 1H), 7.65 (d, J = 8.1, 2H), 7.51 (d, J = 7.9, 2H), 4.64 (dd, J = 13.0, 6.5, 1H), 4.47 – 4.37 (m, 1H), 3.57 (d, J = 13.7, 1H), 3.45 (d, J = 13.7, 1H), 2.86 (d, J = 8.3, 1H), 2.55 (dd, J = 14.1, 9.2, 2H), 2.43 – 2.36 (m, 1H), 2.31 (d, J = 7.8, 1H), 2.26 – 2.20 (m, 1H), 2.14 (s, 1H), 2.04 (dd, J = 12.1, 6.0, 2H), 1.90 – 1.80 (m, 2H), 1.59 (s, 1H), 1.49 (d, J = 11.3, 10H), 1.37 (s, 1H), 0.81 (t, J = 7.3, 3H); MS (ESI+) *m/z* 484 $(M+H)^+$.

Step C: The title compound was prepared by substituting *tert*-Butyl-((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step B for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.19-8.22 (m, 1H), 7.64-7.67 (m, 2H), 7.50-7.53 (m, 2H), 4.37-4.43 (m, 1H), 3.53-3.58 (m, 2H), 3.46 (d, J = 13.7 Hz, 1H), 2.86 (dd, J = 9.0, 2.6 Hz, 1H), 2.49-2.57 (m, 1H), 2.43-2.49 (m, 1H), 2.33-2.36 (m, 2H), 2.19-2.25 (m, 1H), 2.11-2.20 (m, 2H), 2.06-2.14 (m, 1H), 1.91-2.01 (m, 1H), 1.82-1.90 (m, 1H), 1.62-1.69 (m, 1H), 1.38-1.58 (m, 4H), 0.84 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 384 $(M+H)^+$.

Example 383

N^2-ethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting *tert*-butyl ethyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 323 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37-8.39 (m, 1H), 8.32-8.37 (m, 1H), 8.19-8.21 (m, 1H), 7.90-7.93 (m, 1H), 7.73 (t, J = 7.9 Hz, 1H), 4.23-4.29 (m, 1H), 3.86 (d, J = 11.2 Hz, 1H), 3.31 (t, J = 6.9 Hz, 1H), 3.18 (dd, J = 9.7, 2.1 Hz, 1H), 3.16 (dd, J = 9.9, 7.5 Hz, 1H), 2.96 (dd, J = 9.5, 6.5 Hz, 1H), 2.68-2.75 (m, 1H), 2.51-2.63 (m, 3H), 1.90-2.12 (m, 1H), 1.91-1.99 (m, 1H), 1.80-1.91 (m, 2H), 1.66-1.72 (m, 1H), 1.52-1.60 (m, 2H), 1.26-1.34 (m, 1H), 1.06 (t, J = 7.1 Hz, 3H), 0.92 (d, J = 6.6 Hz, 3H), 0.85 (d, J = 6.5 Hz, 3H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Example 384

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 322 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.38-8.39 (bs, 1H), 8.29-8.31 (m, 1H), 8.19-8.21 (m, 1H), 7.91-7.93 (m, 1H), 7.73 (t, J = 7.8 Hz, 1H), 4.24-4.29 (m, 1H), 3.87 (dd, J = 9.9, 2.2 Hz, 1H), 3.17-3.22 (m, 2H), 3.15 (dd, J = 9.8, 7.4 Hz, 1H), 2.95 (dd, J = 9.6, 6.7 Hz, 1H), 2.49-2.60 (m, 2H), 2.39 (s, 3H), 1.93-2.10 (m, 1H), 1.91-1.99 (m, 1H), 1.80-1.91 (m, 2H), 1.68 (ddd, J = 13.5, 7.8, 5.8 Hz, 1H), 1.53-1.59 (m, 2H), 1.25-1.33 (m, 1H), 0.91 (d, J = 6.6 Hz, 3H), 0.85 (d, J = 6.6 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 385

***N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide from Example 269 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.38-8.39 (bs, 1H), 8.19-8.22 (m, 2H), 7.91-7.94 (m, 1H), 7.74 (t, J = 7.8 Hz, 1H), 7.29-7.35 (m, 4H), 7.24-7.29 (m, 1H), 4.92-4.95 (m, 1H), 4.16-4.23 (m, 1H), 3.80 (dd, J = 7.6, 5.7 Hz, 1H), 3.77 (dd, J = 9.8, 2.7 Hz, 1H), 3.32 (dd, J = 13.2, 5.7 Hz, 1H), 3.15 (dd, J = 9.6, 2.9 Hz, 1H), 2.99-3.03 (m, 2H), 2.89 (dd, J = 9.6, 7.6 Hz, 1H), 2.41-2.47 (m, 1H), 2.32-2.37 (m, 1H), 1.98-2.15 (m, 1H), 1.83-1.89 (m, 1H), 1.71-1.77 (m, 1H), 1.35-1.43 (m, 1H), 1.17-1.26 (m, 1H); MS (ESI+) *m/z* 482 $(M+H)^+$.

Example 386

***N*-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide from Example 270 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.39-8.40 (bs, 1H), 8.25 (d, J = 5.1 Hz, 1H), 7.94-7.96 (m, 1H), 7.79 (t, J = 7.8 Hz, 1H), 7.31-7.33 (m, 4H), 7.24-7.28 (m, 1H), 4.17-4.24 (m, 1H), 3.73 (dd, J = 9.9, 2.8 Hz, 1H), 3.45 (t, J = 6.8 Hz, 1H), 3.13-3.20 (m, 2H), 3.01-3.10 (m, 2H), 2.91 (dd, J = 9.6, 7.6 Hz, 1H), 2.39-2.50 (m, 1H), 2.36 (s, 3H), 2.28-2.37 (m, 1H), 2.0 (m, 1H), 1.89-2.26 (m, 1H), 1.84-1.92 (m, 1H), 1.72-1.79 (m, 1H), 1.40-1.48 (m, 1H), 1.18-1.26 (m, 1H); MS (ESI+) *m/z* 496 $(M+H)^+$.

Example 387

***N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-prolinamide**

The title compound was prepared by substituting (*S*)-*tert*-butyl 2-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamoyl)pyrrolidine-1-carboxylate from Example 271 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.35-8.38 (m, 1H), 8.17-8.19 (m, 2H), 7.90-7.92 (m, 1H), 7.72 (t, J = 7.9 Hz, 1H), 4.13-4.19 (m, 1H), 3.86 (dd, J = 8.6, 5.8 Hz, 1H), 3.79 (dd, J = 9.9, 2.6 Hz, 1H), 3.16 (dd, J = 9.6, 2.9 Hz, 1H), 3.02 (dd, J = 9.9, 7.8 Hz, 1H), 2.66-3.18 (m, 1H), 2.79-2.91 (m, 3H), 2.48-2.55 (m, 1H), 2.40-2.45 (m, 1H), 1.99-2.10 (m, 2H), 1.76-1.92 (m, 2H), 1.55-1.65 (m, 1H), 1.48-1.56 (m, 1H), 1.39-1.48 (m, 1H), 1.21-1.29 (m, 1H); MS (ESI+) *m/z* 432 $(M+H)^+$.

Example 388

(3*R*)-3-amino-4-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide

The title compound was prepared by substituting *tert*-butyl (1*R*)-1-isopropyl-3-oxo-3-[((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]propylcarbamate from Example 272 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.74-8.76 (bs, 2H), 8.37-8.38 (bs, 1H), 8.19 (d, *J* = 7.9 Hz, 1H), 7.91 (d, *J* = 7.9 Hz, 1H), 7.72 (t, *J* = 7.8 Hz, 1H), 4.23-4.28 (m, 1H), 3.85 (dd, *J* = 9.9, 2.4 Hz, 1H), 3.14-3.19 (m, 2H), 3.12 (dd, *J* = 9.9, 7.6 Hz, 1H), 2.94 (dd, *J* = 9.6, 6.8 Hz, 1H), 2.50-2.55 (m, 2H), 2.43 (dd, *J* = 14.4, 3.2 Hz, 1H), 2.27 (dd, *J* = 14.4, 9.9 Hz, 1H), 1.92-1.99 (m, 1H), 1.80-1.88 (m, 1H), 1.65-1.90 (m, 1H), 1.50-1.61 (m, 2H), 1.25-1.32 (m, 1H), 0.85 (d, *J* = 6.9 Hz, 3H), 0.83 (d, *J* = 6.9 Hz, 3H); MS (ESI-) *m/z* 446 $(M-H)^-$.

Example 389

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate from Example 273 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.39-8.40 (bs, 1H), 8.24 (d, *J* = 6.9 Hz, 1H), 8.21 (d, *J* = 7.8 Hz, 1H), 7.91-7.93 (m, 1H), 7.73 (t, *J* = 7.8 Hz, 1H), 4.24-4.28 (m, 1H), 3.86 (dd, *J* = 9.9, 2.4 Hz, 1H), 3.18 (dd, *J* = 9.7, 2.4 Hz, 1H), 3.15 (dd, *J* = 9.9, 7.5 Hz, 1H), 2.96 (dd, *J* = 9.6, 6.9 Hz, 1H), 2.88 (d, *J* = 5.9 Hz, 1H), 2.51-2.56 (m, 2H), 2.38 (s, 3H), 2.04-2.14 (m, 1H), 1.88-2.12 (m, 1H), 1.90-1.98 (m, 1H), 1.80-1.88 (m, 1H), 1.51-1.58 (m, 1H), 1.29 (ddt, *J* = 9.6, 12.8, 6.4 Hz, 1H), 1.04 (d, *J* = 6.9 Hz, 3H), 1.01-1.05 (m, 6H), 1.02 (d, *J* = 6.9 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Example 390

(2*S*)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)piperidine-2-carboxamide

The title compound was prepared by substituting *tert*-butyl (2*S*)-2-{[((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]carbonyl}piperidine-1-carboxylate from Example 274 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.35-8.36 (bs, 1H), 8.17-8.19 (m, 1H), 7.90-7.92 (m, 1H), 7.78-7.80 (m, 1H), 7.73 (t, *J* = 7.8 Hz, 1H), 4.16-4.23 (m, 1H), 3.79 (dd, *J* = 9.8, 2.6 Hz, 1H), 3.32 (dd, *J* = 10.3, 3.2 Hz, 1H), 3.15 (dd, *J* = 9.6, 2.9 Hz, 1H), 3.02 (dd, *J* = 9.8, 7.7 Hz, 1H), 2.96-3.00 (m, 1H), 2.89 (dd, *J* = 9.6, 7.4 Hz, 1H), 2.49-2.59 (m, 2H), 2.42-2.49 (m, 1H), 2.18-2.71 (m, 1H), 2.01-2.05 (m, 1H), 1.87-1.95 (m, 1H), 1.75-1.83 (m, 1H), 1.65-1.71 (m, 1H), 1.54-1.61 (m, 1H), 1.44-1.52 (m, 1H), 1.35-1.43 (m, 1H), 1.19-1.35 (m, 3H); MS (ESI+) *m/z* 446 $(M+H)^+$.

Example 391

(3*S*)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide

The title compound was prepared by substituting *tert*-butyl (3*S*)-3-{[((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]carbonyl}-3,4-dihydroisoquinoline-2(1*H*)-carboxylate from Example 275 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (501 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.30-8.31 (bs, 1H), 8.13-8.16 (m, 1H), 7.83-7.85 (m, 1H), 7.68-7.71 (m, 1H), 7.65 (t, *J* = 7.9 Hz, 1H), 7.08-7.12 (m, 3H), 6.97-7.00 (m, 1H), 4.05-4.15 (m, 2H), 3.94-3.98 (m, 1H), 3.66 (dd, *J* = 10.3, 3.4 Hz, 1H), 3.63 (dd, *J* = 9.8, 5.2 Hz, 1H), 3.21-3.26 (m, 1H), 3.11-3.18 (m, 3H), 2.99-3.06 (m, 1H), 2.54-2.58 (m, 1H), 2.47-2.52 (m, 1H), 1.96 (m, 1H), 1.87-1.94 (m, 1H), 1.78-1.85 (m, 1H), 1.45-1.54 (m, 1H), 1.23-1.31 (m, 1H); MS (ESI-) *m/z* 492 $(M-H)^-$.

Example 392

4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate from Example 276 for *tert*-butyl (S)-1-((3aR,4S,6aS)-2-benzyloctahydrocyclopenta[c]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (501 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.30-8.31 (bs, 1H), 8.13-8.16 (m, 1H), 7.82-7.85 (m, 2H), 7.65 (t, *J* = 7.9 Hz, 1H), 4.03-4.10 (m, 1H), 3.69 (dd, *J* = 10.1, 3.4 Hz, 1H), 3.48 (dd, *J* = 7.5, 4.0 Hz, 1H), 3.23-3.27 (m, 1H), 3.11-3.13 (m, 2H), 2.54-2.59 (m, 1H), 2.46-2.51 (m, 1H), 2.07 (dd, *J* = 14.1, 4.0 Hz, 1H), 2.0 (m, 1H), 1.89-1.96 (m, 1H), 1.78-1.87 (m, 1H), 1.65-1.92 (m, 1H), 1.46-1.55 (m, 1H), 1.34 (dd, *J* = 14.1, 7.6 Hz, 1H), 1.23-1.32 (m, 1H), 0.96 (s, 9H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 393

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norleucinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)hexan-2-yl)carbamate from Example 277 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.38-8.39 (bs, 1H), 8.19-8.23 (m, 2H), 7.91-7.93 (m, 1H), 7.73 (t, *J* = 7.8 Hz, 1H), 4.24-4.29 (m, 1H), 3.87 (dd, *J* = 9.9, 2.3 Hz, 1H), 3.18 (dd, *J* = 9.8, 2.3 Hz, 1H), 3.11-3.16 (m, 2H), 2.94 (dd, *J* = 9.6, 6.8 Hz, 1H), 2.53-2.66 (m, 2H), 2.39 (s, 3H), 1.98-2.19 (m, 1H), 1.91-1.99 (m, 1H), 1.78-1.88 (m, 2H), 1.65-1.73 (m, 1H), 1.50-1.59 (m, 1H), 1.35-1.48 (m, 2H), 1.20-1.33 (m, 3H), 0.81 (t, *J* = 7.3 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 394

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 278 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.38-8.39 (bs, 1H), 8.19-8.21 (m, 2H), 7.90-7.93 (m, 1H), 7.72 (t, J = 7.9 Hz, 1H), 4.22-4.29 (m, 1H), 3.87 (dd, J = 9.9, 2.5 Hz, 1H), 3.18 (dd, J = 9.6, 2.4 Hz, 1H), 3.10-3.15 (m, 2H), 2.94 (dd, J = 9.6, 7.0 Hz, 1H), 2.49-2.57 (m, 2H), 2.37 (s, 3H), 1.92-2.22 (m, 1H), 1.89-1.99 (m, 1H), 1.74-1.87 (m, 2H), 1.62-1.70 (m, 1H), 1.40-1.58 (m, 3H), 1.25-1.32 (m, 1H), 0.84 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Example 395

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

Step A: *tert*-Butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Example 222 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.08 (d, J = 8.2, 2H), 7.82 (d, J = 8.2, 2H), 7.51 (d, J = 2.1, 1H), 4.83 (s, 1H), 4.12 – 4.04 (m, 1H), 3.67 (dd, J = 10.2, 3.4, 1H), 3.27 (dd, J = 10.2, 7.8, 1H), 3.14 – 3.09 (m, 2H), 2.94 (s, 3H), 2.63 – 2.46 (m, 2H), 1.95 – 1.68 (m, 4H), 1.60 (td, J = 13.4, 6.8, 1H), 1.54 – 1.47 (m, 1H), 1.46 (s, 9H), 1.27 (ddt, J = 13.3, 9.3, 6.7, 1H), 0.89 (dd, J = 10.7, 6.6, 6H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-

yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.32-8.34 (m, 1H), 8.13-8.16 (m, 2H), 7.90-7.92 (m, 2H), 4.23-4.30 (m, 1H), 3.86 (dd, J = 9.9, 2.4 Hz, 1H), 3.22 (dd, J = 8.2, 5.9 Hz, 1H), 3.18 (dd, J = 9.8, 2.4 Hz, 1H), 3.15 (dd, J = 10.0, 7.6 Hz, 1H), 2.97 (dd, J = 9.6, 6.8 Hz, 1H), 2.53-2.60 (m, 2H), 2.41 (s, 3H), 2.0 (m, 1H), 1.91-1.99 (m, 1H), 1.80-1.91 (m, 2H), 1.69 (ddd, J = 13.5, 7.7, 5.9 Hz, 1H), 1.52-1.60 (m, 2H), 1.26-1.35 (m, 1H), 0.91 (d, J = 6.6 Hz, 3H), 0.85 (d, J = 6.5 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 396

***N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-prolinamide**

The title compound was prepared by substituting (*S*)-*tert*-butyl 2-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamoyl)pyrrolidine-1-carboxylate from Example 266 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.36-8.37 (bs, 1H), 8.17-8.19 (m, 2H), 7.90-7.92 (m, 1H), 7.72 (t, J = 7.8 Hz, 1H), 4.13-4.19 (m, 1H), 3.81-3.85 (m, 2H), 3.17 (dd, J = 9.6, 2.9 Hz, 1H), 3.05 (dd, J = 9.9, 7.8 Hz, 1H), 2.80-2.91 (m, 3H), 2.50-2.55 (m, 1H), 2.39-2.45 (m, 1H), 1.97-2.09 (m, 2H), 1.96 (m, 1H), 1.84-1.91 (m, 1H), 1.76-1.82 (m, 1H), 1.56-1.65 (m, 1H), 1.48-1.56 (m, 1H), 1.40-1.48 (m, 1H), 1.21-1.29 (m, 1H); MS (ESI+) *m/z* 432 $(M+H)^+$.

Example 397

(3*R*)-3-amino-4-methyl-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide

The title compound was prepared by substituting *tert*-butyl (1*R*)-1-isopropyl-3-oxo-3-[((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]propylcarbamate from Example 267 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37-8.38 (bs, 1H), 8.20 (d, J = 7.9 Hz, 1H), 7.90-7.92 (m, 1H), 7.72 (t, J

= 7.8 Hz, 1H), 4.22-4.27 (m, 1H), 3.86 (dd, *J* = 9.9, 2.4 Hz, 1H), 3.12-3.18 (m, 3H), 2.95 (dd, *J* = 9.6, 6.8 Hz, 1H), 2.51-2.56 (m, 2H), 2.45 (dd, *J* = 14.4, 3.2 Hz, 1H), 2.27 (dd, *J* = 14.4, 9.9 Hz, 1H), 1.90-1.98 (m, 1H), 1.79-1.88 (m, 1H), 1.63-1.83 (m, 3H), 1.49-1.62 (m, 2H), 1.24-1.32 (m, 1H), 0.80-0.95 (m, 6H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Example 398

(2*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)piperidine-2-carboxamide

The title compound was prepared by substituting *tert*-butyl (2*S*)-2-{[((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]carbonyl}piperidine-1-carboxylate from Example 268 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.35-8.36 (bs, 1H), 8.17 (d, *J* = 7.9 Hz, 1H), 7.90-7.92 (m, 1H), 7.78-7.80 (m, 1H), 7.72 (t, *J* = 7.8 Hz, 1H), 4.16-4.23 (m, 1H), 3.83 (dd, *J* = 9.9, 2.7 Hz, 1H), 3.30 (dd, *J* = 10.3, 3.2 Hz, 1H), 3.16 (dd, *J* = 9.6, 2.8 Hz, 1H), 3.04 (dd, *J* = 9.8, 7.8 Hz, 1H), 2.95-3.00 (m, 1H), 2.89 (dd, *J* = 9.6, 7.4 Hz, 1H), 2.49-2.59 (m, 2H), 2.41-2.49 (m, 1H), 2.29-2.51 (m, 1H), 1.96-2.04 (m, 1H), 1.86-1.92 (m, 1H), 1.77-1.83 (m, 1H), 1.64-1.70 (m, 1H), 1.52-1.61 (m, 1H), 1.43-1.53 (m, 1H), 1.34-1.43 (m, 1H), 1.20-1.34 (m, 3H); MS (ESI+) *m/z* 446 $(M+H)^+$.

Example 399

(2*S*)-*N*-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}piperidine-2-carboxamide

Step A: *tert*-Butyl (2*S*)-2-{[((3a*S*,4*R*,6a*R*)-2-{[4-fluorophenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]carbonyl}piperidine-1-carboxylate was prepared by substituting *tert*-butyl (2*S*)-2-({[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]amino}carbonyl)piperidine-1-carboxylate from Example 231 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-fluorobenzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.98 – 7.91 (m, 2H), 7.47 – 7.40 (m, 1H), 7.22 (dd, *J* =

12.0, 5.3, 2H), 4.88 – 4.80 (m, 1H), 4.13 – 4.05 (m, 2H), 3.61 (dd, *J* = 10.1, 3.3, 1H), 3.30 (td, *J* = 12.8, 3.2, 1H), 3.23 (dd, *J* = 10.0, 7.8, 1H), 3.07 (dd, *J* = 8.6, 5.3, 2H), 2.60 – 2.46 (m, 2H), 2.19 (dd, *J* = 12.5, 1.1, 1H), 1.97 – 1.89 (m, 1H), 1.85 – 1.77 (m, 1H), 1.66 – 1.49 (m, 5H), 1.47 (s, 9H), 1.31 (dtdd, *J* = 13.3, 6.8, 6.0, 3.1, 2H); MS (ESI+) *m/z* 513 $(M+NH_4)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (2*S*)-2-{[((3a*S*,4*R*,6a*R*)-2-{[4-fluorophenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]carbonyl}piperidine-1-carboxylate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.96-7.99 (m, 2H), 7.78 (d, *J* = 7.0 Hz, 1H), 7.30-7.34 (m, 2H), 4.20 (p, *J* = 7.0 Hz, 1H), 3.75 (dd, *J* = 9.9, 2.9 Hz, 1H), 3.30 (dd, *J* = 10.3, 3.2 Hz, 1H), 3.11 (dd, *J* = 9.6, 2.9 Hz, 1H), 2.96-3.03 (m, 2H), 2.87 (dd, *J* = 9.6, 7.4 Hz, 1H), 2.48-2.60 (m, 2H), 2.42-2.49 (m, 1H), 2.28-2.46 (m, 1H), 2.00-2.05 (m, 1H), 1.86-1.92 (m, 1H), 1.76-1.83 (m, 1H), 1.66-1.71 (m, 1H), 1.44-1.62 (m, 2H), 1.24-1.41 (m, 4H); MS (ESI+) *m/z* 396 $(M+H)^+$.

Example 400

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-valinamide

Step A: *tert*-Butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxobutan-2-yl(methyl)carbamate from Example 232 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-fluorobenzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.97 – 7.89 (m, 2H), 7.74 – 7.63 (m, 1H), 7.25 – 7.18 (m, 2H), 4.34 (d, *J* = 10.1, 1H), 4.08 (dt, *J* = 13.5, 6.7, 1H), 3.57 (dd, *J* = 10.1, 3.3, 1H), 3.22 – 3.16 (m, 1H), 3.07 (d, *J* = 5.5, 2H), 3.01 (s, 3H), 2.57 – 2.50 (m, 1H), 2.50 – 2.43 (m, 1H), 2.38 (qd, *J* = 13.2, 6.6, 1H), 1.94 (td, *J* = 12.2, 6.5, 1H), 1.86 – 1.77 (m, 1H), 1.54 (ddd, *J* = 16.4, 12.6, 7.7, 1H), 1.45 (s, 9H), 1.34 – 1.24 (m, 1H), 0.98 (d, *J* = 6.5, 3H), 0.86 (d, *J* = 6.7, 3H) ; MS (ESI+) *m/z* 498 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-

ylamino)butan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.13-8.31 (m, 1H), 7.99-8.02 (m, 2H), 7.30-7.34 (m, 2H), 4.24-4.29 (m, 1H), 3.78 (dd, J = 9.9, 2.5 Hz, 1H), 3.11-3.14 (m, 2H), 2.94 (dd, J = 9.6, 6.9 Hz, 1H), 2.87 (d, J = 5.8 Hz, 1H), 2.47-2.58 (m, 2H), 2.37 (s, 3H), 2.05-2.14 (m, 1H), 1.92-2.08 (m, 1H), 1.91-1.98 (m, 1H), 1.80-1.87 (m, 1H), 1.51-1.59 (m, 1H), 1.25-1.35 (m, 1H), 0.98-1.08 (m, 6H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Example 401

(2*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)piperidine-2-carboxamide

Step A: *tert*-Butyl (2*S*)-2-{[((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]carbonyl}piperidine-1-carboxylate was prepared by substituting *tert*-butyl (2*S*)-2-({[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]amino}carbonyl)piperidine-1-carboxylate from Example 231 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.08 (d, J = 8.1, 2H), 7.82 (d, J = 8.2, 2H), 7.46 (d, J = 5.2, 1H), 4.84 (d, J = 3.3, 1H), 4.09 (dt, J = 13.3, 6.6, 2H), 3.68 (dd, J = 10.2, 3.3, 1H), 3.34 – 3.24 (m, 2H), 3.12 (d, J = 5.5, 2H), 2.61 – 2.48 (m, 2H), 2.22 – 2.15 (m, 1H), 1.93 (dt, J = 11.8, 6.6, 1H), 1.81 (dtd, J = 12.7, 7.6, 4.8, 1H), 1.65 – 1.49 (m, 5H), 1.47 (s, 9H), 1.40 – 1.24 (m, 2H); MS (ESI+) *m/z* 563 $(M+NH_4)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (2*S*)-2-{[((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]carbonyl}piperidine-1-carboxylate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.10-8.13 (m, 2H), 7.89-7.92 (m, 2H), 7.79 (d, J = 7.0 Hz, 1H), 4.17-4.22 (m, 1H), 3.82 (dd, J = 9.9, 2.8 Hz, 1H), 3.30 (dd, J = 10.3, 3.2 Hz, 1H), 3.16 (dd, J = 9.6, 2.9

Hz, 1H), 3.03-3.07 (m, 1H), 2.96-2.99 (m, 1H), 2.92 (dd, J = 9.6, 7.4 Hz, 1H), 2.50-2.59 (m, 2H), 2.43-2.50 (m, 1H), 2.27-2.53 (m, 1H), 2.00-2.04 (m, 1H), 1.86-1.92 (m, 1H), 1.76-1.83 (m, 1H), 1.64-1.70 (m, 1H), 1.53-1.63 (m, 1H), 1.43-1.53 (m, 1H), 1.35-1.43 (m, 1H), 1.20-1.35 (m, 3H); MS (ESI+) *m/z* 446 $(M+H)^+$.

Example 402

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide

Step A: *tert*-Butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxobutan-2-yl(methyl)carbamate from Example 232 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.07 (d, J = 8.2, 2H), 7.82 (d, J = 8.2, 2H), 7.72 (s, 1H), 4.34 (d, J = 10.4, 1H), 4.09 (dd, J = 13.6, 6.7, 1H), 3.64 (dd, J = 10.2, 3.3, 1H), 3.26 – 3.19 (m, 1H), 3.15 – 3.07 (m, 2H), 3.01 (s, 3H), 2.58 – 2.51 (m, 1H), 2.50 – 2.44 (m, 1H), 2.38 (qd, J = 13.2, 6.6, 1H), 1.93 (td, J = 12.1, 6.5, 1H), 1.82 (td, J = 12.7, 7.5, 1H), 1.53 (ddd, J = 15.6, 12.6, 8.3, 1H), 1.45 (s, 9H), 1.29 (ddd, J = 15.9, 13.2, 6.7, 1H), 0.97 (d, J = 6.5, 3H), 0.86 (d, J = 6.7, 3H); MS (ESI+) *m/z* 548 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.22-8.25 (m, 1H), 8.13-8.15 (m, 2H), 7.89-7.92 (m, 2H), 4.23-4.29 (m, 1H), 3.86 (dd, J = 9.9, 2.6 Hz, 1H), 3.13-3.20 (m, 2H), 2.98 (dd, J = 9.6, 7.0 Hz, 1H), 2.87 (d, J = 5.8 Hz, 1H), 2.50-2.59 (m, 2H), 2.37 (s, 3H), 2.05-2.13 (m, 1H), 1.93-2.11 (m, 1H), 1.90-1.98 (m, 1H), 1.80-1.87 (m, 1H), 1.51-1.58 (m, 1H), 1.26-1.34 (m, 1H), 1.04 (d, J = 6.9 Hz, 3H), 1.02 (d, J = 6.9 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Example 403

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate from Example 330 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.23 (d, J = 7.2 Hz, 1H), 7.98-8.01 (m, 2H), 7.30-7.34 (m, 2H), 4.26 (p, J = 6.8 Hz, 1H), 3.77 (dd, J = 9.9, 2.7 Hz, 1H), 3.09-3.15 (m, 3H), 2.93 (dd, J = 9.6, 7.1 Hz, 1H), 2.47-2.58 (m, 2H), 2.38 (s, 3H), 1.92-2.21 (m, 1H), 1.91-1.99 (m, 1H), 1.75-1.87 (m, 2H), 1.64-1.71 (m, 1H), 1.51-1.60 (m, 1H), 1.38-1.51 (m, 2H), 1.25-1.35 (m, 1H), 0.84 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Example 404

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 331 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.24-8.26 (m, 1H), 8.12-8.15 (m, 2H), 7.89-7.92 (m, 2H), 4.26 (p, J = 6.9 Hz, 1H), 3.85 (dd, J = 9.9, 2.7 Hz, 1H), 3.18 (dd, J = 9.6, 2.7 Hz, 1H), 3.15 (dd, J = 7.7, 3.9 Hz, 1H), 3.13 (d, J = 7.0 Hz, 1H), 2.97 (dd, J = 9.6, 7.2 Hz, 1H), 2.51-2.61 (m, 2H), 2.38 (s, 3H), 1.95-2.31 (m, 1H), 1.92-1.98 (m, 1H), 1.75-1.87 (m, 2H), 1.64-1.72 (m, 1H), 1.51-1.59 (m, 1H), 1.39-1.52 (m, 2H), 1.30 (ddt, J = 9.7, 13.0, 6.5 Hz, 1H), 0.84 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Example 405

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 259 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.20-8.23 (m, 1H), 8.13-8.15 (m, 2H), 7.89-7.92 (m, 2H), 4.22-4.29 (m, 1H), 3.85 (dd, J = 9.9, 2.7 Hz, 1H), 3.18 (dd, J = 9.7, 2.7 Hz, 1H), 3.11-3.16 (m, 2H), 2.96 (dd, J = 9.6, 7.1 Hz, 1H), 2.50-2.61 (m, 2H), 2.38 (s, 3H), 1.98-2.07 (m, 1H), 1.90-1.98 (m, 1H), 1.75-1.87 (m, 2H), 1.63-1.70 (m, 1H), 1.41-1.58 (m, 3H), 1.26-1.33 (m, 1H), 0.84 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Example 406

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate from Example 340 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.39-8.40 (bs, 1H), 8.24 (d, J = 7.2 Hz, 1H), 8.18-8.22 (m, 1H), 7.90-7.92 (m, 1H), 7.72 (t, J = 7.8 Hz, 1H), 4.24-4.30 (m, 1H), 3.86 (dd, J = 9.9, 2.3 Hz, 1H), 3.14-3.20 (m, 2H), 2.96 (dd, J = 9.7, 7.1 Hz, 1H), 2.86 (d, J = 5.8 Hz, 1H), 2.50-2.57 (m, 2H), 2.37 (s, 3H), 2.04-2.13 (m, 1H), 1.88-2.08 (m, 1H), 1.89-1.98 (m, 1H), 1.80-1.89 (m, 1H), 1.50-1.59 (m, 1H), 1.25-1.34 (m, 1H), 1.03 (d, J = 6.9 Hz, 3H), 1.01 (d, J = 7.0 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Example 407

N^1-((3a*S*,4*R*,6a*R*)-2-{[4-fluoro-3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-methyl-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluoro-3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Example 327 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.35 (dd, *J* = 6.5, 1.9 Hz, 1H), 8.31 (d, *J* = 7.3 Hz, 1H), 8.26 (ddd, *J* = 8.5, 4.7, 2.4 Hz, 1H), 7.53-7.58 (m, 1H), 4.24-4.30 (m, 1H), 3.88 (dd, *J* = 9.9, 2.5 Hz, 1H), 3.16-3.20 (m, 3H), 3.00 (dd, *J* = 9.6, 7.2 Hz, 1H), 2.53-2.62 (m, 2H), 2.38 (s, 3H), 1.82-2.01 (m, 4H), 1.67 (ddd, *J* = 13.5, 7.8, 5.7 Hz, 1H), 1.53-1.59 (m, 2H), 1.32 (ddt, *J* = 9.7, 12.9, 6.5 Hz, 1H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.84 (d, *J* = 6.5 Hz, 3H); MS (ESI+) *m/z* 480 $(M+H)^+$.

Example 408

3-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-3,3-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-ylcarbamate from Example 341 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.25 (d, *J* = 6.7 Hz, 1H), 8.12-8.16 (m, 2H), 7.90-7.92 (m, 2H), 4.18-4.24 (m, 1H), 3.82 (dd, *J* = 10.0, 2.3 Hz, 1H), 3.24 (s, 1H), 3.13-3.18 (m, 2H), 2.98 (dd, *J* = 9.5, 6.5 Hz, 1H), 2.49-2.60 (m, 2H), 1.93-2.29 (m, 2H), 1.85-1.95 (m, 1H), 1.77-1.85 (m, 1H), 1.47-1.55 (m, 1H), 1.22-1.31 (m, 1H), 1.12 (s, 9H); MS (ESI-) *m/z* 446 $(M-H)^-$.

Example 409

3-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-3,3-dimethyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-

ylamino)butan-2-ylcarbamate from Example 342 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.23 (d, J = 6.7 Hz, 1H), 8.12-8.14 (m, 2H), 7.89-7.91 (m, 2H), 4.18-4.25 (m, 1H), 3.80 (dd, J = 9.9, 2.7 Hz, 1H), 3.24 (s, 1H), 3.16 (dd, J = 9.7, 2.8 Hz, 1H), 3.10 (dd, J = 9.9, 7.5 Hz, 1H), 2.95 (dd, J = 9.6, 7.2 Hz, 1H), 2.45-2.55 (m, 2H), 1.96-2.22 (m, 2H), 1.88-1.96 (m, 1H), 1.78-1.85 (m, 1H), 1.49-1.57 (m, 1H), 1.20-1.32 (m, 1H), 1.11 (s, 9H).

Example 410

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-isoleucinamide

The title compound was prepared by substituting *tert*-butyl methyl((2*S*,3*S*)-3-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 332 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.39-8.40 (bs, 1H), 8.24 (d, J = 7.2 Hz, 1H), 8.19-8.22 (m, 1H), 7.91-7.93 (m, 1H), 7.73 (d, J = 7.9 Hz, 1H), 4.24-4.30 (m, 1H), 3.87 (dd, J = 9.9, 2.3 Hz, 1H), 3.13-3.20 (m, 2H), 2.95 (d, J = 6.3 Hz, 2H), 2.50-2.58 (m, 2H), 2.38 (s, 3H), 1.89-2.02 (m, 1H), 1.90-1.98 (m, 1H), 1.79-1.89 (m, 2H), 1.72-1.82 (m, 1H), 1.51-1.59 (m, 1H), 1.23-1.40 (m, 2H), 1.00 (d, J = 6.8 Hz, 3H), 0.86 (t, J = 7.4 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 411

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-isoleucinamide

The title compound was prepared by substituting *tert*-butyl methyl((2*S*,3*S*)-3-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 333 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.24-8.26 (m, 1H), 8.13-8.16 (m, 2H), 7.90-7.92 (m, 2H), 4.23-4.30 (m, 1H), 3.86 (dd, J = 9.9, 2.5 Hz, 1H), 3.19 (dd, J = 9.6, 2.4 Hz, 1H), 3.15 (dd, J = 9.8, 7.6 Hz, 1H), 2.97 (dd, J = 9.4, 6.9 Hz, 1H), 2.95 (d, J = 6.0 Hz, 1H), 2.52-2.60 (m, 2H), 2.39 (s, 3H),

1.92-2.04 (m, 1H), 1.91-1.97 (m, 1H), 1.80-1.88 (m, 2H), 1.72-1.80 (m, 1H), 1.51-1.60 (m, 1H), 1.25-1.36 (m, 2H), 1.01 (d, J = 6.9 Hz, 3H), 0.86 (t, J = 7.4 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 412

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-isoleucinamide

The title compound was prepared by substituting *tert*-butyl methyl((2*S*,3*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 334 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.23-8.26 (m, 1H), 8.12-8.16 (m, 2H), 7.89-7.91 (m, 2H), 4.24-4.29 (m, 1H), 3.86 (dd, J = 9.9, 2.5 Hz, 1H), 3.15-3.20 (m, 2H), 2.98 (dd, J = 9.6, 6.9 Hz, 1H), 2.94 (d, J = 6.1 Hz, 1H), 2.50-2.62 (m, 2H), 2.38 (s, 3H), 1.91-2.04 (m, 1H), 1.91-1.98 (m, 1H), 1.80-1.88 (m, 2H), 1.72-1.80 (m, 1H), 1.51-1.59 (m, 1H), 1.24-1.35 (m, 2H), 1.00 (d, J = 6.8 Hz, 3H), 0.85 (t, J = 7.4 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 413

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-isoleucinamide

The title compound was prepared by substituting *tert*-butyl methyl((2*S*,3*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 335 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.38-8.39 (bs, 1H), 8.24 (d, J = 7.0 Hz, 1H), 8.19-8.22 (m, 1H), 7.90-7.92 (m, 1H), 7.72 (t, J = 7.8 Hz, 1H), 4.23-4.30 (m, 1H), 3.86 (dd, J = 9.9, 2.2 Hz, 1H), 3.14-3.20 (m, 2H), 2.97 (dd, J = 9.6, 6.6 Hz, 1H), 2.93 (d, J = 6.1 Hz, 1H), 2.55 (t, J = 4.5 Hz, 2H), 2.37 (s, 3H), 1.92-2.10 (m, 1H), 1.91-1.99 (m, 1H), 1.80-1.89 (m, 2H), 1.71-1.81 (m, 1H), 1.51-1.59 (m, 1H), 1.24-1.40 (m, 2H), 0.99 (d, J = 6.8 Hz, 3H), 0.84 (t, J = 7.4 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 414

N^2,4-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate from Example 336 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.38-8.40 (m, 1H), 8.34 (d, J = 6.9 Hz, 1H), 8.20-8.22 (m, 1H), 7.90-7.93 (m, 1H), 7.73 (d, J = 7.9 Hz, 1H), 4.23-4.28 (m, 1H), 3.89 (dd, J = 9.9, 2.1 Hz, 1H), 3.16-3.21 (m, 2H), 3.15 (dd, J = 9.8, 7.4 Hz, 1H), 2.93-2.97 (m, 1H), 2.50-2.58 (m, 2H), 2.38 (s, 3H), 2.00-2.06 (m, 1H), 1.90-1.99 (m, 1H), 1.90 (dd, J = 14.1, 5.1 Hz, 1H), 1.79-1.87 (m, 1H), 1.51-1.60 (m, 1H), 1.48 (dd, J = 14.0, 6.5 Hz, 1H), 1.25-1.32 (m, 1H), 0.97 (s, 9H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Example 415

N^2,4-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate from Example 337 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37-8.40 (m, 1H), 8.14-8.16 (m, 2H), 7.90-7.92 (m, 2H), 4.23-4.27 (m, 1H), 3.87 (dd, J = 9.9, 2.2 Hz, 1H), 3.22 (t, J = 5.9 Hz, 1H), 3.18 (dd, J = 9.7, 2.1 Hz, 1H), 3.15 (dd, J = 9.9, 7.5 Hz, 1H), 2.95-2.99 (m, 1H), 2.55-2.58 (m, 2H), 2.40 (s, 3H), 1.91-1.98 (m, 1H), 1.92 (dd, J = 14.0, 5.1 Hz, 2H), 1.80-1.86 (m, 1H), 1.52-1.61 (m, 1H), 1.50 (dd, J = 14.0, 6.4 Hz, 1H), 1.25-1.34 (m, 1H), 0.97 (s, 9H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Example 416

N^2,4-dimethyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate from Example 338 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37-8.39 (bs, 1H), 8.33-8.36 (m, 1H), 8.18-8.21 (m, 1H), 7.91 (d, J = 7.0 Hz, 1H), 7.72 (t, J = 7.8 Hz, 1H), 4.23-4.29 (m, 1H), 3.88 (dd, J = 9.9, 2.1 Hz, 1H), 3.12-3.20 (m, 3H), 2.94 (dd, J = 9.6, 6.6 Hz, 1H), 2.54 (t, J = 4.6 Hz, 2H), 2.37 (s, 3H), 1.92-2.00 (m, 1H), 1.75-2.14 (m, 1H), 1.90 (dd, J = 14.0, 5.2 Hz, 1H), 1.80-1.87 (m, 1H), 1.51-1.59 (m, 1H), 1.49 (dd, J = 14.0, 6.6 Hz, 1H), 1.24-1.33 (m, 1H), 0.96 (s, 9H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Example 417

N^2,4-dimethyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate from Example 339 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.36-8.38 (m, 1H), 8.13-8.15 (m, 2H), 7.89-7.91 (m, 2H), 4.22-4.29 (m, 1H), 3.87 (d, J = 10.4 Hz, 1H), 3.16-3.20 (m, 2H), 3.14 (dd, J = 9.9, 7.5 Hz, 1H), 2.96 (dd, J = 9.6, 6.8 Hz, 1H), 2.54-2.59 (m, 2H), 2.38 (s, 3H), 1.91-1.99 (m, 1H), 1.95 (m, 1H), 1.91 (dd, J = 14.0, 5.2 Hz, 1H), 1.79-1.87 (m, 1H), 1.52-1.60 (m, 1H), 1.50 (dd, J = 14.0, 6.6 Hz, 1H), 1.26-1.33 (m, 1H), 0.96 (s, 9H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Example 418

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norleucinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)hexan-2-yl)carbamate from Example 343 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.21-8.24 (m, 1H), 8.13-8.15 (m, 2H), 7.90-7.92 (m, 2H), 4.23-4.30 (m, 1H), 3.86 (dd, J = 9.9, 2.5 Hz, 1H), 3.18 (dd, J = 9.6, 2.6 Hz, 1H), 3.12-3.16 (m, 2H), 2.96 (dd, J = 9.6, 7.0 Hz, 1H), 2.54-2.61 (m, 2H), 2.40 (s, 3H), 1.94-2.28 (m, 1H), 1.91-1.98 (m, 1H), 1.78-1.87 (m, 2H), 1.65-1.73 (m, 1H), 1.51-1.59 (m, 1H), 1.36-1.50 (m, 2H), 1.27-1.34 (m, 1H), 1.24 (h, J = 7.4 Hz, 2H), 0.81 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 419

4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate from Example 344 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.39-8.41 (m, 1H), 8.13-8.15 (m, 2H), 7.90-7.92 (m, 2H), 4.18-4.24 (m, 1H), 3.85 (dd, J = 9.9, 2.6 Hz, 1H), 3.59 (dd, J = 7.4, 4.3 Hz, 1H), 3.16 (dd, J = 9.6, 2.8 Hz, 1H), 3.10 (dd, J = 9.9, 7.4 Hz, 1H), 2.95 (dd, J = 9.6, 7.1 Hz, 1H), 2.48-2.58 (m, 2H), 2.16 (dd, J = 14.0, 4.3 Hz, 1H), 2.06-2.22 (m, 1H), 1.88-1.95 (m, 1H), 1.78-1.83 (m, 1H), 1.47-1.55 (m, 1H), 1.43 (dd, J = 13.9, 7.4 Hz, 1H), 1.23-1.31 (m, 1H), 0.98 (s, 9H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 420

N^2-methyl-N^1-((3a*R*,4*R*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*R*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 328 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.52 (d, J = 7.9 Hz, 1H), 8.10-8.15 (m, 2H), 7.88-7.91 (m, 2H), 4.44-4.50 (m, 1H), 3.63 (dd, J = 9.5, 2.8 Hz, 1H), 3.23-3.26 (m, 1H), 3.14-3.19 (m, 1H), 2.98 (dd, J = 25.4, 9.3 Hz, 3H), 2.49-2.56 (m, 1H), 2.48 (s, 3H), 1.86-1.92 (m, 1H), 1.90 (m, 1H), 1.75-1.83 (m, 1H), 1.69-1.75 (m, 2H), 1.59-1.68 (m, 1H), 1.44-1.59 (m, 2H), 1.33-1.39 (m, 1H), 0.88 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Example 421

N^2-methyl-N^1-((3a*R*,4*R*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*R*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 329 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.60-8.65 (m, 1H), 8.12-8.14 (m, 2H), 7.88-7.91 (m, 2H), 4.45-4.50 (m, 1H), 3.63-3.66 (m, 1H), 3.33-3.37 (m, 1H), 3.15 (dd, J = 9.6, 3.0 Hz, 1H), 2.95-3.05 (m, 3H), 2.51 (s, 3H), 2.46-2.52 (m, 1H), 1.91-1.97 (m, 2H), 1.78-1.83 (m, 1H), 1.72-1.75 (m, 3H), 1.63 (dq, J = 13.0, 8.2 Hz, 1H), 1.34-1.39 (m, 1H), 0.94 (d, J = 6.5 Hz, 3H), 0.88 (d, J = 6.5 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 422

N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

Step A: *tert*-Butyl-((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-

yl)carbamate was prepared by substituting *tert*-butyl ((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 382 Step A for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.13 (d, J = 8.1, 2H), 7.96 (d, J = 8.0, 1H), 7.90 (d, J = 8.3, 2H), 4.60 (dd, J = 14.5, 8.2, 1H), 4.27 – 4.18 (m, 1H), 3.81 (dd, J = 9.8, 1.5, 1H), 3.21 – 3.10 (m, 2H), 2.99 – 2.92 (m, 1H), 2.61 – 2.50 (m, 2H), 2.00 (dd, J = 14.3, 5.4, 1H), 1.84 (ddd, J = 13.4, 11.2, 6.8, 3H), 1.55 – 1.44 (m, 13H), 1.25 (d, J = 8.9, 1H), 0.81 (t, J = 7.3, 3H); MS (ESI+) *m/z* 551 $(M+NH_4)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl-((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.28 (d, J = 7.0 Hz, 1H), 8.11-8.15 (m, 2H), 7.89-7.92 (m, 2H), 4.17-4.24 (m, 1H), 3.82 (dd, J = 9.9, 2.8 Hz, 1H), 3.52 (dd, J = 7.9, 4.9 Hz, 1H), 3.16 (dd, J = 9.6, 2.9 Hz, 1H), 3.09 (dd, J = 9.9, 7.7 Hz, 1H), 2.94 (dd, J = 9.6, 7.3 Hz, 1H), 2.46-2.57 (m, 2H), 2.07-2.18 (m, 2H), 1.88-1.96 (m, 2H), 1.77-1.84 (m, 1H), 1.63 (dddd, J = 13.1, 8.0, 10.1, 5.1 Hz, 1H), 1.40-1.53 (m, 3H), 1.23-1.32 (m, 1H), 0.85 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 434 $(M+H)^+$.

Example 423

N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

Step A: *tert*-Butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl carbamate was prepared by substituting *N*-(*tert*-butoxycarbonyl) L-norvaline for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Example 16 Step E for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.58 (d, J = 7.2, 1H), 7.91 (d, J = 8.3, 1H), 7.42 (d, J = 7.3, 2H), 7.36 (t, J = 7.4, 2H), 7.27 (t, J = 7.2, 1H), 4.64 (dd, J = 14.4, 7.7, 1H), 4.45 – 4.35 (m, 1H), 3.56 (d, J = 13.1, 1H), 3.40 (d, J = 13.2, 1H), 2.74 (d, J = 8.9, 1H), 2.52 – 2.43 (m,

2H), 2.39 – 2.27 (m, 2H), 2.26 – 2.19 (m, 1H), 2.14 (dq, J = 12.0, 6.0, 1H), 2.02 (dt, J = 13.9, 6.7, 1H), 1.85 (td, J = 13.8, 8.2, 2H), 1.65 (td, J = 14.3, 7.3, 1H), 1.49 (d, J = 8.5, 11H), 1.44 – 1.32 (m, 1H), 0.86 – 0.76 (m, 3H); MS (ESI+) m/z 416 $(M+H)^+$.

Step B: *tert*-Butyl-((*S*)-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl carbamate from Step A for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.79 (d, J = 6.8, 1H), 8.11 (d, J = 8.1, 2H), 7.98 (d, J = 8.1, 1H), 7.90 (d, J = 8.3, 2H), 4.59 (dd, J = 14.4, 7.8, 1H), 4.28 – 4.20 (m, 1H), 3.78 (d, J = 9.7, 1H), 3.14 (d, J = 9.6, 1H), 3.05 – 2.98 (m, 1H), 2.93 – 2.86 (m, 1H), 2.50 (d, J = 2.3, 2H), 2.02 – 1.92 (m, 2H), 1.88 – 1.77 (m, 2H), 1.63 – 1.53 (m, 1H), 1.53 – 1.38 (m, 11H), 1.33 – 1.22 (m, 1H), 0.79 (t, J = 7.4, 3H); MS (ESI+) m/z 551 $(M+NH_4)^+$.

Step C: The title compound was prepared by substituting *tert*-butyl-((*S*)-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step B for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.27 (d, J = 7.2 Hz, 1H), 8.10-8.14 (m, 2H), 7.89-7.91 (m, 2H), 4.18-4.24 (m, 1H), 3.83 (dd, J = 9.9, 2.9 Hz, 1H), 3.51 (dd, J = 7.9, 4.9 Hz, 1H), 3.16 (dd, J = 9.6, 2.9 Hz, 1H), 3.08 (dd, J = 9.9, 7.7 Hz, 1H), 2.93 (dd, J = 9.6, 7.4 Hz, 1H), 2.45-2.56 (m, 2H), 2.03-2.23 (m, 2H), 1.88-1.95 (m, 2H), 1.77-1.84 (m, 1H), 1.64 (dddd, J = 13.1, 8.1, 10.1, 5.1 Hz, 1H), 1.38-1.54 (m, 3H), 1.24-1.32 (m, 1H), 0.84 (t, J = 7.3 Hz, 3H); MS (ESI-) m/z 432 $(M-H)^-$.

Example 424

N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

Step A: *tert*-Butyl-((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting *tert*-butyl ((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-

benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 382 Step A for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide in the procedure described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.70 (d, *J* = 6.9, 1H), 8.37 (s, 1H), 8.18 (d, *J* = 7.8, 1H), 7.95 (d, *J* = 8.0, 1H), 7.91 (d, *J* = 7.8, 1H), 7.72 (t, *J* = 7.9, 1H), 4.59 (dd, *J* = 14.1, 7.8, 1H), 4.23 (dt, *J* = 13.0, 6.5, 1H), 3.82 (dd, *J* = 9.7, 1.4, 1H), 3.18 – 3.07 (m, 2H), 2.98 – 2.90 (m, 1H), 2.62 – 2.48 (m, 2H), 2.00 (ddd, *J* = 15.3, 11.0, 6.5, 1H), 1.91 – 1.74 (m, 3H), 1.57 – 1.39 (m, 12H), 1.23 (ddd, *J* = 16.9, 12.6, 6.1, 1H), 0.81 (t, *J* = 7.3, 3H); MS (ESI+) *m/z* 551 $(M+NH_4)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl-((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.36-8.37 (bs, 1H), 8.26 (d, *J* = 6.9 Hz, 1H), 8.17-8.20 (m, 1H), 7.90-7.92 (m, 1H), 7.70-7.74 (m, 1H), 4.18-4.24 (m, 1H), 3.83 (dd, *J* = 9.8, 2.7 Hz, 1H), 3.52 (dd, *J* = 7.9, 4.9 Hz, 1H), 3.16 (dd, *J* = 9.6, 2.8 Hz, 1H), 3.07 (dd, *J* = 9.9, 7.5 Hz, 1H), 2.91 (dd, *J* = 9.6, 7.3 Hz, 1H), 2.44-2.54 (m, 2H), 1.95-2.28 (m, 2H), 1.86-1.99 (m, 2H), 1.77-1.84 (m, 1H), 1.59-1.66 (m, 1H), 1.39-1.54 (m, 3H), 1.22-1.32 (m, 1H), 0.84 (t, *J* = 7.3 Hz, 3H); MS (ESI+) *m/z* 434 $(M+H)^+$.

Example 425

N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

Step A: *tert*-Butyl-((*S*)-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl carbamate from Example 423 Step A for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide in the procedure described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.77 (d, *J* = 6.9, 1H), 8.35 (s, 1H), 8.16 (d, *J* = 7.7, 1H), 7.96 (d, *J* = 8.2, 1H), 7.90 (d, *J* = 8.0, 1H), 7.72 (t, *J* = 7.9, 1H), 4.58 (dd, *J* = 14.4, 8.0, 1H), 4.30 – 4.20 (m, 1H), 3.84 – 3.75 (m, 1H), 3.15 (d, *J* = 9.4, 1H), 3.04 – 2.95 (m, 1H), 2.91 – 2.79 (m, 1H), 2.47 (dd, *J* = 2.3, 1.2, 2H), 2.03 – 1.91 (m, 2H), 1.88 – 1.76 (m, 2H), 1.64 – 1.53 (m, 1H),

1.53 – 1.40 (m, 11H), 1.33 – 1.19 (m, 1H), 0.79 (t, J = 7.3, 3H); MS (ESI+) *m/z* 551 $(M+NH_4)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl-((*S*)-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting *tert*-butyl-((*S*)-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.35-8.37 (m, 1H), 8.27 (d, J = 7.0 Hz, 1H), 8.17-8.19 (m, 1H), 7.90-7.92 (m, 1H), 7.72 (t, J = 7.8 Hz, 1H), 4.18-4.25 (m, 1H), 3.84 (dd, J = 9.9, 2.7 Hz, 1H), 3.51 (dd, J = 7.9, 4.9 Hz, 1H), 3.17 (dd, J = 9.6, 2.8 Hz, 1H), 3.07 (dd, J = 9.9, 7.6 Hz, 1H), 2.91 (dd, J = 9.6, 7.3 Hz, 1H), 2.43-2.54 (m, 2H), 1.96-2.32 (m, 2H), 1.87-1.95 (m, 2H), 1.78-1.84 (m, 1H), 1.59-1.67 (m, 1H), 1.37-1.53 (m, 3H), 1.23-1.32 (m, 1H), 0.83 (t, J = 7.3 Hz, 3H); MS (ESI-) *m/z* 432 $(M-H)^-$.

Example 426

3-cyclohexyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-alaninamide

Step A: *tert*-Butyl (*S*)-3-cyclohexyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)propan-2-ylcarbamate was prepared by substituting (*S*)-2-(*tert*-butoxycarbonylamino)-3-cyclohexylpropanoic acid for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 256 Step A for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.76 (s, 1H), 8.13 (d, J = 8.1, 2H), 8.01 (d, J = 8.3, 1H), 7.90 (d, J = 8.3, 2H), 4.74 – 4.65 (m, 1H), 4.31 – 4.19 (m, 1H), 3.85 – 3.78 (m, 1H), 3.21 – 3.10 (m, 2H), 3.01 – 2.93 (m, 1H), 2.64 – 2.51 (m, 2H), 1.96 – 1.74 (m, 6H), 1.69 – 1.60 (m, 1H), 1.60 – 1.45 (m, 13H), 1.32 – 1.18 (m, 1H), 1.16 – 0.96 (m, 3H), 0.94 – 0.81 (m, 1H), 0.79 – 0.67 (m, 1H); MS (ESI+) *m/z* 605 $(M+NH_4)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (*S*)-3-cyclohexyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-

ylamino)propan-2-ylcarbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.35 (d, J = 7.0 Hz, 1H), 8.12-8.15 (m, 2H), 7.90-7.92 (m, 2H), 4.20-4.26 (m, 1H), 3.83 (dd, J = 9.9, 2.7 Hz, 1H), 3.63 (dd, J = 9.2, 4.7 Hz, 1H), 3.17 (dd, J = 9.7, 2.8 Hz, 1H), 3.10 (dd, J = 9.8, 7.6 Hz, 1H), 2.96 (dd, J = 9.6, 7.2 Hz, 1H), 2.46-2.61 (m, 2H), 1.97-2.47 (m, 2H), 1.86-1.96 (m, 2H), 1.78-1.86 (m, 1H), 1.72-1.78 (m, 1H), 1.65-1.71 (m, 1H), 1.47-1.62 (m, 6H), 1.22-1.33 (m, 1H), 0.99-1.23 (m, 3H), 0.91 (qd, J = 12.5, 3.4 Hz, 1H), 0.79 (qd, J = 12.0, 3.4 Hz, 1H); MS (ESI+) *m/z* 488 $(M+H)^+$.

Example 427

3-cyclohexyl-N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-alaninamide

Step A: *tert*-Butyl (*S*)-3-cyclohexyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)propan-2-yl(methyl)carbamate was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-3-cyclohexylpropanoic acid for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 256 Step A for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.51 (d, J = 6.9, 1H), 8.13 (d, J = 8.2, 2H), 7.90 (d, J = 8.3, 2H), 5.23 – 5.14 (m, 0.4H), 4.89 – 4.79 (m, 0.6H), 4.28 – 4.15 (m, 1H), 3.83 (d, J = 10.6, 1H), 3.17 – 3.01 (m, 5H), 2.94 (dd, J = 9.4, 7.2, 1H), 2.57 – 2.48 (m, 2H), 1.99 – 1.74 (m, 5H), 1.67 (d, J = 13.1, 1H), 1.62 – 1.48 (m, 4H), 1.45 (s, 9H), 1.34 – 1.20 (m, 2H), 1.18 – 1.00 (m, 3H), 0.98 – 0.85 (m, 1H), 0.81 – 0.66 (m, 1H); MS (ESI+) *m/z* 602 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (*S*)-3-cyclohexyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)propan-2-yl(methyl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.30 (d, J = 7.2 Hz, 1H), 8.13-8.16 (m, 2H), 7.89-7.93 (m, 2H), 4.24-4.32 (m, 1H), 3.86 (dd, J = 9.9, 2.3 Hz, 1H), 3.25 (dd, J = 7.8, 5.6 Hz, 1H), 3.13-3.21 (m, 2H),

2.98 (dd, J = 9.5, 6.8 Hz, 1H), 2.47-2.63 (m, 2H), 2.41 (s, 3H), 1.95-2.23 (m, 1H), 1.91-1.99 (m, 1H), 1.79-1.90 (m, 1H), 1.66-1.78 (m, 3H), 1.51-1.62 (m, 6H), 1.26-1.35 (m, 1H), 1.00-1.23 (m, 3H), 0.76-0.93 (m, 2H); MS (ESI+) *m/z* 502 $(M+H)^+$.

Example 428

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-5-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-L-leucinamide

Step A: *tert*-Butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(2-chloror-5-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-ylcarbamate from Example 226 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 2-chlroro-5-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.56 (d, J = 1.9, 1H), 8.14 (d, J = 8.7, 1H), 7.80 (dd, J = 8.3, 1.9, 1H), 7.73 (d, J = 8.3, 1H), 4.92 (s, 1H), 4.70 (td, J = 8.3, 5.1, 1H), 4.34 – 4.25 (m, 1H), 3.91 (dd, J = 10.1, 2.9, 1H), 3.54 (dd, J = 10.2, 7.7, 1H), 3.36 (dd, J = 9.9, 7.5, 1H), 3.27 (dd, J = 10.0, 3.3, 1H), 2.72 – 2.57 (m, 2H), 2.13 (dd, J = 14.1, 4.8, 1H), 1.94 (qd, J = 6.4, 1.2, 1H), 1.86 – 1.77 (m, 2H), 1.60 – 1.52 (m, 1H), 1.49 (s, 9H), 1.35 – 1.25 (m, 1H), 0.96 (s, 9H); MS (ESI+) *m/z* 596 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(2-chloror-5-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.56 (d, J = 2.2 Hz, 1H), 8.41 (d, J = 7.0 Hz, 1H), 7.80 (dd, J = 8.3, 2.2 Hz, 1H), 7.74 (d, J = 8.3 Hz, 1H), 4.25-4.32 (m, 1H), 3.94 (dd, J = 10.2, 2.6 Hz, 1H), 3.58 (dd, J = 7.4, 4.3 Hz, 1H), 3.49 (dd, J = 10.1, 7.2 Hz, 1H), 3.34 (dd, J = 9.9, 7.0 Hz, 1H), 3.30 (dd, J = 9.9, 3.1 Hz, 1H), 2.58-2.66 (m, 2H), 1.87-2.45 (m, 2H), 2.14 (dd, J = 14.0, 4.4 Hz, 1H), 1.96-2.04 (m, 1H), 1.82-1.88 (m, 1H), 1.52-1.60 (m, 1H), 1.41 (dd, J = 13.9, 7.5 Hz, 1H), 1.30-1.38 (m, 1H), 0.97 (s, 9H); MS (ESI-) *m/z* 494 $(M-H)^-$.

Example 429

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-L-leucinamide

Step A: *tert*-Butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(2-chloror-4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-ylcarbamate from Example 226 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 2-chloro-4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.33 (d, J = 8.2, 1H), 8.14 (d, J = 8.7, 1H), 7.99 (s, 1H), 7.75 – 7.71 (m,.1H), 4.95 (s, 1H), 4.71 (td, J = 8.3, 4.9, 1H), 4.33 – 4.25 (m, 1H), 3.92 (dd, J = 10.2, 2.9, 1H), 3.53 (dd, J = 10.2, 7.7, 1H), 3.38 (dd, J = 9.9, 7.4, 1H), 3.30 (dd, J = 10.0, 3.3, 1H), 2.72 – 2.58 (m, 2H), 2.14 (dd, J = 14.1, 4.7, 1H), 1.93 (dt, J = 18.2, 6.2, 1H), 1.86 – 1.77 (m, 2H), 1.57 (ddd, J = 16.4, 12.5, 8.6, 1H), 1.50 (s, 9H), 1.31 (ddd, J = 16.0, 13.2, 6.7, 1H), 0.97 (s, 9H); MS (ESI+) *m/z* 596 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(2-chloro-4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.44 (d, J = 7.0 Hz, 1H), 8.35 (d, J = 8.2 Hz, 1H), 7.99 (d, J = 1.7 Hz, 1H), 7.74 (dd, J = 8.2, 1.7 Hz, 1H), 4.25-4.32 (m, 1H), 3.94 (dd, J = 10.1, 2.8 Hz, 1H), 3.59 (dd, J = 7.4, 4.4 Hz, 1H), 3.49 (dd, J = 10.2, 7.3 Hz, 1H), 3.31-3.39 (m, 2H), 2.58-2.67 (m, 2H), 1.86-2.48 (m, 2H), 2.15 (dd, J = 14.0, 4.4 Hz, 1H), 1.97-2.05 (m, 1H), 1.82-1.88 (m, 1H), 1.53-1.61 (m, 1H), 1.42 (dd, J = 14.0, 7.4 Hz, 1H), 1.31-1.39 (m, 1H), 0.98 (s, 9H); MS (ESI-) *m/z* 494 $(M-H)^-$.

Example 430

***N*-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide**

The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide from Example 258 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.15-8.20 (m, 3H), 7.92-7.96 (m, 2H), 7.29-7.34 (m, 4H), 7.24-7.28 (m, 1H), 3.75 (dd, J = 9.9, 2.9 Hz, 1H), 3.43 (t, J = 6.8 Hz, 1H), 3.13-3.20 (m, 3H), 3.04-3.10 (m, 3H), 2.95 (dd, J = 9.6, 7.6 Hz, 1H), 2.43-2.52 (m, 1H), 2.34 (s, 3H), 1.75-2.16 (m, 1H), 1.84-1.91 (m, 1H), 1.70-1.79 (m, 1H), 1.37-1.47 (m, 1H), 1.19-1.28 (m, 1H); MS (ESI+) *m/z* 496 $(M+H)^+$,554 $(M+CH_3CN+NH_4)^+$.

Example 431

***N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-*N*^{2},4-dimethyl-L-leucinamide**

Step A: *tert*-Butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(2-chloro-4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate from Example 247 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 2-chloro-4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.40 (d, J = 6.9, 1H), 8.34 (d, J = 8.1, 1H), 7.99 (d, J = 1.1, 1H), 7.76 – 7.67 (m, 1H), 5.19 – 5.10 (m, 1H), 4.31 – 4.20 (m, 1H), 3.93 (dd, J = 10.2, 2.0, 1H), 3.53 – 3.44 (m, 1H), 3.39 – 3.28 (m, 2H), 3.01 (s, 3H), 2.67 – 2.53 (m, 2H), 2.22 – 2.11 (m, 1H), 2.00 – 1.88 (m, 1H), 1.85 – 1.74 (m, 1H), 1.70 – 1.60 (m, 1H), 1.60 – 1.49 (m, 1H), 1.44 (d, J = 11.0, 9H), 1.37 – 1.25 (m, 1H), 0.91 (d, J = 8.9, 9H); MS (ESI+) *m/z* 610 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(2-chloro-4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.34-8.37 (m, 2H), 7.99 (d, *J* = 1.7 Hz, 1H), 7.72-7.75 (m, 1H), 4.30-4.35 (m, 1H), 3.96 (dd, *J* = 10.2, 2.3 Hz, 1H), 3.53 (dd, *J* = 10.1, 7.2 Hz, 1H), 3.39 (dd, *J* = 10.0, 7.1 Hz, 1H), 3.35 (dd, *J* = 9.9, 2.9 Hz, 1H), 3.17 (dd, *J* = 6.5, 5.1 Hz, 1H), 2.64-2.70 (m, 2H), 2.38 (s, 3H), 2.03 (dtd, *J* = 12.5, 6.3, 4.2 Hz, 1H), 1.89 (dd, *J* = 14.0, 5.2 Hz, 1H), 1.83-1.92 (m, 1H), 1.67-2.06 (m, 1H), 1.56-1.66 (m, 1H), 1.47 (dd, *J* = 14.0, 6.6 Hz, 1H), 1.32-1.43 (m, 1H), 0.96 (s, 9H); MS (ESI+) *m/z* 510 $(M+H)^+$.

Example 432

N-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-*N*-methyl-L-phenylalaninamide

Step A: *N*-(*tert*-Butoxycarbonyl)-*N*-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-L-phenylalanine for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine from Example 284 Step B for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.69 – 8.55 (m, 1H), 8.37 (d, *J* = 8.2, 1H), 8.01 (d, *J* = 1.1, 1H), 7.76 (dd, *J* = 8.3, 1.0, 1H), 7.28 (d, *J* = 15.4, 4H), 7.23 (d, *J* = 1.3, 1H), 5.38 – 5.26 (m, 1H), 4.38 – 4.20 (m, 1H), 3.95 – 3.80 (m, 1H), 3.65 – 3.48 (m, 1H), 3.48 – 3.40 (m, 1H), 3.37 – 3.25 (m, 2H), 3.15 – 3.07 (m, 1H), 3.05 (s, 3H), 2.59 – 2.48 (m, 1H), 2.48 – 2.39 (m, 1H), 2.06 – 1.86 (m, 1H), 1.83 – 1.70 (m, 1H), 1.61 – 1.43 (m, 1H), 1.39 – 1.20 (m, 10H); MS (ESI+) *m/z* 630 $(M+H)^+$.

Step B: The title compound was prepared by substituting *N*-(*tert*-butoxycarbonyl)-*N*-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-

ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.37 (d, J = 8.2, 1H), 8.20 (d, J = 7.3, 1H), 8.01 (d, J = 1.2, 1H), 7.76 (dd, J = 8.3, 1.1, 1H), 7.35 – 7.23 (m, 5H), 4.34 – 4.24 (m, 1H), 3.85 (dd, J = 10.2, 3.0, 1H), 3.49 – 3.27 (m, 4H), 3.17 (dd, J = 13.3, 6.8, 1H), 3.05 (dd, J = 13.3, 6.8, 1H), 2.61 – 2.50 (m, 1H), 2.49 – 2.39 (m, 1H), 2.34 (s, 3H), 2.10 – 2.01 (m, 1H), 1.96 (dtd, J = 10.8, 6.5, 4.4, 1H), 1.83 – 1.72 (m, 1H), 1.53 – 1.41 (m, 1H), 1.31 (ddt, J = 13.2, 9.6, 6.7, 1H); MS (ESI+) m/z 530 $(M+H)^+$.

Example 433

N^1-cyclopropyl-N^2,4-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

Step A: (3a*R*,4*S*,6a*S*)-*N*-Cyclopropyl-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine was prepared by substituting (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 256 Step A for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and (1-ethoxycyclopropoxy)trimethylsilane for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.19 (d, J = 8.1, 2H), 7.94 (d, J = 8.3, 2H), 3.44 (dd, J = 9.8, 2.9, 1H), 3.17 (dd, J = 9.6, 3.2, 1H), 3.06 (dd, J = 9.8, 7.9, 1H), 2.96 (dd, J = 9.6, 7.7, 1H), 2.88 (dd, J = 13.2, 5.8, 1H), 2.56 – 2.46 (m, 1H), 2.28 (ddd, J = 12.1, 9.0, 2.9, 1H), 2.20 – 2.07 (m, 1H), 1.99 (dq, J = 6.3, 4.0, 1H), 1.89 – 1.79 (m, 2H), 1.37 – 1.18 (m, 2H), 0.42 – 0.25 (m, 4H); MS (ESI+) m/z 375 $(M+H)^+$.

Step B: *tert*-Butyl (*S*)-1-(cyclopropyl((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4,4-dimethylpentanoic acid for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-*N*-cyclopropyl-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Step A for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.12 – 8.07 (m, 2H), 7.86 – 7.80 (m, 2H), 5.85 – 5.57 (m, 1H), 3.93 (s, 1H), 3.56 (dd, J = 10.0, 3.2, 1H), 3.19 (dd, J = 10.0, 3.4, 2H), 3.13 (dd, J = 16.7, 9.1, 1H), 2.98 – 2.88 (m, 4H), 2.76 (ddd, J = 11.0, 7.1, 4.2, 1H), 2.72 – 2.64 (m, 1H), 2.15 (ddd, J = 18.3, 11.1, 7.7, 1H), 2.05 – 1.97 (m, 1H), 1.97 – 1.88 (m, 1H), 1.80 – 1.71 (m, 1H), 1.68 – 1.56 (m, 1H), 1.49 (s, 9H), 1.35 –

1.20 (m, 1H), 1.05 (dtd, J = 10.0, 6.8, 5.0, 1H), 0.99 (s, 9H), 0.88 (dddd, J = 9.6, 8.1, 6.7, 3.3, 2H), 0.79 – 0.70 (m, 1H); MS (ESI+) m/z 616 $(M+H)^+$.

Step C: The title compound was prepared by substituting *tert*-butyl (*S*)-1-(cyclopropyl((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate from Step B for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.08-8.11 (m, 2H), 7.81-7.85 (m, 2H), 4.00 (dd, J = 8.3, 4.1 Hz, 1H), 3.91-3.97 (m, 2H), 3.51 (dd, J = 9.6, 2.8 Hz, 1H), 3.08-3.24 (m, 4H), 2.66-2.77 (m, 1H), 2.60-2.66 (m, 1H), 2.30 (s, 3H), 2.11 (qd, J = 11.1, 7.6 Hz, 1H), 1.89-2.02 (m, 1H), 1.79-1.86 (m, 1H), 1.59 (dd, J = 14.1, 4.0 Hz, 1H), 1.45 (dd, J = 14.2, 8.1 Hz, 1H), 1.27 (tt, J = 11.9, 7.5 Hz, 1H), 1.02 (s, 9H), 0.73-0.97 (m, 4H); MS (ESI+) m/z 516 $(M+H)^+$.

Example 434

N^1-ethyl-N^2,4-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-(ethyl((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate from Example 296 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.08-8.11 (m, 2H), 7.82-7.85 (m, 2H), 4.18-4.25 (m, 1H), 3.66 (d, J = 9.9 Hz, 1H), 3.17-3.54 (m, 4H), 2.84-3.15 (m, 2H), 2.52-2.82 (m, 2H), 2.22-2.50 (m, 3H), 1.87-2.19 (m, 2H), 1.67-1.85 (m, 2H), 1.61 (dd, J = 14.2, 3.8 Hz, 1H), 1.48 (dd, J = 14.2, 8.2 Hz, 1H), 1.27-1.40 (m, 1H), 1.17 (t, J = 7.0 Hz, 3H), 1.04 (s, 9H); MS (ESI+) m/z 505 $(M+H)^+$.

Example 435

N^2,4-dimethyl-N^1-propyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-(propyl((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-

yl)amino)pentan-2-yl(methyl)carbamate from Example 297 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.08-8.11 (m, 2H), 7.82-7.85 (m, 2H), 4.18-4.30 (m, 1H), 3.64-3.75 (m, 2H), 2.97-3.36 (m, 5H), 2.18-2.88 (m, 5H), 1.72-2.14 (m, 4H), 1.55-1.71 (m, 3H), 1.48 (dd, J = 14.3, 8.3 Hz, 1H), 1.28-1.34 (m, 1H), 1.04-1.06 (m, 9H), 0.87 (t, J = 7.4 Hz, 3H); MS (ESI+) *m/z* 518 $(M+H)^+$.

Example 436

N^1-(cyclopropylmethyl)-N^2,4-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((cyclopropylmethyl)((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate from Example 298 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.08-8.11 (m, 2H), 7.82-7.85 (m, 2H), 4.13-4.26 (m, 1H), 3.51-3.78 (m, 2H), 3.20-3.35 (m, 3H), 2.82-3.18 (m, 2H), 2.52-2.81 (m, 2H), 2.29-2.50 (m, 3H), 1.77-2.10 (m, 3H), 1.70-2.15 (m, 1H), 1.65 (dd, J = 14.2, 3.8 Hz, 1H), 1.48 (dd, J = 14.3, 8.2 Hz, 1H), 1.27-1.40 (m, 1H), 1.05 (s, 10H), 0.43-0.72 (m, 2H), 0.31-0.35 (m, 2H); MS (ESI+) *m/z* 530 $(M+H)^+$.

Example 437

N^1,N^2,4-trimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-4,4-dimethyl-1-(methyl((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)-1-oxopentan-2-yl(methyl)carbamate from Example 302 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.08-8.11 (m, 2H), 7.82-7.85 (m, 2H), 4.14-4.96 (m, 1H), 3.62 (dd, J = 9.9, 1.8 Hz, 2H), 3.00-3.30 (m, 3H), 2.89 (s, 3H), 2.49-2.65 (m, 2H), 2.25-

2.47 (m, 3H), 1.59-2.10 (m, 5H), 1.46 (dd, J = 14.2, 7.6 Hz, 1H), 1.22-1.41 (m, 1H), 1.01-1.03 (m, 9H); MS (ESI+) m/z 5490 $(M+H)^+$.

Example 438

N^1,N^2-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

Step A: *tert*-Butyl methyl((*S*)-1-(methyl((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)-1-oxopentan-2-yl)carbamate was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)pentanoic acid for (*S*)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid and (3a*R*,4*S*,6a*S*)-*N*-methyl-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 301 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 266: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.11 (d, J = 8.3, 2H), 7.83 (d, J = 8.3, 2H), 4.69 – 4.57 (m, 1H), 3.59 (dd, J = 9.9, 1.2, 1H), 3.29 – 3.18 (m, 2H), 3.16 (dd, J = 9.8, 3.3, 1H), 2.88 (s, 3H), 2.86 (s, 3H), 2.61 – 2.50 (m, 2H), 1.91 – 1.56 (m, 6H), 1.51 (s, 10H), 1.40 – 1.21 (m, 3H), 0.91 (t, J = 7.4, 3H); MS (ESI+) m/z 562 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-(methyl((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)-1-oxopentan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (400 MHz, pyridine-d_5, temperature 90 °C) δ ppm 8.08-8.11 (m, 2H), 7.82-7.85 (m, 2H), 4.48-4.67 (bs, 1H), 3.61 (dd, J = 10.0, 2.0 Hz, 1H), 3.41-3.56 (m, 1H), 2.93-3.34 (m, 4H), 2.86 (s, 3H), 2.50-2.62 (m, 2H), 2.22-2.49 (m, 3H), 1.80-1.95 (m, 1H), 1.39-1.79 (m, 6H), 1.23-1.38 (m, 1H), 0.89 (t, J = 7.2 Hz, 3H); MS (ESI+) m/z 462 $(M+H)^+$.

Example 439

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^1,N^2,4-trimethyl-L-leucinamide

Step A: *tert*-Butyl (3a*R*,4*S*,6a*S*)-2-(2-chloro-4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate (62 mg, 0.132 mmol) from Example 284 Step A was dissolved in 1,2-dimethoxyethane (1.0 mL) and lithium aluminum hydride (10.04 mg, 0.264 mmol) was added portionwise. The reaction was stirred at 70 °C overnight, then it was quenched with wet sodium sulfate. The crude material was applied to a 4 g silica gel cartridge and purified with a gradient of 1-10% methanol (2 *N* ammonia)/dichloromethane over 20 minutes to give (3a*R*,4*S*,6a*S*)-2-(2-chloro-4-(trifluoromethyl)phenylsulfonyl)-*N*-methyloctahydrocyclopenta[*c*]pyrrol-4-amine: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.46 (s, 1H), 8.34 (d, *J* = 8.2, 1H), 7.99 (s, 1H), 4.92 (s, 3H), 4.32 (dt, *J* = 13.7, 7.0, 1H), 3.89 (dd, *J* = 10.2, 3.0, 1H), 3.49 (dd, *J* = 10.2, 7.5, 1H), 3.41 – 3.30 (m, 2H), 2.70 – 2.59 (m, 2H), 2.48 (dt, *J* = 4.4, 2.2, 1H), 2.01 (td, *J* = 11.8, 6.6, 1H), 1.95 – 1.83 (m, 1H), 1.59 (ddd, *J* = 16.1, 10.8, 7.7, 1H), 1.37 (dt, *J* = 22.2, 6.5, 1H); MS (APCI+) *m/z* 383 $(M+H)^+$.

Step B: *tert*-Butyl (*S*)-1-(((3a*R*,4*S*,6a*S*)-2-(2-chloro-4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)(methyl)amino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4,4-dimethylpentanoic acid for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(2-chloro-4-(trifluoromethyl)phenylsulfonyl)-*N*-methyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: MS (ESI+) *m/z* 625 $(M+H)^+$.

Step C: The title compound was prepared by substituting *tert*-butyl (*S*)-1-(((3a*R*,4*S*,6a*S*)-2-(2-chloro-4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)(methyl)amino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate from Step B for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.30 (d, *J* = 8.2, 1H), 7.90 (s, 1H), 7.69 (d, *J* = 8.1, 1H), 3.80 - 3.72 (m, *J* = 7.3, 1H), 3.68 (d, *J* = 9.8, 1H), 3.50 - 3.27 (m, 3H), 2.94 (s, 3H), 2.74 - 2.58 (m, *J* = 5.3, 11.8, 2H), 2.38 (s, 3H), 1.99 - 1.87 (m, *J* = 8.2, 18.8, 1H), 1.85 - 1.64 (m, 4H), 1.53 (dd, *J* = 7.0, 14.1, 1H), 1.47 - 1.33 (m, 1H), 0.99 (s, 9H). ; MS (ESI+) *m/z* 525 $(M+H)^+$.

Example 440

4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(5-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate from Example 262 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.62 (d, *J* = 2.4 Hz, 1H), 8.48-8.50 (m, 1H), 7.67 (dd, *J* = 8.9, 2.5 Hz, 1H), 6.38 (d, *J* = 8.9 Hz, 1H), 4.35-4.41 (m, 1H), 3.80-3.83 (m, 1H), 3.65 (dd, *J* = 7.5, 4.4 Hz, 1H), 3.60-3.66 (m, 1H), 3.54-3.60 (m, 1H), 3.30-3.34 (m, 1H), 2.68-2.79 (m, 2H), 2.20 (dd, *J* = 14.0, 4.4 Hz, 1H), 1.73-2.56 (m, 2H), 2.10-2.17 (m, 1H), 1.89-1.97 (m, 1H), 1.68 (dq, *J* = 12.7, 8.1 Hz, 1H), 1.47 (dd, *J* = 14.0, 7.5 Hz, 1H), 1.35-1.42 (m, 1H), 1.01 (s, 9H); MS (ESI+) *m/z* 399 $(M+H)^+$.

Example 441

4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(6-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate from Example 264 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.43-8.46 (m, 1H), 7.51 (t, *J* = 7.9 Hz, 1H), 6.98 (d, *J* = 7.2 Hz, 1H), 6.50 (d, *J* = 8.5 Hz, 1H), 4.32-4.38 (m, 1H), 3.71 (dd, *J* = 10.9, 2.9 Hz, 1H), 3.64 (dd, *J* = 7.5, 4.3 Hz, 1H), 3.46-3.60 (m, 2H), 3.27 (dd, *J* = 10.9, 3.5 Hz, 1H), 2.65-2.74 (m, 2H), 2.19 (dd, *J* = 13.9, 4.3 Hz, 1H), 1.71-2.58 (m, 2H), 2.06-2.15 (m, 1H), 1.87-1.97 (m, 1H), 1.65 (dq, *J* = 12.7, 8.0 Hz, 1H), 1.46 (dd, *J* = 14.0, 7.5 Hz, 1H), 1.32-1.39 (m, 1H), 1.01 (s, 9H); MS (ESI+) *m/z* 399 $(M+H)^+$.

Example 442

4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[2-(methylsulfonyl)pyrimidin-5-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-4,4-dimethyl-1-((3a*R*,4*S*,6a*S*)-2-(2-(methylsulfonyl)pyrimidin-5-yl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-ylcarbamate from Example 265 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.45 (s, 2H), 8.43 (d, J = 7.3 Hz, 1H), 4.95 (s, 3H), 4.39 (p, J = 7.0 Hz, 1H), 3.97 (dd, J = 11.9, 3.3 Hz, 1H), 3.76 (dd, J = 12.0, 7.7 Hz, 1H), 3.70 (dd, J = 11.6, 8.1 Hz, 1H), 3.62 (dd, J = 7.5, 4.2 Hz, 1H), 3.44 (dd, J = 11.7, 4.5 Hz, 1H), 2.65-2.75 (m, 2H), 2.18 (dd, J = 14.0, 4.3 Hz, 1H), 2.09-2.16 (m, 1H), 2.02-2.19 (m, 2H), 1.86-1.94 (m, 1H), 1.65 (dq, J = 12.7, 8.2 Hz, 1H), 1.45 (dd, J = 14.0, 7.5 Hz, 1H), 1.33-1.42 (m, 1H), 1.00 (s, 9H); MS (ESI+) *m/z* 411 $(M+H)^+$.

Example 443

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide

Step A: *tert*-Butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 3-fluorobenzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: MS (APCI+) *m/z* 512 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.38 (d, J = 6.6 Hz, 1H), 7.84 (dt, J = 8.2, 2.0 Hz, 1H), 7.77 (d, J = 7.8 Hz, 1H), 7.53 (td, J = 8.0, 5.5 Hz, 1H), 7.38 (td, J = 8.4, 2.4 Hz, 1H), 4.23-4.29 (m, 1H), 3.81 (dd, J = 9.9, 2.3 Hz, 1H), 3.25 (dd, J = 8.1, 5.9 Hz, 1H), 3.11-3.16 (m, 2H), 2.94 (dd, J = 9.6,

6.7 Hz, 1H), 2.53-2.56 (m, 2H), 2.42 (s, 3H), 1.92-2.00 (m, 1H), 1.79-1.92 (m, 2H), 1.9 (m, 1H), 1.68-1.74 (m, 1H), 1.52-1.62 (m, 2H), 1.24-1.36 (m, 1H), 0.90 (d, J = 6.6 Hz, 3H), 0.85 (d, J = 6.5 Hz, 3H); MS (ESI-) m/z 410 $(M-H)^-$.

Example 444

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide

Step A: *tert*-Butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-fluorobenzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: MS (APCI+) m/z 512 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.30 (d, J = 7.2 Hz, 1H), 7.98-8.01 (m, 2H), 7.30-7.35 (m, 2H), 4.25-4.29 (m, 1H), 3.79 (dd, J = 9.9, 2.6 Hz, 1H), 3.19 (dd, J = 8.2, 5.8 Hz, 1H), 3.14 (d, J = 2.9 Hz, 1H), 3.10-3.12 (m, 1H), 2.93 (dd, J = 9.6, 6.9 Hz, 1H), 2.52-2.58 (m, 2H), 2.39 (s, 3H), 1.92-2.00 (m, 1H), 1.78-2.08 (m, 1H), 1.80-1.92 (m, 2H), 1.68 (ddd, J = 13.5, 7.7, 5.8 Hz, 1H), 1.58 (dd, J = 8.1, 6.4 Hz, 1H), 1.52-1.58 (m, 1H), 1.26-1.35 (m, 1H), 0.90 (d, J = 6.6 Hz, 3H), 0.84 (d, J = 6.6 Hz, 3H); MS (ESI+) m/z 412 $(M+H)^+$.

Example 445

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3,4-difluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide

Step A: *tert*-Butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3,4-difluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-

benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 3,4-difluorobenzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: MS (APCI+) *m/z* 530 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3,4-difluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.30 (d, *J* = 7.3 Hz, 1H), 8.00 (ddd, *J* = 9.6, 7.3, 2.2 Hz, 1H), 7.76-7.79 (m, 1H), 7.35-7.49 (m, 1H), 4.24-4.30 (m, 1H), 3.82 (dd, *J* = 9.9, 2.6 Hz, 1H), 3.19 (dd, *J* = 7.5, 5.0 Hz, 1H), 3.13-3.17 (m, 2H), 2.98 (dd, *J* = 9.6, 7.1 Hz, 1H), 2.52-2.62 (m, 2H), 2.39 (s, 3H), 1.86-2.18 (m, 1H), 1.94-2.02 (m, 1H), 1.79-1.92 (m, 2H), 1.63-1.74 (m, 1H), 1.53-1.62 (m, 2H), 1.28-1.40 (m, 1H), 0.90 (d, *J* = 6.7 Hz, 3H), 0.84 (d, *J* = 6.6 Hz, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Example 446

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3,5-difluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide

Step A: *tert*-Butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3,5-difluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 3,5-difluorobenzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: MS (APCI+) *m/z* 530 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3,5-difluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.32 (d, *J* = 7.2 Hz, 1H), 7.66-7.69 (m, 2H), 7.33-7.42 (m, 1H), 4.24-4.30 (m, 1H), 3.84 (dd, *J* = 9.9, 2.5 Hz, 1H), 3.16-3.21 (m, 3H), 3.00 (dd, *J* = 9.7, 7.0 Hz, 1H), 2.48-2.60 (m, 2H), 2.39 (s, 3H), 1.89-2.25 (m, 1H), 1.93-2.01 (m, 1H), 1.81-1.92 (m, 2H),

1.68 (ddd, J = 13.6, 7.8, 5.8 Hz, 1H), 1.52-1.63 (m, 2H), 1.31 (ddt, J = 9.7, 12.9, 6.4 Hz, 1H), 0.90 (d, J = 6.6 Hz, 3H), 0.84 (d, J = 6.6 Hz, 3H); MS (ESI+) m/z 430 $(M+H)^+$.

Example 447

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-chlorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide

Step A: *tert*-Butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-chlorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-chlorobenzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: MS (APCI+) m/z 530 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-chlorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.29-8.31 (m, 1H), 7.91-7.93 (m, 2H), 7.57-7.59 (m, 2H), 4.24-4.31 (m, 1H), 3.80 (dd, J = 9.9, 2.5 Hz, 1H), 3.19 (dd, J = 8.2, 5.8 Hz, 1H), 3.13 (dd, J = 9.4, 2.7 Hz, 1H), 3.11 (dd, J = 9.5, 7.2 Hz, 1H), 2.92 (dd, J = 9.6, 7.0 Hz, 1H), 2.52-2.59 (m, 2H), 2.39 (s, 3H), 1.90-2.16 (m, 1H), 1.92-2.00 (m, 1H), 1.80-1.91 (m, 2H), 1.68 (ddd, J = 13.5, 7.8, 5.8 Hz, 1H), 1.52-1.62 (m, 2H), 1.27-1.34 (m, 1H), 0.90 (d, J = 6.6 Hz, 3H), 0.85 (d, J = 6.5 Hz, 3H); MS (ESI-) m/z 426 $(M-H)^-$.

Example 448

N^2-methyl-N^1-[(3a*S*,4*R*,6a*R*)-2-(phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-leucinamide

Step A: *tert*-Butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and

benzenesulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: MS (APCI+) *m/z* 494 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-chlorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.28 (d, *J* = 7.0 Hz, 1H), 7.97-8.00 (m, 2H), 7.52-7.58 (m, 3H), 4.24-4.31 (m, 1H), 3.79 (dd, *J* = 9.9, 2.4 Hz, 1H), 3.19 (dd, *J* = 8.2, 5.8 Hz, 1H), 3.08-3.15 (m, 2H), 2.91 (dd, *J* = 9.6, 6.7 Hz, 1H), 2.48-2.52 (m, 2H), 2.39 (s, 3H), 1.77-2.03 (m, 4H), 1.68 (ddd, *J* = 13.5, 7.8, 5.8 Hz, 1H), 1.49-1.60 (m, 2H), 1.24-1.33 (m, 1H), 0.90 (d, *J* = 6.6 Hz, 3H), 0.84 (d, *J* = 6.5 Hz, 3H); MS (ESI-) *m/z* 392 $(M-H)^-$.

Example 449

N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

Step A: *tert*-Butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide and 4-(trifluoromethyl)benzaldehyde for 3-(trifluoromethyl)benzaldehyde in the procedure described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.36 – 8.27 (m, 1H), 7.65 (d, *J* = 8.1, 2H), 7.50 (d, *J* = 7.6, 2H), 5.14 (m, 0.4H), 4.78 (m, 0.6H), 4.45 – 4.31 (m, 1H), 3.62 – 3.51 (m, 1H), 3.45 (ddd, *J* = 7.5, 5.3, 3.5, 1H), 3.05 (s, 3H), 2.90 – 2.73 (m, 1H), 2.55 – 2.41 (m, 2H), 2.31 (d, *J* = 5.7, 2H), 2.23 – 2.17 (m, 1H), 2.10 (dt, *J* = 11.5, 5.8, 1H), 1.94 – 1.75 (m, 3H), 1.65 – 1.51 (m, 2H), 1.46 (s, 9H), 1.42 – 1.34 (m, 1H), 0.88 (d, *J* = 6.3, 3H), 0.84 (d, *J* = 6.6, 3H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-

benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.19-8.21 (m, 1H), 7.64-7.67 (m, 2H), 7.51-7.53 (m, 2H), 4.44-4.50 (m, 1H), 3.57-3.61 (m, 1H), 3.47 (d, J = 13.6 Hz, 1H), 3.22 (dd, J = 8.2, 5.8 Hz, 1H), 2.89 (dd, J = 9.0, 2.6 Hz, 1H), 2.48-2.58 (m, 2H), 2.42 (s, 3H), 2.34-2.40 (m, 2H), 2.24 (dd, J = 8.9, 7.0 Hz, 1H), 2.09-2.17 (m, 1H), 1.92-2.08 (m, 1H), 1.84-1.94 (m, 2H), 1.71 (ddd, J = 13.5, 7.8, 5.8 Hz, 1H), 1.56-1.65 (m, 2H), 1.39-1.47 (m, 1H), 0.91 (d, J = 6.5 Hz, 3H), 0.85 (d, J = 6.5 Hz, 3H); MS (ESI+) *m/z* 412 $(M+H)^+$.

Example 450

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide

Step A: *tert*-Butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate was prepared by substituting N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-L-leucinamide from Example 151 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide and 4-fluorobenzaldehyde for 3-(trifluoromethyl)benzaldehyde in the procedure described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.30 (d, J = 6.2, 1H), 7.39 – 7.32 (m, 2H), 7.12 (t, J = 8.8, 2H), 5.18 – 5.11 (m, 1H), 4.44 – 4.33 (m, 1H), 3.54 – 3.46 (m, 1H), 3.38 (t, J = 13.8, 1H), 3.05 (s, 3H), 2.87 – 2.71 (m, 1H), 2.53 – 2.41 (m, 2H), 2.31 (d, J = 6.3, 2H), 2.23 – 2.17 (m, 1H), 2.13 – 2.06 (m, 1H), 1.83 (dd, J = 9.0, 5.2, 3H), 1.64 – 1.52 (m, 2H), 1.46 (s, 9H), 1.42 – 1.33 (m, 1H), 0.88 (d, J = 6.4, 3H), 0.84 (d, J = 6.5, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.23-8.25 (m, 1H), 7.37 (dd, J = 8.3, 5.4 Hz, 2H), 7.13 (t, J = 8.6 Hz, 2H), 4.43-4.48 (m, 1H), 3.53 (d, J = 13.1 Hz, 1H), 3.40 (d, J = 13.1 Hz, 1H), 3.24 (dd, J = 8.1, 5.9 Hz, 1H), 2.85 (dd, J = 9.1, 2.6 Hz, 1H), 2.48-2.56 (m, 2H), 2.42 (s, 3H), 2.39 (dd, J = 8.8, 7.1

Hz, 1H), 2.34 (dd, J = 9.0, 2.3 Hz, 1H), 2.24 (dd, J = 8.9, 6.9 Hz, 1H), 2.13 (dq, J = 11.9, 6.0 Hz, 1H), 1.62-2.52 (m, 1H), 1.85-1.94 (m, 2H), 1.72 (ddd, J = 13.5, 7.7, 5.8 Hz, 1H), 1.56-1.65 (m, 2H), 1.38-1.45 (m, 1H), 0.91 (d, J = 6.6 Hz, 3H), 0.86 (d, J = 6.5 Hz, 3H); MS (ESI+) *m/z* 362 $(M+H)^+$.

Example 451

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide

Step A: *tert*-Butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-3-methylbutanoic acid for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 256 Step A for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.08 (d, J = 8.1, 2H), 7.81 (d, J = 8.3, 2H), 7.58 – 7.53 (m, 1H), 4.31 (d, J = 10.6, 1H), 4.11 – 4.02 (m, 1H), 3.66 (dd, J = 10.2, 3.3, 1H), 3.31 (dd, J = 10.2, 7.8, 1H), 3.19 – 3.09 (m, 2H), 3.00 (s, 3H), 2.63 – 2.47 (m, 2H), 2.43 – 2.33 (m, 1H), 1.94 – 1.75 (m, 2H), 1.55 – 1.47 (m, 1H), 1.45 (s, 9H), 1.28 (ddd, J = 13.0, 8.9, 6.2, 1H), 0.98 (d, J = 6.5, 3H), 0.86 (d, J = 6.7, 3H).

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.25-8.27 (m, 1H), 8.13-8.16 (m, 2H), 7.90-7.92 (m, 2H), 4.23-4.30 (m, 1H), 3.85 (dd, J = 9.9, 2.6 Hz, 1H), 3.13-3.20 (m, 2H), 2.97 (dd, J = 9.6, 7.0 Hz, 1H), 2.88 (d, J = 5.9 Hz, 1H), 2.48-2.62 (m, 2H), 2.39 (s, 3H), 2.05-2.13 (m, 1H), 1.94-2.09 (m, 1H), 1.90-1.97 (m, 1H), 1.80-1.87 (m, 1H), 1.51-1.59 (m, 1H), 1.30 (ddt, J = 9.7, 12.9, 6.4 Hz, 1H), 1.02-1.05 (m, 6H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Example 452

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-valinamide

Step A: *tert*-Butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxobutan-2-yl(methyl)carbamate was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-3-methylbutanoic acid for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 261 Step A for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.94 (dd, J = 8.6, 5.3, 2H), 7.20 (t, J = 8.7, 2H), 4.31 (d, J = 11.2, 1H), 4.07 (dt, J = 13.3, 6.8, 1H), 3.59 (dd, J = 9.9, 3.7, 1H), 3.27 (dd, J = 10.1, 7.8, 1H), 3.15 – 3.03 (m, 2H), 2.99 (s, 3H), 2.61 – 2.46 (m, 2H), 2.38 (dq, J = 17.5, 6.8, 1H), 1.94 – 1.75 (m, 2H), 1.51 (dd, J = 14.6, 6.6, 1H), 1.45 (s, 9H), 1.33 – 1.21 (m, 1H), 0.98 (d, J = 6.5, 3H), 0.86 (d, J = 6.7, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxobutan-2-yl(methyl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.26 (d, J = 6.7 Hz, 1H), 7.99-8.02 (m, 2H), 7.31-7.35 (m, 2H), 4.24-4.31 (m, 1H), 3.78 (dd, J = 9.9, 2.5 Hz, 1H), 3.09-3.14 (m, 2H), 2.93 (dd, J = 9.6, 6.8 Hz, 1H), 2.89 (d, J = 5.9 Hz, 1H), 2.48-2.58 (m, 2H), 2.39 (s, 3H), 2.05-2.13 (m, 1H), 1.92-2.12 (m, 1H), 1.90-1.98 (m, 1H), 1.80-1.87 (m, 1H), 1.52-1.59 (m, 1H), 1.24-1.34 (m, 1H), 1.04 (d, J = 7.2 Hz, 3H), 1.03 (d, J = 7.2 Hz, 3H); MS (ESI-) *m/z* 396 $(M-H)^-$.

Example 453

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-4-methyl-L-leucinamide

Step A: *tert*-Butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-ylcarbamate was prepared by substituting (*S*)-2-(*tert*-butoxycarbonylamino)-4,4-dimethylpentanoic acid for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 261 Step A for

(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.70 (d, *J* = 7.0, 1H), 8.14 (d, *J* = 8.7, 1H), 7.99 (dd, *J* = 8.6, 5.2, 2H), 7.32 (t, *J* = 8.6, 2H), 4.75 – 4.65 (m, 1H), 4.27 – 4.18 (m, 1H), 3.74 (dd, *J* = 9.9, 2.7, 1H), 3.10 (ddd, *J* = 13.9, 9.6, 5.4, 2H), 2.92 (dd, *J* = 9.4, 7.7, 1H), 2.61 – 2.47 (m, 2H), 2.15 (dd, *J* = 14.2, 4.7, 1H), 1.89 – 1.73 (m, 3H), 1.56 – 1.45 (m, 10H), 1.28 – 1.18 (m, 1H), 0.98 (s, 9H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-ylcarbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.38-8.40 (m, 1H), 7.98-8.01 (m, 2H), 7.31-7.38 (m, 2H), 4.20-4.23 (m, 1H), 3.77 (dd, *J* = 9.8, 2.6 Hz, 1H), 3.59 (dd, *J* = 7.4, 4.3 Hz, 1H), 3.11 (dd, *J* = 9.6, 2.7 Hz, 1H), 3.06 (dd, *J* = 9.9, 7.3 Hz, 1H), 2.91 (dd, *J* = 9.6, 7.0 Hz, 1H), 2.46-2.58 (m, 2H), 2.16 (dd, *J* = 14.0, 4.3 Hz, 1H), 1.98-2.31 (m, 2H), 1.88-1.96 (m, 1H), 1.77-1.85 (m, 1H), 1.47-1.57 (m, 1H), 1.43 (dd, *J* = 14.0, 7.6 Hz, 1H), 1.23-1.32 (m, 1H), 0.99 (s, 9H); MS (ESI-) *m/z* 410 $(M-H)^-$.

Example 454

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norleucinamide

Step A: *tert*-Butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxohexan-2-yl(methyl)carbamate was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)hexanoic acid for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 261 Step A for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.45 (d, *J* = 6.8, 1H), 7.99 (dd, *J* = 8.7, 5.2, 2H), 7.32 (t, *J* = 8.7, 2H), 4.94 (s, 3H), 4.28 – 4.15 (m, 1H), 3.75 (d, *J* = 10.4, 1H), 3.07 (dd, *J* = 20.0, 10.4, 4H), 2.89 (dd, *J* = 9.5, 7.2, 1H), 2.57 – 2.46 (m, 2H), 2.13 – 1.98 (m, 1H), 1.93 – 1.68 (m, 3H), 1.45 (s, 9H), 1.26 (d, *J* = 6.0, 5H), 0.78 (s, 3H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxohexan-2-yl(methyl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.20-8.22 (m, 1H), 7.99-8.02 (m, 2H), 7.31-7.38 (m, 2H), 4.24-4.30 (m, 1H), 3.78 (dd, J = 9.9, 2.5 Hz, 1H), 3.08-3.16 (m, 3H), 2.88-2.94 (m, 1H), 2.52-2.59 (m, 2H), 2.40 (s, 3H), 1.92-1.98 (m, 1H), 1.60-2.28 (m, 1H), 1.78-1.87 (m, 2H), 1.65-1.73 (m, 1H), 1.52-1.59 (m, 1H), 1.36-1.50 (m, 2H), 1.27-1.35 (m, 1H), 1.24 (h, J = 7.4 Hz, 2H), 0.81 (t, J = 7.3 Hz, 3H); MS (ESI-) m/z 410 $(M-H)^-$.

Example 455

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide

Step A: *tert*-Butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4-methylpentanoic acid for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 261 Step A for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.94 (dd, J = 8.1, 5.2, 2H), 7.44 – 7.37 (m, 1H), 7.20 (t, J = 8.5, 2H), 4.85 – 4.77 (m, 1H), 4.12 – 4.03 (m, 1H), 3.61 – 3.55 (m, 1H), 3.27 – 3.21 (m, 1H), 3.13 – 3.02 (m, 2H), 2.93 (s, 3H), 2.59 – 2.44 (m, 2H), 1.83 (ddd, J = 37.1, 15.2, 5.0, 4H), 1.50 (d, J = 0.6, 2H), 1.46 (d, J = 0.8, 9H), 1.33 – 1.22 (m, 1H), 0.89 (t, J = 7.2, 6H); MS (ESI+) m/z 512 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.29-8.31 (m, 1H), 7.99-8.02 (m, 2H), 7.31-7.35 (m, 2H), 4.24-4.30 (m, 1H), 3.79 (dd, J = 9.9, 2.4 Hz, 1H), 3.21 (dd, J = 8.2, 5.9 Hz, 1H), 3.09-3.14 (m, 2H), 2.93 (dd, J = 9.6, 6.7 Hz, 1H), 2.53-2.59 (m, 2H), 2.40 (s, 3H), 1.89-2.27 (m, 1H), 1.91-1.99 (m,

1H), 1.79-1.91 (m, 2H), 1.69 (ddd, *J* = 13.5, 7.7, 5.8 Hz, 1H), 1.53-1.59 (m, 2H), 1.25-1.35 (m, 1H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.85 (d, *J* = 6.6 Hz, 3H); MS (ESI-) *m/z* 410 $(M-H)^-$.

Example 456

N^2-methyl-N^1-((3a*S*,4*S*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

Step A: *tert*-Butyl methyl((*S*)-1-oxo-1-((3a*S*,4*S*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate from Example 238 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: MS (ESI+) *m/z* 548 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*S*,4*S*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.52 (d, *J* = 6.8 Hz, 1H), 8.12-8.14 (m, 2H), 7.90-7.92 (m, 2H), 4.47 (p, *J* = 7.6 Hz, 1H), 3.64 (dd, *J* = 9.5, 2.9 Hz, 1H), 3.24 (dd, *J* = 7.3, 5.4 Hz, 1H), 3.16 (dd, *J* = 9.7, 3.1 Hz, 1H), 2.96-3.05 (m, 3H), 2.51 (s, 3H), 2.45-2.54 (m, 1H), 1.79-2.31 (m, 1H), 1.86-1.94 (m, 1H), 1.69-1.75 (m, 3H), 1.47-1.65 (m, 3H), 1.34-1.40 (m, 1H), 0.90 (t, *J* = 7.3 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Example 457

N^2-methyl-N^1-((3a*S*,4*S*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

Step A: *tert*-Butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*S*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Example 239 for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-

benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethyl)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.99 – 8.92 (m, 1H), 8.12 (d, J = 8.0, 2H), 7.91 (d, J = 8.2, 2H), 5.33 – 5.24 (m, 1H), 4.44 – 4.28 (m, 1H), 3.65 (dd, J = 10.0, 2.8, 1H), 3.19 – 3.09 (m, 4H), 3.03 – 2.81 (m, 3H), 2.50 – 2.42 (m, 1H), 2.05 – 1.92 (m, 2H), 1.73 – 1.55 (m, 4H), 1.50 (s, 9H), 1.35 – 1.25 (m, 1H), 0.97 (d, J = 6.6, 3H), 0.89 – 0.79 (m, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*S*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.61 (d, J = 6.9 Hz, 1H), 8.12-8.14 (m, 2H), 7.90-7.92 (m, 2H), 4.48 (s, 1H), 3.65 (dd, J = 9.6, 3.1 Hz, 1H), 3.29-3.33 (m, 1H), 3.16 (dd, J = 9.6, 3.1 Hz, 1H), 3.01-3.06 (m, 1H), 2.98-3.03 (m, 1H), 2.94-2.98 (m, 1H), 2.52 (s, 3H), 2.46-2.52 (m, 1H), 1.90-1.99 (m, 1H), 1.77-1.84 (m, 1H), 1.28-2.16 (m, 1H), 1.67-1.76 (m, 2H), 1.57-1.66 (m, 2H), 1.34-1.40 (m, 1H), 0.97 (d, J = 6.6 Hz, 3H), 0.90 (d, J = 6.6 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 458

N^1-{(3a*R*,4*S*,6a*S*)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide

Step A: *tert*-Butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(3,3-bis(4-fluorophenyl)propyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 313 Step A for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide and 3,3-bis(4-fluorophenyl)propanal for 3-(trifluoromethyl)benzaldehyde in the procedure described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.35 – 8.19 (m, 1H), 7.42 – 7.31 (m, 4H), 7.18 – 7.06 (m, 4H), 4.92-4.88 (m, 1H), 4.52 – 4.42 (m, 1H), 4.28 (dd, J = 10.0, 5.3, 1H), 3.15 – 3.02 (m, 3H), 2.92 (dd, J = 4.9, 4.1, 1H), 2.48 (dd, J = 7.1, 5.7, 2H), 2.41 – 2.35 (m, 1H), 2.33 – 2.27 (m,

2H), 2.26 – 2.17 (m, 3H), 2.15 – 2.08 (m, 2H), 2.08 – 1.99 (m, 2H), 1.93 – 1.75 (m, 2H), 1.62 – 1.50 (m, 1H), 1.48 (d, J = 7.3, 9H), 1.37 – 1.28 (m, 2H), 0.88 – 0.80 (m, 3H); MS (ESI+) m/z 570 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(3,3-bis(4-fluorophenyl)propyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.12-8.15 (m, 1H), 7.34-7.42 (m, 4H), 7.11-7.17 (m, 4H), 4.48-4.54 (m, 1H), 4.28 (t, J = 7.6 Hz, 1H), 3.18 (t, J = 6.5 Hz, 1H), 2.93 (dd, J = 9.0, 2.2 Hz, 1H), 2.49-2.57 (m, 1H), 2.43-2.49 (m, 1H), 2.42 (s, 3H), 2.28-2.33 (m, 2H), 2.18-2.28 (m, 3H), 2.08-2.28 (m, 3H), 1.95-2.15 (m, 1H), 1.89-2.00 (m, 1H), 1.79-1.87 (m, 1H), 1.67-1.75 (m, 1H), 1.43-1.61 (m, 4H), 0.85 (t, J = 7.3 Hz, 3H); MS (ESI+) m/z 470 $(M+H)^+$.

Example 459

2,2-bis(4-fluorophenyl)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide

Step A: *N*-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-2,2-bis(4-fluorophenyl)acetamide (150 mg, 0.336 mmol) from Example 228 and ethanol (20 ml) were added to 20% $Pd(OH)_2$ on carbon, wet (30.0 mg, 0.214 mmol) in a 50 mL pressure bottle and stirred for 2 hours at under 30 psi hydrogen at 50 °C. The mixture was filtered and the solvent removed in vacuo to give 2,2-bis(4-fluorophenyl)-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.09 (d, J = 7.1, 1H), 7.60 – 7.55 (m, 4H), 7.13 (q, J = 8.2, 4H), 5.26 (s, 1H), 4.36 – 4.27 (m, 1H), 3.06 (dd, J = 10.9, 2.7, 1H), 2.92 (dd, J = 10.9, 7.0, 1H), 2.81 (dd, J = 10.7, 7.0, 1H), 2.59 (dd, J = 10.8, 2.8, 1H), 2.52 – 2.41 (m, 2H), 2.33 – 2.25 (m, 1H), 2.06 – 1.96 (m, 1H), 1.83 (td, J = 12.7, 6.9, 1H), 1.65 – 1.52 (m, 1H), 1.26 (ddt, J = 12.3, 8.7, 6.1, 1H); MS (ESI+) m/z 357$(M+H)^+$.

Step B: 2,2-Bis(4-fluorophenyl)-*N*-[(3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide (30 mg, 0.084 mmol) and (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4-methylpentanoic acid (22.71 mg, 0.093 mmol) were dissolved in dichloromethane (0.5 mL) and then treated with 1-hydroxybenzotriazole hydrate (14.18 mg, 0.093 mmol). After 10 minutes, N^1-((ethylimino)methylene)-N^3,N^3-dimethylpropane-1,3-diamine (0.016 mL, 0.093

mmol) was added, and the reaction mixture was stirred at ambient temperature overnight followed by quenching with water. The material in the organic layer was purified with a 4 g silica gel cartridge eluting with 1-10% methanol (2 *N* ammonia)/dichloromethane to give *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-4-(2,2-bis(4-fluorophenyl)acetamido)hexahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)-4-methyl-1-oxopentan-2-yl(methyl)carbamate: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.25 (s, 1H), 7.46 (td, J = 8.5, 5.5, 4H), 7.08 – 6.96 (m, 4H), 5.08 (s, 2H), 4.29 – 4.18 (m, 1H), 3.80 (s, 2H), 3.69 (s, 1H), 3.43 (dd, J = 11.7, 3.5, 1H), 2.93 (s, 3H), 2.63 (s, 2H), 2.10 (td, J = 12.9, 6.9, 1H), 1.91 – 1.69 (m, 3H), 1.63 (dt, J = 13.2, 6.5, 2H), 1.51 (s, 9H), 1.40 – 1.26 (m, 1H), 0.97 (d, J = 6.5, 3H), 0.92 (d, J = 6.6, 3H); MS (ESI+) *m/z* 584(M+H)$^+$.

Step C: The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-4-(2,2-bis(4-fluorophenyl)acetamido)hexahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Step B for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.36 – 8.22 (m, 1H), 7.46 (td, J = 8.4, 5.5, 4H), 7.03 (td, J = 8.7, 3.4, 4H), 5.10 (s, 1H), 4.34 – 4.23 (m, 1H), 3.77 – 3.66 (m, 2H), 3.63 – 3.52 (m, 2H), 3.47 – 3.37 (m, 2H), 2.67 – 2.56 (m, 2H), 2.38 (s, 3H), 2.14 – 2.02 (m, 1H), 1.99 – 1.82 (m, 2H), 1.70 – 1.57 (m, 1H), 1.49 (t, J = 6.7, 2H), 1.36 (dt, J = 15.6, 6.5, 1H), 0.91 (dd, J = 8.7, 6.8, 6H); MS (ESI+) *m/z* 484(M+H)$^+$.

Example 460

2,2-bis(4-fluorophenyl)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-methyl-L-norvalyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide

The title compound was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)pentanoic acid for (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4-methylpentanoic acid in the procedure described in Example 459: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.35 – 8.24 (m, 1H), 7.50 – 7.40 (m, 4H), 7.07 – 6.98 (m, 4H), 5.10 (s, 1H), 4.31 – 4.21 (m, 1H), 3.75 – 3.64 (m, 2H), 3.61 – 3.51 (m, 2H), 3.41 – 3.31 (m, 1H), 2.66 – 2.54 (m, 2H), 2.37 (s, 3H), 2.14 – 2.02 (m, 1H), 1.92 – 1.83 (m, 1H), 1.71 – 1.40 (m, 6H), 1.33 (dd, J = 12.9, 8.1, 1H), 0.87 (t, J = 7.2, 3H); MS (ESI+) *m/z* 470(M+H)$^+$.

Example 461

***N*-[(3a*R*,4*S*,6a*S*)-2-(*N*,4-dimethyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-bis(4-fluorophenyl)acetamide**

The title compound was prepared by substituting (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4,4-dimethylpentanoic acid for (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4-methylpentanoic acid in the procedure described in Example 459: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.36 – 8.25 (m, 1H), 7.49 – 7.40 (m, 4H), 7.03 (ddd, *J* = 8.8, 6.3, 3.9, 4H), 5.10 (s, 1H), 4.35 – 4.20 (m, 1H), 3.77 – 3.66 (m, 2H), 3.63 – 3.51 (m, 2H), 3.49 – 3.38 (m, 1H), 2.68 – 2.54 (m, 2H), 2.36 (s, 3H), 2.16 – 2.00 (m, 1H), 1.95 – 1.78 (m, 2H), 1.71 (dd, *J* = 14.1, 4.9, 1H), 1.66 – 1.56 (m, 1H), 1.53 – 1.43 (m, 1H), 1.41 – 1.27 (m, 1H), 0.99 (s, 9H). ; MS (ESI+) *m/z* 498(M+H)$^+$.

Example 462

2,2-bis(4-fluorophenyl)-*N*-[(3a*R*,4*S*,6a*S*)-2-(4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide

The title compound was prepared by substituting (*S*)-2-(*tert*-butoxycarbonylamino)-4,4-dimethylpentanoic acid for (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4-methylpentanoic acid in the procedure described in Example 459: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.37 – 8.15 (m, 1H), 7.46 (td, *J* = 8.6, 5.6, 4H), 7.09 – 6.96 (m, 4H), 5.09 (s, 1H), 4.32 – 4.18 (m, 1H), 3.76 – 3.63 (m, 4H), 3.62 – 3.51 (m, 2H), 3.51 – 3.32 (m, 1H), 2.68 – 2.52 (m, 2H), 2.12 – 1.99 (m, 1H), 1.93 – 1.77 (m, 2H), 1.62 (td, *J* = 15.7, 7.8, 1H), 1.44 (dd, *J* = 14.1, 7.5, 1H), 1.39 – 1.23 (m, 1H), 0.99 (s, 9H); MS (ESI+) *m/z* 498(M+H)$^+$.

Example 463

***tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-4-((*S*)-2-(*tert*-butoxycarbonylamino)-4,4-dimethylpentanamido)hexahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)-4,4-dimethyl-1-oxopentan-2-ylcarbamate**

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-ylcarbamate from Example 226 for *N*-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-2,2-bis(4-fluorophenyl)acetamide (150 mg, 0.336 mmol) and (*S*)-2-(*tert*-butoxycarbonylamino)-4,4-dimethylpentanoic acid for (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4-methylpentanoic acid in the procedure described in Example 459 Steps A and B: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.76 (d, *J* = 5.2, 1H), 7.02 (d, *J* = 4.7, 1H), 6.97 – 6.86 (m, 1H), 4.78 (td, *J*

= 8.7, 4.5, 1H), 4.49 (td, *J* = 8.2, 4.6, 1H), 4.25 – 4.14 (m, 1H), 3.84 – 3.76 (m, 2H), 3.54 – 3.35 (m, 1H), 2.73 – 2.59 (m, 2H), 2.07 (ddd, *J* = 20.0, 13.7, 5.6, 2H), 1.94 – 1.81 (m, 2H), 1.69 (ddd, *J* = 11.1, 7.4, 3.2, 2H), 1.64 – 1.55 (m, 1H), 1.48 (s, 9H), 1.48 (s, 9H), 1.38 – 1.27 (m, 1H), 1.02 (s, 9H), 0.97 (s, 9H); MS (ESI+) *m/z* 581(M+H)$^+$.

Example 464

4-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-4-((*S*)-2-(*tert*-butoxycarbonylamino)-4,4-dimethylpentanamido)hexahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)-4,4-dimethyl-1-oxopentan-2-ylcarbamate from Example 463 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-4-(2,2-bis(4-fluorophenyl)acetamido)hexahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 459 Step C: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.88 – 7.76 (m, 1H), 4.22 – 4.14 (m, 1H), 3.78 – 3.66 (m, 6H), 3.61 (dddd, *J* = 9.1, 4.5, 2.1, 0.7, 2H), 3.50 (dd, *J* = 7.5, 4.1, 2H), 2.70 – 2.60 (m, 1H), 2.60 – 2.51 (m, 1H), 2.11 – 2.00 (m, 2H), 1.96 – 1.83 (m, 2H), 1.66 – 1.53 (m, 1H), 1.45 (dd, *J* = 14.1, 7.4, 1H), 1.36 (dd, *J* = 14.1, 7.5, 2H), 1.00 (s, 9H), 0.97 (s, 9H); MS (ESI+) *m/z* 381(M+H)$^+$.

Example 465

4-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-L-phenylalanyloctahydrocyclopenta[*c*]pyrrol-4-yl]-L-leucinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-ylcarbamate from Example 226 for *N*-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-2,2-bis(4-fluorophenyl)acetamide and (*S*)-2-(*tert*-butoxycarbonylamino)-3-phenylpropanoic acid for (*S*)-2-(*tert*-butoxycarbonyl(methyl)amino)-4-methylpentanoic acid in the procedure described in Example 459: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.84 – 7.68 (m, 1H), 7.34 – 7.24 (m, 3H), 7.18 (t, *J* = 6.8, 2H), 4.08 (dt, *J* = 14.3, 7.0, 1H), 3.81 – 3.67 (m, 6H), 3.53 – 3.46 (m, 4H), 3.10 (dd, *J* = 13.2, 7.0, 1H), 2.88 (dd, *J* = 13.2, 6.8, 1H), 2.53 (td, *J* = 14.0, 7.9, 1H), 2.41 (dt, *J* = 14.4, 7.0, 1H), 2.10 – 2.04 (m, 1H), 1.98 (ddd, *J* = 19.6, 7.2, 5.1, 1H), 1.80 (dt, *J* = 13.0, 7.8, 1H), 1.53 (dq, *J* = 12.8, 8.1, 1H), 1.35 (dd, *J* = 14.1, 7.6, 1H), 1.25 – 1.05 (m, 1H), 0.97 (s, 9H); MS (ESI+) *m/z* 401(M+H)$^+$.

Example 466

(3a*R*,4*S*,6a*S*)-*N*-benzhydryl-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-amine

(3a*R*,4*S*,6a*S*)-2-(3-(Trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine (60 mg, 0.211 mmol), from Example 156 Step A was combined with (bromomethylene)dibenzene (62.6 mg, 0.253 mmol) and potassium carbonate (87 mg, 0.633 mmol) in *N*,*N*-dimethylformamide (1 mL). The reaction was stirred at room temperature for 72 hours. The reaction was quenched with water and extracted with diethyl ether. The ether extracts were washed with water (3×1 mL) and the solvent removed. The crude material was purified using a 12 g silica gel cartridge eluting with a gradient of 0-3% methanol (2 *N* ammonia)/dichloromethane to give (3a*R*,4*S*,6a*S*)-*N*-benzhydryl-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.71 (s, 1H), 7.64 – 7.59 (m, 4H), 7.52 (d, J = 7.7, 1H), 7.44 (t, J = 7.7, 1H), 7.33 (td, J = 7.6, 4.7, 4H), 7.25 – 7.21 (m, 4H), 5.09 (s, 1H), 3.51 (q, J = 13.5, 2H), 3.02 (dd, J = 12.9, 5.5, 1H), 2.63 – 2.54 (m, 1H), 2.51 (dd, J = 8.8, 2.8, 1H), 2.47 – 2.41 (m, 1H), 2.37 (t, J = 8.0, 1H), 2.32 – 2.25 (m, 2H), 1.98 (td, J = 11.4, 5.6, 1H), 1.89 (ddd, J = 12.7, 10.4, 5.8, 1H), 1.45 (ddd, J = 14.7, 11.9, 8.1, 1H), 1.32 – 1.23 (m, 1H); MS (ESI+) *m/z* 451(M+H)$^+$.

Example 467

(3a*S*,4*R*,6a*R*)-*N*-benzhydryl-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine

The title compound was prepared by substituting (3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine from Example 254 Step A for (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 466: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.35-8.36 (bs, 1H), 8.17-8.19 (m, 1H), 7.92-7.95 (m, 1H), 7.75 (t, J = 7.8 Hz, 1H), 7.61-7.64 (m, 2H), 7.57-7.60 (m, 2H), 7.32-7.38 (m, 4H), 7.22-7.26 (m, 2H), 5.02 (s, 1H), 3.33 (dd, J = 9.7, 3.1 Hz, 1H), 3.07 (dd, J = 9.6, 3.0 Hz, 1H), 3.03 (dd, J = 9.8, 7.9 Hz, 1H), 2.90-2.95 (m, 2H), 2.48-2.57 (m, 1H), 2.39-2.45 (m, 1H), 2.17-2.48 (m, 1H), 1.80-1.88 (m, 2H), 1.31-1.39 (m, 1H), 1.04-1.12 (m, 1H); MS (ESI+) *m/z* 501 (M+H)$^+$.

Example 468

(3a*R*,4*S*,6a*S*)-*N*-benzhydryl-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 252 Step D for (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 466: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.35-8.36 (bs, 1H), 8.17-8.19 (m, 1H), 7.92-7.95 (m, 1H), 7.74 (t, J = 7.8 Hz, 1H), 7.61-7.64 (m, 2H), 7.57-7.60 (m, 2H), 7.31-7.39 (m, 4H), 7.22-7.27 (m, 2H), 5.01-5.06 (m, 1H), 3.33 (dd, J = 9.8, 3.1 Hz, 1H), 3.07 (dd, J = 9.6, 2.9 Hz, 1H), 3.03 (dd, J = 9.5, 8.2 Hz, 1H), 2.90-2.94 (m, 2H), 2.49-2.55 (m, 1H), 2.38-2.45 (m, 1H), 2.28-2.38 (m, 1H), 1.80-1.88 (m, 2H), 1.31-1.39 (m, 1H), 1.04-1.12 (m, 1H); MS (ESI+) *m/z* 501 $(M+H)^+$.

Example 469

N^1-[(3a*S*,4*R*,6a*R*)-2-benzhydryloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide

Step A: *tert*-Butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzhydryloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate was prepared by substituting *tert*-butyl methyl((*S*)-4-methyl-1-((3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl)carbamate from Example 349 for (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 466: MS (APCI+) *m/z* 520 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzhydryloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.16-8.18 (m, 1H), 7.63-7.65 (m, 2H), 7.56-7.62 (m, 2H), 7.27-7.37 (m, 4H), 7.13-7.20 (m, 2H), 4.47-4.54 (m, 1H), 4.21 (s, 1H), 3.20 (dd, J = 8.2, 5.9 Hz, 1H), 2.78-2.85 (m, 1H), 2.48-2.59 (m, 2H), 2.39 (s, 3H), 2.34-2.38 (m, 2H), 2.20-2.28 (m, 2H), 1.87-2.07 (m, 1H), 1.81-1.94 (m, 2H), 1.60-1.71 (m, 2H), 1.52-1.59 (m, 1H), 1.44-1.52 (m, 1H), 0.89 (d, J = 6.6 Hz, 3H), 0.83 (d, J = 6.5 Hz, 3H); MS (ESI+) *m/z* 420 $(M+H)^+$.

Example 470

4-methyl-N^2-propyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 419 for (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and 1-iodopropane for iodoethane in the procedure described in Example 288: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.31-8.34 (m, 1H), 8.14-8.16 (m, 2H), 7.90-7.92 (m, 2H), 4.22-4.27 (m, 1H), 3.86 (d, J = 11.3 Hz, 1H), 3.28 (t, J = 5.7 Hz, 1H), 3.15-3.20 (m, 2H), 2.98 (dd, J = 9.5, 6.5 Hz, 1H), 2.52-2.62 (m, 4H), 1.92-2.00 (m, 1H), 1.89 (dd, J = 14.1, 4.8 Hz, 1H), 1.81-1.88 (m, 1H), 1.65-1.86 (m, 1H), 1.53-1.62 (m, 1H), 1.40-1.54 (m, 3H), 1.27-1.38 (m, 1H), 0.99 (s, 9H), 0.89 (t, J = 7.4 Hz, 3H); MS (ESI+) *m/z* 504 $(M+H)^+$.

Example 471

N^2-(cyclopropylmethyl)-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 419 for (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and (bromomethyl)cyclopropane for iodoethane in the procedure described in Example 288: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.29-8.31 (m, 1H), 8.13-8.15 (m, 2H), 7.89-7.91 (m, 2H), 4.21-4.26 (m, 1H), 3.87 (dd, J = 9.9, 2.3 Hz, 1H), 3.31 (dd, J = 7.0, 4.5 Hz, 1H), 3.18 (dd, J = 9.8, 2.1 Hz, 1H), 3.16 (dd, J = 9.8, 7.5 Hz, 1H), 2.97 (dd, J = 9.6, 6.7 Hz, 1H), 2.49-2.59 (m, 4H), 1.90-2.04 (m, 1H), 1.92-1.98 (m, 1H), 1.90 (dd, J = 14.1, 4.5 Hz, 1H), 1.80-1.87 (m, 1H), 1.53-1.61 (m, 1H), 1.50 (dd, J = 14.1, 7.1 Hz, 1H), 1.26-1.34 (m, 1H), 0.99 (s, 9H), 0.92-1.03 (m, 1H), 0.39-0.47 (m, 2H), 0.13-0.19 (m, 2H); MS (ESI+) *m/z* 516 $(M+H)^+$.

Example 472

N^2-(cyclobutylmethyl)-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 419 for (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and (bromomethyl)cyclobutane for iodoethane in the procedure described in Example 288: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.28-8.30 (m, 1H), 8.14-8.16 (m, 2H), 7.89-7.92 (m, 2H), 4.23-4.27 (m, 1H), 3.88 (dd, J = 9.9, 2.2 Hz, 1H), 3.27 (dd, J = 7.0, 4.6 Hz, 1H), 3.16-3.20 (m, 2H), 2.98 (dd, J = 9.5, 6.5 Hz, 1H), 2.58-2.69 (m, 4H), 2.36-2.47 (m, 1H), 1.94-2.03 (m, 3H), 1.88 (dd, J = 14.0, 4.6 Hz, 1H), 1.74-1.88 (m, 3H), 1.62-1.73 (m, 2H), 1.53-1.62 (m, 1H), 1.48 (dd, J = 14.1, 7.1 Hz, 1H), 1.32 (ddt, J = 9.6, 12.8, 6.4 Hz, 1H), 0.99 (s, 9H); MS (ESI+) *m/z* 530 $(M+H)^+$.

Example 473

N^2-isobutyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 419 for (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and 1-iodo-2-methylpropane for iodoethane in the procedure described in Example 288: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.26-8.28 (m, 1H), 8.14-8.16 (m, 2H), 7.89-7.92 (m, 2H), 4.22-4.28 (m, 1H), 3.86 (dd, J = 10.0, 2.4 Hz, 1H), 3.25 (dd, J = 7.1, 4.6 Hz, 1H), 3.16-3.21 (m, 2H), 2.99 (dd, J = 9.6, 6.8 Hz, 1H), 2.54-2.60 (m, 2H), 2.38-2.46 (m, 2H), 1.96 (dq, J = 11.8, 5.9 Hz, 1H), 1.87 (dd, J = 14.1, 4.7 Hz, 1H), 1.80-1.88 (m, 1H), 1.63-1.77 (m, 1H), 1.62-1.70 (m, 1H), 1.53-1.61 (m, 1H), 1.50 (dd, J = 14.0, 7.2 Hz, 1H), 1.28-1.35 (m, 1H), 0.99 (s, 9H), 0.92 (d, J = 6.7 Hz, 3H), 0.90 (d, J = 6.7 Hz, 3H); MS (ESI+) *m/z* 518 $(M+H)^+$.

Example 474

N^2-(cyclopentylmethyl)-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 419 for (3a*R*,4*S*,6a*S*)-2-(4-

(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and (iodomethyl)cyclopentane for iodoethane in the procedure described in Example 288: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.30-8.32 (m, 1H), 8.13-8.16 (m, 2H), 7.89-7.92 (m, 2H), 4.22-4.27 (m, 1H), 3.87 (dd, J = 9.9, 2.2 Hz, 1H), 3.28 (dd, J = 7.1, 4.5 Hz, 1H), 3.15-3.22 (m, 2H), 2.96-3.01 (m, 1H), 2.46-2.60 (m, 4H), 1.82-2.01 (m, 4H), 1.20-2.29 (m, 1H), 1.67-1.79 (m, 2H), 1.42-1.63 (m, 6H), 1.13-1.36 (m, 3H), 1.00 (s, 9H); MS (ESI+) *m/z* 544 $(M+H)^+$.

Example 475

N^2-(cyclohexylmethyl)-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 419 for (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and (bromomethyl)cyclohexane for iodoethane in the procedure described in Example 288: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.27-8.29 (m, 1H), 8.14-8.16 (m, 2H), 7.89-7.92 (m, 2H), 4.23-4.28 (m, 1H), 3.88 (dd, J = 9.9, 2.2 Hz, 1H), 3.25 (dd, J = 7.1, 4.5 Hz, 1H), 3.16-3.21 (m, 2H), 2.99 (dd, J = 9.6, 6.5 Hz, 1H), 2.59-2.61 (m, 2H), 2.47 (dd, J = 11.1, 6.7 Hz, 1H), 2.43 (dd, J = 11.2, 6.2 Hz, 1H), 1.98 (dq, J = 11.8, 5.9 Hz, 1H), 1.89 (dd, J = 14.2, 4.4 Hz, 1H), 1.82-1.89 (m, 1H), 1.71-1.82 (m, 2H), 1.58-1.79 (m, 1H), 1.56-1.67 (m, 4H), 1.52 (dd, J = 14.0, 7.2 Hz, 1H), 1.28-1.41 (m, 2H), 1.05-1.22 (m, 3H), 1.00 (s, 9H), 0.86-0.98 (m, 2H); MS (ESI+) *m/z* 558 $(M+H)^+$.

Example 476

N^2-butyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 419 for (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and 1-iodobutane for iodoethane in the procedure described in Example 288: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.32-8.34 (m, 1H), 8.14-8.16 (m, 2H), 7.90-7.92 (m, 2H), 4.24-4.29 (m, 1H), 3.87 (dd, J

= 9.9, 2.1 Hz, 1H), 3.29 (dd, J = 6.8, 4.8 Hz, 1H), 3.15-3.21 (m, 2H), 2.99 (dd, J = 9.5, 6.4 Hz, 1H), 2.55-2.66 (m, 4H), 1.94-2.01 (m, 1H), 1.90 (dd, J = 14.0, 4.9 Hz, 1H), 1.82-1.89 (m, 1H), 1.64-1.88 (m, 1H), 1.54-1.63 (m, 1H), 1.51 (dd, J = 14.0, 6.9 Hz, 1H), 1.39-1.47 (m, 2H), 1.26-1.38 (m, 3H), 0.99 (s, 9H), 0.84 (t, J = 7.3 Hz, 3H); MS (ESI-) m/z 516 $(M-H)^-$.

Example 477

N^2-ethyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 419 for (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 288: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.35-8.38 (m, 1H), 8.14-8.16 (m, 2H), 7.90-7.92 (m, 2H), 4.22-4.27 (m, 1H), 3.86 (dd, J = 10.0, 2.2 Hz, 1H), 3.30 (t, J = 5.8 Hz, 1H), 3.14-3.20 (m, 2H), 2.98 (dd, J = 9.5, 6.4 Hz, 1H), 2.65-2.72 (m, 1H), 2.57-2.63 (m, 1H), 2.56-2.60 (m, 2H), 1.92-1.99 (m, 1H), 1.90 (dd, J = 14.0, 5.0 Hz, 1H), 1.79-1.88 (m, 1H), 1.62-1.94 (m, 1H), 1.52-1.63 (m, 1H), 1.50 (dd, J = 14.0, 6.6 Hz, 1H), 1.26-1.40 (m, 1H), 1.06 (t, J = 7.1 Hz, 3H), 0.98 (s, 9H); MS (ESI+) m/z 490 $(M+H)^+$.

Example 478

N^2-(cyclopropylmethyl)-4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 440 for (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and (bromomethyl)cyclopropane for iodoethane in the procedure described in Example 288: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.62-8.63 (bs, 1H), 8.38-8.41 (m, 1H), 7.68 (dd, J = 8.9, 2.5 Hz, 1H), 6.40 (d, J = 8.9 Hz, 1H), 4.38-4.44 (m, 1H), 3.82-3.86 (m, 1H), 3.66-3.70 (m, 1H), 3.56-3.61 (m, 1H), 3.29-3.41 (m, 2H), 2.75-2.78 (m, 2H), 2.57 (dd, J = 6.7, 2.1 Hz, 2H), 2.12-2.21 (m, 1H), 1.92-2.00 (m, 1H), 1.95 (dd, J = 14.0, 4.5 Hz, 1H), 1.71 (dq, J = 12.7, 8.1 Hz, 1H), 1.54 (dd, J = 14.1, 7.0 Hz, 1H), 1.38-1.48 (m, 1H), 1.02 (s, 9H), 0.96-1.05 (m, 1H), 0.45-0.48 (m, 2H), 0.16-0.24 (m, 2H); MS (ESI+) m/z 453 $(M+H)^+$.

Example 479

N^2-(cyclopropylmethyl)-4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 441 for (3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and (bromomethyl)cyclopropane for iodoethane in the procedure described in Example 288: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.34-8.36 (m, 1H), 7.51 (t, J = 7.9 Hz, 1H), 6.98 (d, J = 7.2 Hz, 1H), 6.52 (d, J = 8.5 Hz, 1H), 4.35-4.41 (m, 1H), 3.73 (dd, J = 10.9, 2.9 Hz, 1H), 3.60-3.65 (m, 1H), 3.52 (dd, J = 10.7, 7.3 Hz, 1H), 3.36 (dd, J = 7.1, 4.5 Hz, 1H), 3.29 (dd, J = 10.9, 3.6 Hz, 1H), 2.69-2.77 (m, 2H), 2.55 (dd, J = 6.7, 2.8 Hz, 2H), 2.10-2.16 (m, 1H), 1.94 (dd, J = 14.1, 4.5 Hz, 1H), 1.89-1.96 (m, 1H), 1.74-2.09 (m, 1H), 1.69 (dq, J = 12.7, 7.9 Hz, 1H), 1.53 (dd, J = 14.1, 7.0 Hz, 1H), 1.31-1.42 (m, 1H), 1.02 (s, 9H), 0.95-1.05 (m, 1H), 0.42-0.51 (m, 2H), 0.15-0.25 (m, 2H); MS (ESI+) *m/z* 453 $(M+H)^+$.

Example 480

N^2-isopropyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 419 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.26-8.29 (m, 1H), 8.13-8.16 (m, 2H), 7.89-7.91 (m, 2H), 4.21-4.26 (m, 1H), 3.85 (dd, J = 9.9, 2.3 Hz, 1H), 3.36 (dd, J = 7.5, 4.1 Hz, 1H), 3.15-3.20 (m, 2H), 2.98 (dd, J = 9.6, 6.7 Hz, 1H), 2.83 (hept, J = 6.2 Hz, 1H), 2.51-2.62 (m, 2H), 1.91-1.97 (m, 1H), 1.79-1.88 (m, 2H), 1.63-1.81 (m, 1H), 1.51-1.59 (m, 1H), 1.47 (dd, J = 14.1, 7.5 Hz, 1H), 1.31 (ddt, J = 9.6, 12.8, 6.4 Hz, 1H), 1.03 (dd, J = 6.2, 2.7 Hz, 6H), 0.98 (s, 9H); MS (ESI+) *m/z* 504 $(M+H)^+$.

Example 481

N^2-isopropyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

The title compound was prepared by substituting N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide from Example 422 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.31-8.34 (m, 1H), 8.13-8.15 (m, 2H), 7.89-7.91 (m, 2H), 4.21-4.27 (m, 1H), 3.84 (dd, J = 9.9, 2.7 Hz, 1H), 3.31-3.34 (m, 1H), 3.18 (dd, J = 9.8, 2.8 Hz, 1H), 3.16 (dd, J = 10.2, 7.9 Hz, 1H), 2.98 (dd, J = 9.6, 7.0 Hz, 1H), 2.83 (hept, J = 6.1 Hz, 1H), 2.46-2.60 (m, 2H), 1.94 (dq, J = 11.8, 5.9 Hz, 1H), 1.77-1.87 (m, 2H), 1.59-1.69 (m, 1H), 1.37-1.59 (m, 4H), 1.27-1.35 (m, 1H), 1.05 (d, J = 6.3 Hz, 3H), 1.03 (d, J = 6.3 Hz, 3H), 0.85 (t, J = 7.4 Hz, 3H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Example 482

N^2-isopropyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

The title compound was prepared by substituting N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide from Example 423 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.26-8.28 (m, 1H), 8.11-8.14 (m, 2H), 7.88-7.91 (m, 2H), 4.23 (p, J = 6.9 Hz, 1H), 3.85 (dd, J = 9.9, 2.9 Hz, 1H), 3.30 (dd, J = 7.5, 5.5 Hz, 1H), 3.18 (dd, J = 9.7, 3.0 Hz, 1H), 3.14 (dd, J = 9.9, 7.7 Hz, 1H), 2.97 (dd, J = 9.6, 7.3 Hz, 1H), 2.81 (p, J = 6.2 Hz, 1H), 2.49-2.61 (m, 2H), 1.90-1.99 (m, 1H), 1.81-1.92 (m, 1H), 1.81-1.88 (m, 1H), 1.74-1.81 (m, 1H), 1.59-1.68 (m, 1H), 1.37-1.58 (m, 3H), 1.27-1.36 (m, 1H), 1.02 (dd, J = 6.2, 1.5 Hz, 6H), 0.85 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Example 483

N^2-isopropyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

The title compound was prepared by substituting N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide from Example 424 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.38-8.39 (bs, 1H), 8.26-8.28 (m, 1H), 8.20 (d, J = 7.9 Hz, 1H), 7.90-7.92 (m, 1H), 7.72 (t, J = 7.8 Hz, 1H), 4.20-4.27 (m, 1H), 3.85 (dd, J = 9.9, 2.5 Hz, 1H), 3.29 (dd, J = 7.6, 5.5 Hz, 1H), 3.18 (dd, J = 20.2, 2.5 Hz, 1H), 3.14-3.18 (m, 1H), 2.96 (dd, J = 9.6, 7.0 Hz, 1H), 2.77-2.83 (m, 1H), 2.51-2.57 (m, 2H), 1.89-1.99 (m, 1H), 1.82-1.93 (m, 1H), 1.80-1.88 (m, 1H), 1.73-1.81 (m, 1H), 1.56-1.67 (m, 1H), 1.36-1.56 (m, 3H), 1.25-1.35 (m, 1H), 1.02 (dd, J = 9.4, 6.2 Hz, 6H), 0.85 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Example 484

N^2-isopropyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

The title compound was prepared by substituting N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide from Example 425 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37-8.38 (bs, 1H), 8.26-8.28 (m, 1H), 8.17-8.20 (m, 1H), 7.90-7.92 (m, 1H), 7.71 (t, J = 7.8 Hz, 1H), 4.21-4.27 (m, 1H), 3.86 (dd, J = 9.9, 2.7 Hz, 1H), 3.29 (dd, J = 7.5, 5.5 Hz, 1H), 3.18 (dd, J = 9.6, 2.8 Hz, 1H), 3.14 (dd, J = 9.9, 7.5 Hz, 1H), 2.95 (dd, J = 9.6, 7.2 Hz, 1H), 2.76-2.84 (m, 1H), 2.47-2.58 (m, 2H), 1.91-1.98 (m, 1H), 1.82-1.93 (m, 1H), 1.81-1.89 (m, 1H), 1.73-1.81 (m, 1H), 1.57-1.66 (m, 1H), 1.36-1.57 (m, 3H), 1.25-1.35 (m, 1H), 1.02 (dd, J = 6.2, 2.0 Hz, 6H), 0.84 (t, J = 7.3 Hz, 3H).

Example 485

3-cyclohexyl-N^2-isopropyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-alaninamide

The title compound was prepared by substituting 3-cyclohexyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-alaninamide from Example 426 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.32 (d, J = 7.2 Hz, 1H), 8.13-8.16 (m, 2H), 7.89-7.95 (m, 2H), 4.22-4.30 (m, 1H), 3.85 (dd, J = 10.0, 2.3 Hz, 1H), 3.41 (dd, J = 8.5, 5.2 Hz, 1H), 3.15-3.21 (m, 2H), 2.99 (dd, J = 9.6, 6.7 Hz, 1H), 2.85 (p, J = 6.2 Hz, 1H), 2.56-2.61 (m, 2H), 1.83-2.11 (m, 1H), 1.90-2.00 (m, 1H), 1.79-1.89 (m, 1H), 1.66-1.78 (m, 3H), 1.46-1.65 (m, 6H), 1.25-1.37 (m, 1H), 1.08-1.25 (m, 3H), 1.06 (d, J = 6.3 Hz, 3H), 1.04 (d, J = 6.3 Hz, 3H), 0.75-1.00 (m, 2H); MS (ESI+) *m/z* 530 $(M+H)^+$.

Example 486

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-5-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-isopropyl-4-methyl-L-leucinamide

The title compound was prepared by substituting N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-5-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-L-leucinamide from Example 428 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.57 (d, J = 2.2 Hz, 1H), 8.32-8.35 (m, 1H), 7.81 (dd, J = 8.3, 2.2 Hz, 1H), 7.75 (d, J = 8.3 Hz, 1H), 4.29-4.35 (m, 1H), 3.93 (dd, J = 10.2, 2.2 Hz, 1H), 3.56 (dd, J = 10.1, 6.6 Hz, 1H), 3.35-3.41 (m, 2H), 3.32 (dd, J = 10.0, 2.6 Hz, 1H), 2.83 (hept, J = 6.2 Hz, 1H), 2.66-2.68 (m, 2H), 2.01-2.08 (m, 1H), 1.86-1.93 (m, 1H), 1.84 (dd, J = 14.2, 4.3 Hz, 1H), 1.66-1.81 (m, 1H), 1.56-1.66 (m, 1H), 1.46 (dd, J = 14.1, 7.4 Hz, 1H), 1.35-1.42 (m, 1H), 1.03 (d, J = 6.1 Hz, 3H), 1.02 (d, J = 6.1 Hz, 3H), 0.98 (s, 9H); MS (ESI+) *m/z* 538 $(M+H)^+$.

Example 487

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-isopropyl-4-methyl-L-leucinamide

The title compound was prepared by substituting N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-L-leucinamide from Example 429 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (501 MHz, pyridine-d_5) δ ppm 8.35 (d, J = 8.2 Hz, 1H), 8.29-8.32 (m, 1H), 7.99 (s, 1H), 7.73 (d, J = 9.1 Hz, 1H), 4.29-4.35 (m, 1H), 3.95 (dd, J = 10.2, 2.4 Hz, 1H), 3.54 (dd, J = 10.1, 6.9 Hz, 1H), 3.40 (dd, J = 10.0, 6.5 Hz, 1H), 3.33-3.36 (m, 2H), 2.82 (dq, J = 12.4, 6.2 Hz, 1H), 2.65-2.68 (m, 2H), 2.00-2.07 (m, 1H), 1.85-1.92 (m, 1H), 1.84 (dd, J = 14.1, 4.2 Hz, 1H), 1.65-1.82 (m, 1H), 1.55-1.65 (m, 1H), 1.46 (dd, J = 14.1, 7.6 Hz, 1H), 1.34-1.43 (m, 1H), 1.03 (d, J = 6.1 Hz, 3H), 1.02 (d, J = 6.3 Hz, 3H), 0.98 (s, 9H); MS (ESI+) *m/z* 538 $(M+H)^+$.

Example 488

N^2-isopropyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropyl-4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-leucinamide from Example 464 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.77 – 7.66 (m, 1H), 4.30 – 4.18 (m, 1H), 3.80 – 3.72 (m, 3H), 3.72 – 3.61 (m, 3H), 3.60 – 3.45 (m, 1H), 3.32 (dd, J = 7.3, 4.2, 1H), 2.87 – 2.77 (m, 2H), 2.76 – 2.68 (m, 1H), 2.68 – 2.60 (m, 1H), 2.17 – 2.05 (m, 1H), 2.02 – 1.90 (m, 1H), 1.82 (dd, J = 14.2, 4.2, 1H), 1.64 (dd, J = 14.2, 4.2, 2H), 1.46 (ddd, J = 27.5, 14.2, 7.7, 3H), 1.12 – 0.92 (m, 30H); MS (ESI+) *m/z* 465 $(M+H)^+$.

Example 489

N^2-isopropyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropyl-L-phenylalanyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-L-phenylalanyloctahydrocyclopenta[*c*]pyrrol-4-yl]-L-leucinamide from Example 465 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.74 – 7.61 (m, 1H), 7.36 – 7.23 (m, 4H), 7.22 – 7.15 (m, 2H), 4.19 – 4.02 (m, 2H), 3.77 (dd, J = 11.9, 3.7, 5H), 3.56 – 3.48 (m, 1H), 3.32 (dd, J = 7.3, 4.3, 1H), 3.05 – 2.94 (m, 2H), 2.92 – 2.76 (m, 2H), 2.66 – 2.50 (m, 1H), 2.48 – 2.35 (m, 1H), 2.06 – 1.92 (m, 1H), 1.83 (dd, J = 14.2, 4.3, 2H), 1.55 (dq, J = 12.8, 8.0, 1H), 1.42 (dd, J = 14.2, 7.3, 1H), 1.08 – 1.00 (m, 12H), 0.99 (s, 9H); MS (ESI+) *m/z* 485 $(M+H)^+$.

Example 490

N^2-isopropyl-4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 440 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.62-8.63 (bs, 1H), 8.34-8.36 (m, 1H), 7.68 (dd, J = 8.9, 2.5 Hz, 1H), 6.40 (d, J = 8.9 Hz, 1H), 4.39-4.44 (m, 1H), 3.82-3.85 (m, 1H), 3.67-3.71 (m, 1H), 3.57-3.61 (m, 1H), 3.29-3.44 (m, 2H), 2.88 (hept, J = 6.2 Hz, 1H), 2.74-2.76 (m, 2H), 2.13-2.20 (m, 1H), 1.64-2.00 (m, 4H), 1.51 (dd, J = 14.1, 7.6 Hz, 1H), 1.39-1.46 (m, 1H), 1.08 (d, J = 6.3 Hz, 3H), 1.07 (d, J = 6.3 Hz, 3H), 1.01 (s, 9H); MS (ESI+) *m/z* 441 $(M+H)^+$.

Example 491

N^2-isopropyl-4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 441 for (3a*S*,4*R*,6a*R*)-2-(3-

(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.31-8.34 (m, 1H), 7.51 (t, J = 7.9 Hz, 1H), 6.98 (d, J = 7.2 Hz, 1H), 6.52 (d, J = 8.6 Hz, 1H), 4.36-4.41 (m, 1H), 3.73 (dd, J = 10.9, 3.0 Hz, 1H), 3.63 (dd, J = 10.9, 7.0 Hz, 1H), 3.53 (dd, J = 10.8, 7.4 Hz, 1H), 3.40 (dd, J = 7.5, 4.0 Hz, 1H), 3.29 (dd, J = 10.9, 3.6 Hz, 1H), 2.88 (p, J = 6.2 Hz, 1H), 2.74 (dd, J = 5.6, 2.8 Hz, 2H), 2.09-2.16 (m, 1H), 1.89-1.98 (m, 1H), 1.90 (dd, J = 14.1, 4.0 Hz, 1H), 1.69-1.85 (m, 1H), 1.63-1.73 (m, 1H), 1.50 (dd, J = 14.1, 7.6 Hz, 1H), 1.36-1.43 (m, 1H), 1.07 (d, J = 6.3 Hz, 3H), 1.07 (d, J = 6.1 Hz, 3H), 1.01 (s, 9H); MS (ESI+) *m/z* 441 $(M+H)^+$.

Example 492

2,2-bis(4-fluorophenyl)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropyl-4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide

The title compound was prepared by substituting 2,2-bis(4-fluorophenyl)-*N*-[(3a*R*,4*S*,6a*S*)-2-(4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide from Example 462 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.35 – 8.23 (m, 1H), 7.49 – 7.41 (m, 4H), 7.07 – 6.99 (m, 4H), 5.10 (s, 1H), 4.37 – 4.19 (m, 1H), 3.78 – 3.70 (m, 2H), 3.66-3.41 (m 4H), 2.84 – 2.71 (m, 1H), 2.69 – 2.54 (m, 2H), 2.14 – 2.00 (m, 1H), 1.95 – 1.80 (m, 1H), 1.63 (ddd, J = 12.4, 9.1, 6.0, 2H), 1.48 (dd, J = 14.2, 8.0, 1H), 1.42 – 1.29 (m, 1H), 1.08 – 0.95 (m, 15H); MS (ESI+) *m/z* 526 $(M+H)^+$.

Example 493

N^2-isopropyl-4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[2-(methylsulfonyl)pyrimidin-5-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[2-(methylsulfonyl)pyrimidin-5-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 442 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.45 (s, 2H), 8.31-8.33 (m, 1H), 4.95 (s, 3H), 4.40-4.46 (m, 1H), 3.97 (dd, J = 11.8, 2.8 Hz, 1H), 3.80 (dd, J = 11.9, 7.6 Hz, 1H), 3.73 (dd, J = 11.6, 8.1 Hz, 1H), 3.45 (dd, J =

11.7, 4.1 Hz, 1H), 3.40 (dd, J = 7.5, 4.0 Hz, 1H), 2.86 (hept, J = 6.2 Hz, 1H), 2.70-2.78 (m, 2H), 2.13-2.19 (m, 1H), 1.89-1.98 (m, 1H), 1.89 (dd, J = 14.2, 4.1 Hz, 1H), 1.65-1.81 (m, 1H), 1.63-1.72 (m, 1H), 1.49 (dd, J = 14.1, 7.6 Hz, 1H), 1.38-1.45 (m, 1H), 1.06 (d, J = 6.1 Hz, 3H), 1.05 (d, J = 6.1 Hz, 3H), 1.00 (s, 9H); MS (ESI+) *m/z* 450 $(M+H)^+$.

Example 494

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-isopropyl-L-norvalinamide

Step A: N^1-{(3a*R*,4*S*,6a*S*)-2-Benzyloctahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide was prepared by substituting *tert*-butyl ((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 382 Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.17 (d, J = 7.3, 1H), 7.43 (d, J = 7.4, 2H), 7.36 (t, J = 7.6, 2H), 7.27 (t, J = 7.3, 1H), 4.42 – 4.35 (m, 1H), 3.59 (d, J = 13.2, 1H), 3.53 (dd, J = 7.9, 4.9, 1H), 3.44 (d, J = 13.1, 1H), 2.84 (dd, J = 8.9, 2.4, 1H), 2.54 – 2.42 (m, 2H), 2.41 – 2.33 (m, 2H), 2.23 (dd, J = 8.7, 7.3, 1H), 2.10 (dt, J = 17.7, 5.8, 3H), 1.98 – 1.90 (m, 1H), 1.82 (dt, J = 20.2, 6.2, 1H), 1.69 – 1.61 (m, 1H), 1.58 – 1.34 (m, 4H), 0.84 (t, J = 7.3, 3H); MS (ESI+) *m/z* 316 $(M+H)^+$.

Step B: The title compound was prepared by substituting N^1-{(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide from Step A for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.17-8.19 (m, 1H), 7.43-7.46 (m, 2H), 7.37 (t, J = 7.5 Hz, 2H), 7.28 (t, J = 7.3 Hz, 1H), 4.39-4.44 (m, 1H), 3.61 (d, J = 13.1 Hz, 1H), 3.46 (d, J = 13.1 Hz, 1H), 3.32 (dd, J = 7.6, 5.5 Hz, 1H), 2.81-2.86 (m, 2H), 2.48-2.59 (m, 2H), 2.45 (dd, J = 8.7, 7.2 Hz, 1H), 2.36 (dd, J = 9.0, 2.7 Hz, 1H), 2.28 (dd, J = 8.9, 6.8 Hz, 1H), 2.12 (dq, J = 12.0, 6.0 Hz, 1H), 1.84-1.99 (m, 1H), 1.77-1.89 (m, 2H), 1.40-1.67 (m, 5H), 1.05 (d, J = 6.1 Hz, 3H), 1.04 (d, J = 6.0 Hz, 3H), 0.85 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 358 $(M+H)^+$.

Example 495

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-isopropyl-L-norvalinamide

Step A: *tert*-Butyl ((*S*)-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting *N*-(*tert*-butoxycarbonyl)-L-norvaline for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Example 16 Step D for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.58 (d, J = 7.2, 1H), 7.91 (d, J = 8.3, 1H), 7.42 (d, J = 7.3, 2H), 7.36 (t, J = 7.4, 2H), 7.27 (t, J = 7.2, 1H), 4.64 (dd, J = 14.4, 7.7, 1H), 4.45 – 4.34 (m, 1H), 3.56 (d, J = 13.1, 1H), 3.40 (d, J = 13.2, 1H), 2.74 (d, J = 8.9, 1H), 2.48 (d, J = 0.7, 2H), 2.39 – 2.27 (m, 2H), 2.26 – 2.19 (m, 1H), 2.14 (dq, J = 12.0, 6.0, 1H), 2.07 – 1.96 (m, 1H), 1.85 (td, J = 13.8, 8.2, 2H), 1.65 (td, J = 14.3, 7.3, 1H), 1.49 (d, J = 8.5, 11H), 1.45 – 1.33 (m, 1H), 0.81 (t, J = 7.3, 3H); MS (ESI+) *m/z* 416 $(M+H)^+$.

Step B: N^1-{(3a*S*,4*R*,6a*R*)-2-Benzyloctahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide was prepared by substituting *tert*-butyl-((*S*)-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.19 (d, J = 7.4, 1H), 7.43 (d, J = 7.3, 2H), 7.36 (t, J = 7.6, 2H), 7.27 (t, J = 7.3, 1H), 4.43 – 4.35 (m, 1H), 3.59 (d, J = 13.1, 1H), 3.53 (dd, J = 7.9, 5.0, 1H), 3.43 (d, J = 13.2, 1H), 2.83 (dd, J = 8.9, 2.4, 1H), 2.55 – 2.48 (m, 1H), 2.44 (ddd, J = 9.2, 6.0, 3.6, 1H), 2.41 – 2.33 (m, 2H), 2.23 (dd, J = 8.8, 7.3, 1H), 2.10 (td, J = 11.8, 5.9, 3H), 1.98 – 1.89 (m, 1H), 1.83 (dt, J = 20.4, 6.2, 1H), 1.70 – 1.60 (m, 1H), 1.58 – 1.33 (m, 4H), 0.84 (t, J = 7.3, 3H); MS (ESI+) *m/z* 316 $(M+H)^+$.

Step C: The title compound was prepared by substituting N^1-{(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide from Step B for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.18-8.20 (m, 1H), 7.43-7.45 (m, 2H), 7.37 (t, J = 7.5 Hz, 2H), 7.28 (t, J = 7.3 Hz, 1H), 4.40-4.46 (m, 1H), 3.60 (d, J = 13.1 Hz, 1H), 3.44 (d, J = 13.1 Hz, 1H), 3.32 (dd, J = 7.5, 5.5 Hz, 1H), 2.80-2.86 (m, 2H), 2.46-2.59 (m, 2H), 2.43 (dd, J = 8.8, 7.2 Hz, 1H), 2.35 (dd, J = 8.9, 2.9 Hz, 1H), 2.27 (dd, J = 8.9, 7.1 Hz, 1H), 2.12 (dq, J = 12.0, 6.0 Hz, 1H), 1.86-

2.04 (m, 1H), 1.77-1.90 (m, 2H), 1.55-1.70 (m, 2H), 1.38-1.55 (m, 3H), 1.05 (d, J = 6.9 Hz, 3H), 1.04 (d, J = 6.6 Hz, 3H), 0.85 (t, J = 7.3 Hz, 3H); MS (ESI+) m/z 358 $(M+H)^+$.

Example 496

N^2-isopropyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

Step A: *tert*-Butyl-((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine from 252 Step D for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.75 (d, J = 13.1, 1H), 8.37 (s, 1H), 8.18 (d, J = 7.7, 1H), 8.00 (d, J = 8.4, 1H), 7.91 (d, J = 7.9, 1H), 7.71 (t, J = 7.9, 1H), 4.70 – 4.59 (m, 1H), 4.29 – 4.18 (m, 1H), 3.82 (dd, J = 10.1, 2.4, 1H), 3.15 (dd, J = 9.9, 7.6, 2H), 2.99 – 2.89 (m, 1H), 2.62 – 2.44 (m, 2H), 1.93 – 1.70 (m, 5H), 1.55 – 1.44 (m, 10H), 1.30 – 1.16 (m, 1H), 0.86 (d, J = 5.9, 3H), 0.83 (d, J = 5.9, 3H). ; MS (ESI-) m/z 545 $(M-H)^-$.

Step B: N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(Trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide was prepared by substituting *tert*-butyl-((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.44 – 8.32 (m, 2H), 8.19 (d, J = 7.9, 1H), 7.91 (d, J = 7.9, 1H), 7.79 – 7.66 (m, 1H), 4.72 – 4.38 (m, 3H), 4.29 – 4.15 (m, 1H), 3.84 (dd, J = 9.9, 2.4, 1H), 3.60 (dd, J = 9.3, 4.5, 1H), 3.06 (dt, J = 21.7, 10.8, 1H), 2.92 (dd, J = 9.6, 7.2, 1H), 2.57 – 2.45 (m, 2H), 1.98 – 1.76 (m, 4H), 1.61 – 1.43 (m, 2H), 1.26 (ddt, J = 13.2, 9.9, 6.5, 1H), 0.90 (d, J = 6.4, 3H), 0.84 (d, J = 6.3, 3H); MS (ESI-) m/z 448 $(M-H)^-$.

Step C: The title compound was prepared by substituting N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Step B for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.38 (s, 1H), 8.30-8.33 (m, 1H), 8.20 (d, J = 7.9 Hz, 1H),

7.90-7.93 (m, 1H), 7.72 (t, J = 7.8 Hz, 1H), 4.20-4.26 (m, 1H), 3.86 (dd, J = 9.9, 2.3 Hz, 1H), 3.35 (dd, J = 8.9, 5.1 Hz, 1H), 3.14-3.20 (m, 2H), 2.97 (dd, J = 9.6, 6.8 Hz, 1H), 2.83 (hept, J = 6.2 Hz, 1H), 2.52-2.56 (m, 2H), 2.07-2.81 (m, 1H), 1.78-2.01 (m, 3H), 1.64 (ddd, J = 13.6, 8.4, 5.2 Hz, 1H), 1.47-1.59 (m, 2H), 1.25-1.36 (m, 1H), 1.04 (d, J = 6.3 Hz, 3H), 1.02 (d, J = 6.1 Hz, 3H), 0.91 (d, J = 6.7 Hz, 3H), 0.85 (d, J = 6.6 Hz, 3H); MS (ESI-) m/z 488 $(M-H)^-$.

Example 497

N^2,N^2-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 384 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and formaldehyde for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.37 (s, 1H), 8.26 (d, J = 7.0, 1H), 8.19 (d, J = 7.9, 1H), 7.91 (d, J = 7.9, 1H), 7.72 (t, J = 7.9, 1H), 4.24 (dt, J = 13.3, 6.5, 1H), 3.85 (dd, J = 10.0, 2.0, 1H), 3.20 – 3.11 (m, 3H), 2.94 (dd, J = 9.6, 7.1, 1H), 2.59 – 2.48 (m, 2H), 2.33 (s, 6H), 1.96 (dt, J = 12.3, 6.3, 1H), 1.81 (tdd, J = 14.4, 11.4, 6.9, 3H), 1.56 (ddt, J = 18.7, 13.2, 8.6, 2H), 1.28 (ddt, J = 13.0, 9.8, 6.4, 1H), 0.93 (d, J = 6.5, 3H), 0.90 (d, J = 6.4, 3H); MS (ESI+) m/z 476 $(M+H)^+$.

Example 498

(3*R*)-3-(dimethylamino)-4-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide

The title compound was prepared by substituting (3*R*)-3-amino-4-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide from Example 388 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and formaldehyde for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.47-8.49 (m, 1H), 8.37-8.38 (bs, 1H), 8.20 (d, J = 7.9 Hz, 1H), 7.91 (d, J = 7.9 Hz, 1H), 7.71 (t, J = 7.8 Hz, 1H), 4.24 (p, J = 6.4 Hz, 1H), 3.85 (dd, J = 9.9, 2.4 Hz, 1H), 3.13-3.18 (m, 2H), 2.95-3.01 (m, 2H), 2.48-2.55 (m, 3H), 2.23 (s, 6H), 2.20 (dd, J = 15.1, 5.8 Hz, 1H), 1.95 (dq, J = 11.8, 5.9 Hz, 1H), 1.80-1.88 (m, 1H), 1.63-1.73 (m, 1H), 1.51-1.59 (m,

1H), 1.29 (ddt, J = 9.4, 12.7, 6.4 Hz, 1H), 0.98 (d, J = 6.6 Hz, 3H), 0.92 (d, J = 6.6 Hz, 3H); MS (ESI+) m/z 476 $(M+H)^+$.

Example 499

N^2-cyclopropyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 419 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and (1-ethoxycyclopropoxy)trimethylsilane for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.54-8.56 (m, 1H), 8.14-8.16 (m, 2H), 7.89-7.92 (m, 2H), 4.27-4.31 (m, 1H), 3.89 (dd, J = 9.9, 2.6 Hz, 1H), 3.44 (t, J = 6.0 Hz, 1H), 3.15-3.21 (m, 2H), 2.99 (dd, J = 9.6, 6.9 Hz, 1H), 2.53-2.66 (m, 2H), 2.24-2.28 (m, 1H), 1.94-2.00 (m, 1H), 1.81-1.90 (m, 3H), 1.56-1.64 (m, 1H), 1.51 (dd, J = 13.9, 6.6 Hz, 1H), 1.31 (ddt, J = 9.7, 12.8, 6.4 Hz, 1H), 0.96 (s, 9H), 0.46-0.51 (m, 1H), 0.30-0.45 (m, 3H); MS (ESI+) m/z 502 $(M+H)^+$.

Example 500

N^2,N^2-dicyclopropyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 419 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and (1-ethoxycyclopropoxy)trimethylsilane for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.13-8.15 (m, 2H), 7.88-7.90 (m, 2H), 7.83-7.85 (m, 1H), 4.21 (dq, J = 9.1, 6.2 Hz, 1H), 3.89 (dd, J = 9.9, 2.2 Hz, 1H), 3.53 (dd, J = 9.1, 1.8 Hz, 1H), 3.16 (dd, J = 9.9, 7.4 Hz, 2H), 2.96 (dd, J = 9.6, 6.7 Hz, 1H), 2.62 (dd, J = 13.6, 9.3 Hz, 1H), 2.46-2.57 (m, 2H), 2.23-2.28 (m, 2H), 1.88-1.94 (m, 1H), 1.76-1.82 (m, 1H), 1.65 (dd, J = 13.6, 1.9 Hz, 1H), 1.48-1.58 (m, 1H), 1.23-1.32 (m, 1H), 1.00 (s, 9H), 0.44-0.56 (m, 8H); MS (ESI+) m/z 542 $(M+H)^+$.

Example 501

N^2-cyclopentyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 419 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and cyclopentanone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.34-8.36 (m, 1H), 8.13-8.16 (m, 2H), 7.89-7.91 (m, 2H), 4.23-4.29 (m, 1H), 3.88 (dd, J = 10.0, 2.1 Hz, 1H), 3.34 (dd, J = 7.4, 4.3 Hz, 1H), 3.10-3.22 (m, 3H), 2.96-3.00 (m, 1H), 2.56-2.58 (m, 2H), 1.90-2.02 (m, 1H), 1.81-1.89 (m, 2H), 1.70-1.84 (m, 1H), 1.55-1.75 (m, 5H), 1.36-1.54 (m, 5H), 1.24-1.35 (m, 1H), 0.99 (s, 9H); MS (ESI+) *m/z* 530 $(M+H)^+$.

Example 502

N^2-cyclohexyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 419 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and cyclohexanone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.25-8.27 (m, 1H), 8.13-8.16 (m, 2H), 7.89-7.91 (m, 2H), 4.22-4.28 (m, 1H), 3.86 (dd, J = 9.9, 2.1 Hz, 1H), 3.42 (dd, J = 7.6, 3.8 Hz, 1H), 3.12-3.22 (m, 2H), 2.99 (dd, J = 9.6, 6.4 Hz, 1H), 2.55-2.65 (m, 2H), 2.47-2.53 (m, 1H), 1.91-2.01 (m, 1H), 1.78-1.91 (m, 4H), 1.65-1.76 (m, 1H), 1.60-1.67 (m, 2H), 1.54-1.60 (m, 1H), 1.45-1.52 (m, 2H), 1.28-1.37 (m, 1H), 1.03-1.25 (m, 5H), 1.00 (s, 9H); MS (ESI+) *m/z* 544 $(M+H)^+$.

Example 503

N^2-(1-ethylpropyl)-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 419 for (3a*S*,4*R*,6a*R*)-2-(3-

(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and pentan-3-one for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.25-8.27 (m, 1H), 8.13-8.16 (m, 2H), 7.89-7.92 (m, 2H), 4.21-4.27 (m, 1H), 3.85 (d, *J* = 11.2 Hz, 1H), 3.40 (dd, *J* = 7.0, 4.7 Hz, 1H), 3.18 (dd, *J* = 10.2, 2.7 Hz, 2H), 2.97-3.02 (m, 1H), 2.55-2.59 (m, 2H), 2.45 (p, *J* = 5.7 Hz, 1H), 1.96 (dt, *J* = 11.8, 5.9 Hz, 1H), 1.86 (dd, *J* = 14.1, 4.5 Hz, 1H), 1.78-1.89 (m, 1H), 1.53-1.81 (m, 1H), 1.26-1.63 (m, 7H), 1.00 (s, 9H), 0.92 (t, *J* = 7.4 Hz, 3H), 0.84 (t, *J* = 7.4 Hz, 3H); MS (ESI+) *m/z* 532 $(M+H)^+$.

Example 504

N^2-cyclobutyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 419 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and cyclobutanone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (501 MHz, pyridine-d_5) δ ppm 8.30-8.33 (m, 1H), 8.13-8.16 (m, 2H), 7.89-7.91 (m, 2H), 4.21-4.27 (m, 1H), 3.88 (dd, *J* = 10.0, 2.0 Hz, 1H), 3.31 (t, *J* = 6.5 Hz, 2H), 3.15-3.20 (m, 2H), 2.96-2.99 (m, 1H), 2.56-2.59 (m, 2H), 2.08-2.21 (m, 2H), 2.01-2.16 (m, 1H), 1.92-1.99 (m, 1H), 1.88 (dd, *J* = 14.1, 5.3 Hz, 1H), 1.82-1.86 (m, 2H), 1.70-1.78 (m, 1H), 1.48-1.64 (m, 4H), 1.27-1.34 (m, 1H), 0.98 (s, 9H); MS (ESI+) *m/z* 516 $(M+H)^+$.

Example 505

4-methyl-N^2-neopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 419 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.20-8.22 (m, 1H), 8.14-8.16 (m, 2H), 7.89-7.92 (m, 2H), 4.21-4.28 (m, 1H), 3.86 (dd, *J* = 10.0, 2.8 Hz, 1H), 3.23 (dd, *J* = 7.9, 4.0 Hz, 1H), 3.17-3.21 (m, 2H), 3.00 (dd, *J* = 9.7, 7.2 Hz, 1H), 2.52-2.58 (m, 2H), 2.39 (d, *J* = 11.1 Hz, 1H), 2.31 (d, *J* = 11.1 Hz, 1H), 1.94-2.01 (m, 1H), 1.87 (dd, *J* = 14.1,

4.2 Hz, 1H), 1.83-1.89 (m, 2H), 1.52-1.61 (m, 1H), 1.50 (dd, *J* = 14.0, 7.8 Hz, 1H), 1.29-1.36 (m, 1H), 0.99 (s, 9H), 0.92 (s, 9H); MS (ESI+) *m/z* 532 $(M+H)^+$.

Example 506

N^2-cyclopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

The title compound was prepared by substituting N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide from Example 422 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and cyclopentanone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.30-8.33 (m, 1H), 8.12-8.15 (m, 2H), 7.88-7.91 (m, 2H), 4.21-4.29 (m, 1H), 3.86 (d, *J* = 11.3 Hz, 1H), 3.27 (t, *J* = 6.5 Hz, 1H), 3.12-3.21 (m, 3H), 2.96-3.01 (m, 1H), 2.50-2.64 (m, 2H), 1.89-2.18 (m, 2H), 1.24-1.90 (m, 15H), 0.86 (t, *J* = 7.3 Hz, 3H); MS (ESI+) *m/z* 502 $(M+H)^+$.

Example 507

N^2-cyclohexyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

The title compound was prepared by substituting N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide from Example 422 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and cyclohexanone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.25-8.27 (m, 1H), 8.12-8.15 (m, 2H), 7.89-7.92 (m, 2H), 4.20-4.28 (m, 1H), 3.84 (dd, *J* = 10.0, 2.4 Hz, 1H), 3.35 (dd, *J* = 7.6, 5.4 Hz, 1H), 3.14-3.21 (m, 2H), 2.96-3.01 (m, 1H), 2.51-2.65 (m, 2H), 2.40-2.51 (m, 1H), 1.75-2.01 (m, 6H), 1.44-1.67 (m, 7H), 1.26-1.38 (m, 1H), 1.04-1.24 (m, 5H), 0.87 (t, *J* = 7.3 Hz, 3H); MS (ESI+) *m/z* 516 $(M+H)^+$.

Example 508

N^2-cyclopentyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-cyclopentyl-4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-L-leucinamide

The title compound was prepared by substituting 4-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-leucinamide from Example 464 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and cyclopentanone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.73 (d, J = 5.6, 1H), 4.31 – 4.20 (m, 1H), 3.83 – 3.71 (m, 2H), 3.72-3.49 (m, 3H), 3.31 (dd, J = 7.2, 4.4, 1H), 3.19 – 3.07 (m, 2H), 2.78 – 2.63 (m, 2H), 2.12 (dt, J = 12.6, 6.4, 1H), 1.96 (tt, J = 5.7, 5.0, 1H), 1.86 – 1.59 (m, 12H), 1.57 – 1.33 (m, 12H), 1.04 (s, 9H), 0.99 (s, 9H); MS (ESI+) *m/z* 517 $(M+H)^+$.

Example 509

N^2,N^2-dimethyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 164 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and formaldehyde for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.17-8.20 (m, 1H), 7.76-7.77 (bs, 1H), 7.63-7.65 (m, 2H), 7.50 (t, J = 7.7 Hz, 1H), 4.48-4.54 (m, 1H), 3.74 (d, J = 13.1 Hz, 1H), 3.30 (d, J = 13.1 Hz, 1H), 3.05 (dd, J = 9.0, 5.0 Hz, 1H), 2.74-2.78 (m, 1H), 2.68-2.74 (m, 1H), 2.42-2.47 (m, 1H), 2.33 (s, 7H), 2.21 (dd, J = 9.4, 7.2 Hz, 1H), 2.14 (dd, J = 9.0, 7.5 Hz, 1H), 1.76-1.89 (m, 3H), 1.67-1.74 (m, 1H), 1.53-1.61 (m, 2H), 1.21-1.28 (m, 1H), 0.96 (d, J = 6.6 Hz, 3H), 0.94 (d, J = 6.7 Hz, 3H); MS (ESI-) *m/z* 424 $(M-H)^-$.

Example 510

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-N^2-neopentyl-L-leucinamide

The title compound was prepared by substituting N^1-{(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide from Example 165 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.15-8.17

(m, 1H), 7.43-7.46 (m, 2H), 7.37 (t, J = 7.5 Hz, 2H), 7.28 (t, J = 7.3 Hz, 1H), 4.39-4.45 (m, 1H), 3.61 (d, J = 13.1 Hz, 1H), 3.46 (d, J = 13.1 Hz, 1H), 3.27 (dd, J = 7.9, 6.0 Hz, 1H), 2.85 (dd, J = 8.9, 2.0 Hz, 1H), 2.52-2.58 (m, 2H), 2.46-2.52 (m, 2H), 2.45 (s, 3H), 2.43 (d, J = 13.8 Hz, 1H), 2.29-2.36 (m, 2H), 2.12 (dq, J = 12.2, 6.1 Hz, 1H), 1.82-2.02 (m, 3H), 1.53-1.63 (m, 2H), 1.37-1.47 (m, 1H), 0.95 (d, J = 6.6 Hz, 3H), 0.94 (d, J = 6.6 Hz, 3H), 0.90 (s, 9H); MS (ESI+) *m/z* 414 $(M+H)^+$.

Example 511

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(3,3-dimethylbutyl)-N^2-methyl-L-leucinamide

The title compound was prepared by substituting N^1-{(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide from Example 165 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and 3,3-dimethylbutanal for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.04-8.06 (m, 1H), 7.43-7.46 (m, 2H), 7.37 (t, J = 7.5 Hz, 2H), 7.28 (t, J = 7.4 Hz, 1H), 4.42-4.48 (m, 1H), 3.63 (d, J = 13.1 Hz, 1H), 3.46 (d, J = 13.1 Hz, 1H), 3.33 (dd, J = 8.2, 5.3 Hz, 1H), 2.89-2.92 (m, 1H), 2.55-2.66 (m, 4H), 2.44-2.48 (m, 1H), 2.39 (s, 3H), 2.36-2.39 (m, 1H), 2.27 (dd, J = 8.8, 6.1 Hz, 1H), 2.12 (dq, J = 11.9, 6.0 Hz, 1H), 1.83-1.99 (m, 3H), 1.56-1.63 (m, 2H), 1.40-1.48 (m, 3H), 0.95 (d, J = 6.3 Hz, 6H), 0.89 (s, 9H); MS (ESI+) *m/z* 428 $(M+H)^+$.

Example 512

N^2,N^2-dimethyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide

The title compound was prepared by substituting N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide from Example 184 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and formaldehyde for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.38-8.39 (bs, 1H), 8.18-8.25 (m, 2H), 7.90-7.92 (m, 1H), 7.72 (t, J = 7.8 Hz, 1H), 4.20-4.25 (m, 1H), 3.88 (d, J = 10.8 Hz, 1H), 3.18 (dd, J = 9.8, 2.5 Hz, 1H), 3.11-3.18 (m, 2H), 2.95-2.98 (m, 1H), 2.51-2.60 (m, 2H), 2.32 (s, 6H), 1.90-1.97 (m, 1H), 1.75-1.86 (m,

3H), 1.49-1.60 (m, 2H), 1.24-1.32 (m, 1H), 0.90 (d, J = 6.4 Hz, 3H), 0.90 (d, J = 6.4 Hz, 3H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Example 513

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(4-fluorobenzyl)-N^2-methyl-L-leucinamide

The title compound was prepared by substituting N^1-{(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide from Example 165 for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and 4-fluorobenzaldehyde for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.25-8.27 (m, 1H), 7.36-7.46 (m, 6H), 7.28 (t, J = 7.3 Hz, 1H), 7.13-7.17 (m, 2H), 4.45-4.50 (m, 1H), 3.86 (d, J = 13.7 Hz, 1H), 3.76 (d, J = 13.7 Hz, 1H), 3.63 (d, J = 13.1 Hz, 1H), 3.47 (d, J = 13.1 Hz, 1H), 3.41 (dd, J = 7.7, 6.2 Hz, 1H), 2.91 (dd, J = 9.0, 2.7 Hz, 1H), 2.53-2.64 (m, 2H), 2.49 (dd, J = 8.8, 7.0 Hz, 1H), 2.34-2.39 (m, 1H), 2.36 (s, 3H), 2.30 (dd, J = 8.9, 6.9 Hz, 1H), 2.10-2.22 (m, 1H), 1.84-1.94 (m, 3H), 1.67-1.76 (m, 1H), 1.59-1.67 (m, 1H), 1.39-1.46 (m, 1H), 0.93 (d, J = 6.8 Hz, 3H), 0.91 (d, J = 6.6 Hz, 3H); MS (ESI+) *m/z* 452 $(M+H)^+$.

Example 514

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-(methylsulfonyl)piperidine-2-carboxamide

The title compound was prepared by substituting (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]piperidine-2-carboxamide from Example 350 for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate in the procedure described in Example 242 Step A: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.54 (d, J = 7.2, 1H), 7.43 (d, J = 7.2, 2H), 7.37 (dd, J = 10.2, 4.7, 2H), 7.28 (t, J = 7.2, 1H), 4.89 (d, J = 3.1, 1H), 4.40 – 4.31 (m, 1H), 3.90 – 3.77 (m, 2H), 3.57 (d, J = 13.1, 1H), 3.45 (d, J = 13.1, 1H), 3.15 (s, 3H), 2.79 (dd, J = 9.0, 2.1, 1H), 2.54 – 2.41 (m, 2H), 2.40 – 2.31 (m, 2H), 2.24 (dd, J = 8.8, 6.9, 1H), 2.20 – 2.14 (m, 1H), 2.09 (dq, J = 12.0, 6.0, 1H), 1.88 – 1.78 (m, 1H), 1.67 – 1.53 (m, 4H), 1.51 – 1.34 (m, 3H); MS (ESI+) *m/z* 406 $(M+H)^+$.

Example 515

(3*R*)-4-methyl-3-[(methylsulfonyl)amino]-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide

The title compound was prepared by substituting (3*R*)-3-amino-4-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide from Example 388 for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate in the procedure described in Example 242 Step A: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.77 (d, J = 6.6, 1H), 8.42 – 8.34 (m, 2H), 8.20 (d, J = 7.8, 1H), 7.91 (d, J = 7.8, 1H), 7.72 (t, J = 7.9, 1H), 4.21 (dq, J = 13.4, 6.1, 2H), 3.85 (dd, J = 9.9, 1.7, 1H), 3.23 (s, 3H), 3.17 (dd, J = 9.6, 1.9, 1H), 3.11 (dd, J = 9.8, 7.3, 1H), 2.93 (dd, J = 9.5, 7.1, 1H), 2.76 – 2.65 (m, 2H), 2.56 – 2.45 (m, 2H), 2.11 (dq, J = 13.5, 6.8, 1H), 1.95 (td, J = 12.2, 6.3, 1H), 1.83 (dt, J = 12.5, 6.4, 1H), 1.55 (ddd, J = 15.9, 12.3, 9.1, 1H), 1.28 (ddd, J = 12.8, 9.4, 6.3, 1H), 1.02 (d, J = 6.8, 3H), 0.97 (d, J = 6.8, 3H); MS (ESI+) *m/z* 524 $(M+H)^+$.

Example 516

N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

Step A: *tert*-Butyl (*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate was prepared by substituting (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 156 Step A for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.67 (d, J = 7.2, 1H), 7.96 (d, J = 8.4, 1H), 7.75 (s, 1H), 7.61 (s, 1H), 7.56 (s, 1H), 7.45 (dd, J = 14.3, 6.7, 1H), 4.75 – 4.66 (m, 1H), 4.45 – 4.36 (m, 1H), 3.59 (d, J = 13.5, 1H), 3.46 (d, J = 13.6, 1H), 2.81 (dd, J = 9.1, 2.3, 1H), 2.62 – 2.56 (m, 1H), 2.56 – 2.49 (m, 1H), 2.49 – 2.43 (m, 1H), 2.27 (d, J = 5.3, 2H), 2.03 (td, J = 11.6, 5.7, 1H), 1.94 – 1.78 (m, 4H), 1.65 – 1.56 (m, 1H), 1.50 (s, 9H), 1.35 (dt, J = 13.6, 5.7, 1H), 0.86 (dd, J = 11.2, 5.7, 6H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Step B: N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(Trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide was prepared by substituting *tert*-butyl (*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348:

^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.31 (d, J = 7.5, 1H), 7.76 (s, 1H), 7.62 (d, J = 7.9, 1H), 7.56 (s, 1H), 7.46 (t, J = 7.7, 1H), 4.44 – 4.33 (m, 1H), 3.63 – 3.56 (m, 2H), 3.47 (d, J = 13.5, 1H), 2.83 (dd, J = 9.0, 2.3, 1H), 2.58 – 2.46 (m, 2H), 2.44 – 2.39 (m, 1H), 2.32 (dd, J = 9.0, 2.6, 1H), 2.28 – 2.23 (m, 1H), 2.08 (td, J = 11.9, 5.9, 2H), 1.95 – 1.81 (m, 4H), 1.62 – 1.51 (m, 2H), 1.43 – 1.34 (m, 1H), 0.90 (d, J = 6.3, 3H), 0.85 (d, J = 6.2, 3H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Step C: The title compound was prepared by substituting N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Step B for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate in the procedure described in Example 242 Step A: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.36 (d, J = 8.9, 1H), 9.24 (d, J = 7.3, 1H), 7.78 (s, 1H), 7.62 (d, J = 8.2, 2H), 7.46 (t, J = 7.7, 1H), 4.48 (qd, J = 13.1, 7.5, 2H), 3.62 (d, J = 13.5, 1H), 3.50 (d, J = 13.5, 1H), 3.20 (s, 3H), 2.86 (dd, J = 9.1, 2.9, 1H), 2.64 (dt, J = 8.4, 6.1, 1H), 2.60 – 2.53 (m, 1H), 2.49 (dd, J = 8.8, 7.5, 1H), 2.34 – 2.27 (m, 2H), 2.15 – 2.09 (m, 1H), 2.04 – 1.95 (m, 1H), 1.90 (ddd, J = 14.5, 9.2, 4.2, 2H), 1.78 (ddd, J = 13.9, 8.5, 5.7, 1H), 1.65 (dt, J = 19.1, 7.2, 1H), 1.41 (dq, J = 13.9, 6.1, 1H), 0.83 (d, J = 6.7, 3H), 0.81 (d, J = 6.6, 3H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Example 517

N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide

Step A: *tert*-Butyl (*R*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate was prepared by substituting (3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 156 Step A for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine and *N*-(*tert*-butoxycarbonyl)-D-leucine for *N*-(*tert*-butoxycarbonyl)-L-leucine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.70 (d, J = 7.4, 1H), 7.95 (d, J = 8.4, 1H), 7.73 (s, 1H), 7.59 (s, 1H), 7.56 (s, 1H), 7.45 (t, J = 7.7, 1H), 4.72 (br s, 1H), 4.40 (br s, 1H), 3.57 (d, J = 13.4, 1H), 3.42 (d, J = 13.6, 1H), 2.73 (d, J = 9.0, 1H), 2.50 (s, 2H), 2.39 – 2.32 (m, 1H), 2.25 (dd, J = 12.9, 7.0, 2H), 2.11 (dq, J = 12.3, 6.2, 1H), 1.94 – 1.78 (m, 4H), 1.66 (dq, J = 21.9, 7.3, 1H), 1.50 (s, 9H), 1.39 (d, J = 7.0, 1H), 0.86 (dd, J = 10.2, 5.6, 6H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Step B: N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(Trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide was prepared by

substituting *tert*-butyl (*R*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.33 (d, J = 7.6, 1H), 7.75 (s, 1H), 7.62 (s, 1H), 7.56 (s, 1H), 7.46 (t, J = 7.7, 1H), 4.43 – 4.34 (m, 1H), 3.64 – 3.56 (m, 2H), 3.46 (d, J = 13.5, 1H), 2.82 (dd, J = 9.0, 2.5, 1H), 2.59 – 2.45 (m, 2H), 2.44 – 2.39 (m, 1H), 2.31 (dd, J = 9.0, 2.8, 1H), 2.25 (dd, J = 8.8, 7.1, 1H), 2.09 (td, J = 11.9, 5.9, 2H), 1.88 (tdd, J = 13.5, 8.9, 6.0, 4H), 1.57 (tt, J = 18.0, 6.6, 2H), 1.44 – 1.34 (m, 1H), 0.90 (d, J = 6.4, 3H), 0.85 (d, J = 6.3, 3H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Step C: The title compound was prepared by substituting N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Step B for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate in the procedure described in Example 242 Step A: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.35 (d, J = 8.5, 1H), 9.24 (d, J = 7.2, 1H), 7.76 (s, 1H), 7.63 – 7.56 (m, 2H), 7.45 (dd, J = 14.6, 7.0, 1H), 4.47 (dt, J = 13.0, 8.2, 2H), 3.59 (d, J = 13.6, 1H), 3.48 (d, J = 13.5, 1H), 3.18 (s, 3H), 2.85 (dd, J = 9.1, 2.5, 1H), 2.63 – 2.49 (m, 2H), 2.39 (dd, J = 9.0, 7.1, 1H), 2.33 (dd, J = 9.0, 2.6, 1H), 2.29 – 2.22 (m, 1H), 2.15 (dt, J = 12.2, 6.1, 1H), 2.04 – 1.95 (m, 1H), 1.94 – 1.84 (m, 2H), 1.81 – 1.66 (m, 2H), 1.43 (dt, J = 21.0, 6.4, 1H), 0.85 – 0.79 (m, 6H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Example 518

N^2-ethyl-N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting N^2-ethyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 366 for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate in the procedure described in Example 242 Step A: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.83 (d, J = 7.3, 1H), 7.77 (s, 1H), 7.63 – 7.55 (m, 2H), 7.45 (t, J = 7.7, 1H), 4.71 (t, J = 6.9, 1H), 4.43 – 4.34 (m, 1H), 3.93 (td, J = 13.9, 6.8, 1H), 3.63 – 3.45 (m, 3H), 3.15 (d, J = 5.3, 3H), 2.89 – 2.81 (m, 1H), 2.54 (ddd, J = 29.4, 12.7, 9.2, 2H), 2.46 – 2.42 (m, 1H), 2.39 – 2.30 (m, 1H), 2.24 (dd, J = 17.4, 8.7, 1H), 2.08 (ddt, J = 17.6, 11.7, 5.8, 1H), 1.90 – 1.75 (m, 4H), 1.68 – 1.53 (m, 1H), 1.40 (dd, J = 12.7, 6.4, 1H), 1.36 – 1.30 (m, 3H), 0.85 (d, J = 5.4, 3H), 0.82 (t, J = 5.3, 3H); MS (ESI+) *m/z* 502 $(M+H)^+$.

Example 519

4-methyl-N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

Step A: *tert*-Butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-[4-trifluromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-ylcarbamate was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-ylcarbamate from Example 226 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide in the procedure described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.60 (d, J = 7.5, 1H), 8.12 (d, J = 8.9, 1H), 7.65 (d, J = 8.0, 2H), 7.51 (d, J = 8.0, 2H), 4.75 (td, J = 8.4, 5.1, 1H), 4.45 – 4.37 (m, 1H), 3.56 (d, J = 13.8, 1H), 3.46 (d, J = 13.7, 1H), 2.86 (dd, J = 9.0, 2.2, 1H), 2.62 – 2.46 (m, 2H), 2.42 – 2.36 (m, 1H), 2.30 (dd, J = 8.7, 2.2, 1H), 2.26 – 2.20 (m, 1H), 2.19 – 2.12 (m, 1H), 2.04 (td, J = 11.7, 5.7, 1H), 1.89 – 1.80 (m, 2H), 1.64 – 1.53 (m, 1H), 1.51 (s, 9H), 1.36 (dt, J = 21.2, 7.3, 1H), 0.98 (s, 9H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Step B: 4-Methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-[4-trifluromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-ylcarbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.31 (d, J = 7.7, 1H), 7.65 (d, J = 8.0, 2H), 7.52 (d, J = 7.9, 2H), 4.45 – 4.31 (m, 1H), 3.62 – 3.53 (m, 2H), 3.47 (d, J = 13.9, 1H), 2.89 (d, J = 8.4, 1H), 2.58 – 2.43 (m, 2H), 2.35 (t, J = 7.6, 2H), 2.25 – 2.15 (m, 3H), 2.10 (dt, J = 11.7, 6.7, 2H), 1.87 (td, J = 13.1, 6.6, 1H), 1.57 (dt, J = 14.8, 7.7, 1H), 1.48 – 1.36 (m, 2H), 0.98 (s, 9H); MS (ESI+) *m/z* 412 $(M+H)^+$.

Step C: The title compound was prepared by substituting 4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Step B for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate in the procedure described in Example 242 Step A: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.55 (d, J = 9.7, 1H), 9.30 (d, J = 7.3, 1H), 7.66 (d, J = 8.1, 2H), 7.54 (d, J = 8.0, 2H), 4.57 – 4.51 (m, 1H), 4.51 – 4.44 (m, 1H), 3.60 (d, J = 13.8, 1H), 3.50 (d, J = 13.8, 1H), 3.18 (s, 3H), 2.92 (dd, J = 9.0, 2.5, 1H), 2.67 – 2.61 (m, 1H), 2.58 – 2.50 (m, 1H), 2.43 (dd, J = 8.9, 7.3, 1H), 2.36 (dd, J

= 9.0, 2.6, 1H), 2.25 (dd, J = 8.7, 7.5, 1H), 2.17 – 2.10 (m, 1H), 2.03 (dd, J = 14.1, 5.4, 1H), 1.95 – 1.85 (m, 2H), 1.64 (dtd, J = 12.2, 8.1, 5.8, 1H), 1.46 – 1.37 (m, 1H), 0.96 (s, 9H); MS (ESI+) *m/z* 490 $(M+H)^+$.

Example 520

3-methyl-N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-valinamide

Step A: *tert*-Butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-ylamino)-3,3-dimethyl-1-oxobutan-2-ylcarbamate was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3,3-dimethyl-1-oxobutan-2-ylcarbamate from Example 225 for (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide in the procedure described in Example 303: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.72 (d, J = 9.7, 1H), 7.66 (d, J = 8.1, 2H), 7.52 (d, J = 8.0, 2H), 7.37 (d, J = 3.1, 1H), 4.61 (d, J = 9.8, 1H), 4.46 – 4.39 (m, 1H), 3.60 (d, J = 13.7, 1H), 3.46 (d, J = 13.7, 1H), 2.89 (dd, J = 9.1, 2.5, 1H), 2.63 – 2.57 (m, 1H), 2.57 – 2.50 (m, 1H), 2.46 – 2.41 (m, 1H), 2.35 – 2.29 (m, 1H), 2.28 – 2.22 (m, 1H), 1.99 (dq, J = 11.8, 5.7, 1H), 1.84 (td, J = 12.7, 6.2, 1H), 1.57 – 1.49 (m, 1H), 1.48 (s, 9H), 1.40 – 1.31 (m, 1H), 1.18 (s, 9H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Step B: 3-Methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-valinamide was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-ylamino)-3,3-dimethyl-1-oxobutan-2-ylcarbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.15 – 8.06 (m, 1H), 7.66 (d, J = 8.1, 2H), 7.52 (d, J = 8.0, 2H), 4.47 – 4.40 (m, 1H), 3.59 (d, J = 13.6, 1H), 3.46 (d, J = 13.8, 1H), 3.27 (s, 1H), 2.89 – 2.85 (m, 1H), 2.56 – 2.50 (m, 2H), 2.41 – 2.36 (m, 1H), 2.35 – 2.32 (m, 1H), 2.26 – 2.21 (m, 1H), 2.19 – 2.12 (m, 2H), 2.11 – 2.02 (m, 1H), 1.90 – 1.82 (m, 1H), 1.60 – 1.52 (m, 1H), 1.43 – 1.35 (m, 1H), 1.14 (s, 9H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Step C: The title compound was prepared by substituting 3-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-valinamide from Step B for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate in the procedure

described in Example 242 Step A: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.28 (d, J = 10.4, 1H), 9.13 (d, J = 7.4, 1H), 7.67 (d, J = 8.1, 2H), 7.55 (d, J = 8.1, 2H), 4.54 – 4.46 (m, 1H), 4.19 (d, J = 10.4, 1H), 3.64 (d, J = 13.7, 1H), 3.50 (d, J = 13.7, 1H), 3.13 (s, 3H), 2.92 (dd, J = 9.0, 2.4, 1H), 2.67 – 2.52 (m, 2H), 2.46 (dd, J = 8.8, 7.1, 1H), 2.37 (dd, J = 9.0, 2.5, 1H), 2.30 – 2.23 (m, 1H), 2.09 (dq, J = 11.7, 5.8, 1H), 1.94 – 1.83 (m, 1H), 1.62 – 1.53 (m, 1H), 1.45 – 1.37 (m, 1H), 1.18 (s, 9H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Example 521

N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide

The title compound was prepared by substituting N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide from Example 382 for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate in the procedure described in Example 242 Step A: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.42 (d, J = 9.2, 1H), 9.10 (d, J = 7.4, 1H), 7.66 (d, J = 8.0, 2H), 7.53 (d, J = 8.0, 2H), 4.50 – 4.39 (m, 2H), 3.60 (d, J = 13.7, 1H), 3.49 (d, J = 13.7, 1H), 3.19 (s, 3H), 2.89 (dd, J = 9.1, 2.4, 1H), 2.65 – 2.58 (m, 1H), 2.58 – 2.51 (m, 1H), 2.46 – 2.40 (m, 1H), 2.35 (dd, J = 9.0, 2.5, 1H), 2.28 – 2.23 (m, 1H), 2.13 (dt, J = 11.9, 6.0, 1H), 1.98 (tt, J = 13.2, 6.5, 1H), 1.94 – 1.83 (m, 2H), 1.63 (dt, J = 19.4, 7.6, 1H), 1.58 – 1.47 (m, 2H), 1.42 (dt, J = 14.6, 6.3, 1H), 0.77 (t, J = 7.4, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 522

N^2-(isopropylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 170 Step B for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate and propane-2-sulfonylchloride for methanesulfonyl chloride in the procedure described in Example 242 Step A: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.34 (d, J = 9.2, 1H), 9.12 (d, J = 7.4, 1H), 7.75 (d, J = 12.2, 2H), 7.61 (d, J = 7.5, 1H), 7.45 (t, J = 7.8, 1H), 4.50 – 4.41 (m, 2H), 3.58 (d, J = 13.5, 1H), 3.51 (d, J = 13.4, 1H), 3.38 – 3.31 (m, 1H), 2.89 (d, J = 9.6, 1H), 2.56 (qd, J = 5.6, 1.6, 2H), 2.41 – 2.34 (m, 2H), 2.25 (dd, J = 8.7, 6.7, 1H), 2.19 – 2.12 (m, 1H), 2.06 – 1.97 (m, 1H), 1.95 – 1.86 (m, 3H), 1.79 – 1.66 (m, 2H), 1.46 (d, J = 6.8, 6H), 0.82 (d, J = 6.5, 1H); MS (ESI+) *m/z* 504 $(M+H)^+$.

Example 523

N^2-(phenylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 170 Step B for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate and benzenesulfonyl chloride for methanesulfonyl chloride in the procedure described in Example 242 Step A: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 10.09 – 9.90 (m, 1H), 8.77 (d, J = 7.3, 1H), 8.18 (dd, J = 8.0, 1.5, 2H), 7.78 (s, 1H), 7.62 (d, J = 7.9, 1H), 7.51 – 7.34 (m, 5H), 4.36 (dd, J = 9.4, 5.5, 1H), 4.16 – 4.08 (m, 1H), 3.59 (d, J = 13.5, 1H), 3.49 (d, J = 13.6, 1H), 2.60 (dd, J = 9.1, 3.0, 1H), 2.51 – 2.42 (m, 1H), 2.33 (dd, J = 8.9, 7.6, 1H), 2.27 (dd, J = 11.1, 6.5, 2H), 2.24 – 2.17 (m, 1H), 2.05 (td, J = 12.1, 5.9, 1H), 1.98 (dd, J = 13.8, 6.7, 1H), 1.88 – 1.79 (m, 2H), 1.72 (ddd, J = 13.7, 8.6, 5.4, 1H), 1.58 (dt, J = 19.1, 7.0, 1H), 1.36 (dt, J = 20.4, 6.2, 1H), 0.81 (d, J = 6.7, 3H), 0.77 (d, J = 6.5, 3H); MS (ESI+) *m/z* 538 $(M+H)^+$.

Example 524

N^2-(cyclopentylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide

The title compound was prepared by substituting N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example 170 Step B for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate and cyclopentanesulfonyl chloride for methanesulfonyl chloride in the procedure described in Example 242 Step A: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.30 (d, J = 9.6, 1H), 9.12 (d, J = 7.5, 1H), 7.76 (d, J = 15.6, 2H), 7.45 (dd, J = 17.4, 9.7, 2H), 4.53 – 4.44 (m, 2H), 3.59 (d, J = 13.4, 1H), 3.53 (d, J = 13.7, 1H), 2.91 (d, J = 8.0, 1H), 2.60 – 2.54 (m, 2H), 2.39 (t, J = 9.0, 2H), 2.34 – 2.10 (m, 6H), 2.08 – 1.99 (m, 2H), 1.96 – 1.85 (m, 3H), 1.79 – 1.63 (m, 3H), 1.49 – 1.35 (m, 3H), 0.82 (d, J = 6.6, 6H); MS (ESI+) *m/z* 530 $(M+H)^+$.

Example 525

isopropyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate

The title compound was prepared by substituting 4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide from Example

519 Step B for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate and isopropyl carbonochloridate for methanesulfonyl chloride in the procedure described in Example 242 Step A: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.38 (d, J = 9.0, 1H), 7.65 (d, J = 8.1, 2H), 7.51 (d, J = 8.0, 2H), 5.08 (dt, J = 12.8, 6.5, 1H), 4.81 (td, J = 8.5, 5.3, 1H), 4.46 – 4.38 (m, 1H), 3.57 (d, J = 13.7, 1H), 3.46 (d, J = 13.8, 1H), 2.88 (dd, J = 8.8, 1.7, 1H), 2.63 – 2.54 (m, 1H), 2.49 (tt, J = 4.3, 3.3, 1H), 2.43 – 2.36 (m, 1H), 2.31 (dd, J = 8.9, 2.5, 1H), 2.25 – 2.21 (m, 1H), 2.21 – 2.17 (m, 1H), 2.16 (d, J = 4.8, 1H), 2.10 – 1.99 (m, 1H), 1.90 – 1.77 (m, 2H), 1.59 (ddd, J = 14.7, 12.6, 7.8, 1H), 1.41 – 1.32 (m, 1H), 1.23 (d, J = 6.2, 3H), 1.14 (d, J = 6.2, 3H), 0.98 (s, 9H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Example 526

isopropyl (*S*)-3,3-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-ylcarbamate

The title compound was prepared by substituting 3-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-valinamide from Example 520 Step B for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate and isopropyl carbonochloridate for methanesulfonyl chloride in the procedure described in Example 242 Step A: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.84 (d, J = 7.3, 1H), 8.05 (d, J = 9.6, 1H), 7.66 (d, J = 8.1, 2H), 7.52 (d, J = 8.0, 2H), 5.06 (dt, J = 12.6, 6.3, 1H), 4.67 (d, J = 9.8, 1H), 4.44 (p, J = 7.3, 1H), 3.61 (d, J = 13.8, 1H), 3.47 (d, J = 13.7, 1H), 2.89 (dd, J = 9.0, 2.5, 1H), 2.66 – 2.58 (m, 1H), 2.57 – 2.50 (m, 1H), 2.49 – 2.41 (m, 1H), 2.29 (dt, J = 15.8, 7.5, 2H), 2.00 (td, J = 11.5, 5.3, 1H), 1.85 (dt, J = 20.3, 6.6, 1H), 1.54 (dt, J = 15.1, 7.3, 1H), 1.41 – 1.30 (m, 1H), 1.24 (d, J = 6.2, 3H), 1.19 (s, 9H), 1.12 (d, J = 6.0, 3H); MS (ESI+) *m/z* 484 $(M+H)^+$.

Example 527

cyclopentyl (*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate

The title compound was prepared by substituting N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide from Example 382 for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate and cyclopentyl carbonochloridate for methanesulfonyl chloride in the procedure described in Example 242 Step A: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.76 (d, J = 1.7, 1H), 8.22 (d, J = 8.4, 1H), 7.65 (d, J = 8.1, 2H), 7.51 (d, J = 7.9, 2H), 5.32 – 5.24 (m, 1H), 4.71 (dd, J = 14.3, 7.9, 1H), 4.49 – 4.39 (m, 1H), 3.57 (d, J = 13.7, 1H), 3.46 (d, J = 14.0, 1H), 2.87 (dd, J = 8.8, 1.7, 1H), 2.63 – 2.50 (m, 2H),

2.41 (dd, J = 8.6, 7.5, 1H), 2.31 (dd, J = 8.0, 1.8, 1H), 2.27 – 2.20 (m, 1H), 2.12 – 1.98 (m, 2H), 1.93 – 1.82 (m, 2H), 1.81 – 1.73 (m, 2H), 1.73 – 1.65 (m, 2H), 1.65 – 1.55 (m, 3H), 1.54 – 1.45 (m, 2H), 1.45 – 1.31 (m, 3H), 0.81 (t, J = 7.4, 3H); MS (ESI+) *m/z* 496 $(M+H)^+$.

Example 528

N^2-(2,2-dimethylpropanoyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide

The title compound was prepared by substituting N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide from Example 382 for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate and pivaloyl chloride for methanesulfonyl chloride in the procedure described in Example 242 Step A: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.70 (d, J = 7.6, 1H), 7.72 (d, J = 7.9, 1H), 7.65 (d, J = 8.0, 2H), 7.51 (d, J = 8.0, 2H), 4.45 – 4.36 (m, 1H), 3.57 (d, J = 13.9, 1H), 3.47 (d, J = 13.8, 1H), 2.85 (dd, J = 9.1, 2.0, 1H), 2.60 – 2.51 (m, 2H), 2.42 (dd, J = 8.8, 6.9, 1H), 2.32 (dd, J = 8.9, 2.0, 1H), 2.28 – 2.23 (m, 1H), 2.06 (dq, J = 12.1, 6.0, 1H), 1.97 (dq, J = 9.4, 6.4, 1H), 1.90 – 1.75 (m, 2H), 1.59 (dt, J = 14.2, 7.3, 1H), 1.51 – 1.37 (m, 3H), 1.36 (s, 1H), 1.31 (s, 9H), 0.79 (t, J = 7.4, 3H); MS (ESI+) *m/z* 468 $(M+H)^+$.

Example 529

***tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(3-chloro-4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate**

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 313 Step A for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 3-chloro-4-fluorobenzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: ^{1}H NMR (300 MHz, $CDCl_3$) ppm 7.88 (dd, J = 6.7, 2.2 Hz, 1H), 7.70 (ddd, J = 8.6, 4.4, 2.2 Hz, 1H), 7.26-7.33 (m, 1H), 5.73-6.40 (m, 1H), 4.43 (d, J = 4.3 Hz, 1H), 3.85-3.95 (m, 1H), 3.40-3.52 (m, 1H), 3.09 (dd, J = 9.6, 3.2 Hz, 1H), 3.05 (dd, J = 10.1, 8.3 Hz, 1H), 2.97 (dd, J = 9.6, 7.4 Hz, 1H), 2.73 (s, 3H), 2.63-2.76 (m, 2H), 2.32-2.42 (m, 1H), 1.76-2.09 (m, 3H), 1.58-1.72 (m, 1H), 1.46 (s, 9H), 1.19-1.34 (m, 3H), 0.94 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 532 $(M+H)^+$.

Example 530

***tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(pyridin-3-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 313 Step A for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and pyridine-3-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 9.01-9.04 (bs, 1H), 8.80-8.85 (bs, 1H), 8.09 (ddd, *J* = 8.0, 2.2, 1.7 Hz, 1H), 7.49 (dd, *J* = 8.0, 4.8 Hz, 1H), 5.78-6.33 (m, 1H), 4.32-4.52 (m, 1H), 3.84-3.95 (m, 1H), 3.40-3.52 (m, 1H), 3.05-3.15 (m, 2H), 3.02 (dd, *J* = 9.7, 7.4 Hz, 1H), 2.73 (s, 3H), 2.61-2.75 (m, 1H), 2.33-2.50 (m, 1H), 1.77-2.07 (m, 3H), 1.53-1.71 (m, 2H), 1.46 (s, 9H), 1.18-1.32 (m, 3H), 0.94 (t, *J* = 7.3 Hz, 3H); MS (ESI+) *m/z* 481 $(M+H)^+$.

Example 531

***tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(thiophen-2-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate**

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 313 Step A for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and thiophene-2-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7.62 (dd, *J* = 5.0, 1.3 Hz, 1H), 7.56 (dd, *J* = 3.7, 1.3 Hz, 1H), 7.16 (dd, *J* = 5.0, 3.7 Hz, 1H), 5.75-6.30 (m, 1H), 4.33-4.53 (m, 1H), 3.88-3.97 (m, 1H), 3.37 (dd, *J* = 10.2, 3.6 Hz, 1H), 3.04-3.20 (m, 3H), 2.73 (s, 3H), 2.63-2.75 (m, 1H), 2.36-2.50 (m, 1H), 1.77-2.10 (m, 3H), 1.55-1.71 (m, 1H), 1.46 (s, 9H), 1.35-1.55 (m, 2H), 1.19-1.32 (m, 2H), 0.94 (t, *J* = 7.3 Hz, 3H); MS (ESI+) *m/z* 486 $(M+H)^+$.

Example 532

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethoxy)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

Step A: *tert*-Butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethoxy)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-

yl)carbamate was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 313 Step A for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-(trifluoromethoxy)benzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: MS (APCI+) *m/z* 564 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethoxy)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.99-10.02 (m, 1H), 8.05-8.07 (m, 2H), 7.50-7.52 (m, 2H), 4.55-4.59 (m, 1H), 4.26-4.36 (m, 1H), 3.73 (dd, *J* = 9.9, 2.8 Hz, 1H), 3.18 (dd, *J* = 9.6, 2.9 Hz, 1H), 3.11 (dd, *J* = 9.9, 7.9 Hz, 1H), 2.92 (s, 3H), 2.88-2.94 (m, 1H), 2.73-2.86 (m, 1H), 2.62-2.68 (m, 1H), 2.19-2.40 (m, 2H), 1.97-2.07 (m, 2H), 1.77-1.87 (m, 1H), 1.51-1.75 (m, 2H), 1.31-1.38 (m, 1H), 0.85 (t, *J* = 7.3 Hz, 3H); MS (ESI+) *m/z* 464 $(M+H)^+$.

Example 533

N^2-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(thien-2-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(thiophen-2-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 531 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 10.02-10.04 (m, 1H), 7.86 (d, *J* = 5.4 Hz, 1H), 7.76 (d, *J* = 4.2 Hz, 1H), 7.18-7.22 (m, 1H), 6.93-6.93 (m, 1H), 4.65 (dd, *J* = 9.1, 4.8 Hz, 1H), 4.28-4.36 (m, 1H), 3.72 (dd, *J* = 10.0, 3.0 Hz, 1H), 3.24 (dd, *J* = 10.0, 8.0 Hz, 1H), 3.19 (dd, *J* = 9.7, 3.1 Hz, 1H), 3.04 (dd, *J* = 9.7, 7.7 Hz, 1H), 2.94 (s, 3H), 2.78-2.84 (m, 1H), 2.66-2.72 (m, 1H), 2.35-2.42 (m, 1H), 2.22-2.30 (m, 1H), 1.98-2.11 (m, 2H), 1.81-1.89 (m, 1H), 1.6 6-1.77 (m, 1H), 1.54-1.66 (m, 1H), 1.31-1.38 (m, 1H), 0.86 (t, *J* = 7.3 Hz, 3H); MS (ESI+) *m/z* 386 $(M+H)^+$.

Example 534

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-chloro-4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(3-chloro-4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate from Example 529 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 10.05-10.07 (m, 1H), 8.19 (dd, J = 6.8, 2.2 Hz, 1H), 7.89 (ddd, J = 8.6, 4.4, 2.2 Hz, 1H), 7.44 (t, J = 8.7 Hz, 1H), 4.66 (dd, J = 9.1, 4.8 Hz, 1H), 4.27-4.36 (m, 1H), 3.72 (dd, J = 9.9, 2.9 Hz, 1H), 3.06-3.18 (m, 2H), 2.94 (s, 3H), 2.90-2.93 (m, 1H), 2.80-2.85 (m, 1H), 2.67-2.73 (m, 1H), 2.35-2.42 (m, 1H), 2.22-2.30 (m, 1H), 1.99-2.10 (m, 2H), 1.82-1.90 (m, 1H), 1.66-1.76 (m, 1H), 1.53-1.65 (m, 1H), 1.33-1.40 (m, 1H), 0.85 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 432 $(M+H)^+$.

Example 535

N^2-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(pyridin-3-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-norvalinamide

The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(pyridin-3-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 530 for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 10.18-10.21 (m, 1H), 9.34 (d, J = 2.3 Hz, 1H), 8.92 (dd, J = 4.8, 1.6 Hz, 1H), 8.25 (ddd, J = 8.0, 2.4, 1.6 Hz, 1H), 7.50 (dd, J = 8.0, 4.8 Hz, 1H), 4.73 (dd, J = 9.3, 4.6 Hz, 1H), 4.30 (p, J = 6.3 Hz, 1H), 3.71 (dd, J = 10.0, 2.9 Hz, 1H), 3.08-3.21 (m, 2H), 2.87-3.07 (m, 4H), 2.78-2.83 (m, 1H), 2.64-2.70 (m, 1H), 2.40-2.47 (m, 1H), 2.26-2.34 (m, 1H), 1.98-2.17 (m, 2H), 1.78-1.92 (m, 1H), 1.55-1.77 (m, 2H), 1.29-1.36 (m, 1H), 0.84 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 381 $(M+H)^+$.

Example 536

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-cyanophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide

Step A: *tert*-Butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-[(4-cyanophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 313 Step A for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide and 4-cyanobenzene-1-sulfonyl chloride for 3-(trifluoromethyl)benzene-1-sulfonyl chloride in the procedure described in Example 319: MS (APCI+) *m/z* 505 $(M+H)^+$.

Step B: The title compound was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-[(4-cyanophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Step A for *tert*-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate in the procedure described in Example 348: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 10.09-10.11 (m, 1H), 8.05-8.07 (m, 2H), 7.94-7.96 (m, 2H), 4.68 (dd, *J* = 9.2, 4.6 Hz, 1H), 4.26-4.35 (m, 1H), 3.71 (dd, *J* = 10.0, 3.0 Hz, 1H), 3.14-3.18 (m, 2H), 2.93-2.99 (m, 1H), 2.95 (s, 3H), 2.80-2.86 (m, 1H), 2.67-2.73 (m, 1H), 2.36-2.43 (m, 1H), 2.23-2.31 (m, 1H), 1.99-2.14 (m, 2H), 1.83-1.90 (m, 1H), 1.65-1.75 (m, 1H), 1.55-1.65 (m, 1H), 1.31-1.40 (m, 1H), 0.85 (t, *J* = 7.3 Hz, 3H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Example 537

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-methoxyphenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide

Step A: *tert*-Butyl methyl((*S*)-1-((3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl)carbamate was prepared by substituting *tert*-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate from Example 313 Step A for (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-2-morpholinopentanamide in the procedure described in Example 319 Step A: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.44 – 8.32 (m, 1H), 4.76 – 4.57 (m, 1H), 4.41 – 4.26 (m, 1H), 3.30 (dd, *J* = 11.1, 1.6, 1H), 3.17 – 2.95 (m, 5H), 2.78 (d, *J* = 9.8, 1H), 2.60 (s, 2H), 2.11 – 1.93 (m, 2H), 1.91 – 1.71 (m, 2H),

1.62 – 1.53 (m, 1H), 1.46 (s, 9H), 1.40 – 1.24 (m, 4H), 0.84 (t, J = 6.0, 3H); MS (ESI+) *m/z* 340 $(M+H)^+$.

Step B: The title compound was prepared by combining *tert*-butyl methyl((*S*)-1-((3a*R*,4*S*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl)carbamate (0.075 g, 0.221 mmol) from Step A with 4-methoxybenzene-1-sulfonyl chloride (0.050 g, 0.243 mmol) and diisopropylethylamine (0.042 mL, 0.243 mmol) in dichloromethane (5 mL). The reaction was stirred at ambient temperature overnight and volatiles were removed in vacuo. To the resulting mixture was added 4 *N* HCl/dioxane (5 mL), and the resultant reaction mixture was stirred at ambient temperature for 30 minutes. The volatiles were removed in vacuo, and the crude material was purified by preparative reverse-phase HPLC (Phenomenex® Luna® C8(2) 5 µm 100Å AXIA column, 30×75 mm, 10-95% gradient of acetonitrile in 0.1% aqueous trifluoroacetic acid, flow rate 50 mL/minute) to afford the title compound as the trifluoroacetic acid salt: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.83 (d, J = 6.7 Hz, 1H), 7.94-7.97 (m, 2H), 7.09-7.13 (m, 2H), 4.39 (t, J = 6.8 Hz, 1H), 4.32 (p, J = 6.5 Hz, 1H), 3.73 (s, 3H), 3.69-3.76 (m, 1H), 3.04-3.19 (m, 2H), 2.87-2.95 (m, 1H), 2.90 (s, 3H), 2.64-2.71 (m, 1H), 2.56-2.64 (m, 1H), 2.07-2.19 (m, 2H), 1.96-2.04 (m, 1H), 1.86-1.96 (m, 1H), 1.62-1.71 (m, 1H), 1.47-1.61 (m, 2H), 1.29-1.39 (m, 1H), 0.80 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 410 $(M+H)^+$.

Example 538

N^1-((3a*R*,4*S*,6a*S*)-2-{[3,5-bis(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting 3,5-bis(trifluoromethyl)phenyl-1-sulfonyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.73 (d, J = 6.7 Hz, 1H), 8.84 (s, 1H), 8.63 (s, 2H), 8.46-8.47 (bs, 1H), 4.47 (t, J = 6.7 Hz, 1H), 4.26-4.34 (m, 1H), 3.87 (dd, J = 10.0, 2.6 Hz, 1H), 3.20-3.29 (m, 2H), 3.03 (dd, J = 9.5, 7.7 Hz, 1H), 2.96 (s, 3H), 2.69-2.77 (m, 1H), 2.60-2.69 (m, 1H), 2.04-2.17 (m, 2H), 1.90-2.05 (m, 2H), 1.66-1.74 (m, 1H), 1.43-1.61 (m, 2H), 1.27-1.37 (m, 1H), 0.78 (t, J = 7.3 Hz, 3H).

Example 539

N^1-{(3a*R*,4*S*,6a*S*)-2-[(2-chloro-4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting 2-chloro-4-fluorophenyl-1-sulfonyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.84-9.86 (m, 1H), 8.22 (dd, J = 8.9, 6.0 Hz, 1H), 7.45 (dd, J = 8.5, 2.4 Hz, 1H), 7.19-7.23 (m, 1H), 4.46 (t, J = 6.8 Hz, 1H), 4.30-4.39 (m, 1H), 3.81 (dd, J = 10.1, 3.0 Hz, 1H), 3.48 (dd, J = 10.1, 7.7 Hz, 1H), 3.23-3.35 (m, 2H), 2.94 (s, 3H), 2.75-2.82 (m, 1H), 2.67-2.75 (m, 1H), 2.02-2.19 (m, 3H), 1.92-1.99 (m, 1H), 1.73 (dq, J = 12.5, 8.1 Hz, 1H), 1.47-1.62 (m, 2H), 1.39 (ddt, J = 9.1, 13.0, 6.5 Hz, 1H), 0.80 (t, J = 7.3 Hz, 3H); MS (ESI-) *m/z* 430 $(M-H)^-$.

Example 540

N^2-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(1-naphthylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-norvalinamide

The title compound was prepared by substituting 1-naphthyl-1-sulfonyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.74-9.78 (m, 1H), 9.25 (d, J = 8.7 Hz, 1H), 8.43 (d, J = 7.3 Hz, 1H), 8.12 (d, J = 8.2 Hz, 1H), 7.98 (d, J = 8.2 Hz, 1H), 7.69 (t, J = 7.8 Hz, 1H), 7.54-7.57 (m, 1H), 4.38 (t, J = 6.8 Hz, 1H), 4.26-4.32 (m, 1H), 3.83 (dd, J = 9.9, 2.7 Hz, 1H), 3.29 (dd, J = 9.9, 7.8 Hz, 1H), 3.22 (dd, J = 9.7, 2.7 Hz, 1H), 3.08 (dd, J = 9.6, 7.5 Hz, 1H), 2.89 (s, 3H), 2.59-2.66 (m, 1H), 2.50-2.59 (m, 1H), 2.02-2.15 (m, 2H), 1.80-2.00 (m, 2H), 1.57-1.67 (m, 1H), 1.45-1.55 (m, 2H), 1.23-1.30 (m, 1H), 0.78 (t, J = 7.3 Hz, 3H); MS (ESI-) *m/z* 428 $(M-H)^-$.

Example 541

N^1-((3a*R*,4*S*,6a*S*)-2-{[4-bromo-3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting 4-bromo-3-(trifluoromethyl)phenyl-1-sulfonyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.81-9.83 (m, 1H), 8.32 (d, J = 2.0

Hz, 1H), 8.04 (dd, J = 8.3, 2.0 Hz, 1H), 8.01 (d, J = 8.3 Hz, 1H), 6.60-8.44 (bs, 1H), 4.33-4.38 (m, 1H), 4.26-4.33 (m, 1H), 3.82 (dd, J = 9.9, 2.6 Hz, 1H), 3.21 (dd, J = 9.8, 2.7 Hz, 1H), 3.18 (dd, J = 9.8, 7.9 Hz, 1H), 2.96 (dd, J = 9.6, 7.5 Hz, 1H), 2.89 (s, 3H), 2.69-2.76 (m, 1H), 2.61-2.69 (m, 1H), 2.05-2.17 (m, 2H), 1.97-2.05 (m, 1H), 1.89-1.97 (m, 1H), 1.64-1.72 (m, 1H), 1.45-1.59 (m, 2H), 1.34 (ddt, J = 9.3, 13.0, 6.5 Hz, 1H), 0.79 (t, J = 7.3 Hz, 3H); MS (ESI-) m/z 524 $(M-H)^-$.

Example 542

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3,4-dichlorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting 3,4-dichlorophenyl-1-sulfonyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.84-9.86 (m, 1H), 7.41-8.78 (bs, 1H), 7.82 (dd, J = 8.3, 2.1 Hz, 1H), 7.69 (d, J = 8.3 Hz, 1H), 7.58-7.59 (bs, 1H), 4.45 (t, J = 6.8 Hz, 1H), 4.30 (p, J = 6.7 Hz, 1H), 3.76 (dd, J = 9.9, 2.7 Hz, 1H), 3.16 (dd, J = 9.9, 2.9 Hz, 1H), 3.14 (dd, J = 10.0, 8.0 Hz, 1H), 2.94 (s, 3H), 2.89-2.95 (m, 1H), 2.70-2.75 (m, 1H), 2.62-2.69 (m, 1H), 2.06-2.18 (m, 2H), 1.97-2.04 (m, 1H), 1.90-1.96 (m, 1H), 1.65-1.73 (m, 1H), 1.46-1.62 (m, 2H), 1.30-1.37 (m, 1H), 0.80 (t, J = 7.3 Hz, 3H); MS (ESI-) m/z 446 $(M-H)^-$.

Example 543

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-*tert*-butylphenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting 4-*tert*-butylphenyl -sulfonyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.85 (d, J = 6.8 Hz, 1H), 7.96-7.99 (m, 2H), 7.58-7.66 (m, 2H), 4.43 (t, J = 6.8 Hz, 1H), 4.27-4.33 (m, 1H), 3.78 (dd, J = 9.8, 2.5 Hz, 1H), 3.20 (dd, J = 9.6, 2.6 Hz, 1H), 3.11 (dd, J = 9.8, 7.7 Hz, 1H), 2.93 (s, 3H), 2.90 (dd, J = 9.5, 7.6 Hz, 1H), 2.47-2.62 (m, 2H), 2.08-2.18 (m, 2H), 1.93-2.01 (m, 1H), 1.85-1.92 (m, 1H), 1.60-1.68 (m, 1H), 1.48-1.59 (m, 2H), 1.28-1.39 (m, 1H), 1.26 (s, 9H), 0.81 (t, J = 7.3 Hz, 3H); MS (ESI+) m/z 436 $(M+H)^+$.

Example 544

N^1-[(3a*R*,4*S*,6a*S*)-2-(1,1'-biphenyl-4-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting 1,1'-biphenyl-4-sulfonyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.86-9.88 (m, 1H), 8.07-8.09 (m, 2H), 7.86-7.88 (m, 2H), 7.71-7.75 (m, 2H), 7.48-7.53 (m, 2H), 7.41-7.47 (m, 1H), 4.44 (t, J = 6.8 Hz, 1H), 4.29-4.36 (m, 1H), 3.78 (dd, J = 9.9, 2.7 Hz, 1H), 3.21 (dd, J = 9.7, 2.7 Hz, 1H), 3.15 (dd, J = 9.8, 7.9 Hz, 1H), 2.95 (dd, J = 9.5, 7.7 Hz, 1H), 2.93 (s, 3H), 2.64-2.71 (m, 1H), 2.56-2.64 (m, 1H), 2.06-2.19 (m, 2H), 1.97-2.04 (m, 1H), 1.88-1.97 (m, 1H), 1.62-1.73 (m, 1H), 1.48-1.62 (m, 2H), 1.30-1.40 (m, 1H), 0.80 (t, J = 7.3 Hz, 3H); MS (ESI+) *m/z* 456 $(M+H)^+$.

Example 545

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3,4-dimethoxyphenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting 3,4-dimethoxyphenyl -sulfonyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.86 (d, J = 6.9 Hz, 1H), 7.66 (dd, J = 8.4, 2.0 Hz, 1H), 7.55 (d, J = 2.0 Hz, 1H), 7.08 (d, J = 8.4 Hz, 1H), 4.38-4.43 (m, 1H), 4.31-4.38 (m, 1H), 3.81 (s, 3H), 3.78 (dd, J = 10.2, 2.8 Hz, 1H), 3.76 (s, 3H), 3.17-3.23 (m, 2H), 3.00 (dd, J = 9.6, 7.5 Hz, 1H), 2.91 (s, 3H), 2.68-2.75 (m, 1H), 2.60-2.68 (m, 1H), 2.06-2.18 (m, 2H), 1.98-2.06 (m, 1H), 1.88-1.98 (m, 1H), 1.64-1.73 (m, 1H), 1.49-1.59 (m, 2H), 1.33-1.40 (m, 1H), 0.79 (t, J = 7.3 Hz, 3H); MS (ESI-) *m/z* 438 $(M-H)^-$.

Example 546

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-cyanophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting 3-cyanophenyl -sulfonyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.86-9.88 (m, 1H), 8.56 (s, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.96 (d, J = 7.8 Hz, 1H), 7.66 (t, J = 7.8 Hz, 1H), 4.39-4.44 (m, 1H), 4.23-4.32 (m, 1H), 3.77 (dd, J = 10.0, 2.7 Hz, 1H), 3.18 (dd, J = 9.8, 2.9 Hz, 1H), 3.14 (dd, J = 9.9, 7.8 Hz, 1H), 2.93-2.96 (m, 1H), 2.91 (s, 3H), 2.65-2.72 (m, 1H), 2.58-2.65 (m, 1H), 2.04-2.18 (m, 2H), 1.95-2.03

(m, 1H), 1.87-1.95 (m, 1H), 1.68 (dq, J = 12.3, 8.1 Hz, 1H), 1.45-1.59 (m, 2H), 1.27-1.38 (m, 1H), 0.79 (t, J = 7.3 Hz, 3H); MS (ESI+) m/z 405 $(M+H)^+$.

Example 547

N^1-[(3a*R*,4*S*,6a*S*)-2-(2-furylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting 2-furylsulfonyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.88-9.90 (m, 1H), 7.86-7.87 (m, 1H), 7.26-7.28 (m, 1H), 6.58 (dd, J = 3.4, 1.8 Hz, 1H), 4.42 (t, J = 6.8 Hz, 1H), 4.24-4.33 (m, 1H), 3.79 (dd, J = 10.3, 3.2 Hz, 1H), 3.46 (dd, J = 10.3, 7.8 Hz, 1H), 3.20-3.32 (m, 2H), 2.92 (s, 3H), 2.67-2.75 (m, 1H), 2.60-2.68 (m, 1H), 2.06-2.20 (m, 2H), 1.97-2.05 (m, 1H), 1.88-1.95 (m, 1H), 1.71 (dq, J = 12.5, 8.0 Hz, 1H), 1.46-1.62 (m, 2H), 1.30 (ddt, J = 8.9, 13.0, 6.5 Hz, 1H), 0.81 (t, J = 7.3 Hz, 3H); MS (ESI+) m/z 370 $(M+H)^+$.

Example 548

N^1-{(3a*R*,4*S*,6a*S*)-2-[(2,3-dichlorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting 2,3-dichlorophenylsulfonyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.84-9.86 (m, 1H), 8.14 (dd, J = 7.9, 1.5 Hz, 1H), 7.68 (dd, J = 8.0, 1.5 Hz, 1H), 7.34 (t, J = 8.0 Hz, 1H), 4.49 (t, J = 6.8 Hz, 1H), 4.32-4.38 (m, 1H), 3.84-3.90 (m, 1H), 3.51 (dd, J = 10.2, 7.7 Hz, 1H), 3.26-3.41 (m, 2H), 2.95 (s, 3H), 2.76-2.82 (m, 1H), 2.68-2.75 (m, 1H), 2.09-2.19 (m, 2H), 2.01-2.09 (m, 1H), 1.90-2.00 (m, 1H), 1.73 (dq, J = 12.5, 8.1 Hz, 1H), 1.46-1.64 (m, 2H), 1.35-1.42 (m, 1H), 0.80 (t, J = 7.3 Hz, 3H); MS (ESI+) m/z 448 $(M+H)^+$.

Example 549

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)benzyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

The title compound was prepared by substituting 4-(trifluoromethyl)benzyl -sulfonyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.72-9.74 (m, 1H), 7.79-7.81 (m, 2H), 7.68-7.70 (m,

2H), 4.75-4.75 (bs, 2H), 4.51 (dd, J = 8.3, 6.3 Hz, 1H), 4.33 (p, J = 6.7 Hz, 1H), 3.78 (dd, J = 10.1, 3.1 Hz, 1H), 3.62 (dd, J = 10.2, 7.5 Hz, 1H), 3.45 (dd, J = 9.9, 7.5 Hz, 1H), 3.23 (dd, J = 9.9, 3.7 Hz, 1H), 2.90 (s, 3H), 2.68-2.85 (m, 2H), 2.02-2.15 (m, 3H), 1.91-1.98 (m, 1H), 1.75 (dq, J = 12.4, 8.1 Hz, 1H), 1.43-1.64 (m, 2H), 1.30-1.39 (m, 1H), 0.81 (t, J = 7.3 Hz, 3H); MS (ESI+) m/z 462 $(M+H)^+$.

Example 550

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[2-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide

The title compound was prepared by substituting 2-(trifluoromethyl)phenyl -sulfonyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.81-9.83 (m, 1H), 8.26 (d, J = 7.9 Hz, 1H), 7.93 (d, J = 7.8 Hz, 1H), 7.73 (t, J = 7.7 Hz, 1H), 7.67 (t, J = 7.7 Hz, 1H), 4.50 (t, J = 6.8 Hz, 1H), 4.31 (p, J = 6.7 Hz, 1H), 3.83 (dd, J = 10.1, 2.9 Hz, 1H), 3.36 (dd, J = 10.1, 7.7 Hz, 1H), 3.29 (dd, J = 9.9, 3.1 Hz, 1H), 3.18 (dd, J = 9.9, 7.5 Hz, 1H), 2.95 (s, 3H), 2.75-2.80 (m, 1H), 2.65-2.73 (m, 1H), 2.14 (q, J = 7.5 Hz, 2H), 1.99-2.06 (m, 1H), 1.91-1.98 (m, 1H), 1.68-1.76 (m, 1H), 1.47-1.65 (m, 2H), 1.36 (ddt, J = 9.2, 12.9, 6.5 Hz, 1H), 0.80 (t, J = 7.3 Hz, 3H); MS (ESI+) m/z 448 $(M+H)^+$.

Example 551

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-bromophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting 2-(trifluoromethyl)phenyl -sulfonyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 9.78-9.80 (m, 1H), 8.26 (t, J = 1.8 Hz, 1H), 7.90 (dt, J = 7.8, 1.2 Hz, 1H), 7.78 (ddd, J = 8.0, 1.9, 1.0 Hz, 1H), 7.43 (t, J = 7.9 Hz, 1H), 4.42 (dd, J = 7.9, 5.8 Hz, 1H), 4.29 (p, J = 6.7 Hz, 1H), 3.75 (dd, J = 9.9, 2.7 Hz, 1H), 3.15 (dd, J = 9.7, 2.8 Hz, 1H), 3.10 (dd, J = 9.9, 7.7 Hz, 1H), 2.92 (s, 3H), 2.88 (dd, J = 9.6, 7.5 Hz, 1H), 2.62-2.68 (m, 1H), 2.55-2.61 (m, 1H), 2.04-2.20 (m, 2H), 1.86-2.03 (m, 2H), 1.63-1.70 (m, 1H), 1.48-1.60 (m, 2H), 1.31 (ddt, J = 9.2, 12.9, 6.5 Hz, 1H), 0.80 (t, J = 7.3 Hz, 3H); MS (ESI-) m/z 456 $(M-H)^-$.

Example 552

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting 2-chloro-4-(trifluoromethyl)phenylsulfonyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 10.09-10.11 (m, 1H), 8.33 (d, J = 8.2 Hz, 1H), 7.99-8.00 (bs, 1H), 7.73-7.75 (m, 1H), 4.66-4.70 (m, 1H), 4.35-4.44 (m, 1H), 3.85 (dd, J = 10.3, 3.2 Hz, 1H), 3.55 (d, J = 8.7 Hz, 1H), 3.30-3.42 (m, 2H), 2.95 (s, 3H), 2.88-2.95 (m, 1H), 2.75-2.86 (m, 1H), 2.35-2.41 (m, 1H), 2.22-2.30 (m, 1H), 1.99-2.19 (m, 2H), 1.89-1.95 (m, 1H), 1.54-1.77 (m, 2H), 1.39-1.47 (m, 1H), 0.85 (t, J = 7.3 Hz, 3H); MS (ESI-) *m/z* 480 $(M-H)^-$.

Example 553

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-5-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-methyl-L-norvalinamide

The title compound was prepared by substituting 2-chloro-5-(trifluoromethyl)phenylsulfonyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 10.09-10.12 (m, 1H), 8.54 (d, J = 2.2 Hz, 1H), 7.82 (dd, J = 8.3, 2.2 Hz, 1H), 7.76 (d, J = 8.3 Hz, 1H), 4.73 (dd, J = 9.1, 4.6 Hz, 1H), 4.35-4.43 (m, 1H), 3.84 (dd, J = 10.2, 3.2 Hz, 1H), 3.56 (dd, J = 10.2, 7.8 Hz, 1H), 3.29-3.40 (m, 2H), 2.96 (s, 3H), 2.89-3.00 (m, 1H), 2.76-2.88 (m, 1H), 2.35-2.44 (m, 1H), 2.21-2.33 (m, 1H), 2.05-2.19 (m, 2H), 1.88-1.98 (m, 1H), 1.66-1.79 (m, 1H), 1.53-1.66 (m, 1H), 1.38-1.48 (m, 1H), 0.85 (t, J = 7.3 Hz, 3H); MS (ESI-) *m/z* 480 $(M-H)^-$.

Example 554

N^2-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzoyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide

The title compound was prepared by substituting 3-(trifluoromethyl)benzoyl chloride for 4-methoxybenzene-1-sulfonyl chloride in the procedure described in Example 537: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 7.98 (s, 1H), 7.80 (d, J = 7.7, 1H), 7.65 (d, J = 7.9, 1H), 7.52 –

7.40 (m, 3H), 4.34 – 4.19 (m, 1H), 3.88 – 3.74 (m, 3H), 3.66 (d, J = 8.2, 1H), 3.44 (s, 1H), 2.85 – 2.52 (m, 5H), 2.51 – 2.38 (m, 0H), 2.11 (dt, J = 12.6, 6.2, 1H), 1.91 (dddd, J = 22.0, 15.6, 10.7, 4.6, 3H), 1.72 (dq, J = 12.8, 8.0, 1H), 1.57 – 1.17 (m, 4H), 0.83 (t, J = 7.3, 3H); MS (ESI+) *m/z* 412 $(M+H)^+$.

Example 555

***N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*-isopropyl-3-(trifluoromethyl)benzenesulfonamide**

Step A: (3a*R*,4*S*,6a*S*)-2-Benzyl-*N*-isopropyloctahydrocyclopenta[*c*]pyrrol-4-amine was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Example 33 Step A for (3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-amine and acetone for pivalaldehyde in the procedure described in Example 281: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 7.48 (d, J = 7.5, 2H), 7.39 (t, J = 7.5, 2H), 7.29 (t, J = 7.3, 1H), 3.61 – 3.51 (m, 2H), 3.05 (dd, J = 12.1, 5.4, 1H), 2.87 – 2.78 (m, 1H), 2.61 – 2.51 (m, 2H), 2.43 – 2.36 (m, 2H), 2.35 – 2.30 (m, 1H), 2.28 – 2.21 (m, 1H), 2.00 – 1.93 (m, 1H), 1.93 – 1.87 (m, 1H), 1.42 – 1.28 (m, 3H), 1.05 – 0.98 (m, 6H); MS (ESI+) *m/z* 259 $(M+H)^+$.

Step B: The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyl-*N*-isopropyloctahydrocyclopenta[*c*]pyrrol-4-amine from Step A for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate and 3-(trifluoromethyl)benzene-1-sulfonylchloride for methanesulfonyl chloride in the procedure described in Example 242: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.43 (s, 1H), 8.30 – 8.21 (m, 1H), 7.84 (d, J = 7.6, 1H), 7.66 – 7.59 (m, 1H), 7.40 (ddd, J = 12.7, 8.4, 2.6, 4H), 7.32 – 7.27 (m, 1H), 3.82 – 3.70 (m, 2H), 3.51 (d, J = 2.0, 2H), 2.82 – 2.74 (m, 1H), 2.67 – 2.62 (m, 1H), 2.52 – 2.43 (m, 3H), 2.09 – 2.04 (m, 1H), 1.99 – 1.95 (m, 1H), 1.91 – 1.79 (m, 2H), 1.75 – 1.65 (m, 1H), 1.26 (dd, J = 6.8, 2.6, 6H); MS (ESI+) *m/z* 467 $(M+H)^+$.

Example 556

***N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide**

The title compound was prepared by substituting (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine from Example 33 Step A for (*S*)-*tert*-butyl 2-amino-4-methylpentanoate and 3-(trifluoromethyl)benzene-1-sulfonylchloride for methanesulfonyl chloride in the procedure described in Example 242 Step A: ^{1}H NMR (500

MHz, pyridine-d_5) δ ppm 9.49 (d, J = 7.2, 1H), 8.43 (s, 1H), 8.30 (d, J = 7.9, 1H), 7.81 (d, J = 7.9, 1H), 7.60 (d, J = 7.9, 1H), 7.37 (dd, J = 9.6, 3.8, 4H), 7.33 – 7.26 (m, 1H), 3.83 – 3.75 (m, 1H), 3.50 (d, J = 13.1, 1H), 3.44 (d, J = 13.1, 1H), 2.61 (dd, J = 9.2, 2.0, 1H), 2.56 – 2.43 (m, 2H), 2.35 (dd, J = 9.1, 2.1, 1H), 2.21 – 2.13 (m, 2H), 1.99 (td, J = 11.7, 5.8, 1H), 1.82 (ddd, J = 12.5, 10.2, 5.6, 1H), 1.63 – 1.53 (m, 1H), 1.29 (ddt, J = 12.7, 10.0, 6.4, 1H); MS (ESI+) *m/z* 442 $(M+NH_4)^+$.

Example 557

***N*-isopropyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide**

The title compound was prepared by substituting *N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*-isopropyl-3-(trifluoromethyl)benzenesulfonamide from Example 555 for *N*-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-2,2-bis(4-fluorophenyl)acetamide in the procedure described in Example 459: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.30 (s, 1H), 8.17 (d, J = 7.8, 1H), 7.79 (d, J = 8.1, 1H), 7.61 (t, J = 7.8, 1H), 3.90 – 3.80 (m, 2H), 3.77 – 3.67 (m, 4H), 3.39 (dd, J = 9.0, 4.2, 1H), 3.10 – 3.01 (m, 1H), 2.82 – 2.70 (m, 1H), 2.39 (s, 3H), 2.13 – 2.01 (m, 1H), 2.02 – 1.83 (m, 3H), 1.51 (t, J = 6.7, 2H), 1.29 (d, J = 6.8, 5H), 1.23 (d, J = 6.8, 3H), 0.97 – 0.89 (m, 6H); MS (ESI+) *m/z* 504 $(M+H)^+$.

Example 558

***N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide**

The title compound was prepared by substituting *N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide from Example 556 for *N*-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-2,2-bis(4-fluorophenyl)acetamide in the procedure described in Example 459: ^{1}H NMR (400 MHz, pyridine-d_5) δ ppm 8.88 (qt, J = 7.3, 2.9, 1H), 8.35 (s, 1H), 8.24 (d, J = 7.9, 1H), 7.79 (d, J = 7.9, 1H), 7.59 (t, J = 8.0, 1H), 3.79 – 3.70 (m, 3H), 3.68 – 3.53 (m, 2H), 3.37 (ddd, J = 8.4, 7.7, 2.4, 1H), 2.77 – 2.62 (m, 2H), 2.37 (s, 3H), 2.06 – 1.87 (m, 3H), 1.75 – 1.63 (m, 1H), 1.53 – 1.44 (m, 2H), 1.38 – 1.24 (m, 1H), 0.92 (dd, J = 8.8, 6.7, 7H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Example 559

***N*-cyclopropyl-*N*-[(3a*S**,4*S**,6a*R**)-[2-(*N*-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide**

The title compound was prepared by substituting *N*-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*-cyclopropyl-3-(trifluoromethyl)benzenesulfonamide from Example 199 for *N*-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl)-2,2-bis(4-fluorophenyl)acetamide in the procedure described in Example 459: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.50 (s, 1H), 8.39 – 8.31 (m, 1H), 7.96 (dd, *J* = 20.3, 7.8, 1H), 7.82 – 7.71 (m, 1H), 4.20 (dd, *J* = 13.1, 5.0, 0.5H), 4.12 (dt, *J* = 13.2, 6.7, 0.5H), 4.04 – 3.98 (m, 0.5H), 3.97 – 3.80 (m, 1.5H), 3.72 (ddd, *J* = 22.3, 16.1, 9.9, 1H), 3.60 (dt, *J* = 8.6, 7.6, 0.5H), 3.53 – 3.38 (m, 2H), 3.29 – 3.21 (m, 0.5H), 2.72 – 2.65 (m, 0.5H), 2.63 – 2.52 (m, 0.5H), 2.48 (s, 0.5H), 2.42 (d, *J* = 4.6, 2H), 2.39 (s, 0.5H), 2.15 – 1.97 (m, 3H), 1.92 – 1.82 (m, 1H), 1.75 – 1.68 (m, 1H), 1.67 – 1.34 (m, 5H), 1.04 (d, *J* = 6.6, 1H), 0.99 – 0.94 (m, 3H), 0.91 (dt, *J* = 14.0, 5.1, 3H), 0.85 – 0.71 (m, 1.5H), 0.69 – 0.59 (m, 0.5H); MS (ESI+) *m/z* 502 $(M+H)^+$.

Example 560

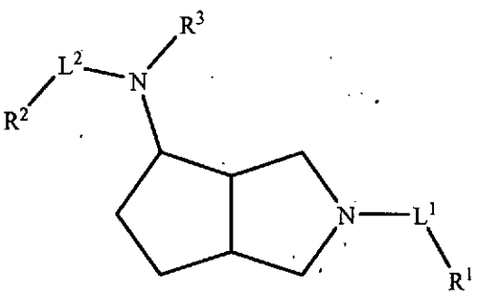
4-fluoro-*N*-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzamide

The title compound was prepared by substituting 4-fluorobenzoic acid for *N*-(*tert*-butoxycarbonyl)-L-leucine and (3a*R*,4*S*,6a*S*)-2-(6-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-amine from Example 264 Step A for (3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-amine in the procedure described in Example 221: ^{1}H NMR (500 MHz, pyridine-d_5) δ ppm 8.90 (d, *J* = 6.9, 1H), 8.27 – 8.21 (m, 2H), 7.55 – 7.50 (m, 1H), 7.20 – 7.14 (m, 2H), 6.99 (d, *J* = 7.2, 1H), 6.53 (d, *J* = 8.6, 1H), 4.61 – 4.54 (m, 1H), 3.80 (dd, *J* = 11.0, 3.7, 1H), 3.63 (dd, *J* = 10.9, 8.2, 1H), 3.51 (dd, *J* = 10.8, 8.4, 1H), 3.30 (dd, *J* = 10.9, 4.6, 1H), 2.88 – 2.81 (m, 1H), 2.76 – 2.67 (m, 1H), 2.23 (ddd, *J* = 19.5, 7.1, 4.7, 1H), 1.93 (dtd, *J* = 12.7, 8.0, 4.6, 1H), 1.81 (ddd, *J* = 16.4, 12.7, 8.1, 1H), 1.40 (dt, *J* = 13.2, 7.6, 1H); MS (ESI+) *m/z* 394 $(M+H)^+$.

Many variations in the invention will suggest themselves to those skilled in the art in light of the foregoing detailed description. All such obvious variations are within the full intended scope of the appended claims.

We claim

1. A compound of formula (I),



(I),

or a pharmaceutically acceptable salt, prodrug, salt of a prodrug, or a combination thereof, wherein

L^1 is C(O), $S(O)_2$, $SO_2N(R^4)$, C(O)O or $-(CR^aR^b)_m-$;

R^1 is alkyl, G^1, $-CH(G^1)_2$, $-(CR^aR^b)_m-G^1$, $-(CR^aR^b)_m-CH(G^1)_2$, $-(CR^eR^f)_n-N(R^5)_2$, $-(CR^eR^f)_n-N(R^5)-C(O)O(alkyl)$, $-(CR^eR^f)_n-N(R^5)-C(O)(alkyl)$, or $-(CR^eR^f)_n-N(R^5)-SO_2R^6$; or

L^1-R^1 taken together are hydrogen, alkyl, hydroxyalkyl, G^1, or $-CH(G^1)_2$;

L^2 is $-(CR^cR^d)_p-$, C(O), $C(O)N(R^4)$, $S(O)_2$, $SO_2N(R^5)$, or C(O)O;

R^2 is alkyl, G^2, $-C(R^c)(G^2)(G^3)$, $-(CR^cR^d)_p-G^2$, $-(CR^cR^d)_p-CH(G^2)(G^3)$, $-(CR^gR^h)_q-N(R^5)-C(O)O(alkyl)$, $-(CR^gR^h)_q-N(R^5)-C(O)O-G^2$, $-(CR^gR^h)_q-N(R^5)-C(O)(alkyl)$, $-(CR^gR^h)_q-N(R^5)-SO_2R^6$, $-(CR^gR^h)_q-N(R^4)(R^5)$, $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-(alkyl)$, or $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-G^2$; or

L^2-R^2 taken together are alkyl, G^2, or $-C(R^c)(G^2)(G^3)$;

m and p, at each occurrence, are each independently 1, 2, 3, 4, 5, or 6;

n and q, at each occurrence, are each independently 1, 2, 3, 4, or 5;

R^a, R^b, R^c, and R^d, at each occurrence, are each independently hydrogen, alkyl, arylalkyl, halogen, haloalkyl or OR^7; or

R^a and R^b, or R^c and R^d, together with the carbon atom to which they are attached, optionally form a C_{3-6} cycloalkyl ring;

R^e, R^f, R^g, and R^h, at each occurrence, are each independently hydrogen, alkyl, halogen, haloalkyl, OR^7, cycloalkylalkyl, heteroaryl, arylalkyl, or heteroarylalkyl; wherein the aryl, cycloalkyl and heteroaryl groups of aryl, cycloalkyl and heteroaryl are each independently unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of alkyl and haloalkyl;

G^1, G^2, and G^3 at each occurrence, are each independently aryl, cycloalkyl, cycloalkenyl, heteroaryl, or heterocycle; wherein G^1, G^2, and G^3 at each occurrence are each independently unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents selected form the group consisting of alkyl, alkenyl, alkynyl, cyano, haloalkyl, halogen, nitro, oxo, phenyl, $N(R^7)_2$, $N(R^7)C(O)R^7$, OR^7, $C(O)R^7$, $C(O)OR^7$, $C(O)N(R^7)_2$, SO_2R^8, and $SO_2N(R^7)_2$; and wherein G^1 is other than quinoline, quinazolinedione, or pyridopyrimidinedione;

R^3 is hydrogen, alkyl, haloalkyl, cycloalkyl, or cycloalkylalkyl;

R^4, R^5, and R^7, at each occurrence, are each independently hydrogen, alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, or haloalkyl; wherein said aryl, the aryl of arylalkyl and cycloalkyl are independently unsubstituted or substituted with 1, 2 3, 4, or 5 substituents independently selected from the group consisting of alkyl, haloalkyl, and halogen;

R^6 is alkyl, aryl, cycloalkyl, cycloalkenyl, heteroaryl, or heterocycle; wherein said aryl, heteroaryl, and heterocycle are independently unsubstituted or substituted with 1, 2 3, 4, or 5 substituents independently selected from the group consisting of alkyl, haloalkyl, and halogen;

R^8 is alkyl or haloalkyl;

with the proviso that L^1-R^1 and L^2-R^2 are not both alkyl at the same time;

and with the proviso that when L^1-R^1 is alkyl, L^2-R^2 is other than $C(O)N(R^4)$, wherein R^4 is alkyl;

and with the further proviso that the compound is other than:

N-(2-trityloctahydrocyclopenta[*c*]pyrrol-4-yl)acetamide;

N-(octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide

N-methyl-*N*-(2-trityloctahydrocyclopenta[*c*]pyrrol-4-yl)acetamide;

N-methyl-*N*-(octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide;

6-(2-(2-(3-fluoro-6-methoxy-1,5-naphthyridin-4-yl)ethyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)methyl-2*H*-pyrido[3,2-*b*][1,4]thiazin-3(4*H*)-one;

tert-butyl 2-(2-(3-fluoro-6-methoxy-1,5-naphthyridin-4-yl)ethyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate;

tert-butyl 2-benzyl octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate; or

tert-butyl octahydrocyclopenta[*c*]pyrrol-4-ylcarbamate.

2. The compound according to claim 1, wherein

L^1 is $-(CR^aR^b)_m-$;

R^a and R^b are each hydrogen;

m is 1;

R^1 is G^1; wherein G^1 is aryl;

L^2 is C(O);

R^2 is $-(CR^cR^d)_p-G^2$; wherein G^2 is aryl;

p is 1;

R^c and R^d, together with the carbon atom to which they are attached form a C_{3-6} cycloalkyl ring; and

R^3 is hydrogen.

3. The compound according to claim 1, wherein

L^1-R^1 together are alkyl; or

L^1 is $-(CR^aR^b)_m-$ or C(O);

R^1 is G^1; wherein G^1 is aryl, cycloalkyl, or heteroaryl;

L^2 is C(O);

R^2 is $-(CR^cR^d)_p-G^2$; wherein G^2 is aryl and p is 1 or 2;

R^a, R^b, R^c, and R^d, at each occurrence are independently hydrogen, alkyl, or arylalkyl; and

R^3 is hydrogen or alkyl.

4. The compound according to claim 1, wherein

L^1 is $-(CR^aR^b)_m-$;

R^a and R^b at each occurrence are each hydrogen;

m is 1 or 2;

R^1 is G^1; wherein G^1 is aryl;

L^2 is $C(O)N(R^4)$, wherein R^4 is alkyl;

R^2 is G^2, wherein G^2 is aryl; and

R^3 is hydrogen.

5. The compound according to claim 1, wherein

L^1 is $-(CR^aR^b)_m-$, C(O) or $S(O)_2$;

R^a and R^b at each occurrence are each hydrogen;

m is 1;

R^1 is alkyl or G^1; wherein G^1 is aryl or cycloalkyl;

L^2 is C(O);

R^2 is $-(CR^cR^d)_p-G^2$; wherein

R^c and R^d at each occurrence are independently hydrogen, alkyl or OR^7;

p is 1;

G^2 is cycloalkyl or heterocycle; wherein said cycloalkyl or heterocycle is unsubstituted or substituted with 1, 2, 3, 4, or 5 substituents independently selected from the group consisting of alkyl, haloalkyl, halogen, oxo and $C(O)OR^7$;

R^7 is hydrogen; and

R^3 is hydrogen.

6. The compound according to claim 1, wherein

L^1 is $-(CR^aR^b)_m-$;

R^a and R^b at each occurrence are each hydrogen;

m is 1;

R^1 is G^1; wherein G^1 is aryl;

L^2-R^2 together are cycloalkyl; and

R^3 is hydrogen or cycloalkyl.

7. The compound according to claim 1, wherein

L^1 is $-(CR^aR^b)_m-$;

R^a and R^b at each occurrence are each hydrogen;

m is 1;

R^1 is G^1; wherein G^1 is aryl;

L^2 is C(O);

R^2 is $-C(R^c)(G^2)(G^3)$, or $-(CR^cR^d)_p-CH(G^2)(G^3)$; wherein G^2 is aryl and G^3 is aryl or cycloalkyl;

R^c and R^d are each hydrogen; and

R^3 is hydrogen.

8. The compound according to claim 1, wherein

L^1-R^1 together is hydrogen or $-CH(G^1)_2$, wherein each G^1 is aryl or heteroaryl; or

L^1 is $-(CR^aR^b)_m-$, C(O), or $S(O)_2$;

R^1 is G^1, $-CH(G^1)_2$, $-(CR^aR^b)_m-G^1$, $-(CR^aR^b)_m-CH(G^1)_2$, $-(CR^eR^f)_n-N(R^5)_2$; wherein each G^1 is aryl or heteroaryl;

R^a and R^b are each hydrogen;

R^e and R^f at each occurrence, are each independently hydrogen or alkyl;

R^5 at each occurrence, is independently hydrogen or alkyl;

L^2 is C(O);

R^2 is $-C(R^c)(G^2)(G^3)$; wherein G^2 and G^3 are each cycloalkyl;

R^c hydrogen or OR^7, wherein R^7 is hydrogen; and

R^3 is hydrogen.

9. The compound according to claim 1, wherein

L^1 is $-(CR^aR^b)_m-$ or $S(O)_2$;

R^a and R^b at each occurrence are each hydrogen;

m is 1;

R^1 is G^1; wherein G^1 is aryl;

L^2 is C(O); and

R^2 is alkyl or G^2, wherein G^2 is cycloalkyl or heterocycle; and

R^3 is hydrogen.

10. The compound according to claim 1, wherein

L^1 is $-(CR^aR^b)_m-$, C(O) or $S(O)_2$;

R^a and R^b at each occurrence are each hydrogen;

m, at each occurrence, is 1 or 2;

R^1 is G^1, $-(CR^aR^b)_m-G^1$, or $-CH(G^1)_2$, wherein G^1, at each occurrence, is independently aryl or heteroaryl;

L^2 is C(O);

R^2 is $-(CR^gR^h)_q-N(R^5)-C(O)O(alkyl)$, $-(CR^gR^h)_q-N(R^5)-C(O)O-G^2$, $-(CR^gR^h)_q-N(R^5)-C(O)(alkyl)$, $-(CR^gR^h)_q-N(R^5)-SO_2-R^6$, $-(CR^gR^h)_q-N(R^4)(R^5)$, $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-(alkyl)$, or $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-G^2$;

q is 1 or 2;

R^g and R^h, at each occurrence, are each independently hydrogen, alkyl, arylalkyl, or cycloalkylalkyl;

R^4 and R^5 at each occurrence, are each independently hydrogen, alkyl, arylalkyl, cycloalkyl or cycloalkylalkyl;

R^6 is alkyl, aryl, or cycloalkyl;

G^2 is aryl or cycloalkyl; and

R^3 is hydrogen, alkyl, cycloalkyl or cycloalkylalkyl.

11. The compound according to claim 1, wherein

L^1-R^1 together are hydrogen or hydroxyalkyl; or

L^1 is $-(CR^aR^b)_m-$, C(O) or $S(O)_2$;

R^1 is G^1, $-(CR^aR^b)_m-G^1$ or $-CH(G^1)_2$, wherein each G^1 is aryl or heteroaryl;

R^a and R^b, at each occurrence, are each independently hydrogen or alkyl;

L^2 is $S(O)_2$;

R^2 is G^2, wherein G^2 is aryl or heteroaryl; or

R^3 is hydrogen, alkyl or cycloalkyl.

12. The compound according to claim 1, wherein

L^1 is $-(CR^aR^b)_m-$;

R^a and R^b are each hydrogen;

R^1 is $-CH(G^1)_2$, wherein each G^1 is aryl;

L^2 is C(O);

R^2 is $-(CR^cR^d)_p-G^2$; wherein G^2 is aryl;

p is 1;

R^c and R^d, at each occurrence, are each independently hydrogen or alkyl; and

R^3 is hydrogen.

13. The compound according to claim 1, wherein

L^1 is C(O), $S(O)_2$ or $-(CR^aR^b)_m-$;

R^a and R^b, at each occurrence, are independently hydrogen or alkyl;

m is 1;

R^1 is G^1 or $-(CR^aR^b)_m-G^1$, wherein G^1 is aryl or heteroaryl;

L^2 is $-(CR^cR^d)_p-$;

R^c and R^d are each hydrogen;

p is 1;

R^2 is G^2, wherein G^2 is aryl, cycloalkyl or heteroaryl; or

L^2-R^2 taken together are alkyl, G^2, or $-C(R^c)(G^2)(G^3)$, wherein G^2 and G^3 are each aryl or heteroaryl and R^c is hydrogen; and

R^3 is hydrogen or alkyl.

14. The compound according to claim 1, wherein

L^1 is C(O);

R^1 is $-(CR^eR^f)_n-N(R^5)_2$;

n is 1 or 2;

R^e and R^f at each occurrence are each independently hydrogen or alkyl;

R^5 at each occurrence is independently hydrogen or alkyl;

L^2 is C(O) or $S(O)_2$;

R^2 is G^2 or $-C(R^c)(G^2)(G^3)$, wherein G^2 and G^3 are each aryl or heteroaryl and R^c is hydrogen; and

R^3 is hydrogen, alkyl, or cycloalkyl.

15. The compound according to claim 1, wherein

L^1 is C(O);

R^1 is $-(CR^eR^f)_n-N(R^5)_2$ or $-(CR^eR^f)_n-N(R^5)C(O)O(alkyl)$;

n is 1 or 2;

R^e and R^f at each occurrence are each independently hydrogen, alkyl, or arylalkyl;

R^5 at each occurrence is independently hydrogen, alkyl or cycloalkyl;

L^2 is C(O);

R^2 is $-(CR^gR^h)_qN(R^4)(R^5)$ or $-(CR^gR^h)_q-N(R^5)C(O)O(alkyl)$;

q is 1 or 2;

R^4 is hydrogen or alkyl;

R^g and R^h at each occurrence are each independently hydrogen or alkyl; and

R^3 is hydrogen.

16. The compound of claim 1, wherein

L^1-R^1 taken together are hydrogen, G^1 or $CH(G^1)_2$, wherein G^1 is aryl or heteroaryl;

L^2 is C(O);

R^2 is $-(CR^gR^h)_qN(R^4)(R^5)$ or $-(CR^gR^h)_q-N(R^5)C(O)O(alkyl)$;

q is 1 or 2;

R^4 is hydrogen, alkyl, or cycloalkylalkyl;

R^5 is hydrogen or alkyl;

R^g and R^h at each occurrence are each independently hydrogen or alkyl; and

R^3 is hydrogen.

17. The compound of claim 1, wherein

L^1-R^1 taken together are G^1, wherein G^1 is aryl or heteroaryl;

L^2 is C(O);

R^2 is G^2, wherein G^2 is aryl or heteroaryl; and

R^3 is hydrogen or alkyl.

18. The compound according to claim 1 or a pharmaceutically acceptable salt thereof, selected from the group consisting of:

N-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclopentanecarboxamide;

N-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclopentanecarboxamide;

N-[(3a*R**,4*R**,6a*S**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclohexyl-2-phenylacetamide;

N-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclohexyl-2-phenylacetamide;

N-[(3a*R**,4*R**,6a*S**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*R**,4*S**,6a*S**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclopentyl-2-phenylacetamide;

N-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclopentyl-2-phenylacetamide;

N-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclohexanecarboxamide;

N-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclohexanecarboxamide;

N-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide;

(2*S*)-2-(3-benzoylphenyl)-*N*-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]propanamide;

(2*S*)-2-(3-benzoylphenyl)-*N*-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]propanamide;

N-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclopentyl-2-phenylacetamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylpropanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-propylpentanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]cycloheptanecarboxamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(4-isobutylphenyl)propanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclohexanecarboxamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,3-diphenylpropanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-methyl-3-phenylpropanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-methyl-2-phenylpropanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclopropanecarboxamide;

2-benzyl-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethylbutanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethyl-2-phenylbutanamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethyl-2-phenylbutanamide;

(2*R*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethyl-2-phenylbutanamide;

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclopentyl-2-phenylacetamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

(2*R*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide;

(2*R*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylpropanamide;

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylpropanamide;

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(4-isobutylphenyl)propanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclopropyl-2-phenylacetamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-cyclobutyl-2-phenylacetamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(4-chlorophenyl)-3-methylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-ethyl-2-phenylpentanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(4-hydroxyphenyl)-3-methylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclohexanecarboxamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-methyl-2-phenylpropanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-phenylcyclopropanecarboxamide;

2-benzyl-*N*-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,3-diphenylpropanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-methyl-3-phenylpropanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3,3-dimethyl-2-phenylbutanamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(2-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[4-fluoro-3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-fluoro-4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

N-{(3a*S*,4*S*,6a*R*)-2-[3,5-bis(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[2-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-methylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(4-methylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethoxy)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

N-{(3a*S*,4*S*,6a*R*)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide;

N-{(3a*S*,4*S*,6a*R*)-2-[6,6-bis(4-fluorophenyl)hexyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide;

N-{(3a*S*,4*S*,6a*R*)-2-[3-(3-chlorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(3-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-phenylpropyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-((3a*S*,4*S*,6a*R*)-2-{3-[4-(trifluoromethyl)phenyl]propyl}octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(pyridin-4-ylmethyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*S*,6a*R*)-2-(pyridin-3-ylmethyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

N-{(3a*S*,4*R*,6a*R*)-2-[3,5-bis(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide;

N-{(3a*S*,4*R*,6a*R*)-2-[6,6-bis(4-fluorophenyl)hexyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide;

2,2-dicyclohexyl-*N*-[(3a*S*,4*R*,6a*R*)-2-(3,3-diphenylpropyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

N-{(3a*S*,4*R*,6a*R*)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide;

N-{(3a*S*,4*R*,6a*R*)-2-[4,4-bis(4-fluorophenyl)butyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2,2-dicyclohexylacetamide;

3-methyl-2-phenyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(cyclohexylmethyl)octahydrocyclopenta[c]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-2-methyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(2-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(3-chlorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(3-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

3-methyl-2-phenyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(3-methoxybenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(3-methylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide;

3-methyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(2-methylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(2,6-dimethylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(2-methoxybenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(4-*tert*-butylbenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(4-methoxybenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(3-cyanobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

3-methyl-2-phenyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

3-methyl-2-phenyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[2-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[4-fluoro-3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[3-fluoro-4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

3-methyl-2-phenyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(thien-2-ylmethyl)octahydrocyclopenta[*c*]pyrrol-4-yl]butanamide;

3-methyl-2-phenyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(pyridin-4-ylmethyl)octahydrocyclopenta[*c*]pyrrol-4-yl]butanamide;

3-methyl-2-phenyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(2-phenylethyl)octahydrocyclopenta[*c*]pyrrol-4-yl]butanamide;

3-methyl-2-phenyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(3-phenylpropyl)octahydrocyclopenta[*c*]pyrrol-4-yl]butanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[3-(4-*tert*-butylphenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[6,6-bis(4-fluorophenyl)hexyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

3-methyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(2-methylphenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2-phenylbutanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[3-(3-chlorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

3-methyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(3-methylphenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-2-phenylbutanamide;

3-methyl-2-phenyl-*N*-((3a*R*,4*S*,6a*S*)-2-{3-[3-(trifluoromethyl)phenyl]propyl}octahydrocyclopenta[*c*]pyrrol-4-yl)butanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[3-(3-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

3-methyl-2-phenyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(4-phenylbutyl)octahydrocyclopenta[*c*]pyrrol-4-yl]butanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[3-(3-chloro-5-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

3-methyl-2-phenyl-*N*-((3a*R*,4*S*,6a*S*)-2-{3-[4-(trifluoromethyl)phenyl]propyl}octahydrocyclopenta[*c*]pyrrol-4-yl)butanamide;

N-[(3a*R*,4*S*,6a*S*)-2-(3,3-diphenylpropyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[4,4-bis(4-fluorophenyl)butyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

N-{(3a*R*,4*S*,6a*S*)-2-[5,5-bis(4-fluorophenyl)pentyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-methyl-2-phenylbutanamide;

N-[(3a*S*,4*S*,6a*R*)-2-benzhydryloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzhydryloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-dicyclohexylacetamide;

3-methyl-2-phenyl-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

3,3-dimethyl-2-phenyl-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

2,2-dicyclohexyl-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2-ethyl-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

2-propyl-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}pentanamide;

N-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}cyclohexanecarboxamide;

N-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}cycloheptanecarboxamide;

N-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}cyclopentanecarboxamide;

6,6-bis(4-fluorophenyl)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}hexanamide;

3,3-diphenyl-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}propanamide;

5,5-bis(4-fluorophenyl)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}pentanamide;

3,3-bis(4-fluorophenyl)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[c]pyrrol-4-yl}propanamide;

4,4-bis(4-fluorophenyl)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

2,2-diphenyl-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-bis(4-fluorophenyl)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^2-(*tert*-butyloxycarbonyl)-N^2-methyl-N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

6,6-bis(4-fluorophenyl)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}hexanamide;

3,3-diphenyl-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}propanamide;

5,5-bis(4-fluorophenyl)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}pentanamide;

3,3-bis(4-fluorophenyl)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}propanamide;

4,4-bis(4-fluorophenyl)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

2,2-diphenyl-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-bis(4-fluorophenyl)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

3,3-dimethyl-2-phenyl-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

N^2-(*tert*-butyloxycarbonyl)-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(*tert*-butyloxycarbonyl)-*N*^{1}-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^2-(*tert*-butyloxycarbonyl)-*N*^{2}-methyl-*N*^{1}-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*^{2}-(*tert*-butyloxycarbonyl)-*N*^{2}-methyl-L-leucinamide;

2,2-dicyclohexyl-2-hydroxy-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

N^2-(*tert*-butyloxycarbonyl)-*N*^{2}-methyl-*N*^{1}-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

2,2-dicyclohexyl-2-hydroxy-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

N^2-(*tert*-butyloxycarbonyl)-*N*^{2}-methyl-*N*^{1}-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

2,2-dicyclohexyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-{(3a*R*,4*R*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^2-methyl-*N*^{1}-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^2-methyl-*N*^{1}-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^2-methyl-*N*^{1}-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*^{2}-methyl-L-leucinamide;

N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[c]pyrrol-4-yl}-L-leucinamide;

N^2-methyl-N^2-(methylsulfonyl)-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-N^2-(methylsulfonyl)-L-leucinamide;

N^2-methyl-N^2-(methylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(methylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(methylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^2-(cyclopropylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(isobutylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(cyclopropylsulfonyl)-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-acetyl-N^2-methyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(2,2-dimethylpropanoyl)-N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(2,2-dimethylpropanoyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

isobutyl (*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

cyclopentyl (*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

N^2-[(*tert*-butylamino)carbonyl]-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-[(cyclopentylamino)carbonyl]-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

3-(trifluoromethyl)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide;

3-(trifluoromethyl)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide;

3-(trifluoromethyl)-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide;

3-(trifluoromethyl)-*N*-{(3a*R*,4*R*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide;

3-(trifluoromethyl)-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide;

N-{(3a*S*,4*R*,6a*R*)-2-[6,6-bis(4-fluorophenyl)hexyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-(trifluoromethyl)benzenesulfonamide;

N-{(3a*S*,4*R*,6a*R*)-2-[3,5-bis(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-(trifluoromethyl)benzenesulfonamide;

N-{(3a*S*,4*R*,6a*R*)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-(trifluoromethyl)benzenesulfonamide;

N-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-3-(trifluoromethyl)benzenesulfonamide;

N-[(3a*S*,4*S*,6a*R*)-2-(4-hydroxybutyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide;

(3a*S**,4*S**,6a*R**)-*N*,*N*-dicyclopropyl-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*S**,4*R**,6a*R**)-2-benzyl-*N*-cyclopropyloctahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*S**,4*S**,6a*R**)-2-benzyl-*N*-cyclopropyloctahydrocyclopenta[*c*]pyrrol-4-amine;

N-[(3a*S**,4*S**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*-cyclopropyl-3-(trifluoromethyl)benzenesulfonamide;

N-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*-cyclopropyl-3-(trifluoromethyl)benzenesulfonamide;

N-cyclopropyl-*N*-[(3a*S**,4*S**,6a*R**)-octahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide;

N-{(3a*S**,4*S**,6a*R**)-2-[6,6-bis(4-fluorophenyl)hexyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-*N*-cyclopropyl-3-(trifluoromethyl)benzenesulfonamide;

N-{(3a*S**,4*S**,6a*R**)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-*N*-cyclopropyl-3-(trifluoromethyl)benzenesulfonamide;

N-cyclopropyl-3-(trifluoromethyl)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzenesulfonamide;

2,2-dicyclohexyl-*N*-((3a*S*,4*S*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide;

2,2-dicyclohexyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[(2-phenylethyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

2,2-dicyclohexyl-*N*-((3a*S*,4*S*,6a*R*)-2-{[2-(1-naphthyl)ethyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide;

2,2-dicyclohexyl-*N*-((3a*S*,4*S*,6a*R*)-2-{[3-(trifluoromethyl)benzyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide;

2,2-dicyclohexyl-*N*-((3a*S*,4*S*,6a*R*)-2-{[2-(4-fluorophenyl)ethyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)acetamide;

(2*S*)-2-phenyl-*N*-{(3a*R*,4*R*,6a*S*)-2-[(1*S*)-1-phenylethyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

(2*S*)-2-phenyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[(1*S*)-1-phenylethyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

(2*S*)-2-phenyl-*N*-{(3a*S*,4*S*,6a*R*)-2-[(1*S*)-1-phenylethyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

(2*S*)-2-phenyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[(1*S*)-1-phenylethyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*,3-dimethyl-2-phenylbutanamide;

N-[(3a*S**,4*R**,6a*R**)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*,3-dimethyl-2-phenylbutanamide;

(3a*R**,4*S**,6a*S**)-*N*-benzyl-2-(3-methyl-2-phenylbutanoyl)octahydrocyclopenta[*c*]pyrrol-4-amine;

2,2-dicyclohexyl-*N*-[(3a*S*,4*R*,6a*R*)-2-(*N*,*N*-dimethyl-D-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzoyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-2-phenylbutanamide;

N'-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*-isopropyl-*N*-phenylurea;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methylpentanamide;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-ylcarbamate;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(ethyl)carbamate;

tert-butyl (2*S*,3*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3,3-dimethyl-1-oxobutan-2-ylcarbamate;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-ylcarbamate;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxohexan-2-yl(methyl)carbamate;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-bis(4-fluorophenyl)acetamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-isopropyl-3-methylbutanamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methylbutanamide;

tert-butyl (2*S*)-2-({[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]amino}carbonyl)piperidine-1-carboxylate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3-methyl-1-oxobutan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-3,3-dimethyl-1-oxobutan-2-ylcarbamate;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-2-isopropyl-3-methylbutanamide;

N-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methylbutanamide;

2-cyclohexyl-2-hydroxy-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}acetamide;

tert-butyl (*S*)-1-((3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate;

S-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(methylsulfonyl)-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(methylsulfonyl)-L-leucinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-neopentyl-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-neopentyl-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-neopentyl-L-norvalinamide;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-ylamino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-morpholin-4-ylpentanamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-pyrrolidin-1-ylpentanamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-piperidin-1-ylpentanamide;

N^2-neopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-neopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-neopentyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-neopentyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-neopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-neopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N-(*tert*-butoxycarbonyl)-*N*-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

N^2-neopentyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-neopentyl-L-leucinamide;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(5-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

isopropyl (*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(5-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(6-(trifluoromethyl)pyridin-2-yl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

tert-butyl (*S*)-4,4-dimethyl-1-((3a*R*,4*S*,6a*S*)-2-(2-(methylsulfonyl)pyrimidin-5-yl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-ylcarbamate;

(*S*)-*tert*-butyl 2-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamoyl)pyrrolidine-1-carboxylate;

tert-butyl (1*R*)-1-isopropyl-3-oxo-3-[((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]propylcarbamate;

tert-butyl (2*S*)-2-{[((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]carbonyl}piperidine-1-carboxylate;

N-(*tert*-butoxycarbonyl)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide;

N-(*tert*-butoxycarbonyl)-*N*-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide;

(*S*)-*tert*-butyl 2-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylcarbamoyl)pyrrolidine-1-carboxylate;

tert-butyl (1*R*)-1-isopropyl-3-oxo-3-[((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]propylcarbamate;

tert-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate;

tert-butyl (2*S*)-2-{[((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]carbonyl}piperidine-1-carboxylate;

tert-butyl (3*S*)-3-{[((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)amino]carbonyl}-3,4-dihydroisoquinoline-2(1*H*)-carboxylate;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)hexan-2-yl)carbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

isopropyl (*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

isopropyl (*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

(3a*S*,4*R*,6a*R*)-*N*-neopentyl-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*-neopentyl-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*-isopropyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}-*N*-isopropyloctahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*S*,4*R*,6a*R*)-*N*-(4-fluorobenzyl)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*-(4-fluorobenzyl)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*-(4-fluorobenzyl)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*-ethyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*,*N*-diethyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*-propyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*,*N*-dipropyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*-(cyclopropylmethyl)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}-*N*-ethyloctahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}-*N*,*N*-diethyloctahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}-*N*-[5-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-amine;

tert-butyl (*S*)-1-(ethyl((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-(propyl((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)pentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((cyclopropylmethyl)((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)-4,4-dimethyl-1-oxopentan-2-yl(methyl)carbamate;

2-nitro-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)benzenesulfonamide;

N-methyl-2-nitro-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)benzenesulfonamide;

(3a*R*,4*S*,6a*S*)-*N*-methyl-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

tert-butyl (*S*)-4,4-dimethyl-1-(methyl((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl)amino)-1-oxopentan-2-yl(methyl)carbamate;

(2*S*)-2-(1,1-dioxidoisothiazolidin-2-yl)-4-methyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}pentanamide;

2-isopropyl-3-methyl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

2-isopropyl-3-methyl-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}butanamide;

tert-butyl (*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

tert-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl ethyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(3-fluoro-4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluoro-3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate;

(2*S*)-4-methyl-2-morpholin-4-yl-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide;

(2*S*)-4-methyl-2-pyrrolidin-1-yl-*N*-((3a*S*,4*R*;6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide;

(2*S*)-4-methyl-2-piperidin-1-yl-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide;

tert-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl ethyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluoro-3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-4-methyl-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*R*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((*S*)-4-methyl-1-oxo-1-((3a*R*,4*R*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl (*S*)-1-((3a*S*,4*R*,6a*R*)-2-(4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((2*S*,3*S*)-3-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((2*S*,3*S*)-3-methyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((2*S*,3*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((2*S*,3*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl(methyl)carbamate;

tert-butyl methyl((*S*)-3-methyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(3-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-yl)carbamate;

tert-butyl (*S*)-3,3-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-ylcarbamate;

tert-butyl (*S*)-3,3-dimethyl-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-ylcarbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)hexan-2-yl)carbamate;

tert-butyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

(2*S*)-4-methyl-2-pyrrolidin-1-yl-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzoyl]octahydrocyclopenta[*c*]pyrrol-4-yl}pentanamide;

(2*S*)-4-methyl-*N*-[(3a*S*,4*R*,6a*R*)-2-(methylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-2-pyrrolidin-1-ylpentanamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-(cyclopropylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-2-pyrrolidin-1-ylpentanamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide;

tert-butyl methyl((*S*)-4-methyl-1-((3a*S*,4*R*,6a*R*)-octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl)carbamate;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]piperidine-2-carboxamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-valinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-isoleucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-isoleucinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2,4-dimethyl-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-L-valinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-methyl-L-valinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2,4-dimethyl-L-leucinamide;

N^1-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide;

N^1-[(3a*S*,4*S*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-L-leucinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norleucinamide;

N^1-[(3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide;

N^1-[(3a*R*,4*R*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide;

N^2-ethyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-valinamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]piperidine-2-carboxamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-valinamide;

(2*S*)-*N*-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}piperidine-2-carboxamide;

N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide;

N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-valinamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[4-fluoro-3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide;

N^2-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide;

N^2-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide;

N^2-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide;

N^2-ethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide;

N-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide;

N-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-prolinamide;

(3*R*)-3-amino-4-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide;

(2*S*)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)piperidine-2-carboxamide;

(3*S*)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-1,2,3,4-tetrahydroisoquinoline-3-carboxamide;

4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norleucinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-prolinamide;

(3*R*)-3-amino-4-methyl-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide;

(2*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)piperidine-2-carboxamide;

(2*S*)-*N*-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}piperidine-2-carboxamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-valinamide;

(2*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)piperidine-2-carboxamide;

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide;

N^1-((3a*S*,4*R*,6a*R*)-2-{[4-fluoro-3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-methyl-L-leucinamide;

3-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide;

3-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-isoleucinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-isoleucinamide;

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-isoleucinamide;

N^2-methyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-isoleucinamide;

N^2,4-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2,4-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2,4-dimethyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2,4-dimethyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norleucinamide;

4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-methyl-N^1-((3a*R*,4*R*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-methyl-N^1-((3a*R*,4*R*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

3-cyclohexyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-alaninamide;

3-cyclohexyl-N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-alaninamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-5-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-L-leucinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-4-methyl-L-leucinamide;

N-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-phenylalaninamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2,4-dimethyl-L-leucinamide;

N-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-*N*-methyl-L-phenylalaninamide;

N^1-cyclopropyl-N^2,4-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^1-ethyl-N^2,4-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2,4-dimethyl-N^1-propyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^1-(cyclopropylmethyl)-N^2,4-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^1,N^2,4-trimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^1,N^2-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^1,N^2,4-trimethyl-L-leucinamide;

4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[2-(methylsulfonyl)pyrimidin-5-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3,4-difluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3,5-difluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-chlorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide;

N^2-methyl-N^1-[(3a*S*,4*R*,6a*R*)-2-(phenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-leucinamide;

N^2-methyl-N^1-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobenzyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-valinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-valinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-4-methyl-L-leucinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norleucinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-leucinamide;

N^2-methyl-N^1-((3a*S*,4*S*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-methyl-N^1-((3a*S*,4*S*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[3,3-bis(4-fluorophenyl)propyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

2,2-bis(4-fluorophenyl)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

2,2-bis(4-fluorophenyl)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-methyl-L-norvalyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

N-[(3a*R*,4*S*,6a*S*)-2-(*N*,4-dimethyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-2,2-bis(4-fluorophenyl)acetamide;

2,2-bis(4-fluorophenyl)-*N*-[(3a*R*,4*S*,6a*S*)-2-(4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-4-((*S*)-2-(*tert*-butoxycarbonylamino)-4,4-dimethylpentanamido)hexahydrocyclopenta[*c*]pyrrol-2(1*H*)-yl)-4,4-dimethyl-1-oxopentan-2-ylcarbamate;

4-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-leucinamide;

4-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-L-phenylalanyloctahydrocyclopenta[*c*]pyrrol-4-yl]-L-leucinamide;

(3a*R*,4*S*,6a*S*)-*N*-benzhydryl-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*S*,4*R*,6a*R*)-*N*-benzhydryl-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

(3a*R*,4*S*,6a*S*)-*N*-benzhydryl-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-amine;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzhydryloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-leucinamide;

4-methyl-N^2-propyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-(cyclopropylmethyl)-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-(cyclobutylmethyl)-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-isobutyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-(cyclopentylmethyl)-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-(cyclohexylmethyl)-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-butyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-ethyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-(cyclopropylmethyl)-4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(cyclopropylmethyl)-4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-isopropyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-isopropyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-isopropyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-isopropyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-isopropyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

3-cyclohexyl-N^2-isopropyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-alaninamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-5-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-isopropyl-4-methyl-L-leucinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-isopropyl-4-methyl-L-leucinamide;

N^2-isopropyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropyl-4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-L-leucinamide;

N^2-isopropyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropyl-L-phenylalanyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-L-leucinamide;

N^2-isopropyl-4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-isopropyl-4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

2,2-bis(4-fluorophenyl)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropyl-4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]acetamide;

N^2-isopropyl-4-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[2-(methylsulfonyl)pyrimidin-5-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-isopropyl-L-norvalinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-isopropyl-L-norvalinamide;

N^2-isopropyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2,N^2-dimethyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

(3*R*)-3-(dimethylamino)-4-methyl-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide;

N^2-cyclopropyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2,N^2-dicyclopropyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-cyclopentyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-cyclohexyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-(1-ethylpropyl)-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-cyclobutyl-4-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

4-methyl-N^2-neopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^2-cyclopentyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-cyclohexyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-cyclopentyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-cyclopentyl-4-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-4-methyl-L-leucinamide;

N^2,N^2-dimethyl-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-N^2-neopentyl-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(3,3-dimethylbutyl)-N^2-methyl-L-leucinamide;

N^2,N^2-dimethyl-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-leucinamide;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-(4-fluorobenzyl)-N^2-methyl-L-leucinamide;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-1-(methylsulfonyl)piperidine-2-carboxamide;

(3*R*)-4-methyl-3-[(methylsulfonyl)amino]-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)pentanamide;

N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-D-leucinamide;

N^2-ethyl-N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

4-methyl-N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

3-methyl-N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-valinamide;

N^2-(methylsulfonyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide;

N^2-(isopropylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(phenylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

N^2-(cyclopentylsulfonyl)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-leucinamide;

isopropyl (*S*)-4,4-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

isopropyl (*S*)-3,3-dimethyl-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)butan-2-ylcarbamate;

cyclopentyl (*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluoromethyl)benzyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-ylcarbamate;

N^2-(2,2-dimethylpropanoyl)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluoromethyl)benzyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide;

tert-butyl (*S*)-1-((3a*R*,4*S*,6a*S*)-2-(3-chloro-4-fluorophenylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)-1-oxopentan-2-yl(methyl)carbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(pyridin-3-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

tert-butyl methyl((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(thiophen-2-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-ylamino)pentan-2-yl)carbamate;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethoxy)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(thien-2-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-chloro-4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

N^2-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(pyridin-3-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-cyanophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-methoxyphenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[3,5-bis(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-methyl-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(2-chloro-4-fluorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

N^2-methyl-N^1-[(3a*R*,4*S*,6a*S*)-2-(1-naphthylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-L-norvalinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[4-bromo-3-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-methyl-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3,4-dichlorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-*tert*-butylphenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-(1,1'-biphenyl-4-ylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3,4-dimethoxyphenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-cyanophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

N^1-[(3a*R*,4*S*,6a*S*)-2-(2-furylsulfonyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-N^2-methyl-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(2,3-dichlorophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluoromethyl)benzyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^2-methyl-N^1-((3a*R*,4*S*,6a*S*)-2-{[2-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-L-norvalinamide;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-bromophenyl)sulfonyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-N^2-methyl-L-norvalinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-4-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-methyl-L-norvalinamide;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-chloro-5-(trifluoromethyl)phenyl]sulfonyl}octahydrocyclopenta[*c*]pyrrol-4-yl)-N^2-methyl-L-norvalinamide;

N^2-methyl-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluoromethyl)benzoyl]octahydrocyclopenta[*c*]pyrrol-4-yl}-L-norvalinamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-*N*-isopropyl-3-(trifluoromethyl)benzenesulfonamide;

N-[(3a*R*,4*S*,6a*S*)-2-benzyloctahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide;

N-isopropyl-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide;

N-[(3a*R*,4*S*,6a*S*)-2-(*N*-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide;

N-cyclopropyl-*N*-[(3a*S**,4*S**,6a*R**)-[2-(*N*-methyl-L-leucyl)octahydrocyclopenta[*c*]pyrrol-4-yl]-3-(trifluoromethyl)benzenesulfonamide; and

4-fluoro-*N*-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluoromethyl)pyridin-2-yl]octahydrocyclopenta[*c*]pyrrol-4-yl}benzamide.

19. A pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier.

20. A method of treating pain in a subject in need thereof, comprising: administering to the subject a therapeutically suitable amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof, wherein the pain is acute pain, chronic pain, neuropathic pain, inflammatory pain, visceral pain, cancer pain, allodynia, fibromyalgia, sciatica, back pain, and headache pain including migraine, or combinations thereof.

21. A method of treating disorders of the central nervous system in a subject in need thereof, comprising the step of: administering a therapeutically suitable amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof, wherein the disorders of the central nervous system include stroke, epilepsy, manic depression, bipolar disorders, depression, anxiety, schizophrenia, migraine, and psychoses; neural degenerative disorders including Alzheimer's disease, AIDS related dementia, Parkinson's disease, neuropathy caused by head injury, and dementia caused by cerebrovascular disorders; disorders of the lower urinary tract including overactive bladder, prostatis, prostadynia, interstitial cystitis, and benign prostatic hyperplasia; disorders caused by psychogenic stress including bronchial asthma, unstable angina, and hypersensitive colon inflammation; cardiovascular disorders including hypertension, atherosclerosis, heart failure, and cardiac arrhythmias; drug addiction withdrawal symptoms, including ethanol addiction withdrawal symptoms; skin disorders

NUEVAS OCTAHIDROCICLOPENTA[C]PIRROL-4-AMINAS SUSTITUIDAS COMO BLOQUEANTES DE LOS CANALES DE CALCIO

CAMPO TÉCNICO Y ANTECEDENTES

La presente solicitud se refiere a compuestos que son bloqueantes de los canales de calcio, a composiciones que comprenden dichos compuestos y a métodos para tratar condiciones y trastornos usando dichos compuestos y composiciones.

Los canales de calcio regulados por el voltaje (VGCC) cumplen una función integral en la regulación de la conductancia iónica de la membrana, la liberación de neurotransmisores y la excitabilidad celular. Los VGCC están compuestos por la subunidad formadora de poros $\alpha 1$ y las subunidades auxiliares $\alpha 2\delta$ y β que modulan la expresión y las propiedades funcionales de los canales (Dolphin, A. C. *A short history of voltage-gated calcium channels. British Journal of Pharmacology* 2006, 147 (Supl. 1), S56-S62.). Estos canales se pueden clasificar en canales activados por voltaje bajo (LVA; tipo T o $Ca_v3.x$) y activados por voltaje alto (HVA; tipo L o $Ca_v1.x$ y tipos N-, P/Q- y R o $Ca_v2.x$). Los canales N-, P/Q y R se activan típicamente a potenciales de membrana más positivos (~ -30 mV) y están relacionados con la neurotransmisión "presináptica" (McGivern J. G. *Targeting N-type and T-type calcium channels for the treatment of pain. Drug Discovery Today* 2006, 11, 245-253.). Los canales tipo T se activan a potenciales de membrana relativamente más negativos (~ -60 mV) y están relacionados primariamente con la excitabilidad "postsináptica" (Shin, H.-S.; et al., *T-type Ca^{2+} channels as therapeutic targets in the nervous system. Curr. Opin. in Pharmacology* 2008, 8, 33-41.).

Las subunidades α_δ del canal tipo N están codificadas por un solo gen (α_1B o $Ca_v2.2$) a diferencia de las corrientes tipo L y T definidas farmacológicamente que están codificadas por múltiple genes de la subunidad α_1. La diversidad de canales tipo N surge debido a un extenso procesamiento alternativo del gen de la subunidad α que genera variantes con diferentes patrones de expresión y propiedades biofísicas moduladas por GPCR (Gray, A. C.; et al., *Neuronal calcium channels:splicing for optimal performance; Cell Calcium*, 2007, 42(4-5), 409-417.). La secuencia primaria de $Ca_v2.2$ está altamente conservada entre especies (las

ratas y humanos comparten un 91% de identidad a nivel de aminoácidos).

Los canales de tipo N se expresan ampliamente en el sistema nervioso central (CNS) (corteza, hipocampo, cuerpo estriado, tálamo, núcleos del tallo cerebral y médula espinal) y en el sistema nervioso periférico (PNS) (sistema nervioso simpático adulto y ganglios de las raíces dorsales) (Ino, M.; et al., *Functional disorders of the sympathetic nervous system in mice lacking the α_{1B} subunit ($Ca_v2.2$) of N-type calcium channels. Proc. Natl. Acad. Sci.* EE.UU., 2001, 98(9), 5323-5328). En las vías del dolor, los canales de tipo N se expresan en la médula ventral rostral, un sitio importante de la modulación descendente del dolor (Urban, M. O.; et al., *Medullary N-type and P/Q-type calcium channels contribute to neuropathy-induced allodynia, Neuroreport*, 2005, 16(6), 563-566) y son los principales contribuyentes de la neurotransmisión sináptica que tiene lugar entre los nociceptores C/Aδ y las neuronas la lámina espinal I (Bao, J.; et al., *Differences in Ca^{2+} channels governing generation of miniature and evoked excitatory synaptic currents in spinal laminae I and II. J Neurosci.* 1998, 18(21), 8740-50. Heinke, B.; et al., *Pre- and postsynaptic contributions of voltage-dependent Ca^{2+} channels to nociceptive transmission in rat spinal lamina I neurons. Eur. J. Neurosci.* 2004, 19(1), 103-111.). Por el contrario, los canales de tipo P/Q se expresan casi exclusivamente en las láminas II-IV de la médula espinal y muestran poca co-localización con la sustancia P y los canales tipo N (Westenbroek, R. E.; et al., *Localization of Ca^{2+} channel subtypes on rat spinal motor neurons, interneurons, and nerve terminals. J. Neurosci.* 1998, 18(16), 6319-6330.).

Después de lesiones en los nervios hay una mayor expresión de $Ca_v2.2$ (Westenbroek, R. E.; et al., *Localization of Ca^{2+} channel subtypes on rat spinal motor neurons, interneurons, and nerve terminals. J. Neurosci.* 1998, 18(16), 6319-6330. Cizkova, D.; et al., *Localization of N-type Ca^{2+} channels in the rat spinal cord following chronic constrictive nerve injury. Exp. Brain Res.* 2002, 147, 456-463. Yokoyama, K.; et al., *Plastic change of N-type calcium channel expression after preconditioning is responsible for prostaglandin E2-induced long-lasting allodynia. Anesthesiology*, 2003, 99(6), 1364-1370.) y las subunidades α2δ1 (Luo, Z. D.; et al., *Upregulation of dorsal root ganglion α2δ calcium channel subunit and its correlation with allodynia in spinal nerve-injured rats. J. Neurosci.* 2001, 21(6), 1868-1875. Newton, R. A.; et al., *Dorsal root ganglion neurons show*

increased expression of the calcium channel α2δ-1 subunit following partial sciatic nerve injury. Mol. Brain Res. 2001, 95(1-2), 1-8.) además de incrementos en las capas superficiales del cuerno dorsal de la médula espinal, lo cual sustenta un rol de los canales tipo N en el dolor neuropático. Recientemente se ha identificado una variante de procesamiento $Ca_v2,2$ específica del nociceptor en el ganglio de la raíz dorsal (Bell, T. J.; et al., *Cell specific alternative splicing increases calcium channel density in the pain pathway. Neuron*, 2004, 41(1), 127-138.). Estos canales tienen distintas propiedades electrofisiológicas y densidades de corriente (Castiglioni, A. J.; et al., *Alternative splicing in the C-terminus of $Ca_V2.2$ controls expression and gating of N-type calcium channels. J. Physiol., 2*006, 576(Pt 1), 119-134.) en comparación con los canales $Ca_v2.2$ de tipo salvaje. En tanto la inhibición del receptor acoplado a proteína G de los canales de tipo N de tipo salvaje típicamente está mediada por $G\beta\gamma$ y es dependiente del voltaje, la variante de procesamiento específica del nociceptor es inhibida por la activación de GPCR (por ejemplo opioides) de una manera independiente del voltaje (Raingo, J.; et al., *Alternative splicing controls G protein-dependent inhibition of N-type calcium channels in nociceptors. Nat. Neurosci.* 2007, 10(3), 285-292.). Este mecanismo incrementa sustancialmente la sensibilidad de los canales $Ca_v2.2$ a los opiàceos y al ácido gamma-aminobutírico (GABA) lo cual sugiere que el procesamiento alternativo específico celular del ARNm para los canales $Ca_v2.2$ sirve como un interruptor molecular que controla la sensibilidad de los canales de tipo N a los neurotransmisores y a las drogas que modulan la nocicepción. En su conjunto estos datos proporcionan un sustento adicional del rol de los canales $Ca_v2.2$ en los estados de dolor.

Las contribuciones relativas de los diversos canales de Ca^{2+} HVA en la señalización nociceptiva fueron evaluadas en estudios con ratones noqueados. Los ratones noqueados para $Ca_v2.2$ tienen buena salud, son fértiles y no presentan déficits neurológicos evidentes (Ino, M.; et al., *Functional disorders of the sympathetic nervous system in mice lacking the alpha 1B subunit ($Ca_v2.2$) of N-type calcium channels. Proc. Natl. Acad. Sci.* EE.UU., 2001, 98(9), 5323-5328. Kim, C.; et al., *Altered nociceptive response in mice deficient in the $alpha_{1B}$ subunit of the voltage-dependent calcium channel. Mol. Cell. Neurosci.* 2001, 18(2), 235-245. Hatakeyama, S.; et al., *Differential nociceptive responses in mice lacking the*

alpha$_{1B}$ subunit of N-type Ca^{2+} channels. *Neuroreport*, 2001, 12(11), 2423-2427. Liu; L.; et al., *In vivo analysis of voltage-dependent calcium channels. J. Bioenerg. Biomembr*. 2003, 35(6), 671-685.). Este hallazgo sugiere que otros tipos de canales Ca_v pueden compensar la falta de canales $Ca_v2.2$ en la mayoría de las sinapsis en estos ratones (Pietrobon, D. *Function and dysfunction of synaptic calcium channels: insights from mouse models. Curr. Opin. Neurobiol.* 2005, 15(3), 257-265.). Los ratones deficientes en $Ca_v2.2$ son resistentes al desarrollo de dolor inflamatorio y neuropático (Kim, C.; et al., *Altered nociceptive response in mice deficient in the alpha$_{1B}$ subunit of the voltage-dependent calcium channel. Mol. Cell. Neurosci.* 2001, 18(2), 235-245. Hatakeyama, S.; et al., *Differential nociceptive responses in mice lacking the alpha$_{1B}$ subunit of N-type Ca^{2+} channels*. Neuroreport 2001, 12(11), 2423-2427. Saegusa, H.; et al., *Suppression of inflammatory and neuropathic pain symptoms in mice lacking the N-type calcium channel. EMBO J.*, 2001, 20(10), 2349-2356.), han disminuido la función del sistema nervioso simpático (Ino, M.; et al., *Functional disorders of the sympathetic nervous system in mice lacking the alpha 1B subunit ($Ca_v2.2$) of N-type calcium channels. Proc. Natl. Acad. Sci.* EE.UU., 2001, 98(9), 5323-5328.), y alterado las respuestas tanto al etanol como a los anestésicos (Newton, R. A.; et al., *Dorsal root ganglion neurons show increased expression of the calcium channel alpha2delta-1 subunit following partial sciatic nerve injury. Brain Res. Mol. Brain Res*. 2001, 95(1-2), 1-8. Takei, R. et al., *Increased sensitivity to halothane but decreased sensitivity to propofol in mice lacking the N-type Ca^{2+} channel. Neurosci. Lett*. 2003, 350(1), 41-45.). Otros estudios de comportamiento indican que los ratones noqueados para $Ca_v2.2$ son menos ansiosos, son hiperactivos y muestran una mayor vigilancia en comparación con sus compañeros de camada de tipo salvaje (Beuckmann, C. T.; et al., *N-type calcium channel alpha$_{1B}$ subunit($Ca_v2.2$) knock-out mice display hyperactivity and vigilance state differences. J. Neurosci.* 2003, 23(17), 6793-6797.).

Los canales de tipo N y P/Q se localizan en las uniones sinápticas neuronales y contribuyen significativamente en la liberación del neurotransmisor (Olivera, B. M.; et al., *Calcium channel diversity and neurotransmitter release: the omega-conotoxins and omega agatoxins. Annu. Rev. Biochem.* 1994, 63, 823-867. Miljanich, G. P.; et al., *Antagonists of neuronal calcium channels: structure,*

function, and therapeutic implications. Annu. Rev. Pharmacol. Toxicol. 1995, 35, 707-734.). Los canales de tipo N cumplen un rol importante en la liberación de glutamato, acetilcolina, dopamina, norepinefrina, GABA y proteína relacionada con el gen de calcitonina (CGRP). Los canales de tipo P/Q pueden estar involucrados en la liberación de glutamato, aspartato, 5HT, GABA y probablemente de glicina (Pietrobon, D. *Function and dysfunction of synaptic calcium channels: insights from mouse models. Curr. Opin. Neurobiol.* 2005, 15(3), 257-265.).

Los canales de tipo L, P/Q y N son bloqueados por antagonistas específicos de los canales, es decir, dihidropiridinas, ω-agatoxina IVA y ω-conotoxina MVIIA/ ziconotida, respectivamente. Se ha demostrado que la agatoxina IVa bloquea la neurotransmisión excitatoria (Luebke, J. I.; et al., *Multiple calcium channel types control glutamatergic synaptic transmission in the hippocampus. Neuron,* 1993, 11(5), 895-902.) así como la inhibidora (Takahashi, T.; et al., *Different types of calcium channels mediate central synaptic transmission. Nature,* 1993, 366(6451), 156-158.). La inyección intratecal de bloqueantes selectivos de canales de tipo N (por ejemplo péptidos derivados de conotoxina, tales como GVIA, MVIIA (ziconotida) y CVID) atenúa significativamente las respuestas al dolor en modelos de animales de dolor neuropático, dolor inducido por formalina y dolor post-operatorio (Chaplan, S. R.; et al., *Role of voltage-dependent calcium channel subtypes in experimental tactile allodynia. J. Pharmacol. Exp. Ther.* 1994,269(3), 1117-1123. Malmberg, A. B.; et al., *Voltage-sensitive calcium channels in spinal nociceptive processing: blockade of N-and P-type channels inhibits formalin-induced nociception. J. Neurosci.* 1994, 14(8), 4882-4890. Bowersox, S. S.; et al., *Selective N-type neuronal voltage-sensitive calcium channel blocker, SNX-111, produced spinal antinociception in rat models of acute, persistent and neuropathic pain. J. Pharmacol. Exp. Ther.* 1996, 279(3), 1243-1249. Wang, Y. X.; et al., *Effects of intrathecal administration of ziconotide, a selective neuronal N-type calcium channel blocker, on mechanical allodynia and heat hyperalgesia in a rat model of postoperative pain. Pain* 2000, 84(2-3), 151-158. Scott, D. A.; et al., *Actions of intrathecal omega-conotoxins CVID, GVIA, MVIIA, and morphine in acute and neuropathic pain in the rat. Eur. J. Pharmacol.* 2002, 451(3), 279-286.). Estos bloqueantes peptídicos se unen a la región del poro del canal, no muestra actividad dependiente del voltaje o la frecuencia y presentan un bloqueo de

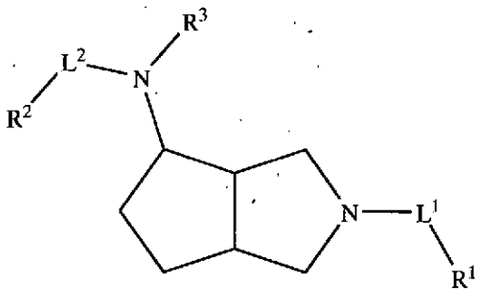
canales irreversible (Feng, Z. P.; et al., *Determinants of inhibition of transiently expressed voltage-gated calcium channels by omega-conotoxins GVIA and MVIIA. J. Biol. Chem.* 2003, 278(22), 20171-20178.). La ziconotida produce un bloqueo potente de la liberación de neurotransmisores en las neuronas del cuerno dorsal de la médula espinal (Matthews, E. A.; et al., *Effects of spinally delivered N-and P-type voltage-dependent calcium channel antagonists on dorsal horn neuronal responses in a rat model of neuropathy. Pain* 2001, 92(1-2), 235-246. Smith, M. T.; et al., *The novel N-type calcium channel blocker, AM336, produces potent dose-dependent antinociception after intrathecal dosing in rats and inhibits substance P release in rat spinal cord slices. Pain* 2002, 96(1-2), 119-127. Heinke, B.; et al., *Pre- and postsynaptic contributions of voltage-dependent Ca^{2+} channels to nociceptive transmission in rat spinal lamina I neurons. Eur. J. Neurosci.* 2004, 19(1), 103-111.) y en las neuronas del ganglio de la raíz dorsal (DRG) (Evans, A. R.; et al., *Differential regulation of evoked peptide release by voltage-sensitive calcium channels in rat sensory neurons.* Brain Res. 1996, 712(2), 265-273. Smith, M. T.; et al., *The novel N-type calcium channel blocker, AM336, produces potent dose-dependent antinociception after intrathecal dosing in rats and inhibits substance P release in rat spinal cord slices. Pain* 2002, 96(1-2), 119-127.). También bloquea de manera potente y completa la liberación inducida por despolarización de la sustancia P de cortes de médula espinal de rata. Por el contrario, la administración intratecal del bloqueante selectivo para el tipo P/Q, ω-agatoxina IVA, no mostró efectos sobre la alodinia mecánica en el modelo de ligación de nervios espinales (Chaplan, S. R.; et al., *Role of voltage-dependent calcium channel subtypes in experimental tactile allodynia. J. Pharmacol. Exp. Ther.* 1994, 269(3), 1117-1123.) o en la hiperalgesia térmica en el modelo de lesión por constricción crónica (Yamamoto, T.; et al., *Differential effects of intrathecally administered N- and P-type voltage-sensitive calcium channel blockers upon two models of experimental mononeuropathy in the rat.* Brain Res. 1998, 794(2), 329-332.) de dolor neuropático.

El dolor es el síntoma más común de enfermedad y la queja más frecuente que los pacientes presentan a los médicos. El manejo inadecuado del dolor en todo el espectro de etiologías del dolor etiologies continúa siendo un problema en la salud pública. En este sentido, el desarrollo de novedosos compuestos

terapéuticos con nuevos mecanismos de acción para el tratamiento del dolor, incluyendo el bloqueo de los canales de calcio, tendrá un impacto significativo sobre la lucha permanente para lograr un equilibrio entre eficacia y seguridad para los pacientes más necesitados. Los compuestos de la presente invención son nuevos bloqueantes de los canales de calcio que son de utilidad en el tratamiento del dolor, entre otras condiciones.

RESUMEN DE LA INVENCIÓN

La invención se dirige a compuestos de fórmula (I)



(I),

o una sal, prodroga, sal de una prodroga aceptables farmacéuticamente, o una combinación de las mismas, donde

L^1 es C(O), $S(O)_2$, $SO_2N(R^4)$, C(O)O o $-(CR^aR^b)_m-$;

R^1 es alquilo, G^1, $-CH(G^1)_2$, $-(CR^aR^b)_m-G^1$, $-(CR^aR^b)_m-CH(G^1)_2$, $-(CR^eR^f)_n-N(R^5)_2$, $-(CR^eR^f)_n-N(R^5)-C(O)O(alquilo)$, $-(CR^eR^f)_n-N(R^5)-C(O)(alquilo)$, o $-(CR^eR^f)_n-N(R^5)-SO_2R^6$; o

L^1-R^1 tomados juntos son hidrógeno, alquilo, hidroxialquilo, G^1, o $-CH(G^1)_2$;

L^2 es $-(CR^cR^d)_p-$, C(O), $C(O)N(R^4)$, $S(O)_2$, $SO_2N(R^5)$, o C(O)O;

R^2 es alquilo, G^2, $-C(R^c)(G^2)(G^3)$, $-(CR^cR^d)_p-G^2$, $-(CR^cR^d)_p-CH(G^2)(G^3)$, $-(CR^gR^h)_q-N(R^5)-C(O)O(alquilo)$, $-(CR^gR^h)_q-N(R^5)-C(O)O-G^2$, $-(CR^gR^h)_q-N(R^5)-C(O)(alquilo)$, $-(CR^gR^h)_q-N(R^5)-SO_2R^6$, $-(CR^gR^h)_q-N(R^4)(R^5)$, $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-(alquilo)$, o $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-G^2$; o

L^2-R^2 tomados juntos son alquilo, G^2, o $-C(R^c)(G^2)(G^3)$;

m y p, en cada caso, son cada uno en forma independiente 1, 2, 3, 4, 5, o 6;

n y q, en cada caso, son cada uno en forma independiente 1, 2, 3, 4, o 5;

R^a, R^b, R^c, y R^d, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, arilalquilo, halógeno, haloalquilo o OR^7; o

R^a y R^b, o R^c y R^d, junto con el átomo de carbono al cual se encuentran

unidos, forman opcionalmente un anillo C_{3-6} cicloalquilo;

R^e, R^f, R^g, y R^h, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, halógeno, haloalquilo, OR^7, cicloalquilalquilo, heteroarilo, arilalquilo, o heteroarilalquilo; donde los grupos arilo, cicloalquilo y heteroarilo de arilo, cicloalquilo y heteroarilo cada uno en forma independiente no se sustituye o se sustituye con 1, 2, 3, 4, o 5 sustituyentes seleccionados en forma independiente entre el grupo que consiste en alquilo y haloalquilo;

G^1, G^2, y G^3 en cada caso, son cada uno en forma independiente arilo, cicloalquilo, cicloalquenilo, heteroarilo, o heterociclo; donde G^1, G^2, y G^3 en cada caso cada uno en forma independiente no se sustituye o se sustituye con 1, 2, 3, 4, o 5 sustituyentes seleccionados entre el grupo que consiste en alquilo, alquenilo, alquinilo, ciano, haloalquilo, halógeno, nitro, oxo, fenilo, $N(R^7)_2$, $N(R^7)C(O)R^7$, OR^7, $C(O)R^7$, $C(O)OR^7$, $C(O)N(R^7)_2$, SO_2R^8, y $SO_2N(R^7)_2$; y donde G^1 no es quinolina, quinazolindiona, o piridopirimidindiona;

R^3 es hidrógeno, alquilo, haloalquilo, cicloalquilo, o cicloalquilalquilo;

R^4, R^5, y R^7, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, arilo, arilalquilo, cicloalquilo, cicloalquilalquilo, o haloalquilo; donde dichos arilo, el arilo de arialquilo y cicloalquilo no se sustituyen o se sustituyen en forma independiente con 1, 2 3, 4, o 5 sustituyentes seleccionados en forma independiente entre el grupo que consiste en alquilo, haloalquilo, y halógeno;

R^6 es alquilo, arilo, cicloalquilo, cicloalquenilo, heteroarilo, o heterociclo; donde dichos arilo, heteroarilo y heterociclo no se sustituyen o se sustituyen en forma independiente con 1, 2 3, 4, o 5 sustituyentes seleccionados en forma independiente entre el grupo que consiste en alquilo, haloalquilo, y halógeno;

R^8 es alquilo o haloalquilo;

con la condición de que L^1-R^1 y L^2-R^2 no son ambos alquilo al mismo tiempo;

y con la condición de que cuando L^1-R^1 es alquilo, L^2-R^2 no es $C(O)N(R^4)$, donde R^4 es alquilo;

y con la condición adicional de que el compuesto no es:

N-(2-tritiloctahidrociclopenta[*c*]pirrol-4–il)acetamida;

N-(octahidrociclopenta[*c*]pirrol-4–il)acetamida

N-metil-*N*-(2-tritiloctahidrociclopenta[*c*]pirrol-4–il)acetamida;

N-metil-*N*-(octahidrociclopenta[*c*]pirrol-4–il)acetamida;

6-(2-(2-(3-fluoro-6-metoxi-1,5-naftiridin-4–il)etil)octahidrociclopenta[*c*]pirrol-4–ilamino)metil-2*H*-pirido[3,2-*b*][1,4]tiazin-3(4*H*)-ona;

2-(2-(3-fluoro-6-metoxi-1,5-naftiridin-4–il)etil)octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo;

octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo 2-bencilo; o

octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo.

Otro aspecto de la invención se relaciona con composiciones farmacéuticas que comprenden una cantidad terapéuticamente eficaz de los compuestos de la invención o sales farmacéuticamente aceptables de los mismos, en combinación con uno o más vehículos farmacéuticamente aceptables. Dichas composiciones pueden administrarse de acuerdo con un método de la invención, típicamente como parte de un régimen terapéutico para el tratamiento o la prevención de afecciones y trastornos relacionados con los canales de calcio. Más particularmente, el método es de utilidad para el tratamiento de condiciones relacionadas con un método de tratamiento del dolor en un sujeto que lo necesita. El método comprende la administración al sujeto de una cantidad terapéuticamente adecuada de un compuesto de la fórmula (I), o una sal farmacéuticamente aceptable del mismo. Las condiciones relacionadas con el dolor incluyen dolor agudo, dolor crónico, dolor neuropático, dolor inflamatorio, dolor visceral, dolor de cáncer, alodinia, fibromialgia, ciática, dolor de espalda y dolor de cabeza incluyendo migraña, o combinaciones de los mismos.

Otro aspecto de la invención proporciona un método de tratamiento de trastornos del sistema nervioso central en un sujeto que lo necesita. El método comprende el paso de: administrar una cantidad terapéuticamente adecuada de un compuesto de la fórmula (I), o una sal farmacéuticamente aceptable del mismo. Los trastornos del sistema nervioso central incluyen accidente cerebrovascular, epilepsia, depresión maníaca, trastornos bipolares, depresión, ansiedad, esquizofrenia, migraña y psicosis; trastornos degenerativos neurales incluyendo mal de Alzheimer, demencia relacionada con SIDA, enfermedad de Parkinson, neuropatía causada por lesión de la cabeza y demencia causada por trastornos cerebrovasculares; trastornos del tracto urinario inferior incluyendo vejiga

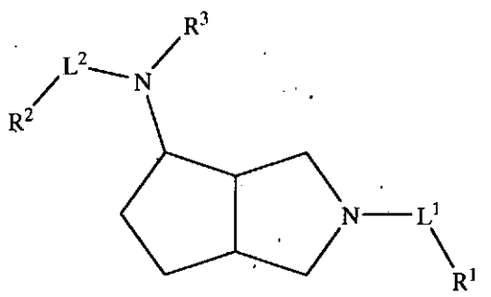
superactiva, prostatis, prostadinia, cistitis intersticial e hiperplasia prostática benigna; trastornos causados por estrés psicogénico incluyendo asma bronquial, angina inestable e inflamación de colon hipersensible; trastornos cardiovasculares incluyendo hipertensión, aterosclerosis, insuficiencia cardíaca y arritmias cardíacas; síntomas de abstinencia por adicción a drogas, incluyendo síntomas de abstinencia por adicción a etanol; trastornos de la piel incluyendo pruritis y dermatitis alérgica, enfermedad de intestino inflamatorio; cáncer; diabetes; y esterilidad y disfunción sexual, o combinaciones de los mismos.

Asimismo, en la presente se describen compuestos, composiciones que comprenden a los compuestos y los métodos para tratar o prevenir afecciones y trastornos mediante la administración de dichos compuestos.

Estos y otros objetos de la invención se describen con mayor detalle en los siguientes párrafos. No debe considerarse que estos objetos puedan limitar el alcance de la invención.

DESCRIPCIÓN DETALLADA

En esta invención se divulgan compuestos de la fórmula (I)



(I),

en donde L^1, L^2, R^1, R^2 y R^3 son como se definieron previamente en la Síntesis de la invención. Se divulgan asimismo composiciones que comprenden dichos compuestos y métodos para el tratamiento de condiciones y trastornos usando dichos compuestos y composiciones.

En distintas formas de realización, la presente invención proporciona por lo menos una variable que aparece más de una vez en cualquier sustituyente o en el compuesto de la invención o en cualquier otra fórmula en la presente. La definición de una variable cada vez que aparece es independiente de su definición en otra aparición. Además, las combinaciones de sustituyentes solamente son posibles si dichas combinaciones dan como resultado compuestos estables. Los

compuestos estables son compuestos que se pueden aislar de una mezcla de reacción.

a. Definiciones

Según se usan en la memoria descriptiva y en las reivindicaciones adjuntas, los siguientes términos tienen el significado que se indica a continuación.

El término "alquenilo", según se usa en la presente, hace referencia a un hidrocarburo de cadena lineal o ramificada, que contiene entre 2 y 10 carbonos y que contiene al menos un enlace doble carbono-carbono formado al remover dos hidrógenos. Los ejemplos representativos de alquenilos incluyen, pero en un sentido no limitativo, etenilo, 2-propenilo, 2-metil-2-propenilo, 3-butenilo, 4-pentenilo, 5-hexenilo, 2-heptenilo, 2-metil-1-heptenilo y 3-decenilo.

El término "alquenileno" hace referencia a un grupo divalente derivado de un hidrocarburo de cadena lineal o ramificada de entre 2 y 4 átomos de carbono que contiene al menos un enlace doble carbono-carbono. Los ejemplos representativos de grupos alquileno incluyen, en un sentido no limitativo, -CH=CH- y $-CH_2CH=CH-$.

El término "alquilo" según se usa en la presente, se refiere a una cadena hidrocarbonada saturada, lineal o ramificada que contiene entre 1 y 10 átomos de carbono. El término "alquilo inferior" o "C_{1-6} alquilo" se refiere a un hidrocarbono de cadena lineal o ramificada que contiene entre 1 y 6 átomos de carbono. El término "C_{1-3} alquilo" se refiere a un hidrocarbono de cadena lineal o ramificada que contiene entre 1 y 3 átomos de carbono. Los ejemplos representativos de alquilo incluyen, en un sentido no limitativo, metilo, etilo, n-propilo, iso-propilo, n-butilo, sec-butilo, iso-butilo, ter-butilo, n-pentilo, isopentilo, neopentilo, n-hexilo, 3-metilhexilo, 2,2-dimetilpentilo, 2,3-dimetilpentilo, n-heptilo, n-octilo, n-nonilo y n-decilo.

El término "alquileno" hace referencia a un grupo divalente derivado de un hidrocarburo de cadena lineal o ramificada de entre 1 y 10 átomos de carbono. Los ejemplos representativos de alquileno incluyen, pero en un sentido no limitativo, $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2-$ y $-CH_2CH(CH_3)CH_2-$.

El término "alquinilo" según se usa en la presente, se refiere a un grupo de cadena hidrocarbonada lineal o ramificada que contiene entre 2 y 10 átomos de carbono y que contiene al menos un enlace triple carbono-carbono. Los ejemplos

representativos de alquinilo incluyen, pero en un sentido no limitativo, acetilenilo, 1-propinilo, 2-propinilo, 3-butinilo, 2-pentinilo y 1-butinilo.

El término "arilo", según se usa en la presente, hace referencia a un fenilo o un arilo bicíclico. El arilo bicíclico es naftilo, un fenilo fusionado a un cicloalquilo monocíclico o un fenilo fusionado a un cicloalquenilo monocíclico. Los ejemplos representativos de grupos arilo incluyen, pero en un sentido no limitativo, dihidroindenilo, indenilo, naftilo, dihidronaftalenilo y tetrahidronaftalenilo. El arilo bicíclico está unido a la porción molecular principal a través de cualquier átomo de carbono localizado en el sistema de anillo. Los grupos arilo de la presente invención pueden estar sustituidos, o no.

El término "arilalcoxi" según se usa en la presente, se refiere a un grupo arilo, definido en la presente, unido a una porción de la molécula principal a través de un grupo alquileno, definido en la presente. Los ejemplos representativos de arilalquilo incluyen, pero en un sentido no limitativo, bencilo, 2-feniletilo, 3-fenilpropilo y 2-naft-2–iletilo.

El término "ciano", según se usa en la presente, se refiere a un grupo -CN.

El término "cicloalquilo" o "cicloalcano" según se usa en la presente, significa un cicloalquilo monocíclico, bicíclico o tricíclico. El cicloalquilo monocíclico es un sistema de anillos carbocíclico que contiene entre 3 y 8 átomos de carbono, cero heteroátomos y cero dobles enlaces. Los ejemplos de sistemas de anillos monocíclicos incluyen ciclopropilo, ciclobutilo, ciclopentilo, ciclohexilo, cicloheptilo y ciclooctilo. El cicloalquilo bicíclico es un cicloalquilo monocíclico fusionado a un anillo cicloalquilo monocíclico, o un sistema de anillos monocíclico con puente en donde dos átomos de carbono no adyacentes del anillo monocíclico se unen a través de un puente alquileno que contiene 1, 2, 3 ó 4 átomos de carbono. Los ejemplos representativos de sistemas de anillos bicíclicos incluyen, pero en un sentido no limitativo, biciclo[3.1.1]heptano, biciclo[2.2.1]heptano, biciclo[2.2.2]octano, biciclo[3.2.2]nonano, biciclo[3.3.1]nonano y biciclo[4.2.1]nonano. Los ejemplos de cicloalquilos tricíclicos son un cicloalquilo bicíclico fusionado a un cicloalquilo monocíclico, o un cicloalquilo bicíclico en donde dos átomos de carbono no adyacentes del sistema de anillos se unen por un puente alquileno de 1, 2, 3 ó 4 átomos de carbono. Los ejemplos representativos de sistemas de anillos tricíclicos incluyen, pero en un sentido no

limitativo, triciclo[3.3.1.$0^{3,7}$]nonano (octahidro-2,5-metanpentaleno o noradamantano) y triciclo[3.3.1.$1^{3,7}$]decano (adamantano). Los cicloalquilos monocíclicos, bicíclicos y tricíclicos pueden estar sustituidos o no, y se unen a la porción molecular principal a través de cualquier átomo del sistema de anillos susceptible de sustitución.

El término "cicloalquilalquilo", según se usa en la presente, hace referencia a un grupo cicloalquilo, definido en la presente, unido a la porción molecular principal a través de un grupo alquilo, definido en la presente.

El término "cicloalquenilo" o "cicloalqueno", según se usa en la presente, significa un sistema de anillos hidrocarbonado monocíclico o bicíclico. El cicloalquenilo monocíclico tiene 4, 5, 6, 7 ú 8 átomos de carbono y cero heteroátomos. Los sistemas de anillos de 4 miembros tienen un doble enlace, los sistemas de anillos de 5 ó 6 miembros tienen 1 ó 2 dobles enlaces y los sistemas de anillos de 7 u 8 miembros tienen 1, 2 ó 3 dobles enlaces. Los ejemplos representativos de grupos cicloalquenilo monocíclicos incluyen, pero en un sentido no limitativo, ciclobutenilo, ciclopentenilo, ciclohexenilo, cicloheptenilo y ciclooctenilo. El cicloalquenilo bicíclico es un cicloalquenilo monocíclico fusionado a un grupo cicloalquilo monocíclico o un cicloalquenilo monocíclico fusionado a un grupo cicloalquenilo monocíclico. El anillo cicloalquenilo monocíclico o bicíclico puede contener 1 ó 2 puentes alquileno, donde cada uno consiste en 1, 2 ó 3 átomos de carbono, cada uno de los cuales une dos átomos de carbono no adyacentes del sistema de anillos. Los ejemplos representativos de grupos cicloalquenilo bicíclicos incluyen, pero en un sentido no limitativo, 4,5,6,7-tetrahidro-3aH-indeno, octahidronaftalenilo y 1,6-dihidro-pentaleno. El cicloalquenilo monocíclico y bicíclico puede estar unido a la porción molecular principal a través de cualquier átomo del sistema de anillos susceptible de sustitución, y puede estar sustituido o no.

El término "halo" ó "halógeno", según se usa en la presente, hace referencia a Cl, Br, I o F.

El término "haloaquilo", según se usa en la presente, hace referencia a un grupo alquilo, definido en la presente, en el cual uno, dos, tres, cuatro, cinco o seis átomos de hidrógeno han sido reemplazados por halógeno. Los ejemplos representativos de haloalquilo incluyen, pero en un sentido no limitativo,

clorometilo, 2-fluoroetilo, 2,2,2-trifluoroetilo, trifluorometilo, difluorometilo, pentafluoroetilo, 2-cloro-3-fluoropentilo y trifluoropropilo tal como 3,3,3-trifluoropropilo.

El término "heterociclo" o "heterocíclico", según se usa en la presente, hace referencia a un heterociclo monocíclico, a un heterociclo bicíclico o a un heterociclo tricíclico. El heterociclo monocíclico es un anillo de tres, cuatro, cinco, seis, siete u ocho miembros que contiene por lo menos un heteroátomo seleccionado de manera independiente del grupo que consiste de O, N y S. El anillo de tres o cuatro miembros contiene cero o un enlace doble, y un heteroátomo seleccionado del grupo que consiste de O, N y S. El anillo de cinco miembros contiene cero o un enlace doble y uno, dos o tres heteroátomos seleccionados del grupo que consiste de O, N y S. El anillo de seis miembros contiene cero, uno o dos enlace dobles y uno, dos o tres heteroátomos seleccionados del grupo que consiste de O, N y S. Los anillos de siete y ocho miembros contiene cero, uno, dos o tres enlaces dobles y uno, dos o tres heteroátomos seleccionados del grupo que consiste de O, N y S. Los ejemplos representativos de heterociclos monocíclicos incluyen, pero en un sentido no limitativo, azetidinilo, azepanilo, aziridinilo, diazepanilo, 1,3-dioxanilo, 1,3-dioxolanilo, 1,3-ditiolanilo, 1,3-ditianilo, imidazolinilo, imidazolidinilo, isotiazolinilo, isotiazolidinilo, isoxazolinilo, isoxazolidinilo, morfolinilo, oxadiazolinilo, oxadiazolidinilo, oxazolinilo, oxazolidinilo, piperazinilo, piperidinilo, piranilo, pirazolinilo, pirazolidinilo, pirrolinilo, pirrolidinilo, tetrahidrofuranilo, tetrahidropiranilo, tetrahidropiridinilo, tetrahidrotienilo, tiadiazolinilo, tiadiazolidinilo, 1,2-tiazinanilo, 1,3-tiazinanilo, tiazolinilo, tiazolidinilo, tiomorfolinilo, 1,1-dioxidotiomorfolinilo (tiomorfolinsulfona), tiopiranilo y tritianilo. El heterociclo bicíclico es un heterociclo monocíclico fusionado a un grupo fenilo o un heterociclo monocíclico fusionado a un cicloalquilo monocíclico o un heterociclo monocíclico fusionado a un cicloalquenilo monocíclico o un heterociclo monocíclico fusionado a un heterociclo monocíclico o un sistema de anillos heterocíclico monocíclico con puente, en donde dos átomos de adyacentes del anillo se unen por un puente alquileno de 1, 2, 3 ó 4 átomos de carbono o por medio de un puente alquenileno de 2, 3 ó 4 átomos de carbono. Los ejemplos representativos de heterociclos bicíclicos incluyen, pero en un sentido no limitativo, benzopiranilo, benzotiopiranilo,

cromanilo, 2,3-dihidrobenzofuranilo, 2,3-dihidrobenzotienilo, 2,3-dihidroisoquinolina, azabiciclo[2.2.1]heptilo (incluyendo 2-azabiciclo[2.2.1]hept-2–ilo), 2,3-dihidro-1H-indolilo, isoindolinilo, octahidrociclopenta[*c*]pirrolilo, octahidropirrolopiridinilo y tetrahidroisoquinolinilo. Los ejemplos de heterociclos tricíclicos incluyen un heterociclo bicíclico fusionado a un grupo fenilo o un heterociclo bicíclico fusionado a un cicloalquilo monocíclico o un heterociclo bicíclico fusionado a un cicloalquenilo monocíclico o un heterociclo bicíclico fusionado a un heterociclo monocíclico o un heterociclo bicíclico en donde dos átomos no adyacentes del anillo bicíclico se unen por un puente alquileno de 1, 2, 3 ó 4 átomos de carbono o por medio de un puente alquenileno de 2, 3 ó 4 átomos de carbono. Los ejemplos de heterociclos tricíclicos incluyen, en un sentido no limitativo, octahidro-2,5-epoxipentaleno, hexahidro-2*H*-2,5-metanociclopenta[*b*]furano, hexahidro-1*H*-1,4-metanociclopenta[*c*]furan, aza-admantano (1-azatriciclo[3,3,1,$1^{3,7}$]decano) y oxa-adamantano (2-oxatriciclo[3,3,1,$1^{3,7}$]decano). Los heterociclos monocíclicos, bicíclicos y tricíclicos están unidos a la porción molecular principal a través de cualquier átomo de carbono o cualquier átomo de nitrógeno contenido en los anillos, y pueden estar sustituidos o no.

El término "heteroarilo", según se usa en la presente, hace referencia a un heteroarilo monocíclico o a un heteroarilo bicíclico. El heteroarilo monocíclico es un anillo de cinco o seis miembros. El anillo de cinco miembros contiene dos enlaces dobles. El anillo de 5 miembros puede contener un heteroátomo seleccionado entre O o S; o 1, 2, 3 ó 4 átomos de nitrógeno y opcionalmente un átomo de oxígeno o azufre. El anillo de 6 miembros contiene tres dobles enlaces y 1, 2, 3 ó 4 átomos de nitrógeno. Los ejemplos representativos de grupos heteroarilo monocíclicos incluyen, pero en un sentido no limitativo, furanilo, imidazolilo, isoxazolilo, isotiazolilo, oxadiazolilo, 1,3-oxazolilo, piridinilo, piridazinilo, pirimidinilo, pirazinilo, pirazolilo, pirrolilo, tetrazolilo, tiadiazolilo, 1,3-tiazolilo, tienilo, triazolilo y triazinilo. Los heteroarilos bicíclicos consisten en un heteroarilo monocíclico fusionado a un fenilo, en un heteroarilo monocíclico fusionado a un cicloalquilo monocíclico, en un heteroarilo monocíclico fusionado a un cicloalquenilo monocíclico, en un heteroarilo monocíclico fusionado a un heteroarilo monocíclico o en un heteroarilo monocíclico fusionado a un heterociclo

monocíclico. Los ejemplos representativos de grupos heteroarilo bicíclicos incluyen, pero en un sentido no limitativo, benzofuranilo, benzotienilo, benzoxazolilo, benzimidazolilo, benzoxadiazolilo, 6,7-dihidro-1,3-benzotiazolilo, imidazo[1,2-*a*]piridinilo, indazolilo, indolilo, isoindolilo, isoquinolinilo, naftiridinilo, piridoimidazolilo, quinolinilo, tiazol[5,4-b]piridin-2–ilo, tiazolo[5,4-d]pirimidin-2–ilo y 5,6,7,8-tetrahidroquinolin-5–ilo. Los grupos heteroarilo monocíclicos y bicíclicos de la presente invención pueden estar sustituidos o no y están unidos a la porción molecular principal a través de cualquier átomo de carbono o cualquier átomo de nitrógeno contenido en los sistemas de anillos.

El término "heteroarilalquilo", según se usa en la presente, se refiere a un grupo heteroarilo unido a la porción molecular principal a través de un grupo alquilo, definido en la presente.

El término "heteroátomo" según se usa en la presente, significa un átomo de nitrógeno, oxígeno o azufre.

El término "hidroxilo" o "hidroxi", según se usa en la presente, se refiere a un grupo -OH.

El término "hidroxialquilo" según se usa en la presente, se refiere a por lo menos un grupo hidroxi, definido en la presente, unido a una porción de la molécula principal a través de un grupo alquileno, definido en la presente. Los ejemplos representativos de hidroxialquilo incluyen, pero en un sentido no limitativo, hidroximatilo, 2-hidroxietilo, 3-hidroxipropilo, 2,3-dihidroxipentilo y 2-etil-4-hidroxiheptilo.

El término "nitro", según se usa en la presente, hace referencia a un grupo -NO_2.

El término "oxo" según se usa en la presente, significa un grupo =O.

b. Compuestos

Los compuestos de la invención tienen la fórmula (I) según se describió anteriormente.

Los valores particulares de los grupos variables en los compuestos de la fórmula (I) son los siguientes. Dichos valores se pueden utilizar, cuando fuera apropiado, con cualquiera de los otros valores, definiciones, reivindicaciones o realizaciones que se han definido o que se definen más adelante en la presente.

Más particularmente, los compuestos de fórmula (I) pueden incluir,

pero no taxativamente, compuestos donde L^1-R^1 tomados juntos son hidrógeno, alquilo, hidroxialquilo, G^1, o $CH(G^1)_2$.

En otra forma de realización , los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde L^1 es C(O), $S(O)_2$, $SO_2N(R^4)$, C(O)O o $-(CR^aR^b)_m-$; donde m es 1,2,3, 4, 5, o 6.

En una forma de realización adicional, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde L^1 es C(O), $S(O)_2$, o $-(CR^aR^b)_m-$.

En otra forma de realización , los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^1 es alquilo, G^1, $CH(G^1)_2$, $-(CR^aR^b)_m-G^1$, $-(CR^aR^b)_m-CH(G^1)_2$, $-(CR^eR^f)_n-N(R^5)_2$, $-(CR^eR^f)_n-N(R^5)$-C(O)O(alquilo), $-(CR^eR^f)_n-N(R^5)$-C(O)(alquilo), o $-(CR^eR^f)_n-N(R^5)-SO_2R^6$; donde m es 1, 2, 3, 4, 5, o 6; y donde n es 1, 2, 3, 4, o 5.

En una forma de realización adicional, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^1 es G^1, $CH(G^1)_2$, $-(CR^aR^b)_m-G^1$, $-(CR^aR^b)_m-CH(G^1)_2$.

En una realización, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde L^2-R^2 tomados juntos son alquilo, G^2, o $C(R^c)(G^2)(G^3)$.

En una forma de realización adicional, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde L^2-R^2 juntos son alquilo, arilo, cicloalquilo, heteroarilo o $-C(R^c)(G^2)(G^3)$, donde R^c es hidrógeno y G^2 y G^3 son cada uno arilo o heteroarilo.

En otra forma de realización , los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde L^2 es $-(CR^cR^d)_p-$, C(O), $C(O)N(R^4)$, $S(O)_2$, $SO_2N(R^5)$, o C(O)O; donde p es 1, 2, 3, 4, 5, o 6.

En una forma de realización adicional, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde L^2 es $-(CR^cR^d)_p-$, C(O), $C(O)N(R^4)$, o $S(O)_2$, donde p es 1.

En otra forma de realización , los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^2 es alquilo, G^2, $-C(R^c)(G^2)(G^3)$, $-(CR^cR^d)_p-G^2$, $-(CR^cR^d)_p-CH(G^2)(G^3)$, $-(CR^gR^h)_q-N(R^5)$-C(O)O(alquilo), $-(CR^gR^h)_q-N(R^5)-C(O)O-G^2$, $-(CR^gR^h)_q-N(R^5)$-C(O)(alquilo), -

$(CR^gR^h)_q$-$N(R^5)$-SO_2R^6, -$(CR^gR^h)_q$-$N(R^4)(R^5)$, -$(CR^gR^h)_q$-$N(R^5)$-$C(O)N(R^5)$-(alquilo), o -$(CR^gR^h)_q$-$N(R^5)$-$C(O)N(R^5)$-G^2; donde q es 1, 2, 3, 4, o 5; y donde p es 1, 2, 3, 4, 5, o 6.

En otra forma de realización , los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^a y R^b, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, arilalquilo, halógeno, o haloalquilo o OR^7.

En una forma de realización adicional, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^a y R^b, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, o arilalquilo.

En aún otra forma de realización , los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^a y R^b, junto con el átomo de carbono al cual se encuentran unidos, forman opcionalmente un anillo C_{3-6} cicloalquilo.

En otra forma de realización , los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^c y R^d, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, arilalquilo, halógeno, o haloalquilo o OR^7.

En una forma de realización adicional, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^c y R^d, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, arilalquilo, o OR^7, donde R^7 es hidrógeno.

En aun otra forma de realización , los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^c y R^d, junto con el átomo de carbono al cual se encuentran unidos, forman opcionalmente un anillo C_{3-6} cicloalquilo.

En una realización, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^e y R^f, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, halógeno, haloalquilo, OR^7, cicloalquilalquilo, heteroarilo, arilalquilo, o heteroarilalquilo; donde los grupos arilo, cicloalquilo y heteroarilo de arilo, cicloalquilo y heteroarilo cada uno en forma independiente no se sustituye o se sustituye con 1, 2, 3, 4, o 5 sustituyentes seleccionados en forma independiente entre el grupo que consiste en alquilo y

haloalquilo.

En otra forma de realización , los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^g, y R^h, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, halógeno, haloalquilo, OR^7, cicloalquilalquilo, heteroarilo, arilalquilo, o heteroarilalquilo; donde los grupos arilo, cicloalquilo y heteroarilo de arilo, cicloalquilo y heteroarilo cada uno en forma independiente no se sustituye o se sustituye con 1, 2, 3, 4, o 5 sustituyentes seleccionados en forma independiente entre el grupo que consiste en alquilo y haloalquilo.

En una forma de realización adicional, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^g, y R^h, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, arilalquilo o cicloalquilo.

En una realización, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde G^1 en cada caso, es en forma independiente arilo, cicloalquilo, cicloalquenilo, heteroarilo, o heterociclo; donde G^1 en cada caso no se sustituye o se sustituye en forma independiente con 1, 2, 3, 4, o 5 sustituyentes seleccionados entre el grupo que consiste en alquilo, alquenilo, alquinilo, ciano, haloalquilo, halógeno, nitro, oxo, fenilo, $N(R^7)_2$, $N(R^7)C(O)R^7$, OR^7, $C(O)R^7$, $C(O)OR^7$, $C(O)N(R^7)_2$, SO_2R^8, y $SO_2N(R^7)_2$.

En otra forma de realización , los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde G^1 en cada caso, es en forma independiente arilo, cicloalquilo, o heteroarilo; donde G^1 en cada caso no se sustituye o se sustituye en forma independiente con 1, 2, o 3 sustituyentes seleccionados entre el grupo que consiste en alquilo, ciano, haloalquilo, halógeno, o OR^7.

En una realización, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde G^2 en cada caso, es en forma independiente arilo, cicloalquilo, cicloalquenilo, heteroarilo, o heterociclo; donde G^2 en cada caso no se sustituye o se sustituye en forma independiente con 1, 2, 3, 4, o 5 sustituyentes seleccionados entre el grupo que consiste en alquilo, alquenilo, alquinilo, ciano, haloalquilo, halógeno, nitro, oxo, fenilo, $N(R^7)_2$, $N(R^7)C(O)R^7$, OR^7, $C(O)R^7$, $C(O)OR^7$, $C(O)N(R^7)_2$, SO_2R^8, y $SO_2N(R^7)_2$.

En una forma de realización adicional, los compuestos de fórmula (I)

pueden incluir, pero no taxativamente, compuestos donde G^2 en cada caso, es en forma independiente arilo, cicloalquilo, heteroarilo o heterociclo; donde G^2 en cada caso no se sustituye o se sustituye en forma independiente con 1, 2, o 3 sustituyentes seleccionados entre el grupo que consiste en alquilo, ciano, haloalquilo, halógeno, nitro, oxo, OR^7, $C(O)R^7$, $C(O)OR^7$ o SO_2R^8,

En una realización, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde G^3 en cada caso, es en forma independiente arilo, cicloalquilo, cicloalquenilo, heteroarilo, o heterociclo; donde G^2 en cada caso no se sustituye o se sustituye en forma independiente con 1, 2, 3, 4, o 5 sustituyentes seleccionados entre el grupo que consiste en alquilo, alquenilo, alquinilo, ciano, haloalquilo, halógeno, nitro, oxo, fenilo, $N(R^7)_2$, $N(R^7)C(O)R^7$, OR^7, $C(O)R^7$, $C(O)OR^7$, $C(O)N(R^7)_2$, SO_2R^8, y $SO_2N(R^7)_2$.

En una forma de realización adicional, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde G^3 en cada caso, es en forma independiente arilo, cicloalquilo, heteroarilo o heterociclo; donde G^2 en cada caso no se sustituye o se sustituye en forma independiente con 1, 2, o 3 sustituyentes seleccionados entre el grupo que consiste en alquilo, ciano, haloalquilo, halógeno, nitro, oxo, OR^7, $C(O)R^7$, $C(O)OR^7$ o SO_2R^8,

En una realización, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^3 es hidrógeno, alquilo, haloalquilo, cicloalquilo, o cicloalquilalquilo.

En una forma de realización adicional, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^3 es hidrógeno, alquilo, o cicloalquilo.

En una realización, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^4 y R^5, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, arilo, arilalquilo, cicloalquilo, cicloalquilalquilo, o haloalquilo; donde dichos arilo, el arilo de arialquilo y cicloalquilo no se sustituyen o se sustituyen en forma independiente con 1, 2 3, 4, o 5 sustituyentes seleccionados en forma independiente entre el grupo que consiste en alquilo, haloalquilo, y halógeno.

En una forma de realización adicional, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^4 y R^5, en cada caso,

son cada uno en forma independiente hidrógeno, alquilo, arilalquilo, cicloalquilo o cicloalquilalquilo.

En una realización; los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^6 es alquilo, arilo, cicloalquilo, cicloalquenilo, heteroarilo, o heterociclo; donde dichos arilo, heteroarilo y heterociclo no se sustituyen o se sustituyen en forma independiente con 1, 2 3, 4, o 5 sustituyentes seleccionados en forma independiente entre el grupo que consiste en alquilo, haloalquilo, y halógeno.

En otra forma de realización , los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^6 es alquilo o cicloalquilo.

En una realización, los compuestos de fórmula (I) pueden incluir, pero no taxativamente; compuestos donde R^7, en cada caso, es en forma independiente hidrógeno, alquilo, arilo, arilalquilo, cicloalquilo, cicloalquilalquilo, o haloalquilo; donde dichos arilo, el arilo de arialquilo y cicloalquilo no se sustituyen o se sustituyen en forma independiente con 1, 2 3, 4, o 5 sustituyentes seleccionados en forma independiente entre el grupo que consiste en alquilo, haloalquilo, y halógeno.

En una forma de realización adicional, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^7, en cada caso, es en forma independiente hidrógeno o alquilo.

En una realización, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^8 es alquilo o haloalquilo.

En una forma de realización adicional, los compuestos de fórmula (I) pueden incluir, pero no taxativamente, compuestos donde R^8 es alquilo.

En una realización, en un compuesto de fórmula (I), L^1 es $-(CR^aR^b)_m-$; R^a y R^b son cada uno hidrógeno; m es 1; R^1 es G^1, donde G^1 es arilo; L^2 es C(O); R^2 es $-(CR^cR^d)_p-G^2$, donde G^2 es arilo y p es 1; R^c y R^d, junto con el átomo de carbono al cual se encuentran unidos forman un anillo C_{3-6} cicloalquilo; y R^3 es hidrógeno.

En otra forma de realización , en un compuesto de fórmula (I), L^1-R^1 juntos son alquilo; o L^1 es $-(CR^aR^b)_m-$ o C(O); y R^1 es G^1; donde G^1 es arilo, cicloalquilo, o heteroarilo; L^2 es C(O); R^2 es $-(CR^cR^d)_p-G^2$; donde G^2 es arilo y p es 1 o 2; R^a, R^b, R^c, y R^d, en cada caso son en forma independiente hidrógeno,

alquilo o arilalquilo; y R^3 es hidrógeno o alquilo.

En una realización, en un compuesto de fórmula (I), L^1 es $-(CR^aR^b)_m-$; m es 1 o 2; R^a y R^b son cada uno hidrógeno; R^1 es G^1, donde G^1 es arilo; L^2 es $C(O)N(R^4)$, donde R^4 es alquilo; R^2 es G^2, donde G^2 es arilo; y R^3 es hidrógeno.

En otra forma de realización , en un compuesto de fórmula (I), L^1 es $-(CR^aR^b)_m-$, C(O), o $S(O)_2$; R^a y R^b en cada caso son cada uno hidrógeno; m es 1; R^1 es alquilo o G^1, donde G^1 es arilo o cicloalquilo; L^2 es C(O); y R^2 es $-(CR^cR^d)_p-G^2$; donde Rc y Rd en cada caso son en forma independiente hidrógeno, alquilo o OR^7; p es 1; G^2 es cicloalquilo o heterociclo; donde dicho cicloalquilo o heterociclo no se sustituye o se sustituye con 1, 2, 3, 4, o 5 sustituyentes seleccionados en forma independiente entre el grupo que consiste en alquilo, haloalquilo, halógeno, oxo $C(O)OR^7$; R^7 es hidrógeno;; y R^3 es hidrógeno.

En una realización, en un compuesto de fórmula (I), L^1 es $-(CR^aR^b)_m-$; R^a y R^b son cada uno hidrógeno; m es 1; R^1 es G^1; donde G^1 es arilo; L^2-R^2 juntos son cicloalquilo; y R^3 es hidrógeno o cicloalquilo.

En otra forma de realización , en un compuesto de fórmula (I), L^1 es $-(CR^aR^b)_m-$; R^a y R^b son cada uno hidrógeno; m es 1; R^1 es G^1; donde G^1 es arilo; L^2 es C(O); R^2 es $-C(R^c)(G^2)(G^3)$ o $-(CR^cR^d)_p-CH(G^2)(G^3)$; donde G^2 es arilo y G^3 es arilo o cicloalquilo; R^c y R^d, en cada caso, son cada uno en forma independiente hidrógeno; p es 1, 2, 3, 4, o 5; y R^3 es hidrógeno.

En una forma de realización adicional, en un compuesto de fórmula (I), L^1-R^1 juntos son hidrógeno o $-CH(G^1)_2$; donde cada G^1 es arilo o heteroarilo; o L^1 es $-(CR^aR^b)_m-$, C(O), o $S(O)_2$; y R^1 es G^1, $-CH(G^1)_2$, $-(CR^aR^b)_m-G^1$, $-(CR^aR^b)_m-CH(G^1)_2$, $-(CR^eR^f)_n-N(R^5)_2$, donde cada G^1 es arilo o heteroarilo; R^a y R^b en cada caso, son cada uno en forma independiente hidrógeno; R^e y R^f en cada caso, son cada uno en forma independiente hidrógeno o alquilo; m es 1, 2, 3, 4, o 5; n es 1 o 2; R^5 es hidrógeno o alquilo; L^2 es C(O); R^2 es $-C(R^c)(G^2)(G^3)$; donde G^2 y G^3 son cada uno cicloalquilo; R^c es hidrógeno o OR^7, R^7 es hidrógeno; y R^3 es hidrógeno.

En una realización, en un compuesto de fórmula (I), L^1 es $-(CR^aR^b)_m-$; R^a y R^b son cada uno hidrógeno; m es 1; R^1 es G^1, donde G^1 es arilo; L^2 es C(O); R^2 es alquilo o G^2; donde G^2 es cicloalquilo o heterociclo; R^3 es hidrógeno.

En otra forma de realización , en un compuesto de fórmula (I), L^1 es $-(CR^aR^b)_m-$, C(O) o $S(O)_2$, donde R^a y R^b son cada uno hidrógeno y m es 1 o 2; R^1

es G^1, $-CH(G^1)_2$ o $-(CR^aR^b)_m-G^1$, donde G^1 en cada caso es arilo o heteroarilo; L^2 es C(O); R^2 es $-(CR^gR^h)_q-N(R^5)-C(O)O$(alquilo), $-(CR^gR^h)_q-N(R^5)--C(O)O-G^2$, $-(CR^gR^h)_q-N(R^5)-C(O)$(alquilo), $-(CR^gR^h)_q-N(R^5)-SO_2R^6$, $-(CR^gR^h)_q-N(R^4)(R^5)$, $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-$(alquilo), o $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-G^2$; q es 1 o 2; R^g y R^h, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, arilalquilo o cicloalquilalquilo; R^4 y R^5 en cada caso, son cada uno en forma independiente hidrógeno, alquilo, arilalquilo, o cicloalquilo; R^6 es alquilo, arilo, o cicloalquilo; G^2 es arilo o cicloalquilo; y R^3 es hidrógeno, alquilo, cicloalquilo o cicloalquilalquilo.

En una realización, en un compuesto de fórmula (I), L^1-R^1 juntos son hidrógeno o hidroxialquilo; o L^1 es $-(CR^aR^b)_m-$, C(O) o $S(O)_2$; y R^1 es G^1 o $-CH(G^1)^2$, donde G^1 es arilo o heteroarilo, y donde R^a y R^b, en cada caso, son cada uno en forma independiente hidrógeno o alquilo; m es 1, 2, 3, 4, o 5; L^2 es $S(O)_2$; R^2 es G^2, donde G^2 es arilo o heteroarilo; y R^3 es hidrógeno, alquilo o cicloalquilo.

En una forma de realización adicional, en un compuesto de fórmula (I), L^1 es $-(CR^aR^b)_m-$; R^a y R^b, en cada caso, son cada uno en forma independiente hidrógeno; m es 1, 2, 3, 4, o 5; L^2 es C(O); R^2 es $-(CR^cR^d)_p-G^2$; donde G^2 es arilo; p es 1; R^c y R^d, en cada caso, son cada uno en forma independiente hidrógeno o alquilo; y R^3 es hidrógeno.

En otra forma de realización , en un compuesto de fórmula (I), L^1 es C(O), $S(O)_2$ o $-(CR^aR^b)_m-$; R^a y R^b, en cada caso, son en forma independiente hidrógeno o alquilo; m es 1; R^1 es G^1 o $-(CR^aR^b)_m-G^1$, donde G^1 es arilo o heteroarilo; L^2 es $-(CR^cR^d)_p-$; R^c y R^d son cada uno hidrógeno; p es 1; R^2 es G^2, donde G^2 es arilo, cicloalquilo o heteroarilo; o L^2-R^2 tomados juntos son alquilo, G^2, o $-C(R^c)(G^2)(G^3)$, donde G^2 y G^3 son cada uno arilo o heteroarilo y R^c es hidrógeno; y R^3 es hidrógeno o alquilo.

En una forma de realización adicional, en un compuesto de fórmula (I), L^1 es C(O); R^1 es $-(CR^eR^f)_n-N(R^5)_2$; n es 1 o 2; R^e y R^f en cada caso son cada uno en forma independiente hidrógeno o alquilo; R^5 en cada caso es en forma independiente hidrógeno o alquilo; L^2 es C(O) o $S(O)_2$; R^2 es G^2 o $-C(R^c)(G^2)(G^3)$, donde G^2 y G^3 son cada uno arilo o heteroarilo y R^c es hidrógeno; y R^3 es hidrógeno, alquilo, o cicloalquilo. En una forma de realización adicional, en un compuesto de fórmula (I), L^1 es C(O); R^1 es $-(CR^eR^f)_n-N(R^5)_2$ o $-(CR^eR^f)_n-$

$N(R^5)C(O)O$(alquil); n es 1 o 2; R^e y R^f en cada caso son cada uno en forma independiente hidrógeno, alquilo, o arilalquilo; R^5 en cada caso es en forma independiente hidrógeno, alquilo o cicloalquilo; L^2 es C(O); R^2 es $-(CR^gR^h)_qN(R^4)(R^5)$ o $-(CR^gR^h)_q-N(R^5)C(O)O$(alquil); q es 1 o 2; R^4 es hidrógeno o alquilo; R^g y R^h en cada caso son cada uno en forma independiente hidrógeno o alquilo; y R^3 es hidrógeno. En otra forma de realización , en un compuesto de fórmula (I), L^1-R^1 tomados juntos son hidrógeno, G^1 o $CH(G^1)_2$, donde G^1 es arilo o heteroarilo; L^2 es C(O); R^2 es $-(CR^gR^h)_qN(R^4)(R^5)$ o $-(CR^gR^h)_q-N(R^5)C(O)O$(alquil); q es 1 o 2; R^4 es hidrógeno, alquilo, o cicloalquilalquilo; R^5 es hidrógeno o alquilo; R^g y R^h en cada caso son cada uno en forma independiente hidrógeno o alquilo; y R^3 es hidrógeno. En una forma de realización adicional, en un compuesto de fórmula (I), L^1-R^1 tomados juntos son G^1, donde G^1 es arilo o heteroarilo; L^2 es C(O); R^2 es G^2, donde G^2 es arilo o heteroarilo; y R^3 es hidrógeno o alquilo.

Las realizaciones específicas de compuestos contemplados como parte de la invención incluyen, pero no se limitan a:

N-[(3a*S**,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclopentancarboxamida;

N-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclopentancarboxamida;

N-[(3a*R**,4*R**,6a*S**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclohexil-2-fenilacetamida;

N-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclohexil-2-fenilacetamida;

N-[(3a*R**,4*R**,6a*S**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*R**,4*S**,6a*S**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*S**,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclopentil-2-fenilacetamida;

N-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclopentil-2-fenilacetamida;

N-[(3a*S**,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclohexanocarboxamida;

N-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclohexanocarboxamida;

N-[(3a*S**,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida;

(2*S*)-2-(3-benzoilfenil)-*N*-[(3a*S**,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]propanamida;

(2*S*)-2-(3-benzoilfenil)-*N*-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]propanamida;

N-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclopentil-2-fenilacetamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilpropanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-propilpentanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]cicloheptancarboxamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(4-isobutilfenil)propanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclohexanocarboxamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,3-difenilpropanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-metil-3-

fenilpropanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-metil-2-fenilpropanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclopropancarboxamida;

2-bencil-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetilbutanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetil-2-fenilbutanamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetil-2-fenilbutanamida;

(2*R*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetil-2-fenilbutanamida;

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclopentil-2-fenilacetamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

(2*R*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida;

(2*R*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilpropanamida;

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilpropanamida;

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(4-isobutilfenil)propanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclopropil-2-fenilacetamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclobutil-2-fenilacetamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(4-clorofenil)-3-metilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-etil-2-fenilpentanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(4-hidroxifenil)-3-metilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclohexanocarboxamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-metil-2-fenilpropanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclopropancarboxamida;

2-bencil-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,3-difenilpropanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-metil-3-fenilpropanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetil-2-fenilbutanamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(2-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[4-fluoro-3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-fluoro-4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

N-{(3a*S*,4*S*,6a*R*)-2-[3,5-bis(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[2-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-metilbencil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(4-metilbencil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometoxi)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

N-{(3a*S*,4*S*,6a*R*)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida;

N-{(3a*S*,4*S*,6a*R*)-2-[6,6-bis(4-fluorofenil)hexil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida;

N-{(3a*S*,4*S*,6a*R*)-2-[3-(3-clorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(3-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-fenilpropil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-((3a*S*,4*S*,6a*R*)-2-{3-[4-(trifluorometil)fenil]propil}octahidrociclopenta[*c*]pirrol-4–il)acetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(piridin-4–ilmetil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(piridin-3–ilmetil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

N-{(3a*S*,4*R*,6a*R*)-2-[3,5-bis(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida;

N-{(3a*S*,4*R*,6a*R*)-2-[6,6-bis(4-fluorofenil)hexil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-2-(3,3-difenilpropil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

N-{(3a*S*,4*R*,6a*R*)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida;

N-{(3a*S*,4*R*,6a*R*)-2-[4,4-bis(4-fluorofenil)butil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida;

3-metil-2-fenil-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(ciclohexilmetil)octahidrociclopenta[c]pirrol-4–il]-3-metil-2-fenilbutanamida;

3-metil-*N*-[(3a*R*,4*S*,6a*S*)-2-metiloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(2-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(3-clorobencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(3-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

3-metil-2-fenil-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(3-metoxibencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

3-metil-*N*-[(3a*R*,4*S*,6a*S*)-2-(3-metilbencil)octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida;

3-metil-*N*-[(3a*R*,4*S*,6a*S*)-2-(2-metilbencil)octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(2,6-dimetilbencil)octahidrociclopenta[*c*]pirrol-4–il]-3-

metil-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(2-metoxibencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(4-*tert*-butilbencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(4-metoxibencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(3-cianobencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

3-metil-2-fenil-*N*-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

3-metil-2-fenil-*N*-{(3a*R*,4*S*,6a*S*)-2-[2-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[4-fluoro-3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[3-fluoro-4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

3-metil-2-fenil-*N*-[(3a*R*,4*S*,6a*S*)-2-(tien-2–ilmetil)octahidrociclopenta[*c*]pirrol-4–il]butanamida;

3-metil-2-fenil-*N*-[(3a*R*,4*S*,6a*S*)-2-(piridin-4–ilmetil)octahidrociclopenta[*c*]pirrol-4–il]butanamida;

3-metil-2-fenil-*N*-[(3a*R*,4*S*,6a*S*)-2-(2-feniletil)octahidrociclopenta[*c*]pirrol-4–il]butanamida;

3-metil-2-fenil-*N*-[(3a*R*,4*S*,6a*S*)-2-(3-fenilpropil)octahidrociclopenta[*c*]pirrol-4–il]butanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[3-(4-*tert*-butilfenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[6,6-bis(4-fluorofenil)hexil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

3-metil-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(2-metilfenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-2-fenilbutanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[3-(3-clorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

3-metil-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(3-metilfenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-2-fenilbutanamida;

3-metil-2-fenil-*N*-((3a*R*,4*S*,6a*S*)-2-{3-[3-(trifluorometil)fenil]propil}octahidrociclopenta[*c*]pirrol-4–il)butanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[3-(3-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

3-metil-2-fenil-*N*-[(3a*R*,4*S*,6a*S*)-2-(4-fenilbutil)octahidrociclopenta[*c*]pirrol-4–il]butanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[3-(3-cloro-5-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

3-metil-2-fenil-*N*-((3a*R*,4*S*,6a*S*)-2-{3-[4-(trifluorometil)fenil]propil}octahidrociclopenta[*c*]pirrol-4–il)butanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(3,3-difenilpropil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[4,4-bis(4-fluorofenil)butil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[5,5-bis(4-fluorofenil)pentil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

N-[(3a*S*,4*S*,6a*R*)-2-benzhidriloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida;

N-[(3a*S*,4*R*,6a*R*)-2-benzhidriloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida;

3-metil-2-fenil-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

3,3-dimetil-2-fenil-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

2,2-diciclohexil-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2-etil-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

2-propil-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-

(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}pentanamida;

N-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}ciclohexanocarboxamida;

N-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}cicloheptancarboxamida;

N-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}ciclopentancarboxamida;

6,6-bis(4-fluorofenil)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}hexanamida;

3,3-difenil-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}propanamida;

5,5-bis(4-fluorofenil)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}pentanamida;

3,3-bis(4-fluorofenil)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[c]pirrol-4–il}propanamida;

4,4-bis(4-fluorofenil)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

2,2-difenil-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-bis(4-fluorofenil)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^2-(*tert*-butiloxicarbonil)-N^2-metil-N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

6,6-bis(4-fluorofenil)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}hexanamida;

3,3-difenil-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}propanamida;

5,5-bis(4-fluorofenil)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}pentanamida;

3,3-bis(4-fluorofenil)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}propanamida;

4,4-bis(4-fluorofenil)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

2,2-difenil-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-bis(4-fluorofenil)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

3,3-dimetil-2-fenil-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^2-(*tert*-butiloxicarbonil)-N^2-metil-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida;

2,2-diciclohexil-2-hidroxi-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

N^2-(*tert*-butiloxicarbonil)-N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

2,2-diciclohexil-2-hidroxi-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

N^2-(*tert*-butiloxicarbonil)-N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

2,2-diciclohexil-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-{(3a*R*,4*R*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–

il}-D-leucinamida;

N^2-metil-*N*^{1}-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^2-metil-*N*^{1}-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^2-metil-*N*^{1}-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*^{2}-metil-L-leucinamida;

N^2-metil-*N*^{1}-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[c]pirrol-4–il}-L-leucinamida;

N^2-metil-*N*^{2}-(metilsulfonil)-*N*^{1}-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*^{2}-metil-*N*^{2}-(metilsulfonil)-L-leucinamida;

N^2-metil-*N*^{2}-(metilsulfonil)-*N*^{1}-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(metilsulfonil)-*N*^{1}-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(metilsulfonil)-*N*^{1}-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^2-(ciclopropilsulfonil)-*N*^{1}-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(isobutilsulfonil)-*N*^{1}-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(ciclopropilsulfonil)-*N*^{1}-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-acetil-*N*^{2}-metil-*N*^{1}-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(2,2-dimetilpropanoil)-N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(2,2-dimetilpropanoil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

(S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de isobutilo;

(S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de ciclopentilo;

N^2-[(*tert*-butilamino)carbonil]-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-[(ciclopentilamino)carbonil]-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

3-(trifluorometil)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida;

3-(trifluorometil)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida;

3-(trifluorometil)-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida;

3-(trifluorometil)-*N*-{(3a*R*,4*R*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida;

3-(trifluorometil)-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida;

N-{(3a*S*,4*R*,6a*R*)-2-[6,6-bis(4-fluorofenil)hexil]octahidrociclopenta[*c*]pirrol-4–

il}-3-(trifluorometil)bencenosulfonamida;

N-{(3a*S*,4*R*,6a*R*)-2-[3,5-bis(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-3-(trifluorometil)bencenosulfonamida;

N-{(3a*S*,4*R*,6a*R*)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-3-(trifluorometil)bencenosulfonamida;

N-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-3-(trifluorometil)bencenosulfonamida;

N-[(3a*S*,4*S*,6a*R*)-2-(4-hidroxibutil)octahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida;

(3a*S**,4*S**,6a*R**)-*N*,*N*-diciclopropil-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4-amina;

(3a*S**,4*R**,6a*R**)-2-bencil-*N*-ciclopropiloctahidrociclopenta[*c*]pirrol-4-amina;

(3a*S**,4*S**,6a*R**)-2-bencil-*N*-ciclopropiloctahidrociclopenta[*c*]pirrol-4-amina;

N-[(3a*S**,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*-ciclopropil-3-(trifluorometil)bencenosulfonamida;

N-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*-ciclopropil-3-(trifluorometil)bencenosulfonamida;

N-ciclopropil-*N*-[(3a*S**,4*S**,6a*R**)-octahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida;

N-{(3a*S**,4*S**,6a*R**)-2-[6,6-bis(4-fluorofenil)hexil]octahidrociclopenta[*c*]pirrol-4–il}-*N*-ciclopropil-3-(trifluorometil)bencenosulfonamida;

N-{(3a*S**,4*S**,6a*R**)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-*N*-ciclopropil-3-(trifluorometil)bencenosulfonamida;

N-ciclopropil-3-(trifluorometil)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida;

2,2-diciclohexil-*N*-((3a*S*,4*S*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)acetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[(2-feniletil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-((3a*S*,4*S*,6a*R*)-2-{[2-(1-naftil)etil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)acetamida;

2,2-diciclohexil-*N*-((3a*S*,4*S*,6a*R*)-2-{[3-(trifluorometil)bencil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)acetamida;

2,2-diciclohexil-*N*-((3a*S*,4*S*,6a*R*)-2-{[2-(4-fluorofenil)etil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)acetamida;

(2*S*)-2-fenil-*N*-{(3a*R*,4*R*,6a*S*)-2-[(1*S*)-1-feniletil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

(2*S*)-2-fenil-*N*-{(3a*R*,4*S*,6a*S*)-2-[(1*S*)-1-feniletil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

(2*S*)-2-fenil-*N*-{(3a*S*,4*S*,6a*R*)-2-[(1*S*)-1-feniletil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

(2*S*)-2-fenil-*N*-{(3a*S*,4*R*,6a*R*)-2-[(1*S*)-1-feniletil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*,3-dimetil-2-fenilbutanamida;

N-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*,3-dimetil-2-fenilbutanamida;

(3a*R**,4*S**,6a*S**)-*N*-bencil-2-(3-metil-2-fenilbutanoil)octahidrociclopenta[*c*]pirrol-4-amina;

2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-2-(*N*,*N*-dimetil-D-leucil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

N-[(3a*R*,4*S*,6a*S*)-2-benzoiloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N'-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*-isopropil-*N*-fenilurea;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida;

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–ilcarbamato de tert-butilo;

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(etil)carbamato de tert-butilo;

(2S,3S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-

metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3,3-dimetil-1-oxobutan-2–ilcarbamato de tert-butilo;

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo;

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxohexan-2–il(metil)carbamato de tert-butilo;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-bis(4-fluorofenil)acetamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-isopropil-3-metilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metilbutanamida;

(2S)-2-({[(3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–il]amino}carbonil)piperidin-1-carboxilato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxobutan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3,3-dimetil-1-oxobutan-2–ilcarbamato de tert-butilo;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-isopropil-3-metilbutanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metilbutanamida;

2-ciclohexil-2-hidroxi-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

(S)-1-((3aS,4S,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aS,4S,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aR,4R,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aR,4R,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

S-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(metilsulfonil)-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(metilsulfonil)-L-leucinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-neopentil-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-neopentil-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-neopentil-L-norvalinamida;

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-morfolin-4–ilpentanamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-pirrolidin-1–ilpentanamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-piperidin-1–ilpentanamida;

N^2-neopentil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-neopentil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-neopentil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-neopentil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-neopentil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-neopentil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-

(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N-(*tert*-butoxicarbonil)-*N*-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida;

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

N^2-neopentil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-neopentil-L-leucinamida;

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(5-(trifluorometil)piridin-2–il)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo;

(S)-1-oxo-1-((3aR,4S,6aS)-2-(5-(trifluorometil)piridin-2–il)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de isopropilo;

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(6-(trifluorometil)piridin-2–il)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo;

(S)-4,4-dimetil-1-((3aR,4S,6aS)-2-(2-(metilsulfonil)pirimidin-5–il)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–ilcarbamato de tert-butilo;

(S)-2-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilcarbamoil)pirrolidin-1-carboxilato de tert-butilo;

(1R)-1-isopropil-3-oxo-3-[((3aS,4R,6aR)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]propilcarbamato de tert-butilo;

(2S)-2-{[((3aS,4R,6aR)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]carbonil}piperidin-1-carboxilato de tert-butilo;

N-(*tert*-butoxicarbonil)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida;

N-(*tert*-butoxicarbonil)-*N*-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida;

(S)-2-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilcarbamoil)pirrolidin-1-

carboxilato de tert-butilo;

(1R)-1-isopropil-3-oxo-3-[((3aR,4S,6aS)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]propilcarbamato de tert-butilo;

metil((S)-3-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo;

(2S)-2-{[((3aR,4S,6aS)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]carbonil}piperidin-1-carboxilato de tert-butilo;

(3S)-3-{[((3aR,4S,6aS)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]carbonil}-3,4-dihidroisoquinolin-2(1H)-carboxilato de tert-butilo;

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo;

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)hexan-2–il)carbamato de tert-butilo;

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

(S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de isopropilo;

(S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de isopropilo;

(3a*S*,4*R*,6a*R*)-*N*-neopentil-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*-neopentil-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*-isopropil-2-{[4-

(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}-*N*-isopropiloctahidrociclopenta[*c*]pirrol-4-amina;

(3a*S*,4*R*,6a*R*)-*N*-(4-fluorobencil)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*-(4-fluorobencil)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*-(4-fluorobencil)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*-etil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*,*N*-dietil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*-propil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*,*N*-dipropil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*-(ciclopropilmetil)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}-*N*-etiloctahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}-*N*,*N*-dietiloctahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}-*N*-[5-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4-amina;

(S)-1-(etil((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-4,4-dimetil-1-oxo-1-(propil((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)pentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((ciclopropilmetil)((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)-4,4-dimetil-1-

oxopentan-2–il(metil)carbamato de tert-butilo;

2-nitro-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)bencenosulfonamida;

N-metil-2-nitro-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)bencenosulfonamida;

(3a*R*,4*S*,6a*S*)-*N*-metil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(S)-4,4-dimetil-1-(metil((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(2*S*)-2-(1,1-dioxidoisotiazolidin-2–il)-4-metil-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}pentanamida;

2-isopropil-3-metil-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

2-isopropil-3-metil-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

(S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo;

metil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

(S)-1-((3aR,4S,6aS)-2-(4-fluorobencil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

etil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-(3-fluoro-4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-(4-fluoro-3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

(S)-1-((3aR,4S,6aS)-2-(4-fluorobencil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo;

metil((S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo;

metil((S)-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-(4-fluorobencil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(2*S*)-4-metil-2-morfolin-4–il-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida;

(2*S*)-4-metil-2-pirrolidin-1–il-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida;

(2*S*)-4-metil-2-piperidin-1–il-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida;

metil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

etil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–

il)carbamato de tert-butilo;

metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-(4-fluoro-3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

metil((S)-1-oxo-1-((3aR,4R,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((S)-4-metil-1-oxo-1-((3aR,4R,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo;

metil((S)-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((2S,3S)-3-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((2S,3S)-3-metil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((2S,3S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((2S,3S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(3-

(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo;

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo;

(S)-4,4-dimetil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo;

(S)-4,4-dimetil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo;

metil((S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo;

(S)-3,3-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–ilcarbamato de tert-butilo;

(S)-3,3-dimetil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–ilcarbamato de tert-butilo;

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)hexan-2–il)carbamato de tert-butilo;

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo;

(2*S*)-4-metil-2-pirrolidin-1–il-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)benzoil]octahidrociclopenta[*c*]pirrol-4–il}pentanamida;

(2*S*)-4-metil-*N*-[(3a*S*,4*R*,6a*R*)-2-(metilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-2-pirrolidin-1–ilpentanamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-(ciclopropilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-pirrolidin-1–ilpentanamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-

leucinamida;

metil((S)-4-metil-1-((3aS,4R,6aR)-octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il)carbamato de tert-butilo;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]piperidin-2-carboxamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-valinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-isoleucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-isoleucinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2,4-dimetil-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-L-valinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-L-valinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2,4-dimetil-L-leucinamida;

N^1-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida;

N^1-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-L-leucinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norleucinamida;

N^1-[(3a*R*,4*R*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida;

N^1-[(3a*R*,4*R*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*^{2}-metil-L-norvalinamida;

N^2-etil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-metil-*N*^{1}-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-valinamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]piperidin-2-carboxamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-*N*^{2}-metil-L-valinamida;

(2*S*)-*N*-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}piperidin-2-carboxamida;

N^2-metil-*N*^{1}-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-*N*^{2}-metil-L-norvalinamida;

N^2-metil-*N*^{1}-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-valinamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-*N*^{2}-metil-L-leucinamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[4-fluoro-3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-*N*^{2}-metil-L-leucinamida;

N^2-metil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida;

N^2-metil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-*N*^{2}-metil-L-norvalinamida;

N^2-metil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-metil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-*N*^{2}-

metil-L-leucinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida;

N^2-etil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida;

N-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida;

N-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-prolinamida;

(3*R*)-3-amino-4-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida;

(2*S*)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)piperidin-2-carboxamida;

(3*S*)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-1,2,3,4-tetrahidroisoquinolin-3-carboxamida;

4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norleucinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-prolinamida;

(3*R*)-3-amino-4-metil-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-

(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida;

(2*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)piperidin-2-carboxamida;

(2*S*)-*N*-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}piperidin-2-carboxamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-valinamida;

(2*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)piperidin-2-carboxamida;

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida;

N^1-((3a*S*,4*R*,6a*R*)-2-{[4-fluoro-3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-metil-L-leucinamida;

3-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida;

3-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-isoleucinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-isoleucinamida;

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-isoleucinamida;

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-isoleucinamida;

N^2,4-dimetil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2,4-dimetil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2,4-dimetil-*N*^{1}-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2,4-dimetil-*N*^{1}-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norleucinamida;

4-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-metil-*N*^{1}-((3a*R*,4*R*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-metil-*N*^{1}-((3a*R*,4*R*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

3-ciclohexil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-alaninamida;

3-ciclohexil-*N*^{2}-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-alaninamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-5-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-4-metil-L-leucinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-4-metil-L-leucinamida;

N-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-

(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-*N*^{2},4-dimetil-L-leucinamida;

N-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-*N*-metil-L-fenilalaninamida;

N^1-ciclopropil-*N*^{2},4-dimetil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^1-etil-*N*^{2},4-dimetil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2,4-dimetil-*N*^{1}-propil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^1-(ciclopropilmetil)-*N*^{2},4-dimetil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^1,*N*^{2},4-trimetil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^1,*N*^{2}-dimetil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-*N*^{1},*N*^{2},4-trimetil-L-leucinamida;

4-metil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

4-metil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

4-metil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[2-(metilsulfonil)pirimidin-5–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-*N*^{2}-metil-L-leucinamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-*N*^{2}-metil-L-leucinamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3,4-difluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–

il}-N^2-metil-L-leucinamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3,5-difluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-clorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida;

N^2-metil-N^1-[(3a*S*,4*R*,6a*R*)-2-(fenilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-L-leucinamida;

N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-valinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-4-metil-L-leucinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norleucinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida;

N^2-metil-N^1-((3a*S*,4*S*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-metil-N^1-((3a*S*,4*S*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

2,2-bis(4-fluorofenil)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-bis(4-fluorofenil)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-metil-L-norvalil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

N-[(3a*R*,4*S*,6a*S*)-2-(*N*,4-dimetil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-2,2-bis(4-fluorofenil)acetamida;

2,2-bis(4-fluorofenil)-*N*-[(3a*R*,4*S*,6a*S*)-2-(4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

(S)-1-((3aR,4S,6aS)-4-((S)-2-(tert-butoxicarbonilamino)-4,4-dimetilpentanamido)hexahidrociclopenta[c]pirrol-2(1H)–il)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo;

4-metil-N^1-[(3a*R*,4*S*,6a*S*)-2-(4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-L-leucinamida;

4-metil-N^1-[(3a*R*,4*S*,6a*S*)-2-L-fenilalanilóctahidrociclopenta[*c*]pirrol-4–il]-L-leucinamida;

(3a*R*,4*S*,6a*S*)-*N*-benzhidril-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4-amina;

(3a*S*,4*R*,6a*R*)-*N*-benzhidril-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*-benzhidril-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzhidriloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida;

4-metil-N^2-propil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-(ciclopropilmetil)-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-(ciclobutilmetil)-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-isobutil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-(ciclopentilmetil)-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-(ciclohexilmetil)-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-butil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-etil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-(ciclopropilmetil)-4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(ciclopropilmetil)-4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-isopropil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-isopropil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-isopropil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-isopropil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-isopropil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

3-ciclohexil-N^2-isopropil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-alaninamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-5-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-isopropil-4-metil-L-leucinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-isopropil-4-metil-L-leucinamida;

N^2-isopropil-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropil-4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-4-metil-L-leucinamida;

N^2-isopropil-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropil-L-fenilalanil)octahidrociclopenta[*c*]pirrol-4–il]-4-metil-L-leucinamida;

N^2-isopropil-4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-isopropil-4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

2,2-bis(4-fluorofenil)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropil-4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

N^2-isopropil-4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[2-(metilsulfonil)pirimidin-5–

il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*^{2}-isopropil-L-norvalinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*^{2}-isopropil-L-norvalinamida;

N^2-isopropil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2,*N*^{2}-dimetil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

(3*R*)-3-(dimetilamino)-4-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida;

N^2-ciclopropil-4-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2,*N*^{2}-diciclopropil-4-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-ciclopentil-4-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-ciclohexil-4-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-(1-etilpropil)-4-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-ciclobutil-4-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

4-metil-*N*^{2}-neopentil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-ciclopentil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-ciclohexil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-ciclopentil-*N*^{1}-[(3a*R*,4*S*,6a*S*)-2-(*N*-ciclopentil-4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-4-metil-L-leucinamida;

N^2,*N*^{2}-dimetil-*N*^{1}-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-N^2-neopentil-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(3,3-dimetilbutil)-N^2-metil-L-leucinamida;

N^2,N^2-dimetil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(4-fluorobencil)-N^2-metil-L-leucinamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-(metilsulfonil)piperidin-2-carboxamida;

(3*R*)-4-metil-3-[(metilsulfonil)amino]-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida;

N^2-(metilsulfonil)-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(metilsulfonil)-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^2-etil-N^2-(metilsulfonil)-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

4-metil-N^2-(metilsulfonil)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

3-metil-N^2-(metilsulfonil)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-valinamida;

N^2-(metilsulfonil)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida;

N^2-(isopropilsulfonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(fenilsulfonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(ciclopentilsulfonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de isopropilo;

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(S)-3,3-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–ilcarbamato de isopropilo;

(S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de ciclopentilo;

N^2-(2,2-dimetilpropanoil)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida;

(S)-1-((3aR,4S,6aS)-2-(3-cloro-4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo;

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(piridin-3–ilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(tiofen-2–ilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometoxi)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-metil-N^1-[(3a*R*,4*S*,6a*S*)-2-(tien-2–ilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-cloro-4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

N^2-metil-N^1-[(3a*R*,4*S*,6a*S*)-2-(piridin-3–ilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-cianofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-metoxifenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[3,5-bis(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-metil-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(2-cloro-4-

fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-*N*^{2}-metil-L-norvalinamida;

N^2-metil-*N*^{1}-[(3a*R*,4*S*,6a*S*)-2-(1-naftilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-L-norvalinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[4-bromo-3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-*N*^{2}-metil-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3,4-diclorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-*N*^{2}-metil-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-*tert*-butilfenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-*N*^{2}-metil-L-norvalinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-(1,1'-bifenil-4–ilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-*N*^{2}-metil-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3,4-dimetoxifenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-*N*^{2}-metil-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-cianofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-*N*^{2}-metil-L-norvalinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-(2-furilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-*N*^{2}-metil-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(2,3-diclorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-*N*^{2}-metil-L-norvalinamida;

N^2-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)bencil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[2-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-bromofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-*N*^{2}-metil-L-norvalinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-*N*^{2}-metil-L-norvalinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-5-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-*N*^{2}-metil-L-norvalinamida;

N^2-metil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[3-

(trifluorometil)benzoil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*-isopropil-3-(trifluorometil)bencenosulfonamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida;

N-isopropil-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida;

N-[(3a*R*,4*S*,6a*S*)-2-(*N*-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida;

N-ciclopropil-*N*-[(3a*S**,4*S**,6a*R**)-[2-(*N*-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida; y

4-fluoro-*N*-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}benzamida.

Cuando hay centros asimétricos o quirales presentes, los compuestos de la presente solicitud pueden existir como estereoisómeros. Estos estereoisómeros son "R" o "S", dependiendo de la configuración de los sustituyentes alrededor del átomo de carbono quiral. Los términos "R" y "S" usados en la presente son las configuraciones definidas en IUPAC, 1974, *Recommendations for Section E, Fundamental Stereochemistry, Pure Appl. Chem.*, 1976, 45: 13-30.

En ocasiones, se conoce la estereoquímica relativa de un par enantiomérico, sin embargo, se desconoce la configuración absoluta. Bajo dicha circunstancia, se usan los términos que describen la estereoquímica relativa "*R**" y "*S**". Los términos "*R**" y "*S**" usados en la presente están definidos en Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; John Wiley & Sons, Inc.: Nueva York, 1994; páginas 119-120 y 1206. En un par enantiomérico particular, se invierten los descriptores relativos para indicar que se desconoce la estereoquímica absoluta de este par de enantiómeros.

En la presente solicitud se contemplan diversos estereoisómeros y mezclas de los mismos, y se los incluye específicamente dentro del alcance de esta solicitud. Los estereoisómeros incluyen enantiómeros y diastereómeros, y mezclas de enantiómeros o diastereómeros. Los estereoisómeros individuales de los compuestos de la presente solicitud se pueden preparar mediante síntesis a

partir de materiales de partida disponibles comercialmente que contienen centros asimétricos o quirales o mediante preparación de las mezclas racémicas seguido por resolución como es bien conocido por los especialistas en la técnica. Estos métodos de resolución se pueden ejemplificar mediante (1) unión de una mezcla de enantiómeros a un auxiliar quiral, separación de la mezcla resultante de diastereómeros por recristalización o cromatografía y liberación del producto ópticamente puro del auxiliar o (2) separación directa de la mezcla de enantiómeros ópticos sobre columnas de cromatografía quiral.

Los compuestos de la presente pueden presentarse como isómeros geométricos. La invención contempla los diversos isómeros geométricos y mezclas de los mismos causados por la disposición de los sustituyentes alrededor de un doble enlace carbono-carbono, un doble enlace carbono-nitrógeno, un grupo cicloalquilo o un grupo heterocíclico. Los sustituyentes que rodean un doble enlace carbono-carbono o un enlace carbono-nitrógeno se denominan según su configuración Z o E y los sustituyentes que rodean un cicloalquilo o heterociclo se denominan según su configuración cis o trans.

Se comprenderá que en la presente invención los compuestos divulgados aquí pueden presentar el fenómeno de tautomería.

Por lo tanto, en las figuras de las fórmulas en esta memoria descriptiva pueden ilustrarse solamente una de las formas tautoméricas o estereoisoméricas posibles. Se debe comprender que la invención abarca a todas las formas tautoméricas o estereoisoméricas, y mezclas de las mismas, y no se la debe limitar a una ninguna de las formas tautoméricas o estereoisoméricas que se utilizan en la nomenclatura de los compuestos o figuras de las fórmulas.

Los compuestos de esta invención pueden existir en una forma isotópica que contiene uno o más átomos que tienen una masa atómica o un número másico diferente de la masa atómica o del número másico más abundante en la naturaleza. Los isótopos de átomos tales como hidrógeno, carbono, fósforo, azufre, flúor, cloro y iodo incluyen, pero en un sentido no limitativo, ^{2}H, ^{3}H, ^{11}C, ^{14}C, ^{32}P, ^{35}S, ^{18}F, ^{36}Cl, y ^{125}I, respectivamente. Los compuestos que contienen otros isótopos de estos y/o de otros átomos se encuentran dentro del alcance de esta invención. Se prefieren en general los compuestos que contienen los radioisótopos tritio (^{3}H) y ^{14}C por su fácil preparación y detectabilidad de

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compuestos marcados radioactivamente. Los compuestos marcados con isótopos de esta invención se pueden preparar mediante los métodos generales bien conocidos por los especialistas en la técnica. Dichos compuestos marcados con isótopos se pueden preparar convenientemente utilizando los procedimientos divulgados en la sección de los Ejemplos y Esquemas por sustitución de un reactivo marcado con isótopos de fácil acceso por un reactivo no marcado.

c. Datos biológicos

Las abreviaturas que se usaron en las descripciones de los Datos biológicos que se describen a continuación son: EDTA por ácido etilendiamintetracético; FBS por suero fetal bovino; FLIPR por lector de placas con imágenes fluorométricas; HBSS por solución balanceada de sales de Hank; HEPES por ácido 4-(2-hidroxietil)-1-piperazinetansulfónico; i.p. por intraperitoneal; MEM por medio mínimo esencial; MEM NEAA por medio mínimo esencial con aminoácidos no esenciales; p.o. por *per orem* (por vía oral/bucal).

(i) Métodos in vitro: Evaluación de la actividad de los canales de calcio usando FLIPR:

Se evaluaron células IMR32 que expresan de manera endógena $Ca_v2.2$ humanos por el influjo de Ca^{2+} usando un colorante indicador de calcio sin lavado (Calcium 4 dye: Molecular Probes) y la tecnología FLIPR (Lubin, M. L.; Reitz, T. L.; Todd, M. J.; Flores, C. M.; Qin, N.; Xin, H. *A nonadherent cell-based HTS assay for N-type calcium channel using calcium 3 dye. Assay and Drug Development Technologies,* 2006, 4(6), 689-694.). Las células IMR32 se mantuvieron en medio MEM que contiene FBS 10% (v/v), antibiótico/antimitótico 1% (v/v), piruvato sodio 1% (v/v) y MEM NEAA 1% (v/v). Después de disociación en tripsina/EDTA 0,05% (v/v), las células se sembraron en placas negras de 96 cavidades (Corning Cellbind) a una densidad de 1-1,2 x 10^5 células/cavidad y se incubaron en el medio de mantenimiento anterior durante 48 horas a 37 °C. Inmediatamente antes de conducir el ensayo, se removió el medio y las células se cargaron por 1,5 horas con 1 x colorante de Calcio 4 preparado en HBSS (NaCl 137 mM, KCl 5,4 mM, Na_2HPO_4 0,25 mM, KH_2PO_4 0,44 mM, $CaCl_2$ 1,3 mM, $MgSO_4$ 1 mM, $NaHCO_3$ 4,2 mM) que contiene HEPES pH 7,4 a temperatura ambiente. Después de cargar el colorante y una subsiguiente pre-incubación de 3 minutos o 60 minutos con los compuestos (diluciones logarítmicas completas de 10 μM a 0,1 nM) en la

presencia de $CaCl_2$ 1,3 mM y nifedipina 2 μM para bloquear los canales tipo L endógenos, se incrementó la concentración externa de Ca^{2+} a $CaCl_2$ 5 mM y las células se despolarizaron concomitantemente con KCl 80 mM para evaluar la actividad de los canales. Para determinar los valores IC_{50}, se determinó el porcentaje de inhibición del compuesto a cada concentración con relación a la actividad en la ausencia de inhibidor, y los datos se ajustaron usando un análisis de una curva de dosis-respuesta sigmoidal por regresión no lineal con GraphPad Prism®.

Ejemplo	**IC_{50} (μM) o porcentaje de inhibición (* indica 3 minutos de incubación, sino es de 60 minutos)**	**Ejemplo**	**IC_{50} (μM) o porcentaje de inhibición (* indica 3 minutos de incubación, sino es de 60 minutos)**
1	3,5*	**271**	3,41
2	4,2*	**272**	5,14
3	91% @ 10 μM	**273**	0,18
4	3,5*	**274**	1,38
5	3,8*	**275**	0,92
6	2,2*	**276**	0,38
7	1,8*	**277**	0,72
8	1,1	**278**	0,34
9	1,8*	**280**	5,04
10	1,3*	**281**	4,18
11	4	**282**	5,24
13	23	**283**	8,69
14	3,8	**284**	3,71
15	15,7	**285**	0,48
16	9,8	**286**	0,38
17	1,6	**287**	3,09
18	2,7	**288**	10,36
19	25% @ 10 μM *	**289**	9,74
20	1,8	**290**	7,80
21	10,1*	**291**	4,40
22	14,7*	**292**	3,91
23	2,5	**293**	4,82
24	2,9*	**294**	7,81
25	3,7*	**295**	2,97
26	17,3*	**296**	2,14
27	9,7*	**297**	7,88
28	13,9*	**298**	9,00
29	5,6*	**299**	3,68
30	1,8	**300**	1,54
31	1,6	**302**	1,14

32	1,4	**303**	3,11
33	7,4	**304**	3,78
34	1,5	**305**	3,51
35	3,3	**306**	0,50
36	44% @ 10 μM*	**307**	1,54
37	15% @ 10 μM*	**308**	1,93
38	27% @ 10 μM*	**309**	1,74
39	92% @ 10 μM*	**310**	0,68
40	3,6*	**311**	2,05
41	56% @ 10 μM*	**312**	1,59
43	1,5	**313**	2,10
44	1,7*	**314**	2,15
46	3,1*	**315**	5,36
47	15,6*	**316**	2,02
48	10,5*	**317**	0,90
49	4,6*	**318**	1,07
50	5,0*	**319**	1,21
51	15,2*	**320**	0,70
52	3,4	**321**	0,44
53	8,6	**322**	0,70
54	0,5	**323**	0,20
55	0,8	**324**	0,69
56	1	**325**	0,25
57	0,3	**326**	1,46
58	1,4	**327**	1,83
59	0,5	**328**	1,38
60	1,5	**329**	2,60
61	1,5	**330**	1,11
62	1,6	**331**	0,75
63	0,6	**332**	0,48
64	1,3	**333**	0,57
65	4,5	**334**	0,69
66	0,9	**335**	0,83
67	1,3	**336**	0,48
68	1,7	**337**	0,78
69	1,7	**338**	0,23
70	1,9	**339**	1,11
71	1,2	**340**	1,03
72	3,2	**341**	2,01
73	3,3	**342**	2,17
74	11,2*	**343**	1,01
75	0,5	**344**	0,99
76	5,7	**345**	4,32
77	9,4	**349**	17,65
78	0,4	**358**	9,00
79	0,9	**361**	24,74
80	1,7	**364**	8,12

81	1,1	**366**	5,28
82	1,5	**367**	7,00
83	2,6*	**368**	12,42
84	5,8% @ 10 μM*	**370**	6,02
85	3,6	**371**	8,89
86	1,6	**373**	7,58
87	3,1	**374**	5,36
88	1,2	**375**	8,22
89	2	**376**	10,63
90	83% @ 10 μM*	**377**	13,37
91	1,8	**379**	8,59
92	2	**380**	9,73
93	3,3	**382**	14,42
94	2,3	**383**	0,80
95	1	**384**	1,14
96	2,4*	**385**	1,85
97	5,3*	**386**	1,62
98	4,9*	**387**	5,88
99	4,8*	**388**	4,53
100	4,2*	**389**	1,48
101	4,7*	**390**	2,46
102	2,8	**391**	1,46
103	31*	**392**	0,95
104	79% @ 10 μM*	**393**	1,08
105	1,5	**394**	0,98
106	5,8*	**395**	2,12
107	1,1	**396**	3,55
108	11,3*	**397**	1,45
109	9,0*	**398**	3,25
110	2,0*	**399**	15,29
111	2,2*	**400**	6,86
112	2,8*	**401**	2,96
113	3,1*	**402**	2,06
114	2,8*	**403**	8,66
115	1,2	**404**	1,02
116	1,2	**405**	3,84
117	0,9	**406**	3,69
118	1	**407**	5,43
119	1,1	**408**	5,11
120	3,4	**409**	5,02
121	14,3	**410**	1,80
122	0,6	**411**	4,22
123	0,6	**412**	4,72
124	0,7	**413**	0,78
125	2,8	**414**	0,90
126	1	**415**	2,97
127	1,5	**416**	1,33

128	1	**417**	1,16
129	2,9	**418**	0,82
130	0,8	**419**	0,80
131	0,7	**420**	5,70
132	1,1	**421**	2,56
133	0,7	**422**	7,83
134	1,2	**423**	6,46
135	0,9	**424**	3,11
136	1,1	**425**	3,21
137	0,6	**426**	1,79
138	0,8	**427**	6,45
139	1	**428**	2,31
140	0,6	**429**	0,96
141	0,6	**430**	1,75
142	0,9	**431**	0,58
143	0,6	**432**	1,67
144	1	**433**	1,26
145	1,2	**434**	2,70
146	0,8	**435**	2,32
147	0,5	**436**	1,77
148	0,8	**437**	2,43
149	0,6	**438**	5,70
150	0,5	**439**	1,43
151	0,7	**440**	3,19
152	0,8	**441**	0,37
153	0,4	**442**	7,18
154	1,3	**443**	7,68
155	0,7	**444**	2,11
156	0,8	**445**	7,96
157	2,1	**446**	4,96
158	3,5	**447**	2,71
159	5,6	**448**	12,35
160	3,8	**449**	4,06
161	3,9	**450**	9,25
162	3,9	**451**	0,80
163	4,6	**452**	9,12
164	1,6	**453**	4,23
165	33,3	**454**	2,03
166	2,7	**455**	3,03
167	1,2	**456**	5,33
168	12,9	**457**	3,07
169	0,9	**458**	3,08
170	4,6	**459**	1,62
171	6,2	**460**	2,69
172	2	**461**	1,88
173	1,8	**462**	2,96
174	1	**463**	2,03

175	1,5	**466**	2,33
176	0,9	**467**	3,49
177	2,6	**468**	2,25
178	1	**469**	2,24
179	0,9	**470**	1,03
180	1,8	**471**	0,65
181	0,9	**472**	1,27
182	1,5	**473**	2,66
183	1,4	**474**	1,74
184	1,5	**475**	1,84
185	0,9	**476**	1,31
186	0,6	**477**	1,88
187	1,2	**478**	0,75
188	0,8	**479**	0,25
189	1	**480**	1,31
190	1,3	**481**	2,28
191	0,5	**482**	1,97
192	2,3	**483**	0,49
193	0,6	**484**	0,97
194	1,4	**485**	1,50
195	22,1	**486**	1,21
196	3,2	**487**	0,56
197	69,7	**488**	7,43
198	40,4	**489**	9,76
199	2,2	**490**	3,12
200	1	**491**	0,26
201	5,2	**492**	2,00
202	0,8	**493**	5,08
203	1,6	**496**	0,53
204	1,3	**497**	0,57
205	3,4	**498**	1,58
206	>100	**499**	2,70
207	>100	**500**	1,70
208	>100	**501**	0,82
209	>100	**502**	0,97
210	76% @ 10 μM*	**503**	0,89
211	3,8	**504**	0,91
212	4,1	**505**	2,24
213	60% @ 10 μM*	**506**	1,72
215	2	**507**	0,87
216	85% @ 10 μM*	**508**	8,60
217	1,3	**509**	4,56
218	56% @ 10 μM*	**510**	1,68
219	63% @ 10 μM*	**511**	2,12
220	>9	**512**	0,47
221	3,93	**513**	2,15
222	2,05	**515**	3,17

223	2,06	**516**	2,99
224	4,64	**517**	4,45
225	9,38	**518**	0,81
226	4,06	**519**	5,14
227	3,17	**520**	12,82
228	2,09	**521**	9,60
229	13,10	**522**	2,90
231	6,14	**523**	4,43
232	3,60	**524**	2,07
233	2,81	**525**	1,39
234	7,40	**526**	2,77
235	14,23	**527**	2,29
237	1,88	**528**	7,23
238	5,73	**529**	0,96
239	3,31	**530**	7,63
240	2,67	**531**	3,49
241	2,09	**532**	3,16
242	7,92	**533**	9,69
243	8,59	**534**	6,38
244	9,10	**536**	8,38
245	8,08	**537**	11,32
246	8,39	**538**	3,76
247	3,62	**539**	4,39
248	1,67	**540**	1,67
252	0,64	**541**	2,57
253	0,36	**542**	2,36
254	0,72	**543**	3,21
255	0,55	**544**	2,15
256	1,38	**546**	6,32
257	0,70	**548**	1,05
258	0,85	**549**	2,74
259	1,14	**550**	2,57
260	1,11	**551**	2,49
261	1,26	**552**	0,78
262	1,80	**553**	1,94
264	0,28	**554**	10,32
265	2,62	**555**	2,51
266	0,87	**556**	2,58
267	14,06	**557**	1,14
268	0,73	**558**	4,88
269	1,90	**559**	1,68
270	0,77	**560**	1,45

(ii) Datos in vivo: Modelo de hiperalgesia mecánica secundaria inducida por capsaicina:

Se restringió brevemente el movimiento de ratas Sprague Dawley, y se

administró capsaicina a una dosis de 10 µg en 10 µl de vehículo por inyección intraplantar en el centro de la pata trasera derecha. Se midió la hiperalgesia mecánica secundaria (SMH) en el talón alejado del sitio de inyección, 180 minutos después de la exposición a capsaicina. Los compuestos y gabapentina (control positivo), se administraron p.o. 60 minutos antes de la prueba (2 horas después de la capsaicina) o i.p. 30 minutos antes de la prueba (2,5 horas después de la capsaicina). La SMH se midió usando filamentos von Frey calibrados (Stoelting, Woodale, IL). Después de 1 hora de habituación en el cuarto de pruebas, las ratas se llevaron a cámaras individuales de plexiglass que descansan sobre una malla de alambre, lo que permitirá estimular la superficie plantar de las patas traseras. Se dejó que las ratas se habituaran a las cámaras nuevas durante 15 minutos antes de comenzar la prueba. El umbral de abstinencia de patas se determinó aumentando y disminuyendo la intensidad del estímulo (fuerza: g) y se calculó usando el método de arriba-abajo [*up-down*] de Dixon (Chaplan, S. R.; Bach, F. W.; Pogrel, J. W.; Chung, J. M.; Yaksh, T. L.; *Quantitative assessment of tactile allodynia in the rat paw. J. Neuroscience Methods* 1994, 53(1), 55-63.). Los filamentos (fuerza máxima de 15,0 g) se mantuvieron en su lugar por 8 segundos o hasta que se observaba una respuesta de abstinencia por la estimulación mecánica.

Ejemplo	% de inhibición @ 30 mg/kg p.o.	Ejemplo	% de inhibición @ 30 mg/kg p.o.
54	38	**405**	32
75	85	**415**	52
156	67	**461**	43
157	57	**478**	57
165	92	**479**	40
170	57	**480**	64
172	85	**488**	55
183	78	**489**	47
220	76	**560**	42
280	38		

d.Métodos de uso de los compuestos

Una forma de realización de la presente invención proporciona un método de tratamiento del dolor en un sujeto que lo necesita. El método comprende la administración al sujeto, incluyendo un mamífero tal como un ser humano, de una

cantidad terapéuticamente adecuada de un compuesto de la fórmula (I), o una sal farmacéuticamente aceptable del mismo. Las condiciones relacionadas con el dolor incluyen dolor agudo, dolor crónico, dolor neuropático, dolor inflamatorio, dolor visceral, dolor de cáncer, alodinia, fibromialgia, ciática, dolor de espalda y dolor de cabeza incluyendo migraña, o combinaciones de los mismos. Preferentemente, el método comprende administrarle al mamífero una cantidad terapéuticamente eficaz de cualquiera de los compuestos que se describen en la presente, o una sal farmacéuticamente aceptable del mismo. En determinadas formas de realización, el método comprende administrarle al mamífero una cantidad terapéuticamente eficaz de cualquier de los compuestos que se describen en la presente, o una sal farmacéuticamente aceptable del mismo, en combinación con uno o más de los siguientes: una droga antiinflamatoria no esteroide (NSAID), un analgésico opioide, un barbiturato, una benzodiazapina, una antagonista de histamina, un sedante, un relajante de la musculatura esquelética, un antagonista del potencial de canales iónicos de un receptor transitorio, un α-adrenérgico, un antidepresivo tricíclico, un anticonvulsionante, un antagonista de taquiquinina, un antagonista muscarínico, un inhibidor selectivo de ciclooxigenasa-2, un neuroléptico, un agonista del receptor vanilloide, un antagonista del receptor vanilloide, un β-adrenérgico, un anestésico local, un corticosteroide, un agonista del receptor 5-HT, un antagonista del receptor 5-HT, un antagonista del receptor 5-HT_{2A}, un analgésico colinérgico, un ligando $\alpha_2\delta$ tal como gabapentina o pregabalina, un ligand del receptor cannabinoide, un antagonista del receptor de glutamato metabotrópico del subtipo 1, un inhibidor de recaptación de serotonina, inhibidor de recaptación de norepinefrina, un inhibidor de recaptación doble de serotonina-noradrenalina, un inhibidor de Rho quinasa, un inhibidor de la óxido nítrico sintasa inducible, un inhibidor de acetilcolinesterasa, un antagonista de prostaglandina E_2 subtipo 4, un antagonista de leucotrieno B4, un inhibidor de 5-lipoxigenasa, un bloqueante de los canales de sodio, un antagonista de 5-HT3, un antagonista del receptor ácido N-metil-D-aspártico y un inhibidor de fosfodiesterasa V.

Aún otra forma de realización de la presente invención se relaciona con un método para tratar trastornos del sistema nervioso central incluyendo accidente cerebrovascular, epilepsia, depresión maníaca, trastornos bipolares, depresión,

ansiedad, esquizofrenia, migraña y psicosis; trastornos degenerativos neurales incluyendo mal de Alzheimer, demencia relacionada con SIDA, enfermedad de Parkinson, neuropatía causada por lesión de la cabeza y demencia causada por trastornos cerebrovasculares; trastornos del tracto urinario inferior incluyendo vejiga superactiva, prostatis, prostadinia, cistitis intersticial e hiperplasia prostática benigna; trastornos causados por estrés psicogénico incluyendo asma bronquial, angina inestable e inflamación de colon hipersensible; trastornos cardiovasculares incluyendo hipertensión, aterosclerosis, insuficiencia cardíaca y arritmias cardíacas; síntomas de abstinencia por adicción a drogas, incluyendo síntomas de abstinencia por adicción a etanol; trastornos de la piel incluyendo pruritis y dermatitis alérgica, enfermedad de intestino inflamatorio; cáncer; diabetes; y esterilidad y disfunción sexual en un mamífero que necesita dicho tratamiento. Este método comprende la administración al mamífero (incluyendo un ser humano) una cantidad terapéuticamente eficaz de un compuesto de la invención o una sal farmacéuticamente aceptable del mismo.

Los bloqueantes de los canales de calcio se han asociado con un riesgo disminuido ligeramente mayor de un accidente cerebrovascular en comparación con otros tipos de agentes antihipertensivos (Angeli, F.; et al., *Calcium channel blockade to prevent stroke in hypertension*. *American Journal of Hypertension*, 2004, 17(9), 817-822). El mayor efecto no se correlaciona con diferencias en la presión sanguínea sistólica y aún se desconoce el mecanismo de acción. Sin embargo, los bloqueantes de los canales de calcio se han asociado con el bloqueo del influjo de calcio neuronal central y la subsiguiente lesión isquémica en dos modelos de roedores (Barone, F. C.; et al., *SB 201823-A antagonizes calcium currents in central neurons and reduces the effects of focal ischemia in rats and mice*. *Stroke*, 1995, 26, 1683-1690.). En otro modelo de isquemia global, un bloqueante de canales de calcio ofreció neuroprotección si bien no de manera permanente (Colbourne, F.; et al., *Continuing postischemic neuronal death in CA1: Influence of ischemia duration and cytoprotective doses of NBQX and SNX-111 in rats. Stroke*, 1999, 30(3), 662-668.). Además, se ha observado un retardo en el avance de aterosclerosis de carótidas con el uso de un bloqueante de canales de calcio (Zanchetti, A.; et al., *Calcium antagonist lacidipine slows down progression of asymptomatic carotid atherosclerosis*. Los principales resultados del estudio

europeo de lacidipina sobre aterosclerosis (ELSA), un ensayo randomizado, doble ciego, a largo plazo. *Circulation*, 2002, 106, r47-r52.).

Se ha correlacionado un incremento en la concentración de calcio intracelular con la actividad de convulsiones (Heinemann, U.; et al., *Extracellular free calcium and potassium during paroxysmal activity in the cerebral cortex of the cat. Exp. Brain Res.* 1977, 27, 237-243.). Diversos estudios han indicado que los bloqueantes de los canales de calcio producen actividad anticonvulsionante (Vezzani, A.; et al., *Effects of various calcium channel blockers on three different models of limbic seizures in rats. Neuropharmacology*, 1988, 27(5), 451-458. Otoom, S.; et al., *Nifedipine inhibits picrotoxin-induced seizure activity: further evidence on the involvement of L-type calcium channel blockers in epilepsy. Fundamental & Clinical Pharmacology*, 2006, 20, 115-119.).

Los bloqueantes de los canales de calcio han sido evaluados en el tratamiento de trastornos bipolares y depresión maníaca por décadas. Se ha sugerido que el subtipo del canal de calcio afecta la eficacia de estos trastornos (Gitlin, M. *Treatment-resistant bipolar disorder. Molecular Psychiatry*, 2006, 11, 227-240. Levy, N. A.; Janicak, P. G., *Bipolar Disorders*, 2000, 2, 108-119.).

Los bloqueantes de los canales de calcio también se han asociado con el tratamiento de ansiedad y depresión (Saade, S.; et al., *The L-type calcium channel blocker nimodipine mitigates "learned helplessness" in rats. Pharmacology, Biochemistry and Behavior*, 2003, 74, 269-278.).

Se ha encontrado que las drogas antiesquizofrénicas son antagonistas de los canales de calcio (Gould, R. J.; et al., *Antischizophrenic drugs of the diphenylbutylpiperidine type act as calcium channel antagonists. Proc. Natl. Acad. Sci.* EE.UU., 1983, 80, 5122-5125.). Se han sugerido otros bloqueantes de los canales de calcio para el tratamiento de esquizofrenia (Tort, A. B. L.; et al., *Atypical antipsychotic profile of flunarizine in animal models. Psychopharmacology*, 2005, 177, 344-348.).

Las migrañas se tratan con bloqueantes de los canales de calcio (Arulmoshi, D. K.; et al., *Migraine: Current concepts and emerging therapies. Vascular Pharmacology*, 2005, 43, 176-187. Gladstone, J. P.; et al., *Current and emerging treatment options for migraine and other primary headache disorders. Expert Rev. Neurotherapeutics*, 2003, 3(6), 845-872.).

Los trastornos del tracto urinario inferior, incluyendo vejiga superactiva, prostatis, prostadinia, cistitis intersticial e hiperplasia prostática benigna, pueden ser tratados con bloqueantes de los canales de calcio (Fraser, M. O.; et al., US20050148587, 2005).

El síndrome de abstinencia de etanol disminuye con los bloqueantes de los canales de calcio (Little, H. J.; et al., *Calcium channel antagonists decrease the ethanol withdrawal syndrome. Life Sciences*, 1986, 39, 2059-2065.).

Diversos trastornos cardíacos son tratados con bloqueantes de los canales de calcio. La aterosclerosis se puede reducir por medio de una disminución en los daños mediados por radicales libres como resultado del efecto sobre las propiedades biofísicas de las membranas (Mason, R. P.; et al., *Antioxidant and cytoprotective activities of the calcium channel blocker mibefradil. Biochemical Pharmacology*, 1998, 55, 1843-1852.). La hipertensión y la angina son tratados ambos con éxito usando con bloqueantes de los canales de calcio (Croom, K. F.; et al., *Modified-release nifedipine: A review of the use of modified-release formulations in the treatment of hypertension and angina pectoris. Drugs*, 2006, 66(4), 497-528.).

Hay datos que sugieren que los bloqueantes de los canales de calcio inhiben la proliferación de células cancerosas (Gray, L. S.; et al.. Publicación Internacional N° WO200059882, 2000.).

Los canales de calcio han sido sugeridos como un blanco para el tratamiento de la diabetes (Bhattacharjee, A.; et al., *T-Type calcium channels facilitate insulin secretion by enhancing general excitability in the insulin-secreting β-cell line, INS-1. Endocrinology*, 1997, 138(9), 3735-3740.).

Los canales iónicos, incluyendo los canales de calcio, cumplen un rol importante en la fisiología del esperma y en la fertilización (Darszon, A.; et al., *Ion channels in sperm physiology. Physiological Reviews*, 1999, 79(2), 481-510).

Los bloqueantes de los canales de calcio modulan la inflamación (Bilici, D.; et al., *Protective effect of T-type calcium channel blocker in histamine-induced paw inflammation in rat. Pharmacological Research*, 2001, 44(6), 527-531.).

Los niveles incrementados de calcio en las neurones se han relacionado con el mal de Alzheimer. Dos mecanismos sugeridos de un influjo de calcio incrementado son que el β-amiloide puede formar canales permeables al calcio

(Bhatia, R.; et al., *Fresh and globular amyloid beta protein (1-42) induces rapid cellular degeneration: evidence for AβP channel-mediated cellular toxicity. FASEB J.* 2000, 14(9), 1233-1243.) o que un receptor acoplado a la proteína G puede ser activado por el β-amiloide (Lorton, D. *β-Amyloid induced IL-1 β release from an activated human monocyte cell line is calcium- and G-protein-dependent. Mech. Ageing Dev.*. 1997, 94(1-3), 199-211.).

Las enfermedades neurodegenerativas, incluyendo el mal de Parkinson y de Alzheimer pueden modularse mediante bloqueantes de los canales de calcio (Rodnitzky, R. L. *Can calcium antagonists provide a neuroprotective effect in Parkinson's disease. Drugs*, 1999, 57(6), 845-849. Vagnucci, A. H., Jr.; et al., *Alzheimer's disease and angiogenesis. The Lancet*, 2003, 361(9357), 605-608. Veng, L. M.; et al., *Age-related working memory impairment is correlated with increases in the L-type calcium channel protein α_{1D} ($Ca_v1.3$) in area CA1 of the hippocampus and both are ameliorated by chronic nimodipine treatment. Molecular Brain Research*, 2203, 110, 193-202. Geldenhuys, W. J.; et al., *Structure-activity relationships of pentacycloundecylamines at the N-methyl-D-aspartate receptor. Bioorganic and Medicinal Chemistry*, 2007, 15, 1525-1532. Cavalli, A.; et al., *Multi-target-directed ligands to combat neurodegenerative diseases. J. Med. Chem.* 2008, 51(3), 347-372.)

Los niveles reales de dosificación de los ingredientes activos en las composiciones farmacéuticas de esta invención se pueden variar con el fin de obtener una cantidad de dichos uno o más compuestos activos que son eficaces para lograr la respuesta teraéutica deseada para un paciente, composiciones y un modo de administración particulares. El nivel de dosificación seleccionado dependerá de la actividad del compuesto particular, la ruta de administración, la severidad de la afección bajo tratamiento y la condición e historia médica previa del paciente bajo tratamiento. Sin embargo, es propio del conocimiento de la técnica comenzar con dosis del compuesto a niveles menores que los requeridos para lograr el efecto terapéutico deseado y para incrementar gradualmente la dosificación hasta obtener el efecto deseado.

Los compuestos también pueden ser administrados como una composición farmacéutica que contiene al compuesto de interés en combinación con uno o más vehículos farmacéuticamente aceptables. La frase, "cantidad terapéuticamente

eficaz" del compuesto de la invención significa una cantidad suficiente del compuesto como para tratar trastornos, con una relación de beneficio/riesgo razonable que se puede aplicar a cualquier tratamiento médico. Se comprenderá, sin embargo, que el uso diario total de los compuestos y las composiciones de la invención será decidido por el médico a cargo dentro del alcance del buen juicio médico. El nivel de dosis terapéuticamente eficaz específico para cualquier paciente en particular dependerá de una variedad de factores que incluyen el trastorno que se está tratando y la gravedad del trastorno; la actividad del compuesto específico que se está empleando; la composición específica que se está empleando; la edad, peso corporal, estado general de salud, sexo y dieta del paciente; el momento de la administración, la ruta de administración, y la tasa de excreción del compuesto específico que se está empleando; la duración del tratamiento; las drogas que se utilizan en combinación o de manera coincidente con el compuesto específico que se está empleando; y otros factores bien conocidos en la ciencia médica. Por ejemplo, es propio del conocimiento de la técnica iniciar con dosis del compuesto a niveles menores que los requeridos para lograr el efecto terapéutico deseado y para incrementar gradualmente la dosificación hasta obtener el efecto deseado.

La dosis diaria total de los compuestos de esta invención administrada a un ser humano u otro animal varía en un rango entre aproximadamente 0,01 mg/kg de peso corporal y aproximadamente 100 mg/kg de peso corporal. Las dosis pueden variar más preferentemente en el rango de entre aproximadamente 0,01 mg/kg de peso corporal y aproximadamente 30 mg/kg de peso corporal. Si se lo desea, la dosis diaria eficaz puede dividirse en múltiples dosis para su administración. En consecuencia, las composiciones de dosis individuales pueden contener dichas cantidades, o submúltiplos de las mismas, hasta conformar la dosis diaria.

e. Composiciones farmacéuticas

La presente invención provee además composiciones farmacéuticas que comprenden compuestos de la presente invención o una sal o solvato farmacéuticamente aceptable de los mismos. Las composiciones farmacéuticas comprenden compuestos de la presente invención que pueden formularse con uno o más vehículos no tóxicos farmacéuticamente aceptables.

Otro aspecto de la presente invención es una composición farmacéutica que comprende compuestos de la invención, o una sal farmacéuticamente aceptable de los mismos, y uno o más vehículos farmacéuticamente aceptables, solos o en combinación con una o más drogas antiinflamatorias no esteroides (NSAID), analgésicos opioides, barbituratos, benzodiazepinas, antagonistas de histamina, sedantes, relajantes de la musculatura esquelética, antagonistas del potencial de canales iónicos de un receptor transitorio, α-adrenérgicos, antidepresivos tricíclicos, anticonvulsionantes, antagonistas de taquiquinina, antagonistas muscarínicos, inhibidores selectivos de ciclooxigenasa-2, neurolépticos, agonistas del receptor vanilloide, antagonistas del receptor vanilloide, β-adrenérgicos, anestésicos locales, corticosteroides, agonistas del receptor 5-HT, antagonistas del receptor 5-HT, antagonistas del receptor 5-HT_{2A}, analgésicos colinérgicos, ligandos $\alpha_2\delta$ tal como gabapentina o pregabalina, ligandos del receptor cannabinoide, antagonistas del receptor de glutamato metabotrópico del subtipo 1, inhibidores de la recaptación de serotonina, inhibidores de la recaptación de norepinefrina, inhibidores de de la recaptación doble de serotonina-noradrenalina, inhibidores de Rho quinasa, inhibidores inducibles de óxido nítrico sintasa, inhibidores acetilcolinesterasa, antagonistas de prostaglandina E_2 subtipo 4, antagonistas de leucotrieno B4, inhibidores de 5-lipoxigenasa, bloqueantes de los canales de sodio, antagonistas de 5-HT3, antagonistas del receptor de ácido N-metil-D-aspártico e inhibidores de la fosfodiesterasa V.

Las composiciones farmacéuticas de esta invención se pueden administrar a seres humanos y otros mamíferos por vía oral, rectal, parenteral, intracistérnica, intravaginal, intraperitoneal, tópica (tal como por medio de polvos, ungüentos o gotas), bucal o como un rocío oral o nasal. El término "por vía parenteral", según se usa en la presente, se refiere a modos de administración que incluyen la inyección y la infusión intravenosa, intramuscular, intraperitoneal, intraesternal, subcutánea e intraarticular.

El término "vehículo farmacéuticamente aceptable", según se usa en la presente, se refiere a un diluyente, un material encapsulante o un auxiliar de formulación no tóxico, inerte, sólido, semisólido o líquido de cualquier tipo. Algunos ejemplos de materiales que pueden servir como vehículos

farmacéuticamente aceptables son azúcares tales como, pero de manera no limitativa, lactosa, glucosa y sacarosa; almidones tales como, pero de manera no limitativa, almidón de maíz y almidón de papa; celulosa y sus derivados tales como, pero de manera no limitativa, carboximetilcelulosa sódica, etilcelulosa y acetato de celulosa; goma tragacanto en polvo; malta; gelatina; talco; excipientes tales como, pero de manera no limitativa, manteca de cacao y ceras para supositorios; aceites tales como, pero de manera no limitativa, aceite de maní, aceite de algodón, aceite de cártamo, aceite de sésamo, oliva, aceite de maíz y aceite de soja; glicoles; tales como propilenglicol; ésteres tales como, pero de manera no limitativa, oleato de etilo y laurato de etilo; ágar agar; agentes amortiguadores de pH tales como, pero de manera no limitativa, hidróxido de magnesio e hidróxido de aluminio; ácido algínico; agua libre de pirógenos; solución salina isotónica; solución de Ringer; alcohol etílico, y soluciones amortiguadoras de pH al fosfato, así como otros lubricantes no tóxicos compatibles tales como, pero de manera no limitativa, lauril sulfato de sodio y estearato de magnesio; de acuerdo con el juicio de quien realice la fórmula en la composición también pueden haber presentes agentes colorantes, agentes de despegue, agentes de recubrimiento, agentes endulzantes, saborizantes y de perfume, conservantes y antioxidantes.

Las composiciones farmacéuticas para inyecciones parenterales también pueden comprender soluciones, dispersiones, suspensiones o emulsiones estériles acuosos o no acuosos farmacéuticamente aceptables, así como polvos estériles para su reconstitución en soluciones o dispersiones inyectables estériles justo antes del uso. Los ejemplos de vehículos, diluyentes, solventes o vehículos acuosos y no acuosos apropiados incluyen agua, etanol, polioles (tales como glicerol, propilenglicol, polietilenglicol etcétera), aceites vegetales (tales como aceite de oliva), ésteres orgánicos inyectables (tales como oleato de etilo) y mezclas apropiadas de los mismos. Se puede mantener una fluidez adecuada, por ejemplo, mediante el uso de materiales de recubrimiento tales como lecitina, manteniendo el tamaño de partícula deseado en el caso de las dispersiones y por medio del uso de agentes tensioactivos.

Dichas composiciones también pueden contener coadyuvantes tales como conservantes, agentes humectantes, agentes emulsionantes y agentes

dispersantes. La prevención de la acción de microorganismos se puede asegurar incluyendo diversos agentes antibacterianos y antifúngicos, por ejemplo, parabeno, clorobutanol, fenol, ácido sórbico y semejantes. También puede ser deseable incluir agentes isotónicos, tales como azúcares, cloruro de sodio y semejantes. La absorción prolongada de una forma farmacéutica inyectable se puede lograr por inclusión de agentes que demoran la absorción, tales como monoestearato de aluminio y gelatina.

En algunos casos, para prolongar el efecto de la droga, es deseable demorar la absorción de la droga de una inyección subcutánea o intramuscular. Esto se puede lograr usando una suspensión líquida de un material cristalino o amorfo con baja solubilidad en agua. Entonces, la velocidad de absorción de la droga depende de su velocidad de disolución que, a su vez, puede depender del tamaño de los cristales y de la forma cristalina. Como alternativa, la absorción demorada de una droga administrada en forma parenteral se lleva a cabo por medio de la disolución o dispersión de la droga en un vehículo oleoso.

Las formas de depósito inyectables se preparan formando matrices microencapsuladas de la droga en polímeros biodegradables, tales como poliláctido-poliglicólido. Dependiendo de la relación de droga a polímero y de la naturaleza del polímero en particular que se emplee, se puede controlar la velocidad de liberación de la droga. Los ejemplos de otros polímeros biodegradables incluyen poli(ortoésteres) y poli(anhídridos). También se pueden preparar formulaciones inyectables de depósito atrapando la droga en liposomas o microemulsiones, que sean compatibles con los tejidos corporales.

Las formulaciones inyectables se pueden esterilizar, por ejemplo, por filtración a través de un filtro que retiene bacterias, o incorporando esterilizando agentes en la forma de composiciones sólidas estériles que se pueden disolver o dispersar en agua estéril u otro medio inyectable estéril justo antes de su uso.

Las formas de dosificación sólidas para administración oral incluyen cápsulas, tabletas, píldoras, polvos y gránulos. En dichas formas de dosificación sólidas, el compuesto activo se puede mezclar con por lo menos un vehículo o excipiente inerte, farmacéuticamente aceptable, como por ejemplo citrato de sodio o fosfato dicálcico y/o a) cargas o diluyentes sólidos tales como almidones, lactosa, sacarosa, glucosa, manitol y ácido silícico; b) aglutinantes tales como

carboximetilcelulosa, alginatos, gelatina, polivinilpirrolidona, sacarosa y goma de acacia; c) humectantes tales como glicerol; d) agentes desintegrantes tales como ágar agar, carbonato de calcio, almidón de papa o tapioca, ácido algínico, ciertos silicatos y carbonato de sodio; e) agentes retardadores de la solución tales como parafina; f) aceleradores de absorción tales como compuestos de amonio cuaternario; g) agentes humectantes tales como alcohol cetílico y monoestearato de glicerol; h) absorbentes tales como caolín y arcilla de bentonita y i) lubricantes tales como talco, estearato de calcio, estearato de magnesio, polietilenglicoles sólidas, laurilsulfato de sodio y mezclas de los mismos. En el caso de las cápsulas, las tabletas y las píldoras, la forma de dosificación también puede comprender agentes reguladores del pH.

También se pueden emplear composiciones sólidas de un tipo similar como rellenos en cápsulas de gelatina blanda y dura usando vehículos tales como lactosa o azúcar de leche así como polietilenglicoles de alto peso molecular, etcétera.

Las formas de dosificación sólidas de tabletas, grageas, cápsulas, píldoras y gránulos se pueden preparar con recubrimientos y revestimientos tales como recubrimientos entéricos y otros recubrimientos bien conocidos en el arte de la formulación farmacéutica. Los mismos pueden contener opcionalmente agentes opacificantes y también pueden tener una composición tal que liberen el(los) ingrediente(s) activo(s) solo, o preferentemente, en cierta parte del tracto intestinal, opcionalmente, de una manera retardada. Los ejemplos de composiciones de embebido que pueden usarse incluyen sustancias poliméricas y ceras.

Los compuestos activos también pueden estar en forma microencapsulada, de ser apropiado, con uno o más de los vehículos mencionados anteriormente.

Las formas de dosificación líquidas para la administración oral incluyen emulsiones, soluciones, suspensiones, jarabes y elixires farmacéuticamente aceptables. Además de los compuestos activos, las formas de dosificación líquidas pueden contener diluyentes inértes que se usan comúnmente en la técnica tales como, por ejemplo, agua u otros solventes, agentes solubilizantes y emulsionantes tales como alcohol etílico, alcohol isopropílico, carbonato de etilo, acetato de etilo, alcohol bencílico, benzoato de bencilo, propilenglicol, 1,3-

butilenglicol, dimetilformamida, aceites (en particular, aceites de semilla de algodón, maní, de maíz, de germen de trigo, de oliva, de ricino, y de sésamo), glicerol, alcohol tetrahidrofurfurílico, polietilenglicoles y ésteres de ácido graso y sorbitan, y mezclas de los mismos.

Junto con los diluyentes inertes, las composiciones orales también pueden incluir coadyuvantes tales como agentes humectantes, emulsionantes y agentes de suspensión, agentes endulzantes, saborizantes, y aromatizantes.

Además de los compuestos activos, las suspensiones pueden contener agentes de suspensión, por ejemplo, alcoholes isoestearílicos etoxilados, polioxietilén sorbitol y ésteres de sorbitan, celulosa microcristalina, metahidróxido de aluminio, bentonita, ágar agar, tragacanto y mezclas de los mismos.

Las composiciones para administración rectal o vaginal son preferentemente supositorios que se pueden preparar mezclando los compuestos de la presente invención con vehículos no irritantes apropiados o vehículos tales como manteca de cacao, polietilenglicol o una cera para supositorios que sea sólida a temperatura ambiente pero líquida a la temperatura corporal y que por lo tanto se funda en el recto o la cavidad vaginal y libera el compuesto activo.

Los compuestos de la presente invención también se pueden administrar en la forma de liposomas. Según se sabe en la técnica, los liposomas derivan en general de fosfolípidos u otras sustancias lípidas. Los liposomas se forman con cristales líquidos hidratados mono o multilaminares, que se dispersan en un medio acuoso. Se puede usar cualquier lípido no tóxico, aceptable para uso fisiológico y metabolizable capaz de formar liposomas. Las formas de composiciones en liposomas de la presente pueden contener, además de un compuesto de la presente invención, estabilizantes, conservantes, excipientes, etcétera. Los lípidos preferidos son los fosfolípidos naturales y sintéticos, y las fosfatidilcolinas (lecitinas), usados por separado o juntos.

Los métodos para formar liposomas son conocidos en la técnica. Véase, por ejemplo, Prescott, editor, *Methods in Cell Biology*, Volumen XIV, Academic Press, Nueva York, N. Y., (1976), p. 33 *y sig.*.

Las formas de dosificación para la administración tópica de un compuesto de esta invención incluyen polvos, rocíos, ungüentos e inhalantes. El compuesto activo se puede mezclar bajo condiciones estériles con un vehículo

farmacéuticamente aceptable y los preservantes, amortiguadores o propelentes que puedan ser necesarios. Dentro del alcance de esta invención también se contemplan las formulaciones oftálmicas, los ungüentos para los ojos, los polvos y las soluciones.

Los compuestos de la presente invención se pueden usar en la forma de sales farmacéuticamente aceptables derivadas de ácidos inorgánicos u orgánicos. La frase "sal farmacéuticamente aceptable" equivale a aquellas sales que, dentro del juicio médico reconocido, son apropiadas para su uso en contacto con los tejidos de seres humanos y animales inferiores, sin una toxicidad, una irritación o una respuesta inapropiada, y semejantes, y satisfacen una relación de beneficio/riesgo razonable.

Las sales farmacéuticamente aceptables son bien conocidas en la técnica. Por ejemplo, S. M. Berge, *et al.* describe sales farmacéuticamente aceptables en detalle en J. Pharmaceutical Sciences, 1977, 66: 1 y sig.). Las sales se pueden preparar *in situ* durante los procedimientos finales de aislamiento y purificación de los compuestos de la invención, o por separado mediante reacción de la función base libre con un ácido orgánico apropiado. Las sales de adición ácida representativas incluyen, pero en un sentido no limitativo, sales de acetato, adipato, alginato, citrato, aspartato, benzoato, bencensulfonato, bisulfato, butirato, alcanforato, alcanforsulfonato, digluconato, glicerofosfato, hemisulfato, heptanoato, hexanoato, fumarato, clorhidrato, bromohidrato, iodohidrato, 2-hidroxietansulfonato (isetionato), lactato, malato, maleato, metansulfonato, nicotinato, 2-naftalensulfonato, oxalato, palmitoato, pectinato, persulfato, 3-fenilproprionato, picrato, pivalato, propionato, succinato, tartrato, tiocianato, fosfato, glutamato, bicarbonato, p-toluensulfonato y undecanoato. Además, los grupos que contienen nitrógeno básico pueden ser cuaternizados con agentes tales como haluros de alquilo inferior tales como, pero en un sentido no limitativo, cloruro, bromuros y yoduros de metilo, etilo, propilo y butilo; sulfatos de dialquilo tal como sulfatos de dimetilo, dietilo, dibutilo y diamilo, haluros de cadena larga tales como, pero en un sentido no limitativo, cloruros, bromuros y yoduros de decilo, laurilo, miristilo y estearilo, haluros de fenilalquilo como bromuro de bencilo y fenetilo, y otros. De esa manera se obtienen productos solubles o dispersables en agua o aceite. Los ejemplos de ácidos que se pueden emplear para formar sales de adición ácida

farmacéuticamente aceptables incluyen ácidos inorgánicos, tales como ácido clorhídrico, ácido bromhídrico, ácido sulfúrico y ácido fosfórico, y ácidos orgánicos tales como ácido acético, ácido fumárico, ácido maleico, ácido 4-metilbencensulfónico, ácido succínico y ácido cítrico.

Las sales de adición básica pueden prepararse in situ durante el aislamiento final y la purificación de los compuestos, haciendo reaccionar un grupo carboxilo con una base apropiada, tal como, sin limitaciones, hidróxido, carbonato o bicarbonato de un catión metálico, o con amoníaco o una amina orgánica primaria, secundaria o terciaria. Las sales farmacéuticamente aceptables incluyen, pero en un sentido no limitativo, sales basadas en cationes de metales alcalinos o metales alcalinos térreos, tales como, sin limitaciones, sales de sodio, litiol, potasio, calcio, magnesio, aluminio, y semejantes, y también sales no tóxicas de cationes de aminas cuaternarias y amonio, tales como amonio, tetrametilamonio, tetraetilamonio, metilamina, dimetilamina, trimetilamina, trietilamina, dietilamina, etilamina y semejantes. Otras aminas orgánicas representativas útiles para la formación de sales de adición básica incluyen etilendiamina, etanolamina, dietanolamina, piperidina, piperazina y semejantes.

El término "prodroga aceptable para el uso farmacéutico" o "prodroga", según se usa en la presente, representa aquellas prodrogas de los compuestos de la invención que, dentro del juicio médico reconocido, son apropiadas para usar en contacto con los tejidos de los seres humanos y los animales inferiores, sin una toxicidad, una irritación o una respuesta inapropiada, y semejantes, satisfacen una relación beneficio/riesgo razonable, y son efectivas para el uso que pretende dársele.

La presente invención contempla compuestos de la invención formadas por medio de síntesis o formadas mediante biotransformación *in vivo* de una prodroga.

Los compuestos de la invención pueden existir en formas no solvatadas y también solvatadas, que incluyen formas hidratadas, como por ejemplo hemi-hidratos. En general, a los efectos de la invención, las formas solvatadas, con solventes farmacéuticamente aceptables tales como agua y etanol entre otros, son equivalentes a las formas no solvatadas.

f. Síntesis general

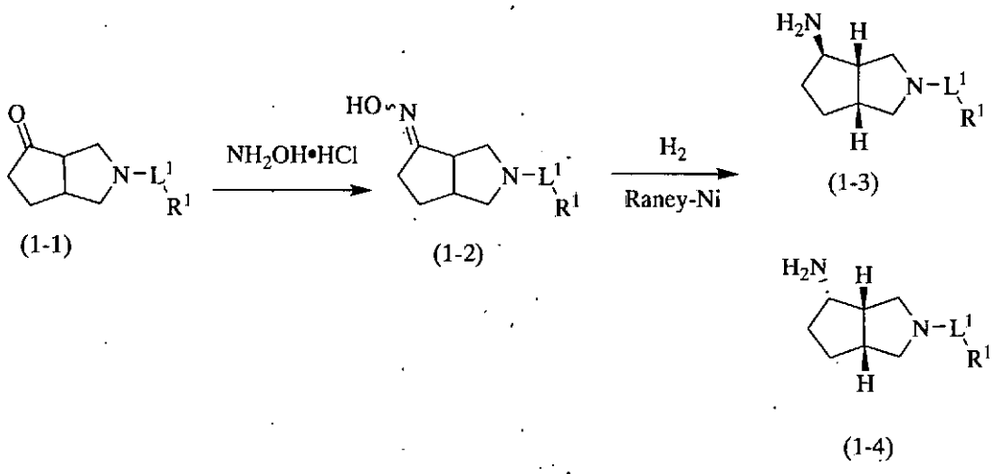
Esta invención pretende abarcar los compuestos de la invención cuando se

preparan mediante procesos de síntesis o mediante procesos metabólicos. La preparación de los compuestos mediante procesos metabólicos incluye los que tienen lugar en el cuerpo humano o de un animal (*in vivo*) o los procesos que tienen lugar *in vitro*.

Los compuestos de la invención se pueden preparar mediante una variedad de procesos bien conocidos para la preparación de los compuestos de esta clase. Por ejemplo, los compuestos de la invención, en donde los grupos L^1, L^2, R^1, R^2, R^3,R^4, R^5, R^6, R^e, R^f, R^g, R^h, n, q y G^1 tienen los significados expresados en la sección de Síntesis de la invención a menos que se indique de otra manera, se pueden sintetizar como se muestra en los Esquemas 1-20.

A continuación se detallan las abreviaturas que se utilizaron en las descripciones de los esquemas y de los ejemplos. Ac por acetilo; $AlMe_3$ por trimetilaluminio; Boc por *t*-butoxicarbonilo; Boc_2O por dicarbonato de di-*ter*-butilo; Bu por butilo; Et por etilo, EtOH por etanol; DMF o *N,N*-dimetilformamida; DMSO por dimetilsulfóxido; lcms por cromatografía líquida/espect. de masa; MeOH por metanol; MsCl por cloruro de metansulfonilo; NEt_3 por trietilamina; OAc por acetato; Ph por fenilo; PPh_3 por trifenilfosfina; PS-cianoborohidruro por cianoborohidruro sobre soporte polimérico; psi por libras por pulgadas cuadradas; tBu por *ter*-butilo; THF por tetrahidrofurano y tlc por cromatografía en capa delgada.

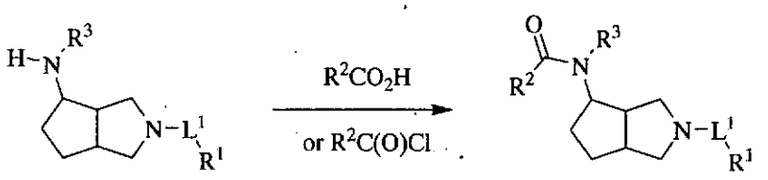
Esquema 1



Los compuestos de la fórmula (1-3) y (1-4), en donde L^1 y R^1 son como se definen en la Síntesis de la invención, se pueden preparar según se ilustra en el Esquema 1. Los compuestos de la fórmula (1-1) se pueden tratar con clorhidrato de

hidroxilamina en la presencia de una base tal como carbonato de sodio, bicarbonato de sodio o acetato de sodio en un solvente, tal como agua o metanol acuoso, y opcionalmente calentar para obtener las oximas de la fórmula (1-2). Las oximas de la fórmula (1-2) se pueden reducir luego en la presencia de hidrógeno (30 psi) en la presencia de níquel Raney® en un solvente tal como amoníaco en metanol 20% a temperatura ambiente sobre un período de 1 a 24 horas para proporcionar una mezcla diastereomérica de aminas, los compuestos de las fórmulas (1-3) y (1-4). Las aminas diastereoméricas se pueden separar mediante técnicas conocidas por el especialista en la técnica, tal como cromatografía.

Esquema 2



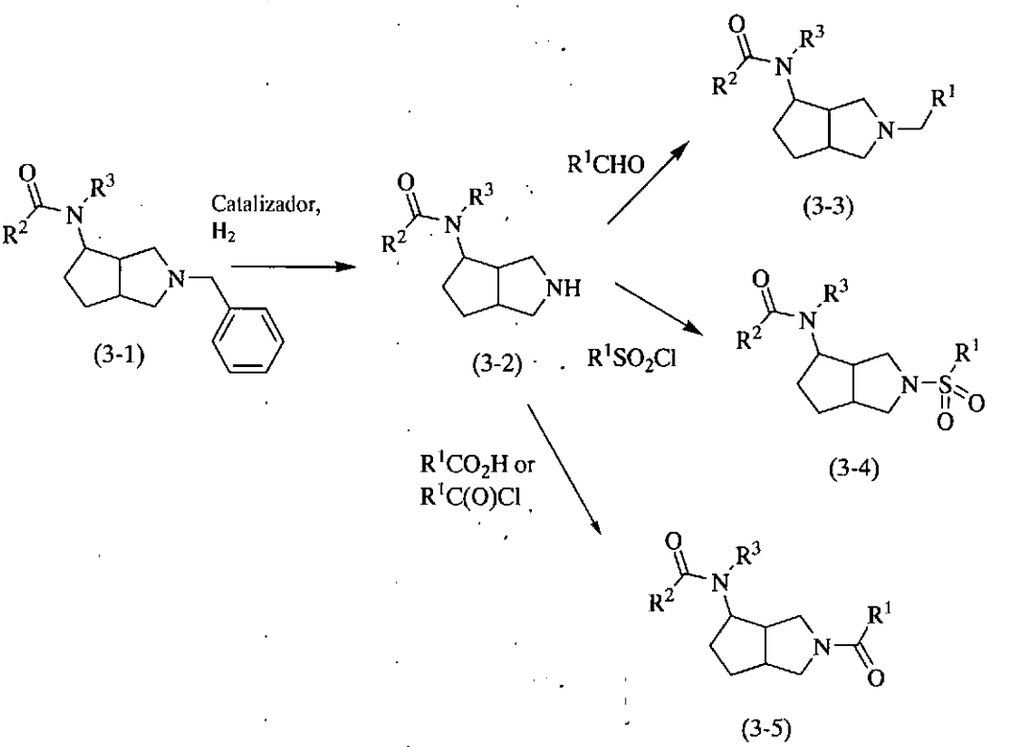
(2-1) (2-2)

Los compuestos de la fórmula (2-2) que son representativos de los compuestos de la fórmula (I), en donde L^1, R^1, R^2 y R^3 son como se describieron en la Síntesis de la invención, se preparan por reacción de compuestos de la fórmula (2-1) con ácidos carboxílicos de la fórmula R^2CO_2H bajo condiciones de acoplamiento de enlaces de amida. Los ejemplos de condiciones conocidas por generar amidas a partir de una mezcla de un ácido carboxílico y una amina incluyen, pero en un sentido no limitativo, adición de un reactivo de acoplamiento tal como, pero en un sentido no limitativo, *N*-(3-dimetilaminopropil)-*N'*-etilcarbodiimida (EDC o EDCI), 1,3-diciclohexilcarbodiimida (DCC), cloruro de bis(2-oxo-3-oxazolidinil)fosfínico (BOPCl), hexafluorofosfato O-(7-azabenzotriazol-1–il)-*N,N,N',N'*-tetrametiluronio (HATU), tetrafluoroborato de O-benzotriazol-1–il-*N,N,N',N'*-tetrametiluronio (TBTU) y hexafluorofosfato(V) de 2-(1*H*-benzo[*d*][1,2,3]triazol-1–il)-1,1,3,3-tetrametilisouronio (HBTU). Los reactivos de acoplamiento se pueden agregar como un sólido, una solución o como el reactivo unido a una resina de soporte sólido. Además de los reactivos de acoplamiento, los reactivos de acoplamiento auxiliaresy pueden facilitar la reacción de acoplamiento. Los reactivos de acoplamiento auxiliares que con frecuencia se usan en las reacciones de acoplamiento incluyen, pero en un sentido no limitativo, (dimetilamino)piridina

(DMAP), 1-hidroxi-7-azabenzotriazol (HOAT) y 1-hidroxibenzotriazol (HOBT). La reacción se puede conducir opcionalmente en la presencia de una base tal como trietilamina o diisopropiletilamina. La reacción de acoplamiento se puede conducir en solventes tales como, pero en un sentido no limitativo, tetrahidrofurano, *N,N*-dimetilformamida, diclorometano y acetato de etilo. La reacción se puede conducir a temperatura ambiente o a temperaturas elevadas.

Como alternativa, los compuestos de la fórmula (2-2) se pueden preparar a partir de los compuestos de la fórmula (2-1) por reacción con un cloruro ácido de la fórmula $R^2C(O)Cl$. Los compuestos de la fórmula (2-1) se pueden tratar con $R_2C(O)Cl$ en un solvente, tal como diclorometano, en la presencia de una amina tal como trietilamina o diisopropiletilamina a temperatura ambiente sobre un período de 1 a 24 horas para obtener los compuestos de la fórmula (2-2).

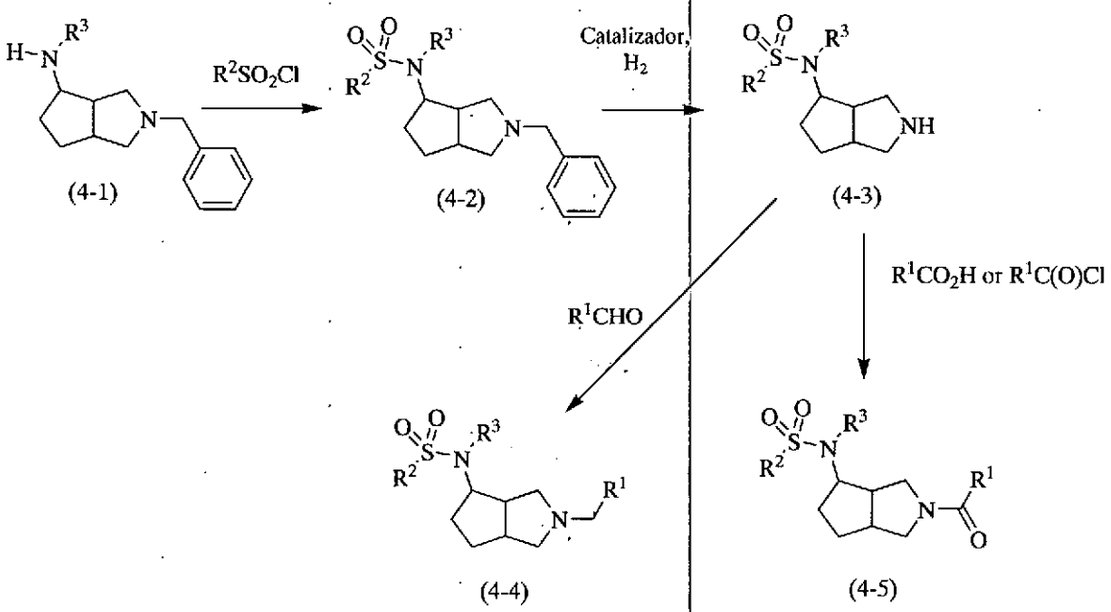
Esquema 3



Según se ilustra en el Esquema 3, los compuestos de las fórmulas (3-3), (3-4) y (3-5) que son representativos de los compuestos de la fórmula (I), y en donde R^1, R^2 y R^3 son como se definen en la Síntesis de la invención, se pueden obtener a partir de compuestos de la fórmula (3-1). Los compuestos de la fórmula (3-1) se pueden convertir en compuestos de la fórmula (3-2) mediante tratamiento con

hidrógeno (15-60 psi) en la presencia de un catalizador, tal como hidróxido de paladio sobre carbón o paladio sobre carbón, en un solvente tal como metanol o etanol a temperatura ambiente sobre un período de 3-36 horas. Los compuestos de la fórmula (3-2) se pueden aminar luego bajo condiciones reductoras con aldehídos de la fórmula R^1CHO en la presencia de un agente reductor, tal como PS-cianoborohidruro, cianoborohidruro de sodio o triacetoxiborohidruro de sodio y ácido acético en un solvente tal como metanol o diclorometano a temperatura ambiente sobre un período de 4-24 horas para suministrar los compuestos de la fórmula (3-3). Como alternativa, los compuestos de la fórmula (3-2) se pueden hacer reaccionar con un cloruro de sulfonilo de la fórmula R^1SO_2Cl en la presencia de una base, tal como trietilamina o diisopropilamina, opcionalmente en la presencia de (dimetilamino)piridina en un solvente tal como diclorometano a temperatura ambiente sobre un período de 4-24 horas para suministrar los compuestos de la fórmula (3-4). Los compuestos de la fórmula (3-5) también se pueden preparar a partir de compuestos de la fórmula (3-2). Los compuestos de la fórmula (3-2) se pueden tratar con un ácido carboxílico de la fórmula R^1CO_2H o y un cloruro ácido de la fórmula $R^1C(O)Cl$ bajo las condiciones formadoras de enlaces amida que se describieron en el Esquema 2 para dar los compuestos de la fórmula (3-5).

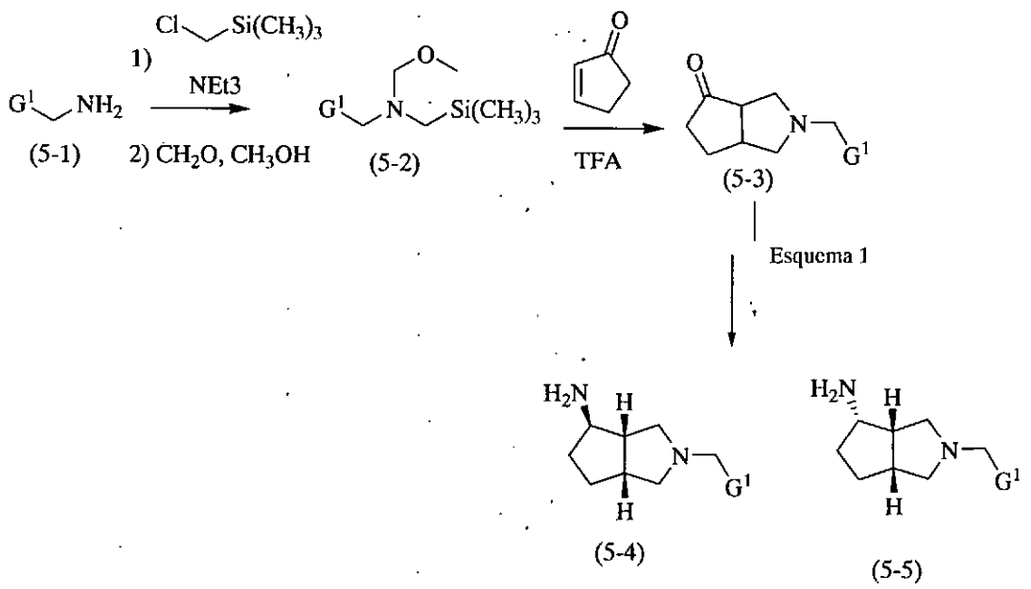
Esquema 4



Según se ilustra en el Esquema 4, los compuestos de las fórmulas (4-2), (4-3), (4-

4) y (4-5) que son representativos de los compuestos de la fórmula (I), en donde R^1, R^2 y R^3 son como se definen en la Síntesis de la invención, se pueden obtener a partir de compuestos de la fórmula (4-1). Por consiguiente, los compuestos de la fórmula (4-1) se pueden tratar con cloruros de sulfonilo de la fórmula R_2SO_2Cl usando las condiciones que se describieron en el Esquema 3 para dar compuestos de la fórmula (4-2). El grupo bencilo se puede clivar bajo condiciones reductoras con hidrógeno y un catalizador de paladio como se describe en el Esquema 3 para proporcionar compuestos de la fórmula (4-3). Los compuestos de la fórmula (4-3) se pueden alquilar bajo condiciones reductoras con aldehídos de la fórmula R^1CHO bajo las condiciones de reacción que se describen en el Esquema 3 para dar compuestos de la fórmula (4-4). La amina secundaria de los compuestos de la fórmula (4-3) se puede acoplar con un ácido carboxílico o un cloruro ácido bajo las condiciones que se describieron en el Esquema 2 para dar amidas de la fórmula (4-5).

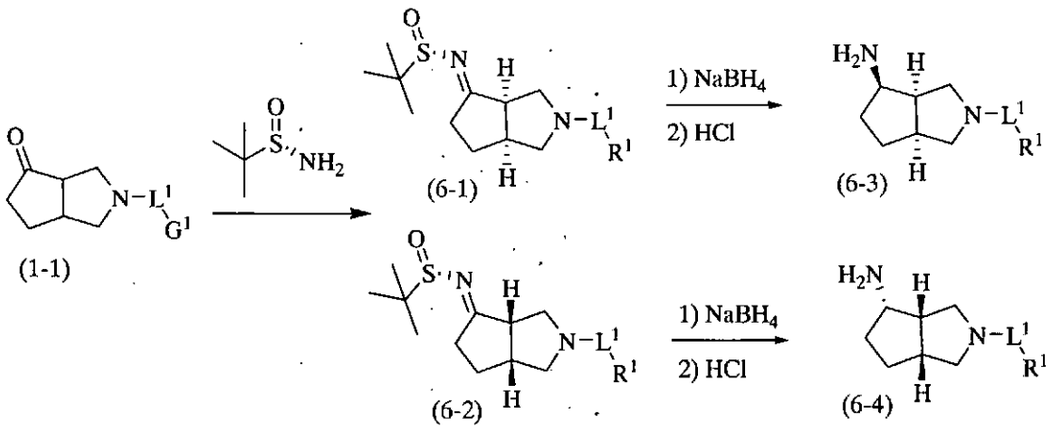
Esquema 5



Los compuestos de la fórmula (5-4) y (5-5), en donde G^1 es arilo o heteroarilo y están sustituidos o no están sustituidos como se describe en la Síntesis de la invención, se pueden preparar a partir de compuestos de la fórmula (5-1) como se describe en el Esquema 5. Los compuestos de la fórmula (5-1) se pueden combinar con clorometiltrimetilsilano y trietilamina y llevar a reflujo durante 8-24 horas. El intermediario se puede hacer reaccionar luego con formaldehído en la

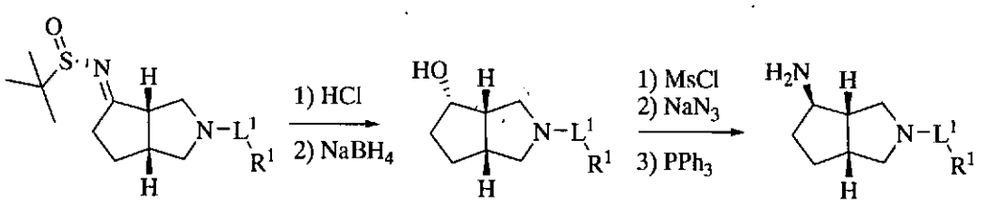
presencia de carbonato de potasio y en metanol para dar compuestos de la fórmula (5-2). Los compuestos de la fórmula (5-2) se pueden hacer reaccionar con ciclopent-2-enona a temperatura ambiente en la presencia de ácido trifluoroacético en un solvente tal como diclorometano para dar compuestos de la fórmula (5-3). Los compuestos de la fórmula (5-3) se pueden transformar en los compuestos de las fórmulas (5-4) y (5-5) mediante tratamiento primero con clorhidrato de hidroxilamina y a continuación con hidrógeno en la presencia de Níquel Raney® como se describe en el Esquema 1.

Esquema 6



Los compuestos quirales de las fórmulas (6-3) y (6-4), en donde L^1 y R^1 son como se definen en la Síntesis de la invención, se pueden sintetizar como se describe en el Esquema 6. Para tal fin, los compuestos de la fórmula (1-1) se pueden tratar con una sulfinamida quiral, tal como (*S*)-2-metilpropan-2-sulfinamida, en la presencia de tetraetóxido de titanio en un solvente tal como tetrahidrofurano y calentar a 30-65 °C durante 4 a 24 horas para dar los compuestos diastereoméricos (6-1) y (6-2). Los diastereómeros quirales se pueden separar cromatográficamente y luego tratar individualmente en la siguiente secuencia. Los compuestos quirales de la fórmula (6-1) se pueden reducir con borohidruro de sodio en metanol a -78 °C con calentamiento gradual hasta temperatura ambiente sobre un período de 8 a 20 horas. La subsiguiente hidrólisis con ácido clorhídrico en metanol provee compuestos quirales de la fórmula (6-3). De manera similar, los compuestos quirales de la fórmula (6-2) se pueden convertir en los compuestos quirales de la fórmula (6-4).

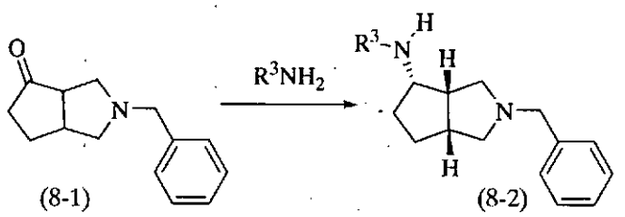
Esquema 7



(6-2) (7-1) (7-2)

Según se ilustra en el Esquema 7, los compuestos quirales de la fórmula (7-2), en donde L^1 y R^1 son como se definen en la Síntesis de la invención, se pueden obtener a partir de los compuestos quirales de la fórmula (6-2). Los compuestos quirales de la fórmula (6-2) se pueden hidrolizar con ácido clorhídrico en tetrahidrofurano a temperatura ambiente sobre un período de 1-8 horas. La subsiguiente reducción con borohidruro de sodio en metanol a una temperatura entre -40 °C y temperatura ambiente sobre un período de 8-24 horas suministra alcoholes quirales (7-1). Los alcoholes (7-1) se pueden transformar en las aminas quirales (7-2) en un proceso de tres pasos. Los compuestos de la fórmula (7-1) se pueden tratar con cloruro de metansulfónilo en la presencia de trietilamina en diclorometano a temperatura ambiente durante 10 minutos a 2 horas. Los sulfonatos se pueden desplazar luego con inversion con azida sódica en *N*,*N*-dimetilacetamida caliente sobre un período de 8-24 horas. Las azidas derivadas se pueden reducir finalmente con trifenilfosfina en una mezcla caliente de agua y tetrahidrofurano para dar compuestos quirales de la fórmula (7-2).

Esquema 8

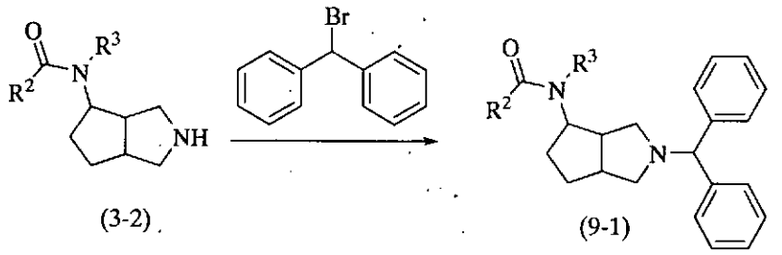


(8-1) (8-2)

Como se describe en el Esquema 8, los compuestos de la fórmula (8-1) se pueden convertir en compuestos de la fórmula (8-2) en donde R^3 es alquilo, haloalquilo, cicloalquilo o cicloalquilalquilo. Los compuestos de la fórmula (8-1) se pueden tratar con aminas de la fórmula R^3NH_2 en la presencia de PS-cianoborohidruro, cianoborohidruro de sodio o triacetoxi borohidruro y ácido acético en diclorometano a temperatura ambiente durante 1-6 horas para dar los compuestos

de la fórmula (8-2). Los compuestos de la fórmula (8-2) se pueden usar en el Esquema 4 en lugar de los compuestos de la fórmula (4-1).

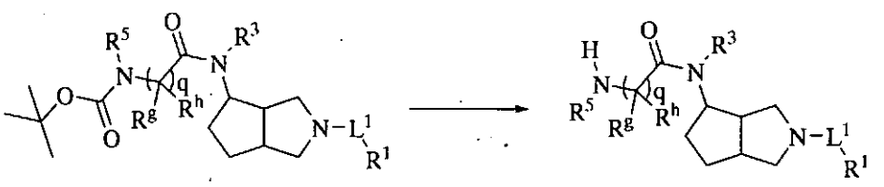
Esquema 9



(3-2) (9-1)

Según se ilustra en el Esquema 9, los compuestos de la fórmula (9-1), en donde R^2 y R^3 son como se definen en la Síntesis de la invención, se pueden obtener a partir de los compuestos de la fórmula (3-2). Los compuestos de la fórmula (3-2) se pueden hacer reaccionar con (bromometilen)dibenceno en la presencia de ioduro de potasio, y carbonato de sodio en metil etil cetona calentada a 90 °C por 6 a 24 horas para dar compuestos de la fórmula (9-1) que son representativos de los compuestos de la fórmula (I).

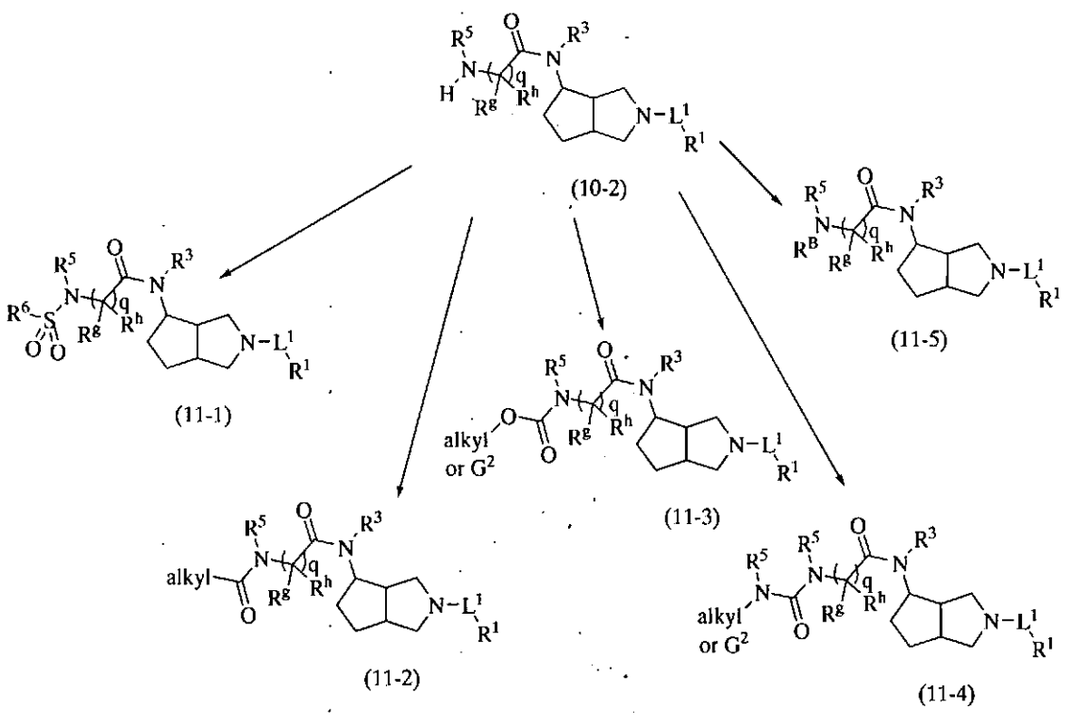
Esquema 10



(10-1) (10-2)

Según se ilustra en el Esquema 10, los compuestos de la fórmula (10-2) que son representativos de los compuestos de la fórmula (I) y en donde L^1, R^1, R^3, R^5, R^g, R^h y q son como se definen en la Síntesis de la invención se pueden obtener a partir de los compuestos de la fórmula (10-1). Los compuestos de la fórmula (10-1) se pueden tratar con un ácido tal como ácido clorhídrico o ácido trifluoroacético a temperatura ambiente en un solvente tal como éter, dioxano o diclorometano por 2-24 horas para suministrar los compuestos de la fórmula (10-2).

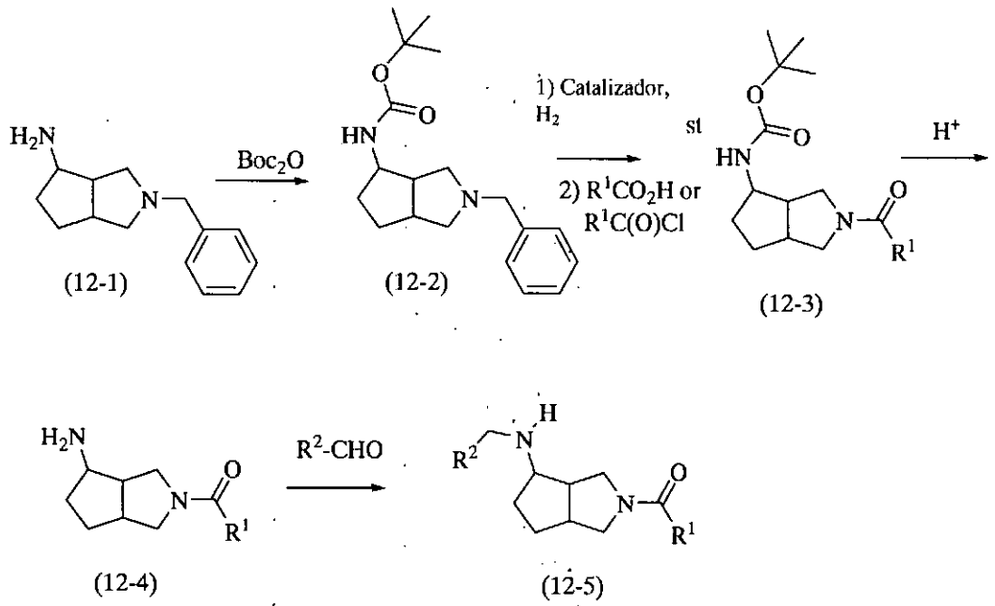
Esquema 11



Según se ilustra en el Esquema 11, los compuestos de la fórmula (11-1), (11-2), (11-3), (11-4) y (11-5) que son representativos de los compuestos de la fórmula (I) y en donde L^1, R^1, R^3, R^5, R^g, R^h, q y G^2 son como se definen en la Síntesis de la invención, se pueden obtener a partir de los compuestos de la fórmula (10-2). Los compuestos de la fórmula (10-2) se pueden tratar con un cloruro de sulfonilo de la fórmula R^6SO_2Cl en diclorometano en la presencia de diisopropiletilamina a temperatura ambiente por 2-24 horas para proporcionar los compuestos de la fórmula (11-1). De manera similar, los compuestos de la fórmula (11-2) se pueden obtener mediante tratamiento de los compuestos de la fórmula (10-2) con un anhidruro o cloruro ácido en diclorometano a temperatura ambiente en la presencia de diisopropiletilamina sobre un período de 2-24 horas. Los compuestos de la fórmula (11-3) se obtienen a partir de los compuestos de la fórmula (10-2) mediante tratamiento con un cloroformiato en la presencia de diisopropiletilamina en diclorometano a temperatura ambiente sobre un período de 2-24 horas. De manera similar, los compuestos de la fórmula (11-4) se elaboran a partir de los compuestos de la fórmula (10-2) mediante reacción con un isocianato en diclorometano a temperatura ambiente sobre un período de 2-24 horas. Los compuestos de la fórmula (11-5), en donde R^B es alquilo, arilalquilo, cicloalquilo,

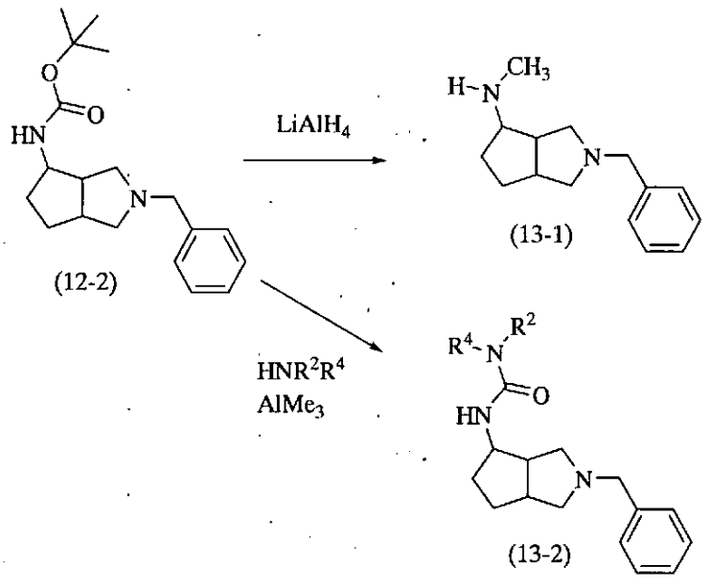
cicloalquilalquilo o heteroarilalquilo, se pueden preparar ya sea por alquilación o por aminación reductora de los compuestos de la fórmula (10-2) usando la metodología conocida por el especialista en la técnica.

Esquema 12



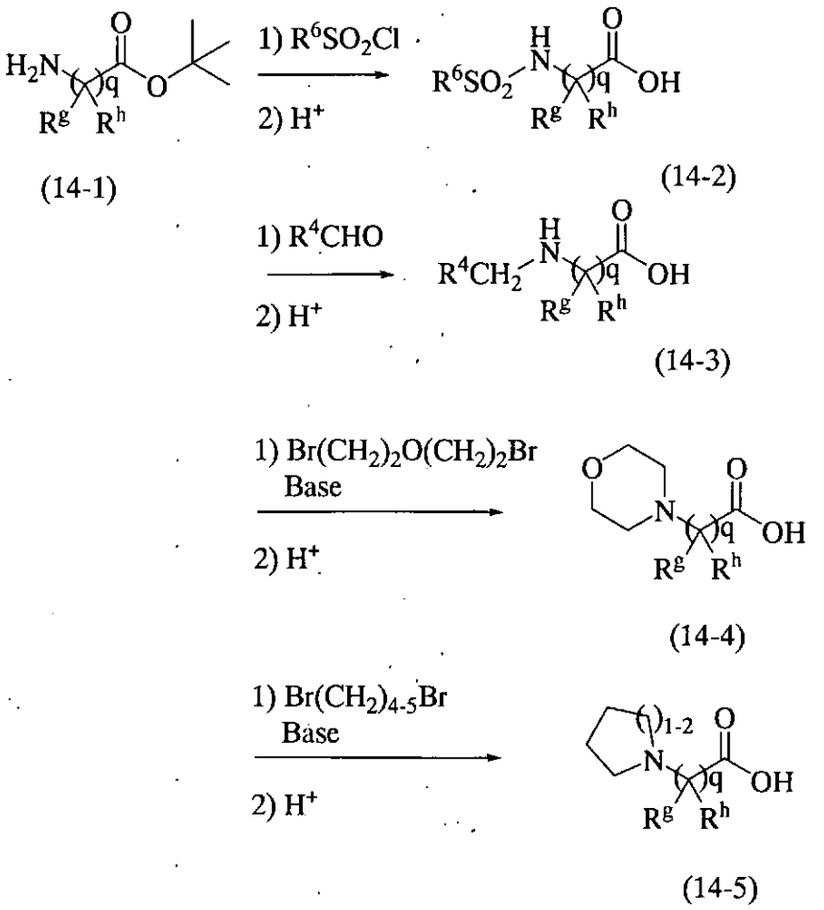
Según se ilustra en el Esquema 12, los compuestos de la fórmula (12-5) que son representativos de los compuestos de la fórmula (I) y en donde R^1 y R^2 son como se definen en la Síntesis de la invención, se pueden obtener a partir del compuesto de la fórmula (12-1). El compuesto (12-1) se puede hacer reaccionar con dicarbonato de di-*ter*-butilo en la presencia de (dimetilamino)piridina en un solvente tal como diclorometano o dioxano a temperatura ambiente durante 20 minutos a 4 horas para proporcionar un compuesto de la fórmula (12-2). El grupo bencilo de los compuestos de la fórmula (12-2) se puede remover con hidrógeno en la presencia de un catalizador de paladio como se ha descrito y luego se puede acoplar con un ácido carboxílico o un cloruro ácido como se describió en los métodos del Esquema 3 para proporcionar los compuestos de la fórmula (12-3). La eliminación del grupo *ter*-butoxicarbonilo de los compuestos de la fórmula (12-3) bajo las condiciones ácidas que se describieron en el Esquema 10 suministra los compuestos de la fórmula (12-4). Los compuestos de la fórmula (12-4) se pueden aminar bajo condiciones reductoras con aldehídos de la fórmula R^2-CHO usando las condiciones que se describen en el Esquema 3 para dar los compuestos de la fórmula (12-5).

Esquema 13



Según se ilustra en el Esquema 13, los compuestos de la fórmula (13-2) que son representativos de los compuestos de la fórmula (I), en donde R^2 y R^4 son como se definen en la Síntesis de la invención, y los compuestos de la fórmula (13-1) se pueden obtener a partir del compuesto de la fórmula (12-2). Los compuestos de la fórmula (12-2) se pueden tratar con hidruro de aluminio y litio en tetrahidrofurano, inicialmente a temperatura ambiente y luego se pueden calentar a reflujo para obtener los compuestos de la fórmula (13-1). Los compuestos de la fórmula (13-1) se pueden usar en los métodos que se describen en los Esquemas 2 y 4. El compuesto de la fórmula (12-2) se puede tratar con una amina en la presencia de trimetilaluminio en tolueno inicialmente a 0 °C y luego a 90 °C durante 6 a 24 horas para proporcionar los compuestos de urea de la fórmula (13-2).

Esquema 14



(14-1) (14-2) (14-3) (14-4) (14-5)

Según se muestra en el Esquema 14, los compuestos de las fórmulas (14-2), (14-3), (14-4) y (14-5), en donde R^4, R^6, R^g, R^h y q son como se definen en la Síntesis de la invención, se pueden obtener a partir de los compuestos de la fórmula (14-1). Los compuestos de la fórmula (14-1) se pueden tratar con un cloruro de sulfonilo de la fórmula R^6SO_2Cl en la presencia de una base tal como trietilamina o diisopropiletilamina en un solvente tal como diclorometano. La subsiguiente eliminción del grupo *t*-butilo bajo condiciones ácidas proporcionan los compuestos de la fórmula (14-2). Los compuestos de la fórmula (14-1) también se pueden aminar bajo condiciones reductoras con un aldehído de la fórmula R^4CHO y un reductor tal como cianoborohidruro de sodio, una resina de cianoborohidruro sobre soporte polimérico o triacetoxiborohidruro de sodio, opcionalmente en la presencia de un ácido tal como ácido acético en solventes tales como diclorometano o metanol. La eliminación ácida del grupo *t*-butilo suministra los compuestos de la fórmula (14-3). Los compuestos de la fórmula (14-1) también se pueden dialquilar

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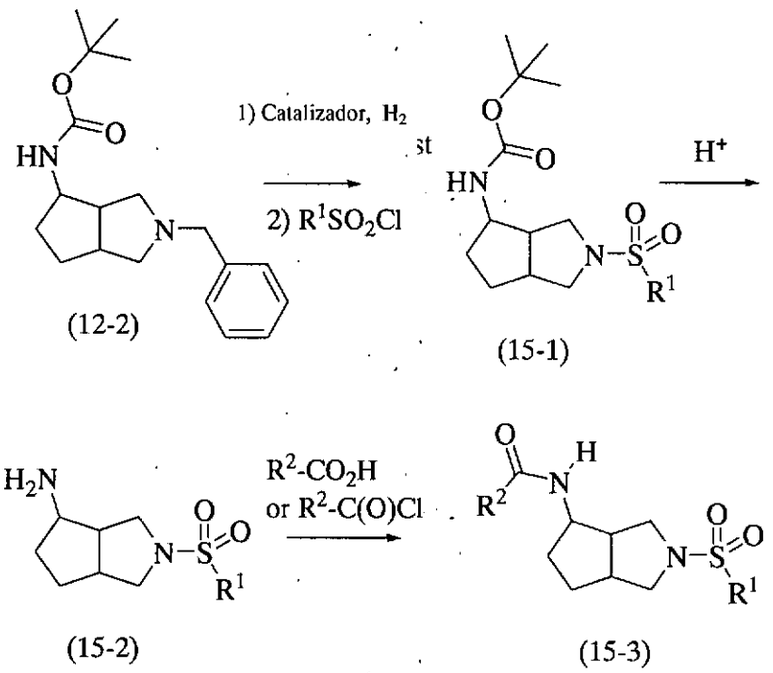
con compuestos dibromo. Por consiguiente, la alquilación de (14-1) con 1-bromo-2-(2-bromoetoxi)etano en acetonitrilo caliente en la presencia de una base seguido por eliminación de *t*-butilo catalizado por un ácido provee los compuestos de la fórmula (14-4). La alquilación con 1,4-dibromobutano o 1,5-dibromopentano bajo condiciones similares seguido por la eliminación de t-butilo catalizado por un ácido provee los compuestos de la fórmula (14-5). Los compuestos de las fórmulas (14-2), (14-3), (14-4) y (14-5) se pueden usar en los Esquemas 2, 3, 4 y 12.

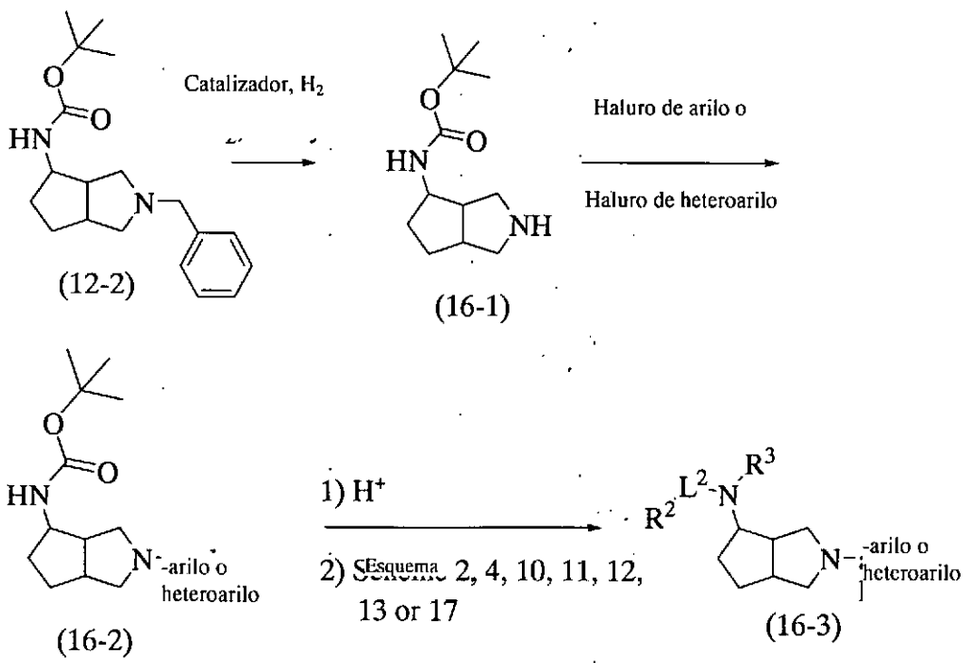
Esquema 15



Según se ilustra en el Esquema 15, los compuestos de la fórmula (15-3) que son representativos de los compuestos de la fórmula (I) y en donde R^1 y R^2 son como se definen en la Síntesis de la invención, puede obtenerse a partir del compuesto de la fórmula (12-2). El grupo bencilo de los compuestos de la fórmula (12-2) se puede remover con hidrógeno en la presencia de un catalizador de paladio como se describe en el Esquema 3 y luego se puede acoplar con un cloruro de sulfonilo de la fórmula R^1SO_2Cl como se describe en los métodos del Esquema 3 para proporcionar los compuestos de la fórmula (15-1). La eliminación del grupo *ter*-butoxicarbonilo de los compuestos de la fórmula (15-1) bajo las condiciones ácidas que se describieron en el Esquema 10 suministra los compuestos de la fórmula (15-2). Los compuestos de la fórmula (15-2) se pueden acoplar con ácidos carboxílicos de la fórmula R^2-CO_2H o cloruros ácidos de la fórmula R^2-C(O)Cl bajo

las condiciones de reacción que se describen en el Esquema 2 para dar los compuestos de la fórmula (15-3).

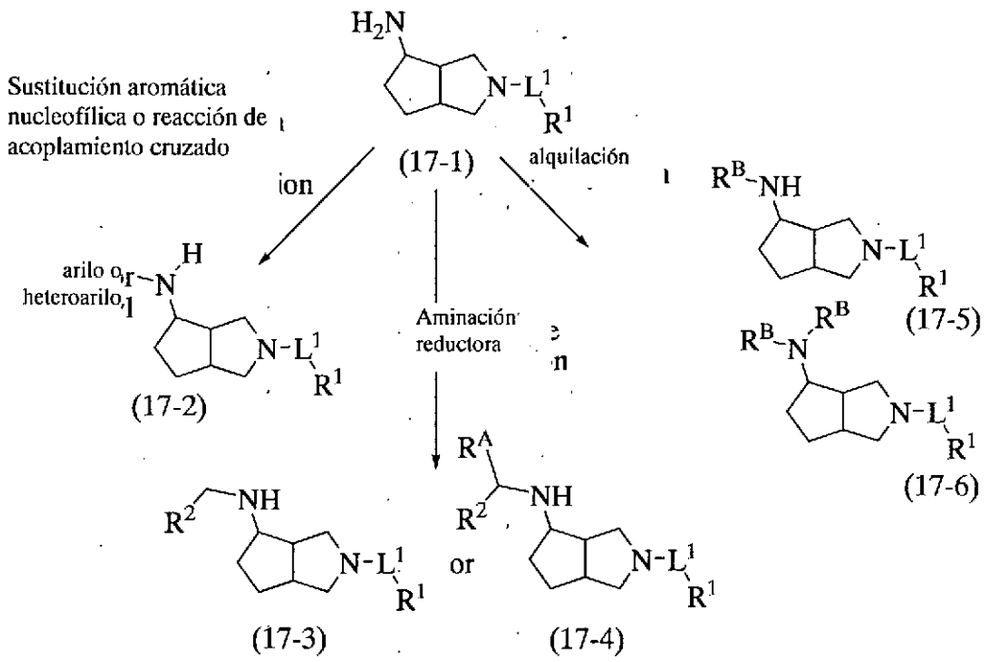
Esquema 16



(12-2) (16-1) (16-2) (16-3)

Según se ilustra en el Esquema 17, los compuestos de las fórmulas (16-3) que son representativos de los compuestos de la fórmula (I), en donde L^2, R^1, R^2 y R^3 son como se definen en la Síntesis de la invención, se pueden obtener a partir de compuestos de la fórmula (12-2). Los compuestos de la fórmula (12-1) se pueden convertir en compuestos de la fórmula (3-2) mediante tratamiento con hidrógeno (15-60 psi) en la presencia de un catalizador, tal como hidróxido de paladio sobre carbón o paladio sobre carbón, en un solvente tal como metanol o etanol a temperatura ambiente sobre un período de 16-36 horas. Los compuestos de la fórmula (16-1) se pueden hacer reaccionar luego con un haluro de arilo o un haluro de heteroarilo adecuado para una reacción de substitución aromática nucleofílica para obtener los compuestos de la fórmula (16-2). Por ejemplo, se puede calentar un compuesto de la fórmula (16-1) en un solvente tal como etanol en la presencia de una base y bromuro de heteroarilo para suministrar los compuestos de la fórmula (16-2). Los compuestos de la fórmula (16-2) se pueden desproteger luego bajo condiciones ácidas y funcionalizar luego como se describe, pero en un sentido no limitativo, en los Esquemas 2, 4, 10, 11, 12, 13 ó 17 para dar compuestos de la fórmula (16-3).

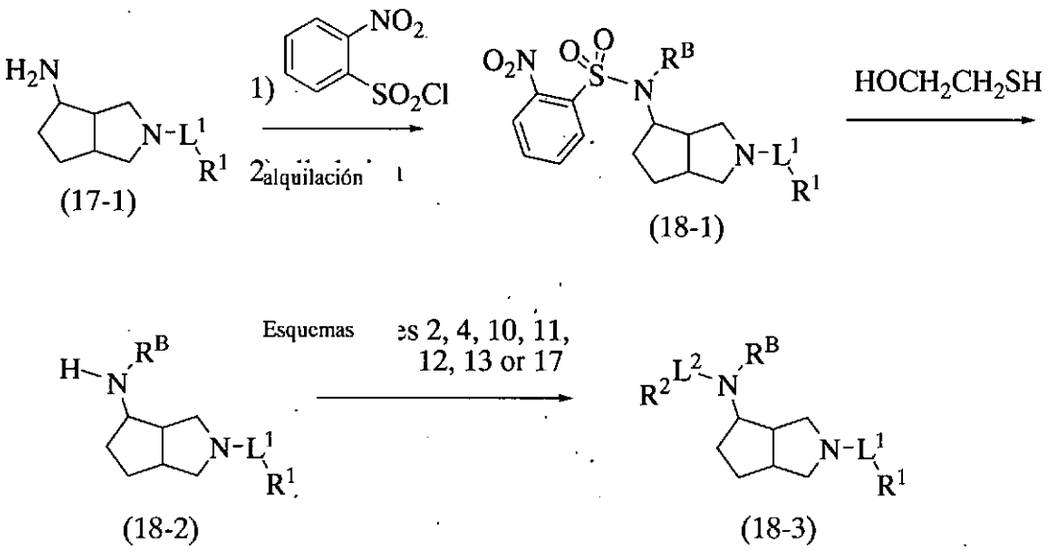
Esquema 17



Según se ilustra en el Esquema 17, los compuestos de la fórmula (17-1) se pueden transformar en los compuestos de las fórmulas (17-2), (17-3), (17-4), (17-5) y (17-6) que son representativos de los compuestos de la fórmula (I), en donde L^1, R^1 y R^2 son como se definen en la Síntesis de la invención. Los compuestos de la fórmula (17-1) se pueden convertir en compuestos de la fórmula (17-2) mediante una reacción de substitución aromática nucleofílica bajo las condiciones que se describieron en el Esquema 16 o bajo las condiciones de reacción de acoplamiento cruzado conocidas por el especialista en la técnica. Los compuestos de la fórmula (17-1) también se pueden aminar bajo condiciones reductoras con un aldehído para dar los compuestos de la fórmula (17-3) o con una cetona para dar los compuestos de la fórmula (17-4), en donde R^A es alquilo, arilo, arilalquilo, cicloalquilo, cicloalquilalquilo, heteroarilo o heteroarilalquilo. Como alternativa, en los compuestos de la fórmula (17-4), R^A y R^2 se pueden unir, junto con el átomo a los cuales están unidos, para formar un grupo cíclico. Las condiciones de una aminación reductora se describen, pero en un sentido no limitativo, en los Esquemas 3, 4, 8, 12 y 14. Los compuestos de la fórmula (17-1) se pueden mono-alquilar para dar los compuestos de la fórmula (17-5) o di-alquilar para dar los compuestos de la fórmula (17-6). Los compuestos de la fórmula (17-1) se pueden tratar con un haluro o sulfonato de alquilo, arilalquilo, cicloalquilo,

cicloalquilalquilo o heteroarilalquilo, opcionalmente en la presencia de una base opcionalmente en un solvente caliente tal como tetrahidrofurano o *N,N*-dimetilformamida para dar los compuestos de la fórmula (17-5), en donde R^B es alquilo, arilalquilo, cicloalquilo, cicloalquilalquilo o heteroarilalquilo. Un exceso de agente alquilante conduce a los compuestos de la fórmula (17-6).

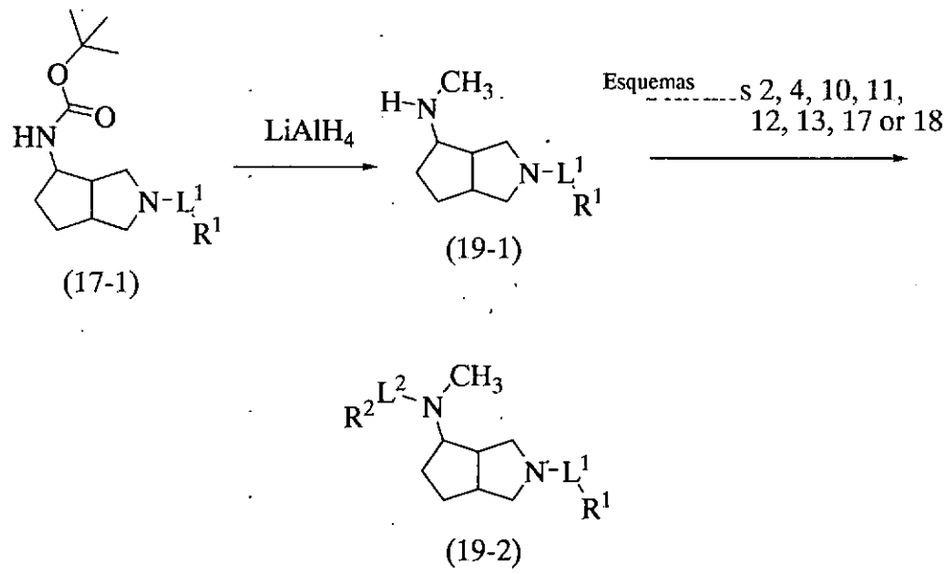
Esquema 18



(17-1) (18-1) (18-2) (18-3)

Según se ilustra en el Esquema 18, los compuestos de la fórmula (17-1) se pueden convertir en compuestos de las fórmulas (18-1), (18-2) y (18-3) que son representativos de los compuestos de la fórmula (I), en donde, L^1, L^2, R^1 y R^2 son como se definen en la Síntesis de la invención y R^B es alquilo, arilalquilo, cicloalquilo, cicloalquilalquilo o heteroarilalquilo. Los compuestos de la fórmula (17-1) se pueden hacer reaccionar con cloruro de 2-nitrobenceno-1-sulfonilo en la presencia de una base. La sulfonamida resultante se puede alquilar luego bajo las condiciones conocidas por el especialista en la técnica para dar los compuestos de la fórmula (18-1). El tratamiento con 2-mercaptoetanol en la presencia de una base en un solvente tal como *N,N*-dimetilformamida permite obtener los compuestos de la fórmula (18-2). Los compuestos de la fórmula (18-2) se pueden hacer reaccionar como se describe en los Esquemas 2, 4, 10, 11, 12, 13 ó 17 para dar los compuestos de la fórmula (18-3).

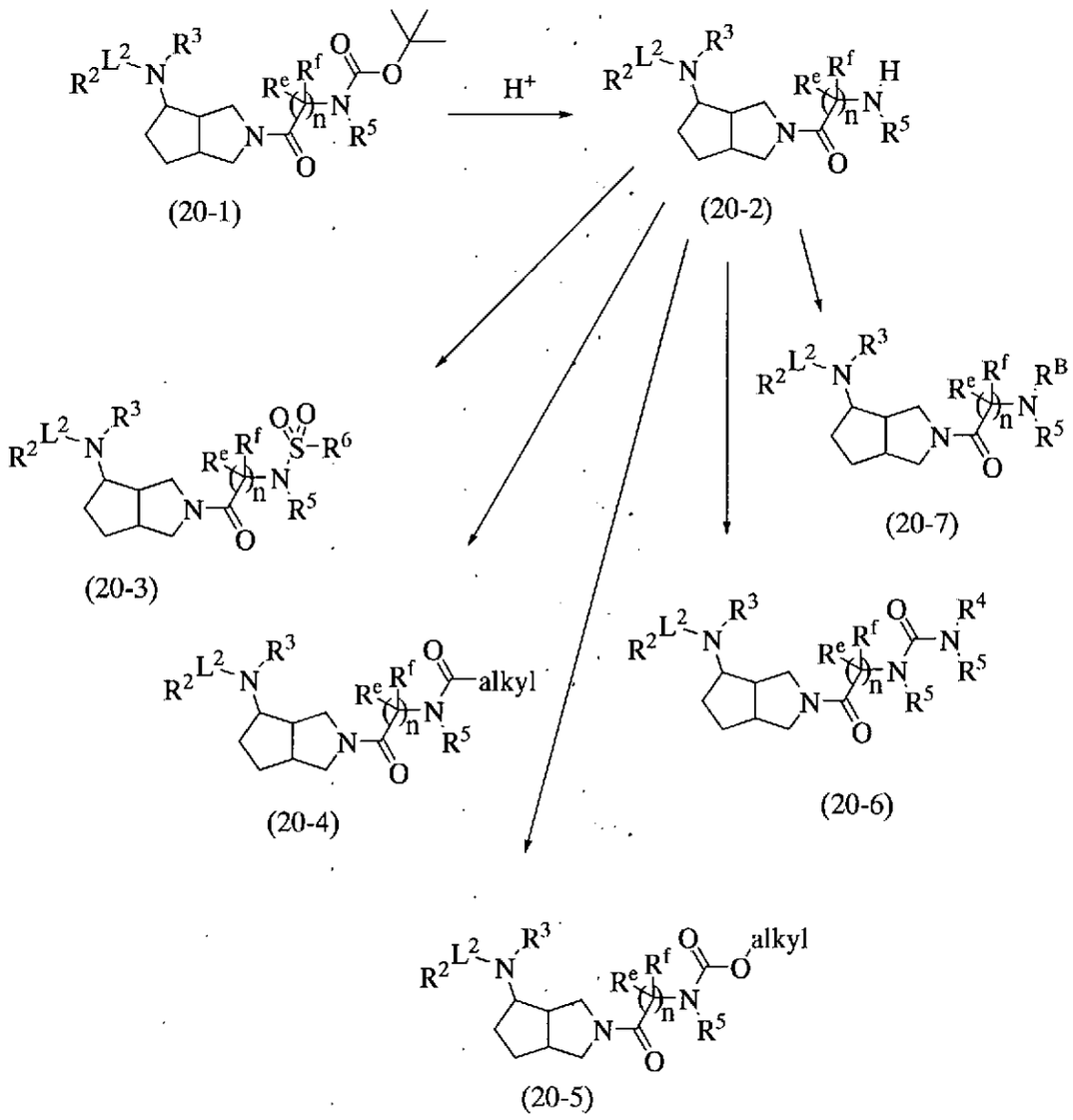
Esquema 19



(17-1) (19-1) (19-2)

Según se ilustra en el Esquema 19, los compuestos de la fórmula (19-2) que son representativos de los compuestos de la fórmula (I), en donde L^1, L^2, R^1 y R^2 son como se definen en la Síntesis de la invención, se pueden obtener a partir de compuestos de la fórmula (17-1). El compuesto de la fórmula (17-1) se puede tratar con hidruro de aluminio y litio en tetrahidrofurano inicialmente a temperatura ambiente y luego se puede calentar a reflujo para obtener compuestos de la fórmula (19-1). Los compuestos de la fórmula (19-1) se pueden usar en los métodos que se describen en los Esquemas 2, 4, 10, 11, 12, 13, 17 ó 18 para dar los compuestos de la fórmula (19-2).

Esquema 20



Según se ilustra en el Esquema 20, los compuestos de la fórmula (20-3), (20-4), (20-5), (20-6) y (20-7) que son representativos de los compuestos de la fórmula (I) y en donde L^2, R^2, R^3, R^4, R^5, R^6, R^e, R^f y n son como se definen en la Síntesis de la invención, se pueden obtener a partir de los compuestos de la fórmula (20-2). Los compuestos de la fórmula (20-2) se obtienen a partir de los compuestos de la fórmula (20-1) mediante tratamiento con un ácido tal como ácido trifluoroacético en diclorometano o ácido clorhídrico en dioxano. Los compuestos de la fórmula (20-2) se pueden tratar con un cloruro de sulfonilo de la fórmula R^6SO_2Cl en diclorometano en la presencia de diisopropiletilamina a temperatura ambiente por 2-24 horas para proporcionar los compuestos de la fórmula (20-3). De manera

similar, los compuestos de la fórmula (20-4) se pueden obtener mediante tratamiento de los compuestos de la fórmula (20-2) con un anhidruro o cloruro ácido en diclorometano a temperatura ambiente en la presencia de diisopropiletilamina sobre un período de 2-24 horas. Los compuestos de la fórmula (20-5) se obtienen a partir de los compuestos de la fórmula (20-2) mediante tratamiento con un cloroformiato en la presencia de diisopropiletilamina en diclorometano a temperatura ambiente sobre un período de 2-24 horas. De manera similar, los compuestos de la fórmula (20-6) se elaboran a partir de los compuestos de la fórmula (20-2) mediante reacción con un isocianato en diclorometano a temperatura ambiente sobre un período de 2-24 horas. Los compuestos de la fórmula (20-7), en donde R^B es alquilo, arilalquilo, cicloalquilo, cicloalquilalquilo o heteroarilalquilo, se pueden preparar ya sea por alquilación o por aminación reductora de los compuestos de la fórmula (20-2) usando la metodología conocida por el especialista en la técnica.

Se podrá apreciar que los esquemas de síntesis y los ejemplos específicos que se ilustran en la sección de los Ejemplos se ofrecen a modo ilustrativo y no se deben interpretar como limitantes del alcance de la invención definida en las reivindicaciones adjuntas. Todas las alternativas, modificaciones, y equivalentes de los métodos de síntesis y ejemplos específicos se incluyen dentro del alcance de las reivindicaciones.

Las condiciones de reacción y los tiempos de reacción óptimos para cada paso individual pueden variar dependiendo de los reactivos que se empleen en particular y de los sustituyentes presentes en los reactivos que se utilicen. A no ser que se especifique de otra manera, el especialista en la técnica puede seleccionar fácilmente los solventes, temperaturas y otras condiciones de reacción. Los procedimientos específicos se indican en la sección de Ejemplos. Las reacciones se pueden desarrollar de la manera convencional, por ejemplo eliminando el solvente del residuo y seguir con la purificación de acuerdo con metodologías conocidas en general en la técnica, tales como, pero de manera no limitativa, cristalización, destilación, extracción, trituración y cromatografía. A menos que se indique lo contrario, los materiales de partida y los reactivos se pueden obtener comercialmente o los especialistas en la técnica los pueden preparar a partir de materiales que se pueden obtener comercialmente usando los

métodos descritos en la literatura química.

El alcance de la invención incluye los experimentos de rutina, que incluyen la apropiada manipulación de las condiciones de reacción, reactivos y la secuencia de la ruta de síntesis, protección de toda funcionalidad química que pueda no ser compatible con las condiciones de reacción y desprotección en un punto apropiado en la secuencia de la reacción del método. Los grupos protectores apropiados y los métodos para proteger y desproteger diferentes sustituyentes usando dichos grupos protectores apropiados son bien conocidos por aquellos con experiencia en la técnica; cuyos ejemplos se pueden consultar en T. Greene y P. Wuts, *Protecting Groups in Chemical Synthesis* (3ª ed.), John Wiley & Sons, NY (1999), que se incorpora aquí como referencia en su totalidad. La síntesis de los compuestos de la invención se puede llevar a cabo usando métodos análogos a aquellos descritos en los esquemas de síntesis descritos aquí anteriormente y en los ejemplos específicos.

Si los materiales de partida no se pueden obtener comercialmente, se pueden preparar mediante procedimientos que se pueden seleccionar entre técnicas estándar de la química orgánica, técnicas análogas a las síntesis de compuestos conocidos, estructuralmente similares, o técnicas que son análogas a los esquemas descritos anteriormente o los procedimientos descritos en la sección de síntesis de los Ejemplos.

Cuando fuera necesaria una forma ópticamente activa de un compuesto de la invención, la misma se puede obtener llevando a cabo uno de los procedimientos que se describen aquí usando una materia prima ópticamente activa (preparada, por ejemplo, por inducción asimétrica de un paso de reacción apropiado), o por resolución de una mezcla de los estereoisómeros del compuesto o intermediarios usando un procedimiento estándar (tal como separación cromatográfica, recristalización o resolución enzimática).

De manera similar, cuando se necesita un isómero geométrico puro de un compuesto de la invención, el mismo se puede obtener llevando a cabo uno de los procedimientos anteriores usando un isómero geométrico puro como materia prima, o por resolución de una mezcla de los isómeros geométricos del compuesto o intermediarios usando un procedimiento estándar tal como la separación cromatográfica.

g. Ejemplos

Ejemplo 1 y Ejemplo 2

***N*-[(3a*S**,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclopentancarboxamida (Ejemplo 1) y *N*-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclopentancarboxamida (Ejemplo 2)**

Se agregó 1-hidroxibenzotriazol (33 mg, 0,24 mmol) y *N*-(3-dimetilaminopropil)-*N*'-etilcarbodiimida (43 µL, 0,24 mmol) a una solución de ácido 1-fenilciclopentancarboxílico (46 mg, 0,24 mmol) en diclorometano (2 ml). La reacción se agitó a temperatura ambiente por 10 minutos, luego se agregó (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina (52 mg, 0,24 mmol) y la reacción se agitó a temperatura ambiente durante la noche. La reacción se detuvo con agua, y se extrajo con diclorometano, luego se purificó mediante cromatografía sobre gel de sílice usando metanol al 1-10% (amoníaco 2 N)/cloroformo como eluyente para dar los compuestos del título.

Ejemplo 1: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,52 – 7,28 (m, 9H), 7,25 (d, *J* = 7,7, 1H), 4,43 – 4,34 (m, 1H), 3,56 (d, *J* = 12,9, 1H), 3,17 (d, *J* = 12,9, 1H), 2,83 – 2,67 (m, 2H), 2,59 – 2,50 (m, 1H), 2,50 – 2,44 (m, 1H), 2,35 – 2,29 (m, 2H), 2,04 – 1,87 (m, 4H), 1,84 – 1,54 (m, 6H), 1,43 – 1,26 (m, 1H), 1,04 – 0,94 (m, 1H); MS (ESI+) *m/z* 389 $(M+H)^+$.

Ejemplo 2: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,52 – 7,47 (m, 2H), 7,41 (d, *J* = 7,4, 2H), 7,38 – 7,29 (m, 4H), 7,25 (q, *J* = 7,3, 2H), 4,36 (m, 1H), 3,57 (d, *J* = 13,2, 1H), 3,40 (d, *J* = 13,2, 1H), 2,78 (m, 3H), 2,33 (m, 3H), 2,27 (d, *J* = 8,7, 1H), 2,21 – 2,13 (m, 1H), 1,99 (dt, *J* = 5,8, 11,7, 3H), 1,87 – 1,75 (m, 2H), 1,71 – 1,60 (m, 3H), 1,44 (ddd, *J* = 7,7, 12,1, 14,5, 1H), 1,31 (m, 1H); MS (ESI+) *m/z* 389 $(M+H)^+$.

Ejemplo 3 y Ejemplo 4

***N*-[(3a*R**,4*R**,6a*S**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclohexil-2-fenilacetamida (Ejemplo 3) y *N*-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclohexil-2-fenilacetamida (Ejemplo 4)**

Los compuestos del título se prepararon utilizando ácido 2-ciclohexil-2-fenilacético en lugar de ácido 1-fenilciclopentancarboxílico en el procedimiento que describe la preparación de los Ejemplos 1 y 2.

Ejemplo 3: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,10 (s, 1H), 7,67 (d, *J* = 7,2, 1H), 7,44 (dd, *J* = 5,7, 12,3, 3H), 7,40 – 7,35 (m, 3H), 7,33 (t, *J* = 7,4, 1H), 7,27 (dd, *J* = 7,6, 16,2, 1H), 4,43 – 4,37 (m, 0,5H), 4,36 – 4,29 (m, 0,5H), 3,56 (d, *J* = 12,6, 0,5H), 3,42 (t, *J* = 11,7, 1H), 3,26 (dd, *J* = 6,6, 11,7, 1H), 3,14 (d, *J* = 10,5, 0,5H), 2,80 (d, *J* = 8,3, 1H), 2,63 (d, *J* = 6,9, 0,5H), 2,24 – 2,13 (m, 1,5H), 2,02 (d, *J* = 12,5, 0,5H), 1,91 (d, *J* = 7,0, 1H), 1,74 – 1,59 (m, 2,5H), 1,58 – 1,34 (m, 4H), 1,33 – 1,19 (m, 1,5H), 1,18 – 0,99 (m, 3H), 0,87 (d, *J* = 14,3, 0,5H), 0,81 – 0,68 (m, 1H); MS (ESI+) *m/z* 417 $(M+H)^+$.

Ejemplo 4: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,65 – 8,56 (m, 1H), 7,66 (dd, *J* = 3,1, 7,3, 2H), 7,43 (d, *J* = 7,4, 1H), 7,39 – 7,30 (m, 5H), 7,27 (dd, *J* = 5,0, 7,6, 2H), 4,35 (s, 1H), 3,59 (d, *J* = 13,1, 0,5H), 3,52 (d, *J* = 13,2, 0,5H), 3,44 (d, *J* = 13,1, 0,5H), 3,33 (dd, *J* = 8,2, 11,7, 1,5H), 2,89 (dd, *J* = 3,1, 9,1, 0,5H), 2,63 – 2,54 (m, 1H), 2,53 – 2,45 (m, 1H), 2,36 (m, 2H), 2,28 (t, *J* = 8,0, 1H), 2,22 (t, *J* = 7,0, 2H), 2,16 (dd, *J* = 6,0, 12,2, 1H), 1,92 (dd, *J* = 6,1, 12,2, 0,5H), 1,84 (dd, *J* = 7,5, 12,6, 0,5H), 1,71 (dd, *J* = 6,2, 12,8, 2H), 1,44 (dd, *J* = 20,6, 55,0, 4H), 1,29 (m, 1,5H), 1,18 (m, 1H), 1,06 (m, 2H), 0,70 (m, 1H); MS (ESI+) *m/z* 389 $(M+H)^+$.

Ejemplo 5 y Ejemplo 6

***N*-[(3a*R**,4*R**,6a*S**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida (Ejemplo 5) y *N*-[(3a*R**,4*S**,6a*S**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida (Ejemplo 6)**

Los compuestos del título se prepararon utilizando ácido 3-metil-2-fenilbutanoico en lugar de ácido 1-fenilciclopentancarboxílico en el procedimiento que describe la preparación de los Ejemplos 1 y 2.

Ejemplo 5: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,13 – 8,03 (m, 1H), 7,65 (d, *J* = 7,2, 1H), 7,55 (d, *J* = 7,3, 1H), 7,44 (d, *J* = 4,3, 2H), 7,41 (d, *J* = 7,0, 1H), 7,36 (t, *J* = 6,9, 3H), 7,28 (ddd, *J* = 7,3, 14,7, 17,5, 2H), 4,40 (dd, *J* = 6,7, 13,3, 0,5H), 4,35 – 4,27 (m, 0,5H), 3,55 (d, *J* = 12,7, 0,5H), 3,40 (dd, *J* = 4,5, 12,8, 1H), 3,26 (d, *J* = 12,9, 0,5H), 3,16 (d, *J* = 10,5, 0,5H), 3,05 (d, *J* = 10,5, 0,5H), 2,78 (dd, *J* = 8,1, 15,8, 1H), 2,69 – 2,54 (m, 1,5H), 2,43 – 2,26 (m, 3H), 2,23 – 2,13 (m, 1H), 1,94 – 1,82 (m, 1H), 1,73 – 1,57 (m, 1,5H), 1,50 (dt, *J* = 7,1, 15,0, 0,5H), 1,38 (td, *J* = 6,4, 12,2, 0,5H), 1,27 (m, 0,5H), 1,19 (d, *J* = 6,4, 1,5H), 1,11 (dd, *J* = 5,7, 12,0, 0,5H), 1,03 (d, *J* = 6,5, 1,5H), 0,73 (dd, *J* = 6,7, 10,7, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Ejemplo 6: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,56 (d, *J* = 12,9, 1H), 7,67 – 7,61 (m, 2H), 7,43 (d, *J* = 7,1, 1H), 7,39 – 7,31 (m, 5H), 7,29 – 7,24 (m, 2H), 4,40 – 4,28 (m, 1H), 3,60 (d, *J* = 13,1, 0,5H), 3,52 (d, *J* = 13,1, 0,5H), 3,44 (d, *J* = 13,2, 0,5H), 3,33 (d, *J* = 13,2, 0,5H), 3,22 (d, *J* = 10,4, 1H), 2,89 (dd, *J* = 3,0, 9,1, 0,5H), 2,64 (m, 1H), 2,55 (m 1H), 2,51 – 2,44 (m, 1H), 2,36 (s, 1H), 2,28 (t, *J* = 8,3, 1H), 2,24 – 2,10 (m, 2H), 1,95 – 1,87 (m, 0,5H), 1,81 (d, *J* = 8,1, 0,5H), 1,77 – 1,62 (m, 1H), 1,36 (m, 1,5H), 1,20 (dt, *J* = 5,3, 10,6, 3H), 0,70 (dd, *J* = 1,6, 6,7, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Ejemplo 7 y Ejemplo 8

_N_-[(3a_S_*,4_S_*,6a_R_*)-2-benciloctahidrociclopenta[_c_]pirrol-4–il]-2-ciclopentil-2-fenilacetamida (Ejemplo 7) y _N_-[(3a_S_*,4_R_*,6a_R_*)-2-benciloctahidrociclopenta[_c_]pirrol-4–il]-2-ciclopentil-2-fenilacetamida (Ejemplo 8)

Los compuestos del título se prepararon utilizando ácido 2-ciclopentil-2-fenilacético en lugar de ácido 1-fenilciclopentancarboxílico en el procedimiento que describe la preparación de los Ejemplos 1 y 2.

Ejemplo 7: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,06 (dd, *J* = 6,8, 23,5, 1H), 7,67 (d, *J* = 7,2, 1H), 7,46 – 7,39 (m, 3H), 7,40 – 7,29 (m, 4H), 7,29 – 7,22 (m, 1H), 4,45 – 4,37 (m, 0,5H), 4,35 – 4,27 (m, 0,5H), 3,54 (d, *J* = 12,7, 0,5H), 3,42 (dd, *J* = 4,0, 12,8, 1H), 3,34 – 3,19 (m, 1,5H), 2,97 – 2,77 (m, 2,5H), 2,63 (d, *J* = 7,2, 0,5H), 2,46– 2,27 (m, 3H), 2,26 – 2,05 (m, 1,5H), 2,03 – 1,84 (m, 1,5H), 1,71 (dt, *J* = 7,0, 14,1, 0,5H), 1,65 – 1,36 (m, 8H), 1,33 – 1,22 (m, 0,5H), 1,20 – 0,98 (m, 2H); MS (ESI+) *m/z* 403 $(M+H)^+$.

Ejemplo 8: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,60 – 8,49 (m, 1H), 7,67 (dd, *J* = 2,3, 7,6, 2H), 7,44 (d, *J* = 7,2, 1H), 7,36 (dt, *J* = 5,0, 7,6, 5H), 7,26 (t, *J* = 6,9, 2H), 4,36 (m, 1H), 3,61 (d, *J* = 13,1, 0,5H), 3,52 (d, *J* = 13,1, 0,5H), 3,45 (d, *J* = 13,2, 0,5H), 3,36 (dd, *J* = 12,0, 16,0, 1,5H), 2,95 – 2,83 (m, 1,5H), 2,63 – 2,55 (m, 1H), 2,53 – 2,46 (m, 1H), 2,38 (s, 1H), 2,29 (dd, *J* = 7,0, 12,8, 1,5H), 2,22 (dd, *J* = 6,1, 12,3, 1H), 2,18– 2,504 (m, 1,5H), 1,94 (dd, *J* = 6,1, 12,2, 0,5H), 1,84 (dd, *J* = 7,5, 12,7, 0,5H), 1,79 – 1,66 (m, 1H), 1,65 – 1,24 (m, 8,5H), 1,09 – 0,92 (m, 1H); MS (ESI+) *m/z* 403 $(M+H)^+$.

Ejemplo 9 y Ejemplo 10

***N*-[(3a*S**,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclohexanocarboxamida (Ejemplo 9) y *N*-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclohexanocarboxamida (Ejemplo 10)**

Los compuestos del título se prepararon utilizando ácido 1-fenilciclohexanocarboxílico en lugar de ácido 1-fenilciclopentancarboxílico en el procedimiento que describe la preparación de los Ejemplos 1 y 2.

Ejemplo 9: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,57 – 7,54 (m, 2H), 7,45 (t, *J* = 7,3, 2H), 7,37 (dd, *J* = 7,6, 15,3, 5H), 7,29 (d, *J* = 6,9, 1H), 7,25 (t, *J* = 7,3, 1H), 4,41 (m, 1H), 3,59 (d, *J* = 12,9, 1H), 3,18 (d, *J* = 12,9, 1H), 2,52 (dd, *J* = 8,9, 17,6, 4H), 2,34 (dd, *J* = 8,5, 15,2, 2H), 2,01 – 1,92 (m, 2H), 1,91 – 1,80 (m, 2H), 1,79 – 1,68 (m, 3H), 1,61 (d, *J* = 25,2, 4H), 1,43 – 1,33 (m, 1H), 1,27 (d, *J* = 8,7, 1H), 1,04 – 0,93 (m, 1H); MS (ESI+) *m/z* 403 $(M+H)^+$.

Ejemplo 10: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,60 (s, 1H), 7,42 (d, *J* = 7,2, 2H), 7,36 (t, *J* = 6,7, 4H), 7,27 (d, *J* = 7,5, 2H), 4,42 (m, 1H), 3,58 (d, *J* = 13,2, 1H), 3,40 (d, *J* = 13,1, 1H), 2,81 (d, *J* = 8,1, 1H), 2,68 (m, 2H), 1,41 – 2,24 (m, 4H), 2,18 (m, 1H), 2,00 (m, 1H), 1,80 (m, 4H), 1,73 – 1,54 (m, 4H), 1,52 – 1,39 (m, 1H), 1,36 – 1,18 (m, 2H); MS (ESI+) *m/z* 403 $(M+H)^+$.

Ejemplo 11

***N*-[(3a*S**,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida**

Se combinó (3a*S**,6aR*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina (500 mg, 2,311 mmol), ácido 2,2-diciclohexilacético (570 mg, 2,54 mmol), y 1-hidroxibenzotriazol (389 mg, 2,54 mmol) en diclorometano (20 ml). La reacción se agitó a temperatura ambiente por 10 minutos, luego se agregó *N*-(3-dimetilaminopropil)-*N*'-etilcarbodiimida (0,449 ml, 2,54 mmol) por goteo. La reacción se agitó a temperatura ambiente por 20 horas, y luego la reacción se detuvo con 10 ml de agua. La reacción se extrajo con 2x20 ml de diclorometano, el solvente se eliminó al vacío, y el material crudo se cromatografió sobre un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-40) eluyendo con 30-50% acetato de etilo/hexanos para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,60 (d, *J* = 5,1, 1H), 7,45 – 7,38 (m, 4H), 7,35 (m, 1H),

4,49 – 4,41 (m, 1H), 3,57 (d, *J* = 12,6, 1H), 3,37 (d, *J* = 12,5, 1H), 2,76 (d, *J* = 9,6, 1H), 2,69 (dd, *J* = 7,9, 15,7, 1H), 2,50 (d, *J* = 9,1, 1H), 2,48 – 2,41 (m, 1H), 2,28 (t, *J* = 8,2, 1H), 2,15 – 2,08 (m, 1H), 1,99 – 1,06 (m, 26H), 1,04 – 0,92 (m, 1H); MS (ESI+) *m/z* 423 $(M+H)^+$.

Ejemplo 12 y Ejemplo 13

(2*S*)-2-(3-benzoilfenil)-*N*-[(3a*S,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]propanamida (Ejemplo 12) y (2*S*)-2-(3-benzoilfenil)-*N*-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]propanamida (Ejemplo 13)**

Los compuestos del título se prepararon utilizando ácido (S)-2-(3-benzoilfenil)propanoico en lugar de ácido 1-fenilciclopentancarboxílico en el procedimiento que describe la preparación de los Ejemplos 1 y 2.

Ejemplo 12: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,28 (d, *J* = 6,9, 0,5H), 8,21 (d, *J* = 7,1, 0,5H), 8,13 (d, *J* = 15,9, 1H), 7,92 – 7,82 (m, 2H), 7,75 (t, *J* = 9,1, 2H), 7,56 – 7,52 (m, 1H), 7,50 – 7,25 (m, 8H), 4,49 – 4,32 (m, 1H), 3,90 (q, *J* = 7,1, 0,5H), 3,81 (t, *J* = 7,0, 0,5H), 3,45 (q, *J* = 12,8, 1,5H), 3,25 (d, *J* = 13,0, 0,5H), 2,75 (d, *J* = 9,2, 1,5H), 2,49 (dd, *J* = 2,9, 9,5, 0,5H), 2,44 – 2,31 (m, 1,5H), 2,24 (dt, *J* = 7,7, 16,5, 1,5H), 2,14 (d, *J* = 9,6, 0,5H), 2,09 – 2,01 (m, 0,5H), 1,90 – 1,71 (m, 1H), 1,66 – 1,44 (m, 5H), 1,20 (dd, *J* = 5,4, 28,1, 1H); MS (ESI+) *m/z* 453 $(M+H)^+$.

Ejemplo 13: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,67 (d, *J* = 7,1, 1H), 8,10 (s, 1H), 7,91 – 7,86 (m, 2H), 7,83 (d, *J* = 7,7, 1H), 7,74 (d, *J* = 7,6, 1H), 7,56 – 7,51 (m, 1H), 7,47 – 7,32 (m, 7H), 7,30 – 7,24 (m, 1H), 4,47 – 4,29 (m, 1H), 3,93 (q, *J* = 6,9, 1H), 3,56 (t, *J* = 12,3, 1H), 3,44 (d, *J* = 13,1, 0,5H), 3,37 (d, *J* = 13,1, 0,5H), 2,81 (dd, *J* = 3,0, 9,1, 0,5H), 2,72 (d, *J* = 7,0, 0,5H), 2,53 (m, 0,5H), 2,49 – 2,39 (m, 2H), 2,37 – 2,32 (m, 0,5H), 2,31 – 2,18 (m, 2H), 2,12 (dd, *J* = 6,0, 12,1, 0,5H), 2,03 (dd, *J* = 6,0, 12,2, 0,5H), 1,86 – 1,71 (m, 1H), 1,63 (t, *J* = 9,9, 3H), 1,57 – 1,47 (m, 1H), 1,40 – 1,27 (m, 1H); MS (ESI+) *m/z* 453 $(M+H)^+$.

Ejemplo 14

***N*-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida**

Paso A: Se combinó 2-bencilhexahidrociclopenta[*c*]pirrol-4(5*H*)-ona (16,28 g, 76 mmol), tetraetóxido de titanio (28,5 ml, 137 mmol), y (*S*)-2-metilpropan-2-sulfinamida (10,452 g, 86 mmol) en tetrahidrofurano (200 ml). La reacción se

calentó a 60 °C durante la noche. La reacción luego se redujo en volumen a aproximadamente la mitad y se vertió en 150 ml de cloruro de amonio acuoso saturado. El precipitado se recogió mediante filtración y se lavó con acetato de etilo. El material filtrado se vertió en un embudo de separación y la capa orgánica se retiró. La capa acuosa se extrajo con acetato de etilo (3×100 ml). Los lavados orgánicos se combinaron y se lavó con salmuera, se secó (Na_2SO_4) y se concentró. El material crudo se cromatografió usando un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS65-400) eluyendo con 5-100% acetato de etilo/hexanos para dar (*S*,*E*)-*N*-((3a*R*,6a*S*)-2-bencilhexahidrociclopenta[*c*]pirrol-4(5*H*)–iliden)-2-metilpropan-2-sulfinamida y (*S*,*E*)-*N*-((3a*S*,6a*R*)-2-bencilhexahidrociclopenta[*c*]pirrol-4(5*H*)–iliden)-2-metilpropan-2-sulfinamida.

Paso B: Una mezcla de (*S*,*E*)-*N*-((3a*S*,6a*R*)-2-bencilhexahidrociclopenta[*c*]pirrol-4(5*H*)–iliden)-2-metilpropan-2-sulfinamida (0,940 g, 2,95 mmol) del Paso A en metanol (20 ml) se enfrió a -78 °C en un baño de hielo seco/acetona. Se agregó borhidruro de sodio (0,335 g, 8,85 mmol), y la reacción se dejó calentar a temperatura ambiente durante la noche. La reacción se detuvo con cloruro de amonio acuoso saturado, se diluyó con agua, y se extrajo con 3×100 ml de acetato de etilo. Los extractos se secaron (Na_2SO_4) y se filtró. El solvente se eliminó al vacío, y el material crudo se cromatografió usando un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-40) con 5-50% acetona/hexanos para dar (*S*)-*N*-((3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-2-metilpropan-2-sulfinamida: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,37 – 7,11 (m, 5H), 4,85 (d, *J* = 7,0, 1H), 3,90 – 3,71 (m, 2H), 3,28 (d, *J* = 13,0, 1H), 3,09 (d, *J* = 9,8, 1H), 2,72 – 2,50 (m, 2H), 2,46 (d, *J* = 9,6, 1H), 2,32 – 2,12 (m, 2H), 1,82 (td, *J* = 5,5, 12,7, 1H), 1,68 – 1,60 (m, *J* = 10,6, 2H), 1,35 – 1,24 (m, 1H), 1,20 (s, *J* = 5,5, 9H).

Paso C: Se combinó (*S*)-*N*-((3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-2-metilpropan-2-sulfinamida (855 mg, 2,67 mmol) del Paso B y HCl 2 N (10 ml, 40,0 mmol) en metanol (10 ml). Luego de 30 minutos, el solvente se eliminó y el material crudo se purificó en un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-25) cargado con una solución al 10% de metanol(amoníaco 2 N)/diclorometano y eluyendo con metanol al 2-10% (amoníaco 2 N)/diclorometano para dar (3a*S*,4*S*,6a*R*)-2-

benciloctahidrociclopenta[*c*]pirrol-4-amina: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,44 (d, *J* = 7,4, 2H), 7,36 (t, *J* = 7,5, 2H), 7,28 (t, *J* = 7,3, 1H), 3,52 (q, *J* = 13,0, 2H), 3,29 (q, *J* = 7,3, 1H), 2,84 (dd, *J* = 3,7, 9,3, 1H), 2,55 – 2,43 (m, 3H), 2,37 – 2,30 (m, 1H), 2,24 (d, *J* = 5,3, 1H), 1,74 – 1,64 (m, 2H), 1,62 – 1,53 (m, 1H), 1,34 (dd, *J* = 5,0, 10,1, 1H).

Paso D: Se combinó ácido 3-metil-2-fenilbutanoico (1,049 mmol), hidrato de 1-hidroxibenzotriazol (1,049 mmol), y *N*-(3-dimetilaminopropil)-*N'*-etilcarbodiimida (185 µL, 1,049 mmol) en diclorometano (4 ml). La mezcla se agitó a temperatura ambiente por 10 minutos, luego se agregó (3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina (1,049 mmol) del Paso C en 2 ml de diclorometano. La reacción se agitó a temperatura ambiente por 3,5 horas, y luego se detuvo con 0,5 ml de agua. La capa orgánica se separó y se cromatografió usando un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-12) eluyendo con 1-10% metanol(amoníaco)/diclorometano para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,08 (dd, *J* = 7,2, 14,4, 1H), 7,64 (dd, *J* = 7,5, 14,5, 1H), 7,56 – 7,52 (m, 1H), 7,43 (d, *J* = 4,4, 2H), 7,42 – 7,40 (m, 1H), 7,38 – 7,22 (m, 5H), 4,40 (dt, *J* = 7,2, 14,3, 0,5H), 4,35 – 4,28 (m, 0,5H), 3,55 (d, *J* = 12,7, 0,5H), 3,40 (dd, *J* = 4,5, 12,8, 1H), 3,26 (d, *J* = 12,9, 0,5H), 3,15 (d, *J* = 10,5, 0,5H), 3,05 (d, *J* = 10,5, 0,5H), 2,83 – 2,74 (m, 1H), 2,70 – 2,55 (m, 1,5H), 2,43 – 2,26 (m, 3H), 2,23 – 2,13 (m, 1H), 1,94 – 1,83 (m, 1H), 1,74 – 1,57 (m, 1,5H), 1,50 (dt, *J* = 7,1, 15,3, 0,5H), 1,37 (td, *J* = 6,5, 12,1, 0,5H), 1,31 – 1,23 (m, 0,5H), 1,18 (d, *J* = 6,5, 1,5H), 1,10 (dt, *J* = 6,5, 11,5, 0,5H), 1,03 (d, *J* = 6,5, 1,5H), 0,73 (dd, *J* = 6,7, 10,7, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Ejemplo 15

N-[(3aS,4S,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–il]-2,2-diciclohexilacetamida

El compuesto del título se preparó utilizando ácido 2,2-diciclohexilacético en lugar de ácido 3-metil-2-fenilbutanoico en el procedimiento usado para preparar el Ejemplo 14: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,44 – 7,38 (m, 4H), 7,37 – 7,32 (m, 1H), 4,49 – 4,38 (m, 1H), 3,57 (d, *J* = 12,6, 1H), 3,37 (d, *J* = 12,5, 1H), 2,77 (dd, *J* = 1,7, 9,6, 1H), 2,68 (td, *J* = 2,0, 9,3, 1H), 2,51 (dd, *J* = 1,9, 9,0, 1H), 2,45 (dd, *J* = 7,1, 15,9, 1H), 2,30 – 2,25 (m, 1H), 2,11 (dd, *J* = 7,1, 9,6, 1H), 1,98 – 1,83 (m, 3H), 1,83 – 1,58 (m, 12H), 1,57 – 1,51 (m, 1H), 1,48 (d, *J* = 13,0, 1H), 1,44 –

1,37 (m, 1H), 1,36 – 1,09 (m, 9H), 1,04 – 0,94 (m, 1H); MS (ESI+) *m/z* 423 $(M+H)^+$.

Ejemplo 16

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida

Paso A: Se combinó (*S*,*E*)-*N*-((3a*S*,6a*R*)-2-bencilhexahidrociclopenta[*c*]pirrol-4(5*H*)–ilidén)-2-metilpropan-2-sulfinamida (2,67 g, 8,38 mmol) del Ejemplo 14 Paso A y HCl acuoso 2,0 N (18,86 ml, 37,7 mmol) en tetrahidrofurano (25 ml). La reacción se agitó a temperatura ambiente por 2 horas y el tetrahidrofurano se retiró al vacío y la porción acuosa restante se hizo ligeramente básica con solución acuosa de bicarbonato de sodio. La capa acuosa se extrajo con 3×200 ml de diclorometano. Las capas orgánicas combinadas se separaron, y el solvente se eliminó al vacío. El material crudo se purificó en un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS25-25) eluyendo con acetato de etilo/hexanos para dar (3a*S*,6a*R*)-2-bencilhexahidrociclopenta[*c*]pirrol-4(5*H*)-ona: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,35 – 7,16 (m, 5H), 3,61 (d, *J* = 13,1, 1H), 3,48 (d, *J* = 13,1, 1H), 3,02 (dd, *J* = 1,8, 9,1, 1H), 2,96 – 2,82 (m, 1H), 2,71 – 2,56 (m, 2H), 2,43 (dt, *J* = 8,2, 17,4, 3H), 2,34 – 2,21 (m, 1H), 2,12 (ddd, *J* = 8,3, 13,0, 16,9, 1H), 1,79 (dddd, *J* = 4,2, 6,4, 9,2, 13,2, 1H).

Paso B: Una mezcla de (3a*S*,6a*R*)-2-bencilhexahidrociclopenta[*c*]pirrol-4(5*H*)-ona (1,462 g, 6,79 mmol) del Paso A en metanol (20ml) se enfrió en un baño de hielo seco/acetona a -40 °C. Se agregó borhidruro de sodio (0,514 g, 13,58 mmol) en porciones durante 5 minutos. La reacción se dejó calentar a temperatura ambiente durante la noche, luego se detuvo con cloruro de amonio acuoso saturado, se diluyó con agua, y se extrajo con 3×150 ml de acetato de etilo. Los extractos combinados se secaron (Na_2SO_4) y el solvente se eliminó al vacío para dar (3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-ol: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,38 – 7,16 (m, 5H), 4,21 – 4,04 (m, 1H), 3,66 (d, *J* = 12,8, 1H), 3,51 (d, *J* = 12,8, 1H), 3,07 (d, *J* = 9,3, 1H), 2,65 – 2,53 (m, *J* = 11,8, 2H), 2,52 – 2,43 (m, 1H), 2,18 – 2,07 (m, *J* = 7,5, 16,3, 2H), 2,05 – 1,94 (m, *J* = 8,7, 12,6, 1H), 1,84 – 1,74 (m, *J* = 6,2, 1H), 1,49 – 1,34 (m, 3H).

Paso C: Se combinó (3a*S*,4*S*,6a*R*)-2-Benciloctahidrociclopenta[*c*]pirrol-4-ol (1,476 g, 6,79 mmol) del Paso B y trietilamina (1,420 ml, 10,19 mmol) en

diclorometano (30 ml). Se agregó cloruro de metansulfonilo (0,635 ml, 8,15 mmol) como una solución en 20mL de diclorometano por goteo a través de un embudo de adición. La reacción se agitó a temperatura ambiente por 30 minutos y se concentró. El material crudo se adsorbió sobre gel de sílice y se cromatografió sobre un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS25-25) eluyendo con 20-100% acetato de etilo/hexanos para dar metansulfonato de (3aS,4S,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilo: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,35 – 7,27 (m, 4H), 7,27 – 7,20 (m, 1H), 4,96 (ddd, *J* = 6,1, 7,6, 9,1, 1H), 3,71 – 3,44 (m, 1H), 2,94 (s, *J* = 13,5, 3H), 2,85 (ddd, *J* = 4,9, 8,1, 16,0, 1H), 2,75 – 2,68 (m, 2H), 2,67 – 2,55 (m, 1H), 2,54 – 2,44 (m, 1H), 2,31 (dd, *J* = 4,1, 8,7, 1H), 2,20 – 2,04 (m, 1H), 1,97 (dtd, *J* = 3,4, 6,2, 9,6, 1H), 1,79 – 1,63 (m, 1H), 1,61 – 1,49 (m, 2H).

Paso D: Se combinó metansulfonato de (3aS,4S,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilo (1,686 g, 5,71 mmol) del Paso C y azida de sodio (0,557 g, 8,56 mmol) en *N,N*-dimetilacetamida (10 ml). La reacción se calentó a 90 °C por 15 horas. La reacción se enfrió y se diluyó con 200 ml de acetato de etilo y luego se detuvo con 30mL agua. La capa orgánica se retiró y se lavó con 2×20 ml de agua, luego 20 ml de salmuera. El solvente se eliminó al vacío para dar (3a*S*,4*R*,6a*R*)-4-azido-2-benciloctahidrociclopenta[*c*]pirrol: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,36 – 7,27 (m, 4H), 7,22 (dd, *J* = 2,9, 5,8, 1H), 3,72 – 3,61 (m, 1H), 3,54 (s, 2H), 2,76 – 2,60 (m, 1H), 2,55 – 2,40 (m, 4H), 2,35 (dd, *J* = 3,5, 9,1, 1H), 2,07 – 1,86 (m, 2H), 1,72 – 1,60 (m, 1H), 1,49 – 1,38 (m, 1H).

Paso E: Se agregó trifenilfosfina (4,49 g, 17,13 mmol) y agua (1,234 ml, 68,5 mmol) en forma sucesiva a una mezcla de (3a*S*,4*R*,6a*R*)-4-azido-2-benciloctahidrociclopenta[*c*]pirrol (1,384 g, 5,71 mmol) en tetrahidrofurano (30 ml). La reacción se mantuvo a reflujo a 80 °C por 2 horas. El material crudo se adsorbió sobre gel de sílice y se aplicó a un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-40) y se eluyó con 1-10% metanol (amoníaco 2 N)/cloroformo para dar (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,45 (d, *J* = 7,4, 2H), 7,38 (t, *J* = 7,5, 2H), 7,29 (t, *J* = 7,3, 1H), 3,52 (s, 2H), 3,14 (dd, *J* = 5,7, 10,7, 1H), 2,62 – 2,55 (m, 1H), 2,52 (dd, *J* = 3,2, 9,0, 1H), 2,38 – 2,29 (m, 3H), 2,20 – 2,13 (m, 1H), 2,01 – 1,84 (m, 2H), 1,40 – 1,29 (m, 2H).

Paso F: Se combinó ácido (S)-2-fenilbutanoico (41,7 mg, 0,254 mmol), 1-hidroxibenzotriazol (38,9 mg, 0,254 mmol), y *N*-(3-dimetilaminopropil)-*N'*-etilcarbodiimida (0,045 ml, 0,254 mmol) en diclorometano (1 ml). La reacción se agitó a temperatura ambiente por 10 minutos, y luego (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina (50 mg, 0,231 mmol) del Paso E se agregó en 0,5 ml de diclorometano. La reacción se agitó a temperatura ambiente por 20 horas, y luego se detuvo con 0,5 ml de agua. La capa orgánica se separó. El material crudo se cromatografió usando un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-4) eluyendo con 1-10% metanol(amoníaco)/diclorometano para dar el compuesto del título: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,47 (d, *J* = 7,0, 1H), 7,59 (m, 2H), 7,42 (d, *J* = 7,1, 2H), 7,34 (dd, *J* = 7,6, 16,5, 4H), 7,25 (dt, *J* = 5,0, 10,1, 2H), 4,45 – 4,29 (m, 1H), 3,62 – 3,51 (m, 2H), 3,44 (d, *J* = 13,2, 1H), 2,85 (dd, *J* = 2,7, 9,0, 1H), 2,58 – 2,50 (m, 1H), 2,50 – 2,42 (m, 2H), 2,40 – 2,31 (m, 1H), 2,31 – 2,22 (m, 2H), 1,97 (dq, *J* = 6,1, 12,1, 1H), 1,85 (td, *J* = 6,9, 13,6, 1H), 1,74 (dt, *J* = 6,4, 14,3, 1H), 1,46 (dt, *J* = 7,1, 19,2, 1H), 1,31 (dt, *J* = 6,2, 20,5, 1H), 0,96 (dd, *J* = 5,5, 9,1, 3H); MS (ESI+) *m/z* 363 $(M+H)^+$.

Ejemplo 17

***N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-il]-2-ciclopentil-2-fenilacetamida**

El compuesto del título se preparó utilizando ácido 2-ciclopentil-2-fenilacético en lugar de ácido (S)-2-fenilbutanoico en el Paso F de el procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,61 (dd, *J* = 7,4, 10,6, 1H), 7,69 (dd, *J* = 1,5, 8,1, 2H), 7,44 (d, *J* = 7,3, 1H), 7,36 (dt, *J* = 7,2, 15,3, 5H), 7,30 – 7,25 (m, 2H), 4,42 – 4,29 (m, 1H), 3,61 (d, *J* = 13,1, 0,5H), 3,52 (d, *J* = 13,2, 0,5H), 3,43 (dd, *J* = 12,0, 18,8, 1,5H), 3,34 (d, *J* = 13,2, 0,5H), 2,96 – 2,83 (m, 1,5H), 2,55 (dt, *J* = 15,9, 16,3, 2H), 2,41 (t, *J* = 18,3, 1H), 2,31 (d, *J* = 9,0, 0,5H), 2,28 (d, *J* = 6,3, 1H), 2,23 (d, *J* = 5,0, 1H), 2,20 – 2,04 (m, 1,5H), 1,94 (dt, *J* = 7,1, 12,1, 0,5H), 1,89 – 1,81 (m, 0,5H), 1,80 – 1,67 (m, 1H), 1,65 – 1,26 (m, 7H), 1,05 – 0,94 (m, 1H); MS (ESI+) *m/z* 403 $(M+H)^+$.

Ejemplo 18

N-[(3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4-il]-3-metil-2-fenilbutanamida

El compuesto del título se preparó utilizando ácido 3-metil-2-fenilbutanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F de el procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,64 (dd, *J* = 7,3, 11,3, 1H), 7,66 (dd, *J* = 2,4, 7,5, 2H), 7,43 (d, *J* = 7,5, 1H), 7,40 – 7,30 (m, 5H), 7,29 – 7,23 (m, 2H), 4,40 – 4,28 (m, 1H), 3,60 (d, *J* = 13,2, 0,5H), 3,52 (d, *J* = 13,1, 0,5H), 3,44 (d, *J* = 13,1, 0,5H), 3,33 (d, *J* = 13,1, 0,5H), 3,25 (d, *J* = 10,5, 1H), 2,88 (dd, *J* = 3,1, 9,1, 0,5H), 2,66 (s, 1H), 2,60 – 2,56 (m, 0,5H), 2,55 – 2,46 (m, 1,5H), 2,39 (t, *J* = 18,7, 1H), 2,28 (t, *J* = 8,0, 1,5H), 2,22 (d, *J* = 5,1, 1H), 2,18 – 2,09 (m, 0,5H), 1,91 (dd, *J* = 6,0, 12,0, 0,5H), 1,84 (dd, *J* = 7,1, 13,4, 0,5H), 1,72 (ddd, *J* = 6,5, 12,3, 25,1, 1H), 1,49 – 1,40 (m, 0,5H), 1,33 (ddd, *J* = 13,3, 19,9, 32,3, 1H), 1,20 (dd, *J* = 5,0, 6,4, 3H), 0,70 (dd, *J* = 1,7, 6,7, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Ejemplo 19

(2S)-N-[(3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4-il]-2-fenilpropanamida

El compuesto del título se preparó utilizando ácido (S)-2-fenilpropanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F de el procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,41 (d, *J* = 6,8, 1H), 7,54 (d, *J* = 7,0, 2H), 7,41 (t, *J* = 9,7, 2H), 7,38 – 7,30 (m, 4H), 7,26 (dd, *J* = 5,3, 16,7, 2H), 4,43 – 4,32 (m, 1H), 3,84 (q, *J* = 7,0, 1H), 3,56 (t, *J* = 12,3, 1H), 3,40 (dd, *J* = 13,1, 33,2, 1H), 2,81 (dd, *J* = 2,9, 9,0, 1H), 2,51 (m, 1H), 2,48 – 2,36 (m, 2H), 2,33 – 2,17 (m, 2H), 2,14 (s, 3H, OAc), 2,00 (dq, *J* = 6,1, 12,1, 1H), 1,73 (dt, *J* = 6,3, 14,2, 1H), 1,60 (d, *J* = 7,0, 3H), 1,47 (dt, *J* = 7,1, 14,8, 1H), 1,39 – 1,24 (m, 1H); MS (ESI+) *m/z* 349 $(M+H)^+$.

Ejemplo 20

N-[(3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4-il]-2,2-diciclohexilacetamida

El compuesto del título se preparó utilizando ácido 2,2-diciclohexilacético en lugar de ácido (S)-2-fenilbutanoico en el Paso F de el procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,12 (d, *J* = 7,2, 1H),

7,45 (d, *J* = 7,4, 2H), 7,36 (t, *J* = 7,5, 2H), 7,27 (t, *J* = 7,3, 1H), 4,52 – 4,43 (m, 1H), 3,63 (d, *J* = 13,1, 1H), 3,48 (d, *J* = 13,1, 1H), 2,89 (dd, *J* = 2,7, 8,9, 1H), 2,65 – 2,50 (m, 3H), 2,35 (d, *J* = 4,5, 2H), 2,18 – 2,10 (m, 1H), 2,03 (t, *J* = 7,4, 1H), 1,96 (d, *J* = 13,0, 2H), 1,87 (dt, *J* = 7,4, 13,9, 3H), 1,80 (d, *J* = 12,6, 2H), 1,76 – 1,64 (m, 5H), 1,60 (d, *J* = 10,7, 2H), 1,51 – 1,38 (m, 3H), 1,30 – 1,05 (m, 8H); MS (ESI+) *m/z* 423 $(M+H)^+$.

Ejemplo 21

***N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-propilpentanamida**

El compuesto del título se preparó utilizando ácido 2-propilpentanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F de el procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,36 (d, *J* = 7,2, 1H), 7,43 (d, *J* = 7,4, 2H), 7,36 (t, *J* = 7,5, 2H), 7,27 (t, *J* = 7,3, 1H), 4,56 – 4,38 (m, 1H), 3,60 (d, *J* = 11,8, 1H), 3,45 (d, *J* = 13,1, 1H), 2,85 (dd, *J* = 2,8, 9,0, 1H), 2,61 – 2,50 (m, 2H), 2,50 – 2,45 (m, 1H), 2,39 – 2,25 (m, 3H), 2,20 – 2,09 (m, 1H), 1,93 – 1,79 (m, 3H), 1,66 (dd, *J* = 7,7, 12,2, 1H), 1,53 – 1,29 (m, 7H), 0,87 (td, *J* = 3,1, 7,2, 6H); MS (ESI+) *m/z* 343 $(M+H)^+$.

Ejemplo 22

***N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]cicloheptancarboxamida**

El compuesto del título se preparó utilizando ácido cicloheptancarboxílico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,08 (d, *J* = 7,2, 1H), 7,44 (d, *J* = 7,4, 2H), 7,36 (t, *J* = 7,6, 2H), 7,27 (t, *J* = 7,3, 1H), 4,50 – 4,34 (m, 1H), 3,60 (d, *J* = 13,7, 1H), 3,44 (d, *J* = 13,1, 1H), 2,83 (d, *J* = 9,0, 1H), 2,54 (s, 2H), 2,49 – 2,41 (m, 2H), 2,33 (d, *J* = 6,8, 1H), 2,30 – 2,25 (m, 1H), 2,19 – 2,10 (m, 1H), 2,01 – 1,81 (m, 5H), 1,74 – 1,58 (m, 3H), 1,47 – 1,37 (m, 5H), 1,31 (s, 2H); MS (ESI+) *m/z* 341 $(M+H)^+$.

Ejemplo 23

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(4-isobutilfenil)propanamida

El compuesto del título se preparó utilizando ácido (S)-2-(3-isobutilfenil)propanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del

procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37 (d, *J* = 7,2, 1H), 7,49 (d, *J* = 8,0, 2H); 7,42 (d, *J* = 7,5, 2H), 7,36 (t, *J* = 7,5, 2H), 7,27 (t, *J* = 7,3, 1H), 7,14 (d, *J* = 8,0, 2H), 4,43 – 4,31 (m, 1H), 3,84 (q, *J* = 7,0, 1H), 3,58 (d, *J* = 13,1, 1H), 3,44 (d, *J* = 13,1, 1H), 2,82 (dd, *J* = 2,8, 9,1, 1H), 2,55 – 2,48 (m, 1H), 2,48 – 2,42 (m, 2H), 2,39 (d, *J* = 7,2, 2H), 2,31 – 2,21 (m, 2H), 2,00 (dt, *J* = 6,0, 12,1, 1H), 1,83 – 1,69 (m, 2H), 1,63 (d, *J* = 7,0, 3H), 1,48 (dt, *J* = 7,0, 19,1, 1H), 1,36 – 1,25 (m, 1H), 0,86 – 0,77 (m, 6H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Ejemplo 24

***N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclohexanocarboxamida**

El compuesto del título se preparó utilizando ácido 1-fenilciclohexanocarboxílico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,73 (d, *J* = 7,8, 1H), 7,63 – 7,59 (m, 1H), 7,41 (d, *J* = 7,3, 2H), 7,39 – 7,31 (m, 4H), 7,29 – 7,23 (m, 3H), 4,45 – 4,35 (m, 1H), 3,58 (d, *J* = 13,2, 1H), 3,40 (d, *J* = 13,2, 1H), 2,80 (d, *J* = 7,7, 1H), 2,69 – 2,59 (m, 2H), 2,41 – 2,31 (m, 3H), 2,28 (d, *J* = 8,6, 1H), 2,20 – 2,13 (m, 1H), 2,00 (td, *J* = 5,7, 11,7, 1H), 1,87 – 1,75 (m, 4H), 1,74 – 1,54 (m, *J* = 9,1, 18,8, 38,4, 4H), 1,46 (dt, *J* = 7,8, 14,8, 1H), 1,36 – 1,19 (m, 2H); MS (ESI+) *m/z* 403 $(M+H)^+$.

Ejemplo 25

***N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,3-difenilpropanamida**

El compuesto del título se preparó utilizando ácido 2,3-difenilpropanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,52 (dd, *J* = 7,3, 13,3, 1H), 7,65 (d, *J* = 7,4, 2H), 7,44 (d, *J* = 7,1, 1H), 7,41 – 7,29 (m, 8H), 7,26 (dt, *J* = 4,8, 10,9, 4H), 4,35 – 4,22 (m, 1H), 3,96 (dt, *J* = 5,0, 10,0, 1H), 3,77 (ddd, *J* = 3,7, 10,1, 13,5, 1H), 3,52 (dt, *J* = 13,2, 18,8, 1,5H), 3,33 (d, *J* = 13,1, 0,5H), 3,05 (dt, *J* = 4,7, 13,0, 1H), 2,77 (d, *J* = 8,9, 0,5H), 2,56 (d, *J* = 6,2, 0,5H), 2,38 – 2,23 (m, 3H), 2,23 – 2,17 (m, *J* = 8,7, 1H), 1,94 (ddd, *J* = 5,7, 11,8, 23,8, 1H), 1,72 – 1,57 (m, *J* = 6,0, 1H), 1,51 – 1,19 (m, 3H); MS (ESI+) *m/z* 425 $(M+H)^+$.

Ejemplo 26

***N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-metil-3-fenilpropanamida**

El compuesto del título se preparó utilizando ácido 2-metil-3-fenilpropanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,12 (dd, *J* = 7,0, 21,5, 1H), 7,47 – 7,22 (m, 10H), 4,43 – 4,29 (m, 1H), 3,58 (dd, *J* = 6,6, 13,2, 1H), 3,45 (dd, *J* = 13,2, 21,2, 1H), 3,20 (ddd, *J* = 4,6, 10,8, 15,0, 1H), 2,81 – 2,66 (m, 3H), 2,48 – 2,19 (m, 5H), 2,04 (ddt, *J* = 6,0, 12;1, 24,4, 1H), 1,82 – 1,63 (m, 1H), 1,47 (ddd, *J* = 7,1, 15,9, 18,8, 1H), 1,39 – 1,30 (m, 1H), 1,28 (d, *J* = 6,3, 3H); MS (ESI+) *m/z* 363 $(M+H)^+$.

Ejemplo 27

***N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-metil-2-fenilpropanamida**

El compuesto del título se preparó utilizando ácido 2-metil-2-fenilpropanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,44 (dd, *J* = 7,9, 16,1, 4H), 7,31 (ddd, *J* = 7,7, 14,5, 22,6, 6H), 7,12 – 7,03 (m, 1H), 4,46 – 4,36 (m, 1H), 3,58 (d, *J* = 13,2, 1H), 3,43 (d, *J* = 13,2, 1H), 2,84 (d, *J* = 6,5, 1H), 2,39 – 2,26 (m, *J* = 6,9, 20,1, 4H), 2,23 – 2,14 (m, *J* = 6,7, 1H), 2,04 (dd, *J* = 5,8, 11,8, 1H), 1,67 (s, 7H), 1,54 – 1,40 (m, 1H), 1,38 – 1,24 (m, 1H); MS (ESI+) *m/z* 363 $(M+H)^+$.

Ejemplo 28

***N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclopropancarboxamida**

El compuesto del título se preparó utilizando ácido 1-fenilciclopropancarboxílico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,42 (dd, *J* = 7,2, 16,3, 4H), 7,33 (dt, *J* = 7,6, 17,1, 4H), 7,25 (dd, *J* = 5,8, 13,1, 2H), 6,27 (d, *J* = 7,5, 1H), 4,41 – 4,24 (m, *J* = 5,8, 1H), 3,56 (d, *J* = 13,2, 1H), 3,40 (d, *J* = 13,2, 1H), 2,87 – 2,74 (m, 1H), 2,37 – 2,19 (m, 4H), 2,12 (t, *J* = 8,0, 1H), 2,03 – 1,94 (m, 1H), 1,75 (dd, *J* = 3,5, 6,6, 2H), 1,68 – 1,58 (m, *J* = 8,7, 16,8, 1H), 1,37 – 1,23 (m, 2H), 1,01 (dd, *J* = 3,5, 6,6, 2H); MS (ESI+) *m/z* 361 $(M+H)^+$.

Ejemplo 29

2-bencil-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetilbutanamida

El compuesto del título se preparó utilizando ácido 2-bencil-3,3-dimetilbutanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,08 (dd, *J* = 7,4, 13,5, 1H), 7,46 (d, *J* = 7,3, 1H), 7,44 – 7,32 (m, 5H), 7,32 – 7,23 (m, 4H), 4,33 (s, 1H), 3,58 (dd, *J* = 13,2, 16,9, 1H), 3,50 (d, *J* = 13,1, 0,5H), 3,40 (d, *J* = 13,1, 0,5H), 3,25 (q, *J* = 11,9, 1H), 2,80 – 2,66 (m, 2H), 2,45 (d, *J* = 6,9, 1H), 2,41 – 2,23 (m, 3,5H), 2,20 (t, *J* = 8,3; 0,5H), 2,16 – 2,09 (m, 0,5H), 2,06 (dd, *J* = 5,8, 11,6, 0,5H), 1,89 (dd, *J* = 5,8, 11,8, 0,5H), 1,75 (s, 0,5H), 1,61 (s, 0,5H), 1,47 (s, 0,5H), 1,38 – 1,20 (m, 2H), 1,16 (s, 9H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Ejemplo 30

***N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetil-2-fenilbutanamida**

El compuesto del título se preparó utilizando ácido 3,3-dimetil-2-fenilbutanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,57 – 8,49 (m, 1H), 7,73 (dd, *J* = 3,3, 5,3, 2H), 7,44 (d, *J* = 7,1, 1H), 7,41 – 7,24 (m, 7H), 4,41 – 4,29 (m, *J* = 6,9, 13,0, 1H), 3,62 (d, *J* = 13,2, 0,5H), 3,53 (d, *J* = 13,1, 0,5H), 3,43 (s, 0,5H), 3,35 (d, *J* = 13,1, 0,5H), 2,90 (dd, *J* = 3,1, 8,9, 1H), 2,63 – 2,46 (m, 2H), 2,44 – 2,37 (m, 0,5H), 2,36 – 2,30 (m, *J* = 8,3, 1H), 2,28 (d, *J* = 5,3, 1H), 2,23 (d, *J* = 5,5, 1H), 2,15 (dt, *J* = 6,2, 12,5, 0,5H), 1,91 (dt, *J* = 6,1, 12,2, 0,5H), 1,88 – 1,79 (m, 0,5H), 1,77 – 1,66 (m, 1H), 1,46 – 1,35 (m, 1H), 1,34 – 1,23 (m, 1H), 1,15 (s, 4,5H), 1,14 (s, 4,5H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Ejemplo 31 y Ejemplo 32

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetil-2-fenilbutanamida (Ejemplo 31) y

(2*R*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetil-2-fenilbutanamida (Ejemplo 32)

El material del Ejemplo 30 se sometió a separación mediante cromatografía quiral de fluido supercrítico en una columna ChiralCel® OD-H (21×250 mm, 5 µm, Chiral Technologies, Inc.), 5-50% metanol:CO_2 (100 bar), a 40 ml/minute durante

10 minutos para dar los compuestos del título.

Ejemplo 31: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,50 (d, *J* = 7,1, 1H), 7,74 – 7,70 (m, 1H), 7,44 (d, *J* = 7,2, 2H), 7,40 – 7,24 (m, *J* = 8,0, 15,4, 18,2, 7H), 4,43 – 4,31 (m, 1H), 3,63 (d, *J* = 13,1, 1H), 3,49 – 3,41 (m, *J* = 6,6, 2H), 2,91 (dd, *J* = 3,0, 8,9, 1H), 2,63 – 2,43 (m, 3H), 2,28 (d, *J* = 5,3, 2H), 1,92 (dq, *J* = 6,1, 12,1, 1H), 1,78 – 1,68 (m, 1H), 1,41 (dt, *J* = 7,0, 18,9, 1H), 1,30 (dt, *J* = 6,4, 14,5, 1H), 1,14 (s, 9H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Ejemplo 32: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,52 (d, *J* = 7,0, 1H), 7,72 (d, *J* = 7,0, 2H), 7,41 – 7,24 (m, *J* = 7,2, 21,5, 29,9, 8H), 4,41 – 4,25 (m, 1H), 3,53 (d, *J* = 13,1, 1H), 3,45 (s, 1H), 3,35 (d, *J* = 13,1, 1H), 2,57 (d, *J* = 5,7, 1H), 2,45 – 2,36 (m, 1H), 2,31 (dd, *J* = 5,1, 10,5, 2H), 2,25 – 2,20 (m, 2H), 2,15 (td, *J* = 6,4, 12,4, 1H), 1,83 (td, *J* = 6,8, 14,8, 1H), 1,69 (td, *J* = 6,7, 13,4, 1H), 1,38 (td, *J* = 6,7, 12,4, 1H), 1,14 (s, 9H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Ejemplo 33

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida

Paso A: (3a*R*,4*S*,6a*S*)-2-Benciloctahidrociclopenta[*c*]pirrol-4-amina se preparó de acuerdo con el procedimiento descrito en Ejemplo 16 Pasos A-E utilizando (*S,E*)-*N*-((3a*R*,6a*S*)-2-bencilhexahidrociclopenta[*c*]pirrol-4(5*H*)–iliden)-2-metilpropan-2-sulfinamida del Paso A en Ejemplo 14 en lugar de (*S,E*)-*N*-((3a*S*,6a*R*)-2-bencilhexahidrociclopenta[*c*]pirrol-4(5*H*)–iliden)-2-metilpropan-2-sulfinamida en el Paso A de Ejemplo 16 para dar (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,34 – 7,28 (m, 4H), 7,25 – 7,18 (m, 1H), 3,54 (s, 2H), 3,09 (dd, *J* = 4,8, 10,9, 1H), 2,75 – 2,58 (m, 1H), 2,48 (dd, *J* = 8,6, 16,5, 2H), 2,40 (dd, *J* = 3,9, 9,3, 1H), 2,30 (dd, *J* = 3,9, 9,0, 1H), 2,21 – 2,09 (m, 1H), 2,01 – 1,84 (m, *J* = 6,9, 12,0, 2H), 1,47 – 1,25 (m, 4H).

Paso B: El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,55 (d, *J* = 4,5, 1H), 7,59 (s, *J* = 5,1, 1H), 7,39 (d, *J* = 7,2, 2H), 7,34 (dd, *J* = 7,7, 16,5, 4H), 7,25 (dd, *J* = 7,6, 16,2, 3H), 4,43 – 4,33 (m, 1H), 3,59 – 3,50 (m, 2H), 3,36 (d, *J* = 13,1,

1H), 2,69 – 2,61 (m, 1H), 2,43 – 2,28 (m, 4H), 2,28 – 2,23 (m, 1H), 2,22 – 2,18 (m, 1H), 2,13 (dq, *J* = 6,3, 12,3, 1H), 1,89 – 1,77 (m, 2H), 1,65 (td, *J* = 7,0, 14,2, 1H), 1,40 – 1,32 (m, 1H), 0,97 (t, *J* = 7,3, 3H); MS (ESI+) *m/z* 363 $(M+H)^+$.

Ejemplo 34

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclopentil-2-fenilacetamida**

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y utilizando ácido 2-ciclopentil-2-fenilacético en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,54 (d, *J* = 14,7, 1H), 7,66 (dd, *J* = 2,5, 7;5, 2H), 7,43 (d, *J* = 7,4, 1H), 7,40 – 7,31 (m, 5H), 7,26 (t, *J* = 6,9, 2H), 4,41 – 4,30 (m, 1H), 3,61 (d, *J* = 13,1, 0,5H), 3,52 (d, *J* = 13,1, 0,5H), 3,45 (d, *J* = 13,2, 0,5H), 3,36 (app. t, *J* = 12,7, 1,5H), 2,89 (d, *J* = 9,0, 1H), 2,61 – 2,55 (m, 1H), 2,53 – 2,46 (m, 1H), 2,44 – 2,33 (m, 1H), 2,29 (dd, *J* = 7,3, 12,8, 1,5H), 2,22 (t, *J* = 4,9, 1H), 2,19 – 2,04 (m, 1,5H), 1,98 – 1,89 (m, 0,5H), 1,88 – 1,80 (m, 0,5H), 1,79 – 1,65 (m, 1H), 1,65 – 1,25 (m, 8H), 1,05 – 0,95 (m, 1H); MS (ESI+) *m/z* 403 $(M+H)^+$.

Ejemplo 35

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida**

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y utilizando ácido 3-metil-2-fenilbutanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,64 – 8,49 (m, *J* = 20,1, 1H), 7,67 – 7,61 (m, 2H), 7,43 (d, *J* = 7,0, 1H), 7,39 – 7,30 (m, 5H), 7,29 – 7,24 (m, 2H), 4,41 – 4,27 (m, 1H), 3,60 (d, *J* = 13,1, 0,5H), 3,52 (d, *J* = 13,1, 0,5H), 3,44 (d, *J* = 13,2, 0,5H), 3,33 (d, *J* = 13,2, 0,5H), 3,23 (d, *J* = 10,5, 1H), 2,89 (dd, *J* = 3,0, 9,1, 0,5H), 2,69 – 2,60 (m, *J* = 10,0, 1H), 2,59 – 2,53 (m, *J* = 3,0, 9,0, 1H), 2,52 – 2,44 (m, 1H), 2,44 – 2,33 (m, 1H), 2,30 – 2,25 (m, *J* = 6,4, 10,0, 1,5H), 2,25 – 2,20 (m, 1H), 2,14 (dd, *J* = 5,9, 12,3, 0,5H), 1,91 (dd, *J* = 6,1, 12,1, 0,5H), 1,86 – 1,79 (m, *J* = 4,7, 0,5H), 1,78 – 1,64 (m, 1H), 1,47 – 1,24

(m, *J* = 30,2, 37,0, 1,5H), 1,20 (dd, *J* = 4,9, 6,4, 3H), 0,70 (dd, *J* = 1,6, 6,7, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Ejemplo 36

(2*R*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y utilizando ácido (R)-2-fenilbutanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7,38 – 7,21 (m, 10H), 5,29 (d, *J* = 6,9, 1H), 4,04 – 3,90 (m, 1H), 3,65 (d, *J* = 12,9, 1H), 3,52 (d, *J* = 12,9, 1H), 3,15 (t, *J* = 7,6, 1H), 2,68 (t, *J* = 8,6, 1H), 2,64 – 2,48 (m, *J* = 8,5, 3H), 2,30 – 2,22 (m, *J* = 3,7, 8,3, 1,5H), 2,14 (ddd, *J* = 7,4, 13,9, 19,9, 1,5H), 1,93 (dt, *J* = 6,2, 12,5, 1H), 1,84 – 1,62 (m, *J* = 7,6, 14,5, 20,6, 2H), 1,45 – 1,27 (m, 2H), 0,95 – 0,80 (m, 4H); MS (ESI+) *m/z* 363 $(M+H)^+$.

Ejemplo 37

(2*R*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilpropanamida

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y utilizando ácido (R)-2-fenilpropanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7,37 – 7,26 (m, *J* = 5,5, 7,5, 8H), 7,25 – 7,18 (m, 2H), 5,19 (d, *J* = 5,9, 1H), 4,06 – 3,89 (m, 1H), 3,59 (d, *J* = 13,0, 1H), 3,48 (ddd, *J* = 7,6, 13,7, 21,0, 2H), 2,60 – 2,46 (m, 3H), 2,43 – 2,33 (m, *J* = 7,0, 14,4, 1H), 2,26 (dd, *J* = 3,8, 9,0, 1H), 2,20 – 2,07 (m, *J* = 34,2, 1H), 2,03 – 1,93 (m, 1H), 1,49 (d, *J* = 7,2, 3H), 1,44 – 1,22 (m, 3H); MS (ESI+) *m/z* 349 $(M+H)^+$.

Ejemplo 38

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilpropanamida

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de

(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y utilizando ácido (S)-2-fenilpropanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7,38 – 7,26 (m, 8H), 7,25 – 7,20 (m, 2H), 5,20 (d, *J* = 6,7, 1H), 4,03 – 3,91 (m, 1H), 3,60 (d, *J* = 13,0, 1H), 3,52 – 3,43 (m, 2H), 2,54 (dd, *J* = 5,7, 13,8, 2H), 2,43 (dd, *J* = 7,1, 16,0, 1H), 2,29 – 2,23 (m, 1H), 2,22 – 2,08 (m, 2H), 1,98 (ddd, *J* = 5,8, 11,9, 15,7, 1H), 1,74 – 1,60 (m, 1H), 1,50 (t, *J* = 6,4, 3H), 1,44 – 1,30 (m, 2H); MS (ESI+) *m/z* 349 $(M+H)^+$.

Ejemplo 39

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(4-isobutilfenil)propanamida

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y utilizando ácido (S)-2-(4-isobutilfenil)propanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7,28 (d, *J* = 4,4, 3H), 7,25 – 7,18 (m, 1H), 7,15 (dd, *J* = 2,3, 8,2, 2H), 7,09 (dd, *J* = 1,8, 8,2, 2H), 5,17 (d, *J* = 7,2, 1H), 4,03 – 3,89 (m, 1H), 3,58 (d, *J* = 13,0, 1H), 3,51 – 3,41 (m, 2H), 2,55 – 2,48 (m, 3H), 2,45 (d, *J* = 7,2, 2H), 2,39 (dd, *J* = 7,3, 9,0, 1H), 2,27 – 2,20 (m, 1H), 2,19 – 2,06 (m, 1H), 2,05 – 1,91 (m, 1H), 1,85 (dt, *J* = 6,8, 13,5, 1H), 1,72 – 1,61 (m, 2H), 1,48 (d, *J* = 7,2, 3H), 1,44 – 1,28 (m, 2H), 0,89 (d, *J* = 6,6, 6H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Ejemplo 40

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida**

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y utilizando ácido 2,2-diciclohexilacético en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7,32 – 7,27 (m, *J* = 6,3, 4H), 7,24 – 7,18 (m, 1H), 5,22 (d, *J* = 6,9, 1H), 4,11 – 3,99 (m, 1H), 3,62 (d, *J* = 13,0, 1H), 3,46 (d, *J* = 13,0, 1H), 2,67 – 2,58 (m, 2H), 2,54 (dd, *J* = 4,2, 9,4, 1H), 2,51 – 2,43 (m, 1H), 2,31 (dt, *J* = 4,0, 7,6, 1H), 2,25 (dd,

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J = 4,2, 9,0, 1H), 2,08 – 1,99 (m, 1H), 1,87 – 1,76 (m, 1H), 1,67 (dd, *J* = 15,7, 26,7, 10H), 1,55 (s, 3H), 1,50 – 1,38 (m, 2H), 1,31 – 1,02 (m, 8H), 1,00 – 0,85 (m, 2H); MS (ESI+) *m/z* 423 $(M+H)^+$.

Ejemplo 41

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclopropil-2-fenilacetamida**

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y utilizando ácido 2-ciclopropil-2-fenilacético en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7,36 – 7,26 (m, 8H), 7,25 – 7,18 (m, 2H), 5,57 – 5,40 (m, 1H), 4,08 – 3,97 (m, 1H), 3,60 (dd, *J* = 5,8, 13,0, 1H), 3,46 (dd, *J* = 3,0, 13,0, 1H), 2,65 (d, *J* = 9,5, 1H), 2,62 – 2,50 (m, 2H), 2,46 – 2,38 (m, 1H), 2,30 – 2,18 (m, 2H), 2,03 (ddd, *J* = 6,0, 12,1, 18,9, 1H), 1,80 – 1,69 (m, 1H), 1,49 – 1,30 (m, 4H), 0,71 (ddd, *J* = 5,7, 9,1, 10,4, 1H), 0,60 – 0,51 (m, 1H), 0,38 (td, *J* = 4,7, 9,0, 1H), 0,19 (dq, *J* = 4,7, 9,4, 1H); MS (ESI+) *m/z* 375 $(M+H)^+$.

Ejemplo 42

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclobutil-2-fenilacetamida**

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y utilizando ácido 2-ciclobutil-2-fenilacético en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,51 (t, *J* = 6,2, 1H), 7,61 (d, *J* = 7,7, 2H), 7,43 (dd, *J* = 7,3, 16,6, 2H), 7,38 – 7,30 (m, 4H), 7,30 – 7,23 (m, 2H), 4,42 – 4,31 (m, 1H), 3,67 (d, *J* = 10,7, 1H), 3,59 (dd, *J* = 13,1, 28,6, 1H), 3,43 (dd, *J* = 13,0, 35,2, 1H), 3,34 – 3,23 (m, 1H), 2,85 (d, *J* = 7,5, 0,5H), 2,67 (d, *J* = 7,1, 0,5H), 2,61 – 2,47 (m, *J* = 9,6, 29,9, 1,5H), 2,46 – 2,33 (m, 1,5H), 2,28 (d, *J* = 17,6, 3H), 2,12 (dt, *J* = 4,5, 12,2, 0,5H), 2,03 – 1,91 (m, 1,5H), 1,87 – 1,55 (m, *J* = 7,8, 17,0, 28,7, 5H), 1,47 (dt, *J* = 7,8, 14,5, 0,5H), 1,42 – 1,26 (m, *J* = 16,4, 37,6, 1,5H); MS (ESI+) *m/z* 389 $(M+H)^+$.

Ejemplo 43

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(4-clorofenil)-3-metilbutanamida**

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y utilizando ácido 2-(4-clorofenil)-3-metilbutanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,69 (s, 1H), 7,54 (dd, *J* = 2,9, 8,4, 2H), 7,47 (d, *J* = 7,5, 1H), 7,42 (d, *J* = 7,3, 1H), 7,38 – 7,31 (m, 4H), 7,28 (t, *J* = 7,5, 1H), 4,36 (s, 1H), 3,66 (d, *J* = 13,1, 0,5H), 3,58 (d, *J* = 13,1, 0,5H), 3,51 (d, *J* = 13,1, 0,5H), 3,42 (d, *J* = 13,1, 0,5H), 3,19 (d, *J* = 10,4, 1H), 2,94 (d, *J* = 5,0, 0,5H), 2,66 (d, *J* = 5,0, 0,5H), 2,62 – 2,49 (m, 2,5H), 2,40 (m, 1,5H), 2,34 (m, 1H), 2,31 – 2,25 (m, 1H), 2,14 (dt, *J* = 6,2, 12,3, 0,5H), 2,01 – 1,91 (m, *J* = 4,7, 13,4, 0,5H), 1,87 – 1,62 (m, 1,5H), 1,52 – 1,43 (m, 0,5H), 1,42 – 1,33 (m, *J* = 10,3, 30,3, 1H), 1,17 (t, *J* = 5,9, 3H), 0,67 (dd, *J* = 2,2, 6,7, 3H); MS (ESI+) *m/z* 411 $(M+H)^+$.

Ejemplo 44

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-etil-2-fenilpentanamida**

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y utilizando ácido 3-etil-2-fenilpentanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,69 – 8,62 (m, 1H), 7,65 (s, 2H), 7,45 (s, 1H), 7,41 (d, *J* = 7,8, 1H), 7,38 – 7,31 (m, 4H), 7,27 (d, *J* = 7,0, 2H), 4,34 (dd, *J* = 5,5, 10,8, 1H), 3,68 – 3,62 (m, 0,5H), 3,60 – 3,47 (m, 2H), 3,45 – 3,32 (m, 0,5H), 2,97 – 2,86 (m, 0,5H), 2,67 – 2,21 (m, 5H), 2,19 – 2,08 (m, 0,5H), 1,94 – 1,55 (m, 4H), 1,48 – 1,38 (m, 2H), 1,12 – 1,00 (m, 1H), 0,97 (q, *J* = 7,5, 3H), 0,93 – 0,84 (m, 1,5H), 0,83 – 0,74 (m, 0,5H), 0,61 (t, *J* = 6,6, 3H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Ejemplo 45

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(4-hidroxifenil)-3-metilbutanamida**

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y ácido 2-(4-hidroxifenil)-3-metilbutanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,53 – 8,46 (m, 1H), 7,56 (d, *J* = 2,8, 1H), 7,43 (d, *J* = 7,2, 1H), 7,36 (dt, *J* = 7,5, 18,2, 4H), 7,26 (q, *J* = 7,1, 1H), 7,16 (dd, *J* = 3,0, 8,6, 2H), 4,44 – 4,32 (m, 1H), 3,60 (d, *J* = 13,1, 0,5H), 3,53 (d, *J* = 13,1, 0,5H), 3,44 (d, *J* = 13,2, 0,5H), 3,33 (d, *J* = 13,1, 0,5H), 3,18 (d, *J* = 10,4, 1H), 2,90 (dd, *J* = 3,0, 9,1, 0,5H), 2,66 (s, 1H), 2,58 (d, *J* = 8,8, 1H), 2,49 (t, *J* = 10,5, 1H), 2,44 – 2,35 (m, *J* = 10,0, 1H), 2,33 – 2,11 (m, 2H), 1,99 – 1,89 (m, 0,5H), 1,88 – 1,63 (m, 1,5H), 1,53 – 1,42 (m, 0,5H), 1,41 – 1,24 (m, 2H), 1,22 (dd, *J* = 4,4, 6,3, 3H), 0,97 – 0,82 (m, *J* = 21,9, 35,1, 1H), 0,79 (d, *J* = 6,7, 3H); MS (ESI+) *m/z* 393 $(M+H)^+$.

Ejemplo 46

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclohexanocarboxamida**

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y ácido 1-fenilciclohexanocarboxílico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,73 (d, *J* = 8,2, 1H), 7,59 (s, 1H), 7,41 (d, *J* = 7,4, 2H), 7,36 (td, *J* = 2,7, 7,6, 4H), 7,26 (dd, *J* = 6,0, 8,7, 2H), 4,45 – 4,33 (m, 1H), 3,58 (d, *J* = 13,2, 1H), 3,40 (d, *J* = 13,2, 1H), 2,81 (d, *J* = 7,3, 1H), 2,68 – 2,59 (m, *J* = 10,2, 2H), 2,41 – 2,31 (m, *J* = 6,2, 14,8, 3H), 2,28 (d, *J* = 8,8, 1H), 2,20 – 2,13 (m, 1H), 1,99 (dt, *J* = 7,4, 14,8, 1H), 1,88 – 1,75 (m, *J* = 9,0, 4H), 1,74 – 1,53 (m, *J* = 8,8, 36,2, 4H), 1,50 – 1,40 (m, 1H), 1,36 – 1,20 (m, 2H); MS (ESI+) *m/z* 403 $(M+H)^+$.

Ejemplo 47

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-metil-2-fenilpropanamida**

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y ácido 2-metil-2-fenilpropanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,49 – 7,38 (m, 4H), 7,31 (ddd, *J* = 7,3, 14,4, 22,5, 5H), 7,08 (d, *J* = 7,3, 1H), 4,46 – 4,35 (m, 1H), 3,58 (d, *J* = 13,2, 1H), 3,43 (d, *J* = 13,2, 1H), 2,84 (d, *J* = 6,7, 1H), 2,36 (d, *J* = 4,8, 3H), 2,31 (d, *J* = 9,6, 1H), 2,21 – 2,13 (m, 1H), 2,04 (td, *J* = 5,9, 11,7, 1H), 1,70 (dd, *J* = 6,7, 12,3, 1H), 1,67 (s, 6H), 1,53 – 1,41 (m, 1H), 1,38 – 1,26 (m, 1H); MS (ESI+) *m/z* 363 $(M+H)^+$.

Ejemplo 48

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclopropancarboxamida**

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y ácido 1-fenilciclopropancarboxílico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,46 – 7,37 (m, 4H), 7,33 (dt, *J* = 7,5, 11,5, 4H), 7,28 – 7,22 (m, 2H), 6,22 (d, *J* = 7,3, 1H), 4,31 (dd, *J* = 6,7, 12,7, 1H), 3,56 (d, *J* = 13,2, 1H), 3,40 (d, *J* = 13,2, 1H), 2,81 (dd, *J* = 2,1, 8,9, 1H), 2,39 – 2,18 (m; *J* = 7,3, 12,5, 18,1, 4H), 2,13 (dd, *J* = 7,3, 8,9, 1H), 1,99 (dt, *J* = 5,6, 11,0, 1H), 1,75 (q, *J* = 3,6, 2H), 1,67 – 1,58 (m, *J* = 8,3, 16,6, 1H), 1,38 – 1,22 (m, 2H), 1,01 (q, *J* = 3,6, 2H); MS (ESI+) *m/z* 361 $(M+H)^+$.

Ejemplo 49

2-bencil-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetilbutanamida

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y ácido 2-bencil-3,3-

dimetilbutanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,08 (dd, *J* = 7,4, 13,6, 1H), 7,46 (d, *J* = 7,3, 1H), 7,44 – 7,40 (m, 1H), 7,38 (dd, *J* = 7,6, 15,7, 2H), 7,34 (d, *J* = 4,3, 2H), 7,31 – 7,23 (m, 4H), 4,36 – 4,29 (m, 1H), 3,59 (d, *J* = 13,1, 0,5H), 3,53 (dd, *J* = 13,2, 32,6, 1H), 3,40 (d, *J* = 13,1, 0,5H), 3,25 (q, *J* = 12,0, 1H), 2,79 – 2,67 (m, 2H), 2,48 – 2,42 (m, *J* = 7,0, 1H), 2,41 – 2,23 (m, 3,5H), 2,20 (t, *J* = 8,3, 0,5H), 2,12 (d, *J* = 6,7, 0,5H), 2,06 (dd, *J* = 5,9, 11,7, 0,5H), 1,88 (dd, *J* = 5,8, 11,7, 0,5H), 1,74 (dd, *J* = 9,4, 16,4, 0,5H), 1,60 (dd, *J* = 7,0, 13,2, 0,5H), 1,51 – 1,42 (m, 0,5H), 1,37 – 1,21 (m, 2H), 1,15 (s, 9H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Ejemplo 50

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,3-difenilpropanamida**

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y ácido 2,3-difenilpropanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,53 (dd, *J* = 7,3, 13,7, 1H), 7,66 (d, *J* = 7,4, 2H), 7,44 (d, *J* = 7,1, 1H), 7,41 – 7,22 (m, 12H), 4,36 – 4,23 (m, *J* = 7,5, 14,9, 1H), 3,97 (dt, *J* = 4,9, 9,9, 1H), 3,77 (ddd, *J* = 3,7, 10,1, 13,5, 1H), 3,52 (dt, *J* = 13,1, 18,6, 1H), 3,33 (d, *J* = 13,1, 0,5H), 3,05 (dt, *J* = 4,7, 13,0, 1H), 2,77 (dd, *J* = 2;6, 9,0, 0,5H), 2,55 (d, *J* = 6,3, 0,5H), 2,38 – 2,24 (m, 3H), 2,21 (d, *J* = 9;2, 1,5H), 2,03 – 1,86 (m, 1,5H), 1,72 – 1,56 (m, 1H), 1,52 – 1,20 (m, 2,5H); MS (ESI+) *m/z* 425 $(M+H)^+$.

Ejemplo 51

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-metil-3-fenilpropanamida**

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y ácido 2-metil-3-fenilpropanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,13 (dd, *J* = 7,0, 21,3, 1H), 7,40 (ddd, *J* = 7,5, 15,5, 25,3, 4H), 7,31 – 7,22

(m, 6H), 4,42 – 4,27 (m, 1H), 3,58 (dd, *J* = 6,6, 13,1, 1H), 3,45 (dd, *J* = 13,1, 21,0, 1H), 3,25 – 3,15 (m, 1H), 2,81 – 2,67 (m, 3H), 2,49 – 2,19 (m, 5H), 2,04 (ddd, *J* = 6,0, 12,1, 24,6, 1H), 1,82 – 1,64 (m, 1H), 1,57 – 1,40 (m, 1H), 1,40 – 1,30 (m, 1H), 1,28 (d, *J* = 6,4, 3H); MS (ESI+) *m/z* 363 $(M+H)^+$.

Ejemplo 52

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetil-2-fenilbutanamida**

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y ácido 3,3-dimetil-2-fenilbutanoico en lugar de ácido (S)-2-fenilbutanoico en el Paso F del procedimiento usado para preparar el Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,53 (dd, *J* = 7,4, 10,9, 1H), 7,73 (dd, *J* = 3,3, 5,3, 2H), 7,44 (d, *J* = 7,0, 1H), 7,41 – 7,24 (m, 7H), 4,41 – 4,30 (m, 1H), 3,62 (d, *J* = 13,1, 0,5H), 3,53 (d, *J* = 13,1, 0,5H), 3,45 (d, *J* = 15,0, 0,5H), 3,35 (d, *J* = 13,1, 0,5H), 2,90 (dd, *J* = 3,1, 8,9, 0,5H), 2,63 – 2,45 (m, 2,5H), 2,44 – 2,36 (m, 0,5H), 2,31 (d, *J* = 6,5, 1H), 2,28 (d, *J* = 5,3, 1H), 2,23 (d, *J* = 5,8, 1H), 2,15 (dd, *J* = 5,9, 12,3, 0,5H), 1,92 (dd, *J* = 6,1, 12,2, 0,5H), 1,84 (dd, *J* = 8,1, 12,6, 0,5H), 1,72 (ddd, *J* = 6,5, 12,5, 18,9, 1H), 1,46 – 1,25 (m, 2H), 1,14 (d, *J* = 1,8, 9H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Ejemplo 53

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida

Se agregó *N*-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida (2,65 g, 6,27 mmol) del Ejemplo 15 y metanol 60 ml a hidróxido de paladio al 20% sobre carbono, (húmedo, 0,530 g, 3,77 mmol) en una botella de presión de 250 ml. La reacción se agitó por 16 horas bajo hidrógeno (30 psi) a temperatura ambiente. La mezcla se filtró a través de una membrana de nylon y el solvente se eliminó al vacío. El material crudo se cromatografió sobre un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS25-25) eluyendo con 1-10% metanol (amoníaco 2 N)/diclorometano para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,97 (d, *J* = 7,1, 1H), 4,57 (dt, *J* = 7,0, 13,8, 1H), 3,03 (dd, *J* = 3,2, 10,1, 1H), 2,89 (dd, *J* = 7,8, 9,7, 1H), 2,78 (dd, *J* = 7,4, 10,1, 1H), 2,71 (ddd, *J* = 3,2, 7,5, 16,7, 1H), 2,58 (dd, *J* = 3,2, 9,8, 1H), 2,50 – 2,39 (m, *J* = 8,3, 1H), 1,98 – 1,89 (m, 3H), 1,89 – 1,80 (m, 3H), 1,79 – 1,67 (m, *J* = 6,4,

14,9, 7H), 1,66 – 1,56 (m, 3H), 1,49 – 1,36 (m, 2H), 1,36 – 1,28 (m, 1H), 1,28 – 1,02 (m, 8H); MS (ESI+) *m/z* 333 $(M+H)^+$.

Ejemplo 54

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida

Se combinó 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida (154 mg, 0,463 mmol) del Ejemplo 53 y 3-(trifluorometil)benzaldehido (0,062 ml, 0,463 mmol) en diclorometano (5 ml), y luego se agregó 2 ml de ácido acético. La reacción se agitó a temperatura ambiente por 20 minutos, y luego se agregó PS-cianoborohidruro (396 mg, 0,926 mmol). La reacción se agitó a temperatura ambiente durante la noche, luego se filtró y la resina se lavó con diclorometano. El solvente se eliminó al vacío, y el material crudo se purificó usando un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-25) eluyendo con 1-10% metanol (amoníaco 2 N)/diclorometano para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,73 (s, 1H), 7,66 (d, *J* = 7,7, 1H), 7,56 (s, 1H), 7,50 (t, *J* = 7,7, 1H), 4,51 – 4,43 (m, 1H), 3,55 (d, *J* = 12,9, 1H), 3,46 (d, *J* = 12,9, 1H), 2,75 (d, *J* = 8,6, 2H), 2,52 – 2,41 (m, *J* = 8,5, 19,1, 2H), 2,34 – 2,29 (m, 1H), 2,20 (dd, *J* = 7,7, 9,8, 1H), 2,14 (s, 3H, OAc), 1,96 – 1,54 (m, 15H), 1,49 – 1,05 (m, 12H), 1,03 – 0,93 (m, *J* = 11,7, 21,1, 1H); MS (ESI+) *m/z* 491 $(M+H)^+$.

Ejemplo 55

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(2-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]acetamida

El compuesto del título se preparó utilizando 2-fluorobenzaldehido en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,55 (s, 1H), 7,36 (dt, *J* = 6,6, 24,8, 2H), 7,20 – 7,15 (m, 2H), 4,44 (s, 1H), 3,68 (d, *J* = 12,6, 1H), 3,44 (d, *J* = 12,6, 1H), 2,77 (d, *J* = 9,6, 1H), 2,64 (dd, *J* = 7,5, 15,0, 1H), 2,53 (d, *J* = 9,0, 1H), 2,49 – 2,40 (m, 1H), 2,29 (t, *J* = 8,3, 1H), 2,16 – 2,09 (m, 1H), 1,98 – 1,64 (m, 12H), 1,61 (d, *J* = 11,4, 2H), 1,55 – 1,37 (m, *J* = 13,8, 20,5, 31,3, 3H), 1,34 – 1,08 (m, 9H), 1,00 (dd, *J* = 13,4, 22,1, 1H); MS (ESI+) *m/z* 441 $(M+H)^+$.

Ejemplo 56

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]acetamida

El compuesto del título se preparó utilizando 4-fluorobenzaldehido en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,54 (d, *J* = 6,0, 1H), 7,40 – 7,29 (m, 2H), 7,18 (d, *J* = 8,7, 2H), 4,53 – 4,38 (m, 1H), 3,55 (d, *J* = 12,5, 1H), 3,29 (d, *J* = 12,6, 1H), 2,72 (dd, *J* = 8,6, 17,7, 2H), 2,56 – 2,39 (m, 2H), 2,29 (t, *J* = 8,3, 1H), 2,10 (t, *J* = 8,1, 1H), 1,98 – 1,07 (m, 26H), 0,99 (dd, *J* = 10,2, 22,0, 1H); MS (ESI+) *m/z* 441 $(M+H)^+$.

Ejemplo 57

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[4-fluoro-3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida

El compuesto del título se preparó utilizando 4-fluoro-3-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,69 (d, *J* = 6,9, 1H), 7,56 – 7,54 (m, 1H), 7,36 – 7,28 (m, 1H), 4,52 – 4,42 (m, 1H), 3,53 (d, *J* = 12,9, 1H), 3,39 (d, *J* = 12,9, 1H), 2,85 – 2,68 (m, 2H), 2,53 – 2,41 (m, 2H), 2,34 (t, *J* = 8,3, 1H), 2,24 – 2,16 (m, 1H), 1,96 – 1,56 (m, 16H), 1,49 (d, *J* = 12,4, 1H), 1,44 – 1,05 (m, 10H), 1,05 – 0,94 (m, 1H); MS (ESI+) *m/z* 509 $(M+H)^+$.

Ejemplo 58

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-fluoro-4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida

El compuesto del título se preparó utilizando 3-fluoro-4-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,62 (d, *J* = 7,5, 2H), 7,32 (d, *J* = 11,8, 1H), 7,25 (d, *J* = 8,0, 1H), 4,51 – 4,40 (m, 1H), 3,54 (d, *J* = 13,5, 1H), 3,42 (d, *J* = 13,5, 1H), 2,84 (dd, *J* = 7,5, 16,5, 1H), 2,76 (dd, *J* = 2,6, 9,5, 1H), 2,56 – 2,47 (m, 1H), 2,44 (dd, *J* = 2,6, 8,8, 1H), 2,40 – 2,34 (m, 1H), 2,23 (dd, *J* = 7,7, 9,3, 1H), 1,97 – 1,52 (m, 16H), 1,45 – 0,97 (m, *J* = 14,9, 40,1, 72,1, 11H); MS (ESI+) *m/z* 509 $(M+H)^+$.

Ejemplo 59

***N*-{(3a*S*,4*S*,6a*R*)-2-[3,5-bis(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida**

El compuesto del título se preparó utilizando 3,5-bis(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,10 (s, 1H), 7,97 (s, 2H), 4,53 – 4,44 (m, 1H), 3,64 – 3,55 (m, 2H), 2,85 – 2,75 (m, 2H), 2,55 – 2,46 (m, 1H), 2,45 – 2,35 (m, 2H), 2,31 (t, *J* = 8,3, 1H), 1,95 – 1,55 (m, 15H), 1,48 (d, *J* = 12,6, 1H), 1,44 – 0,92 (m, 12H); MS (ESI+) *m/z* 559 $(M+H)^+$.

Ejemplo 60

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[2-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida

El compuesto del título se preparó utilizando 2-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,74 (d, *J* = 7,8, 1H), 7,64 (d, *J* = 7,7, 1H), 7,55 (d, *J* = 7,6, 1H), 7,43 (dd, *J* = 7,0, 13,9, 2H), 4,51 – 4,43 (m, 1H), 3,82 (d, *J* = 13,7, 1H), 3,54 (d, *J* = 13,7, 1H), 2,81 – 2,70 (m, 2H), 2,53 – 2,43 (m, 2H), 2,35 (t, *J* = 8,1, 1H), 2,23 – 2,17 (m, 1H), 1,95 – 1,68 (m, 10H), 1,67 – 1,52 (m, 5H), 1,46 – 1,04 (m, 11H), 0,97 – 0,86 (m, 1H); MS (ESI+) *m/z* 491 $(M+H)^+$.

Ejemplo 61

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-metilbencil)octahidrociclopenta[*c*]pirrol-4–il]acetamida

El compuesto del título se preparó utilizando 3-metilbenzaldehido en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,53 (d, *J* = 5,8, 1H), 7,32 (t, *J* = 7,5, 1H), 7,24 – 7,22 (m, 1H), 7,20 – 7,14 (m, 2H), 4,50 – 4,42 (m, 1H), 3,57 (d, *J* = 12,4, 1H), 3,34 (d, *J* = 12,3, 1H), 2,78 (d, *J* = 9,4, 1H), 2,66 (dd, *J* = 7,5, 15,1, 1H), 2,55 (d, *J* = 8,8, 1H), 2,50 – 2,42 (m, 1H), 2,33 (s, 3H), 2,31 – 2,24 (m, 1H), 2,14 – 2,07 (m, 1H), 1,98 – 1,57 (m, 13H), 1,53 (ddd, *J* = 6,4, 11,9, 18,4, 1H), 1,42 (t, *J* = 10,0, 2H), 1,38 – 1,08 (m, 10H), 1,02 – 0,92 (m, 1H); MS (ESI+) *m/z* 437 $(M+H)^+$.

Ejemplo 62

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(4-metilbencil)octahidrociclopenta[*c*]pirrol-4–il]acetamida

El compuesto del título se preparó utilizando 4-metilbenzaldehido en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,54 (d, *J* = 7,8, 1H), 7,30 (d, *J* = 7,7, 2H), 7,21 – 7,18 (m, 2H), 4,49 – 4,42 (m, 1H), 3,58 (d, *J* = 12,3, 1H), 3,31 (d, *J* = 12,4, 1H), 2,77 (d, *J* = 9,5, 1H), 2,66 (dd, *J* = 8,3, 15,9, 1H), 2,54 (d, *J* = 8,8, 1H), 2,50 – 2,41 (m, 1H), 2,32 (s, 3H), 2,30 – 2,23 (m, 2H), 2,11 – 2,03 (m, 1H), 1,99 – 1,58 (m, 13H), 1,57 – 1,08 (m, 12H), 1,03 – 0,90 (m, 1H); MS (ESI+) *m/z* 437 $(M+H)^+$.

Ejemplo 63

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometoxi)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida

El compuesto del título se preparó utilizando 3-(trifluorometoxi)benzaldehido en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,60 (d, *J* = 7,3, 1H), 7,42 (t, *J* = 7,9, 1H), 7,37 (s, 1H), 7,30 (dd, *J* = 7,9, 16,8, 2H), 4,51 – 4,44 (m, 1H), 3,50 (d, *J* = 13,0, 1H), 3,45 (d, *J* = 13,0, 1H), 2,80 – 2,72 (m, *J* = 4,8, 16,2, 2H), 2,51 – 2,42 (m, *J* = 8,7, 2H), 2,29 (t, *J* = 8,3, 1H), 2,20 (dd, *J* = 7,2, 9,2, 1H), 1,96 – 1,89 (m, 2H), 1,89 – 1,78 (m, 4H), 1,77 – 1,65 (m, 5H), 1,64 – 1,51 (m, 4H), 1,42 (dd, *J* = 9,4, 23,0, 1H), 1,36 – 1,09 (m, 10H), 1,08 – 0,98 (m, 1H); MS (ESI+) *m/z* 507 $(M+H)^+$.

Ejemplo 64

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]acetamida

El compuesto del título se preparó utilizando 3-fluorobenzaldehido en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,36 (dd, *J* = 7,8, 13,9, 1H), 7,19 – 7,11 (m, 3H), 4,49 – 4,42 (m, 1H), 3,55 (d, *J* = 12,8, 1H), 3,34 (d, *J* = 12,8, 1H), 2,78 – 2,69 (m, *J* = 8,0, 15,6, 2H), 2,51 – 2,43 (m, *J* = 10,6, 2H), 2,29 (t, *J* = 8,4, 1H), 2,13 (dd, *J* = 7,2, 9,5, 1H), 1,97 – 1,77 (m, 7H), 1,77 – 1,64 (m, 5H), 1,63 – 1,47 (m, 4H), 1,42 (ddd, *J* = 3,0, 12,2, 23,0, 1H), 1,33 (dd, *J* = 9,7, 23,2, 1H), 1,29 – 1,08 (m, 8H), 1,02 (dd, *J* = 11,8, 22,6, 1H); MS (ESI+) *m/z* 441 $(M+H)^+$.

Ejemplo 65

***N*-{(3a*S*,4*S*,6a*R*)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida**

El compuesto del título se preparó utilizando 3,3-bis(4-fluorofenil)propanal en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,77 (d, J = 7,3, 1H), 7,39 – 7,31 (m, 4H), 7,20 – 7,13 (m, 4H), 4,58 – 4,50 (m, 1H), 4,13 (d, J = 7,5, 1H), 2,85 (dd, J = 2,2, 9,4, 1H), 2,74 (dd, J = 7,2, 14,4, 1H), 2,47 (d, J = 7,4, 2H), 2,38 – 2,26 (m, 4H), 2,22 (t, J = 8,6, 1H), 2,12 (dd, J = 7,4, 9,3, 1H), 1,98 – 1,90 (m, 4H), 1,90 – 1,82 (m, 2H), 1,82 – 1,76 (m, J = 8,6, 2H), 1,76 – 1,66 (m, 5H), 1,65 – 1,57 (m, 3H), 1,47 – 1,33 (m, 3H), 1,30 – 1,18 (m, 4H), 1,18 – 1,03 (m, 4H); MS (ESI+) *m/z* 563 $(M+H)^+$.

Ejemplo 66

***N*-{(3a*S*,4*S*,6a*R*)-2-[6,6-bis(4-fluorofenil)hexil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida**

El compuesto del título se preparó utilizando 6,6-bis(4-fluorofenil)hexanal en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,80 (d, J = 6,7, 1H), 7,35 (ddd, J = 2,1, 5,4, 7,9, 4H), 7,16 (td, J = 3,1, 8,8, 4H), 4,56 – 4,47 (m, 1H), 3,99 (t, J = 7,8, 1H), 2,82 (d, J = 9,3, 1H), 2,65 (d, J = 7,7, 1H), 2,49 (dd, J = 8,5, 19,2, 2H), 2,30 (d, J = 31,9, 2H), 2,16 – 2,01 (m, 4H), 1,99 – 1,68 (m, 11H), 1,67 – 1,57 (m, 2H), 1,57 – 1,04 (m, 14H); MS (ESI+) *m/z* 605 $(M+H)^+$.

Ejemplo 67

***N*-{(3a*S*,4*S*,6a*R*)-2-[3-(3-clorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida**

El compuesto del título se preparó utilizando 3-(3-clorofenil)propanal en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,87 (s, 1H), 7,31 (d, J = 13,4, 2H), 7,27 (t, J = 7,6, 1H), 7,13 (d, J = 7,3, 1H), 4,57 – 4,49 (m, 1H), 2,86 (d, J = 8,6, 1H), 2,74 (dd, J = 7,3, 14,6, 1H), 2,62 (dd, J = 7,0, 15,3, 2H), 2,53 – 2,45 (m, J = 6,7, 2H), 2,39 – 2,32 (m, J = 6,1, 2H), 2,23 (t, J = 8,0, 1H), 2,01 – 1,68 (m, 16H), 1,65 – 1,56 (m, 3H), 1,48 – 1,33 (m, 3H), 1,32 – 1,18 (m, 4H), 1,17 – 1,04 (m, J = 12,5, 25,1, 4H); MS (ESI+) *m/z* 485 $(M+H)^+$.

Ejemplo 68

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(3-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}acetamida

El compuesto del título se preparó utilizando 3-(3-fluorofenil)propanal en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,81 (d, *J* = 3,1, 1H), 7,31 (dd, *J* = 7,3, 14,5, 1H), 7,10 – 7,02 (m, *J* = 11,5, 3H), 4,60 – 4,46 (m, 1H), 2,85 (d, *J* = 8,2, 1H), 2,76 – 2,59 (m, 3H), 2,55 – 2,43 (m, 2H), 2,41 – 2,28 (m, 2H), 2,25 – 2,16 (m, 1H), 2,15 – 2,06 (m, 1H), 2,00 – 1,90 (m, 4H), 1,89 – 1,67 (m, *J* = 37,4, 11H), 1,67 – 1,54 (m, 3H), 1,49 – 1,33 (m, 3H), 1,30 – 1,18 (m, *J* = 10,6, 4H), 1,17 – 1,05 (m, 4H); MS (ESI+) *m/z* 469 $(M+H)^+$.

Ejemplo 69

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-fenilpropil)octahidrociclopenta[*c*]pirrol-4–il]acetamida

El compuesto del título se preparó utilizando 3-fenilpropanal en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,83 (d, *J* = 5,1, 1H), 7,38 (t, *J* = 7,6, 2H), 7,28 (d, *J* = 7,4, 3H), 4,57 – 4,48 (m, 1H), 2,85 (d, *J* = 8,7, 1H), 2,75 – 2,61 (m, 3H), 2,48 (dd, *J* = 8,7, 19,0, 2H), 2,35 (dd, *J* = 7,0, 17,3, 2H), 2,17 (t, *J* = 7,8, 1H), 2,12 – 2,07 (m, 1H), 1,93 (dd, *J* = 8,6, 14,2, 4H), 1,89 – 1,75 (m, 7H), 1,71 (d, *J* = 10,9, 4H), 1,65 – 1,53 (m, *J* = 6,0, 14,1, 3H), 1,49 – 1,32 (m, 3H), 1,30 – 1,18 (m, 4H), 1,17 – 1,04 (m, *J* = 9,5, 21,4, 4H); MS (ESI+) *m/z* 451 $(M+H)^+$.

Ejemplo 70

2,2-diciclohexil-*N*-((3a*S*,4*S*,6a*R*)-2-{3-[4-(trifluorometil)fenil]propil}octahidrociclopenta[*c*]pirrol-4–il)acetamida

El compuesto del título se preparó utilizando 3-(4-(trifluorometil)fenil)propanal en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,82 (d, *J* = 7,1, 1H), 7,67 (d, *J* = 8,1, 2H), 7,36 (d, *J* = 8,1, 2H), 4,57 – 4,50 (m, 1H), 2,85 (d, *J* = 9,5, 1H), 2,70 (tt, *J* = 7,0, 14,1, 3H), 2,49 (d, *J* = 7,5, 2H), 2,35 (t, *J* = 6,4, 2H), 2,22 (t, *J* = 8,5, 1H), 2,16 – 2,09 (m, 1H), 1,98 – 1,89 (m, 4H), 1,89 – 1,74 (m, 7H), 1,70 (d, *J* = 8,5, 4H), 1,60 (dd, *J* = 4,9, 12,1, 3H), 1,41 (dt, *J* = 9,0, 20,3, 3H), 1,30 – 1,17 (m, 4H), 1,10 (dt, *J* = 10,4, 12,0, 4H); MS (ESI+) *m/z* 519 $(M+H)^+$.

Ejemplo 71

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}acetamida

El compuesto del título se preparó utilizando 3-(4-fluorofenil)propanal en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,94 – 7,77 (m, 1H), 7,25 – 7,20 (m, 2H), 7,14 (t, *J* = 8,7, 2H), 4,61 – 4,47 (m, 1H), 2,93 – 2,80 (m, 1H), 2,79 – 2,69 (m, 1H), 2,62 (dd, *J* = 7,6, 15,5, 2H), 2,55 – 2,44 (m, 2H), 2,43 – 2,29 (m, 2H), 2,27 – 2,08 (m, 2H), 2,02 – 1,90 (m, 4H), 1,89 – 1,75 (m, 7H), 1,70 (d, *J* = 11,2, 4H), 1,60 (d, *J* = 6,9, 3H), 1,49 – 1,32 (m, 3H), 1,30 – 1,17 (m, 4H), 1,12 (dd, *J* = 12,0, 24,1, 4H); MS (ESI+) *m/z* 469 $(M+H)^+$.

Ejemplo 72

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(piridin-4–ilmetil)octahidrociclopenta[*c*]pirrol-4–il]acetamida

El compuesto del título se preparó utilizando isonicotinaldehido en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,76 (d, *J* = 5,7, 2H), 7,75 – 7,69 (m, 1H), 7,31 (d, *J* = 5,5, 2H), 4,48 (dd, *J* = 6,9, 13,1, 1H), 3,47 (d, *J* = 13,5, 1H), 3,39 (d, *J* = 13,5, 1H), 2,87 – 2,75 (m, *J* = 9,2, 21,0, 2H), 2,53 – 2,45 (m, 1H), 2,43 (d, *J* = 9,0, 1H), 2,34 (t, *J* = 8,3, 1H), 2,26 – 2,20 (m, 1H), 1,97 – 1,87 (m, 4H), 1,87 – 1,76 (m, 4H), 1,75 – 1,64 (m, *J* = 6,5, 12,2, 17,6, 5H), 1,63 – 1,56 (m, *J* = 13,2, 3H), 1,43 (dd, *J* = 10,1, 22,9, 1H), 1,35 (dd, *J* = 5,6, 12,1, 1H), 1,30 – 1,18 (m, *J* = 12,4, 24,4, 4H), 1,17 – 1,08 (m, *J* = 10,1, 19,2, 4H), 1,09 – 0,99 (m, 1H); MS (ESI+) *m/z* 424 $(M+H)^+$.

Ejemplo 73

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(piridin-3–ilmetil)octahidrociclopenta[*c*]pirrol-4–il]acetamida

El compuesto del título se preparó utilizando nicotinaldehido en lugar de 3-(trifluorometil)benzaldehido en Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,80 (d, *J* = 1,7, 1H), 7,64 (d, *J* = 6,4, 2H), 7,30 (dd, *J* = 4,8, 7,7, 1H), 4,49 – 4,41 (m, 1H), 3,54 (d, *J* = 12,9, 1H), 3,35 (d, *J* = 12,8, 1H), 2,80 – 2,71 (m, *J* = 7,7, 2H), 2,51 – 2,42 (m, *J* = 8,7, 2H), 2,31 (t, *J* = 8,3, 1H), 2,16 (t, *J* = 8,8, 1H), 1,91 (dd, *J* = 6,4, 11,9, 2H), 1,86 – 1,64 (m, 10H), 1,57 (dd, *J* = 11,4, 24,2, 4H), 1,42 (d, *J* = 12,8, 1H), 1,35 – 1,08 (m, 10H), 1,03 (d, *J* = 14,0, 1H); MS (ESI+) *m/z* 424 $(M+H)^+$.

Ejemplo 74

2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida

El compuesto del título se preparó utilizando *N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida del Ejemplo 20 en lugar de *N*-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida en Ejemplo 53: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 5,31 (d, *J* = 7,5, 1H), 3,97 – 3,82 (m, 1H), 3,09 – 2,85 (m, 3H), 2,66 (dd, *J* = 3,7, 12,5, 2H), 2,40 – 2,26 (m, 1H), 2,10 – 1,80 (m, 6H), 1,79 – 1,53 (m, 11H), 1,52 – 1,30 (m, *J* = 21,5, 31,0, 2H), 1,29 – 1,03 (m, 7H), 0,93 (dd, *J* = 11,9, 23,1, 2H); MS (ESI+) *m/z* 333 $(M+H)^+$.

Ejemplo 75

2,2-diciclohexil-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida

El compuesto del título se preparó utilizando 2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida del Ejemplo 74 en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,07 (d, *J* = 7,2, 1H), 7,75 (s, 1H), 7,63 – 7,54 (m, 2H), 7,43 (t, *J* = 7,8, 1H), 4,51 – 4,42 (m, 1H), 3,61 (d, *J* = 13,6, 1H), 3,46 (d, *J* = 13,5, 1H), 2,87 (dd, *J* = 2,4, 8,9, 1H), 2,64 – 2,52 (m, 2H), 2,52 – 2,46 (m, 1H), 2,30 (s, 2H), 2,18 – 2,08 (m, 1H), 2,03 (t, *J* = 7,3, 1H), 1,99 – 1,76 (m, 7H), 1,75 – 1,55 (m, 7H), 1,51 – 1,35 (m, 3H), 1,31 – 1,03 (m, 8H); MS (ESI+) *m/z* 491 $(M+H)^+$.

Ejemplo 76

2,2-diciclohexil-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida

El compuesto del título se preparó utilizando 3-fluoro-4-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido y 2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida del Ejemplo 74 en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,16 (d, *J* = 7,3, 1H), 7,59 (d, *J* = 10,3, 1H), 7,33 (d, *J* = 11,7, 1H), 7,28 (d, *J* = 8,0, 1H), 4,52 – 4,44 (m, 1H), 3,56 (d, *J* = 14,2, 1H), 3,45 (d, *J* = 14,2, 1H), 2,92 (dd, *J* = 1,8, 8,9, 1H), 2,63 – 2,52 (m, *J* =

11,3, 2H), 2,43 (dd, *J* = 6,9, 8,8, 1H), 2,34 (dd, *J* = 2,0, 9,0, 1H), 2,29 – 2,23 (m, 1H), 2,13 (dq, *J* = 5,9, 11,8, 1H), 2,04 (t, *J* = 7,4, 1H), 2,00 – 1,84 (m, 5H), 1,80 (d, *J* = 12,4, 2H), 1,76 – 1,56 (m, 7H), 1,46 (dd, *J* = 10,4, 23,5, 3H), 1,30 – 1,18 (m, 4H), 1,17 – 1,05 (m, 4H); MS (ESI+) *m/z* 509 $(M+H)^+$.

Ejemplo 77

***N*-{(3a*S*,4*R*,6a*R*)-2-[3,5-bis(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida**

El compuesto del título se preparó utilizando 3,5-bis(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido y 2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida del Ejemplo 74 en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,16 (d, *J* = 7,1, 1H), 7,99 (s, 3H), 4,50 – 4,42 (m, 1H), 3,69 (d, *J* = 13,9, 1H), 3,54 (d, *J* = 13,9, 1H), 2,92 (dd, *J* = 2,7, 9,0, 1H), 2,65 – 2,56 (m, *J* = 10,2, 15,6, 2H), 2,55 – 2,50 (m, 1H), 2,31 (d, *J* = 4,2, 2H), 2,10 (dq, *J* = 5,9, 11,8, 1H), 2,03 (t, *J* = 7,4, 1H), 1,99 – 1,83 (m, 5H), 1,80 (d, *J* = 12,4, 2H), 1,75 – 1,64 (m, *J* = 12,4, 18,4, 5H), 1,63 – 1,56 (m, *J* = 8,7, 2H), 1,44 (td, *J* = 7,6, 21,0, 3H), 1,31 – 1,16 (m, 4H), 1,16 – 1,04 (m, 4H); MS (ESI+) *m/z* 559 $(M+H)^+$.

Ejemplo 78

***N*-{(3a*S*,4*R*,6a*R*)-2-[6,6-bis(4-fluorofenil)hexil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida**

El compuesto del título se preparó utilizando 6,6-bis(4-fluorofenil)hexanal en lugar de 3-(trifluorometil)benzaldehido y 2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida del Ejemplo 74 en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H *N*MR (500 MHz, piridin-d_5) δ ppm 8,14 (d, *J* = 7,3, 1H), 7,33 (dd, *J* = 5,6, 8,5, 4H), 7,14 (t, *J* = 8,7, 4H), 4,52 – 4,44 (m, 1H), 3,96 (t, *J* = 7,8, 1H), 2,94 (d, *J* = 8,8, 1H), 2,58 (s, 2H), 2,42 (d, *J* = 8,1, 2H), 2,31 (d, *J* = 22,9, 3H), 2,17 – 2,09 (m, 1H), 2,08 – 1,85 (m, 8H), 1,85 – 1,77 (m, 2H), 1,76 – 1,64 (m, 5H), 1,61 (d, *J* = 12,0, 2H), 1,52 – 1,42 (m, 5H), 1,41 – 1,34 (m, 2H), 1,31 – 1,19 (m, 5H), 1,18 – 1,07 (m, 5H); MS (ESI+) *m/z* 605 $(M+H)^+$.

Ejemplo 79

2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-2-(3,3-difenilpropil)octahidrociclopenta[*c*]pirrol-4–il]acetamida

El compuesto del título se preparó utilizando 3,3-difenilpropanal en lugar de 3-(trifluorometil)benzaldehido y 2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida del Ejemplo 74 en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,10 (d, *J* = 7,7, 1H), 7,45 (d, *J* = 7,3, 2H), 7,42 (d, *J* = 7,1, 3H), 7,38 – 7,30 (m, 5H), 4,56 – 4,48 (m, 1H), 4,27 (t, *J* = 7,5, 1H), 2,92 – 2,86 (m, 1H), 2,59 – 2,48 (m, *J* = 6,7, 14,0, 2H), 2,38 – 2,26 (m, 5H), 2,21 – 2,12 (m, 2H), 2,05 (t, *J* = 7,4, 1H), 1,97 (dd, *J* = 8,3, 17,0, 2H), 1,94 – 1,85 (m, 4H), 1,81 (d, *J* = 11,8, 2H), 1,72 (d, *J* = 13,2, 4H), 1,66 (dd, *J* = 7,4, 11,8, 1H), 1,61 (d, *J* = 12,6, 2H), 1,48 (ddd, *J* = 3,4, 12,8, 15,5, 3H), 1,30 – 1,19 (m, 4H), 1,19 – 1,06 (m, 4H); MS (ESI+) *m/z* 527 $(M+H)^+$.

Ejemplo 80

***N*-{(3a*S*,4*R*,6a*R*)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida**

El compuesto del título se preparó utilizando 3,3-bis(4-fluorofenil)propanal en lugar de 3-(trifluorometil)benzaldehido y 2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida del Ejemplo 74 en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,13 (s, 1H), 7,41 (dd, *J* = 5,5, 8,7, 2H), 7,35 (dd, *J* = 5,1, 13,8, 3H), 7,14 (dt, *J* = 8,8, 14,7, 4H), 4,60 – 4,51 (m, *J* = 21,3, 1H), 4,30 (t, *J* = 7,7, 1H), 2,95 (d, *J* = 8,9, 1H), 2,57 – 2,51 (m, 2H), 2,40 (d, *J* = 8,7, 1H), 2,30 (d, *J* = 7,0, 3H), 2,26 – 2,12 (m, 4H), 2,05 (t, *J* = 7,4, 1H), 2,02 – 1,94 (m, *J* = 12,5, 2H), 1,94 – 1,85 (m, *J* = 6,7, 18,0, 2H), 1,82 (d, *J* = 11,7, 2H), 1,72 (d, *J* = 11,8, 4H), 1,67 – 1,57 (m, *J* = 10,6, 16,3, 3H), 1,48 (qd, *J* = 3,3, 12,7, 3H), 1,25 (dd, *J* = 15,5, 28,8, 4H), 1,13 (t, *J* = 18,3, 4H); MS (ESI+) *m/z* 563 $(M+H)^+$.

Ejemplo 81

***N*-{(3a*S*,4*R*,6a*R*)-2-[4,4-bis(4-fluorofenil)butil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida**

El compuesto del título se preparó utilizando 4,4-bis(4-fluorofenil)butanal en lugar de 3-(trifluorometil)benzaldehido y 2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida del Ejemplo 74 en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,12 (d, *J* = 7,5, 1H), 7,36 (ddd, *J* = 5,5, 8,6, 16,2, 4H), 7,17 (t, *J* = 8,8, 2H), 7,11 (t, *J* = 8,8, 2H), 4,52 – 4,45 (m, 1H), 3,99 (t, *J* = 7,9, 1H), 2,91 (d, *J* = 9,1, 1H), 2,59 – 2,50 (m, 2H), 2,36 (t, *J* = 7,1, 3H), 2,24 – 2,16 (m, *J* = 6,6, 13,0, 2H), 2,14 – 2,02 (m, *J* = 9,6, 17,5, 3H), 2,02 – 1,86 (m, *J* = 9,2, 27,4, 5H), 1,81 (t, *J* = 10,7, 2H), 1,73 (d, *J* = 9,6, 4H), 1,68 – 1,57 (m, *J* = 13,6, 3H), 1,53 – 1,37 (m, 6H), 1,31 – 1,19 (m, *J* = 11,2, 23,8, 4H), 1,18 – 1,07 (m, *J* = 10,5, 22,1, 4H); MS (ESI+) *m/z* 577 $(M+H)^+$.

Ejemplo 82

3-metil-2-fenil-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida

Paso A: Se preparó 3-Metil-*N*-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida utilizando *N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida del Ejemplo 18 en lugar de *N*-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida en el procedimiento descrito por ejemplo 53: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,31 (dd, *J* = 1,5, 6,6, 2H), 5,50 – 5,38 (m, *J* = 3,8, 9,7, 1H), 3,84 (dd, *J* = 4,1, 13,5, 1H), 2,92 (ddd, *J* = 10,1, 15,8, 20,7, 3H), 2,76 (dt, *J* = 3,7, 11,5, 2H), 2,65 – 2,53 (m, *J* = 7,9, 12,1, 3H), 2,47 – 2,25 (m, *J* = 9,8, 17,7, 31,5, 2H), 2,20 – 2,07 (m, *J* = 9,3, 17,5, 1H), 2,05 – 1,80 (m, 2H), 1,53 – 1,39 (m, 1H), 1,27 (s, 2H), 1,03 (dd, *J* = 3,4, 6,5, 3H), 0,70 (d, *J* = 6,7, 3H); MS (ESI+) *m/z* 287 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando 3-metil-*N*-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz,

piridin-d_5) δ ppm 8,60 (t, *J* = 7,9, 1H), 7,73 (d, *J* = 26,6, 1H), 7,63 (dd, *J* = 2,0, 7,5, 1H), 7,57 – 7,52 (m, 2H), 7,43 (dd, *J* = 7,7, 17,9, 1H), 7,33 (td, *J* = 4,1, 7,5, 2H), 7,26 (dt, *J* = 3,6, 7,2, 1H), 4,38 – 4,28 (m, 1H), 3,60 (d, *J* = 13,6, 0,5H), 3,52 (d, *J* = 13,5, 0,5H), 3,46 (d, *J* = 13,6, 0,5H), 3,35 (d, *J* = 13,5, 0,5H), 3,22 (dd, *J* = 1,4, 10,4, 1H), 2,90 (dd, *J* = 3,0, 9,1, 0,5H), 2,70 – 2,60 (m, *J* = 5,3, 11,8, 1H), 2,59 – 2,53 (m, 1H), 2,52 – 2,46 (m, 1H), 2,44 – 2,32 (m, 1H), 2,28 (d, *J* = 9,1, 0,5H), 2,25 (d, *J* = 5,1, 1H), 2,20 (dd, *J* = 2,4, 4,7, 1H), 2,13 – 2,07 (m, 1,5H), 1,92 – 1,80 (m, 1H), 1,75 (dt, *J* = 6,3, 18,8, 0,5H), 1,71 – 1,64 (m, 0,5H), 1,47 – 1,39 (m, 0,5H), 1,39 – 1,32 (m, 0,5H), 1,32 – 1,24 (m, *J* = 4,2, 16,6, 0,5H), 1,20 (dd, *J* = 4,3, 6,4, 3H), 0,70 (d, *J* = 6,7, 3H); MS (ESI+) *m/z* 445 $(M+H)^+$.

Ejemplo 83

***N*-[(3a*R*,4*S*,6a*S*)-2-(ciclohexilmetil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida**

Paso A: 3-Metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida se preparó utilizando *N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida del Ejemplo 35 en lugar de *N*-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida en Ejemplo 53: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,61 (d, *J* = 6,9, 1H), 7,65 (dd, *J* = 4,6, 6,9, 2H), 7,34 (t, *J* = 7,5, 2H), 7,26 (t, *J* = 7,3, 1H), 4,24 (tt, *J* = 6,2, 12,6, 1H), 3,23 (d, *J* = 10,4, 1H), 3,19 (dd, *J* = 2,7, 10,8, 0,5H), 2,99 (dd, *J* = 7,2, 10,9, 0,5H), 2,84 – 2,72 (m, 2H), 2,70 – 2,61 (m, 1H), 2,58 (dd, *J* = 2,8, 10,7, 0,5H), 2,53 (dd, *J* = 3,3, 10,5, 1H), 2,49 – 2,44 (m, 0,5H), 2,43 – 2,35 (m, *J* = 10,5, 0,5H), 2,35 – 2,28 (m, *J* = 12,5, 0,5H), 2,06 (dq, *J* = 6,1, 12,2, 0,5H), 1,91 – 1,72 (m, 1,5H), 1,66 (dt, *J* = 7,2, 19,4, 0,5H), 1,42 (dd, *J* = 7,9, 19,3, 0,5H), 1,30 – 1,13 (m, 4 H), 0,71 (d, *J* = 6,7, 3H); MS (ESI+) *m/z* 287 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando ciclohexanocarbaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,57 (dd, *J* = 7,0, 10,9, 1H), 7,64 (dd, *J* = 4,9, 7,0, 2H), 7,34 (t, *J* = 7,6, 2H), 7,25 (t, *J* = 7,4, 1H), 4,37 – 4,28 (m, 1H), 3,23 (d, *J* = 10,4, 1H), 2,85 (dd, *J* = 2,8, 9,0, 0,5H), 2,70 – 2,60 (m, 1H), 2,59 – 2,53 (m, *J* = 4,6, 11,8, 0,5H), 2,51

(dd, *J* = 3,1, 9,1, 1H), 2,44 – 2,38 (m, 1H), 2,37 – 2,32 (m, 0,5H), 2,31 – 2,28 (m, 0,5H), 2,27 – 2,08 (m, 3,5H), 2,08 – 1,99 (m, 1H), 1,93 – 1,73 (m, 3,5H), 1,73 – 1,54 (m, 3,5H), 1,47 – 1,27 (m, 2,5H), 1,22 (dd, *J* = 6,5, 10,5, 3H), 1,19 – 1,06 (m, 3H), 0,90 – 0,75 (m, 2H), 0,71 (dd, *J* = 2,2, 6,7, 3H); MS (ESI+) *m/z* 383 $(M+H)^+$.

Ejemplo 84

3-metil-*N*-[(3a*R*,4*S*,6a*S*)-2-metiloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida

El compuesto del título se preparó utilizando formaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,55 (t, *J* = 5,4, 1H), 7,65 (t, *J* = 6,5, 2H), 7,34 (ddd, *J* = 3,7, 7,6, 10,9, 2H), 7,29 – 7,25 (m, 1H), 4,42 – 4,28 (m, 1H), 3,22 (d, *J* = 10,5, 1H), 2,91 (dd, *J* = 2,2, 9,0, 0,5H), 2,65 (dt, *J* = 6,7, 17,3, 1H), 2,53 (dd, *J* = 2,5, 9,2, 1H), 2,46 (dd, *J* = 4,4, 10,2, 0,5H), 2,42 – 2,35 (m, 0,5H), 2,30 (d, *J* = 8,8, 1,5H), 2,25 (dd, *J* = 2,8, 9,0, 0,5H), 2,19 (s, 1,5H), 2,16 – 2,05 (m, 3,5H), 1,85 (td, *J* = 6,2, 12,0, 1H), 1,75 (dd, *J* = 6,6, 13,8, 0,5H), 1,63 (dt, *J* = 7,0, 15,3, 0,5H), 1,39 (dt, *J* = 8,1, 14,4, 1H), 1,31 (dt, *J* = 2,9, 9,4, 0,5H), 1,22 (dd, *J* = 6,5, 11,7, 3H), 0,71 (dd, *J* = 2,9, 6,7, 3H); MS (ESI+) *m/z* 301 $(M+H)^+$.

Ejemplo 85

***N*-[(3a*R*,4*S*,6a*S*)-2-(2-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida**

El compuesto del título se preparó utilizando 2-fluorobenzaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,66 – 8,58 (m, 1H), 7,63 (dd, *J* = 3,1, 7,4, 2H), 7,53 (t, *J* = 7,4, 1H), 7,33 (td, *J* = 2,2, 7,6, 2H), 7,28 – 7,22 (m, *J* = 7,4, 9,9, 2H), 7,17 – 7,06 (m, *J* = 8,2, 14,8, 26,9, 2H), 4,34 (dd, *J* = 6,0, 11,5, 1H), 3,75 (d, *J* = 13,6, 0,5H), 3,71 – 3,62 (m, 1H), 3,57 (d, *J* = 13,6, 0,5H), 3,22 (dd, *J* = 2,2, 10,4, 1H), 3,00 (d, *J* = 6,7, 0,5H), 2,69 – 2,48 (m, *J* = 23,7, 34,8, 3H), 2,47 – 2,28 (m, 3,5H), 2,17 – 2,07 (m, 0,5H), 1,93 – 1,78 (m, *J* = 6,7, 12,4, 20,1, 1H), 1,78 – 1,62 (m, 1H), 1,49 – 1,27 (m, *J* = 10,3, 19,5,

9707.01

26,3, 1,5H), 1,20 (dd, *J* = 2,9, 6,4, 3H), 0,70 (dd, *J* = 1,4, 6,6, 3H); MS (ESI+) *m/z* 395 $(M+H)^+$.

Ejemplo 86

N-[(3aR,4S,6aS)-2-(3-clorobencil)octahidrociclopenta[c]pirrol-4–il]-3-metil-2-fenilbutanamida

El compuesto del título se preparó utilizando 3-clorobenzaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,62 (t, *J* = 6,5, 1H), 7,64 (dd, *J* = 4,3, 7,0, 2H), 7,51 (s, 0,5H), 7,46 (s, 0,5H), 7,33 (td, *J* = 2,5, 7,5, 3H), 7,30 – 7,28 (m, 1H), 7,28 – 7,23 (m, 2H), 4,37 – 4,28 (m, 1H), 3,60 (d, *J* = 13,4, 0,5H), 3,51 (d, *J* = 13,4, 0,5H), 3,45 (d, *J* = 13,4, 0,5H), 3,33 (d, *J* = 13,4, 0,5H), 3,22 (dd, *J* = 2,2, 10,4, 1H), 2,93 (d, *J* = 6,3, 0,5H), 2,69 – 2,48 (m, 3H), 2,31 (dddd, *J* = 8,9, 13,2, 14,5, 20,2, 3H), 2,16 – 2,05 (m, 1H), 1,92 – 1,79 (m, 1H), 1,78 – 1,62 (m, 1H), 1,49 – 1,40 (m, 0,5H), 1,37 (dd, *J* = 5,8, 12,6, 0,5H), 1,30 (dd, *J* = 7,2, 13,5, 0,5H), 1,20 (dd, *J* = 3,0, 6,5, 3H), 0,70 (dd, *J* = 1,5, 6,7, 3H); MS (ESI+) *m/z* 411 $(M+H)^+$.

Ejemplo 87

N-[(3aR,4S,6aS)-2-(3-fluorobencil)octahidrociclopenta[c]pirrol-4–il]-3-metil-2-fenilbutanamida

El compuesto del título se preparó utilizando 3-fluorobenzaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,61 (t, *J* = 8,0, 1H), 7,64 (dd, *J* = 4,1, 7,0, 2H), 7,37 – 7,16 (m, 5H), 7,13 (d, *J* = 7,6, 1H), 7,04 (s, 1H), 4,33 (dd, *J* = 5,7, 12,4, 1H), 3,57 (d, *J* = 13,5, 0,5H), 3,48 (d, *J* = 13,4, 0,5H), 3,42 (d, *J* = 13,5, 0,5H), 3,30 (d, *J* = 13,5, 0,5H), 3,23 (d, *J* = 10,5, 1H), 2,90 (dd, *J* = 2,9, 9,1, 0,5H), 2,70 – 2,61 (m, 1H), 2,59 – 2,53 (m, 1H), 2,53 – 2,45 (m, 1H), 2,44 – 2,31 (m, *J* = 18,5, 1H), 2,27 (t, *J* = 7,7, 1H), 2,19 (dd, *J* = 6,3, 13,0, 1H), 2,12 (dd, *J* = 6,0, 12,3, 0,5H), 1,93 – 1,80 (m, *J* = 6,9, 12,4, 20,6, 1H), 1,79 – 1,64 (m, 1H), 1,47 – 1,24 (m, 2H), 1,20 (dd, *J* = 3,1, 6,4, 3H), 0,70 (d, *J* =

6,7, 3H); MS (ESI+) *m/z* 395 $(M+H)^+$.

Ejemplo 88

3-metil-2-fenil-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida

El compuesto del título se preparó utilizando 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,60 (t, *J* = 7,6, 1H), 7,76 (s, 0,5H), 7,71 (s, 0,5H), 7,64 (d, *J* = 7,8, 2H), 7,57 – 7,53 (m, *J* = 7,1, 2H), 7,43 (dd, *J* = 7,8, 17,8, 1H), 7,36 – 7,30 (m, 2H), 7,28 – 7,23 (m, 1H), 4,33 (dd, *J* = 5,8, 12,3, 1H), 3,61 (d, *J* = 13,6, 0,5H), 3,53 (d, *J* = 13,5, 0,5H), 3,47 (d, *J* = 13,5, 0,5H), 3,36 (d, *J* = 13,5, 0,5H), 3,22 (dd, *J* = 1,5, 10,4, 1H), 2,91 (dd, *J* = 3,0, 9,0, 0,5H), 2,69 – 2,59 (m, 1H), 2,55 (dd, *J* = 3,0, 9,0, 1H), 2,52 – 2,47 (m, 1H), 2,44 – 2,32 (m, *J* = 10,5, 32,1, 1H), 2,29 (d, *J* = 8,9, 0,5H), 2,26 (d, *J* = 5,2, 1H), 2,22 – 2,18 (m, 1H), 2,16 – 2,06 (m, 0,5H), 1,92 – 1,79 (m, 1H), 1,79 – 1,63 (m, 1H), 1,48 – 1,25 (m, 1,5H), 1,20 (dd, *J* = 4,5, 6,4, 3H), 0,70 (d, *J* = 5,8, 3H); MS (ESI+) *m/z* 445 $(M+H)^+$.

Ejemplo 89

***N*-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida**

El compuesto del título se preparó utilizando 4-fluorobenzaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,61 (t, *J* = 7,2, 1H), 7,64 (dd, *J* = 2,4, 7,5, 2H), 7,39 (dd, *J* = 5,8, 8,2, 1H), 7,33 (dt, *J* = 5,8, 11,6, 3H), 7,28 – 7,23 (m, 1H), 7,11 (dd, *J* = 8,8, 19,1, 2H), 4,34 (dd, *J* = 5,8, 12,6, 1H), 3,56 (d, *J* = 13,3, 0,5H), 3,45 (dd, *J* = 13,3, 16,8, 1H), 3,31 (d, *J* = 13,1, 0,5H), 3,22 (dd, *J* = 2,3, 10,5, 1H), 2,92 (d, *J* = 6,5, 0,5H), 2,69 – 2,60 (m, 1H), 2,57 (d, *J* = 6,6, 1H), 2,51 (d, *J* = 8,4, 1H), 2,46 – 2,33 (m, 1H), 2,29 (d, *J* = 4,4, 1H), 2,22 (d, *J* = 6,5, 1H), 2,14 (dq, *J* = 6,2, 12,2, 0,5H), 1,95 – 1,80 (m, *J* = 7,1, 12,4, 20,7, 1H), 1,79 – 1,72 (m, 0,5H), 1,71 – 1,64 (m, 1H), 1,48 – 1,23 (m, 1,5H), 1,20 (t, *J* = 6,1, 3H), 0,70 (dd, *J* = 2,1, 6,7, 3H); MS (ESI+) *m/z* 395 $(M+H)^+$.

Ejemplo 90

N-[(3aR,4S,6aS)-2-(3-metoxibencil)octahidrociclopenta[c]pirrol-4–il]-3-metil-2-fenilbutanamida

El compuesto del título se preparó utilizando 3-metoxibenzaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,61 – 8,54 (m, 1H), 7,63 (d, *J* = 7,6, 2H), 7,36 – 7,24 (m, *J* = 5,6, 12,0, 20,6, 4H), 7,17 (s, 0,5H), 7,11 (s, 0,5H), 7,06 (d, *J* = 7,8, 0,5H), 7,00 (d, *J* = 7,5, 0,5H), 6,95 – 6,88 (m, 1H), 4,42 – 4,29 (m, 1H), 3,72 (s, 1,5H), 3,70 (s, 1,5H), 3,60 (d, *J* = 13,3, 0,5H), 3,52 (d, *J* = 13,2, 0,5H), 3,48 (d, *J* = 13,3, 0,5H), 3,36 (d, *J* = 13,2, 0,5H), 3,23 – 3,19 (m, 1H), 2,93 (dd, *J* = 2,7, 9,0, 0,5H), 2,68 – 2,61 (m, 1H), 2,58 (dd, *J* = 3,0, 8,9, 1H), 2,52 – 2,46 (m, 1H), 2,45 – 2,20 (m, 3H), 2,18 – 2,11 (m, 1H), 1,91 (dd, *J* = 6,0, 12,0, 0,5H), 1,87 – 1,80 (m, 0,5H), 1,78 – 1,64 (m, 1H), 1,48 – 1,26 (m, *J* = 28,4, 35,4, 1,5H), 1,20 (t, *J* = 6,7, 3H), 0,70 (dd, *J* = 2,8, 6,7, 3H); MS (ESI+) *m/z* 407 $(M+H)^+$.

Ejemplo 91

3-metil-N-[(3aR,4S,6aS)-2-(3-metilbencil)octahidrociclopenta[c]pirrol-4–il]-2-fenilbutanamida

El compuesto del título se preparó utilizando 3-metilbenzaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,62 – 8,50 (m, 1H), 7,64 (d, *J* = 7,5, 2H), 7,33 (td, *J* = 3,7, 7,5, 2H), 7,29 – 7,23 (m, *J* = 5,5, 11,0, 3H), 7,18 (s, 1H), 7,07 (d, *J* = 7,0, 1H), 4,42 – 4,29 (m, 1H), 3,60 (d, *J* = 13,1, 0,5H), 3,51 (d, *J* = 13,0, 0,5H), 3,45 (d, *J* = 13,1, 0,5H), 3,33 (d, *J* = 13,0, 0,5H), 3,22 (d, *J* = 10,4, 1H), 2,90 (dd, *J* = 2,9, 8,9, 0,5H), 2,64 (tt, *J* = 6,8, 13,6, 1H), 2,59 – 2,46 (m, *J* = 5,3, 12,0, 23,8, 2H), 2,44 – 2,34 (m, 1H), 2,30 (d, *J* = 5,3, 1H), 2,28 – 2,23 (m, *J* = 8,0, 4H), 2,13 (dt, *J* = 6,3, 12,4, 1H), 1,94 – 1,78 (m, 1H), 1,78 – 1,64 (m, 1H), 1,48 – 1,25 (m, 1,5H), 1,20 (t, *J* = 6,1, 3H), 0,70 (dd, *J* = 1,9, 6,7, 3H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Ejemplo 92

3-metil-*N*-[(3a*R*,4*S*,6a*S*)-2-(2-metilbencil)octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida

El compuesto del título se preparó utilizando 2-metilbenzaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,57 – 8,51 (m, 1H), 7,63 (dd, *J* = 3,5, 7,1, 2H), 7,43 – 7,36 (m, 1H), 7,36 – 7,30 (m, 3H), 7,25 (dd, *J* = 6,9, 9,6, 2H), 7,20 – 7,13 (m, *J* = 10,0, 2H), 4,31 (dd, *J* = 5,5, 11,3, 1H), 3,57 (d, *J* = 13,1, 0,5H), 3,48 (d, *J* = 13,0, 0,5H), 3,39 (d, *J* = 13,0, 0,5H), 3,29 (d, *J* = 13,0, 0,5H), 3,21 (d, *J* = 10,3, 1H), 2,92 (dd, *J* = 2,8, 9,0, 0,5H), 2,68 – 2,60 (m, 1H), 2,60 – 2,53 (m, 1H), 2,51 – 2,45 (m, 1H), 2,35 (s, 1,5H), 2,30 (s, 1,5H), 2,28 – 2,17 (m, 2H), 2,15 – 2,06 (m, 1H), 1,84 (ddd, *J* = 6,8, 12,4, 20,0, 1H), 1,76 – 1,62 (m, 1H), 1,42 (dt, *J* = 7,2, 19,2, 0,5H), 1,33 (dt, *J* = 7,0, 12,5, 0,5H), 1,29 – 1,22 (m, 0,5H), 1,20 (d, *J* = 6,5, 3H), 0,70 (d, *J* = 6,7, 3H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Ejemplo 93

***N*-[(3a*R*,4*S*,6a*S*)-2-(2,6-dimetilbencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida**

El compuesto del título se preparó utilizando 2,6-dimetilbenzaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,54 – 8,50 (m, *J* = 6,7, 1H), 7,65 – 7,60 (m, 2H), 7,32 (t, *J* = 7,1, 2H), 7,28 – 7,23 (m, 1H), 7,11 (dd, *J* = 6,2, 14,3, 1H), 7,04 (t, *J* = 8,3, 2H), 4,27 – 4,19 (m, 1H), 3,57 (d, *J* = 12,5, 0,5H), 3,44 (dd, *J* = 12,5, 15,5, 1H), 3,34 (d, *J* = 12,5, 0,5H), 3,20 (d, *J* = 10,4, 1H), 2,92 (d, *J* = 5,9, 0,5H), 2,68 – 2,58 (m, *J* = 10,2, 18,3, 1H), 2,55 – 2,51 (m, *J* = 4,5, 1H), 2,48 – 2,42 (m, 0,5H), 2,39 (s, 3H), 2,34 (s, 3H), 2,32 – 2,18 (m, 3H), 2,07 (td, *J* = 6,6, 12,6, 0,5H), 1,87 – 1,73 (m, 1H), 1,72 – 1,62 (m, 1H), 1,33 (dd, *J* = 19,1, 78,6, 2,5H), 1,19 (dd, *J* = 4,9, 6,3, 3H), 0,69 (d, *J* = 6,6, 3H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Ejemplo 94

N-[(3aR,4S,6aS)-2-(2-metoxibencil)octahidrociclopenta[c]pirrol-4–il]-3-metil-2-fenilbutanamida

El compuesto del título se preparó utilizando 2-metoxibenzaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,50 (t, *J* = 7,3, 1H), 7,62 (d, *J* = 7,3, 2H), 7,55 (d, *J* = 7,8, 1H), 7,32 (dq, *J* = 3,8, 11,6, 2H), 7,25 (dd, *J* = 3,6, 7,5, 2H), 7,04 (dt, *J* = 7,4, 11,4, 1H), 6,89 (t, *J* = 8,3, 1H), 4,43 – 4,31 (m, 1H), 3,80 – 3,57 (m, 5H), 3,21 (d, *J* = 10,4, 1H), 2,99 (d, *J* = 6,2, 0,5H), 2,61 (ddd, *J* = 4,5, 12,6, 15,9, 2,5H), 2,52 – 2,45 (m, 0,5H), 2,45 – 2,31 (m, 3,5H), 2,19 – 2,09 (m, 0,5H), 2,00 – 1,80 (m, 1H), 1,72 (ddd, *J* = 6,5, 12,3, 19,3, 1H), 1,47 – 1,25 (m, 2,5H), 1,20 (dd, *J* = 3,0, 6,4, 3H), 0,70 (d, *J* = 6,7, 3H); MS (ESI+) *m/z* 407 $(M+H)^+$.

Ejemplo 95

N-[(3aR,4S,6aS)-2-(4-*tert*-butilbencil)octahidrociclopenta[c]pirrol-4–il]-3-metil-2-fenilbutanamida

El compuesto del título se preparó utilizando 4-*tert*-butilbenzaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,57 (dd, *J* = 6,7, 11,0, 1H), 7,63 (dd, *J* = 3,4, 7,1, 2H), 7,44 – 7,30 (m, 6H), 7,25 (t, *J* = 7,4, 1H), 4,36 (tt, *J* = 6,3, 12,6, 1H), 3,63 (d, *J* = 13,1, 0,5H), 3,55 (d, *J* = 13,0, 0,5H), 3,46 (d, *J* = 13,0, 0,5H), 3,35 (d, *J* = 13,0, 0,5H), 3,21 (d, *J* = 10,4, 1H), 2,90 (dd, *J* = 2,7, 8,7, 0,5H), 2,65 (dt, *J* = 6,6, 16,9, 1H), 2,58 – 2,44 (m, 2H), 2,44 – 2,34 (m, 1H), 2,32 (d, *J* = 8,6, 0,5H), 2,30 (d, *J* = 5,2, 1H), 2,24 (d, *J* = 5,0, 1H), 2,19 – 2,12 (m, 1H), 1,92 (dq, *J* = 6,1, 12,1, 0,5H), 1,82 (td, *J* = 7,3, 14,3, 0,5H), 1,70 (dq, *J* = 8,1, 14,7, 1H), 1,48 – 1,30 (m, *J* = 22,3, 41,1, 1H), 1,27 (s, *J* = 1,6, 9H), 1,20 (dd, *J* = 3,5, 6,4, 3H), 0,70 (d, *J* = 6,4, 3H); MS (ESI+) *m/z* 433 $(M+H)^+$.

Ejemplo 96

N-[(3aR,4S,6aS)-2-(4-metoxibencil)octahidrociclopenta[c]pirrol-4–il]-3-metil-2-fenilbutanamida

El compuesto del título se preparó utilizando 4-metoxibenzaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,57 (dd, *J* = 8,3, 10,9, 1H), 7,63 (dd, *J* = 2,8, 7,4, 2H), 7,39 – 7,28 (m, 4H), 7,28 – 7,23 (m, 1H), 6,98 (dd, *J* = 8,7, 10,2, 2H), 4,41 – 4,30 (m, 1H), 3,68 (s, 3H), 3,57 (d, *J* = 12,9, 0,5H), 3,48 (d, *J* = 12,9, 0,5H), 3,42 (d, *J* = 12,9, 0,5H), 3,31 (d, *J* = 12,8, 0,5H), 3,21 (d, *J* = 10,4, 1H), 2,90 (dd, *J* = 2,8, 8,9, 0,5H), 2,69 – 2,59 (m, 1H), 2,56 (dd, *J* = 2,9, 9,0, 1H), 2,53 – 2,46 (m, 1H), 2,45 – 2,33 (m, 1H), 2,32 – 2,26 (m, *J* = 10,0, 1H), 2,24 (t, *J* = 5,2, 1H), 2,15 (dt, *J* = 6,3, 12,3, 0,5H), 1,96 – 1,88 (m, 0,5H), 1,88 – 1,79 (m, 0,5H), 1,79 – 1,65 (m, 1H), 1,48 – 1,24 (m, *J* = 19,9, 48,8, 3H), 1,20 (dd, *J* = 4,3, 6,4, 3H), 0,70 (dd, *J* = 2,0, 6,7, 2H); MS (ESI+) *m/z* 407 $(M+H)^+$.

Ejemplo 97

N-[(3aR,4S,6aS)-2-(3-cianobencil)octahidrociclopenta[c]pirrol-4–il]-3-metil-2-fenilbutanamida

El compuesto del título se preparó utilizando 3-formilbenzonitrilo en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,60 (t, *J* = 7,1, 1H), 7,63 (d, *J* = 5,9, 2H), 7,56 – 7,50 (m, 2H), 7,39 – 7,30 (m, 3H), 7,29 – 7,23 (m, *J* = 8,9, 13,2, 2H), 4,32 (dd, *J* = 5,7, 11,2, 1H), 3,53 (d, *J* = 13,6, 0,5H), 3,44 (d, *J* = 13,5, 0,5H), 3,40 (d, *J* = 13,6, 0,5H), 3,28 (d, *J* = 13,6, 0,5H), 3,21 (dd, *J* = 1,3, 10,4, 1H), 2,90 (dd, *J* = 2,8, 9,1, 0,5H), 2,64 (qd, *J* = 6,6, 13,2, 1H), 2,59 – 2,47 (m, 1H), 2,46 – 2,37 (m, 1H), 2,37 – 2,30 (m, 0,5H), 2,26 – 2,20 (m, 1H), 2,19 – 2,13 (m, 1H), 2,10 (dt, *J* = 6,2, 12,3, 0,5H), 1,89 – 1,79 (m, 1H), 1,75 (dt, *J* = 6,1, 20,0, 0,5H), 1,66 (dt, *J* = 7,0, 19,3, 0,5H), 1,47 – 1,38 (m, 0,5H), 1,38 – 1,23 (m, 2H), 1,20 (dd, *J* = 3,6, 6,4, 3H), 0,70 (d, *J* = 6,7, 3H); MS (ESI+)

m/z 402 $(M+H)^+$.

Ejemplo 98

3-metil-2-fenil-*N*-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida

El compuesto del título se preparó utilizando 4-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,62 (t, *J* = 7,8, 1H), 7,64 (dd, *J* = 7,0, 11,8, 4H), 7,51 (d, *J* = 8,0, 1H), 7,46 (d, *J* = 7,9, 1H), 7,33 (dd, *J* = 7,4, 12,1, 2H), 7,29 – 7,24 (m, 1H), 4,40 – 4,30 (m, 1H), 3,58 (d, *J* = 13,7, 0,5H), 3,48 (t, *J* = 13,8, 1H), 3,35 (d, *J* = 13,7, 0,5H), 3,23 (dd, *J* = 1,4, 10,4, 1H), 2,92 (dd, *J* = 2,7, 9,0, 0,5H), 2,69 – 2,60 (m, 1H), 2,57 (dd, *J* = 2,7, 9,1, 1H), 2,54 – 2,47 (m, 0,5H), 2,47 – 2,39 (m, 1H), 2,39 – 2,32 (m, 0,5H), 2,31 – 2,20 (m, 2H), 2,19 – 2,11 (m, 1H), 1,95 – 1,82 (m, *J* = 6,4, 37,0, 1H), 1,77 (dt, *J* = 6,4, 13,8, 0,5H), 1,69 (dt, *J* = 6,9, 19,1, 0,5H), 1,50 – 1,25 (m, *J* = 34,6, 62,0, 1,5H), 1,21 (t, *J* = 6,4, 3H), 0,70 (d, *J* = 5,1, 3H); MS (ESI+) *m/z* 445 $(M+H)^+$.

Ejemplo 99

3-metil-2-fenil-*N*-{(3a*R*,4*S*,6a*S*)-2-[2-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida

El compuesto del título se preparó utilizando 2-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,61 (d, *J* = 6,0, 1H), 7,93 (d, *J* = 7,6, 0,5H), 7,85 (d, *J* = 7,8, 0,5H), 7,63 (t, *J* = 5,8, 3H), 7,53 (dd, *J* = 7,9, 16,0, 1H), 7,38 – 7,23 (m, 5H), 4,36 (dd, *J* = 5,7, 13,2, 1H), 3,76 (q, *J* = 14,5, 1H), 3,66 (q, *J* = 15,0, 1H), 3,23 (dd, *J* = 2,2, 10,5, 1H), 3,03 (dd, *J* = 2,2, 9,0, 0,5H), 2,69 – 2,60 (m, *J* = 5,6, 17,6, 1H), 2,59 – 2,47 (m, 1H), 2,47 – 2,40 (m, *J* = 10,2, 17,4, 1H), 2,39 – 2,12 (m, 3H), 1,96 – 1,82 (m, 1H), 1,78 (dt, *J* = 6,2, 20,1, 0,5H), 1,68 (dt, *J* = 7,2, 13,8, 0,5H), 1,48 – 1,24 (m, 1,5H), 1,20 (t, *J* = 6,7, 3H), 0,70 (dd, *J* = 1,7, 6,7, 3H); MS (ESI+) *m/z* 445 $(M+H)^+$.

Ejemplo 100

***N*-{(3a*R*,4*S*,6a*S*)-2-[4-fluoro-3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida**

El compuesto del título se preparó utilizando 4-fluoro-3-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,63 (t, *J* = 7,0, 1H), 7,69 (d, *J* = 6,3, 1H), 7,64 (d, *J* = 7,6, 2H), 7,55 – 7,49 (m, 1H), 7,33 (dd, *J* = 7,2, 13,6, 2H), 7,25 (dd, *J* = 7,6, 15,5, 2H), 4,33 (dd, *J* = 5,7, 11,4, 1H), 3,54 (d, *J* = 13,5, 0,5H), 3,44 (t, *J* = 14,0, 1H), 3,31 (d, *J* = 13,4, 0,5H), 3,22 (d, *J* = 10,4, 1H), 2,91 (dd, *J* = 2,6, 9,0, 0,5H), 2,69 – 2,60 (m, *J* = 7,5, 13,7, 1H), 2,55 (dd, *J* = 3,1, 9,1, 1H), 2,53 – 2,39 (m, 2H), 2,38 – 2,32 (m, *J* = 8,0, 0,5H), 2,29 – 2,21 (m, 1H), 2,19 (d, *J* = 4,0, 1H), 2,12 (dd, *J* = 6,1, 12,1, 0,5H), 1,91 – 1,81 (m, *J* = 10,9, 16,7, 1H), 1,77 (dt, *J* = 6,3, 19,8, 0,5H), 1,68 (td, *J* = 7,0, 14,0, 0,5H), 1,44 (dt, *J* = 7,6, 14,7, 0,5H), 1,40 – 1,25 (m, 1H), 1,20 (t, *J* = 5,7, 3H), 0,70 (d, *J* = 6,4, 3H); MS (ESI+) *m/z* 463 $(M+H)^+$.

Ejemplo 101

***N*-{(3a*R*,4*S*,6a*S*)-2-[3-fluoro-4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida**

El compuesto del título se preparó utilizando 3-fluoro-4-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,63 (t, *J* = 6,6, 1H), 7,64 (dd, *J* = 3,0, 7,5, 2H), 7,37 – 7,30 (m, 3H), 7,30 – 7,23 (m, 3H), 4,38 – 4,30 (m, 1H), 3,56 (d, *J* = 14,1, 0,5H), 3,46 (t, *J* = 13,4, 1H), 3,33 (d, *J* = 14,1, 0,5H), 3,23 (d, *J* = 10,4, 1H), 2,94 (dd, *J* = 2,5, 9,0, 0,5H), 2,65 (dt, *J* = 6,2, 10,9, 1H), 2,58 (dd, *J* = 2,8, 9,2, 1H), 2,54 – 2,48 (m, 0,5H), 2,47 – 2,39 (m, 1H), 2,39 – 2,32 (m, 0,5H), 2,28 (dd, *J* = 2,7, 8,9, 0,5H), 2,26 – 2,20 (m, 1H), 2,19 – 2,09 (m, 1H), 1,87 (ddd, *J* = 6,4, 12,3, 18,7, 1H), 1,78

(dt, *J* = 6,2, 19,6, 0,5H), 1,68 (dt, *J* = 7,5, 14,6, 0,5H), 1,49 – 1,24 (m, 2H), 1,21 (dd, *J* = 4,3, 6,2, 3H), 0,70 (d, *J* = 6,7, 3H); MS (ESI+) *m/z* 463 $(M+H)^+$.

Ejemplo 102

3-metil-2-fenil-*N*-[(3a*R*,4*S*,6a*S*)-2-(tien-2–ilmetil)octahidrociclopenta[*c*]pirrol-4–il]butanamida

El compuesto del título se preparó utilizando tiofen-2-carbaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,62 – 8,53 (m, 1H), 7,63 (dd, *J* = 4,4, 7,0, 2H), 7,33 (t, *J* = 7,6, 3H), 7,28 – 7,23 (m, 1H), 6,98 (dd, *J* = 4,8, 9,3, 1H), 6,94 (d, *J* = 3,0, 1H), 4,33 (dd, *J* = 7,7, 13,5, 1H), 3,77 (d, *J* = 13,7, 0,5H), 3,68 (dd, *J* = 4,6, 13,7, 1H), 3,57 (d, *J* = 13,7, 0,5H), 3,21 (d, *J* = 10,4, 1H), 2,94 (d, *J* = 8,5, 0,5H), 2,69 – 2,44 (m, 3H), 2,44 – 2,28 (m, 3H), 2,28 – 2,22 (m, 0,5H), 2,18 – 2,09 (m, 0,5H), 1,90 (td, *J* = 6,1, 12,1, 0,5H), 1,86 – 1,79 (m, 0,5H), 1,78 – 1,63 (m, 1H), 1,47 – 1,35 (m, 1H), 1,32 (dd, *J* = 7,1, 13,2, 0,5H), 1,20 (dd, *J* = 2,0, 6,4, 3H), 0,70 (d, *J* = 6,7, 3H); MS (ESI+) *m/z* 383 $(M+H)^+$.

Ejemplo 103

3-metil-2-fenil-*N*-[(3a*R*,4*S*,6a*S*)-2-(piridin-4–ilmetil)octahidrociclopenta[*c*]pirrol-4–il]butanamida

El compuesto del título se preparó utilizando isonicotinaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,70 (d, *J* = 5,9, 2H), 8,62 (s, 1H), 7,64 (dd, *J* = 3,0, 7,5, 2H), 7,36 – 7,30 (m, 2H), 7,25 (dd, *J* = 7,0, 12,4, 3H), 4,39 – 4,30 (m, 1H), 3,51 (d, *J* = 14,2, 0,5H), 3,41 (dd, *J* = 11,5, 14,2, 1H), 3,28 (d, *J* = 14,3, 0,5H), 3,23 (dd, *J* = 1,8, 10,5, 1H), 2,94 (dd, *J* = 2,6, 9,2, 0,5H), 2,69 – 2,60 (m, 1H), 2,57 (dd, *J* = 2,9, 9,2, 1H), 2,52 – 2,46 (m, 0,5H), 2,42 (dd, *J* = 7,2, 8,8, 1H), 2,38 – 2,31 (m, 0,5H), 2,28 (dd, *J* = 2,7, 9,0, 0,5H), 2,24 – 2,18 (m, 1H), 2,17 – 2,11 (m, 1H), 1,95 – 1,82 (m, 1H), 1,77 (dt, *J* = 5,8, 12,3, 0,5H), 1,73 – 1,64 (m, 0,5H), 1,49 – 1,25 (m, 2H), 1,23 – 1,17 (m, 3H),

0,70 (d, *J* = 6,5, 3H); MS (ESI+) *m/z* 378 $(M+H)^+$.

Ejemplo 104

3-metil-2-fenil-*N*-[(3a*R*,4*S*,6a*S*)-2-(2-feniletil)octahidrociclopenta[*c*]pirrol-4–il]butanamida

El compuesto del título se preparó utilizando 2-fenilacetaldehido en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,57 (dd, *J* = 5,2, 12,0, 1H), 7,65 (t, *J* = 7,1, 2H), 7,38 – 7,23 (m, 8H), 4,40 – 4,29 (m, 1H), 3,23 (d, *J* = 10,5, 1H), 3,00 (dd, *J* = 2,6, 9,0, 0,5H), 2,80 (t, *J* = 7,8, 1H), 2,75 – 2,70 (m, 1H), 2,70 – 2,61 (m, 1H), 2,61 – 2,52 (m, 1H), 2,52 – 2,46 (m, 1H), 2,43 (dd, *J* = 7,6, 8,7, 0,5H), 2,38 (dd, *J* = 2,7, 8,8, 1H), 2,34 (dd, *J* = 2,7, 8,5, 1H), 2,26 (d, *J* = 8,3, 0,5H), 2,24 – 2,18 (m, 1H), 2,12 (td, *J* = 6,4, 12,4, 0,5H), 1,91 – 1,82 (m, 1H), 1,76 (dt, *J* = 6,2, 18,7, 0,5H), 1,70 – 1,61 (m, 0,5H), 1,46 – 1,26 (m, 2H), 1,23 (dd, *J* = 6,5, 13,5, 3H), 0,97 – 0,83 (m, 1H), 0,71 (dd, *J* = 2,7, 6,7, 3H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Ejemplo 105

3-metil-2-fenil-*N*-[(3a*R*,4*S*,6a*S*)-2-(3-fenilpropil)octahidrociclopenta[*c*]pirrol-4–il]butanamida

El compuesto del título se preparó utilizando 3-fenilpropanal en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,60 (t, *J* = 6,8, 1H), 7,69 – 7,63 (m, 2H), 7,39 – 7,22 (m, 8H), 4,41 – 4,31 (m, 1H), 3,25 (d, *J* = 10,4, 1H), 2,95 (dd, *J* = 2,5, 8,9, 0,5H), 2,68 (td, *J* = 2,7, 7,2, 2H), 2,65 – 2,60 (m, 1H), 2,58 (dd, *J* = 2,8, 9,2, 0,5H), 2,56 – 2,52 (m, 0,5H), 2,51 – 2,46 (m, 0,5H), 2,44 – 2,38 (m, 0,5H), 2,37 – 2,26 (m, 3H), 2,23 (t, *J* = 7,2, 1H), 2,18 (d, *J* = 7,3, 0,5H), 2,13 (t, *J* = 8,8, 1,5H), 1,88 (dd, *J* = 6,1, 12,1, 1H), 1,79 (dd, *J* = 7,2, 14,5, 1,5H), 1,74 – 1,64 (m, 1,5H), 1,48 – 1,37 (m, 1H), 1,37 – 1,28 (m, 0,5H), 1,23 (dd, *J* = 6,5, 12,2, 3H), 0,71 (dd, *J* = 3,0, 6,7, 3H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Ejemplo 106

***N*-{(3a*R*,4*S*,6a*S*)-2-[3-(4-*tert*-butilfenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida**

El compuesto del título se preparó utilizando 3-(4-*tert*-butilfenil)propanal en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,57 (t, *J* = 8,5, 1H), 7,65 (t, *J* = 6,6, 2H), 7,40 (dd, *J* = 5,4, 8,0, 2H), 7,34 (t, *J* = 7,4, 2H), 7,30 – 7,23 (m, 3H), 4,37 (dt, *J* = 6,1, 11,1, 1H), 3,23 (d, *J* = 10,4, 1H), 2,96 (dd, *J* = 1,9, 8,9, 0,5H), 2,67 (ddd, *J* = 6,7, 11,6, 23,3, 2H), 2,59 (dd, *J* = 2,6, 9,3, 0,5H), 2,57 – 2,51 (m, 0,5H), 2,50 – 2,44 (m, 0,5H), 2,43 – 2,38 (m, 0,5H), 2,35 (t, *J* = 8,1, 2H), 2,29 (dd, *J* = 2,6, 8,8, 0,5H), 2,25 (t, *J* = 7,1, 1H), 2,19 (d, *J* = 7,2, 0,5H), 2,17 – 2,11 (m, 1H), 1,92 – 1,85 (m, 1H), 1,81 (dt, *J* = 7,7, 15,5, 1H), 1,74 (dt, *J* = 7,9, 15,9, 1H), 1,69 – 1,63 (m, 0,5H), 1,46 – 1,31 (m, 2H), 1,28 (s, 9H), 1,23 (dd, *J* = 6,5, 13,4, 3H), 0,94 – 0,84 (m, 2H), 0,71 (dd, *J* = 3,2, 6,6, 3H); MS (ESI+) *m/z* 461 $(M+H)^+$.

Ejemplo 107

***N*-{(3a*R*,4*S*,6a*S*)-2-[6,6-bis(4-fluorofenil)hexil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida**

El compuesto del título se preparó utilizando 6,6-bis(4-fluorofenil)hexanal en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,59 (t, *J* = 6,4, 1H), 7,65 (dd, *J* = 4,9, 6,9, 2H), 7,33 (dd, *J* = 6,8, 11,6, 6H), 7,25 (dd, *J* = 6,5, 8,2, 1H), 7,14 (dd, *J* = 1,4, 8,7, 4H), 4,40 – 4,30 (m, 1H), 3,97 (q, *J* = 7,7, 1H), 3,23 (d, *J* = 10,4, 1H), 2,96 (d, *J* = 6,8, 0,5H), 2,71 – 2,61 (m, 1H), 2,59 (dd, *J* = 2,5, 9,0, 0,5H), 2,56 – 2,46 (m, 1H), 2,40 (dd, *J* = 8,4, 16,1, 1H), 2,37 – 2,33 (m, 1H), 2,30 (dd, *J* = 4,4, 8,1, 1H), 2,20 (t, *J* = 6,2, 2H), 2,17 – 2,10 (m, 1H), 2,01 (ddd, *J* = 7,8, 11,6, 15,5, 2H), 1,88 (dq, *J* = 6,0, 11,8, 1H), 1,78 (dt, *J* = 6,3, 20,2, 0,5H), 1,67 (td, *J* = 7,1, 14,5, 0,5H), 1,49 – 1,30 (m, 6H), 1,29 – 1,25 (m, 2H), 1,22 (dd, *J* = 6,5, 11,0, 3H), 0,71 (dd, *J* = 3,2, 6,7, 3H); MS (ESI+) *m/z* 559 $(M+H)^+$.

Ejemplo 108

3-metil-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(2-metilfenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-2-fenilbutanamida

El compuesto del título se preparó utilizando 3-*o*-tolilpropanal en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,57 (dd, *J* = 7,2, 14,2, 1H), 7,68 – 7,62 (m, 2H), 7,34 (t, *J* = 7,5, 2H), 7,29 – 7,23 (m, 2H), 7,23 – 7,22 (m, 1H), 7,17 (dd, *J* = 2,6, 3,9, 2H), 4,42 – 4,31 (m, 1H), 3,23 (d, *J* = 10,4, 1H), 2,98 (dd, *J* = 2,3, 8,8, 0,5H), 2,69 – 2,64 (m, 2H), 2,64 – 2,59 (m, 2H), 2,58 – 2,51 (m, 0,5H), 2,51 – 2,45 (m, 0,5H), 2,45 – 2,39 (m, 0,5H), 2,39 – 2,34 (m, 2H), 2,32 (dd, *J* = 2,7, 8,9, 1H), 2,28 (s, 1,5H), 2,25 (s, 1,5H), 2,19 (d, *J* = 8,1, 0,5H), 2,17 – 2,11 (m, 1,5H), 1,93 – 1,85 (m, 1H), 1,84 – 1,77 (m, 0,5H), 1,73 (dd, *J* = 7,6, 15,1, 1H), 1,66 (dt, *J* = 7,4, 9,4, 1,5H), 1,43 (dt, *J* = 7,5, 13,8, 1H), 1,38 – 1,30 (m, 1H), 1,23 (dd, *J* = 6,5, 12,1, 3H), 0,71 (dd, *J* = 2,8, 6,7, 3H); MS (ESI+) *m/z* 419 $(M+H)^+$.

Ejemplo 109

***N*-{(3a*R*,4*S*,6a*S*)-2-[3-(3-clorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida**

El compuesto del título se preparó utilizando 3-(3-clorofenil)propanal en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,60 (d, *J* = 4,6, 1H), 7,66 (dd, *J* = 4,3, 7,0, 2H), 7,35 (dd, *J* = 10,9, 18,3, 3H), 7,29 – 7,23 (m, 3H), 7,16 (d, *J* = 6,8, 0,5H), 7,12 (d, *J* = 7,0, 0,5H), 4,41 – 4,31 (m, 1H), 3,24 (d, *J* = 10,4, 1H), 2,98 (d, *J* = 8,9, 0,5H), 2,72 – 2,62 (m, 2H), 2,62 – 2,55 (m, 2H), 2,55 – 2,51 (m, 0,5H), 2,50 – 2,45 (m, 0,5H), 2,43 – 2,37 (m, 0,5H), 2,31 (ddd, *J* = 2,6, 7,2, 12,1, 3H), 2,23 – 2,16 (m, 1H), 2,15 – 2,09 (m, 1H), 1,91 – 1,84 (m, 1H), 1,80 (td, *J* = 6,3, 12,5, 1H), 1,72 (dd, *J* = 7,5, 14,5, 1H), 1,69 – 1,61 (m, 1H), 1,46 – 1,37 (m, 1H), 1,37 – 1,28 (m, 1H), 1,23 (dd, *J* = 6,5, 13,3, 3H), 0,71 (dd, *J* = 3,9, 6,7, 3H); MS (ESI+) *m/z* 439 $(M+H)^+$.

000502

Ejemplo 110

3-metil-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(3-metilfenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-2-fenilbutanamida

El compuesto del título se preparó utilizando 3-*m*-tolilpropanal en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,57 (dd, *J* = 7,1, 13,5, 1H), 7,65 (dd, *J* = 4,8, 7,0, 2H), 7,34 (t, *J* = 7,5, 2H), 7,29 – 7,22 (m, 2H), 7,12 (d, *J* = 5,9, 1H), 7,09 (d, *J* = 7,1, 1H), 7,06 – 7,02 (m, 1H), 4,42 – 4,31 (m, 1H), 3,24 (d, *J* = 10,4, 1H), 2,97 (d, *J* = 6,8, 0,5H), 2,71 – 2,58 (m, 4H), 2,56 – 2,44 (m, 1H), 2,43 – 2,38 (m, 0,5H), 2,35 (t, *J* = 6,6, 3H), 2,29 (s, 1,5H), 2,27 (s, 1,5H), 2,27 – 2,23 (m, 1H), 2,17 – 2,11 (m, 1,5H), 1,89 (dt, *J* = 6,1, 11,8, 1H), 1,79 (dd, *J* = 7,4, 14,7, 1,5H), 1,72 (dt, *J* = 7,6, 15,1, 1H), 1,66 (dd, *J* = 5,9, 13,1, 0,5H), 1,42 (dt, *J* = 7,5, 12,0, 1H), 1,37 – 1,30 (m, 0,5H), 1,23 (dd, *J* = 6,5, 11,7, 3H), 0,71 (dd, *J* = 3,0, 6,6, 3H); MS (ESI+) *m/z* 419 $(M+H)^+$.

Ejemplo 111

3-metil-2-fenil-*N*-((3a*R*,4*S*,6a*S*)-2-{3-[3-(trifluorometil)fenil]propil}octahidrociclopenta[*c*]pirrol-4–il)butanamida

El compuesto del título se preparó utilizando 3-(3-(trifluorometil)fenil)propanal en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,61 (d, *J* = 6,4, 1H), 7,69 – 7,62 (m, 3H), 7,53 (d, *J* = 6,5, 1H), 7,46 (t, *J* = 7,8, 1H), 7,42 (d, *J* = 5,5, 1H), 7,34 (t, *J* = 7,5, 2H), 7,26 (t, *J* = 7,3, 1H), 4,37 (tt, *J* = 6,4, 12,7, 1H), 3,24 (d, *J* = 10,5, 1H), 3,00 (dd, *J* = 1,9, 8,9, 0,5H), 2,78 – 2,63 (m, 3H), 2,61 (dd, *J* = 2,3, 9,1, 0,5H), 2,57 – 2,45 (m, 1H), 2,40 (dd, *J* = 7,1, 14,3, 0,5H), 2,37 – 2,26 (m, 3H), 2,24 – 2,07 (m, 3H), 1,93 – 1,83 (m, 1H), 1,83 – 1,71 (m, 2H), 1,71 – 1,63 (m, 1H), 1,48 – 1,37 (m, 1H), 1,37 – 1,30 (m, 0,5H), 1,23 (dd, *J* = 6,5, 13,6, 3H), 0,72 (dd, *J* = 4,4, 6,6, 3H); MS (ESI+) *m/z* 473 $(M+H)^+$.

000593
9707.01

Ejemplo 112

N-{(3aR,4S,6aS)-2-[3-(3-fluorofenil)propil]octahidrociclopenta[c]pirrol-4–il}-3-metil-2-fenilbutanamida

El compuesto del título se preparó utilizando 3-(3-fluorofenil)propanal en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,52 (s, 1H), 7,69 – 7,61 (m, 2H), 7,33 (t, *J* = 7,5, 2H), 7,27 (ddd, *J* = 3,5, 7,6, 10,6, 2H), 7,14 – 6,95 (m, 3H), 4,43 – 4,29 (m, 1H), 3,23 (d, *J* = 10,4, 1H), 2,97 (dd, *J* = 2,2, 8,8, 0,5H), 2,72 – 2,58 (m, 3H), 2,57 – 2,44 (m, 1H), 2,44 – 2,38 (m, 0,5H), 2,36 – 2,26 (m, 3H), 2,25 – 2,16 (m, 1H), 2,16 – 2,09 (m, 1H), 1,93 – 1,83 (m, 1H), 1,77 (dt, *J* = 7,2, 14,6, 1,5H), 1,72 – 1,63 (m, 1,5H), 1,47 – 1,27 (m, 2H), 1,22 (dd, *J* = 6,5, 10,4, 3H), 0,94 – 0,83 (m, 1H), 0,71 (dd, *J* = 2,7, 6,7, 3H); MS (ESI+) *m/z* 423 $(M+H)^+$.

Ejemplo 113

3-metil-2-fenil-N-[(3aR,4S,6aS)-2-(4-fenilbutil)octahidrociclopenta[c]pirrol-4–il]butanamida

El compuesto del título se preparó utilizando 4-fenilbutanal en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,58 (dd, *J* = 9,0, 16,5, 1H), 7,66 (t, *J* = 6,4, 2H), 7,34 (t, *J* = 5,6, 4H), 7,29 – 7,22 (m, 4H), 4,39 – 4,29 (m, 1H), 3,24 (d, *J* = 10,4, 1H), 2,91 (dd, *J* = 2,4, 9,0, 0,5H), 2,66 (ddd, *J* = 6,5, 10,6, 13,1, 1H), 2,57 (ddd, *J* = 5,3, 12,3, 17,7, 3H), 2,51 – 2,45 (m, 1H), 2,43 – 2,29 (m, 3H), 2,26 (dd, *J* = 3,0, 8,8, 0,5H), 2,24 – 2,08 (m, 2H), 1,91 – 1,83 (m, 1H), 1,81 – 1,72 (m, 1H), 1,71 – 1,58 (m, 2H), 1,49 (dt, *J* = 7,8, 15,9, 1H), 1,41 (dt, *J* = 6,9, 17,2, 2H), 1,31 (ddd, *J* = 6,7, 13,2, 20,5, 1H), 1,23 (dd, *J* = 6,5, 13,0, 3H), 0,71 (dd, *J* = 2,6, 6,6, 3H); MS (ESI+) *m/z* 419 $(M+H)^+$.

Ejemplo 114

N-{(3aR,4S,6aS)-2-[3-(3-cloro-5-fluorofenil)propil]octahidrociclopenta[c]pirrol-4–il}-3-metil-2-fenilbutanamida

El compuesto del título se preparó utilizando 3-(3-cloro-5-fluorofenil)propanal en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,61 (d, *J* = 7,4, 1H), 7,66 (dd, *J* = 3,2, 7,5, 2H), 7,35 (dd, *J* = 7,5, 15,0, 2H), 7,25 (dd, *J* = 6,1, 13,7, 2H), 7,12 (d, *J* = 7,5, 1H), 7,06 – 6,95 (m, 1H), 4,43 – 4,31 (m, 1H), 3,24 (d, *J* = 10,4, 1H), 3,01 (dd, *J* = 1,3, 8,7, 0,5H), 2,73 – 2,64 (m, 1H), 2,62 (dd, *J* = 6,0, 9,0, 1H), 2,59 – 2,54 (m, 1H), 2,53 – 2,45 (m, 1H), 2,43 – 2,38 (m, 0,5H), 2,37 – 2,25 (m, 3H), 2,24 – 2,06 (m, 3H), 1,93 – 1,76 (m, 2H), 1,75 – 1,58 (m, 2H), 1,47 – 1,28 (m, 2H), 1,23 (dd, *J* = 6,5, 14,4, 3H), 0,72 (dd, *J* = 5,0, 6,2, 3H); MS (ESI+) *m/z* 457 $(M+H)^+$.

Ejemplo 115

3-metil-2-fenil-N-((3aR,4S,6aS)-2-{3-[4-(trifluorometil)fenil]propil}octahidrociclopenta[c]pirrol-4–il)butanamida

El compuesto del título se preparó utilizando 3-(4-(trifluorometil)fenil)propanal en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,69 – 7,62 (m, 4H), 7,39 (d, *J* = 8,0, 1H), 7,37 – 7,32 (m, 3H), 7,26 (t, *J* = 7,3, 1H), 4,41 – 4,33 (m, 1H), 3,25 (d, *J* = 10,5, 1H), 3,00 (dd, *J* = 2,2, 9,0, 0,5H), 2,76 – 2,59 (m, 3H), 2,56 – 2,46 (m, 1H), 2,44 – 2,39 (m, 0,5H), 2,37 (dd, *J* = 2,1, 8,9, 0,5H), 2,31 (dt, *J* = 5,8, 14,1, 2H), 2,23 – 2,07 (m, 3H), 1,94 – 1,71 (m, 2,5H), 1,67 (ddd, *J* = 5,6, 7,9, 11,8, 1H), 1,47 – 1,28 (m, 2H), 1,23 (dd, *J* = 6,5, 13,1, 3H), 0,89 (dt, *J* = 7,2, 24,8, 1H), 0,72 (dd, *J* = 3,7, 6,7, 3H); MS (ESI+) *m/z* 473 $(M+H)^+$.

Ejemplo 116

***N*-[(3a*R*,4*S*,6a*S*)-2-(3,3-difenilpropil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida**

El compuesto del título se preparó utilizando 3,3-difenilpropanal en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,59 (dd, *J* = 2,9, 7,0, 1H), 7,65 (d, *J* = 8,1, 2H), 7,46 (d, *J* = 7,2, 1H), 7,44 – 7,37 (m, 4H), 7,33 (tt, *J* = 3,7, 7,7, 6H), 7,28 – 7,24 (m, 1H), 7,23 – 7,18 (m, 1H), 4,44 – 4,34 (m, 1H), 4,28 (d, *J* = 7,2, 1H), 4,20 (dd, *J* = 5,4, 9,1, 1H), 3,24 (d, *J* = 10,4, 1H), 2,93 (dd, *J* = 2,4, 9,0, 0,5H), 2,71 – 2,61 (m, 1H), 2,56 (dd, *J* = 2,7, 9,2, 0,5H), 2,54 – 2,50 (m, 0,5H), 2,50 – 2,43 (m, 0,5H), 2,43 – 2,36 (m, 0,5H), 2,35 – 2,28 (m, 3H), 2,24 (tt, *J* = 5,1, 10,0, 2H), 2,18 – 2,07 (m, 2H), 1,94 – 1,83 (m, 1H), 1,82 – 1,74 (m, 0,5H), 1,68 (td, *J* = 7,0, 14,3, 0,5H); 1,47 – 1,37 (m, 1H), 1,37 – 1,29 (m, 0,5H), 1,22 (dd, *J* = 4,6, 6,4, 3H), 0,71 (dd, *J* = 1,7, 6,7, 3H); MS (ESI+) *m/z* 481 $(M+H)^+$.

Ejemplo 117

***N*-{(3a*R*,4*S*,6a*S*)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida**

El compuesto del título se preparó utilizando 3,3-bis(4-fluorofenil)propanal en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,62 (d, *J* = 5,3, 1H), 7,65 (d, *J* = 7,3, 2H), 7,42 (dd, *J* = 5,6, 8,6, 1H), 7,39 – 7,29 (m, 5H), 7,26 (td, *J* = 5,3, 7,2; 1H), 7,19 – 7,09 (m, 4H), 4,47 – 4,37 (m, 1H), 4,29 (t, *J* = 7,7, 0,5H), 4,21 (t, *J* = 7,6, 0,5H), 3,24 (d, *J* = 10,4, 1H), 3,02 (dd, *J* = 1,2, 8,9, 0,5H), 2,71 – 2,60 (m, 1H), 2,57 – 2,46 (m, 1H), 2,44 – 2,30 (m, 3H), 2,27 – 2,20 (m, 2H), 2,19 – 2,09 (m, 4H), 1,90 (dq, *J* = 6,0, 17,7, 1H), 1,81 (dq, *J* = 6,2, 18,7, 0,5H), 1,67 (ddd, *J* = 7,6, 12,3, 14,8, 0,5H), 1,48 – 1,38 (m, 1H), 1,38 – 1,30 (m, 0,5H), 1,22 (dd, *J* = 2,5, 6,5, 3H), 0,71 (dd, *J* = 1,4, 6,7, 3H); MS (ESI+) *m/z* 517 $(M+H)^+$.

Ejemplo 118

***N*-{(3a*R*,4*S*,6a*S*)-2-[4,4-bis(4-fluorofenil)butil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida**

El compuesto del título se preparó utilizando 4,4-bis(4-fluorofenil)butanal en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,61 (d, *J* = 7,0, 1H), 7,66 (dd, *J* = 5,3, 7,0, 2H), 7,44 – 7,31 (m, 6H), 7,26 (t, *J* = 7,4, 1H), 7,19 – 7,08 (m, 4H), 4,41 – 4,30 (m, 1H), 4,03 – 3,92 (m, 1H), 3,24 (d, *J* = 10,4, 1H), 2,95 (dd, *J* = 2,3, 8,9, 0,5H), 2,67 (ddd, *J* = 6,6, 13,3, 17,1, 1H), 2,56 (dd, *J* = 2,8, 9,1, 0,5H), 2,54 – 2,43 (m, 1H), 2,42 – 2,30 (m, 2H), 2,29 – 2,20 (m, 2,5H), 2,19 – 2,02 (m, 4H), 1,90 – 1,72 (m, 1,5H), 1,65 (dt, *J* = 7,1, 19,2, 0,5H), 1,52 – 1,34 (m, 3H), 1,34 – 1,26 (m, 0,5H), 1,23 (dd, *J* = 6,5, 15,3, 3H), 0,71 (dd, *J* = 5,0, 6,5, 3H); MS (ESI+) *m/z* 531 $(M+H)^+$.

Ejemplo 119

***N*-{(3a*R*,4*S*,6a*S*)-2-[5,5-bis(4-fluorofenil)pentil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida**

El compuesto del título se preparó utilizando 5,5-bis(4-fluorofenil)pentanal en lugar de 3-(trifluorometil)benzaldehido y 3-metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,61 (s, 1H), 7,66 (dd, *J* = 4,3, 7,3, 2H), 7,37 – 7,30 (m, 5H), 7,25 (dd, *J* = 5,6, 13,1, 2H), 7,19 – 7,11 (m, 4H), 4,38 – 4,29 (m, 1H), 3,96 (dd, *J* = 7,9, 18,0, 1H), 3,25 (d, *J* = 10,5, 1H), 2,96 (d, *J* = 10,4, 0,5H), 2,72 – 2,62 (m, 1H), 2,62 – 2,57 (m, ,50H), 2,56 – 2,51 (m, 0,5H), 2,50 – 2,45 (m, 0,5H), 2,43 – 2,36 (m, 1H), 2,36 – 2,31 (m, 1H), 2,30 – 2,26 (m, 1H), 2,23 – 2,06 (m, 3H), 2,07 – 1,96 (m, 2H), 1,86 (dt, *J* = 6,0, 12,2, 1H), 1,81 – 1,72 (m, 1H), 1,66 (dt, *J* = 7,0, 19,1, 1H), 1,56 – 1,49 (m, 1H), 1,48 – 1,40 (m, 1H), 1,38 – 1,26 (m, 3H), 1,23 (dd, *J* = 6,5, 9,7, 3H), 0,71 (dd, *J* = 2,5, 6,7, 3H); MS (ESI+) *m/z* 545 $(M+H)^+$.

Ejemplo 120

***N*-[(3a*S*,4*S*,6aR)-2-benzhidriloctahidrociclopenta[c]pirrol-4–il]-2,2-diciclohexilacetamida**

Se combinó yoduro de potasio (12,48 mg, 0,075 mmol) y carbonato de sodio (80 mg, 0,752 mmol) con metiletilcetona (5ml) y luego se agregó 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida (200 mg, 0,601 mmol) del Ejemplo 53 seguido por la adición de (bromometilen)dibenceno (124 mg, 0,501 mmol). La reacción se calentó durante la noche a 90 °C. La mezcla de la reacción se concentró con una corriente de nitrógeno y luego se purificó mediante cromatografía sobre gel de sílice eluyendo con metanol al 2-10% (amoníaco 2 N)/diclorometano para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,74 (dd, *J* = 6,7, 15,4, 1H), 7,61 (t, *J* = 6,7, 3H), 7,35 (t, *J* = 7,6, 4H), 7,28 – 7,23 (m, 3H), 4,42 (dt, *J* = 7,4, 14,4, 1H), 4,16 (s, 1H), 2,96 (qd, *J* = 4,2, 8,0, 1H), 2,63 (dd, *J* = 4,1, 9,8, 1H), 2,57 – 2,48 (m, 1H), 2,42 (dt, *J* = 9,4, 14,6, 2H), 2,33 (dd, *J* = 3,7, 9,3, 1H), 2,09 – 1,90 (m, 3H), 1,90 – 1,80 (m, 3H), 1,79 – 1,70 (m, 4H), 1,69 – 1,55 (m, 6H), 1,46 (d, *J* = 14,7, 1H), 1,39 (s, 1H), 1,33 – 1,00 (m, 8H), 1,00 – 0,89 (m, 1H); MS (ESI+) *m/z* 499 $(M+H)^+$.

Ejemplo 121

***N*-[(3aS,4*R*,6a*R*)-2-benzhidriloctahidrociclopenta[c]pirrol-4–il]-2,2-diciclohexilacetamida**

El compuesto del título se preparó utilizando 2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida del Ejemplo 74 en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito por ejemplo 120: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,11 (d, *J* = 7,2, 1H), 7,64 (d, *J* = 7,1, 2H), 7,32 (t, *J* = 7,6, 4H), 7,20 – 7,15 (m, 4H), 4,55 – 4,48 (m, 1H), 4,21 (s, 1H), 2,81 (dd, *J* = 2,9, 9,4, 1H), 2,63 – 2,57 (m, 1H), 2,57 – 2,51 (m, 1H), 2,41 (dd, *J* = 7,0, 9,2, 1H), 2,36 – 2,24 (m, 3H), 2,01 (t, *J* = 7,4, 1H), 1,99 – 1,90 (m, 3H), 1,86 (ddd, *J* = 3,3, 8,1, 15,4, 2H), 1,82 – 1,76 (m, 2H), 1,70 (ddd, *J* = 8,9, 13,9, 15,3, 5H), 1,63 – 1,55 (m, 2H), 1,51 – 1,37 (m, 3H), 1,28 – 1,01 (m, 8H); MS (ESI+) *m/z* 499 $(M+H)^+$.

Ejemplo 122

3-metil-2-fenil-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida**

Paso A: Se combinó ordenadamente (3-(trifluorometil)fenil)metanamina (25 g, 143 mmol), (clorometil)trimetilsilano (19,92 ml, 143 mmol), y trietilamina (23,87 ml, 171 mmol) y la mezcla resultante se sometió a reflujo durante la noche. La reacción se enfrió a temperatura ambiente y se agregó 150 ml de heptano. Las sales de HCl se eliminaron mediante filtración y se lavó con heptano. El solvente se eliminó colocando la mezcla bajo vacío centralizado y luego alto vacío. Se aisló *N*-(3-(Trifluorometil)bencil)-1-(trimetilsilil)metanamina mediante destilación al vacío (punto de ebullición 70-90 °C/3,2 torr): ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,59 (s, 1H), 7,53 – 7,38 (m, 3H), 3,86 (s, 2H), 2,04 (s, 2H), 1,34 (s, 1H), 0,06 (s, 9H).

Paso B: Se combinó formaldehido (4,08 g, 50,2 mmol) y metanol (2,032 ml, 50,2 mmol), y la mezcla se enfrió a 0 °C (baño de hielo). Se agregó *N*-(3-(trifluorometil)bencil)-1-(trimetilsilil)metanamina (10,94 g, 41,9 mmol) por goteo a través de un embudo de adición durante 30 minutos. Se agregó carbonato de potasio (4,63 g, 33,5 mmol), y la reacción se agitó a 0 °C por 2 horas adicionales. El producto de la reacción se decantó a partir del carbonato de potasio, se trató con más carbonato de potasio, y se decantó nuevamente. Los sólidos de carbonato de potasio se lavaron varias veces con éter, y estos lavados se agregaron a la solución del producto. El solvente se eliminó al vacío para dar 1-metoxi-*N*-(3-(trifluorometil)bencil)-*N*-((trimetilsilil)metil)metanamina la cual se usó directamente en el siguiente paso.

Paso C: Se combinó ciclopent-2-enona (3,31 g, 40,4 mmol) y ácido trifluoroacético (0,031 ml, 0,404 mmol) en diclorometano (40 ml). Se agregó 1-metoxi-*N*-(3-(trifluorometil)bencil)-*N*-((trimetilsilil)metil)metanamina (12,33 g, 40,4 mmol) del Paso B como una solución en 10 ml de diclorometano por goteo a través de un embudo de adición durante 45 minutos a temperatura ambiente bajo nitrógeno. La reacción se detuvo con bicarbonato de sodio acuoso y se extrajo con 2×100 ml de diclorometano. Los lavados orgánicos se combinaron y se lavó con salmuera. El solvente se eliminó al vacío para dar 2-(3-(trifluorometil)bencil)hexahidrociclopenta[*c*]pirrol-4(5*H*)-ona: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,54 – 7,34 (m, 4H), 3,66 (d, *J* = 13,4, 1H), 3,52 (d, *J* = 13,4, 1H),

3,04 (dd, *J* = 1,8, 8,9, 1H), 2,91 (ddd, *J* = 2,8, 7,4, 11,7, 1H), 2,72 – 2,65 (m, 1H), 2,62 (d, *J* = 8,9, 1H), 2,52 – 2,23 (m, 4H), 2,15 (ddd, *J* = 8,1, 12,9, 17,1, 1H), 1,85 – 1,70 (m, 1H).

Paso D: Se disolvió clorhidrato de hidroxilamina (3,47 g, 50,0 mmol) y acetato de sodio (4,27 g, 52,0 mmol) en 15 ml de agua y se agregó a una solución de 2-(3-(trifluorometil)bencil)hexahidrociclopenta[*c*]pirrol-4(5*H*)-ona (11,33 g, 40 mmol) del Paso C en etanol (80 ml). La reacción se llevó a reflujo por 5 minutos y se dejó enfriar a 70 °C. Luego de 1 hora, la mezcla de la reacción se enfrió, y el solvente se eliminó al vacío para dar oxima de (E)-2-(3-(trifluorometil)bencil)hexahidrociclopenta[c]pirrol-4(5H)-ona la cual se usó sin purificación adicional en el siguiente paso.

Paso E: Se agregó oxima de (E)-2-(3-(trifluorometil)bencil)hexahidrociclopenta[c]pirrol-4(5H)-ona (11,9 g, 39,9 mmol) del Paso D en amoníaco al 20% -metanol (115 ml) a níquel de Raney® lavado con metanol, (humedecido con agua, 38,52 g, 295 mmol) en una botella de presión de 500 ml. El recipiente se presurizó con hidrógeno (30 psi), y la mezcla se agitó por 16 horas a temperatura ambiente. La mezcla se filtró a través de una membrana de nylon, el solvente se eliminó al vacío, y el material crudo se adsorbió sobre gel de sílice. La cromatografía sobre gel de sílice usando un cartucho (Analogix®, Burlington, Wisconsin, SF65-400) eluyendo con 1-10% metanol (amoníaco 2 N)/diclorometano dio los siguientes diastereómeros.
(3a*S**,4*R**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina: ^{1}H NMR (300 MHz, piridin-d_5) δ ppm 7,58 (s, 1H), 7,50 (t, *J* = 6,7, 2H), 7,45 – 7,37 (m, 1H), 3,59 (s, 2H), 3,26 (dt, *J* = 6,3, 12,6, 1H), 2,67 – 2,50 (m, 4H), 2,38 (dd, *J* = 6,6, 8,4, 1H), 2,31 – 2,20 (m, 1H), 1,79 – 1,62 (m, 2H), 1,60 – 1,33 (m, 4H); y
(3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina: ^{1}H NMR (300 MHz, piridin-d_5) δ ppm 7,58 (s, 1H), 7,50 (t, *J* = 7,2, 2H), 7,45 – 7,37 (m, 1H), 3,59 (s, 2H), 3,09 (dd, *J* = 4,9, 11,4, 1H), 2,77 – 2,57 (m, *J* = 3,9, 1H), 2,52 – 2,38 (m, 3H), 2,34 (dd, *J* = 3,7, 9,0, 1H), 2,22 – 2,09 (m, 1H), 2,03 – 1,85 (m, *J* = 4,7, 7,0, 10,8, 2H), 1,42 – 1,21 (m, 4H).

Paso F: El compuesto del título se preparó utilizando ácido 3-metil-2-fenilbutanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Paso E en lugar de

(3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en Ejemplo 1: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,23 (d, *J* = 6,9, 0,5H), 8,13 (d, *J* = 7,1, 0,5H), 7,73 (s, 0,5H), 7,67 (s, 0,5H), 7,63 (dd, *J* = 6,7, 8,0, 2H), 7,56 – 7,53 (m, 1H), 7,50 (t, *J* = 8,5, 2H), 7,38 – 7,22 (m, 3H), 4,45 – 4,38 (m, 0,5H), 4,33 – 4,26 (m, 0,5H), 3,50 (s, 1H), 3,44 (d, *J* = 13,4, 0,5H), 3,21 (d, *J* = 13,4, 0,5H), 3,17 (d, *J* = 10,5, 0,5H), 3,10 (d, *J* = 10,5, 0,5H), 2,91 (qd, *J* = 3,4, 7,9, 0,5H), 2,79 (dd, *J* = 3,4, 9,5, 0,5H), 2,74 – 2,56 (m, 1,5H), 2,47 – 2,31 (m, 2,5H), 2,27 (dd, *J* = 3,1, 8,9, 0,5H), 2,21 (d, *J* = 2,7, 0,5H), 1,98 – 1,93 (m, 0,5H), 1,89 – 1,79 (m, 0,5H), 1,74 – 1,56 (m, 1,5H), 1,53 – 1,46 (m, 0,5H), 1,46 – 1,39 (m, 0,5H), 1,30 – 1,23 (m, 1H), 1,19 (d, *J* = 6,5, 1,5H), 1,17 – 1,11 (m, 0,5H), 1,08 (d, *J* = 6,5, 1,5H), 0,72 (dd, *J* = 6,7, 9,6, 3H); MS (ESI+) *m/z* 445 $(M+H)^+$.

Ejemplo 123

3,3-dimetil-2-fenil-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[c]pirrol-4–il}butanamida**

El compuesto del título se preparó utilizando ácido 3,3-dimetil-2-fenilbutanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 1: ^{1}H *N*MR (500 MHz, piridin-d_5) δ ppm 8,32 (d, *J* = 6,7, 0,5H), 8,13 (d, *J* = 7,1, 0,5H), 7,74 – 7,70 (m, 1H), 7,69 – 7,66 (m, 1H), 7,61 (t, *J* = 8,6, 3H), 7,48 – 7,43 (m, 1H), 7,37 – 7,24 (m, 3H), 4,48 – 4,39 (m, 0,5H), 4,36 – 4,28 (m, 0,5H), 3,51 (q, *J* = 13,1, 0,5H), 3,41 (d, *J* = 17,1, 1H), 3,35 (d, *J* = 13,3, 0,5H), 3,13 (d, *J* = 13,4, 0,5H), 2,98 (qd, *J* = 4,0, 8,2, 0,5H), 2,81 (dd, *J* = 3,9, 9,5, 0,5H), 2,74 (ddd, *J* = 3,4, 7,8, 16,6, 0,5H), 2,49 – 2,37 (m, 2H), 2,31 (dd, *J* = 3,4, 9,6, 0,5H), 2,24 – 2,15 (m, 2H), 2,01 – 1,94 (m, 0,5H), 1,84 (ddd, *J* = 8,1, 11,7, 14,5, 0,5H), 1,73 – 1,65 (m, 1H), 1,64 – 1,56 (m, 0,5H), 1,52 – 1,38 (m, 1H), 1,27 (dt, *J* = 5,6, 12,2, 1H), 1,16 (s, 4,5H), 1,11 (s, 4,5H); MS (ESI+) *m/z* 459 $(M+H)^+$.

Ejemplo 124

2,2-diciclohexil-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida**

El compuesto del título se preparó utilizando ácido 2,2-diciclohexilacético en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-

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SOLICITUD DE

PATENTE DE INVENCION
PCT ENTRADA EN FASE NACIONAL

21. EXPEDIENTE No. _____

54. TITULO: **NUEVAS OCTAHIDROCICLOPENTA[C]PIRROL-4-AMINAS SUSTITUIDAS COMO BLOQUEANTES DE LOS CANALES DE CALCIO**

52. CLASIFICACION INTERNACIONAL: **C07D 209/02, A61K 31/403**

71. SOLICITANTE: **ABBOTT LABORATORIES**

DOMICILIO: **100 Abbott Park Road, Abbott Park, Illinois 60064, ESTADOS UNIDOS DE AMERICA**

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(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 1: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,73 (s, 1H), 7,65 (d, *J* = 7,6, 1H), 7,57 – 7,44 (m, 3H), 4,46 (dt, *J* = 6,4, 12,6, 1H), 3,55 (d, *J* = 12,9, 1H), 3,47 (d, *J* = 12,8, 1H), 2,75 (d, *J* = 8,1, 2H), 2,53 – 2,39 (m, 2H), 2,32 (t, *J* = 8,2, 1H), 2,21 (t, *J* = 8,3, 1H), 1,97 – 1,53 (m, 15H), 1,50 – 1,04 (m, 11H), 0,98 (dd, *J* = 11,3, 23,1, 1H); MS (ESI+) *m/z* 491 $(M+H)^+$.

Ejemplo 125

2-etil-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida**

El compuesto del título se preparó utilizando ácido 2-etilbutanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 1: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,90 (d, *J* = 6,7, 1H), 7,71 (s, 1H), 7,61 (d, *J* = 7,7, 1H), 7,54 (d, *J* = 7,7, 1H), 7,46 (t, *J* = 7,7, 1H), 4,51 – 4,43 (m, 1H), 3,49 (s, 2H), 2,83 (ddd, *J* = 2,9, 7,8, 16,8, 1H), 2,75 (dd, *J* = 2,9, 9,5, 1H), 2,52 – 2,43 (m, 1H), 2,37 (dd, *J* = 2,9, 9,1, 1H), 2,35 – 2,30 (m, 1H), 2,25 (dd, *J* = 7,6, 9,4, 1H), 2,01 (tt, *J* = 4,8, 9,5, 1H), 1,89 (dt, *J* = 7,3, 11,6, 1H), 1,77 (ddt, *J* = 7,5, 9,3, 15,2, 2H), 1,70 – 1,60 (m, 2H), 1,51 – 1,37 (m, 2H), 1,34 – 1,26 (m, 1H), 0,95 (t, *J* = 7,4, 3H), 0,83 (t, *J* = 7,4, 3H); MS (ESI+) *m/z* 383 $(M+H)^+$.

Ejemplo 126

2-propil-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}pentanamida**

El compuesto del título se preparó utilizando ácido 2-propilpentanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 1: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,94 (d, *J* = 6,9, 1H), 7,72 (s, 1H), 7,62 (d, *J* = 7,7, 1H), 7,56 (d, *J* = 7,7, 1H), 7,47 (t, *J* = 7,7, 1H), 4,48 (dt, *J* = 7,3, 14,6, 1H), 3,52 (d, *J* = 13,0, 1H), 3,48 (d, *J* = 13,0, 1H), 2,84 (ddd, *J* = 3,0, 7,7, 16,7, 1H), 2,74 (dd, *J* = 3,1, 9,5, 1H), 2,52 – 2,45 (m, 1H),

2,38 – 2,34 (m, 2H), 2,27 (dd, *J* = 7,6, 9,5, 1H); 2,22 (td, *J* = 4,6, 9,5, 1H), 1,90 (dt, *J* = 7,3, 11,5, 1H), 1,84 – 1,75 (m, 2H), 1,73 – 1,61 (m, 2H), 1,48 – 1,27 (m, 6H), 1,20 – 1,08 (m, 1H), 0,88 (t, *J* = 7,0, 3H), 0,83 (t, *J* = 7,1, 3H); MS (ESI+) *m/z* 411 $(M+H)^+$.

Ejemplo 127

***N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4-il}ciclohexanocarboxamida**

El compuesto del título se preparó utilizando ácido ciclohexanocarboxílico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 1: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,74 (d, *J* = 6,1, 1H), 7,71 (s, 1H), 7,62 (d, *J* = 7,7, 1H), 7,57 (d, *J* = 9,2, 1H), 7,47 (t, *J* = 7,7, 1H), 4,48 – 4,41 (m, 1H), 3,53 (d, *J* = 13,2, 1H), 3,47 (d, *J* = 13,2, 1H), 2,84 (ddd, *J* = 2,8, 7,9, 10,3, 1H), 2,75 (dd, *J* = 2,8, 9,5, 1H), 2,51 – 2,43 (m, 1H), 2,37 (dd, *J* = 2,8, 9,1, 1H), 2,34 – 2,29 (m, 1H), 2,27 – 2,19 (m, 2H), 1,94 – 1,83 (m, 2H), 1,80 (d, *J* = 12,9, 1H), 1,73 – 1,60 (m, 6H), 1,57 – 1,51 (m, 1H), 1,35 – 1,27 (m, 1H), 1,22 – 1,10 (m, 3H); MS (ESI+) *m/z* 395 $(M+H)^+$.

Ejemplo 128

***N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4-il}cicloheptancarboxamida**

El compuesto del título se preparó utilizando ácido cicloheptancarboxílico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 1: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,79 (d, *J* = 6,9, 1H), 7,71 (s, 1H), 7,62 (d, *J* = 7,7, 1H), 7,56 (s, 1H), 7,47 (t, *J* = 7,7, 1H), 4,48 – 4,40 (m, 1H), 3,54 (d, *J* = 13,2, 1H), 3,46 (d, *J* = 13,2, 1H), 2,86 (ddd, *J* = 3,0, 7,8, 16,6, 1H), 2,76 (dd, *J* = 3,0, 9,5, 1H), 2,51 – 2,39 (m, 2H), 2,37 – 2,30 (m, 2H), 2,26 (dd, *J* = 7,5, 9,4, 1H), 2,00 – 1,80 (m, 5H), 1,75 – 1,60 (m, 4H), 1,49 – 1,41 (m, 4H), 1,33 (ddt, *J* = 7,2, 8,9, 12,1, 3H); MS (ESI+) *m/z* 409 $(M+H)^+$.

Ejemplo 129

***N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}ciclopentancarboxamida**

El compuesto del título se preparó utilizando ácido ciclopentancarboxílico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 1: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,82 (d, *J* = 6,9, 1H), 7,71 (s, 1H), 7,61 (d, *J* = 7,7, 1H), 7,55 (d, *J* = 7,7, 1H), 7,46 (t, *J* = 7,7, 1H), 4,48 – 4,41 (m, 1H), 4,07 (q, *J* = 7,1, 1H), 2,82 (ddd, *J* = 2,9, 7,8, 16,7, 1H), 2,72 (dd, *J* = 2,9, 9,5, 1H), 2,66 (p, *J* = 7,9, 1H), 2,50 – 2,42 (m, 1H), 2,37 (dd, *J* = 2,9, 9,0, 1H), 2,34 – 2,29 (m, 1H), 2,21 (dd, *J* = 7,5, 9,4, 1H), 2,03 (dt, *J* = 7,0, 15,3, 1H), 1,86 (dddd, *J* = 7,4, 12,3, 20,5, 23,4, 3H), 1,75 – 1,60 (m, 5H), 1,53 – 1,41 (m, 2H), 1,30 (td, *J* = 4,7, 11,1, 1H), 1,11 (t, *J* = 7,1, 1H); MS (ESI+) *m/z* 381 $(M+H)^+$.

Ejemplo 130

6,6-bis(4-fluorofenil)-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}hexanamida**

El compuesto del título se preparó utilizando ácido 6,6-bis(4-fluorofenil)hexanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 1: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,99 (d, *J* = 7,1, 1H), 7,69 (s, 1H), 7,58 (s, 1H), 7,54 (d, *J* = 7,6, 1H), 7,42 (dd, *J* = 6,9, 14,5, 1H), 7,26 (dd, *J* = 5,5, 8,6, 4H), 7,14 – 7,08 (m, 4H), 4,51 – 4,41 (m, 1H), 3,91 (t, *J* = 7,8, 1H), 3,47 (d, *J* = 2,3, 2H), 2,84 (qd, *J* = 3,0, 8,0, 1H), 2,69 (dd, *J* = 3,1, 9,5, 1H), 2,53 – 2,43 (m, 1H), 2,38 – 2,20 (m, 5H), 1,99 (dd, *J* = 7,8, 15,6, 2H), 1,89 – 1,78 (m, 3H), 1,70 – 1,59 (m, 2H), 1,37 – 1,25 (m, 3H); MS (ESI+) *m/z* 571 $(M+H)^+$.

Ejemplo 131

3,3-difenil-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}propanamida**

El compuesto del título se preparó utilizando ácido 3,3-difenilpropanoico en

lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 1: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,10 (d, *J* = 7,0, 1H), 7,72 (s, 1H), 7,62 (d, *J* = 7,8, 1H), 7,48 (t, *J* = 7,7, 1H), 7,39 (dd, *J* = 2,6, 7,5, 5H), 7,26 (dt, *J* = 7,6, 15,1, 5H), 7,17 (dd, *J* = 6,2, 13,5, 2H), 4,38 – 4,27 (m, 1H), 3,54 (d, *J* = 13,4, 1H), 3,38 (d, *J* = 13,4, 1H), 3,15 – 3,09 (m, 2H), 2,75 (qd, *J* = 3,6, 7,9, 1H), 2,44 – 2,35 (m, 2H), 2,32 (t, *J* = 8,3, 1H), 2,20 (dd, *J* = 3,3, 8,9, 1H), 2,08 (dd, *J* = 7,8, 9,5, 1H), 1,70 (t, *J* = 7,9, 1H), 1,58 – 1,46 (m, 2H), 1,18 – 1,10 (m, 1H); MS (ESI+) *m/z* 493 $(M+H)^+$.

Ejemplo 132

5,5-bis(4-fluorofenil)-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}pentanamida**

El compuesto del título se preparó utilizando ácido 5,5-bis(4-fluorofenil)pentanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 1: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,06 (d, *J* = 7,0, 1H), 7,70 (s, 1H), 7,60 (d, *J* = 8,0, 1H), 7,54 (d, *J* = 7,7, 1H), 7,44 (t, *J* = 7,7, 1H), 7,26 (dd, *J* = 5,6, 8,4, 4H), 7,08 (td, *J* = 1,2, 8,8, 4H), 4,51 – 4,42 (m, 1H), 3,96 (t, *J* = 7,8, 1H), 2,86 (qd, *J* = 3,2, 7,9, 1H), 2,69 (dd, *J* = 3,2, 9,5, 1H), 2,52 – 2,43 (m, 1H), 2,43 – 2,29 (m, 5H), 2,24 (dd, *J* = 7,7, 9,4, 1H), 2,15 – 2,06 (m, 3H), 1,85 (dt, *J* = 9,9, 17,8, 1H), 1,76 (dt, *J* = 7,3, 15,3, 2H), 1,70 – 1,59 (m, 2H), 1,33 – 1,26 (m, 1H); MS (ESI+) *m/z* 557 $(M+H)^+$.

Ejemplo 133

3,3-bis(4-fluorofenil)-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}propanamida**

El compuesto del título se preparó utilizando ácido 3,3-bis(4-fluorofenil)propanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 1: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,13 (d, *J* = 7,0, 1H), 7,71 (s, 1H), 7,61 (d, *J* = 7,7, 1H), 7,56 (s, 1H),

7,47 (t, *J* = 7,7, 1H), 7,32 (ddd, *J* = 3,7, 5,4, 8,8, 4H), 7,11 – 7,02 (m, 4H), 4,94 (d, *J* = 8,0, 1H), 4,39 – 4,25 (m, 1H), 3,52 (d, *J* = 13,4, 1H), 3,41 (d, *J* = 13,4, 1H), 3,06 (d, *J* = 7,9, 2H), 2,76 (qd, *J* = 3,4, 7,9, 1H), 2,43 (dd, *J* = 3,3, 9,5, 2H), 2,31 (t, *J* = 8,3, 1H), 2,23 (dd, *J* = 3,1, 9,0, 1H), 2,10 (dd, *J* = 7,8, 9,4, 1H), 1,76 – 1,67 (m, 1H), 1,59 – 1,49 (m, 2H), 1,22 – 1,11 (m, 1H); MS (ESI+) *m/z* 529 $(M+H)^+$.

Ejemplo 134

4,4-bis(4-fluorofenil)-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[c]pirrol-4–il}butanamida**

El compuesto del título se preparó utilizando ácido 4,4-bis(4-fluorofenil)butanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 1: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,16 (d, *J* = 6,9, 1H), 7,66 (s, 1H), 7,58 (s, 1H), 7,50 (d, *J* = 7,7, 1H), 7,38 (t, *J* = 7,7, 1H), 7,28 (dd, *J* = 5,5, 7,3, 4H), 7,10 – 7,02 (m, 4H), 4,49 (dt, *J* = 7,6, 14,7, 1H), 4,10 (t, *J* = 7,9, 1H), 3,50 (d, *J* = 13,4, 1H), 3,42 (d, *J* = 13,4, 1H), 2,92 (qd, *J* = 3,6, 7,9, 1H), 2,67 (dd, *J* = 3,5, 9,5, 1H), 2,55 (dd, *J* = 7,2, 15,0, 2H), 2,52 – 2,46 (m, 1H), 2,40 (t, *J* = 8,3, 1H), 2,36 – 2,24 (m, 4H), 1,91 – 1,82 (m, 1H), 1,71 (td, *J* = 5,8, 11,3, 1H), 1,67 – 1,60 (m, 1H), 1,35 – 1,27 (m, 1H); MS (ESI+) *m/z* 543 $(M+H)^+$.

Ejemplo 135

2,2-difenil-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida**

El compuesto del título se preparó utilizando ácido 2,2-difenilacético en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 1: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,50 (s, 1H), 7,71 (d, *J* = 7,5, 2H), 7,63 (d, *J* = 7,2, 2H), 7,45 (d, *J* = 7,4, 2H), 7,39 – 7,28 (m, 5H), 7,25 (dd, *J* = 5,8, 8,9, 3H), 4,51 – 4,42 (m, 1H), 3,44 (d, *J* = 13,3, 1H), 3,25 (d, *J* = 13,3, 1H), 2,85 (qd, *J* = 3,2, 7,9, 1H), 2,59 (dd, *J* = 3,4, 9,5, 1H), 2,47 – 2,37 (m, 1H), 2,26 (t, *J* = 8,3, 1H), 2,21 – 2,13 (m, 2H), 1,85 – 1,76 (m, 1H), 1,67 – 1,52 (m, 3H), 1,27 – 1,18 (m, 1H); MS (ESI+) *m/z* 479 $(M+H)^+$.

Ejemplo 136

2,2-bis(4-fluorofenil)-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida**

El compuesto del título se preparó utilizando ácido 2,2-bis(4-fluorofenil)acético en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 1: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,68 (d, *J* = 7,0, 1H), 7,64 (s, 1H), 7,60 (t, *J* = 6,4, 1H), 7,57 – 7,54 (m, 2H), 7,52 – 7,43 (m, 4H), 7,17 – 7,07 (m, 4H), 4,48 – 4,41 (m, 1H), 3,46 (d, *J* = 13,3, 1H), 3,30 (d, *J* = 13,3, 1H), 2,90 (qd, *J* = 3,5, 8,0, 1H), 2,59 (dd, *J* = 3,5, 9,5, 1H), 2,50 – 2,42 (m, 1H), 2,32 (t, *J* = 8,3, 1H), 2,25 – 2,19 (m, 3H), 1,87 – 1,77 (m, 1H), 1,66 (td, *J* = 5,7, 11,4, 1H), 1,62 – 1,54 (m, 1H), 1,29 – 1,20 (m, 1H); MS (ESI+) *m/z* 515 $(M+H)^+$.

Ejemplo 137

N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*R,4*R**,6a*S**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida**

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-L-leucina en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en Ejemplo el procedimiento descrito en el Ejemplo 1: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,50 (d, *J* = 7,1, 0,5H), 8,46 (d, *J* = 6,8, 0,5H), 8,03 (dd, *J* = 8,2, 17,0, 1H), 7,74 (s, 1H), 7,71 (d, *J* = 7,7, 0,5H), 7,61 (d, *J* = 6,5, 0,5H), 7,47 (t, *J* = 7,7, 1H), 4,67 (dd, *J* = 8,2, 14,1, 0,5H), 4,61 (dd, *J* = 8,1, 14,7, 0,5H), 4,53 – 4,39 (m, 1H), 3,81 (d, *J* = 13,1, 0,5H), 3,70 (d, *J* = 13,3, 0,5H), 3,44 (d, *J* = 13,3, 0,5H), 3,29 (d, *J* = 13,2, 0,5H), 2,93 – 2,86 (m, 1H), 2,85 – 2,74 (m, 1H), 2,46 (d, *J* = 4,1, 1H), 2,39 – 2,21 (m, 3H), 1,96 – 1,76 (m, 5H), 1,73 – 1,55 (m, 2H), 1,50 (s, 4,5H), 1,50 (s, 4,5H), 1,34 – 1,23 (m, 1H), 0,91 – 0,82 (m, 6H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Ejemplo 138

N^2-(tert-butiloxicarbonil)-N^1-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida**

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-D-

leucina en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 1: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,50 (d, *J* = 7,0, 0,5H), 8,46 (d, *J* = 6,8, 0,5H), 8,03 (dd, *J* = 8,1, 17,2, 1H), 7,74 (s, 1H), 7,71 (d, *J* = 7,7, 1H), 7,61 (d, *J* = 5,8, 1H), 7,48 (t, *J* = 7,7, 1H), 4,67 (dd, *J* = 8,3, 14,3, 0,5H), 4,61 (dd, *J* = 7,9, 14,5, 0,5H), 4,47 (ddd, *J* = 7,0, 13,9, 17,8, 1H), 3,81 (d, *J* = 13,1, 0,5H), 3,70 (d, *J* = 13,1, 0,5H), 3,44 (d, *J* = 13,3, 0,5H), 3,29 (d, *J* = 13,2, 0,5H), 2,89 (t, *J* = 13,2, 1H), 2,85 – 2,75 (m, 1H), 2,51 – 2,42 (m, 1H), 2,39 – 2,30 (m, 1H), 2,28 (dd, *J* = 6,1, 15,3, 2H), 1,97 – 1,77 (m, 4H), 1,73 – 1,55 (m, 2H), 1,50 (s, 4,5H), 1,50 (s, 4,5H), 1,34 – 1,22 (m, 1H), 0,91 – 0,81 (m, 6H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Ejemplo 139

N^2-(tert-butiloxicarbonil)-N^2-metil-N^1-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida**

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-D-leucina en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 1: ^{1}H NMR (300 MHz, piridin-d_5) δ ppm 7,76 (d, *J* = 15,9, 2H), 7,57 (s, 3H), 7,54 – 7,43 (m, 1H), 7,42 – 7,36 (m, 0,5H), 7,34 – 7,21 (m, 1H), 4,86 (t, *J* = 9,6, 0,5H), 4,48 – 4,35 (m, 0,5H), 3,71 (d, *J* = 13,3, 0,5H), 3,52 (d, *J* = 13,4, 0,5H), 3,40 (d, *J* = 13,2, 0,5H), 2,98 (s, 1,5H), 2,97 (s, 1,5H), 2,77 (ddd, *J* = 2,0, 7,2, 9,8, 2H), 2,57 – 2,46 (m, 1H), 2,43 (dd, *J* = 2,9, 9,2, 0,5H), 2,36 (dd, *J* = 2,3, 6,4, 0,5H), 2,34 – 2,22 (m, 2H), 1,93 (dddd, *J* = 2,0, 6,2, 8,1, 14,3, 1H), 1,85 – 1,59 (m, 4H), 1,52 (s, 4,5H), 1,50 (s, 4,5H), 1,39 – 1,28 (m, 1H), 0,96 – 0,89 (m, 6H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Ejemplo 140

6,6-bis(4-fluorofenil)-*N*-{(3a*S,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}hexanamida**

El compuesto del título se preparó utilizando ácido 6,6-bis(4-fluorofenil)hexanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*R**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del

Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 2: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,31 (d, *J* = 7,3, 1H), 7,77 (s, 1H), 7,61 (t, *J* = 7,4, 1H), 7,57 (d, *J* = 7,2, 1H), 7,45 (t, *J* = 7,7, 1H), 7,25 (dd, *J* = 5,6, 8,2, 4H), 7,10 (t, *J* = 8,7, 4H), 4,46 – 4,37 (m, 1H), 3,90 (t, *J* = 7,8, 1H), 3,61 (d, *J* = 13,5, 1H), 3,47 (d, *J* = 13,5, 1H), 2,85 – 2,79 (m, 1H), 2,49 (d, *J* = 16,3, 2H), 2,47 – 2,41 (m, 1H), 2,30 (ddd, *J* = 8,1, 15,0, 20,0, 4H), 2,15 – 2,06 (m, 1H), 1,98 (dd, *J* = 7,8, 15,5, 2H), 1,90 – 1,79 (m, 3H), 1,60 (dt, *J* = 7,4, 19,3, 1H), 1,44 – 1,36 (m, 1H), 1,32 (dq, *J* = 7,8, 15,3, 2H); MS (ESI+) *m/z* 571 $(M+H)^+$.

Ejemplo 141

3,3-difenil-*N*-{(3a*S,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}propanamida**

El compuesto del título se preparó utilizando ácido 3,3-difenilpropanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*R**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 2: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,28 (d, *J* = 7,4, 1H), 7,74 (s, 1H), 7,45 (t, *J* = 7,7, 1H), 7,38 (dd, *J* = 1,8, 7,4, 4H), 7,28 (dt, *J* = 7,6, 9,4, 4H), 7,20 – 7,17 (m, 4H), 5,00 (t, *J* = 7,8, 1H), 4,34 – 4,26 (m, 1H), 3,56 (d, *J* = 13,5, 1H), 3,43 (d, *J* = 13,5, 1H), 3,14 (d, *J* = 7,9, 2H), 2,65 (dd, *J* = 2,1, 8,3, 1H), 2,45 – 2,36 (m, 1H), 2,36 – 2,28 (m, 2H), 2,26 – 2,19 (m, 2H), 1,98 – 1,89 (m, 1H), 1,72 (ddd, *J* = 6,3, 12,5, 14,5, 1H), 1,43 (dt, *J* = 7,4, 14,1, 1H), 1,34 – 1,25 (m, 1H); MS (ESI+) *m/z* 493 $(M+H)^+$.

Ejemplo 142

5,5-bis(4-fluorofenil)-*N*-{(3a*S,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}pentanamida**

El compuesto del título se preparó utilizando ácido 5,5-bis(4-fluorofenil)pentanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*R**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 2: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,36 (d, *J* = 7,2, 1H), 7,75 (s, 1H), 7,62 – 7,54 (m, 2H), 7,44 (t, *J* = 7,7, 1H), 7,24 (dt, *J* = 5,7, 11,3, 4H), 7,07 (t, *J* = 8,7, 4H), 4,47 – 4,39 (m, 1H), 3,96 (t, *J*

= 7,8, 1H), 3,59 (d, *J* = 13,5, 1H), 3,46 (d, *J* = 13,5, 1H), 2,84 (d, *J* = 9,0, 1H), 2,51 (s, 2H), 2,42 (dd, *J* = 7,0, 14,2, 3H), 2,30 (d, *J* = 7,1, 1H), 2,27 – 2,22 (m, 1H), 2,15 – 2,06 (m, 3H), 1,85 (dd, *J* = 6,2, 13,9, 1H), 1,78 (dt, *J* = 7,4, 15,1, 2H), 1,60 (dt, *J* = 7,6, 14,6, 1H), 1,43 – 1,34 (m, 1H); MS (ESI+) *m/z* 557 $(M+H)^+$.

Ejemplo 143

3,3-bis(4-fluorofenil)-*N*-{(3a*S,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}propanamida**

El compuesto del título se preparó utilizando ácido 3,3-bis(4-fluorofenil)propanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*R**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 2: : ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,36 (d, *J* = 7,4, 1H), 7,74 (s, 1H), 7,62 – 7,56 (m, 2H), 7,45 (t, *J* = 7,7, 1H), 7,32 (ddd, *J* = 2,0, 5,4, 7,8, 4H), 7,07 (dt, *J* = 8,7, 11,2, 4H), 4,36 – 4,26 (m, 1H), 3,56 (d, *J* = 13,5, 1H), 3,45 (d, *J* = 13,5, 1H), 3,09 (d, *J* = 7,9, 2H), 2,70 – 2,63 (m, 1H), 2,47 – 2,37 (m, 1H), 2,33 (t, *J* = 6,7, 3H), 2,26 (dd, *J* = 3,0, 9,0, 1H), 2,24 – 2,18 (m, 1H), 1,96 (tt, *J* = 6,0, 11,8, 1H), 1,79 – 1,70 (m, 1H), 1,44 (dt, *J* = 7,6, 14,4, 1H), 1,35 – 1,26 (m, 1H); MS (ESI+) *m/z* 529 $(M+H)^+$.

Ejemplo 144

4,4-bis(4-fluorofenil)-*N*-{(3a*S,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida**

El compuesto del título se preparó utilizando ácido 4,4-bis(4-fluorofenil)butanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*R**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 2: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,39 (d, *J* = 7,2, 1H), 7,77 (s, 1H), 7,62 (d, *J* = 7,9, 2H), 7,45 (t, *J* = 7,7, 1H), 7,25 (dd, *J* = 5,5, 7,3, 4H), 7,05 (t, *J* = 8,7, 4H), 4,50 – 4,40 (m, 1H), 4,08 (t, *J* = 7,9, 1H), 3,61 (d, *J* = 13,5, 1H), 3,49 (d, *J* = 13,5, 1H), 2,87 (dd, *J* = 1,4, 8,8, 1H), 2,56 (dd, *J* = 7,7, 15,3, 4H), 2,48 (d, *J* = 8,8, 1H), 2,31 (dd, *J* = 8,0, 15,4, 4H), 2,13 (dq, *J* = 6,0, 12,0, 1H), 1,87 (td, *J* = 6,3, 12,5, 1H), 1,62 (dt, *J* = 7,4, 14,3, 1H), 1,41 (dd, *J* = 11,7, 20,8, 1H); MS (ESI+) *m/z* 543 $(M+H)^+$.

Ejemplo 145

2,2-difenil-*N*-{(3a*S,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida**

El compuesto del título se preparó utilizando ácido 2,2-difenilacético en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*R**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 2: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,94 (d, *J* = 6,8, 1H), 7,74 (s, 2H), 7,64 (d, *J* = 7,8, 4H), 7,47 – 7,40 (m, 1H), 7,38 – 7,29 (m, 5H), 7,28 – 7,23 (m, 3H), 4,45 – 4,37 (m, 1H), 3,57 (d, *J* = 13,5, 1H), 3,42 (d, *J* = 13,5, 1H), 2,76 (dd, *J* = 3,0, 9,1, 1H), 2,54 – 2,47 (m, 1H), 2,47 – 2,42 (m, 1H), 2,39 (dd, *J* = 7,3, 9,0, 1H), 2,23 (d, *J* = 3,0, 2H), 2,06 (dq, *J* = 6,2, 12,2, 1H), 1,83 – 1,74 (m, 1H), 1,59 (dt, *J* = 6,9, 14,5, 1H), 1,33 (dt, *J* = 6,3, 19,6, 1H); MS (ESI+) *m/z* 479 $(M+H)^+$.

Ejemplo 146

2,2-bis(4-fluorofenil)-*N*-{(3a*S,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida**

El compuesto del título se preparó utilizando ácido 2,2-bis(4-fluorofenil)acético en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*R**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 2: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,07 (d, *J* = 7,1, 1H), 7,74 (s, 1H), 7,59 (s, 1H), 7,56 (d, *J* = 5,3, 5H), 7,44 (t, *J* = 7,7, 1H), 7,12 (q, *J* = 8,6, 4H), 5,23 (s, 1H), 4,45 – 4,36 (m, 1H), 3,57 (d, *J* = 13,5, 1H), 3,44 (d, *J* = 13,5, 1H), 2,78 (dd, *J* = 2,9, 9,1, 1H), 2,56 – 2,49 (m, 1H), 2,49 – 2,44 (m, 1H), 2,41 (dd, *J* = 7,3, 8,9, 1H), 2,27 – 2,22 (m, 2H), 2,07 (dq, *J* = 6,1, 12,1, 1H), 1,86 – 1,76 (m, 1H), 1,60 (td, *J* = 7,2, 14,6, 1H), 1,35 (td, *J* = 6,3, 12,6, 1H); MS (ESI+) *m/z* 515 $(M+H)^+$.

Ejemplo 147

3,3-dimetil-2-fenil-*N*-{(3a*S,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida**

El compuesto del título se preparó utilizando ácido 3,3-dimetil-2-fenilbutanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*R**,6a*R**)-2-

(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 2: ^{1}H NMR (400 MHz,) δ ppm 8,47 (t, *J* = 6,7, 1H), 7,77 (s, 0,5H), 7,71 (d, *J* = 7,3, 2H), 7,60 (d, *J* = 7,7, 0,5H), 7,54 (s, 1H), 7,43 (dd, *J* = 8,1, 16,6, 1H), 7,35 – 7,24 (m, 4H), 4,39 – 4,29 (m, 1H), 3,62 (d, *J* = 13,6, 0,5H), 3,53 (d, *J* = 13,5, 0,5H), 3,47 (d, *J* = 13,6, 0,5H), 3,44 (s, 1H), 3,38 (d, *J* = 13,5, 0,5H), 2,92 (dd, *J* = 2,9, 9,0, 0,5H), 2,62 – 2,54 (m, 1H), 2,54 – 2,46 (m, 1H), 2,46 – 2,36 (m, 0,5H), 2,32 (dd, *J* = 9,1, 12,0, 1H), 2,27 (d, *J* = 5,2, 1H), 2,21 (d, *J* = 5,6, 1H), 2,17 – 2,07 (m, 0,5H), 1,86 (ddd, *J* = 6,4, 13,3, 21,3, 1H), 1,71 (tdd, *J* = 6,4, 13,0, 19,3, 1H), 1,36 (ddt, *J* = 8,2, 14,4, 20,6, 1,5H), 1,14 (d, *J* = 1,3, 9H); MS (ESI+) *m/z* 459 $(M+H)^+$.

Ejemplo 148

N^2-(tert-butiloxicarbonil)-N^1-{(3a*S,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida**

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-L-leucina en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*R**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 2: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,66 (dd, *J* = 7,6, 11,3, 1H), 7,98 (d, *J* = 6,0, 1H), 7,74 (d, *J* = 7,5, 1H), 7,58 (d, *J* = 21,6, 2H), 7,44 (t, *J* = 7,8, 1H), 4,74 – 4,66 (m, 1H), 4,45 – 4,36 (m, 1H), 3,58 (t, *J* = 13,6, 1H), 3,43 (dd, *J* = 13,6, 20,1, 1H), 2,81 (s, 0,5H), 2,73 (s, 0,5H), 2,57 (s, 0,5H), 2,47 (d, *J* = 9,1, 2H), 2,34 (s, 0,5H), 2,26 (d, *J* = 6,7, 1H), 2,24 – 2,20 (m, 0,5H), 2,11 (s, 1H), 2,07 – 1,99 (m, 0,5H), 1,87 (s, 4H), 1,71 – 1,62 (m, 0,5H), 1,61 – 1,55 (m, 0,5H), 1,50 (d, *J* = 2,8, 9H), 1,40 (s, 1H), 0,87 (d, *J* = 5,8, 3H), 0,84 (d, *J* = 5,5, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Ejemplo 149

N^2-(tert-butiloxicarbonil)-N^1-{(3a*S,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida**

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-D-leucina en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*R**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el

procedimiento descrito en el Ejemplo 2: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,66 (dd, *J* = 7,4, 11,1, 1H), 7,97 (d, *J* = 6,0, 1H), 7,74 (d, *J* = 7,6, 1H), 7,57 (d, *J* = 10,9, 2H), 7,44 (dd, *J* = 5,9, 13,6, 1H), 4,74 – 4,66 (m, 1H), 4,41 (dd, *J* = 6,2, 11,5, 1H), 3,58 (t, *J* = 13,4, 1H), 3,43 (dd, *J* = 13,6, 19,7, 1H), 2,82 (dd, *J* = 2,4, 9,0, 0,5H), 2,74 (d, *J* = 8,7, 0,5H), 2,62 – 2,54 (m, 0,5H), 2,54 – 2,43 (m, 2H), 2,37 – 2,32 (m, 0,5H), 2,27 (d, *J* = 6,7, 1H), 2,24 – 2,19 (m, 0,5H), 2,16 – 2,08 (m, 0,5H), 2,06 – 1,99 (m, 0,5H), 1,94 – 1,78 (m, 4,5H), 1,66 (dt, *J* = 7,2, 19,6, 0,5H), 1,62 – 1,56 (m, 0,5H), 1,50 (d, *J* = 2,9, 9H), 1,43 – 1,31 (m, 1H), 0,86 (dd, *J* = 5,7, 13,5, 6H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Ejemplo 150

N^2-(tert-butiloxicarbonil)-N^2-metil-N^1-{(3a*S,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida**

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-D-leucina en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S**,4*R**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Ejemplo 2: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,31 (s, 1H), 7,75 (s, 1H), 7,57 (d, *J* = 11,6, 2H), 7,44 (t, *J* = 7,7, 1H), 5,18 – 5,09 (m, 0,5H), 4,84 – 4,73 (m, 0,5H), 4,44 – 4,32 (m, 1H), 3,59 (d, *J* = 13,5, 1H), 3,47 (d, *J* = 13,6, 1H), 3,07 (d, *J* = 25,1, 2,5H), 2,83 (d, *J* = 8,5, 0,5H), 2,79 – 2,72 (m, 0,5H), 2,55 – 2,44 (m, 2H), 2,44 – 2,39 (m, 1H), 2,37 – 2,33 (m, 0,5H), 2,29 (d, *J* = 7,4, 1H), 2,23 (dd, *J* = 7,9, 15,2, 1H), 2,08 (dt, *J* = 5,2, 11,8, 1H), 1,88 – 1,78 (m, 3H), 1,64 – 1,51 (m, 2H), 1,46 (s, 9H), 1,41 – 1,33 (m, 1H), 0,88 (d, *J* = 6,4, 3H), 0,84 (d, *J* = 6,5, 3H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Ejemplo 151

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(tert-butiloxicarbonil)-N^2-metil-L-leucinamida

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-leucina en lugar de ácido 1-fenilciclopentancarboxílico en el procedimiento descrito en el Ejemplo 2: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,28 (d, *J* = 6,6, 1H), 7,41 (s, 2H), 7,38 – 7,34 (m, 2H), 7,27 (t, *J* = 7,3, 1H), 5,16 – 5,11 (m, 0,5H), 4,82 – 4,74 (m, 0,5H), 4,44 – 4,33 (m, 1H), 3,57 (s, 1H), 3,46 – 3,38 (m, 1H), 3,07 (d, *J* = 26,9, 3H), 2,89 – 2,82 (m, 0,5H), 2,80 – 2,73 (m, 1H), 2,50 – 2,43 (m, 2H), 2,40 –

2,29 (m, 2H), 2,24 – 2,19 (m, 1H), 2,10 (dq, *J* = 5,8, 11,6, 1H), 1,92 – 1,87 (m, 0,5H), 1,83 (dd, *J* = 5,2, 9,3, 2H), 1,64 – 1,51 (m, 2H), 1,46 (s, 9H), 1,42 – 1,35 (m, 1H), 0,88 (d, *J* = 6,3, 3H), 0,84 (d, *J* = 6,6, 3H); MS (ESI+) *m/z* 444 $(M+H)^+$.

Ejemplo 152

2,2-diciclohexil-2-hidroxi-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida

Paso A: Se preparó (3a*S*,4*S*,6a*R*)-2-(3-(Trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina de acuerdo con el procedimiento descrito en Ejemplo 14 Paso A-C. Utilizando 2-(3-(trifluorometil)bencil)hexahidrociclopenta[*c*]pirrol-4(5*H*)-ona de los Pasos A-C en Ejemplo 122 en lugar de 2-bencilhexahidrociclopenta[*c*]pirrol-4(5*H*)-ona en el Paso A de Ejemplo 14 se obtuvo (*S*,*E*)-2-metil-*N*-((3a*R*,6a*S*)-2-(3-(trifluorometil)bencil)hexahidrociclopenta[*c*]pirrol-4(5*H*)–iliden)propan-2-sulfinamida y (*S*,*E*)-2-metil-*N*-((3a*S*,6a*R*)-2-(3-(trifluorometil)bencil)hexahidrociclopenta[*c*]pirrol-4(5*H*)–iliden)propan-2-sulfinamida. Se usó (*S*,*E*)-2-metil-*N*-((3a*S*,6a*R*)-2-(3-(trifluorometil)bencil)hexahidrociclopenta[*c*]pirrol-4(5*H*)–iliden)propan-2-sulfinamida como se describe en Ejemplo 14 Pasos B-C para dar (3a*S*,4*S*,6a*R*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,72 (s, 1H), 7,59 (d, *J* = 12,2, 1H), 7,54 (d, *J* = 7,7, 1H), 7,39 (t, *J* = 7,7, 1H), 3,71 – 3,66 (m, 1H), 3,64 (d, *J* = 13,3, 1H), 3,49 (d, *J* = 13,3, 1H), 3,22 (dd, *J* = 3,7, 9,9, 1H), 2,77 (qd, *J* = 3,8, 7,9, 1H), 2,49 (dd, *J* = 8,9, 16,7, 2H), 2,39 (t, *J* = 8,3, 1H), 2,29 (dd, *J* = 3,4, 9,0, 1H), 2,10 (ddd, *J* = 6,1, 9,7, 15,6, 1H), 1,90 (td, *J* = 5,9, 12,0, 1H), 1,69 – 1,60 (m, 1H), 1,42 (dt, *J* = 5,6, 12,2, 1H); MS (ESI+) *m/z* 284 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando ácido 2,2-diciclohexil-2-hidroxiacético en lugar de ácido 3-metil-2-fenilbutanoico y (3a*S*,4*S*,6a*R*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Paso A en lugar de (3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Paso D de Ejemplo 14: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,45 (br s, 1H), 7,85 (s, 1H), 7,75 (d, *J* = 7,4, 1H), 7,54 (d, *J* = 7,6, 1H), 7,36 (dd, *J* = 5,4, 13,2, 1H), 5,93 (br s, 1H), 4,64 – 4,57 (m, 1H), 3,85 (d, *J* = 13,2, 1H), 3,29 (d, *J* = 13,2, 1H), 2,92 (d, *J* = 9,5, 1H), 2,66 (dd, *J* = 7,4, 15,2, 1H), 2,49 – 2,41 (m, 1H), 2,39 (d, *J* = 9,1, 1H), 2,24 – 2,01 (m, 5H), 1,96 – 1,83 (m, 4H), 1,83 – 1,70 (m, 6H),

1,63 (t, *J* = 13,2, 2H), 1,58 – 1,49 (m, 1H), 1,45 – 1,08 (m, 10H); MS (ESI+) *m/z* 507 $(M+H)^+$.

Ejemplo 153

N^2-(tert-butiloxicarbonil)-N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-leucina en lugar de ácido 3-metil-2-fenilbutanoico y (3a*S*,4*S*,6a*R*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del 152 Paso A en lugar de (3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Paso D de Ejemplo 14: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,01 (s, 1H), 7,83 (s, 1H), 7,76 (s, 1H), 7,64 (d, *J* = 7,7, 2H), 5,12 – 5,04 (m, 1H), 4,42 (s, 1H), 3,61 (s, 1H), 3,52 (s, 1H), 3,12 – 2,97 (m, 3H), 2,78 (s, 1H), 2,72 (d, *J* = 9,5, 1H), 2,50 – 2,41 (m, 1H), 2,37 (d, *J* = 7,3, 1H), 2,32 – 2,16 (m, 2H), 1,98 – 1,72 (m, 3H), 1,64 (dt, *J* = 6,8, 14,9, 1H), 1,60 – 1,53 (m, 2H), 1,50 (s, 9H), 1,33 – 1,20 (m, 1H), 0,89 (d, *J* = 6,5, 6H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Ejemplo 154

2,2-diciclohexil-2-hidroxi-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida

Paso A: (3a*S*,4*R*,6a*R*)-2-(3-(Trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina se preparó de acuerdo con el procedimiento descrito en Ejemplo 16 Pasos A-E utilizando (*S*,*E*)-2-metil-*N*-((3a*S*,6a*R*)-2-(3-(trifluorometil)bencil)hexahidrociclopenta[*c*]pirrol-4(5*H*)–iliden)propan-2-sulfinamida del Paso A en Ejemplo 152 en lugar de (*S*,*E*)-*N*-((3a*S*,6a*R*)-2-bencilhexahidrociclopenta[*c*]pirrol-4(5*H*)–iliden)-2-metilpropan-2-sulfinamida en el Paso A-E de Ejemplo 16 para dar (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,78 (s, 1H), 7,59 (d, *J* = 6,0, 2H), 7,45 (t, *J* = 7,7, 1H), 4,94 (br s, 2H), 3,53 (s, 2H), 3,13 (dd, *J* = 5,1, 11,6, 1H), 2,63 – 2,54 (m, 1H), 2,49 (dd, *J* = 3,3, 9,0, 1H), 2,35 (dd, *J* = 7,5, 9,0, 1H), 2,32 (d, *J* = 5,9, 2H), 2,21 – 2,13 (m, 1H), 1,96 (dt, *J* = 6,0, 8,7, 1H), 1,88 (td, *J* = 3,9, 9,7, 1H), 1,38 – 1,29 (m, 2H); MS (ESI+) *m/z* 284 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Paso A en lugar de

(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y ácido 2,2-diciclohexil-2-hidroxiacético en lugar de ácido (S)-2-fenilbutanoico en el procedimiento descrito en el Paso F de Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,75 (s, 1H), 7,70 (d, *J* = 7,8, 1H), 7,63 – 7,54 (m, 1H), 7,44 (t, *J* = 7,7, 1H), 6,25 – 6,09 (m, 1H), 4,45 – 4,37 (m, 1H), 3,61 (d, *J* = 13,5, 1H); 3,44 (d, *J* = 13,5, 1H), 2,91 (dd, *J* = 2,1, 9,0, 1H), 2,58 – 2,46 (m, 1H), 2,40 (dd, *J* = 7,1, 8,8, 1H), 2,33 (dd, *J* = 2,3, 8,9, 1H), 2,22 (dd, *J* = 7,0, 8,7, 1H), 2,19 – 2,04 (m, 5H), 1,94 – 1,82 (m, 4H), 1,82 – 1,71 (m, 4H), 1,63 (s, 3H), 1,58 – 1,46 (m, 1H); 1,37 (s, 4H), 1,25 (s, 7H); MS (ESI+) *m/z* 507 $(M+H)^+$.

Ejemplo 155

N^2-(tert-butiloxicarbonil)-N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 154 Paso A en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y *N*-(*tert*-butoxicarbonil)-*N*-metil-L-leucina en lugar de ácido (S)-2-fenilbutanoico en el procedimiento descrito en el Paso F de Ejemplo 16: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,30 (s, 1H), 7,74 (s, 1H), 7,57 (d, *J* = 9,4, 2H), 7,44 (t, *J* = 7,7, 1H), 5,21 – 5,04 (m, 1H), 4,37 (s, 1H), 3,58 (d, *J* = 12,2, 1H), 3,44 (d, *J* = 13,8, 1H), 3,07 (d, *J* = 25,6, 3H), 2,77 (d, *J* = 8,6, 1H), 2,47 (s, 2H), 2,41 – 2,32 (m, 1H), 2,29 (d, *J* = 7,2, 1H), 2,25 – 2,18 (m, 1H), 2,08 (dq, *J* = 5,8, 11,7, 1H), 1,83 (dd, *J* = 5,4, 9,0, 3H), 1,64 – 1,52 (m, 2H), 1,46 (s, 9H), 1,41 – 1,32 (m, 1H), 0,88 (d, *J* = 6,3, 3H), 0,84 (d, *J* = 6,5, 3H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Ejemplo 156

2,2-diciclohexil-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida

Paso A: (3a*R*,4*S*,6a*S*)-2-(3-(Trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina se preparó de acuerdo con el procedimiento descrito en Ejemplo 16 Paso A-E utilizando (*S*,*E*)-2-metil-*N*-((3a*R*,6a*S*)-2-(3-(trifluorometil)bencil)hexahidrociclopenta[*c*]pirrol-4(5*H*)–iliden)propan-2-sulfinamida del Ejemplo 152 Paso A en lugar de (*S*,*E*)-*N*-((3a*S*,6a*R*)-2-bencilhexahidrociclopenta[*c*]pirrol-4(5*H*)–iliden)-2-metilpropan-2-sulfinamida preparada en el Paso A de Ejemplo 14 para dar (3a*R*,4*S*,6a*S*)-2-(3-

(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,78 (s, 1H), 7,59 (d, *J* = 11,1, 2H), 7,45 (t, *J* = 7,7, 1H), 4,94 (br s, 2H), 3,14 (dd, *J* = 5,2, 11,5, 1H), 2,58 (tt, *J* = 5,1, 10,1, 1H), 2,49 (dd, *J* = 3,3, 9,0, 1H), 2,35 (dd, *J* = 7,5, 9,0, 1H), 2,31 (d, *J* = 5,8, 2H), 2,21 – 2,14 (m, 1H), 2,01 – 1,91 (m, 1H), 1,88 (td, *J* = 4,2, 9,9, 1H), 1,38 – 1,29 (m, 2H).

Paso B: El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Paso A en lugar de (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y ácido 2,2-diciclohexilacético en lugar de ácido (S)-2-fenilbutanoico en el procedimiento descrito en el Ejemplo 16 Paso F: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,13 (d, *J* = 7,2, 1H), 7,76 (s, 1H), 7,63 – 7,53 (m, 2H), 7,44 (t, *J* = 7,9, 1H), 4,51 – 4,43 (m, 1H), 3,61 (d, *J* = 13,5, 1H), 3,46 (d, *J* = 13,5, 1H), 2,88 (dd, *J* = 2,8, 9,0, 1H), 2,63 – 2,52 (m, 2H), 2,49 (dd, *J* = 7,1, 8,9, 1H), 2,32 – 2,27 (m, 2H), 2,13 (dq, *J* = 6,1, 11,9, 1H), 2,03 (t, *J* = 7,4, 1H), 1,96 (d, *J* = 13,0, 2H), 1,92 – 1,83 (m, 3H), 1,80 (d, *J* = 12,2, 2H), 1,75 – 1,68 (m, 4H), 1,67 – 1,63 (m, 1H), 1,63 – 1,57 (m, 2H), 1,50 – 1,37 (m, 3H), 1,30 – 1,18 (m, 4H), 1,12 (dtd, *J* = 2,7, 12,5, 24,6, 4H); MS (ESI+) *m/z* 491 $(M+H)^+$.

Ejemplo 157

2,2-diciclohexil-*N*-{(3a*R*,4*R*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida

Paso A: (3a*R*,4*R*,6a*S*)-2-(3-(Trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina se preparó de acuerdo con el procedimiento descrito en Ejemplo 14 Pasos B-C utilizando (*S*,*E*)-2-metil-*N*-((3a*R*,6a*S*)-2-(3-(trifluorometil)bencil)hexahidrociclopenta[*c*]pirrol-4(5*H*)–iliden)propan-2-sulfinamida del Ejemplo 152 Paso A en lugar de (*S*,*E*)-*N*-((3a*S*,6a*R*)-2-bencilhexahidrociclopenta[*c*]pirrol-4(5*H*)–iliden)-2-metilpropan-2-sulfinamida preparada en el Paso A de Ejemplo 14 para dar (3a*R*,4*R*,6a*S*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,78 (s, 1H), 7,59 (d, *J* = 11,1, 2H), 7,45 (t, *J* = 7,7, 1H), 4,94 (br s, 2H), 3,14 (dd, *J* = 5,2, 11,5, 1H), 2,58 (tt, *J* = 5,1, 10,1, 1H), 2,49 (dd, *J* = 3,3, 9,0, 1H), 2,35 (dd, *J* = 7,5, 9,0, 1H), 2,31 (d, *J* = 5,8, 2H), 2,21 – 2,14 (m, 1H), 2,00 – 1,92 (m, 1H), 1,88 (td, *J* = 4,2, 9,9, 1H), 1,39 – 1,29 (m, 2H); MS (ESI+) *m/z* 284 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando ácido 2,2-diciclohexilacético en lugar de ácido 3-metil-2-fenilbutanoico en y (3a*R*,4*R*,6a*S*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Paso A en lugar de (3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en el Paso D de Ejemplo 14: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,73 (s, 1H), 7,66 (d, *J* = 7,7, 1H), 7,55 (d, *J* = 7,3, 2H), 7,50 (t, *J* = 7,7, 1H), 4,50 – 4,43 (m, 1H), 3,54 (d, *J* = 12,9, 1H), 3,46 (d, *J* = 12,9, 1H), 2,74 (td, *J* = 2,6, 10,5, 2H), 2,51 – 2,42 (m, 2H), 2,31 (t, *J* = 8,3, 1H), 2,20 (dd, *J* = 7,8, 9,8, 1H), 1,94 – 1,54 (m, 15H), 1,46 (d, *J* = 13,0, 1H), 1,40 (d, *J* = 14,4, 1H), 1,35 – 1,07 (m, 9H), 0,98 (qd, *J* = 3,0, 12,3, 1H); MS (ESI+) *m/z* 491 $(M+H)^+$.

Ejemplo 158

N^1-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4-il}-L-leucinamida**

Se combinó N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4-il}-L-leucinamida (140 mg, 0,281 mmol) del Ejemplo 137 y HCl 2 N (2,5 ml, 5,00 mmol) en éter, y la reacción se agitó a temperatura ambiente durante la noche. Los sólidos se recogieron y se secó para dar el compuesto del título como la sal clorhidrato: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,59 (s, 0,5H), 8,48 (s, 0,5H), 7,89 (s, 0,5H), 7,83 (s, 0,5H), 7,69 (t, *J* = 6,8, 1H), 7,60 (d, *J* = 7,8, 1H), 7,50 – 7,44 (m, 1H), 4,96 (br s, 2H), 4,57 – 4,48 (m, 1H), 3,73 (d, *J* = 13,2, 0,5H), 3,67 (s, 1H), 3,64 (d, *J* = 13,2, 1H), 3,39 (d, *J* = 13,1, 0,5H), 3,35 (d, *J* = 13,2, 0,5H), 2,81 – 2,70 (m, 2H), 2,45 (dd, *J* = 7,5, 15,3, 1H), 2,39 – 2,31 (m, 1H), 2,27 – 2,14 (m, 2H), 1,95 – 1,79 (m, 2,5H), 1,72 – 1,56 (m, 2H), 1,53 – 1,46 (m, 0,5H), 1,33 – 1,23 (m, 1,5H), 0,90 (dt, *J* = 6,2, 14,1, 6H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Ejemplo 159

N^1-{(3a*R,4*R**,6a*S**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4-il}-D-leucinamida**

El compuesto del título se preparó utilizando N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4-il}-D-leucinamida del Ejemplo 138 en lugar de N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4-il}-L-leucinamida en el procedimiento descrito en el Ejemplo 158: ^{1}H NMR (500 MHz,

piridin-d_5) δ ppm 8,67 (d, J = 7,4, 0,5H), 8,57 (d, J = 7,6, 0,5H), 7,88 (s, 0,5H), 7,81 (s, 0,5H), 7,68 (d, J = 7,3, 1H), 7,61 (s, 1H), 7,48 (dd, J = 7,3, 14,5, 1H), 4,56 – 4,47 (m, 1H), 3,79 – 3,70 (m, 1H), 3,65 (d, J = 13,2, 0,5H), 3,38 (t, J = 13,5, 1H), 2,82 – 2,71 (m, 2H), 2,50 – 2,42 (m, 1H), 2,38 – 2,31 (m, 1H), 2,27 – 2,16 (m, 2H), 2,08 (dt, J = 6,8, 19,9, 0,5H), 1,96 – 1,88 (m, 1,5H), 1,88 – 1,80 (m, 1H), 1,70 – 1,59 (m, 2H), 1,58 – 1,52 (m, 0,5H), 1,42 – 1,20 (m, 4H), 0,90 (dt, J = 6,1, 13,2, 6H); MS (ESI+) m/z 398 $(M+H)^+$.

Ejemplo 160

N^2-metil-N^1-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida**

El compuesto del título se preparó utilizando N^2-(*tert*-butiloxicarbonil)-N^2-metil-N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida del Ejemplo 139 en lugar de N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida en el procedimiento descrito en el Ejemplo 158: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,52 (s, 0,5H), 8,29 (s, 0,5H), 7,92 (s, 0,5H), 7,79 (s, 0,5H), 7,69 (dd, J = 7,6, 18,7, 1H), 7,62 (d, J = 7,6, 1H), 7,48 (dd, J = 7,8, 18,2, 1H), 4,59 – 4,48 (m, 1H), 3,82 (d, J = 13,2, 0,5H), 3,63 (d, J = 13,1, 0,5H), 3,42 (d, J = 13,1, 0,5H), 3,31 – 3,18 (m, 1H), 2,81 (dd, J = 1,9, 9,4, 0,5H), 2,74 (dd, J = 8,5, 18,2, 1H), 2,50 – 2,43 (m, 1H), 2,41 (s, 1,5H), 2,40 (s, 1,5H), 2,33 (dd, J = 1,9, 9,0, 0,5H), 2,25 (dd, J = 7,3, 9,4, 0,5H), 2,21 – 2,03 (m, 1,5H), 1,92 – 1,81 (m, 2H), 1,80 – 1,48 (m, 4H), 1,42 – 1,21 (m, 3,5H), 0,94 (d, J = 6,6, 1,5H), 0,93 (d, J = 6,6, 1,5H), 0,90 (d, J = 6,6, 1,5H), 0,87 (d, J = 6,6, 1,5H); MS (ESI+) m/z 412 $(M+H)^+$.

Ejemplo 161

N^1-{(3a*S,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida**

El compuesto del título se preparó utilizando N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 148 en lugar de N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida en el procedimiento descrito en el Ejemplo 158: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,33 (s, 1H), 7,76 (s, 1H), 7,63 – 7,58 (m, 2H), 7,45 (d, J = 4,3, 1H), 4,40 (dd, J = 6,5, 12,5, 1H), 3,63 – 3,53 (m, 1H), 3,46 (dd, J = 6,1, 13,6, 1H),

2,82 – 2,73 (m, 1H), 2,69 – 2,51 (m, 2H), 2,48 – 2,38 (m, 1H), 2,33 (dd, *J* = 8,8, 16,3, 1H), 2,24 (dd, *J* = 7,6, 16,5, 1H), 2,16 – 1,88 (m, 5H), 1,85 (dt, *J* = 7,8, 15,2, 0,5H), 1,76 – 1,62 (m, 1H), 1,39 (qd, *J* = 6,6, 14,9, 1,5H), 1,31 – 1,20 (m, 2H), 0,95 (d, *J* = 6,0, 3H), 0,91 (dd, *J* = 3,2, 5,6, 3H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Ejemplo 162

N^1-{(3a*S,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida**

El compuesto del título se preparó utilizando N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida del Ejemplo 149 en lugar de N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida en el procedimiento descrito en el Ejemplo 158: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,31 (s, 1H), 7,75 (s, 1H), 7,62 – 7,53 (m, 2H), 7,44 (dd, *J* = 7,4, 15,0, 1H), 4,44 – 4,35 (m, 1H), 3,60 (d, *J* = 13,5, 2H), 3,46 (dd, *J* = 5,5, 13,5, 1H), 2,87 – 2,79 (m, 1H), 2,57 – 2,43 (m, 2H), 2,42 – 2,37 (m, 1H), 2,32 (dt, *J* = 3,0, 8,8, 1H), 2,27 – 2,20 (m, 1H), 2,08 (td, *J* = 6,0, 12,2, 1H), 1,96 – 1,80 (m, 3H), 1,61 – 1,50 (m, 2H), 1,44 – 1,35 (m, 1H), 1,30 – 1,19 (m, 2H), 0,90 (d, *J* = 6,2, 3H), 0,85 (d, *J* = 6,2, 3H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Ejemplo 163

N^2-metil-N^1-{(3a*S,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida**

El compuesto del título se preparó utilizando N^2-(*tert*-butiloxicarbonil)-N^2-metil-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida del Ejemplo 150 en lugar de N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida en el procedimiento descrito en el Ejemplo 158: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,32 (d, *J* = 6,0, 1H), 7,76 (s, 1H), 7,61 (d, *J* = 7,6, 1H), 7,55 (d, *J* = 14,8, 1H), 7,45 (t, *J* = 7,7, 1H), 4,47 – 4,40 (m, 1H), 3,61 (d, *J* = 13,5, 1H), 3,47 (dd, *J* = 3,1, 13,6, 1H), 3,30 (t, *J* = 6,7, 1H), 2,86 (d, *J* = 8,9, 1H), 2,59 – 2,51 (m, 1H), 2,46 (d, *J* = 2,5, 3H), 2,42 (dd, *J* = 8,5, 15,4, 1H), 2,35 – 2,30 (m, 1H), 2,28 – 2,23 (m, 1H), 2,14 – 2,05 (m, 1H), 1,93 – 1,82 (m, 2H), 1,74 (ddd, *J* = 4,0, 9,7, 13,7, 1H), 1,62 (dt, *J* = 7,4, 15,4, 1H), 1,40 (dt, *J* = 14,2, 15,7, 1H), 1,3 – 1,22 (m, 3H), 0,91 (dt, *J* = 3,0, 6,0, 3H), 0,85 (d, *J* = 6,7, 3H); MS (ESI+) *m/z* 412 $(M+H)^+$.

Ejemplo 164

N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando N^2-(*tert*-butiloxicarbonil)-N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 153 en lugar de N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida en el procedimiento descrito en el Ejemplo 158: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,56 (d, *J* = 7,4, 1H), 7,91 (s, 1H), 7,67 (d, *J* = 7,6, 1H), 7,61 (d, *J* = 7,8, 1H), 7,47 (t, *J* = 7,7, 1H), 4,54 (dt, *J* = 6,6, 13,2, 1H), 3,81 (d, *J* = 13,2, 1H), 3,32 (dd, *J* = 6,0, 7,9, 1H), 3,28 (d, *J* = 13,2, 1H), 2,81 (d, *J* = 9,5, 1H), 2,78 – 2,71 (m, 1H), 2,48 – 2,44 (m, 1H), 2,42 (s, 3H), 2,33 (d, *J* = 9,1, 1H), 2,26 (dd, *J* = 7,4, 9,3, 1H), 2,16 – 2,11 (m, 1H), 1,91 – 1,83 (m, 2H), 1,82 – 1,75 (m, 1H), 1,65 (ddq, *J* = 6,3, 12,1, 18,8, 3H), 1,26 (td, *J* = 6,2, 12,7, 1H), 0,95 (d, *J* = 6,5, 3H), 0,90 (d, *J* = 6,6, 3H); MS (ESI+) *m/z* 412 $(M+H)^+$.

Ejemplo 165

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida

El compuesto del título se preparó utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida del Ejemplo 151 en lugar de N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida en el procedimiento descrito en el Ejemplo 158: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,35 (d, *J* = 6,9, 1H), 7,44 (d, *J* = 7,4, 2H), 7,37 (t, *J* = 7,6, 2H), 7,27 (t, *J* = 7,3, 1H), 4,50 – 4,42 (m, 1H), 3,61 (d, *J* = 13,1, 1H), 3,45 (d, *J* = 13,2, 1H), 3,33 (t, *J* = 7,0, 1H), 2,87 (d, *J* = 8,7, 1H), 2,56 – 2,50 (m, 1H), 2,47 (s, 3H), 2,43 (dd, *J* = 5,5, 14,6, 1H), 2,37 (d, *J* = 8,7, 1H), 2,29 – 2,23 (m, 1H), 2,17 – 2,04 (m, 1H), 1,94 – 1,82 (m, 2H), 1,79 – 1,73 (m, 1H), 1,68 – 1,57 (m, 1H), 1,41 (dd, *J* = 7,2, 13,5, 1H), 1,27 (s, 2H), 0,92 (d, *J* = 6,6, 3H), 0,85 (d, *J* = 6,6, 3H); MS (ESI+) *m/z* 344 $(M+H)^+$.

Ejemplo 166

N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando N^2-(*tert*-butiloxicarbonil)-N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 155 en lugar de N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida en el procedimiento descrito en el Ejemplo 158: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,09 – 7,97 (m, 1H), 7,76 (s, 1H), 7,63 – 7,61 (m, 1H), 7,45 (d, *J* = 7,6, 1H), 7,42 (d, *J* = 7,6, 1H), 4,49 – 4,40 (m, 1H), 3,60 (d, *J* = 12,4, 1H), 3,47 (d, *J* = 13,6, 1H), 2,87 (d, *J* = 7,6, 1H), 2,59 (d, *J* = 9,4, 4H), 2,43 (dt, *J* = 7,2, 9,1, 1H), 2,34 (dd, *J* = 1,7, 8,9, 1H), 2,28 – 2,23 (m, 1H), 2,16 – 2,03 (m, 2H), 1,98 – 1,77 (m, 3H), 1,70 – 1,61 (m, 1H), 1,46 – 1,33 (m, 1H), 1,32 – 1,21 (m, 2H), 0,93 (d, *J* = 6,4, 3H), 0,86 (d, *J* = 6,4, 3H); MS (ESI+) *m/z* 412 $(M+H)^+$.

Ejemplo 167

N^2-metil-N^2-(metilsulfonil)-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

A N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 164 (122 mg, 0,296 mmol) en diclorometano (0,5 ml) *N,N*-diisopropiletilamina (78 µL, 0,445 mmol) seguido por cloruro de metansulfonilo (25,4 µL, 0,326 mmol), y la mezcla de la reacción se agitó a temperatura ambiente durante la noche. La reacción se redujo en volumen y se cargó en un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-12). El compuesto del título se eluyó con un gradiente demetanol de 0% a 5% (amoníaco 2 N)/diclorometano a lo largo de 20 minutos: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,59 (d, *J* = 6,7, 1H), 7,73 (s, 1H), 7,66 (d, *J* = 7,6, 1H), 7,62 (d, *J* = 7,8, 1H), 7,51 (t, *J* = 7,7, 1H), 4,78 (dd, *J* = 6,2, 9,5, 1H), 4,41 – 4,33 (m, 1H), 3,67 (d, *J* = 13,3, 1H), 3,16 (s, 3H), 3,15 (s, 3H), 2,90 (qd, *J* = 3,3, 7,9, 1H), 2,75 (dd, *J* = 3,3, 9,6, 1H), 2,53 – 2,44 (m, 1H), 2,38 – 2,29 (m, 3H), 1,89 – 1,70 (m, 4H), 1,70 – 1,58 (m, 3H), 1,36 – 1,26 (m, 1H), 0,83 (d, *J* = 6,6, 3H), 0,81 (d, *J* = 6,5, 3H); MS (ESI+) *m/z* 490 $(M+H)^+$.

Ejemplo 168

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-N^2-(metilsulfonil)-L-leucinamida

El compuesto del título se preparó utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida del Ejemplo 165 en lugar de N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida en el procedimiento descrito en Ejemplo 167: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,97 (d, *J* = 7,0, 1H), 7,43 (d, *J* = 7,3, 2H), 7,37 (d, *J* = 7,3, 2H), 7,30 – 7,25 (m, 1H), 4,78 (dd, *J* = 5,1, 10,2, 1H), 4,42 – 4,35 (m, 1H), 3,58 (d, *J* = 13,1, 1H), 3,46 (d, *J* = 13,2, 1H), 3,21 (s, 3H), 3,12 (s, 3H), 2,83 (d, *J* = 8,7, 1H), 2,55 – 2,47 (m, 2H), 2,36 (dd, *J* = 8,1, 14,7, 2H), 2,26 – 2,22 (m, 1H), 2,13 (dt, *J* = 5,9, 11,7, 1H), 1,93 – 1,82 (m, 2H), 1,70 – 1,61 (m, 2H), 1,44 – 1,36 (m, 1H), 0,82 (d, *J* = 6,2, 3H), 0,73 (d, *J* = 5,9, 3H); MS (ESI+) *m/z* 422 $(M+H)^+$.

Ejemplo 169

N^2-metil-N^2-(metilsulfonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 166 en lugar de N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida en el procedimiento descrito en Ejemplo 167: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,98 (d, *J* = 7,4, 1H), 7,77 (s, 1H), 7,62 – 7,58 (m, 2H), 7,45 (t, *J* = 7,7, 1H), 4,78 (dd, *J* = 5,0, 10,2, 1H), 4,41 – 4,33 (m, 1H), 3,59 (d, *J* = 13,5, 1H), 3,48 (d, *J* = 13,6, 1H), 3,21 (s, 3H), 3,12 (s, 3H), 2,84 (d, *J* = 7,4, 1H), 2,51 (t, *J* = 5,4, 2H), 2,37 (dd, *J* = 6,9, 8,9, 1H), 2,32 (d, *J* = 7,1, 1H), 2,23 (dd, *J* = 6,8, 8,9, 1H), 2,11 (dd, *J* = 5,8, 11,8, 1H), 1,93 – 1,82 (m, 2H), 1,70 – 1,61 (m, 3H), 1,44 – 1,35 (m, 1H), 0,82 (d, *J* = 6,2, 3H), 0,73 (d, *J* = 6,0, 3H); MS (ESI+) *m/z* 490 $(M+H)^+$.

Ejemplo 170

N^2-(metilsulfonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

Paso A: *N*-(*tert*-Butoxicarbonil)-L-leucina (180 mg, 0,778 mmol), hidroxibenzotriazol (119 mg, 0,778 mmol), y (3a*S*,4*R*,6a*R*)-2-(3-

(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina (201 mg, 0,707 mmol) del Ejemplo 154 Paso A se combinaron en diclorometano (1 ml). Luego de 20 minutos, se agregó *N*-(3-dimetilaminopropil)-*N'*-etilcarbodiimida (0,138 ml, 0,778 mmol) y la reacción se agitó a temperatura ambiente por 24 horas. La reacción se detuvo con agua, y las capas se separaron. La capa acuosa se extrajo con 1 ml de diclorometano. Las capas orgánicas combinadas se aplicaron a un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS15-24) y se eluyó con 1-10% metanol (amoníaco 2 N)/diclorometano para dar N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,66 (d, *J* = 7,1, 1H), 7,97 (d, *J* = 8,5, 1H), 7,73 (s, 1H), 7,56 (s, 2H), 7,44 (t, *J* = 7,7, 1H), 4,70 (dd, *J* = 5,9, 11,0, 1H), 4,40 (br s, 1H), 3,56 (d, *J* = 13,5, 1H), 3,41 (d, *J* = 13,5, 1H), 2,74 (d, *J* = 8,9, 1H), 2,48 (s, 2H), 2,37 – 2,31 (m, 1H), 2,27 (d, *J* = 8,4, 1H), 2,24 – 2,19 (m, 1H), 2,12 (dq, *J* = 6,0, 12,0, 1H), 1,91 – 1,81 (m, 4H), 1,66 (td, *J* = 7,4, 14,7, 1H), 1,50 (s, 9H), 1,43 – 1,35 (m, 1H), 0,87 (d, *J* = 5,9, 3H), 0,84 (d, *J* = 5,6, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Paso B: Se trató N^2-(*tert*-Butiloxicarbonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Paso A (0,731 g, 1,469 mmol) en etanol (5 ml) con HCl (4 *N* en dioxano, 10,0 ml, 40,0 mmol). La reacción se agitó a temperatura ambiente por 2 horas y el solvente se eliminó al vacío. La reacción se detuvo con bicarbonato de sodio acuoso saturado y se extrajo con 3×50 ml de diclorometano. El solvente se eliminó al vacío para dar N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,27 (d, *J* = 7,6, 1H), 7,75 (s, 1H), 7,63 – 7,54 (m, 2H), 7,44 (dd, *J* = 6,9; 14,6, 1H), 4,44 – 4,33 (m, 1H), 3,62 – 3,53 (m, 2H), 3,45 (d, *J* = 13,5, 1H), 2,84 (dd, *J* = 2,5, 8,9, 1H), 2,52 (dd, *J* = 7,2, 14,0, 1H), 2,50 – 2,43 (m, 1H), 2,42 – 2,37 (m, 1H), 2,32 (dd, *J* = 2,8, 9,0, 1H), 2,23 (dd, *J* = 7,2, 8,8, 1H), 2,09 (td, *J* = 6,0, 12,0, 2H), 1,94 – 1,81 (m, 4H), 1,61 – 1,50 (m, 2H), 1,39 (ddt, *J* = 6,3, 8,7, 12,6, 1H), 0,90 (d, *J* = 6,4, 3H), 0,84 (d, *J* = 6,3, 3H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Paso C: El compuesto del título se preparó utilizando N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Paso B en lugar de N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-

(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida en el procedimiento descrito en Ejemplo 167: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,41 (d, *J* = 9,4, 1H), 9,22 (d, *J* = 7,3, 1H), 7,76 (s, 1H), 7,59 (d, *J* = 14,0, 2H), 7,43 (dd, *J* = 6,2, 13,9, 1H), 4,47 (tt, *J* = 6,3, 12,5, 2H), 3,59 (d, *J* = 13,5, 1H), 3,48 (d, *J* = 13,6, 1H), 3,17 (s, 3H), 2,87 (dd, *J* = 2,3, 9,1, 1H), 2,59 – 2,50 (m, 2H), 2,38 (dd, *J* = 7,0, 9,0, 1H), 2,34 (dd, *J* = 2,3, 9,0, 1H), 2,24 (dd, *J* = 6,9, 8,8, 1H), 2,20 – 2,12 (m, 1H), 1,99 (dq, *J* = 6,7, 20,2, 1H), 1,89 (ddd, *J* = 6,0, 10,8, 15,0, 2H), 1,80 – 1,66 (m, 2H), 1,43 (ddd, *J* = 6,3, 10,7, 12,2, 1H), 0,82 (d, *J* = 6,7, 3H), 0,79 (d, *J* = 6,6, 3H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Ejemplo 171

N^2-(metilsulfonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-D-leucina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina en el procedimiento descrito en el Paso A y luego siguiendo los procedimientos descritos en Pasos B y C de Ejemplo 170: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,42 (d, *J* = 9,3, 1H), 9,22 (d, *J* = 7,3, 1H), 7,78 (s, 1H), 7,61 (d, *J* = 7,7, 2H), 7,44 (dd, *J* = 8,7, 16,4, 1H), 4,51 – 4,41 (m, 2H), 3,62 (d, *J* = 13,5, 1H), 3,49 (d, *J* = 13,6, 1H), 3,19 (s, 3H), 2,87 (dd, *J* = 2,8, 9,1, 1H), 2,66 – 2,60 (m, 1H), 2,55 (dd, *J* = 9,0, 15,6, 1H), 2,49 (dd, *J* = 7,3, 9,0, 1H), 2,33 (dd, *J* = 3,0, 9,0, 1H), 2,30 – 2,25 (m, 1H), 2,12 (dq, *J* = 5,8, 11,9, 1H), 1,98 (td, *J* = 6,7, 13,5, 1H), 1,93 – 1,83 (m, 2H), 1,77 (ddd, *J* = 5,6, 8,5, 13,8, 1H), 1,63 (dt, *J* = 7,5, 19,4, 1H), 1,45 – 1,36 (m, 1H), 0,82 (d, *J* = 6,7, 3H), 0,78 (d, *J* = 6,5, 3H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Ejemplo 172

N^2-(ciclopropilsulfonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando cloruro de ciclopropansulfonilo en lugar de cloruro de metansulfonilo y N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 170 Paso B en lugar de N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida en el procedimiento descrito en Ejemplo 167: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,34 (d, *J* = 9,4, 1H), 9,03 (d, *J* = 7,2, 1H), 7,76 (s, 1H), 7,60 (d, *J* = 10,5, 2H), 7,44 (dd,

J = 6,1, 13,8, 1H), 4,45 (dd, *J* = 6,4, 11,7, 2H), 3,57 (d, *J* = 13,5, 1H), 3,49 (d, *J* = 13,5, 1H), 2,84 (dd, *J* = 2,4, 9,1, 1H), 2,80 – 2,73 (m, 1H), 2,61 – 2,50 (m, 2H), 2,38 (dd, *J* = 7,0, 8,9, 1H), 2,34 (dd, *J* = 2,5, 9,0, 1H), 2,28 – 2,23 (m, 1H), 2,18 (td, *J* = 5,8, 11,9, 1H), 2,04 (dt, *J* = 6,9, 20,3, 1H), 1,91 (ddd, *J* = 4,1, 7,2, 14,3, 2H), 1,77 (ddd, *J* = 5,3, 8,7, 13,8, 1H), 1,73 – 1,65 (m, 1H), 1,44 (ddd, *J* = 6,1, 12,3, 18,6, 1H), 1,33 (td, *J* = 4,7, 11,0, 1H), 1,22 – 1,16 (m, 1H), 0,91 (ddd, *J* = 4,5, 8,5, 11,2, 1H), 0,88 – 0,85 (m, 1H), 0,84 (d, *J* = 6,7, 3H), 0,82 (d, *J* = 6,6, 3H); MS (ESI+) *m/z* 502 $(M+H)^+$.

Ejemplo 173

N^2-(isobutilsulfonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando cloruro de 2-metilpropan-1-sulfonilo en lugar de cloruro de metansulfonilo y N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 170 Paso B en lugar de N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida en el procedimiento descrito en Ejemplo 167: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,34 (d, *J* = 9,3, 1H), 9,20 (d, *J* = 7,4, 1H), 7,77 (s, 1H), 7,62 (d, *J* = 7,6, 1H), 7,60 – 7,55 (m, 1H), 7,45 (t, *J* = 7,7, 1H), 4,52 – 4,43 (m, 2H), 3,61 (d, *J* = 13,5, 1H), 3,52 (d, *J* = 13,6, 1H), 3,19 – 3,16 (m, 2H), 2,91 (dd, *J* = 2,0, 9,0, 1H), 2,63 – 2,46 (m, 3H), 2,42 (dd, *J* = 6,8, 8,9, 1H), 2,37 (dd, *J* = 2,1, 9,0, 1H), 2,27 (dd, *J* = 6,9, 8,8, 1H), 2,18 (td, *J* = 5,8, 11,7, 1H), 2,01 (tt, *J* = 6,7, 13,4, 1H), 1,96 – 1,85 (m, 2H), 1,73 (tdd, *J* = 6,3, 10,3, 14,9, 2H), 1,45 (ddt, *J* = 6,2, 9,0, 12,2, 1H), 1,08 (d, *J* = 6,7, 3H), 1,04 (d, *J* = 6,7, 3H), 0,81 (app t, *J* = 7,0, 6H); MS (ESI+) *m/z* 518 $(M+H)^+$.

Ejemplo 174

N^2-(ciclopropilsulfonil)-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

Paso A: Se preparó N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida como se describe en los procedimientos en Ejemplo 170 Pasos A-B utilizando (3a*S*,4*S*,6a*R*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina de 152 Paso A en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina: ^{1}H NMR (500 MHz,

piridin-d_5) δ ppm 8,57 - 8,51 (m, 1H), 7,90 (bs, 1H), 7,71 - 7,65 (m, 1H), 7,47 (t, *J* = 7,7, 1H), 4,57 - 4,49 (m, 1H), 3,73 (d, *J* = 13,1, 1H), 3,66 - 3,59 (m, 1H), 3,35 (d, *J* = 13,1, 1H), 2,80 (dd, *J* = 2,6, 9,4, 1H), 2,78 - 2,69 (m, 1H), 2,49 - 2,40 (m, 1H), 2,35 (dd, *J* = 2,5, 9,0, 1H), 2,24 - 1,79 (m, 7H), 1,73 - 1,50 (m, 3H), 1,47 - 1,21 (m, 2H), 0,95 - 0,85 (m, 6H).

Paso B: A N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Paso A (80 mg, 0,184 mmol) en diclorometano (0,5 ml) se agregó trietilamina (0,064 ml, 0,461 mmol) seguido por cloruro de ciclopropansulfonilo (38,9 mg, 0,277 mmol) en una solución de 300 µL diclorometano y la mezcla de la reacción se agitó a temperatura ambiente durante la noche. La reacción se redujo en volumen y se cargó en un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-12). El compuesto del título se eluyó con un gradiente de acetato de etilo del 20% al 100%/hexanos a lo largo de 20 minutos para dar N^2-(ciclopropilsulfonil)-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,34 (d, *J* = 9,0, 1H), 8,84 (d, *J* = 6,8, 1H), 7,73 (s, 1H), 7,64 (d, *J* = 7,5, 1H), 7,59 (d, *J* = 12,3, 1H), 7,43 (dd, *J* = 6,6, 14,3, 1H), 4,53 – 4,42 (m, 2H), 3,76 (d, *J* = 13,2, 1H), 3,41 (d, *J* = 13,2, 1H), 2,99 (qd, *J* = 4,2, 8,0, 1H), 2,90 (dd, *J* = 3,6, 9,5, 1H), 2,82 – 2,74 (m, 1H), 2,57 – 2,48 (m, 1H), 2,40 (dd, *J* = 8,5, 19,8, 2H), 2,30 (dd, *J* = 3,4, 9,2, 1H), 2,02 (td, *J* = 6,5, 13,7, 1H), 1,94 – 1,85 (m, 2H), 1,85 – 1,78 (m, 1H), 1,71 (td, *J* = 6,2, 11,6, 1H), 1,67 – 1,58 (m, 1H), 1,40 – 1,28 (m, 2H), 1,22 (dt, *J* = 4,7, 10,8, 1H), 0,93 (ddd, *J* = 6,6, 12,3, 14,0, 2H), 0,87 (d, *J* = 6,5, 3H), 0,84 (d, *J* = 6,7, 3H); MS (ESI+) *m/z* 502 $(M+H)^+$.

Ejemplo 175

N^2-acetil-N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

A N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida (123 mg, 0,299 mmol) del Ejemplo 164 en diclorometano (0,5 ml) se agregó *N*,*N*-diisopropiletilamina (78 µL, 0,448 mmol) seguido por anhídrido acético (33,9 µL, 0,359 mmol), y la mezcla de la reacción se agitó a temperatura ambiente durante la noche. La reacción se redujo en volumen y se cargó en un cartucho de gel de

sílice (Analogix®, Burlington, Wisconsin, RS-12), y el producto se eluyó con un gradiente demetanol de 0% a 5% (amoníaco 2 N)/diclorometano a lo largo de 20 minutos. El solvente se eliminó al vacío para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,10 (d, J = 7,1, 1H), 7,81 (d, J = 7,5, 1H), 7,76 (s, 1H), 7,63 (d, J = 7,8, 1H), 7,56 (d, J = 7,7, 1H), 5,54 (dd, J = 6,5, 9,2, 1H), 4,41 (dt, J = 7,3, 14,5, 1H), 3,62 (d, J = 13,2, 1H), 3,49 (d, J = 13,2, 1H), 3,01 (s, 3H), 2,84 – 2,77 (m, 1H), 2,73 (dd, J = 2,8, 9,5, 1H), 2,48 – 2,41 (m, 1H), 2,34 (dd, J = 2,8, 9,0, 1H), 2,25 (dt, J = 7,7, 17,0, 2H), 2,09 (s, 3H), 1,85 (ddd, J = 5,6, 9,9, 13,2, 1H), 1,81 – 1,70 (m, 2H), 1,66 – 1,46 (m, 3H), 1,30 – 1,23 (m, 1H), 0,87 (d, J = 2,7, 3H), 0,85 (d, J = 2,6, 3H); MS (ESI+) m/z 454 $(M+H)^+$.

Ejemplo 176

N^2-(2,2-dimetilpropanoil)-N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

A N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida (38,9 mg, 0,095 mmol) del Ejemplo 166 en diclorometano (0,5 ml) se agregó *N*,*N*-diisopropiletilamina (24,77 µL, 0,142 mmol) seguido por cloruro de pivaloilo (12,79 µL, 0,104 mmol), y la mezcla de reacción resultante se agitó a temperatura ambiente durante la noche. La reacción se redujo en volumen y se cargó en un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-4). El compuesto del título se eluyó con un gradiente de acetato de etilo ente 0% y 100%/hexanos a lo largo de 15 minutos: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,81 (d, J = 7,4, 1H), 7,74 (s, 1H), 7,60 – 7,55 (m, 2H), 7,43 (dd, J = 6,6, 14,3, 1H), 5,45 (dd, J = 7,0, 8,7, 1H), 4,35 – 4,29 (m, 1H), 3,57 (d, J = 13,5, 1H), 3,44 (d, J = 13,5, 1H), 3,13 (s, 3H), 2,73 (dd, J = 2,6, 8,9, 1H), 2,53 – 2,45 (m, 1H), 2,41 (ddd, J = 2,7, 8,3, 12,0, 1H), 2,37 – 2,32 (m, 1H), 2,29 (dd, J = 3,0, 9,0, 1H), 2,26 – 2,21 (m, 1H), 2,05 (dq, J = 6,0, 12,0, 1H), 1,86 – 1,80 (m, 3H), 1,55 (ddd, J = 6,9, 12,8, 19,6, 2H), 1,41 – 1,31 (m, 1H), 1,30 (s, 9H), 0,88 (d, J = 6,7, 3H), 0,82 (d, J = 6,6, 3H); MS (ESI+) m/z 496 $(M+H)^+$.

Ejemplo 177

N^2-(2,2-dimetilpropanoil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó como se describe en Ejemplo 176

utilizando N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 170 Paso B en lugar de N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,77 (d, *J* = 7,3, 1H), 7,86 (d, *J* = 8,4, 1H), 7,73 (s, 1H), 7,60 – 7,55 (m, *J* = 10,6, 2H), 7,45 (t, *J* = 7,7, 1H), 4,42 – 4,35 (m, 1H), 3,55 (d, *J* = 13,5, 1H), 3,41 (d, *J* = 13,5, 1H), 2,71 (d, *J* = 9,0, 1H), 2,50 (s, 2H), 2,34 (dd, *J* = 6,9, 8,9, 1H), 2,29 – 2,20 (m, 2H), 2,12 (dq, *J* = 6,1, 12,3, 1H), 1,94 – 1,74 (m, 5H), 1,66 (dt, *J* = 7,1, 19,3, 1H), 1,39 (d, *J* = 6,9, 1H), 1,33 (s, 9H), 0,84 (d, *J* = 6,1, 3H), 0,82 (d, *J* = 6,1, 3H); MS (ESI+) *m/z* 482 $(M+H)^+$.

Ejemplo 178

(S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de isobutilo

El compuesto del título se preparó utilizando cloroformiato de isobutilo en lugar de cloruro de metansulfonilo y N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 170 Paso B en lugar de N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida en el procedimiento descrito en Ejemplo 167: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,83 (d, *J* = 6,8, 1H), 8,42 (d, *J* = 8,5, 1H), 7,73 (s, 1H), 7,65 – 7,53 (m, 2H), 7,46 – 7,40 (m, 1H), 4,77 (dd, *J* = 7,5, 15,2, 1H), 4,48 – 4,39 (m, 1H), 4,01 (dd, *J* = 6,7, 10,3, 1H), 3,92 (dd, *J* = 6,7, 10,4, 1H), 3,56 (d, *J* = 13,4, 1H), 3,40 (d, *J* = 13,5, 1H), 2,77 (d, *J* = 7,0, 1H), 2,57 – 2,45 (m, 2H), 2,38 – 2,32 (m, 1H), 2,30 – 2,24 (m, 1H), 2,23 – 2,19 (m, 1H), 2,14 (td, *J* = 5,9, 11,9, 1H), 1,95 – 1,79 (m, 5H), 1,73 – 1,63 (m, 1H), 1,45 – 1,34 (m, 1H), 0,87 (d, *J* = 5,9, 3H), 0,84 (d, *J* = 5,8, 3H), 0,82 (d, *J* = 4,3, 3H), 0,80 (d, *J* = 4,3, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Ejemplo 179

(S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de ciclopentilo

El compuesto del título se preparó utilizando cloroformiato de ciclopentilo en lugar de cloruro de metansulfonilo y N^1-{(3a*S*,4*R*,6a*R*)-2-[3-

(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 170 Paso B en lugar de N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida en el procedimiento describe en Ejemplo 167: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,82 (d, *J* = 7,0, 1H), 8,26 (d, *J* = 8,6, 1H), 7,73 (s, 1H), 7,62 – 7,53 (m, 2H), 7,43 (t, *J* = 7,8, 1H), 5,32 – 5,24 (m, 1H), 4,77 (dd, *J* = 7,0, 15,0, 1H), 4,47 – 4,36 (m, 1H), 3,56 (d, *J* = 13,4, 1H), 3,40 (d, *J* = 13,6, 1H), 2,76 (d, *J* = 9,0, 1H), 2,55 – 2,46 (m, 2H), 2,38 – 2,31 (m, 1H), 2,27 (d, *J* = 7,2, 1H), 2,21 (t, *J* = 7,9, 1H), 2,13 (dq, *J* = 6,2, 12,5, 1H), 1,94 – 1,83 (m, 4H), 1,77 (dd, *J* = 6,9, 12,4, 2H), 1,73 – 1,64 (m, 3H), 1,58 (dt, *J* = 8,0, 14,7, 2H), 1,39 (td, *J* = 9,0, 14,1, 3H), 0,87 (d, *J* = 5,9, 3H), 0,84 (d, *J* = 5,3, 3H); MS (ESI+) *m/z* 510 $(M+H)^+$.

Ejemplo 180

N^2-[(tert-butilamino)carbonil]-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

A N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida (113 mg, 0,284 mmol) del Ejemplo 170 Paso B en diclorometano (0,5 ml) se agregó 2-isocianato-2-metilpropano (35,1 µL, 0,313 mmol) y la mezcla de la reacción se agitó a temperatura ambiente durante la noche. La reacción se redujo en volumen y se cargó en un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-12). El compuesto del título se eluyó con un gradiente de metanol entre 0% y 10% (amoníaco 2 N)/diclorometano a lo largo de 20 minutos: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,74 (d, *J* = 8,3, 1H), 7,73 (s, 1H), 7,57 (d, *J* = 9,5, 2H), 7,44 (t, *J* = 7,7, 1H), 6,56 (d, *J* = 8,6, 1H), 6,33 (s, 1H), 4,88 (td, *J* = 5,6, 8,9, 1H), 4,41 – 4,33 (m, 1H), 3,56 (d, *J* = 13,5, 1H), 3,41 (d, *J* = 13,6, 1H), 2,71 (dd, *J* = 1,7, 9,2, 1H), 2,55 – 2,45 (m, 2H), 2,35 (dd, *J* = 6,9, 8,9, 1H), 2,29 – 2,20 (m, 2H), 2,11 (dq, *J* = 6,1, 12,1, 1H), 1,92 – 1,77 (m, 3H), 1,73 – 1,64 (m, 2H), 1,44 (s, 9H), 1,43 – 1,35 (m, 1H), 0,85 (d, *J* = 3,3, 3H), 0,84 (d, *J* = 3,2, 3H); MS (ESI+) *m/z* 497 $(M+H)^+$.

Ejemplo 181

N^2-[(ciclopentilamino)carbonil]-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando isocianatociclopentano en lugar de 2-isocianato-2-metilpropano como se describe en el procedimiento en

Ejemplo 180: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,84 (d, J = 7,2, 1H), 7,73 (s, 1H), 7,64 – 7,53 (m, 2H), 7,44 (t, J = 9,1, 2H), 6,60 (d, J = 7,4, 1H), 6,57 (d, J = 8,8, 1H), 4,42 – 4,36 (m, 2H), 3,56 (d, J = 13,7, 1H), 3,40 (d, J = 13,6, 1H), 2,73 (dd, J = 1,9, 9,3, 1H), 2,53 – 2,49 (m, 2H), 2,34 (dd, J = 7,0, 9,0, 1H), 2,26 (dd, J = 1,8, 8,9, 1H), 2,24 – 2,20 (m, 1H), 2,16 – 2,09 (m, 1H), 1,90 (tdd, J = 5,7, 12,5, 18,4, 4H), 1,80 (ddd, J = 5,7, 7,9, 13,6, 1H), 1,76 – 1,65 (m, 2H), 1,51 (dt, J = 6,3, 14,9, 3H), 1,41 (tt, J = 7,2, 11,8, 4H), 0,85 (d, J = 6,5, 6H); MS (ESI+) *m/z* 509 $(M+H)^+$.

Ejemplo 182

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

Paso A: Se preparó N^1-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida del Ejemplo 151 en lugar de *N*-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida en Ejemplo 53.

Paso B: A N^1-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida del Paso A (220 mg, 0,622 mmol) en diclorometano (5,0 ml) se agregó trietilamina (0,130 ml, 0,934 mmol) seguido por cloruro de 3-(trifluorometil)bencen-1-sulfonilo (0,110 ml, 0,685 mmol) y la mezcla de la reacción se agitó a temperatura ambiente durante la noche. La reacción se redujo en volumen y se cargó en un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-24). El compuesto del título se eluyó con un gradiente de metanol entre 0% y 10% (amoníaco 2 N)/diclorometano a lo largo de 20 minutos para dar N^2-(*tert*-butiloxicarbonil)-N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,32 (bs, 1H), 8,18 – 8,13 (m, 1H), 8,02 – 7,95 (m, 1H), 7,90 – 7,84 (m, 1H), 7,68 (t, J = 7,9, 1H), 4,17 – 4,09 (m, 1H), 3,77 – 3,69 (m, 1H), 3,20 – 3,11 (m, 2H), 3,05 – 2,97 (m, 4H), 2,53 – 2,47 (m, 2H), 1,98 – 1,88 (m, 1H), 1,87 – 1,71 (m, 3H), 1,62 – 1,48 (m, 3H), 1,46 (s, 9H), 1,32 – 1,22 (m, 1H), 0,87 (dd, J = 6,6, 15,5, 6H).

Paso C: El compuesto del título se preparó utilizando N^2-(*tert*-butiloxicarbonil)-N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-

(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida en lugar de N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida en el procedimiento descrito en Ejemplo 158: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,38 (s, 1H), 8,30 (d, *J* = 6,8, 1H), 8,20 (d, *J* = 7,8, 1H), 7,91 (d, *J* = 8,0, 1H), 7,72 (t, *J* = 7,8, 1H), 4,31 – 4,24 (m, 1H), 3,87 (dd, *J* = 2,2, 10,0, 1H), 3,21 – 3,17 (m, 2H), 3,15 (dd, *J* = 7,4, 9,9, 1H), 2,95 (dd, *J* = 7,2, 9,6, 1H), 2,60 – 2,49 (m, 2H), 2,38 (s, 3H), 2,00 – 1,92 (m, 2H), 1,91 – 1,80 (m, 2H), 1,68 (ddd, *J* = 5,8, 7,9, 13,6, 1H), 1,60 – 1,52 (m, 2H), 1,29 (ddd, *J* = 6,4, 12,8, 16,2, 1H), 0,89 (d, *J* = 6,6, 3H), 0,84 (d, *J* = 6,6, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 183

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó como se describe en Ejemplo 182 utilizando cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el Paso B: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,30 (d, *J* = 7,1, 1H), 8,14 (d, *J* = 8,2, 2H), 7,90 (d, *J* = 8,3, 2H), 4,30 – 4,23 (m, 1H), 3,86 (dd, *J* = 2,6, 10,0, 1H), 3,22 – 3,13 (m, 3H), 2,97 (dd, *J* = 7,3, 9,6, 1H), 2,61 – 2,50 (m, 2H), 2,39 (s, 3H), 2,00 – 1,92 (m, 2H), 1,91 – 1,80 (m, 2H), 1,68 (ddd, *J* = 5,9, 7,9, 13,7, 1H), 1,61 – 1,52 (m, 2H), 1,30 (ddt, *J* = 6,7, 9,9, 13,4, 1H), 0,90 (d, *J* = 6,6, 3H), 0,84 (d, *J* = 6,6, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 184

N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

Paso A: Se preparó N^1-[(3a*S*,4*R*,6a*R*)-2-Benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-L-leucinamida utilizando *N*-(*tert*-butoxicarbonil)-L-leucina en lugar de ácido (S)-2-fenilbutanoico en el procedimiento descrito en Ejemplo 16 Paso F: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,64 (d, *J* = 7,1, 1H), 7,97 (d, *J* = 8,5, 1H), 7,41 (d, *J* = 7,3, 2H), 7,36 (t, *J* = 7,5, 2H), 7,27 (t, *J* = 7,3, 1H), 4,71 (s, 1H), 4,41 (s, 1H), 3,56 (d, *J* = 13,1, 1H), 3,39 (d, *J* = 13,1, 1H), 2,74 (d, *J* = 8,9, 1H), 2,48 (s, 2H), 2,39 - 2,19 (m, 3H), 2,14 (td, *J* = 6,3, 12,4, 1H), 2,00 - 1,78 (m, 4H), 1,73 - 1,55 (m, 1H), 1,50 (s, 9H), 1,39 (d, *J* = 7,0, 1H), 0,86 (dd, *J* = 5,8, 13,4, 6H).

Paso B: El compuesto del título se preparó como se describe con los procedimientos en Ejemplo 182 Pasos A-C utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-L-leucinamida del Paso A en lugar de N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37 (s, 1H), 8,33 (d, *J* = 6,9, 1H), 8,18 (d, *J* = 7,9, 1H), 7,91 (d, *J* = 7,8, 1H), 7,72 (t, *J* = 7,9, 1H), 4,27 – 4,19 (m, 1H), 3,84 (dd, *J* = 2,5, 9,9, 1H), 3,55 (dd, *J* = 4,4, 9,3, 1H), 3,17 (dd, *J* = 2,7, 9,7, 1H), 3,07 (dd, *J* = 7,6, 9,8, 1H), 2,91 (dd, *J* = 7,3, 9,6, 1H), 2,55 – 2,45 (m, 2H), 2,09 (s, 1H), 1,97 – 1,78 (m, 5H), 1,52 (ddd, *J* = 4,5, 9,5, 18,5, 2H), 1,27 (ddt, *J* = 6,7, 9,6, 13,2, 1H), 0,89 (d, *J* = 6,4, 3H), 0,83 (d, *J* = 6,3, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Ejemplo 185 y Ejemplo 186

3-(trifluorometil)-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida (Ejemplo 185) y**

3-(trifluorometil)-*N*-{(3a*S,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida (Ejemplo 186)**

A (3a*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 122 Paso E (200 mg, 0,703 mmol) en diclorometano (2 ml) se agregó trietilamina (0,147 ml, 1,055 mmol) seguido por cloruro de 3-(trifluorometil)bencen-1-sulfonilo (0,124 ml, 0,774 mmol), y la mezcla de la reacción se agitó a temperatura ambiente durante la noche. La reacción se detuvo con agua y se extrajo con diclorometano. Los orgánicos se redujeron en volumen y se cargó en un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-24). Los compuestos del título se eluyeron con un gradiente de metanol entre 0% y 10% (amoníaco 2 N)/diclorometano a lo largo de 20 minutos.

Ejemplo 185: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,42 (s, 1H), 8,27 (d, *J* = 7,9, 1H), 7,82 (d, *J* = 7,8, 1H), 7,64 (s, 1H), 7,61 (d, *J* = 7,8, 1H), 7,57 (d, *J* = 8,2, 2H), 7,50 (d, *J* = 7,7, 1H), 7,40 (t, *J* = 7,7, 1H), 3,91 – 3,84 (m, 1H), 3,47 (d, *J* = 13,4, 1H), 3,37 (d, *J* = 13,4, 1H), 2,78 (dd, *J* = 4,3, 9,6, 1H), 2,69 (dd, *J* = 4,4, 7,7, 1H), 2,47 – 2,39 (m, 2H), 2,22 (dt, *J* = 8,0, 12,6, 2H), 1,89 (qd, *J* = 7,1, 11,0, 1H), 1,65 (dtd, *J* = 2,9, 6,2, 8,9, 1H), 1,57 – 1,47 (m, 1H), 1,34 – 1,26 (m, 1H); MS (ESI+) *m/z*

493 $(M+H)^+$.

Ejemplo 186: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,51 (d, *J* = 7,3, 1H), 8,43 (s, 1H), 8,30 (d, *J* = 7,9, 1H), 7,81 (d, *J* = 7,7, 1H), 7,72 (s, 1H), 7,60 (dd, *J* = 3,2, 7,9, 2H), 7,55 (d, *J* = 7,7, 1H), 7,46 (t, *J* = 7,7, 1H), 3,82 – 3,74 (m, 1H), 3,54 – 3,44 (m, 2H), 2,61 (dd, *J* = 1,9, 9,2, 1H), 2,57 – 2,44 (m, 2H), 2,33 (dd, *J* = 2,0, 9,0, 1H), 2,18 (ddd, *J* = 6,8, 9,0, 12,7, 2H), 1,96 (td, *J* = 5,9, 11,8, 1H), 1,89 – 1,79 (m, 1H), 1,64 – 1,54 (m, 1H), 1,29 (ddt, *J* = 6,4, 10,0, 12,6, 1H); MS (ESI+) *m/z* 493 $(M+H)^+$.

Ejemplo 187

3-(trifluorometil)-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida

El compuesto del título se preparó utilizando (3a*S*,4*S*,6a*R*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 152 Paso A en lugar de (3a*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 185: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,26 (s, 1H), 8,41 (s, 1H), 8,27 (d, *J* = 7,9, 1H), 7,82 (d, *J* = 7,8, 1H), 7,62 (d, *J* = 7,9, 1H), 7,57 (d, *J* = 9,8, 2H), 7,50 (d, *J* = 7,7, 1H), 7,40 (t, *J* = 7,7, 1H), 3,87 (dd, *J* = 7,1, 16,1, 1H), 3,48 (d, *J* = 13,4, 1H), 3,38 (d, *J* = 13,4, 1H), 2,77 (dd, *J* = 4,3, 9,6, 1H), 2,73 – 2,65 (m, 1H), 2,47 – 2,41 (m, 2H), 2,26 – 2,19 (m, 2H), 1,89 (qd, *J* = 7,1, 10,9, 1H), 1,65 (dtd, *J* = 2,9, 6,2, 8,9, 1H), 1,52 (dq, *J* = 8,3, 12,8, 1H), 1,34 – 1,26 (m, 1H); MS (ESI+) *m/z* 493 $(M+H)^+$.

Ejemplo 188

3-(trifluorometil)-*N*-{(3a*R*,4*R*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida

El compuesto del título se preparó utilizando (3a*R*,4*R*,6a*S*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 157 Paso A en lugar de (3a*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 185: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,27 (s, 1H), 8,42 (s, 1H), 8,27 (d, *J* = 7,9, 1H), 7,82 (d, *J* = 7,8, 1H), 7,64 (s, 1H), 7,62 (d, *J* = 7,9, 1H), 7,57 (d, *J* = 9,2, 1H), 7,50 (d, *J* = 7,6, 1H), 7,40 (t, *J* = 7,7, 1H), 3,87 (dd, *J* = 7,1, 16,2, 1H), 3,47 (d, *J* = 13,4, 1H), 3,37 (d, *J* = 13,4, 1H), 2,77 (dd, *J* = 4,3, 9,6, 1H), 2,73 – 2,66 (m, 1H), 2,47 – 2,41 (m, 2H), 2,26 – 2,19 (m, 2H), 1,89 (qd, *J* = 7,1, 11,0, 1H), 1,65 (dtd, *J* = 2,9, 6,2, 8,9, 1H), 1,52 (dq, *J* = 8,4, 12,9, 1H), 1,33 – 1,26 (m, 1H); MS (ESI+) *m/z* 493 $(M+H)^+$.

Ejemplo 189

3-(trifluorometil)-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida

El compuesto del título se preparó utilizando (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 154 Paso A en lugar de (3a*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 185: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,51 (d, *J* = 6,7, 1H), 8,43 (s, 1H), 8,30 (d, *J* = 7,8, 1H), 7,81 (d, *J* = 7,9, 1H), 7,72 (s, 1H), 7,62 – 7,52 (m, 3H), 7,45 (t, *J* = 7,6, 1H), 3,82 – 3,74 (m, 1H), 3,54 – 3,44 (m, 2H), 2,61 (d, *J* = 9,4, 1H), 2,57 – 2,44 (m, 2H), 2,33 (dd, *J* = 1,9, 9,0, 1H), 2,18 (ddd, *J* = 6,9, 9,0, 13,4, 2H), 1,96 (ddd, *J* = 5,1, 11,0, 16,3, 1H), 1,84 (dt, *J* = 7,5, 12,3, 1H), 1,58 (dt, *J* = 9,3, 12,1, 1H), 1,35 – 1,25 (m, 1H); MS (ESI+) *m/z* 493 $(M+H)^+$.

Ejemplo 190

***N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida**

El compuesto del título se preparó utilizando (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 16 Paso E en lugar de (3a*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 185: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,49 (d, *J* = 7,0, 1H), 8,43 (s, 1H), 8,29 (d, *J* = 7,9, 1H), 7,81 (d, *J* = 7,8, 1H), 7,60 (d, *J* = 8,0, 1H), 7,38 (d, *J* = 4,7, 4H), 7,33 – 7,27 (m, 1H), 3,84 – 3,75 (m, 1H), 3,47 (q, *J* = 13,1, 2H), 2,61 (dd, *J* = 2,0, 9,2, 1H), 2,56 – 2,43 (m, 2H), 2,35 (dd, *J* = 2,0, 9,0, 1H), 2,21 – 2,12 (m, 2H), 1,99 (td, *J* = 5,9, 11,7, 1H), 1,87 – 1,77 (m, 1H), 1,64 – 1,53 (m, 1H), 1,29 (ddt, *J* = 6,4, 10,0, 12,6, 1H); MS (ESI+) *m/z* 425 $(M+H)^+$.

Ejemplo 191

***N*-{(3a*S*,4*R*,6a*R*)-2-[6,6-bis(4-fluorofenil)hexil]octahidrociclopenta[*c*]pirrol-4–il}-3-(trifluorometil)bencenosulfonamida**

Paso A: *N*-((3a*S*,4*R*,6a*R*)-Octahidrociclopenta[*c*]pirrol-4–il)-3-(trifluorometil)bencenosulfonamida se preparó utilizando *N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida del Ejemplo 190 en lugar de *N*-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida en el procedimiento descrito en Ejemplo 53.

Paso B: El compuesto del título se preparó utilizando 6,6-bis(4-fluorofenil)hexanal en lugar de 3-(trifluorometil)benzaldehido y *N*-((3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il)-3-(trifluorometil)bencenosulfonamida del Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito en el Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,53 (d, *J* = 6,8, 1H), 8,46 (s, 1H), 8,33 (d, *J* = 7,9, 1H), 7,82 (d, *J* = 7,8, 1H), 7,63 (t, *J* = 7,8, 1H), 7,36 – 7,31 (m, 4H), 7,15 (t, *J* = 8,7, 4H), 3,97 (t, *J* = 7,8, 1H), 3,83 – 3,74 (m, 1H), 2,66 (d, *J* = 9,4, 1H), 2,56 – 2,43 (m, 2H), 2,39 (d, *J* = 8,5, 1H), 2,24 (dt, *J* = 5,8, 12,0, 2H), 2,10 – 2,04 (m, 2H), 2,04 – 1,99 (m, 2H), 1,99 – 1,91 (m, 1H), 1,87 (dt, *J* = 6,8, 11,4, 1H), 1,62 – 1,52 (m, 1H), 1,34 (ddd, *J* = 6,9, 17,6, 29,2, 7H); MS (ESI+) *m/z* 607 $(M+H)^+$.

Ejemplo 192

***N*-{(3a*S*,4*R*,6a*R*)-2-[3,5-bis(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-3-(trifluorometil)bencenosulfonamida**

El compuesto del título se preparó utilizando 3,5-bis(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido y *N*-((3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il)-3-(trifluorometil)bencenosulfonamida del Ejemplo 191 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito en el Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,53 (d, *J* = 7,4, 1H), 8,42 (s, 1H), 8,30 (d, *J* = 7,9, 1H), 8,03 (s, 1H), 7,96 (s, 2H), 7,81 (d, *J* = 7,8, 1H), 7,60 (t, *J* = 7,9, 1H), 3,82 – 3,74 (m, 1H), 3,59 (s, 2H), 2,68 – 2,64 (m, 1H), 2,59 – 2,49 (m, 2H), 2,38 – 2,33 (m, 1H), 2,23 (dt, *J* = 5,9, 8,9, 2H), 1,97 – 1,81 (m, 2H), 1,59 (ddd, *J* = 8,2, 11,8, 13,0, 1H), 1,35 – 1,24 (m, 1H); MS (ESI+) *m/z* 561 $(M+H)^+$.

Ejemplo 193

***N*-{(3a*S*,4*R*,6a*R*)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-3-(trifluorometil)bencenosulfonamida**

El compuesto del título se preparó utilizando 3,3-bis(4-fluorofenil)propanal en lugar de 3-(trifluorometil)benzaldehido y *N*-((3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il)-3-(trifluorometil)bencenosulfonamida del Ejemplo 191 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito en el

Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,56 (d, *J* = 7,4, 1H), 8,46 (s, 1H), 8,35 (d, *J* = 7,9, 1H), 7,80 (d, *J* = 7,8, 1H), 7,61 (d, *J* = 7,8, 1H), 7,37 (dd, *J* = 5,6, 8,4, 2H), 7,34 – 7,30 (m, 2H), 7,16 (dt, *J* = 8,7, 12,8, 4H), 4,19 (t, *J* = 7,7, 1H), 3,87 – 3,78 (m, 1H), 2,69 (d, *J* = 9,1, 1H), 2,55 – 2,44 (m, 2H), 2,39 (d, *J* = 8,7, 1H), 2,28 – 2,24 (m, 2H), 2,17 (dd, *J* = 7,8, 15,3, 2H), 2,06 (dd, *J* = 9,2, 16,3, 2H), 1,98 (dt, *J* = 5,7, 16,5, 1H), 1,89 (dd, *J* = 12,0, 19,0, 1H), 1,64 – 1,53 (m, 1H), 1,38 – 1,23 (m, 1H); MS (ESI+) *m/z* 565 $(M+H)^+$.

Ejemplo 194

***N*-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-3-(trifluorometil)bencenosulfonamida**

El compuesto del título se preparó utilizando 3-fluoro-4-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido y *N*-((3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il)-3-(trifluorometil)bencenosulfonamida del Ejemplo 191 Paso A en lugar de 2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida en el procedimiento descrito en el Ejemplo 54: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,56 (d, *J* = 6,8, 1H), 8,44 (s, 1H), 8,33 (d, *J* = 7,9, 1H), 7,82 (d, *J* = 7,6, 1H), 7,65 – 7,59 (m, 2H), 7,29 (d, *J* = 11,8, 1H), 7,21 (s, 1H), 3,81 – 3,74 (m, 1H), 3,46 (s, 2H), 2,64 (d, *J* = 9,3, 1H), 2,55 (ddd, *J* = 8,5, 13,8, 27,5, 2H), 2,35 (d, *J* = 8,7, 1H), 2,17 (dd, *J* = 7,9, 15,7, 2H), 1,99 (dt, *J* = 5,9, 16,5, 1H), 1,87 (dt, *J* = 7,3, 12,1, 1H), 1,60 (dt, *J* = 8,3, 10,0, 1H), 1,35 – 1,26 (m, 1H); MS (ESI+) *m/z* 510 $(M+H)^+$.

Ejemplo 195

***N*-[(3a*S*,4*S*,6a*R*)-2-(4-hidroxibutil)octahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida**

Paso A: *N*-((3a*S*,4*S*,6a*R*)-2-Benciloctahidrociclopenta[*c*]pirrol-4–il)-3-(trifluorometil)bencenosulfonamida se preparó utilizando (3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 14 Paso C en lugar de (3a*S**,6a*R**)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 185.

Paso B: *N*-((3a*S*,4*S*,6a*R*)-2-Benciloctahidrociclopenta[*c*]pirrol-4–il)-3-(trifluorometil)bencenosulfonamida (0,4237 g, 0,998 mmol) del Paso A en tetrahidrofurano (10 ml) se agregó a hidróxido de paladio al 20% sobre carbono

(húmedo, 0,085 g, 0,603 mmol) en una botella de presión de 50 ml bajo nitrógeno. La mezcla de la reacción luego se colocó bajo una atmósfera de hidrógeno (30 psi) y se agitó a 50 °C por 18 horas. La mezcla se filtró a través de una membrana de nylon y el solvente se eliminó al vacío. El material crudo se purificó mediante cromatografía sobre gel de sílice usando metanol al 1-10% (amoníaco 2 N)/diclorometano para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,50 (s, 1H), 8,38 (d, *J* = 7,9, 1H), 7,85 (d, *J* = 7,8, 1H), 7,68 (t, *J* = 7,8, 1H), 3,89 (dd, *J* = 8,4, 14,2, 1H), 3,82 (t, *J* = 6,2, 2H), 2,82 (dd, *J* = 3,3, 9,7, 1H), 2,62 (qd, *J* = 3,4, 7,9, 1H), 2,42 – 2,36 (m, 1H), 2,32 (d, *J* = 4,5, 2H), 2,26 (dd, *J* = 6,8, 11,7, 2H), 2,10 (t, *J* = 8,7, 1H), 1,91 – 1,82 (m, 1H), 1,74 – 1,67 (m, 2H), 1,64 – 1,49 (m, 5H), 1,32 (dd, *J* = 6,1, 9,6, 1H); MS (ESI+) *m/z* 407 $(M+H)^+$.

Ejemplo 196

(3a*S,4*S**,6a*R**)-*N*,*N*-diciclopropil-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4-amina**

Se combinó (3a*S**,4*S**,6a*R**)-2-(3-(Trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina (228 mg, 0,802 mmol) del Ejemplo 122 Paso E y (1-etoxiciclopropoxi)trimetilsilano (140 mg, 0,802 mmol) en diclorometano (1,5 ml) y se agregó 5 ml de ácido acético. La reacción se agitó a temperatura ambiente por 20 minutos, y luego se agregó PS-cianoborohidruro (343 mg, 0,802 mmol). La reacción se calentó a 40 °C durante la noche. La cromatografía sobre gel de sílice eluyendo con 1-10% metanol (amoníaco 2 N)/diclorometano dio el compuesto del título: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,58 (s, 1H), 7,48 (d, *J* = 7,6, 2H), 7,42 (d, *J* = 7,6, 1H), 3,64 (d, *J* = 13,6, 1H), 3,51 (d, *J* = 13,6, 1H), 2,94 – 2,82 (m, 3H), 2,80 – 2,71 (m, 2H), 2,55 (dd, *J* = 5,4, 9,4, 3H), 2,41 (t, *J* = 8,3, 1H), 2,16 (dd, *J* = 4,7, 8,7, 1H), 1,97 – 1,70 (m, 7H), 1,70 – 1,59 (m, 3H), 1,40 (dd, *J* = 6,7, 12,6, 1H); MS (ESI+) *m/z* 365 $(M+H)^+$.

Ejemplo 197 y Ejemplo 198

(3a*S,4*R**,6a*R**)-2-bencil-*N*-ciclopropiloctahidrociclopenta[*c*]pirrol-4-amina (Ejemplo 197) y**

(3a*S,4*S**,6a*R**)-2-bencil-*N*-ciclopropiloctahidrociclopenta[*c*]pirrol-4-amina (Ejemplo 198)**

Se combinó 2-bencilhexahidrociclopenta[*c*]pirrol-4(5*H*)-ona (0,578 g, 2,68

mmol), ciclopropilamina (0,189 ml, 2,68 mmol), y ácido acético (10 ml) en diclorometano (20 ml). Se agregó PS-Cianoborohidruro (1,147 g, 2,68 mmol). La reacción se agitó a temperatura ambiente por 2 horas, luego se filtró y la resina se lavó con diclorometano. El solvente se eliminó al vacío, y el material crudo se aplicó a una columna de gel de sílice y se eluyó con 1-10% metanol(amoníaco 2 N)/diclorometano para dar los compuestos del título.

(3a*S**,4*R**,6a*R**)-2-bencil-*N*-ciclopropiloctahidrociclopenta[*c*]pirrol-4-amina (Ejemplo 197): ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,34 – 7,29 (m, 2H), 7,28 – 7,20 (m, 2H), 3,56 (s, 2H), 3,14 (ddd, *J* = 5,7, 7,3, 10,5, 1H), 2,84 (t, *J* = 8,4, 1H), 2,77 – 2,55 (m, 3H), 2,41 (dd, *J* = 6,2, 9,4, 1H), 2,14 – 2,02 (m, 2H), 1,83 – 1,72 (m, 2H), 1,63 – 1,47 (m, 3H), 1,46 – 1,35 (m, 1H), 0,40 (tdd, *J* = 1,3, 3,0, 4,7, 2H), 0,31 (ddd, *J* = 2,8, 4,3, 6,2, 2H); MS (ESI+) *m/z* 256 $(M+H)^+$.

(3a*S**,4*S**,6a*R**)-2-bencil-*N*-ciclopropiloctahidrociclopenta[*c*]pirrol-4-amina (Ejemplo 198): ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,34 – 7,29 (m, 4H), 7,29 – 7,20 (m, 1H), 3,66 – 3,50 (m, 2H), 3,04 – 2,92 (m, 1H), 2,63 (s, 1H), 2,54 – 2,50 (m, 2H), 2,48 – 2,40 (m, 1H), 2,34 (dd, *J* = 3,8, 9,0, 1H), 2,26 (dt, *J* = 5,0, 16,3, 1H), 2,13 – 2,04 (m, 2H), 2,03 – 1,82 (m, 2H), 1,46 – 1,35 (m, 2H), 0,46 – 0,38 (m, 2H), 0,36 – 0,30 (m, 2H); MS (ESI+) *m/z* 256 $(M+H)^+$.

Ejemplo 199

_N_-[(3a_S_*,4_S_*,6a_R_*)-2-benciloctahidrociclopenta[_c_]pirrol-4–il]-_N_-ciclopropil-3-(trifluorometil)bencenosulfonamida

Se combinó (3a*S**,4*S**,6a*R**)-2-bencil-*N*-ciclopropiloctahidrociclopenta[*c*]pirrol-4-amina (382 mg, 1,490 mmol) del Ejemplo 198, trietilamina (312 µL, 2,235 mmol), y cloruro de 3-(trifluorometil)bencen-1-sulfonilo (262 µL, 1,639 mmol) en tetrahidrofurano (7 ml). Se agregó una cantidad catalítica de (dimetilamino)piridina, y la mezcla de la reacción se agitó a temperatura ambiente durante la noche. El solvente se redujo en volumen, y el material crudo se aplicó a gel de sílice y se eluyó con acetato de etilo del 20% al 100%/hexanos para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,46 (s, 1H), 8,31 (d, *J* = 7,9, 1H), 7,93 (d, *J* = 7,8, 1H), 7,74 (t, *J* = 7,9, 1H), 7,41 (d, *J* = 7,2, 2H), 7,36 (t, *J* = 7,4, 2H), 7,29 (t, *J* = 7,2, 1H), 3,97 (ddd, *J* = 6,1, 7,7, 13,5, 1H), 3,54 – 3,45 (m, 2H), 3,17 (dt, *J* = 5,9, 11,8, 1H), 2,82 (dd, *J* = 3,6, 9,7, 1H), 2,55 (t, *J* = 8,2, 1H), 2,51 – 2,43 (m, 2H), 2,36 – 2,22 (m, 2H), 1,88 – 1,82

(m, 1H), 1,57 (dt, *J* = 5,9, 11,6, 1H), 1,43 – 1,32 (m, 3H), 1,05 – 0,98 (m, 1H), 0,80 (ddd, *J* = 6,9, 9,8, 12,4, 1H), 0,73 – 0,65 (m, 1H); MS (ESI+) *m/z* 465 $(M+H)^+$.

Ejemplo 200

***N*-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*-ciclopropil-3-(trifluorometil)bencenosulfonamida**

El compuesto del título se preparó utilizando (3a*S**,4*R**,6a*R**)-2-bencil-*N*-ciclopropiloctahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 197 en lugar de (3a*S**,4*S**,6a*R**)-2-bencil-*N*-ciclopropiloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 199: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,45 (s, 1H), 8,29 (d, *J* = 7,8, 1H), 7,92 (d, *J* = 7,8, 1H), 7,69 (t, *J* = 7,9, 1H), 7,49 (d, *J* = 7,4, 2H), 7,41 (t, *J* = 7,6, 2H), 7,31 (t, *J* = 7,3, 1H), 4,41 (dd, *J* = 7,7, 17,3, 1H), 3,63 (d, *J* = 13,2, 1H), 3,53 (d, *J* = 13,2, 1H), 2,87 (d, *J* = 8,9, 1H), 2,70 (dd, *J* = 8,2, 15,9, 1H), 2,49 (d, *J* = 8,9, 1H), 2,46 – 2,37 (m, 1H), 2,16 – 2,07 (m, 2H), 1,99 – 1,94 (m, 1H), 1,84 – 1,77 (m, 1H), 1,73 – 1,65 (m, 1H), 1,65 – 1,57 (m, 1H), 1,35 – 1,25 (m, 1H), 1,18 (ddd, *J* = 5,1, 6,9, 10,5, 1H), 0,99 (dq, *J* = 4,7, 6,7, 1H), 0,81 – 0,74 (m, 1H), 0,69 (ddd, *J* = 6,9, 10,8, 11,8, 1H); MS (ESI+) *m/z* 465 $(M+H)^+$.

Ejemplo 201

***N*-ciclopropil-*N*-[(3a*S**,4*S**,6a*R**)-octahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida**

Se agregó (3a*S**,4*S**,6a*R**)-2-bencil-*N*-ciclopropiloctahidrociclopenta[*c*]pirrol-4-amina (0,308 g, 0,663mmol) del Ejemplo 199 y metanol (2ml) a hidróxido de paladio al 20% sobre carbono (húmedo, 4 mg) en una botella de presión de 50 ml. La reacción se agitó por 16 horas bajo hidrógeno (30 psi) a temperatura ambiente. La mezcla se filtró a través de una membrana de nylon y el solvente se eliminó al vacío. El material crudo se cromatografió sobre un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS15-24) eluyendo con 1-10% metanol (amoníaco 2 N)/diclorometano para dar el compuesto del título: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 8,14 (s, 1H), 8,07 (d, *J* = 7,9, 1H), 7,87 (d, *J* = 7,9, 1H), 7,70 (t, *J* = 7,8, 1H), 3,80 – 3,69 (m, 1H), 3,25 (dd, *J* = 7,8, 10,7, 1H), 3,06 – 2,88 (m, 2H), 2,79 – 2,71 (m, 1H), 2,63 – 2,51 (m, 1H), 2,46 (dd, *J* = 5,9, 10,8, 1H), 2,05 (qd, *J* = 7,0, 12,1, 1H), 1,79 (ddd, *J* = 3,9, 6,8, 10,7, 1H), 1,72 – 1,63 (m, 2H), 1,56 (dd, *J* = 4,8, 6,1, 1H), 1,48 (td, *J* = 6,9, 12,8, 1H), 1,31 (ddd, *J* = 2,7, 5,5, 8,8, 1H), 0,92 – 0,70 (m, 3H); MS (ESI+) *m/z*

375 $(M+H)^+$.

Ejemplo 202

***N*-{(3a*S**,4*S**,6a*R**)-2-[6,6-bis(4-fluorofenil)hexil]octahidrociclopenta[*c*]pirrol-4–il}-*N*-ciclopropil-3-(trifluorometil)bencenosulfonamida**

Se combinó *N*-ciclopropil-*N*-[(3a*S**,4*S**,6a*R**)-octahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida del Ejemplo 201 (140mg, 0,374 mmol) y 6,6-bis(4-fluorofenil)hexanal (108 mg, 0,374 mmol) en diclorometano (2 ml) y luego se agregó ácido acético (1 ml). La reacción se agitó a temperatura ambiente por 20 minutos, luego se agregó PS-cianoborohidruro (306 mg, 0,748 mmol). La reacción se agitó a temperatura ambiente durante la noche, luego se filtró y la resina se lavó con diclorometano. El solvente se eliminó al vacío y el material crudo se purificó usando un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-12) eluyendo con 1-10% metanol (amoníaco 2 N)/diclorometano para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,50 (s, 1H), 8,36 (d, J = 7,9, 1H), 7,95 (d, J = 7,9, 1H), 7,76 (dd, J = 6,4, 14,2, 1H), 7,33 (dd, J = 5,6, 8,3, 4H), 7,18 – 7,11 (m, 4H), 3,96 (dd, J = 8,0, 16,3, 2H), 3,18 – 3,10 (m, 1H), 2,82 (dd, J = 3,5, 9,5, 1H), 2,50 – 2,44 (m, 2H), 2,39 (t, J = 8,0, 1H), 2,31 – 2,21 (m, 4H), 2,03 (dd, J = 7,8, 15,3, 2H), 1,91 (dt, J = 3,5, 10,4, 1H), 1,59 (dt, J = 5,6, 11,5, 1H), 1,51 (dd, J = 10,6, 16,2, 1H), 1,46 – 1,33 (m, 6H), 1,28 (dd, J = 7,4, 15,1, 2H), 1,08 (td, J = 5,0, 10,5, 1H), 0,84 (dt, J = 6,9, 12,6, 1H), 0,75 – 0,66 (m, 1H); MS (ESI+) *m/z* 647 $(M+H)^+$.

Ejemplo 203

***N*-{(3a*S**,4*S**,6a*R**)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-*N*-ciclopropil-3-(trifluorometil)bencenosulfonamida**

El compuesto del título se preparó utilizando 3,3-bis(4-fluorofenil)propanal en lugar de 6,6-bis(4-fluorofenil)hexanal en el procedimiento descrito en el Ejemplo 202: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,49 (s, 1H), 8,35 (d, J = 7,9, 1H), 7,94 (d, J = 7,8, 1H), 7,77 (t, J = 7,9, 1H), 7,34 (ddd, J = 2,1, 5,5, 8,4, 4H), 7,14 (td, J = 2,2, 8,8, 4H), 4,16 (t, J = 7,3, 1H), 3,97 – 3,90 (m, 1H), 3,24 – 3,15 (m, 1H), 2,77 (dd, J = 4,1, 9,1, 1H), 2,54 (t, J = 8,1, 1H), 2,47 (dd, J = 7,1, 15,3, 2H), 2,32 – 2,20 (m, 6H), 1,91 (dt, J = 3,5, 10,5, 1H), 1,63 (dt, J = 5,8, 11,6, 1H), 1,52 – 1,36 (m, 3H), 1,03 (dt, J = 4,5, 10,6, 1H), 0,83 (dt, J = 6,8, 12,6, 1H), 0,78 – 0,70 (m, 1H); MS (ESI+) *m/z* 605 $(M+H)^+$.

000541
9707.01

Ejemplo 204

N-ciclopropil-3-(trifluorometil)-N-{(3aS*,4S*,6aR*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[c]pirrol-4–il}bencenosulfonamida

El compuesto del título se preparó utilizando 3-(trifluorometil)benzaldehido en lugar de 6,6-bis(4-fluorofenil)hexanal en el procedimiento descrito en el Ejemplo 202: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,46 (s, 1H), 8,32 (d, *J* = 7,9, 1H), 7,93 (d, *J* = 7,8, 1H), 7,76 – 7,72 (m, 2H), 7,52 (d, *J* = 7,7, 1H), 7,44 (t, *J* = 7,7, 1H), 4,00 – 3,93 (m, 1H), 3,50 (d, *J* = 13,2, 1H), 3,43 (d, *J* = 13,2, 1H), 3,15 (qd, *J* = 3,8, 7,8, 1H), 2,78 (dd, *J* = 3,8, 9,7, 1H), 2,52 – 2,43 (m, 2H), 2,39 (dd, *J* = 8,0, 9,5, 1H), 2,32 – 2,22 (m, 2H), 1,90 – 1,82 (m, 1H), 1,59 (dt, *J* = 5,9, 11,5, 1H), 1,48 – 1,32 (m, 4H), 0,99 – 0,93 (m, 1H), 0,81 (ddd, *J* = 6,9, 9,8, 12,4, 1H), 0,75 – 0,67 (m, 1H); MS (ESI+) *m/z* 533 $(M+H)^+$.

Ejemplo 205

2,2-diciclohexil-N-((3aS,4S,6aR)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)acetamida

Se combinó 2,2-diciclohexil-*N*-((3a*S*,4*S*,6a*R*)-octahidrociclopenta[c]pirrol-4–il)acetamida del Ejemplo 53 (101 mg, 0,304 mmol), trietilamina (0,042 ml, 0,304 mmol), y cloruro de 3-(trifluorometil)bencen-1-sulfonilo (0,049 ml, 0,304 mmol) en diclorometano (2 ml). Se agregó una cantidad catalítica de *N,N*-dimetilaminopiridina. La reacción se agitó a temperatura ambiente por 1 hora y lcms mostró producto, y tlc mostró no más material de partida. La reacción se detuvo con bicarbonato de sodio acuoso y la capa acuosa se separó. Las capas orgánicas se concentraron para dar un precipitado. El precipitado se lavó con agua y éter y se secó bajo una corriente de nitrógeno para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,49 (d, *J* = 6,3, 1H), 8,34 (s, 1H), 8,19 (d, *J* = 7,9, 1H), 7,93 (d, *J* = 7,8, 1H), 7,73 (t, *J* = 7,8, 1H), 4,46 – 4,38 (m, 1H), 3,73 (dd, *J* = 3,4, 9,3, 1H), 3,17 (dd, *J* = 2,8, 9,7, 1H), 3,07 (ddd, *J* = 6,4, 12,0, 23,6, 3H), 2,49 (dd, *J* = 8,0, 15,9, 1H), 2,12 (t, *J* = 7,2, 1H), 2,02 – 1,77 (m, 8H), 1,73 (dd, *J* = 5,3, 9,0, 4H), 1,68 – 1,58 (m, 3H), 1,52 (ddd, *J* = 3,2, 12,5, 14,7, 1H), 1,43 (ddd, *J* = 3,1, 12,6, 15,0, 1H), 1,37 – 1,03 (m, 9H); MS (ESI+) *m/z* 541 $(M+H)^+$.

Ejemplo 206

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[(2-feniletil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}acetamida

El compuesto del título se preparó utilizando cloruro de 2-feniletansulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 205: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,35 (d, *J* = 7,0, 1H), 7,33 – 7,25 (m, 4H), 4,60 – 4,51 (m, 1H), 3,79 (dd, *J* = 4,8, 10,2, 1H), 3,56 – 3,39 (m, 4H), 3,27 (t, *J* = 8,3, 2H), 3,24 – 3,16 (m, 2H), 2,66 – 2,57 (m, 1H), 2,09 (t, *J* = 7,4, 1H), 2,00 – 1,76 (m, 9H), 1,72 (d, *J* = 12,9, 4H), 1,67 – 1,64 (m, 1H), 1,59 (t, *J* = 13,7, 2H), 1,54 – 1,36 (m, 3H), 1,30 – 1,18 (m, 4H), 1,18 – 1,06 (m, 4H); MS (ESI+) *m/z* 501 $(M+H)^+$.

Ejemplo 207

2,2-diciclohexil-*N*-((3a*S*,4*S*,6a*R*)-2-{[2-(1-naftil)etil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)acetamida

El compuesto del título se preparó utilizando cloruro de 2-(naftalen-1–il)etansulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 205: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37 (d, *J* = 6,8, 1H), 8,13 (d, *J* = 9,0, 1H), 7,97 – 7,94 (m, 1H), 7,85 (d, *J* = 8,2, 1H), 7,53 (p, *J* = 6,9, 2H), 7,46 – 7,40 (m, 1H), 7,36 (t, *J* = 7,9, 1H), 4,60 – 4,49 (m, 1H), 3,81 (dd, *J* = 4,8, 10,2, 1H), 3,75 (t, *J* = 8,3, 2H), 3,57 – 3,46 (m, 4H), 3,27 – 3,16 (m, 2H), 2,67 – 2,59 (m, 1H), 2,09 (t, *J* = 7,3, 1H), 1,95 (t, *J* = 13,3, 2H), 1,89 – 1,76 (m, 5H), 1,72 (d, *J* = 12,2, 4H), 1,66 (dd, *J* = 5,1, 7,2, 1H), 1,60 (t, *J* = 10,5, 2H), 1,46 (dt, *J* = 10,8, 20,4, 3H), 1,29 – 1,18 (m, 4H), 1,18 – 1,03 (m, 5H); MS (ESI+) *m/z* 551 $(M+H)^+$.

Ejemplo 208

2,2-diciclohexil-*N*-((3a*S*,4*S*,6a*R*)-2-{[3-(trifluorometil)bencil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)acetamida

El compuesto del título se preparó utilizando cloruro de (3-(trifluorometil)fenil)metansulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 205: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,32 (d, *J* = 6,7, 1H), 7,96 (s, 1H), 7,81 (d, *J* = 7,7, 1H), 7,64 (d, *J* = 7,7, 1H), 7,46 (t, *J* = 7,7, 1H), 4,69 (q, *J* = 13,5, 2H), 4,58 – 4,49 (m, 1H), 3,81 (dd, *J* = 4,9, 10,4, 1H), 3,52 (dd, *J* = 6,3, 13,7, 2H), 3,26 (dd, *J* = 3,1, 9,9, 1H), 3,23 – 3,15

(m, 1H), 2,65 – 2,58 (m, 1H), 2,06 (t, *J* = 7,3, 1H), 1,93 (d, *J* = 13,8, 2H), 1,82 (dt, *J* = 9,9, 14,4, 6H), 1,71 (t, *J* = 10,2, 4H), 1,67 (dd, *J* = 7,0, 11,0, 1H), 1,60 (d, *J* = 9,5, 2H), 1,51 – 1,35 (m, 3H), 1,29 – 1,02 (m, 8H); MS (ESI+) *m/z* 555 $(M+H)^+$.

Ejemplo 209

2,2-diciclohexil-*N*-((3a*S*,4*S*,6a*R*)-2-{[2-(4-fluorofenil)etil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)acetamida

El compuesto del título se preparó utilizando cloruro de 2-(4-fluorofenil)etansulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 205: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37 (d, *J* = 6,8, 1H), 7,18 (dd, *J* = 5,6, 8,5, 2H), 7,09 (t, *J* = 8,7, 2H), 4,60 – 4,49 (m, 1H), 3,80 (dd, *J* = 4,9, 10,3, 1H), 3,57 – 3,39 (m, 4H), 3,27 – 3,16 (m, 4H), 2,67 – 2,59 (m, 1H), 2,09 (t, *J* = 7,3, 1H), 1,99 – 1,77 (m, 8H), 1,72 (d, *J* = 12,4, 4H), 1,66 (dd, *J* = 3,0, 8,1, 1H), 1,59 (t, *J* = 14,2, 2H), 1,46 (ddd, *J* = 7,9, 16,4, 33,2, 3H), 1,24 (ddd, *J* = 3,2, 12,7, 25,7, 4H), 1,18 – 1,03 (m, 4H); MS (ESI+) *m/z* 519 $(M+H)^+$.

Ejemplos 210 y Ejemplo 211

(2*S*)-2-fenil-*N*-{(3a*R*,4*R*,6a*S*)-2-[(1*S*)-1-feniletil]octahidrociclopenta[*c*]pirrol-4–il}butanamida (Ejemplo 210) y

(2*S*)-2-fenil-*N*-{(3a*R*,4*S*,6a*S*)-2-[(1*S*)-1-feniletil]octahidrociclopenta[*c*]pirrol-4–il}butanamida (Ejemplo 211)

Paso A: (3a*R*,6a*S*)-2-((*S*)-1-Feniletil)hexahidrociclopenta[c]pirrol-4(5*H*)-ona y (3a*S*,6a*R*)-2-((*S*)-1-feniletil)hexahidrociclopenta[c]pirrol-4(5*H*)-ona se prepararon como se describe en el procedimiento descrito en Ejemplo 122 Paso C utilizando *S*(-)-*N*-metoximetil-*N*-(trifluorosilil)metil-1-feniletilamina en lugar de 1-metoxi-*N*-(3-(trifluorometil)bencil)-*N*-((trimetilsilil)metil)metanamina.

(3a*R*,6a*S*)-2-((*S*)-1-feniletil)hexahidrociclopenta[c]pirrol-4(5*H*)-ona: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,34 – 7,16 (m, 5H), 3,23 (d, *J* = 8,9, 1H), 3,12 (q, *J* = 6,6, 1H), 2,80 (dt, *J* = 7,5, 14,9, 1H), 2,60 (t, *J* = 8,6, 1H), 2,48 (dd, *J* = 2,0, 9,5, 1H), 2,44 – 2,20 (m, 5H), 2,08 (ddd, *J* = 8,2, 13,0, 17,0, 1H), 1,72 (ddd, *J* = 6,7, 10,1, 17,4, 1H), 1,31 (d, *J* = 6,6, 3H); MS (ESI+) *m/z* 230 $(M+H)^+$.

(3a*S*,6a*R*)-2-((*S*)-1-feniletil)hexahidrociclopenta[c]pirrol-4(5*H*)-ona: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,39 – 7,13 (m, 5H), 3,15 (dd, *J* = 6,5, 13,1, 1H), 2,88 (dd, *J* = 7,1, 13,7, 1H), 2,76 (t, *J* = 9,0, 3H), 2,54 (dd, *J* = 9,9, 18,1, 2H), 2,45 – 2,35 (m,

2H), 2,34 – 2,26 (m, 1H); 2,13 (ddd, *J* = 6,5, 10,8, 17,2, 1H), 1,91 – 1,77 (m, 1H), 1,33 (d, *J* = 6,2, 3H); MS (ESI+) *m/z* 230 $(M+H)^+$.

Paso B: Se preparó (3a*R*,6a*S*)-2-((*S*)-1-Feniletil)octahidrociclopenta[*c*]pirrol-4-amina como se describe en Ejemplo 122 Paso D-E utilizando (3a*R*,6a*S*)-2-((*S*)-1-feniletil)hexahidrociclopenta[c]pirrol-4(5*H*)-ona del Paso A en lugar de 2-(3-(trifluorometil)bencil)hexahidrociclopenta[*c*]pirrol-4(5*H*)-ona: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,47 – 7,09 (m, 5H), 3,12 (dd, *J* = 6,1, 12,5, 1H), 2,75 (br s, 2H), 2,48 (d, *J* = 6,5, 3H), 2,33 – 2,20 (m, 1H), 2,11 – 1,95 (m, 1H), 1,94 – 1,73 (m, 2H), 1,73 – 1,54 (m, 2H), 1,43 (s, 3H), 1,35 (d, *J* = 6,3, 3H); MS (ESI+) *m/z* 231 $(M+H)^+$.

Paso C: Los compuestos del título se prepararon utilizando ácido (S)-2-fenilbutanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*R*,6a*S*)-2-((*S*)-1-feniletil)octahidrociclopenta[*c*]pirrol-4-amina en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplos 1 y 2.

Ejemplo 210: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 11,04 (d, *J* = 6,9, 1H), 10,39 (d, *J* = 7,2, 2H), 10,16 (q, *J* = 8,0, 4H), 10,13 – 10,04 (m, 4H), 7,19 (dt, *J* = 7,1, 14,1, 1H), 6,36 (dd, *J* = 6,3, 8,7, 1H), 5,82 (q, *J* = 6,5, 1H), 5,69 (dd, *J* = 2,5, 9,4, 1H), 5,56 (qd, *J* = 2,7, 7,7, 1H), 5,22 – 5,07 (m, 2H), 4,99 – 4,92 (m, 2H), 4,90 (dd, *J* = 2,7, 9,2, 1H), 4,65 (td, *J* = 6,8, 13,6, 1H), 4,55 (dt, *J* = 7,1, 11,8, 1H), 4,32 – 4,20 (m, 2H), 4,11 (d, *J* = 6,5, 3H), 3,86 – 3,80 (m, 1H), 3,75 (t, *J* = 7,3, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Ejemplo 211: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 11,35 (d, *J* = 7,1, 1H), 10,40 (d, *J* = 7,1, 2H), 10,13 (dt, *J* = 7,6, 15,2, 6H), 10,04 (dt, *J* = 4,6, 14,8, 2H), 7,22 – 7,14 (m, 1H), 6,36 (dd, *J* = 6,3, 8,8, 1H), 5,78 (q, *J* = 6,5, 1H), 5,55 (d, *J* = 8,8, 1H), 5,22 – 5,09 (m, 3H), 5,04 – 4,98 (m, 1H), 4,92 (dd, *J* = 8,9, 15,9, 3H), 4,70 – 4,60 (m, 1H), 4,59 – 4,52 (m, 1H), 4,42 (dt, *J* = 6,9, 19,0, 1H), 4,10 (dd, *J* = 6,6, 18,3, 1H), 4,01 (d, *J* = 6,5, 3H), 3,75 (t, *J* = 7,3, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Ejemplo 212 y Ejemplo 213

(2*S*)-2-fenil-*N*-{(3a*S*,4*S*,6a*R*)-2-[(1*S*)-1-feniletil]octahidrociclopenta[*c*]pirrol-4-il}butanamida (Ejemplo 212) y

(2*S*)-2-fenil-*N*-{(3a*S*,4*R*,6a*R*)-2-[(1*S*)-1-feniletil]octahidrociclopenta[*c*]pirrol-4-il}butanamida (Ejemplo 213)

Paso A: Se preparó (3a*S*,6a*R*)-2-((*S*)-1-feniletil)octahidrociclopenta[*c*]pirrol-4-amina como se describe en Ejemplo 122 Pasos D-E utilizando (3a*S*,6a*R*)-2-((*S*)-1-feniletil)hexahidrociclopenta[*c*]pirrol-4(5*H*)-ona del Ejemplo 210 Paso A en lugar de 2-(3-(trifluorometil)bencil)hexahidrociclopenta[*c*]pirrol-4(5*H*)-ona: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,47 – 7,09 (m, 5H), 3,12 (dd, *J* = 6,1, 12,5, 1H), 2,75 (br s, 2H), 2,48 (d, *J* = 6,5, 3H), 2,33 – 2,20 (m, 1H), 2,11 – 1,95 (m, 1H), 1,94 – 1,73 (m, 2H), 1,73 – 1,54 (m, 2H), 1,43 (br s, 2H), 1,35 (d, *J* = 6,3, 3H); MS (ESI+) *m/z* 231 $(M+H)^+$.

Paso B: Los compuestos del título se prepararon utilizando ácido (S)-2-fenilbutanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*S*,6a*R*)-2-((*S*)-1-feniletil)octahidrociclopenta[*c*]pirrol-4-amina en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplos 1 y 2.

Ejemplo 212: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 10,86 (d, *J* = 6,3, 1H), 10,31 (d, *J* = 7,3, 2H), 10,18 – 10,07 (m, 7H), 10,04 (t, *J* = 7,3, 1H), 7,12 (dt, *J* = 7,2, 14,6, 1H), 6,31 (dd, *J* = 6,4, 8,6, 1H), 5,77 (q, *J* = 6,6, 1H), 5,61 – 5,53 (m, 1H), 5,21 – 5,08 (m, 3H), 4,99 (dd, *J* = 4,6, 9,8, 1H), 4,94 (dd, *J* = 8,3, 16,1, 2H), 4,70 – 4,60 (m, 2H), 4,46 (dt, *J* = 5,8, 16,8, 1H), 4,41 – 4,33 (m, 1H), 4,13 – 4,06 (m, 1H), 4,01 (d, *J* = 6,6, 3H), 3,75 (t, *J* = 7,3, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Ejemplo 213: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,50 (d, *J* = 7,1, 1H), 7,56 (s, 1H), 7,45 (d, *J* = 7,3, 2H), 7,34 (dt, *J* = 7,6, 16,7, 4H), 7,25 (dd, *J* = 7,3, 13,4, 3H), 4,37 – 4,30 (m, 1H), 3,52 (dd, *J* = 6,2, 8,8, 1H), 3,11 (q, *J* = 6,5, 1H), 2,60 (dd, *J* = 2,3, 8,1, 1H), 2,56 – 2,44 (m, 3H), 2,37 – 2,27 (m, 3H), 2,04 – 1,96 (m, 1H), 1,85 – 1,74 (m, 2H), 1,49 (dq, *J* = 6,8, 13,3, 1H), 1,38 – 1,32 (m, 1H), 1,29 (d, *J* = 6,6, 3H), 0,92 (t, *J* = 7,3, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Ejemplo 214

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*,3-dimetil-2-fenilbutanamida**

Paso A: Se combinó dicarbonato de di-tert-butilo (0,429 ml, 1,849 mmol), (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina (200 mg, 0,925 mmol) del Ejemplo 33 Paso A, y (dimetilamino)piridina (22,59 mg, 0,185 mmol) en diclorometano (5ml). La mezcla de la reacción se agitó a temperatura ambiente por 30 minutos. El material crudo se purificó en un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-4) eluyendo con acetato de etilo/hexanos para dar (3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo: ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm 7,39 – 7,12 (m, 5H), 4,47 (s, 1H), 3,74 (s, 1H), 3,61 (s, 1H), 3,52 (s, 1H), 2,55 (t, *J* = 31,6, 4H), 2,31 (s, 2H), 2,03 (d, *J* = 6,1, 1H), 1,83 (d, *J* = 8,0, 1H), 1,58 (s, 1H), 1,43 (s, 9H), 0,98 – 0,79 (m, 1H); MS (ESI+) *m/z* 317 $(M+H)^+$.

Paso B: Se trató (3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo (59 mg, 0,187mmol) del Paso A con hidruro de litio y aluminio (0,374 mmol) en tetrahidrofurano (0,5 ml). La reacción se agitó a temperatura ambiente por 1 hora y luego se calentó a reflujo por 2 horas. La reacción se enfrió a temperatura ambiente y se detuvo con la adición por goteo de sulfato de sodio acuoso saturado (50 µL) para dar un precipitado. El precipitado se lavó con tetrahidrofurano, y luego el solvente se eliminó para dar (3a*R*,4*S*,6a*S*)-2-bencil-*N*-metiloctahidrociclopenta[*c*]pirrol-4-amina: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,34 – 7,28 (m, 4H), 7,25 – 7,19 (m, 1H), 3,60 – 3,51 (m, 2H), 2,76 (q, *J* = 5,6, 1H), 2,64 (d, *J* = 15,7, 1H), 2,58 – 2,53 (m, 1H), 2,51 – 2,46 (m, 1H), 2,40 – 2,35 (m, 4H), 2,31 – 2,22 (m, 2H), 1,98 – 1,85 (m, 2H), 1,39 (dt, *J* = 5,7, 10,6, 3H); MS (ESI+) *m/z* 231 $(M+H)^+$.

Paso C: El compuesto del título se preparó utilizando ácido 3-metil-2-fenilbutanoico en lugar de ácido 1-fenilciclopentancarboxílico y (3a*R*,4*S*,6a*S*)-2-bencil-*N*-metiloctahidrociclopenta[*c*]pirrol-4-amina en lugar de (3a*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 2: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,59 – 7,41 (m, 5H), 7,39 – 7,16 (m, 5H), 3,64 (d, *J* = 13,2, 1H), 3,50 (d, *J* = 9,5, 1H), 2,69 – 2,52 (m, 2H), 2,50 – 2,33 (m, 3H), 2,25 – 2,15 (m, 1H), 2,05 (dd, *J* = 6,3, 9,2, 1H), 1,88 – 1,67 (m, 2H), 1,34 (dd, *J* =

13,4, 19,6, 3H), 1,08 (d, *J* = 6,4, 3H), 1,03 – 0,95 (m, 1H), 0,79 – 0,66 (m, 6H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Ejemplo 215

N-[(3a*S,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*,3-dimetil-2-fenilbutanamida**

El compuesto del título se preparó como se describe en Ejemplo 214 utilizando (3a*R**,4*S**,6a*S**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina (Publicación Internacional N° WO2006/012396) en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en Ejemplo 214 Paso A: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,61 – 7,41 (m, 5H), 7,26 (dd, *J* = 15,4, 37,9, 5H), 3,65 (d, *J* = 13,2, 1H), 3,54 (dd, *J* = 7,6, 19,9, 2H), 2,70 – 2,53 (m, 2H), 2,50 – 2,36 (m, 2H), 2,25 – 2,15 (m, 1H), 2,07 (s, 1H), 1,87 – 1,66 (m, 2H), 1,43 – 1,26 (m, 3H), 1,19 (d, *J* = 6,4, 2H), 1,08 (d, *J* = 6,5, 2H), 1,01 (d, *J* = 6,4, 1H), 0,79 – 0,63 (m, 5H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Ejemplo 216

(3a*R,4*S**,6a*S**)-*N*-bencil-2-(3-metil-2-fenilbutanoil)octahidrociclopenta[*c*]pirrol-4-amina**

Paso A: Se preparó (3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo como se describe en Ejemplo 214 Paso A utilizando (3a*R**,4*S**,6a*S**)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina (Publicación Internacional N° WO2006/012396) en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina: MS (ESI+) *m/z* 317 $(M+H)^+$.

Paso B: Se combinó (3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo (100 mg, 0,316 mmol) del Paso A y formato de amonio (100 mg, 1,580 mmol) en etanol. La reacción se desoxigenó a baja temperatura, y se agregó paladio sobre carbono (3,36 mg, 0,032 mmol). La reacción se calentó a reflujo bajo nitrógeno. Luego de 3 horas, tlc y lcms mostraron mayoritariamente material de partida. Se agregó catalizador de Degussa y 5 equivalentes más de formato de amonio y la mezcla de la reacción se sometió a reflujo bajo nitrógeno durante la noche. Se agregó más formato de amonio y catalizador de Degussa y la reacción se calentó a 90 °C. Luego de 2 horas, tlc y lcms mostraron que no quedaba más material de partida. La reacción se filtró a través de tierra diatomea gel de sílice funcionalizado con carbonato (Silicicle, Quebec, Canada) con

metanol. La eliminación del solvente al vacío dio (3aR,4S,6aS)-octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo: MS (ESI+) *m/z* 226 $(M+H)^+$.

Paso C: Se combinó ácido 3-metil-2-fenilbutanoico (63 mg, 0,353 mmol), 1-hidroxibenzotriazol (54,1 mg, 0,353 mmol), y *N*-(3-dimetilaminopropil)-*N'*-etilcarbodiimida (0,063 ml, 0,353 mmol) en diclorometano (5 ml). La reacción se agitó a temperatura ambiente por 20 minutos, y luego se agregó (3aR,4S,6aS)-octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo (80 mg, 0,353 mmol) del Paso B. Luego de 30 minutos, la reacción se detuvo con agua y se extrajo con diclorometano. Los extractos combinados se concentraron, y el material crudo se purificó usando acetato de etilo al 10-100%/hexanos para dar (3aR,4S,6aS)-2-(3-metil-2-fenilbutanoil)octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo: MS (ESI+) *m/z* 387 $(M+H)^+$.

Paso D: Se combinó (3aR,4S,6aS)-2-(3-metil-2-fenilbutanoil)octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo (39 mg, 0,101 mmol) del Paso C con HCl 4 M en dioxano (5 ml, 20,00 mmol) en éter (5 ml). Luego de aproximadamente 2 horas, el solvente se eliminó al vacío para dar sal de ácido clorhídrico de 1-((3aR,4S,6aS)-4-aminohexahidrociclopenta[c]pirrol-2(1H)–il)-3-metil-2-fenilbutan-1-ona la cual se usó en el siguiente paso sin purificación adicional: MS (ESI+) *m/z* 287 $(M+H)^+$.

Paso E: Se combinó sal de ácido clorhídrico de 1-((3aR,4S,6aS)-4-aminohexahidrociclopenta[c]pirrol-2(1H)–il)-3-metil-2-fenilbutan-1-ona (49 mg, 0,152 mmol) y benzaldehido (0,023 ml, 0,228 mmol) en diclorometano (1,5 ml). Se agregó ácido acético (1,5 ml). La reacción se agitó a temperatura ambiente por 30 minutos, luego se agregó PS-cianoborohidruro (64,9 mg, 0,152 mmol). Luego de 72 horas, lcms de la reacción mostró no más material de partida. La mezcla de la reacción se filtró, y el solvente se eliminó bajo una corriente de nitrógeno. El material crudo se purificó usando un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-4) eluyendo con metanol al 1-10% (amoníaco 2 N)/diclorometano para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,69 – 7,60 (m, 2H), 7,54 – 7,44 (m, 2H), 7,44 – 7,34 (m, 5H), 7,29 (tdd, *J* = 4,8, 7,8, 13,0, 2H), 3,90 – 3,36 (m, 4H), 3,29 (dd, *J* = 3,8, 10,6, 0,5H), 2,99 (dd, *J* = 5,7, 11,4, 0,5H), 2,93 (dd, *J* = 6,0, 11,3, 0,5H), 2,75 – 2,63 (m, 1H), 2,59 – 2,48 (m,

1H), 2,46 – 2,31 (m, 1H), 2,25 (dt, *J* = 4,1, 8,7, 0,5H), 1,97 (dt, *J* = 9,3, 11,6, 1H), 1,93 – 1,85 (m, 0,5H), 1,84 – 1,74 (m, 1H), 1,65 – 1,55 (m, 0,5H), 1,51 – 1,35 (m, 1H), 1,33 – 1,21 (m, 1H), 1,18 – 1,10 (m, 3H), 1,01 (td, *J* = 7,7, 13,1, 0,5H), 0,87 (dt, *J* = 6,6, 12,9, 0,5H), 0,75 (t, *J* = 7,2, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Ejemplo 217

2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-2-(*N*,*N*-dimetil-D-leucil)octahidrociclopenta[*c*]pirrol-4–il]acetamida

Paso A: Se combinó *N*-(*tert*-Butoxicarbonil)-D-leucina (72,7 mg, 0,314 mmol), 2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida (95 mg, 0,286 mmol) del Ejemplo 74, y hidroxibenzotriazol (48,1 mg, 0,314 mmol) en diclorometano (10 ml). Luego de 20 minutos, se agregó *N*-(3-dimetilaminopropil)-*N'*-etilcarbodiimida (0,056 ml, 0,314 mmol), y la mezcla de la reacción se agitó a temperatura ambiente por 18 horas. La reacción se detuvo con agua. La capa orgánica separada se redujo en volumen, y el material crudo se aplicó a un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-12) y se eluyó primero con acetato de etilo entre 10% y 100%/hexanos y luego con metanol al 1-10% (amoníaco 2 N)/diclorometano para dar (R)-1-((3aS,4R,6aR)-4-(2,2-diciclohexilacetamido)hexahidrociclopenta[c]pirrol-2(1H)–il)-4-metil-1-oxopentan-2–ilcarbamato de tert-butilo: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,26 (dd, *J* = 7,2, 24,0, 1H), 7,91 (d, *J* = 8,6, 1H), 4,48 – 4,36 (m, 1H), 4,12 – 3,96 (m, 1H), 3,87 (dd, *J* = 7,4, 10,3, 1H), 3,70 (ddd, *J* = 8,0, 14,4, 23,7, 1H), 3,40 (dd, *J* = 5,7, 12,3, 1H), 2,77 (s, 1H), 2,58 (d, *J* = 6,1, 1H), 2,08 (s, 1H), 2,01 (dd, *J* = 5,6, 10,4, 2H), 1,96 – 1,55 (m, 17H), 1,54 – 1,50 (m, 9H), 1,49 – 1,37 (m, 2H), 1,19 (qdd, *J* = 12,3, 22,3, 24,7, 11H), 1,00 (t, *J* = 6,6, 3H), 0,88 (d, *J* = 6,6, 1H).

Paso B: Se combinó (R)-1-((3aS,4R,6aR)-4-(2,2-diciclohexilacetamido)hexahidrociclopenta[c]pirrol-2(1H)–il)-4-metil-1-oxopentan-2–ilcarbamato de tert-butilo (185 mg, 0,339 mmol) del Paso A, y HCl 2 N en éter (2,5 ml, 5,00 mmol) en éter (1 ml). La mezcla de la reacción se agitó a temperatura ambiente durante la noche. Los sólidos se recogieron y se secó para dar *N*-((3a*S*,4*R*,6a*R*)-2-((*R*)-2-amino-4-metilpentanoil)octahidrociclopenta[*c*]pirrol-4–il)-2,2-diciclohexilacetamida: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,34 – 8,24 (m, 1H), 4,92 (br s, 2H), 4,46 – 4,31 (m, 1H), 4,07 (d, *J* = 9,2, 0,5H), 3,91 – 3,81 (m, 1,5H), 3,77 (dd, *J* = 8,8, 12,1, 1H), 3,72 – 3,64 (m, 0,5H), 3,59 – 3,53 (m, 0,5H),

3,45 (dd, *J* = 5,2, 12,2, 0,5H), 3,32 (d, *J* = 6,5, 0,5H), 2,82 – 2,69 (m, 1H), 2,63 (dd, *J* = 8,4, 14,5, 0,5H), 2,54 (dd, *J* = 8,0, 16,4, 0,5H), 2,21 – 2,06 (m, 2H), 2,02 (q, *J* = 7,6, 1H), 1,99 – 1,55 (m, 15H), 1,50 – 1,38 (m, 3H), 1,37 – 1,12 (m, 9H), 1,09 (d, *J* = 6,5, 3H), 1,01 (d, *J* = 6,6, 2H), 0,96 (d, *J* = 6,4, 1H), 0,91 (d, *J* = 6,6, 1H). MS (ESI+) *m/z* 466 $(M+H)^+$.

Paso C: A *N*-((3a*S*,4*R*,6a*R*)-2-((*R*)-2-amino-4-metilpentanoil)octahidrociclopenta[*c*]pirrol-4–il)-2,2-diciclohexilacetamida (0,133 g, 0,298 mmol) del Paso B se agregó formaldehido (0,228 ml, 2,98 mmol) en diclorometano (0,5 ml). Se agregó ácido acético (0,5 ml). La reacción se agitó a temperatura ambiente por 30 minutos, luego se agregó PS-cianoborohidruro (0,255 g, 0,597 mmol), y la mezcla de la reacción se agitó a temperatura ambiente durante la noche. La reacción se filtró, y el solvente se eliminó al vacío. El material crudo se purificó sobre cromatografía sobre gel de sílice en un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-12) eluyendo con metanol al 1-10% (amoníaco 2 N)/diclorometano para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,29 (dd, *J* = 7,1, 15,9, 1H), 4,46 – 4,35 (m, 1H), 4,09 – 3,99 (m, 1H), 3,92 – 3,80 (m, 1H), 3,70 (dd, *J* = 8,6, 12,4, 1H), 3,66 – 3,58 (m, 2H), 3,45 (dd, *J* = 4,8, 9,1, 0,5H), 2,78 – 2,64 (m, 1H), 2,63 – 2,53 (m, 1H), 2,42 (s, 3H), 2,38 (s, 3H), 2,23 – 2,14 (m, 0,5H), 2,13 – 1,99 (m, 2H), 1,99 – 1,82 (m, 5H), 1,82 – 1,63 (m, 8H), 1,60 (d, *J* = 14,0, 1H), 1,57 – 1,51 (m, 1H), 1,45 (ddd, *J* = 8,6, 18,8, 29,3, 3H), 1,36 – 1,05 (m, 9H), 1,01 (d, *J* = 6,6, 3H), 0,91 (dd, *J* = 6,6, 19,9, 3H); MS (ESI+) *m/z* 474 $(M+H)^+$.

Ejemplo 218

N-[(3a*R*,4*S*,6a*S*)-2-benzoiloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida

Se combinó 3-Metil-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida del Ejemplo 83 Paso A (25 mg, 0,087 mmol), trietilamina (0,018 ml, 0,131 mmol), y cloruro de benzoilo (10,12 µL, 0,087 mmol) en diclorometano (5 ml). Luego de 5 minutos, tlc mostró no más material de partida. La mezcla de reacción cruda se concentró y se aplicó a un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-4) eluyendo con metanol al 1-10%(amoníaco 2 N)/diclorometano para dar el compuesto del título: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,49 – 7,42 (m, 2H), 7,41 – 7,35 (m, 3H), 7,33 – 7,27 (m, 3H), 5,43 (d, *J* = 6,7,

1H), 3,97 (m, 1H), 3,74 (m, 2H), 3,56 (m, 2H), 3,39 (m, 1H), 2,74 (m, 2H), 2,48 (m, 1H), 2,38 (m, 2H), 2,07 (dd, *J* = 4,6, 10,8, 1H), 1,94 (m, 1H), 1,52 – 1,31 (m, 2H), 1,01 (d, *J* = 6,3, 3H), 0,68 (d, *J* = 6,6, 3H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Ejemplo 219

***N'*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*-isopropil-*N*-fenilurea**

Se agregó trimetilaluminio 2 M en tolueno (0,198ml, 0,395 mmol) por goteo a *N*-isopropilanilina (0,068 ml, 0,474 mmol) en tolueno (2 ml) a 0 °C. La reacción se calentó a temperatura ambiente y se agitó por 1 hora. La solución de aluminio amida luego se agregó por goteo a una solución de (3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo del Ejemplo 214 Paso A (50 mg, 0,158 mmol) en 1 ml de tolueno a 0 °C. La reacción se calentó a 90 °C durante la noche, y luego la reacción se detuvo con 1 ml de hidróxido de sodio acuoso al 5%. La capa de tolueno separada se aplicó directamente a un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS-4) eluyendo con metanol al 1-10% (amoníaco 2 N)/diclorometano para dar el compuesto del título: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,40 (ddd, *J* = 1,8, 3,2, 5,7, 3H), 7,29 (d, *J* = 4,4, 4H), 7,24 – 7,18 (m, 1H), 7,14 (t, *J* = 2,0, 1H), 7,13 – 7,10 (m, 1H), 4,87 (dt, *J* = 6,8, 13,6, 1H), 3,94 – 3,84 (m, 1H), 3,74 (d, *J* = 7,1, 1H), 3,60 (d, *J* = 13,0, 1H), 3,44 (d, *J* = 13,0, 1H), 2,53 (t, *J* = 5,5, 2H), 2,48 – 2,40 (m, 1H), 2,40 – 2,33 (m, 1H), 2,22 (dd, *J* = 3,7, 8,8, 1H), 2,07 (ddd, *J* = 5,1, 9,2, 11,7, 1H), 1,95 (td, *J* = 6,0, 12,0, 1H), 1,63 – 1,52 (m, 1H), 1,40 – 1,30 (m, 1H), 1,29 – 1,17 (m, 1H), 1,05 (d, *J* = 3,2, 3H), 1,02 (d, *J* = 3,2, 3H); MS (ESI+) *m/z* 378 $(M+H)^+$.

Quiral

Ejemplo 220

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida

Paso A: Se disolvió clorhidrato de (S)-2-amino-4-metilpentanoato de tert-butilo (0,516 g, 2,306 mmol) en diclorometano (15 ml) y se agregó trietilamina (1,061 ml, 7,61 mmol). Se agregó cloruro de 3-cloropropan-1-sulfonilo (0,337 ml, 2,77 mmol) por goteo, y la mezcla de la reacción se agitó a temperatura ambiente durante la noche. El solvente se eliminó al vacío, y el material crudo se colocó en

éter, se filtró, y se concentró para dar (S)-2-(3-cloropropilsulfonamido)-4-metilpentanoato de tert-butilo: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 4,70 (d, *J* = 9,7, 1H), 4,02 - 3,91 (m, 1H), 3,77 - 3,60 (m, 2H), 3,25 - 2,96 (m, 3H), 2,31 (tdd, *J* = 2,2, 6,6, 9,2, 2H), 1,83 (dq, *J* = 6,5, 13,0, 1H), 1,58 - 1,53 (m, 8H), 1,38 (t, *J* = 7,3, 1H), 0,96 (dd, *J* = 2,1, 6,6, 6H); MS (ESI+) *m/z* 345 $(M+NH_4)^+$.

Paso B: Se disolvió (S)-2-(3-cloropropilsulfonamido)-4-metilpentanoato de tert-butilo (0,756 g, 2,306 mmol) del Paso A en tetrahidrofurano y se agregó tert-butóxido de potasio (0,517 g, 4,61 mmol). La reacción se agitó a temperatura ambiente durante la noche. El solvente se eliminó al vacío, y el material crudo se particionó entre éter y agua. La capa de éter se separó, se lavó con salmuera, se secó (Na_2SO_4), y se concentró al vacío para dar (2S)-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanoato de tert-butilo: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 4,17 - 4,05 (m, 1H), 3,68 (dd, *J* = 7,9, 16,6, 1H), 3,40 - 3,28 (m, 1H), 3,21 - 3,09 (m, 2H), 2,39 (td, *J* = 5,3, 13,6, 2H), 1,68 (m, 3H), 1,47 (s, 9H), 0,97 (dd, *J* = 3,2, 6,2, 6H).

Paso C: Se combinó (2S)-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanoato de tert-butilo (0,656 g, 2,251 mmol) del Paso B con HCl (4 *N* en dioxano, 5 ml, 20,00 mmol). La mezcla de la reacción se agitó a temperatura ambiente por 24 horas, luego el solvente se eliminó al vacío para obtener ácido (2S)-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanoico: MS (DCI+) *m/z* 253 $(M+NH_4)^+$.

Paso D: Se combinó ácido (2S)-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanoico (359 mg, 1,526 mmol) con trietilamina (0,387 ml, 2,77 mmol) en diclorometano (10 ml). Se agregó 1-hidroxibenzotriazol (234 mg, 1,526 mmol) y *N*-(3-dimetilaminopropil)-*N*'-etilcarbodiimida (0,270 ml, 1,526 mmol), y la mezcla de la reacción se agitó por 15 minutos. Luego se agregó (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina (300 mg, 1,387 mmol) del Ejemplo 16 Paso E, y la mezcla de la reacción se agitó a temperatura ambiente por 24 horas. La reacción se detuvo con 10 ml de bicarbonato de sodio acuoso y se extrajo con 3x20 ml de diclorometano. El solvente se eliminó al vacío. El material crudo se aplicó a un cartucho de gel de sílice (Analogix®, Burlington, Wisconsin, RS15-24) y se eluyó con metanol al 1-10% (amoníaco 2 N)/diclorometano para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,76 (d, *J* = 6,9, 1H), 7,46 - 7,39 (m, 2H), 7,40 - 7,33 (m, 2H), 7,26 (dd, *J* = 9,9, 17,2, 1H), 4,52 (t, *J* = 7,7, 1H), 4,44 - 4,34 (m, 1H), 3,93 (dt, *J* = 7,0, 14,5, 1H), 3,57 (dd, *J* = 5,4, 13,1,

1H), 3,49 - 3,36 (m, 2H), 3,30 - 3,20 (m, 2H), 2,83 - 2,74 (m, 1H), 2,62 - 2,45 (m, 2H), 2,44 - 2,37 (m, 1H), 2,33 - 2,17 (m, 4H), 2,11 (qd, *J* = 6,5, 12,5, 1H), 1,92 - 1,78 (m, 3H), 1,77 - 1,59 (m, 2H), 1,45 - 1,32 (m, 1H), 0,88 (d, *J* = 6,6, 3H), 0,83 (dd, *J* = 2,5, 6,5, 3H); MS (ESI+) *m/z* 434 $(M+H)^+$.

Ejemplo 221

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–ilcarbamato de tert-butilo

Se combinó *N*-(*tert*-butoxicarbonil)-L-leucina (0,374 g, 1,617 mmol), hidrato de 1-hidroxibenzotriazol (0,248 g, 1,617 mmol), y (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 33 (0,318g, 1,470 mmol) en diclorometano (3,0 ml). Luego de 20 minutos, se agregó N^1-((etilimino)metilen)-N^3,N^3-dimetilpropan-1,3-diamina (0,286 ml, 1,617 mmol), y la reacción se agitó a temperatura ambiente durante la noche. La reacción se detuvo con agua y se extrajo con de diclorometano (2×2ml), y los extractos se aplicaron directamente a un cartucho de 25 g de gel de sílice y se purificó con un gradiente de 5-40% acetona/hexanos a lo largo de 30 minutos para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,61-8,64 (m, 1H), 7,96-7,99 (m, 1H), 7,42-7,44 (m, 2H), 7,36 (t, *J* = 7,4 Hz, 2H), 7,28 (d, *J* = 7,3 Hz, 1H), 4,65-4,73 (m, 1H), 4,37-4,45 (m, 1H), 3,59 (d, *J* = 13,1 Hz, 1H), 3,43 (d, *J* = 13,1 Hz, 1H), 2,81-2,84 (m, 1H), 2,55-2,58 (m, 1H), 2,44-2,54 (m, 2H), 2,24-2,36 (m, 2H), 2,02-2,13 (m, 1H), 1,78-1,94 (m, 4H), 1,53-1,66 (m, 1H), 1,50 (s, 9H), 1,26-1,43 (m, 1H), 0,87 (d, *J* = 5,5 Hz, 3H), 0,83-0,85 (m, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Ejemplo 222

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-leucina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,23-8,32 (m, 1H), 7,42-7,44 (m, 2H), 7,36 (t, *J* = 7,5 Hz, 2H), 7,27 (t, *J* = 7,4 Hz, 1H), 5,02 (m, 0,7H), 4,69 (m, 0,3H), 4,37-4,43 (m, 1H), 3,58 (d, *J* = 13,1 Hz, 1H), 3,45 (d, *J* = 13,1 Hz, 1H), 3,04-3,11 (m, 3H), 2,82-2,91 (m, 1H), 2,40-2,52 (m, 3H), 2,31-2,34 (m, 1H), 2,21-2,25 (m, 1H), 1,99-2,14 (m, 1H), 1,77-1,94 (m, 3H), 1,51-1,62 (m, 2H), 1,47 (s, 9H), 1,34-1,37 (m, 1H), 0,88 (d, *J* = 6,4 Hz, 3H), 0,85 (d, *J* = 6,4 Hz, 3H); MS (ESI+) *m/z*

444 $(M+H)^+$.

Ejemplo 223

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(etil)carbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-etil-L-leucina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,11-8,14 (m, 1H), 7,42-7,44 (m, 2H), 7,36 (t, *J* = 7,4 Hz, 2H), 7,27 (t, *J* = 7,3 Hz, 1H), 4,36-4,41 (m, 1H), 3,59 (d, *J* = 13,1 Hz, 1H), 3,43-3,47 (m, 3H), 2,80-2,85 (m, 1H), 2,47-2,51 (m, 2H), 2,39-2,43 (m, 1H), 2,33-2,35 (m, 1H), 2,22-2,25 (m, 1H), 2,05-2,13 (m, 1H), 1,94-2,04 (m, 1H), 1,81-1,84 (m, 1H), 1,72-1,78 (m, 1H), 1,52-1,61 (m, 1H), 1,46-1,49 (m, 9H), 1,34-1,41 (m, 2H), 1,17-1,33 (m, 3H), 0,89-0,91 (m, 6H); MS (ESI+) *m/z* 458 $(M+H)^+$.

Ejemplo 224

(2S,3S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-isoleucina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,43 (d, *J* = 8,7 Hz, 1H), 7,43 (s, 1H), 7,37 (t, *J* = 7,4 Hz, 2H), 7,25-7,30 (m, 1H), 4,68-4,72 (m, 1H), 4,34-4,44 (m, 1H), 3,61 (d, *J* = 13,1 Hz, 1H), 3,46 (d, *J* = 13,1 Hz, 1H), 3,22-3,26 (m, 1H), 3,13-3,14 (m, 2H), 2,87-2,90 (m, 1H), 2,46-2,54 (m, 3H), 2,25-2,35 (m, 3H), 2,00-2,12 (m, 1H), 1,82 (dq, *J* = 12,7, 6,3 Hz, 1H), 1,52-1,63 (m, 1H), 1,48-1,50 (m, 9H), 1,32-1,43 (m, 3H), 0,96-1,10 (m, 4H), 0,78-0,86 (m, 3H); MS (ESI+) *m/z* 444 $(M+H)^+$.

Ejemplo 225

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3,3-dimetil-1-oxobutan-2–ilcarbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-*tert*-leucina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,71 (m, 1H), 7,70 (d, *J* = 9,6 Hz, 1H), 7,43-7,45 (m, 2H), 7,37 (t, *J* = 7,5 Hz, 2H), 7,26-7,30 (m, 1H), 4,61 (d, *J* = 9,7 Hz, 1H), 4,39-4,45 (m, 1H), 3,63 (d, *J* = 13,1 Hz, 1H), 3,44 (d, *J* =

13,1 Hz, 1H), 2,86 (dd, *J* = 9,0, 2,9 Hz, 1H), 2,57-2,63 (m, 1H), 2,45-2,55 (m, 2H), 2,26-2,33 (m, 2H), 2,00 (dd, *J* = 12,1, 6,1 Hz, 1H), 1,77-1,84 (m, 1H), 1,48-1,56 (m, 1H), 1,48 (s, 9H), 1,25-1,38 (m, 1H), 1,18 (s, 9H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Ejemplo 226

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-L-neopentilglicina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,54-8,57 (m, 1H), 8,10-8,13 (m, 1H), 7,41-7,45 (m, 2H), 7,36 (t, *J* = 7,4 Hz, 2H), 7,25-7,29 (m, 1H), 4,72-4,76 (m, 1H), 4,38-4,42 (m, 1H), 3,59 (d, *J* = 13,1 Hz, 1H), 3,43 (d, *J* = 13,1 Hz, 1H), 2,84 (dd, *J* = 9,0, 2,9 Hz, 1H), 2,53-2,60 (m, 1H), 2,46-2,53 (m, 1H), 2,42-2,46 (m, 1H), 2,29-2,32 (m, 1H), 2,22-2,27 (m, 1H), 2,16 (dd, *J* = 14,1, 4,8 Hz, 1H), 2,01-2,07 (m, 1H), 1,77-1,87 (m, 2H), 1,54-1,62 (m, 1H), 1,50 (s, 9H), 1,31-1,41 (m, 1H), 0,98 (s, 9H); MS (ESI+) *m/z* 444 $(M+H)^+$.

Ejemplo 227

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxohexan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-norleucina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,21-8,24 (m, 1H), 7,42-7,44 (m, 2H), 7,36 (t, *J* = 7,4 Hz, 2H), 7,24-7,31 (m, 1H), 5,02 (m, 0,7H), 4,66 (m, 0,3H), 4,34-4,47 (m, 1H), 3,59 (d, *J* = 13,1 Hz, 1H), 3,45 (d, *J* = 13,1 Hz, 1H), 3,05-3,10 (m, 3H), 2,82-2,85 (m, 1H), 2,45-2,50 (m, 2H), 2,37-2,45 (m, 1H), 2,31-2,37 (m, 1H), 2,24 (t, *J* = 7,5 Hz, 1H), 2,05-2,12 (m, 2H), 1,79-1,84 (m, 2H), 1,53-1,62 (m, 1H), 1,47 (s, 9H), 1,34-1,38 (m, 1H), 1,21-1,29 (m, 4H), 0,75-0,81 (m, 3H); MS (ESI+) *m/z* 444 $(M+H)^+$.

Ejemplo 228

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-bis(4-fluorofenil)acetamida**

El compuesto del título se preparó utilizando ácido 2,2-bis(4-fluorofenil)acético en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,04 (d, *J* = 7,0,

1H), 7,57 – 7,52 (m, 4H), 7,42 (d, *J* = 7,1, 2H), 7,36 (t, *J* = 7,5, 2H), 7,27 (t, *J* = 7,3, 1H), 7,12 (dt, *J* = 15,8, 8,0, 4H), 5,23 (s, 1H), 4,45 – 4,37 (m, 1H), 3,57 (d, *J* = 13,1, 1H), 3,43 (d, *J* = 13,1, 1H), 2,78 (dd, *J* = 9,1, 2,9, 1H), 2,54 – 2,47 (m, 1H), 2,47 – 2,43 (m, 1H), 2,40 (dd, *J* = 8,9, 7,3, 1H), 2,29 (dd, *J* = 9,0, 3,0, 1H), 2,27 – 2,21 (m, 1H), 2,10 (dq, *J* = 12,2, 6,2, 1H), 1,84 – 1,75 (m, 1H), 1,60 (td, *J* = 14,6, 7,3, 1H), 1,41 – 1,31 (m, 1H); MS (ESI+) *m/z* 447 $(M+H)^+$.

Ejemplo 229

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-isopropil-3-metilbutanamida

El compuesto del título se preparó utilizando ácido 2-isopropil-3-metilbutanoico en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,18 (d, *J* = 7,5, 1H), 7,44 (d, *J* = 7,5, 2H), 7,37 (t, *J* = 7,6, 2H), 7,27 (t, *J* = 7,3, 1H), 4,52 – 4,37 (m, 1H), 3,62 (d, *J* = 13,2, 1H), 3,44 (d, *J* = 13,1, 1H), 2,83 (dd, *J* = 9,0, 2,8, 1H), 2,62 – 2,51 (m, 2H), 2,48 (dd, *J* = 8,8, 7,1, 1H), 2,34 – 2,26 (m, 2H), 2,17 – 2,05 (m, 3H), 1,92 – 1,81 (m, 2H), 1,64 (dt, *J* = 19,2, 7,1, 1H), 1,44 – 1,34 (m, 1H), 1,13 (dd, *J* = 6,6, 3,9, 6H), 0,98 (d, *J* = 6,8, 6H); MS (ESI+) *m/z* 343 $(M+H)^+$.

Ejemplo 230

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metilbutanamida

El compuesto del título se preparó utilizando ácido 3-metilbutanoico en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,36 (d, *J* = 7,8, 1H), 7,44 (d, *J* = 7,6, 2H), 7,37 (t, *J* = 7,5, 2H), 7,28 (t, *J* = 7,2, 1H), 4,48 – 4,40 (m, 1H), 3,60 (d, *J* = 13,1, 1H), 3,45 (d, *J* = 13,2, 1H), 2,82 (dd, *J* = 9,0, 2,2, 1H), 2,59 – 2,50 (m, 2H), 2,50 – 2,43 (m, 1H), 2,31 (tt, *J* = 19,8, 7,9, 3H), 2,23 (d, *J* = 7,3, 2H), 2,17 – 2,08 (m, 1H), 1,87 (dd, *J* = 13,1, 6,7, 1H), 1,68 – 1,58 (m, 1H), 1,46 – 1,34 (m, 1H), 0,95 (d, *J* = 6,6, 5H); MS (ESI+) *m/z* 343 $(M+H)^+$.

Ejemplo 231

(2S)-2-({[(3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–il]amino}carbonil)piperidin-1-carboxilato de tert-butilo

El compuesto del título se preparó utilizando ácido (*S*)-1-(*tert*-butoxicarbonil)piperidin-2-carboxílico en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso E de Ejemplo

16 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5, temperatura 90 °C) δ ppm 7,35-7,39 (m, 2H), 7,30 (t, *J* = 7,5 Hz, 2H), 7,21 (t, *J* = 7,2 Hz, 2H), 4,86-4,88 (m, 1H), 4,25-4,30 (m, 1H), 4,08-4,12 (m, 1H), 3,58 (d, *J* = 13,2 Hz, 1H), 3,47 (d, *J* = 13,1 Hz, 1H), 3,29 (td, *J* = 12,8, 3,1 Hz, 1H), 2,80 (d, *J* = 6,1 Hz, 1H), 2,49-2,56 (m, 1H), 2,42-2,47 (m, 2H), 2,36 (dd, *J* = 9,0, 3,2 Hz, 1H), 2,32 (d, *J* = 7,7 Hz, 1H), 2,22-2,26 (m, 1H), 2,03-2,11 (m, 1H), 1,79-1,93 (m, 1H), 1,49-1,68 (m, 5H), 1,48 (s, 9H), 1,32-1,44 (m, 2H); MS (ESI+) *m/z* 428 $(M+H)^+$.

Ejemplo 232

(S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxobutan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)- *N*-metil-L-valina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso E de Ejemplo 16 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (501 MHz, piridin-d_5, temperatura 90 °C) δ ppm 7,35-7,39 (m, 3H), 7,29 (t, *J* = 7,5 Hz, 2H), 7,21 (t, *J* = 7,3 Hz, 1H), 4,30-4,38 (m, 1H), 4,20-4,29 (m, 1H), 3,56 (d, *J* = 13,0 Hz, 1H), 3,47 (d, *J* = 13,2 Hz, 1H), 3,00-3,02 (m, 3H), 2,76 (d, *J* = 6,5 Hz, 1H), 2,48-2,55 (m, 1H), 2,33-2,47 (m, 4H), 2,28-2,32 (m, 1H), 2,04-2,12 (m, 1H), 1,81-1,88 (m, 1H), 1,49-1,59 (m, 1H), 1,46 (s, 9H), 1,36-1,45 (m, 1H), 1,00 (d, *J* = 6,5 Hz, 3H), 0,87 (d, *J* = 6,7 Hz, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Ejemplo 233

(S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-norvalina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso E de Ejemplo 16 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5, temperatura 90 °C) δ ppm 7,36-7,38 (m, 2H), 7,28-7,31 (m, 3H), 7,21 (t, *J* = 7,2 Hz, 1H), 4,70-4,79 (m, 1H), 4,23-4,29 (m, 1H), 3,57 (d, *J* = 13,2 Hz, 1H), 3,47 (d, *J* = 13,2 Hz, 1H), 2,95 (s, 3H), 2,77-2,81 (m, 1H), 2,48-2,52 (m, 1H), 2,39-2,46 (m, 2H), 2,36 (dd, *J* = 9,0, 2,9

Hz, 1H), 2,30 (t, *J* = 8,0 Hz, 1H), 2,07 (dq, *J* = 12,1, 6,1 Hz, 1H), 1,92-2,03 (m, 1H), 1,72-1,86 (m, 2H), 1,50-1,59 (m, 1H), 1,47 (s, 9H), 1,36-1,44 (m, 1H), 1,25-1,35 (m, 2H), 0,86 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Ejemplo 234

(S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3,3-dimetil-1-oxobutan-2–ilcarbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-L-*tert*-leucina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso E de Ejemplo 16 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,71 (m, 1H), 7,69 (d, *J* = 9,6 Hz, 1H), 7,39-7,42 (m, 2H), 7,36 (t, *J* = 7,5 Hz, 2H), 7,25-7,29 (m, 1H), 4,61 (d, *J* = 9,7 Hz, 1H), 4,32-4,42 (m, 1H), 3,53-3,56 (m, 1H), 3,37-3,40 (m, 1H), 2,63-2,66 (m, 1H), 2,41-2,51 (m, 2H), 2,27-2,33 (m, 2H), 2,20-2,25 (m, 1H), 2,11-2,19 (m, 1H), 1,80-1,91 (m, 1H), 1,61-1,73 (m, 1H), 1,48 (s, 9H), 1,35-1,44 (m, 1H), 1,18 (s, 9H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Ejemplo 235

***N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-isopropil-3-metilbutanamida**

El compuesto del título se preparó utilizando ácido 2-isopropil-3-metilbutanoico en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso E de Ejemplo 16 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,18 (d, *J* = 7,1, 1H), 7,44 (d, *J* = 7,3, 2H), 7,36 (t, *J* = 7,6, 2H), 7,27 (t, *J* = 7,3, 1H), 4,51 – 4,37 (m, 1H), 3,61 (d, *J* = 13,1, 1H), 3,44 (d, *J* = 13,2, 1H), 2,83 (dd, *J* = 9,0, 2,8, 1H), 2,61 – 2,51 (m, 2H), 2,48 (dd, *J* = 8,8, 7,2, 1H), 2,35 – 2,24 (m, 2H), 2,16 – 2,06 (m, 3H), 1,93 – 1,81 (m, 2H), 1,64 (dt, *J* = 14,6, 7,1, 1H), 1,44 – 1,35 (m, 1H), 1,13 (dd, *J* = 6,6, 3,9, 6H), 0,98 (d, *J* = 6,7, 6H); MS (ESI+) *m/z* 343 $(M+H)^+$.

Ejemplo 236

***N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metilbutanamida**

El compuesto del título se preparó utilizando ácido 3-metilbutanoico en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*R*,6a*R*)-2-

benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso E de Ejemplo 16 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,30 – 8,17 (m, 1H), 7,43 (dd, *J* = 11,2, 4,2, 2H), 7,37 (t, *J* = 7,5, 2H), 7,27 (t, *J* = 7,3, 1H), 4,49 – 4,39 (m, 1H), 3,60 (d, *J* = 13,1, 1H), 3,45 (d, *J* = 13,1, 1H), 2,89 – 2,78 (m, 1H), 2,55 – 2,49 (m, 2H), 2,45 (dd, *J* = 10,4, 5,3, 1H), 2,36 – 2,24 (m, 3H), 2,21 (d, *J* = 7,1, 2H), 2,17 – 2,08 (m, 1H), 1,90 – 1,79 (m, 1H), 1,62 (ddd, *J* = 15,1, 12,3, 7,2, 1H), 1,40 (dtd, *J* = 9,2, 8,2, 6,1, 1H), 0,95 (d, *J* = 6,6, 6H); MS (ESI+) *m/z* 301 $(M+H)^+$.

Ejemplo 237

2-ciclohexil-2-hidroxi-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida

El compuesto del título se preparó utilizando ácido 2-ciclohexil-2-hidroxiacético en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*S*,6a*R*)-2-(3-trifluorometil)benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 152 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,59 (d, *J* = 7,9, 0,5H), 8,40 – 8,33 (m, 0,5H), 7,97 (s, 0,5H), 7,77 (dd, *J* = 42,9, 9,6, 1,5H), 7,48 – 7,39 (m, 1,5H), 7,29 (d, *J* = 5,3, 0,5H), 4,67 – 4,57 (m, 1H), 4,37 (t, *J* = 3,8, 1H), 3,80 (dd, *J* = 21,0, 13,1, 1H), 3,27 (dd, *J* = 64,7, 13,0, 1H), 2,86 (dd, *J* = 13,0, 4,7, 1H), 2,73 – 2,61 (m, 1H), 2,50 – 2,40 (m, 1H), 2,36 (d, *J* = 9,1, 1H), 2,28 – 2,08 (m, 3H), 2,03 (dd, *J* = 14,3, 6,2, 0,5H), 2,00 – 1,93 (m, 0,5H), 1,92 – 1,88 (m, 0,5H), 1,86 – 1,45 (m, 9,5H), 1,35 – 1,06 (m, 4H); MS (ESI+) *m/z* 425$(M+H)^+$.

Ejemplo 238

(S)-1-((3aS,4S,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-norvalina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso C de Ejemplo 14 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (501 MHz, piridin-d_5, temperatura 90 °C) δ ppm 7,44-7,45 (bs, 2H), 7,35-7,40 (m, 2H), 7,30-7,37 (m, 1H), 7,25-7,29 (m, 1H), 4,70-4,75 (bs, 1H), 4,37-4,43 (m, 1H), 3,56 (d, *J* = 12,9 Hz, 1H), 3,52 (d, *J* = 12,8 Hz, 1H), 2,95 (s, 3H), 2,71 (d, *J* = 8,9 Hz, 1H), 2,62-2,68 (m, 1H), 2,44-2,48 (m, 2H),

2,25 (t, *J* = 8,5 Hz, 1H), 2,14 (t, *J* = 8,3 Hz, 1H), 1,91-1,99 (m, 1H), 1,66-1,80 (m, 3H), 1,56-1,63 (m, 1H), 1,50 (s, 9H), 1,26-1,38 (m, 3H), 0,88 (t, *J* = 7,4 Hz, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Ejemplo 239

(S)-1-((3aS,4S,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-leucina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso C de Ejemplo 14 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (501 MHz, piridin-d_5, temperatura 90 °C) δ ppm 7,44-7,49 (m, 2H), 7,36-7,40 (m, 2H), 7,32-7,39 (m, 1H), 7,27 (t, *J* = 7,4 Hz, 1H), 4,82-4,89 (m, 1H), 4,37-4,43 (m, 1H), 3,63 (d, *J* = 13,2 Hz, 1H), 3,50 (d, *J* = 13,0 Hz, 1H), 2,94 (s, 3H), 2,73 (dd, *J* = 9,7, 1,8 Hz, 1H), 2,64-2,70 (m, 1H), 2,44-2,47 (m, 2H), 2,22-2,28 (m, 1H), 2,15-2,19 (m, 1H), 1,88 (ddd, *J* = 14,1, 8,2, 6,0 Hz, 1H), 1,64-1,81 (m, 3H), 1,55-1,65 (m, 2H), 1,50 (s, 9H), 1,28-1,38 (m, 1H), 0,90-0,93 (m, 6H); MS (ESI+) *m/z* 444 $(M+H)^+$.

Ejemplo 240

(S)-1-((3aR,4R,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo

Paso A: Se preparó (3a*R*,4*R*,6a*S*)-2-Benciloctahidrociclopenta[*c*]pirrol-4-amina de acuerdo con el procedimiento descrito en Ejemplo 14 Pasos B-C utilizando (*S*,*E*)-*N*-((3a*R*,6a*S*)-2-bencilhexahidrociclopenta[*c*]pirrol-4(5*H*)–iliden)-2-metilpropan-2-sulfinamida del Ejemplo 14 Paso A en lugar de (*S*,*E*)-*N*-((3a*S*,6a*R*)-2-bencilhexahidrociclopenta[*c*]pirrol-4(5*H*)–iliden)-2-metilpropan-2-sulfinamida preparada en el Paso A de Ejemplo 14 para dar (3a*R*,4*R*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,44 (d, *J* = 7,4, 2H), 7,36 (t, *J* = 7,5, 2H), 7,28 (t, *J* = 7,3, 1H), 3,52 (q, *J* = 13,0, 2H), 3,29 (q, *J* = 7,3, 1H), 2,84 (dd, *J* = 3,7, 9,3, 1H), 2,55 – 2,43 (m, 3H), 2,37 – 2,30 (m, 1H), 2,24 (d, *J* = 5,3, 1H), 1,74 – 1,64 (m, 2H), 1,62 – 1,53 (m, 1H), 1,34 (dd, *J* = 5,0, 10,1, 1H).

Paso B: El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-norvalina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y

(3a*R*,4*R*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,40 (d, *J* = 7,4, 2H), 7,34 (t, *J* = 7,5, 2H), 7,25 (t, *J* = 7,3, 1H), 4,79 – 4,68 (m, 1H), 4,44 – 4,32 (m, 1H), 3,82 (d, *J* = 13,2, 1H), 3,36 (d, *J* = 13,0, 1H), 2,94 (s, 3H), 2,80 – 2,65 (m, 2H), 2,46 (s, 1H), 2,35 (dd, *J* = 9,2, 2,7, 1H), 2,31 – 2,25 (m, 2H), 1,99 (dt, *J* = 14,0, 7,0, 1H), 1,83 – 1,72 (m, 2H), 1,70 – 1,56 (m, 2H), 1,49 (d, *J* = 4,5, 1H), 1,48 (s, 9H), 1,41 – 1,23 (m, 3H), 0,89 (t, *J* = 7,4, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Ejemplo 241

(S)-1-((3aR,4R,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-leucina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*R*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 240 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 7,40-7,43 (m, 2H), 7,31-7,37 (m, 3H), 7,23-7,30 (m, 1H), 4,82-4,89 (m, 1H), 4,35-4,42 (m, 1H), 3,35 (d, *J* = 12,9 Hz, 1H), 2,95 (s, 3H), 2,68-2,78 (m, 2H), 2,42-2,50 (m, 1H), 2,26-2,36 (m, 3H), 1,89 (ddd, *J* = 14,1, 8,2, 5,9 Hz, 1H), 1,71-1,82 (m, 2H), 1,60-1,70 (m, 3H), 1,48-1,51 (m, 1H), 1,48 (s, 9H), 1,22-1,35 (m, 1H), 0,88-0,98 (m, 6H); MS (ESI+) *m/z* 444 $(M+H)^+$.

Ejemplo 242

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(metilsulfonil)-L-leucinamida

Paso A: Se disolvió clorhidrato de (S)-2-amino-4-metilpentanoato de tert-butilo (1,53 g, 6,84 mmol) en diclorometano y trietilamina (3,15 ml, 22,57 mmol). Se agregó cloruro de metansulfonilo (0,638 ml, 8,21 mmol) por goteo, y la reacción se agitó a temperatura ambiente por 1 hora. La reacción se detuvo con $NaHCO_3$ acuoso saturado y se extrajo con diclorometano (3×50ml). El solvente se eliminó al vacío para dar (S)-4-metil-2-(metilsulfonamido)pentanoato de tert-butilo: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 4,71 (d, *J* = 9,7, 1H), 3,98 (td, *J* = 9,5, 5,5, 1H), 2,92 (s, 3H), 1,84 (dt, *J* = 13,1, 6,6, 1H), 1,54 (s, 9H), 1,44-1,48 br s, 1H), 0,96 (dd, *J* = 6,6, 2,4, 6H); MS (ESI-) *m/z* 264$(M-H)^-$. Se disolvió (S)-4-metil-2-

(metilsulfonamido)pentanoato de tert-butilo en 10 ml de HCl 4 N en dioxano y se agitó a temperatura ambiente durante la noche. El solvente se eliminó bajo una corriente de nitrógeno y bajo alto vacío para dar ácido (S)-4-metil-2-(metilsulfonamido)pentanoico: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 4,86 (d, *J* = 9,6, 1H), 4,17 (td, *J* = 9,6, 4,8, 1H), 3,18 – 3,07 (m, 1H), 2,99 (s, 3H), 1,96 – 1,80 (m, 1H), 1,64 (dddd, *J* = 23,4, 13,9, 9,1, 5,0, 2H), 1,40 (t, *J* = 7,3, 1H), 0,98 (dd, *J* = 6,6, 3,3, 6H).

Paso B: El compuesto del título se preparó utilizando ácido (S)-4-metil-2-(metilsulfonamido)pentanoico del Paso A en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,41 (d, *J* = 9,4, 1H), 9,21 (d, *J* = 7,3, 1H), 7,45 (d, *J* = 7,2, 2H), 7,37 (t, *J* = 7,5, 2H), 7,29 (t, *J* = 7,3, 1H), 4,53 – 4,42 (m, 2H), 3,62 (d, *J* = 13,1, 1H), 3,47 (d, *J* = 13,1, 1H), 3,19 (s, 3H), 2,87 (dd, *J* = 9,1, 2,9, 1H), 2,66 – 2,58 (m, 1H), 2,57 – 2,45 (m, 2H), 2,35 (dd, *J* = 9,0, 3,0, 1H), 2,31 – 2,25 (m, 1H), 2,14 (dq, *J* = 12,0, 6,0, 1H), 1,99 (dq, *J* = 13,2, 6,5, 1H), 1,93 – 1,82 (m, 2H), 1,77 (ddd, *J* = 13,8, 8,5, 5,6, 1H), 1,63 (dt, *J* = 19,3, 7,2, 1H), 1,46 – 1,35 (m, 1H), 0,82 (d, *J* = 6,7, 3H), 0,79 (d, *J* = 6,5, 3H); MS (ESI+) *m/z* 408 $(M+H)^+$.

Ejemplo 243

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(metilsulfonil)-L-leucinamida

El compuesto del título se preparó utilizando ácido (S)-4-metil-2-(metilsulfonamido)pentanoico del Paso A de Ejemplo 242 en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso E de Ejemplo 16 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,40 (d, *J* = 9,4, 1H), 9,21 (d, *J* = 7,2, 1H), 7,43 (d, *J* = 7,5, 2H), 7,36 (t, *J* = 7,6, 2H), 7,27 (t, *J* = 7,3, 1H), 4,52 – 4,38 (m, 2H), 3,57 (d, *J* = 13,1, 1H), 3,47 (d, *J* = 13,1, 1H), 3,17 (s, 3H), 2,85 (dd, *J* = 9,1, 2,2, 1H), 2,59 – 2,48 (m, 2H), 2,37 (dd, *J* = 9,0, 6,8, 2H), 2,25 (dd, *J* = 8,7, 7,1, 1H), 2,19 (dq, *J* = 11,9, 5,9, 1H), 1,99 (dq, *J* = 13,1, 6,5, 1H), 1,94 – 1,84 (m, 2H), 1,80 – 1,66 (m, 2H), 1,44 (ddd, *J* = 18,9, 12,5, 6,2, 1H), 0,82 (d, *J* = 6,7, 3H), 0,79 (d, *J* = 6,5, 3H). ; MS (ESI+) *m/z* 408 $(M+H)^+$.

Ejemplo 244

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-neopentil-L-leucinamida

Paso A: Se combinó clorhidrato de (S)-2-amino-4-metilpentanoato de tert-butilo (1,022 g, 4,57 mmol) y pivalaldehido (0,502 ml, 4,57 mmol) en diclorometano (25 ml). Se agregó ácido acético (1,0 ml). La reacción se agitó a temperatura ambiente por 5 minutos, luego se agregó PS-cianoborohidruro (3,90 g, 9,14 mmol). La reacción se agitó a temperatura ambiente durante la noche, luego se filtró y el solvente se eliminó al vacío. El material crudo se diluyó con diclorometano y se basificó usando bicarbonato de sodio acuoso saturado para dar (S)-4-metil-2-(neopentilamino)pentanoato de tert-butilo: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 3,04 (t, *J* = 7,4, 1H), 2,40 (d, *J* = 11,1, 1H), 2,09 (d, *J* = 11,1, 1H), 1,86 – 1,70 (m, 1H), 1,46 (s, 10H), 1,40 (t, *J* = 7,2, 3H), 0,95 – 0,89 (m, 6H), 0,89 (s, 9H). Se disolvió (S)-4-metil-2-(neopentilamino)pentanoato de tert-butilo en 10 ml de HCl 4 N en dioxano y se agitó a temperatura ambiente durante la noche. El solvente se eliminó bajo una corriente de nitrógeno y bajo alto vacío para dar ácido (S)-4-metil-2-(neopentilamino)pentanoico: ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8,89 – 8,37 (m, 1H), 8,34 – 8,03 (m, 1H), 3,82 (t, *J* = 6,5, 1H), 2,88 (d, *J* = 12,3, 1H), 2,62 (d, *J* = 12,2, 1H), 1,83 – 1,67 (m, 2H), 1,67 – 1,56 (m, 1H), 1,00 (s, 9H), 0,97 – 0,88 (m, 6H).

Paso B: El compuesto del título se preparó utilizando ácido (S)-4-metil-2-(neopentilamino)pentanoico del Paso A en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,06-8,08 (m, 1H), 7,43-7,46 (m, 2H), 7,37 (t, *J* = 7,5 Hz, 2H), 7,28 (t, *J* = 7,3 Hz, 1H), 4,39-4,46 (m, 1H), 3,61 (d, *J* = 13,1 Hz, 1H), 3,46 (d, *J* = 13,1 Hz, 1H), 3,27 (dd, *J* = 8,5, 5,6 Hz, 1H), 2,84 (dd, *J* = 8,7, 2,5 Hz, 1H), 2,49-2,61 (m, 2H), 2,43-2,49 (m, 2H), 2,36 (dd, *J* = 9,1, 2,9 Hz, 1H), 2,32-2,36 (m, 1H), 2,30 (dd, *J* = 8,8, 7,0 Hz, 1H), 2,15 (dq, *J* = 12,1, 6,1 Hz, 1H), 1,80-1,96 (m, 2H), 1,55-1,76 (m, 4H), 1,39-1,46 (m, 1H), 0,94 (s, 9H), 0,93 (d, *J* = 6,8 Hz, 3H), 0,87 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 400 $(M+H)^+$.

Ejemplo 245

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-il]-N^2-neopentil-L-leucinamida

El compuesto del título se preparó utilizando ácido (S)-4-metil-2-(neopentilamino)pentanoico del Paso A de Ejemplo 244 en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina de Paso E del Ejemplo 16 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,07-8,09 (m, 1H), 7,43-7,45 (m, 2H), 7,37 (t, *J* = 7,5 Hz, 2H), 7,28 (t, *J* = 7,3 Hz, 1H), 4,43 (p, *J* = 6,2 Hz, 1H), 3,60 (d, *J* = 13,1 Hz, 1H), 3,45 (d, *J* = 13,1 Hz, 1H), 3,26 (dd, *J* = 8,6, 5,6 Hz, 1H), 2,86 (dd, *J* = 8,9, 2,6 Hz, 1H), 2,47-2,60 (m, 2H), 2,42-2,47 (m, 2H), 2,36 (dd, *J* = 9,1, 3,0 Hz, 1H), 2,29-2,35 (m, 1H), 2,29 (dd, *J* = 8,7, 7,3 Hz, 1H), 2,14 (dq, *J* = 12,1, 6,0 Hz, 1H), 1,81-1,95 (m, 2H), 1,52-1,76 (m, 4H), 1,44 (dq, *J* = 13,2, 6,6 Hz, 1H), 0,94 (s, 9H), 0,93 (d, *J* = 6,6 Hz, 3H), 0,87 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 400 $(M+H)^+$.

Ejemplo 246

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-il]-N^2-neopentil-L-norvalinamida

Paso A: Se preparó clorhidrato de ácido (S)-2-(neopentilamino)pentanoico utilizando (S)-2-aminopentanoato de tert-butilo en lugar de (*S*)-2-amino-4-metilpentanoato de *tert*-butilo en el procedimiento descrito en el Paso A de Ejemplo 244: ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 8,49 (ddd, *J* = 34,9, 23,2, 14,1, 2H), 3,84 (dd, *J* = 8,0, 5,2, 1H), 2,86 (d, *J* = 12,3, 1H), 2,66 (d, *J* = 12,3, 1H), 1,99 – 1,73 (m, 2H), 1,58 – 1,42 (m, 1H), 1,41 – 1,26 (m, 1H), 1,00 (s, 9H), 0,92 (t, *J* = 7,3, 3H); MS (ESI+) *m/z* 188 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando ácido (*S*)-2-(neopentilamino)pentanoico del Paso A en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso E de Ejemplo 16 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,00-8,03 (m, 1H), 7,43-7,45 (m, 2H), 7,37 (t, *J* = 7,5 Hz, 2H), 7,28 (t, *J* = 7,3 Hz, 1H), 4,40-4,45 (m, 1H), 3,60 (d, *J* = 13,1 Hz, 1H), 3,45 (d, *J* = 13,1 Hz, 1H), 3,20 (t, *J* = 6,5 Hz, 1H), 2,85 (dd, *J* = 8,8, 2,6 Hz, 1H), 2,52-2,60 (m, 1H), 2,46-2,52 (m,

1H), 2,38-2,46 (m, 2H), 2,31-2,38 (m, 2H), 2,28 (dd, *J* = 8,8, 7,3 Hz, 1H), 2,13 (dq, *J* = 12,1, 6,0 Hz, 1H), 1,79-1,92 (m, 2H), 1,71-1,80 (m, 1H), 1,65-1,73 (m, 1H), 1,57-1,65 (m, 1H), 1,39-1,57 (m, 3H), 0,93 (s, 9H), 0,86 (t, *J* = 7,3 Hz, 3H); MS (ESI-) *m/z* 384 $(M-H)^-$.

Ejemplo 247

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo

Paso A: Se disolvió ácido (*S*)-2-(*tert*-butoxicarbonilamino)-4,4-dimetilpentanoico (50 mg, 0,204 mmol) y yodometano (0,102 ml, 1,631 mmol) en tetrahidrofurano (2 ml) a 0 °C y se agregó hidruro de sodio (24,46 mg, 0,611 mmol). La reacción se agitó a 0 °C por media hora y a temperatura ambiente durante la noche. La reacción se enfrió a 0 °C y se agregó acetato de etilo (1 ml) seguido por la detención por goteo con agua (2 ml). El solvente se eliminó al vacío y el material crudo se particionó entre éter y agua. La capa de éter se separó. La capa acuosa se acidificó a pH~5 usando ácido cítrico 1 N y se extrajo con acetato de etilo. La capa orgánica se lavó con tiosulfato de sodio 1 N y salmuera, se secó (Na_2SO_4) y se concentró al vacío. El compuesto se purificó usando un cartucho de 4 g de gel de sílice con un gradiente de metanol al 0-3%/diclorometano a lo largo de 20 minutos para dar ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4,4-dimetilpentanoico: ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 12,63 (s, 1H), 4,57 (ddd, *J* = 74,4, 9,5, 3,1, 1H), 2,69 (s, 3H), 1,83 – 1,53 (m, 2H), 1,39 (s, 9H), 0,89 (s, 9H); MS (DSI+) *m/z* 260$(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4,4-dimetilpentanoico del Paso A en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 7,35-7,38 (m, 2H), 7,29 (t, *J* = 7,5 Hz, 2H), 7,20 (t, *J* = 7,3 Hz, 1H), 6,98-7,02 (m, 1H), 4,85-4,90 (m, 1H), 4,20-4,26 (m, 1H), 3,56 (d, *J* = 13,2 Hz, 1H), 3,48 (d, *J* = 13,2 Hz, 1H), 2,92 (s, 3H), 2,79 (d, *J* = 6,5 Hz, 1H), 2,51-2,55 (m, 1H), 2,39-2,47 (m, 2H), 2,37 (dd, *J* = 9,0, 3,1 Hz, 1H), 2,32 (dd, *J* = 8,9, 7,2 Hz, 1H), 2,19 (dd, *J* = 14,3, 5,6 Hz, 1H), 2,00-2,08 (m, 1H), 1,77-1,86 (m, 1H), 1,62 (dd, *J* = 14,3, 6,9 Hz, 1H), 1,50-1,56 (m, 1H), 1,48 (s, 9H), 1,35-1,47 (m, 1H), 0,95 (s, 9H); MS (DSI+) *m/z* 458$(M+H)^+$.

Ejemplo 248

(S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4,4-dimetilpentanoico del Paso A de Ejemplo 247 en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso E de Ejemplo 16 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,41-7,43 (m, 2H), 7,36 (t, *J* = 7,5 Hz, 2H), 7,25-7,29 (m, 1H), 5,14 (m, 0,7H), 4,79 (m, 0,2H), 4,35 (dd, *J* = 5,6, 2,9 Hz, 1H), 3,56-3,60 (m, 1H), 3,40-3,44 (m, 1H), 3,02-3,09 (m, 3H), 2,76-2,84 (m, 1H), 2,42-2,51 (m, 2H), 2,31-2,40 (m, 2H), 2,17-2,24 (m, 2H), 2,06-2,15 (m, 1H), 1,79-1,83 (m, 1H), 1,62-1,70 (m, 1H), 1,51-1,63 (m, 2H), 1,47 (s, 9H), 1,32-1,42 (m, 1H), 0,94 (s, 9H); MS (ESI+) *m/z* 458 $(M+H)^+$.

Ejemplo 249

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-morfolin-4–ilpentanamida

Paso A: Se combinó (S)-2-amino-4-metilpentanoato de tert-butilo (1,0042 g, 5,36 mmol), carbonato de potasio (2,446 g, 17,69 mmol), y 1-bromo-2-(2-bromoetoxi)etano (1,368 g, 5,90 mmol) en acetonitrilo (30 ml). La reacción se calentó a 80 °C durante la noche. La reacción se enfrió y se filtró y el solvente se eliminó al vacío. El material crudo se purificó mediante cromatografía sobre gel de sílice usando acetato de etilo al 5-50%/hexanos para dar (S)-4-metil-2-morfolinopentanoato de tert-butilo: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 3,76 - 3,58 (m, 4H), 3,11 (dd, *J* = 6,9, 8,1, 1H), 2,74 - 2,53 (m, 4H), 1,71 - 1,55 (m, 2H), 1,51 - 1,34 (m, 10H), 0,92 (dd, *J* = 6,6, 7,3, 6H). (S)-4-metil-2-morfolinopentanoato de tert-butilo (0,637 g, 2,475 mmol) y ácido clorhídrico 4 N en dioxano (5 ml) se combinaron. La mezcla de la reacción se agitó a temperatura ambiente por 24 horas, luego el solvente se eliminó al vacío para dar clorhidrato de ácido (S)-4-metil-2-morfolinopentanoico: MS (DCI+) *m/z* 202$(M+H)^+$.

Paso B: Se combinó clorhidrato de ácido (S)-4-metil-2-morfolinopentanoico (363 mg, 1,526 mmol) y trietilamina (0,387 ml, 2,77 mmol) en diclorometano (10 ml). Se agregó hidrato de 1-hidroxibenzotriazol (234 mg, 1,526 mmol) y *N*^{1}-

((etilimino)metilen)-N^3,N^3-dimetilpropan-1,3-diamina (0,270 ml, 1,526 mmol), y la reacción se agitó por 15 minutos. Luego se agregó (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina (300 mg, 1,387 mmol) del Ejemplo 16 Paso E, y la mezcla de la reacción se agitó a temperatura ambiente por 24 horas. La reacción se detuvo con bicarbonato de sodio acuoso y se extrajo con diclorometano. El solvente se eliminó al vacío y el material crudo se purificó mediante cromatografía sobre gel de sílice usando metanol al 1-10% (amoníaco 2 N)/diclorometano para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,27 (d, *J* = 7,3, 1H), 7,44 (d, *J* = 7,4, 2H), 7,37 (t, *J* = 7,5, 2H), 7,27 (dd, *J* = 9,8, 17,3, 1H), 4,51 - 4,39 (m, 1H), 3,74 (t, *J* = 4,5, 4H), 3,62 (d, *J* = 13,1, 1H), 3,45 (d, *J* = 13,1, 1H), 3,29 - 3,21 (m, 1H), 2,87 (dd, *J* = 2,4, 9,0, 1H), 2,79 (dt, *J* = 4,5, 9,3, 2H), 2,75 - 2,68 (m, 2H), 2,55 (d, *J* = 14,8, 2H), 2,49 - 2,43 (m, 1H), 2,35 (dd, *J* = 2,6, 8,9, 1H), 2,32 - 2,26 (m, 1H), 2,11 (dq, *J* = 6,1, 12,1, 1H), 1,86 (dd, *J* = 6,6, 12,2, 3H), 1,67 - 1,55 (m, 2H), 1,41 (dt, *J* = 6,2, 20,1, 1H), 0,94 (dd, *J* = 6,2, 11,1, 6H); MS (ESI+) *m/z* 400(M+H)$^+$.

Ejemplo 250

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-pirrolidin-1–ilpentanamida

El compuesto del título se preparó utilizando 1,4-dibromobutano en lugar de 1-bromo-2-(2-bromoetoxi)etano en el Paso A de Ejemplo 249: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,98 - 7,93 (m, 1H), 7,47 - 7,41 (m, 2H), 7,36 (t, *J* = 7,4, 2H), 7,31 - 7,24 (m, 1H), 4,45 (t, *J* = 5,2, 1H), 3,61 (d, *J* = 13,1, 1H), 3,45 (d, *J* = 13,1, 1H), 3,16 (dd, *J* = 5,1, 9,3, 1H), 2,87 (d, *J* = 7,9, 1H), 2,73 - 2,65 (m, 2H), 2,66 - 2,52 (m, 4H), 2,44 (dd, *J* = 6,2, 8,9, 1H), 2,36 (dd, *J* = 2,1, 9,0, 1H), 2,30 - 2,23 (m, 1H), 2,12 (dq, *J* = 6,0, 11,9, 1H), 1,95 - 1,78 (m, 3H), 1,66 - 1,54 (m, 6H), 1,47 - 1,36 (m, 1H), 1,00 (d, *J* = 6,4, 3H), 0,91 (d, *J* = 6,4, 3H); MS (ESI+) *m/z* 384(M+H)$^+$.

Ejemplo 251

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-piperidin-1–ilpentanamida

El compuesto del título se preparó utilizando 1,5-dibromopentano en lugar de 1-bromo-2-(2-bromoetoxi)etano en el Paso A de Ejemplo 249: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,09 (d, *J* = 7,5, 1H), 7,44 (d, *J* = 7,3, 2H), 7,36 (d, *J* = 7,7,

2H), 7,28 (t, *J* = 7,3, 1H), 4,46 – 4,36 (m, 1H), 3,61 (d, *J* = 13,1, 1H), 3,45 (d, *J* = 13,1, 1H), 3,21 (dd, *J* = 8,1, 5,4, 1H), 2,85 (d, *J* = 8,8, 1H), 2,70 – 2,50 (m, 6H), 2,49 – 2,44 (m, 1H), 2,32 (dt, *J* = 27,0, 7,9, 2H), 2,11 (dq, *J* = 12,1, 6,1, 1H), 1,95 – 1,79 (m, 3H), 1,63 – 1,47 (m, 6H), 1,45 – 1,32 (m, 3H), 0,94 (d, *J* = 5,8, 6H); MS (ESI+) *m/z* 398(M+H)$^+$.

Ejemplo 252

N^2-neopentil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

Paso A: Se disolvió (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina (0,83 g, 3,84 mmol) del Paso A de Ejemplo 33 en diclorometano anhidro (5 ml) bajo nitrógeno y se agregó trietilamina (0,588 ml, 4,22 mmol) seguido por dicarbonato de di-tert-butilo (1,010 ml, 4,22 mmol). La reacción se agitó a 25 °C por 1 hora. La cromatografía de capa fina (SiO_2, 5% metanol/diclorometano) mostró reacción completa. Los volátiles se eliminaron al vacío, y el material crudo se purificó usando un cartucho de 24 g de gel de sílice eluyendo con un gradiente de metanol al 1-5% (amoníaco 2 N)/diclorometano a lo largo de 20 minutos para dar (3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,54 (d, *J* = 6,3, 1H), 7,43 (d, *J* = 7,3, 2H), 7,36 (t, *J* = 7,4, 2H), 7,27 (t, *J* = 7,2, 1H), 4,12 (q, *J* = 12,1, 1H), 3,59 (d, *J* = 12,9, 1H), 3,43 (d, *J* = 13,0, 1H), 2,78 (s, 1H), 2,59 – 2,49 (m, 2H), 2,49 – 2,41 (m, 1H), 2,37 – 2,25 (m, 2H), 2,16 – 2,05 (m, 1H), 1,88 (td, *J* = 13,1, 6,1, 1H), 1,65 (td, *J* = 14,8, 7,3, 1H), 1,52 (s, 9H), 1,43 – 1,35 (m, 1H); MS (ESI+) *m/z* 317(M+H)$^+$.

Paso B: Se agregó (3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo (1,06 g, 3,35 mmol) del Paso A y etanol (20 ml) a Pd(OH)#2 al 20% sobre carbono, húmedo (212,0 mg, 1,51 mmol) en una botella de presión de acero inoxidable de 250 ml. La mezcla de la reacción se agitó por 16 horas bajo 30 psi de hidrógeno a temperatura ambiente. La mezcla se filtró a través de una membrana de nylon y el solvente se eliminó al vacío para dar (3aR,4S,6aS)-octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 4,02-3,99 (m, 1H), 3,03 (d, *J* = 10,4, 1H), 2,98 – 2,89 (m, 1H), 2,84 (dd, *J* = 10,1, 6,4, 1H), 2,61-2,50 (m, 3H), 2,06 – 1,98 (m, 1H), 1,91 (td, *J* = 12,9, 6,7, 1H), 1,63 (dt, *J* = 19,5, 7,6, 1H), 1,53 (s, 9H), 1,29-1,23 (m, 1H); MS (ESI+) *m/z* 227(M+H)$^+$.

Paso C: Se combinó (3aR,4S,6aS)-octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo (0,71 g, 3,14 mmol) del Paso B, trietilamina (0,656 ml, 4,71 mmol), y cloruro de 3-(trifluorometil)bencen-1-sulfonilo (0,552 ml, 3,45 mmol) en diclorometano (10,0 ml). La reacción se agitó a temperatura ambiente por 16 horas y se detuvo con $NaHCO_3$ acuoso saturado. La capa orgánica se separó y se concentró al vacío. El material crudo resultante se aplicó a un cartucho SF-25-60g (Analogix®, Burlington, Wisconsin) y se purificó con un gradiente de metanol al 0-2%/diclorometano a lo largo de 20 minutos para dar (3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,30 (s, 1H), 8,14 (d, *J* = 7,8, 1H), 7,84 (d, *J* = 7,8, 1H), 7,65 (t, *J* = 7,8, 1H), 6,83 – 6,71 (m, 1H), 3,88 – 3,76 (m, 1H), 3,61 (dd, *J* = 10,1, 3,3, 1H), 3,24 (dd, *J* = 9,8, 8,1, 1H), 3,12 (d, *J* = 5,6, 2H), 2,64 – 2,44 (m, 2H), 1,99 – 1,78 (m, 2H), 1,55 (tt, *J* = 12,4, 7,7, 1H), 1,48 (s, 9H), 1,38 – 1,20 (m, 1H); MS (ESI-) *m/z* 433(M-H)$^-$.

Paso D: Se combinó (3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo (0,814 g, 1,874 mmol) del Paso C y HCl (26,2 ml, 52,5 mmol, 2 *M* en éter) en etanol (3 ml). La reacción se agitó a temperatura ambiente durante la noche y luego los volátiles se eliminaron. El compuesto se purificó usando un cartucho de 24 g de gel de sílice con un gradiente de metanol al 1-10% (amoníaco 2 N)/diclorometano a lo largo de 20 minutos para dar (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37 (s, 1H), 8,21 (d, *J* = 7,9, 1H), 7,93 (d, *J* = 7,9, 1H), 7,75 (t, *J* = 7,9, 1H), 3,41 (dd, *J* = 9,8, 2,8, 1H), 3,13 (dd, *J* = 9,7, 3,1, 1H), 3,03 – 2,98 (m, 1H), 2,97 – 2,89 (m, 2H), 2,56 – 2,45 (m, 1H), 2,14 (tdd, *J* = 8,7, 5,9, 2,9, 1H), 1,5-2,0 (m, 2H)1,95 – 1,85 (m, 1H), 1,79 – 1,69 (m, 1H), 1,32 – 1,15 (m, 2H); MS (ESI+) *m/z* 335(M+H)$^+$.

Paso E: El compuesto del título se preparó utilizando ácido (S)-4-metil-2-(neopentilamino)pentanoico del Paso A de Ejemplo 244 en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso D en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,38 (s, 1H), 8,19-

8,22 (m, 2H), 7,90-7,93 (m, 1H), 7,72 (t, *J* = 7,8 Hz, 1H), 4,21-4,29 (m, 1H), 3,87 (dd, *J* = 9,9, 2,6 Hz, 1H), 3,25 (dd, *J* = 8,6, 5,6 Hz, 1H), 3,15-3,21 (m, 2H), 2,97 (dd, *J* = 9,6, 7,0 Hz, 1H), 2,43-2,60 (m, 3H), 2,28-2,32 (m, 1H), 1,79-2,01 (m, 3H), 1,67-1,78 (m, 1H), 1,69 (ddd, *J* = 13,6, 7,9, 5,7 Hz, 1H), 1,51-1,60 (m, 2H), 1,32 (ddt, *J* = 9,3, 12,8, 6,4 Hz, 1H), 0,93 (d, *J* = 6,6 Hz, 3H), 0,93 (s, 9H), 0,86 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 518 $(M+H)^+$.

Ejemplo 253

N^2-neopentil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

El compuesto del título se preparó utilizando ácido (S)-2-(neopentilamino)pentanoico del Paso A de Ejemplo 246 en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso D de Ejemplo 252 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,38-8,39 (bs, 1H), 8,19-8,21 (m, 1H), 8,13-8,16 (m, 1H), 7,90-7,93 (m, 1H), 7,72 (t, *J* = 7,8 Hz, 1H), 4,21-4,28 (m, 1H), 3,87 (dd, *J* = 9,9, 2,8 Hz, 1H), 3,15-3,21 (m, 3H), 2,97 (dd, *J* = 9,6, 7,3 Hz, 1H), 2,45-2,59 (m, 2H), 2,40 (d, *J* = 11,2 Hz, 1H), 2,31 (d, *J* = 11,2 Hz, 1H), 1,93-2,00 (m, 1H), 1,76-1,89 (m, 2H), 1,61-1,93 (m, 1H), 1,61-1,70 (m, 1H), 1,41-1,58 (m, 3H), 1,31 (ddt, *J* = 9,4, 13,0, 6,5 Hz, 1H), 0,92 (s, 9H), 0,86 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 504 $(M+H)^+$.

Ejemplo 254

N^2-neopentil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

Paso A: Se preparó (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina utilizando (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso E de Ejemplo 16 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el Paso A de Ejemplo 252 y siguiendo los pasos B-D en Ejemplo 252: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37 (s, 1H), 8,20 (d, *J* = 7,9, 1H), 7,93 (d, *J* = 7,8, 1H), 7,74 (t, *J* = 7,8, 1H), 3,40 (dd, *J* = 9,8, 2,8, 1H), 3,13 (dd, *J* = 9,7, 3,1, 1H), 3,00 (dd, *J* = 12,9, 5,7, 1H), 2,93 (ddd, *J* = 12,0, 9,7, 7,9, 2H), 2,52 (qd, *J* = 8,6, 4,3, 1H), 2,17 –

2,09 (m, 1H), 1,94 – 1,84 (m, 1H), 1,78 – 1,69 (m, 1H), 1,67 – 1,33 (m, 2H), 1,30 – 1,15 (m, 2H); MS (ESI+) *m/z* 335(M+H)$^+$.

Paso B: El compuesto del título se preparó utilizando ácido (S)-4-metil-2-(neopentilamino)pentanoico del Paso A de Ejemplo 244 en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37-8,38 (bs, 1H), 8,15-8,19 (m, 2H), 7,90-7,92 (m, 1H), 7,71 (t, *J* = 7,8 Hz, 1H), 4,22-4,28 (m, 1H), 3,88 (dd, *J* = 9,9, 2,8 Hz, 1H), 3,23 (dd, *J* = 8,5, 5,7 Hz, 1H), 3,19 (dd, *J* = 9,7, 2,8 Hz, 1H), 3,15 (dd, *J* = 9,9, 7,6 Hz, 1H), 2,96 (dd, *J* = 9,6, 7,2 Hz, 1H), 2,50-2,59 (m, 2H), 2,41-2,44 (m, 1H), 2,32 (d, *J* = 11,2 Hz, 1H), 1,92-2,01 (m, 1H), 1,82-1,92 (m, 2H), 1,60-1,78 (m, 1H), 1,69 (ddd, *J* = 13,5, 7,8, 5,7 Hz, 1H), 1,50-1,59 (m, 2H), 1,32 (ddt, *J* = 9,4, 13,0, 6,5 Hz, 1H), 0,92 (s, 9H), 0,92 (d, *J* = 6,6 Hz, 3H), 0,86 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 518 (M+H)$^+$.

Ejemplo 255

N^2-neopentil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-il)-L-norvalinamida

El compuesto del título se preparó utilizando ácido (S)-2-(neopentilamino)pentanoico del Paso A de Ejemplo 246 en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 254 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37-8,38 (bs, 1H), 8,18 (d, *J* = 7,9 Hz, 1H), 8,09-8,11 (m, 1H), 7,90-7,92 (m, 1H), 7,71 (t, *J* = 7,8 Hz, 1H), 4,20-4,27 (m, 1H), 3,88 (dd, *J* = 9,9, 2,8 Hz, 1H), 3,20 (dd, *J* = 6,6, 3,1 Hz, 1H), 3,16-3,20 (m, 1H), 3,14 (dd, *J* = 9,9, 7,8 Hz, 1H), 2,96 (dd, *J* = 9,6, 7,3 Hz, 1H), 2,46-2,61 (m, 2H), 2,38 (d, *J* = 11,3 Hz, 1H), 2,33 (d, *J* = 11,3 Hz, 1H), 1,92-1,99 (m, 1H), 1,83-1,90 (m, 1H), 1,76-1,83 (m, 1H), 1,66-1,87 (m, 1H), 1,61-1,70 (m, 1H), 1,38-1,58 (m, 3H), 1,26-1,37 (m, 1H), 0,92 (s, 9H), 0,85 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 504 (M+H)$^+$.

Ejemplo 256

N^2-neopentil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

Paso A: Se preparó (3a*R*,4*S*,6a*S*)-2-(4-(Trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina utilizando cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el Paso C de Ejemplo 252 y siguiendo el procedimiento de Paso D en Ejemplo 252: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,15 (d, *J* = 8,2, 2H), 7,92 (d, *J* = 8,3, 2H), 3,40 (dd, *J* = 9,8, 2,9, 1H), 3,13 (dd, *J* = 9,7, 3,2, 1H), 3,06 – 2,93 (m, 3H), 2,54 (s, 1H), 2,21 – 2,12 (m, 1H), 1,93 – 1,85 (m, 1H), 1,78 – 1,69 (m, 1H), 1,67 – 1,33 (m, 2H),1,33 – 1,15 (m, 2H); MS (ESI+) *m/z* 335(M+H)$^+$.

Paso B: El compuesto del título se preparó utilizando ácido (S)-4-metil-2-(neopentilamino)pentanoico del Paso A de Ejemplo 244 en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,20-8,23 (m, 1H), 8,13-8,16 (m, 2H), 7,89-7,92 (m, 2H), 4,21-4,29 (m, 1H), 3,86 (dd, *J* = 9,9, 2,8 Hz, 1H), 3,22-3,28 (m, 1H), 3,15-3,22 (m, 2H), 2,99 (dd, *J* = 9,6, 7,0 Hz, 1H), 2,50-2,62 (m, 2H), 2,43-2,47 (m, 1H), 2,28-2,32 (m, 1H), 1,92-2,02 (m, 1H), 1,80-1,92 (m, 2H), 1,64-1,76 (m, 1H), 1,69 (ddd, *J* = 13,5, 7,7, 5,8 Hz, 1H), 1,50-1,61 (m, 2H), 1,25-1,40 (m, 1H), 0,93 (d, *J* = 6,8 Hz, 3H), 0,93 (s, 9H), 0,86 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 518 (M+H)$^+$.

Ejemplo 257

N^2-neopentil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

El compuesto del título se preparó útilizando ácido (S)-2-(neopentilamino)pentanoico del Paso A de Ejemplo 246 en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 256 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5)

δ ppm 8,37-8,38 (bs, 1H), 8,13-8,18 (m, 3H), 7,89-7,91 (m, 2H), 4,21-4,28 (m, 1H), 3,86 (dd, *J* = 9,9, 2,9 Hz, 1H), 3,16-3,22 (m, 3H), 2,98 (dd, *J* = 9,6, 7,3 Hz, 1H), 2,47-2,61 (m, 2H), 2,41 (d, *J* = 11,2 Hz, 1H), 2,32 (d, *J* = 11,2 Hz, 1H), 1,93-2,00 (m, 1H), 1,78-1,88 (m, 2H), 1,63-1,70 (m, 1H), 1,41-1,58 (m, 3H), 1,28-1,36 (m, 1H), 0,93 (s, 9H), 0,86 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 504 $(M+H)^+$.

Ejemplo 258

_N_-(*tert*-butoxicarbonil)-_N_-metil-_N_-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-fenilalanina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 256 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,09-8,12 (m, 2H), 7,83-7,86 (m, 2H), 7,52-7,59 (bs, 1H), 7,28-7,32 (m, 2H), 7,23-7,28 (m, 2H), 7,15-7,21 (m, 1H), 4,95-5,12 (m, 1H), 4,09 (p, *J* = 6,9 Hz, 1H), 3,62 (dd, *J* = 10,4, 3,4 Hz, 1H), 3,48 (dd, *J* = 14,0, 7,0 Hz, 1H), 3,26 (dd, *J* = 10,1, 7,9 Hz, 1H), 3,10-3,18 (m, 1H), 3,04-3,13 (m, 1H), 2,97 (s, 3H), 2,46-2,57 (m, 1H), 2,36-2,46 (m, 1H), 1,86-1,96 (m, 1H), 1,74-1,83 (m, 1H), 1,44-1,55 (m, 1H), 1,42-1,46 (m, 1H), 1,38 (s, 9H), 1,21-1,32 (m, 1H); MS (ESI+) *m/z* 596 $(M+H)^+$.

Ejemplo 259

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-norvalina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 256 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,06-8,09 (m, 2H), 7,79-7,82 (m, 2H), 7,40 (d, *J* = 3,1 Hz, 1H), 4,66-4,76 (m, 1H), 4,07 (p, *J* = 6,8 Hz, 1H), 3,65 (dd, *J* = 10,2, 3,4 Hz, 1H), 3,28 (dd, *J* = 10,2, 7,7 Hz, 1H), 3,06-3,17 (m, 2H), 2,93 (s, 3H), 2,53-2,62 (m,

1H), 2,45-2,53 (m, 1H), 1,93-2,02 (m, 1H), 1,86-1,95 (m, 1H), 1,70-1,85 (m, 2H), 1,47-1,57 (m, 1H), 1,45 (s, 9H), 1,27-1,37 (m, 2H), 1,22-1,32 (m, 1H), 0,86 (t, *J* = 7,4 Hz, 3H); MS (ESI+) *m/z* 548 $(M+H)^+$.

Ejemplo 260

N^2-neopentil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

Paso A: Se preparó (3a*S*,4*R*,6a*R*)-2-(4-(Trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina siguiendo los procedimientos descritos en Ejemplo 252 Pasos A-D utilizando (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Paso E de Ejemplo 16 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el Paso A de Ejemplo 252 y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en el Paso C de Ejemplo 252: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,15 (d, *J* = 8,2, 2H), 7,92 (d, *J* = 8,3, 2H), 3,40 (dd, *J* = 9,8, 2,9, 1H), 3,13 (dd, *J* = 9,7, 3,2, 1H), 3,06 – 2,93 (m, 3H), 2,54 (s, 1H), 2,21 – 2,12 (m, 1H), 1,93 – 1,85 (m, 1H), 1,78 – 1,69 (m, 1H), 1,67 – 1,33 (m, 2H),1,33 – 1,15 (m, 2H); MS (ESI+) *m/z* 335$(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando ácido (S)-2-(neopentilamino)pentanoico del Paso A de Ejemplo 246 en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*R*,6a*R*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,09-8,14 (m, 3H), 7,88-7,91 (m, 2H), 4,20-4,26 (m, 1H), 3,88 (dd, *J* = 9,9, 2,9 Hz, 1H), 3,13-3,21 (m, 3H), 2,98 (dd, *J* = 9,6, 7,4 Hz, 1H), 2,49-2,64 (m, 2H), 2,38 (d, *J* = 11,2 Hz, 1H), 2,33 (d, *J* = 11,2 Hz, 1H), 1,91-1,99 (m, 1H), 1,76-1,90 (m, 2H), 1,66-1,95 (m, 1H), 1,62-1,71 (m, 1H), 1,41-1,58 (m, 3H), 1,33 (ddt, *J* = 9,5, 13,0, 6,5 Hz, 1H), 0,92 (s, 9H), 0,86 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 504 $(M+H)^+$.

Ejemplo 261

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-neopentil-L-leucinamida

Paso A: Se preparó (3a*R*,4*S*,6a*S*)-2-(4-

fluorofenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina utilizando cloruro de 4-fluorobencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el Paso C de Ejemplo 252 y siguiendo Paso D en Ejemplo 252: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,05 – 7,96 (m, 2H), 7,38 – 7,31 (m, 2H), 3,34 (dd, *J* = 9,8, 3,0, 1H), 3,08 (dd, *J* = 9,7, 3,3, 1H), 3,05 – 2,98 (m, 1H), 2,97 – 2,89 (m, 2H), 2,59 – 2,49 (m, 1H), 2,20 – 2,10 (m, 1H), 1,95 – 1,85 (m, 1H), 1,79 – 1,69 (m, 1H), 1,67 – 1,33 (m, 2H) 1,31 – 1,15 (m, 2H); MS (ESI+) *m/z* 285(M+H)$^+$.

Paso B: El compuesto del título se preparó utilizando ácido (S)-4-metil-2-(neopentilamino)pentanoico del Paso A de Ejemplo 244 en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(4-fluorofenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,21-8,23 (m, 1H), 7,99-8,02 (m, 2H), 7,32 (t, *J* = 8,5 Hz, 2H), 4,23-4,29 (m, 1H), 3,78 (dd, *J* = 9,9, 2,9 Hz, 1H), 3,26 (dd, *J* = 8,5, 5,7 Hz, 1H), 3,12-3,18 (m, 2H), 2,96 (dd, *J* = 9,6, 7,1 Hz, 1H), 2,51-2,60 (m, 2H), 2,44-2,47 (m, 1H), 2,29-2,32 (m, 1H), 1,93-2,01 (m, 1H), 1,81-1,93 (m, 2H), 1,67-1,79 (m, 1H), 1,70 (ddd, *J* = 13,5, 7,8, 5,7 Hz, 1H), 1,53-1,60 (m, 2H), 1,23-1,36 (m, 1H), 0,93 (d, *J* = 6,7 Hz, 3H), 0,93 (s, 9H), 0,87 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 468 (M+H)$^+$.

Ejemplo 262

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(5-(trifluorometil)piridin-2–il)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo

Paso A: Se combinó (3aR,4S,6aS)-octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo del Paso B de Ejemplo 252 (250 mg, 1,105 mmol), 2-bromo-5-(trifluorometil)piridina (250 mg, 1,105 mmol), y trietilamina (0,462 ml, 3,31 mmol) en etanol (0,6 ml). La reacción se calentó a 81 °C por 16 horas. A la mezcla de la reacción se agregó agua al 50%/etanol (5 ml), y el precipitado se recogió mediante filtración. Este material crudo se purificó usando un cartucho de 12 g de gel de sílice con un gradiente de metanol al 0-1,5% (amoníaco 2 N)/diclorometano a lo largo de 20 minutos para dar (3aR,4S,6aS)-2-(5-(trifluorometil)piridin-2–il)octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,62 (s, 1H), 7,76 (d, *J* = 6,4, 1H), 7,68 (d, *J* = 8,6, 1H), 6,38 (d, *J* = 8,8, 1H), 4,10 (s, 1H), 3,73 (d, *J* = 10,4, 1H), 3,65 (s, 1H), 3,61 – 3,53 (m, 1H),

3,32 (d, *J* = 10,1, 1H), 2,82 – 2,71 (m, 2H), 2,15 (td, *J* = 12,6, 6,8, 1H), 1,97 (dt, *J* = 13,1, 6,4, 1H), 1,74 (dq, *J* = 15,6, 7,9, 1H), 1,54 (s, 9H), 1,45 – 1,34 (m, 1H); MS(DCI+) *m/z* 372(M+H)$^+$.

Paso B: Se combinó (3aR,4S,6aS)-2-(5-(trifluorometil)piridin-2–il)octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo (282 mg, 0,759 mmol) del Paso A con HCl 4 N en 1,4-dioxano (2,5 ml, 9,87 mmol). La reacción se agitó a temperatura ambiente durante la noche y luego los volátiles se eliminaron al vacío. El compuesto se purificó usando un cartucho de 12 g de gel de sílice eluyendo con un gradiente de metanol al 0-7,5% (amoníaco 2 N)/diclorometano a lo largo de 20 minutos para dar (3a*R*,4*S*,6a*S*)-2-(5-(trifluorometil)piridin-2–il)octahidrociclopenta[*c*]pirrol-4-amina: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,64 (s, 1H), 7,69 (dd, *J* = 8,9, 2,5, 1H), 6,38 (d, *J* = 8,9, 1H), 4,95 (s, 2H), 3,56 (dd, *J* = 23,7, 14,1, 3H), 3,25 (d, *J* = 6,2, 1H), 3,11 (q, *J* = 6,0, 1H), 2,83 – 2,68 (m, 1H), 2,35 (ddd, *J* = 13,1, 7,9, 5,3, 1H), 2,02 (dtd, *J* = 13,5, 8,3, 5,5, 1H), 1,92 (ddd, *J* = 18,3, 7,4, 5,6, 1H), 1,46 – 1,30 (m, 2H); MS (ESI+) *m/z* 272(M+H)$^+$.

Paso C: El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-L-neopentilglicina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(5-(trifluorometil)piridin-2–il)octahidrociclopenta[*c*]pirrol-4-amina del Paso B en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,52 (s, 1H), 7,81 (d, *J* = 5,8, 1H), 7,60 (dd, *J* = 8,9, 2,5, 1H), 7,07 (d, *J* = 7,0, 1H), 6,35 (d, *J* = 8,9, 1H), 4,53 (td, *J* = 8,3, 4,7, 1H), 4,30 – 4,18 (m, 1H), 3,72 (dd, *J* = 11,3, 3,5, 1H), 3,65 (dd, *J* = 11,3, 7,6, 1H), 3,57 (dd, *J* = 11,1, 7,8, 1H), 3,31 (dd, *J* = 11,2, 3,9, 1H), 2,80 – 2,67 (m, 2H), 2,10 (ddd, *J* = 19,9, 13,5, 5,8, 2H), 1,93 (td, *J* = 13,1, 7,7, 1H), 1,74 (dd, *J* = 14,3, 8,0, 1H), 1,64 (dq, *J* = 12,9, 7,8, 1H), 1,50 (s, 9H), 1,44 – 1,33 (m, 1H), 1,00 (s, 9H); MS (ESI+) *m/z* 499(M+H)$^+$.

Ejemplo 263

(S)-1-oxo-1-((3aR,4S,6aS)-2-(5-(trifluorometil)piridin-2–il)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de isopropilo

Paso A: Se disolvió ácido (S)-2-aminopentanoico (1,874 g, 16mmol) en dioxano (16 ml) y se agregó 16 ml de NaOH 1 N a 0 °C. Se agregó cloroformiato de isopropilo 1 M en tolueno (16,00 ml, 16,00 mmol) simultáneamente con 16 ml de NaOH 1 N por goteo usando embudos de adición. La reacción se agitó a 0 °C

por 3 horas y se dejó calentar a temperatura ambiente durante la noche para dar una solución bifásica pH 8-9. El solvente se redujo en volumen. La capa acuosa se lavó con éter, se acidificó con $KHSO_4$ 1 M, y se extrajo con acetato de etilo para dar ácido (S)-2-(isopropoxicarbonilamino)pentanoico: ^{1}H NMR (300 MHz, DMSO-d_6) δ ppm 12,43 (s, 1H), 7,25 (d, *J* = 8,0, 1H), 4,73 (hept, *J* = 6,3, 1H), 3,89 (td, *J* = 8,6, 5,2, 1H), 1,68 – 1,46 (m, 2H), 1,41 – 1,22 (m, 2H), 1,16 (d, *J* = 6,2, 6H), 0,85 (t, *J* = 7,3, 3H); MS (DCI+) *m/z* 204(M+H)$^+$

Paso B: El compuesto del título se preparó utilizando ácido (S)-2-(isopropoxicarbonilamino)pentanoico del Paso A en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(5-(trifluorometil)piridin-2–il)octahidrociclopenta[*c*]pirrol-4-amina del Paso B de Ejemplo 262 en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,52 (d, *J* = 1,0, 1H), 7,94 (dd, *J* = 4,3, 2,4, 1H), 7,60 (dd, *J* = 8,9, 2,5, 1H), 7,07 (d, *J* = 7,0, 1H),6,35 (d, *J* = 8,9, 1H), 5,03 (dt, *J* = 12,5, 6,2, 1H), 4,49 (dd, *J* = 13,9, 8,0, 1H), 4,35 – 4,19 (m, 1H), 3,73 (dd, *J* = 11,3, 3,6, 1H), 3,66 (dd, *J* = 11,3, 7,6, 1H), 3,57 (dd, *J* = 11,0, 8,0, 1H), 3,32 (dd, *J* = 11,2, 3,9, 1H), 2,81 – 2,66 (m, 2H), 2,10 (dt, *J* = 12,4, 7,0, 1H), 2,04 – 1,88 (m, 2H), 1,86 – 1,75 (m, 1H), 1,72 – 1,60 (m, 1H), 1,57 – 1,46 (m, 2H), 1,45 – 1,33 (m, 1H), 1,21 (d, *J* = 6,2, 3H), 1,18 (d, *J* = 6,2, 3H), 0,87 (t, *J* = 7,4, 3H). ;MS (ESI+) *m/z* 457(M+H)$^+$.

Ejemplo 264

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(6-(trifluorometil)piridin-2–il)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo

Paso A: Se preparó (3a*R*,4*S*,6a*S*)-2-(6-(trifluorometil)piridin-2–il)octahidrociclopenta[*c*]pirrol-4-amina como se describe en el Ejemplo 262 Pasos A-B utilizando 2-bromo-6-(trifluorometil)piridina en lugar de 2-bromo-5-(trifluorometil)piridina en el Paso A de Ejemplo 262: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,53 (t, *J* = 7,9, 1H), 6,98 (d, *J* = 7,2, 1H), 6,51 (d, *J* = 8,6, 1H), 3,49 (dd, *J* = 20,2, 8,4, 3H), 3,19 (dd, *J* = 10,7, 4,8, 1H), 3,08 (q, *J* = 6,0, 1H), 2,78 – 2,69 (m, 1H), 2,32 (td, *J* = 12,2, 5,8, 1H), 2,04 – 1,95 (m, 1H), 1,89 (dt, *J* = 12,7, 5,7, 1H), 1,80 – 1,49 (m, 2H), 1,44 – 1,36 (m, 1H), 1,35 – 1,27 (m, 1H); MS (ESI+) *m/z* 272(M+H)$^+$.

Paso B: El compuesto del título se preparó utilizando *N*-(*tert*-

butoxicarbonil)-L-neopentilglicina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(6-(trifluorometil)piridin-2–il)octahidrociclopenta[*c*]pirrol-4-amina del Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,78 (s, 1H), 7,45 (s, 1H), 7,05 (s, 1H), 6,91 (d, *J* = 7,3, 1H), 6,47 (d, *J* = 8,6, 1H), 4,53 (td, *J* = 8,3, 4,7, 1H), 4,28 – 4,19 (m, 1H), 3,67 – 3,56 (m, 2H), 3,52 (dd, *J* = 10,9, 7,9, 1H), 3,27 (dd, *J* = 11,0, 3,7, 1H), 2,76 – 2,66 (m, 2H), 2,13 (dd, *J* = 14,3, 4,6, 1H), 2,06 (dt, *J* = 12,8, 6,4, 1H), 1,91 (td, *J* = 13,3, 7,9, 1H), 1,73 (dd, *J* = 14,3, 8,0, 1H), 1,62 (dq, *J* = 15,1, 7,7, 1H), 1,50 (s, 9H), 1,37 (qd, *J* = 7,9, 4,9, 1H), 1,00 (s, 9H). ;MS (ESI+) *m/z* 499(M+H)$^+$.

Ejemplo 265

(S)-4,4-dimetil-1-((3aR,4S,6aS)-2-(2-(metilsulfonil)pirimidin-5–il)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–ilcarbamato de tert-butilo

Paso A: (3a*R*,4*S*,6a*S*)-2-(2-(Metilsulfonil)pirimidin-5–il)octahidrociclopenta[*c*]pirrol-4-amina se preparó como se describe en Ejemplo 262 Pasos A-B utilizando 5-bromo-2-(metilsulfonil)pirimidina en lugar de 2-bromo-5-(trifluorometil)piridina en el Paso A de Ejemplo 262: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,48 (s, 2H), 4,96 (s, 3H), 3,71 (dd, *J* = 11,6, 8,6, 1H), 3,66 (d, *J* = 6,1, 2H), 3,41 (dd, *J* = 11,7, 4,9, 1H), 3,11 (q, *J* = 6,0, 1H), 2,80 – 2,71 (m, 1H), 2,37 – 2,30 (m, 1H), 2,00 (ddd, *J* = 21,4, 10,5, 6,5, 1H), 1,90 (td, *J* = 12,5, 5,6, 1H), 1,82 – 1,51 (m, 2H), 1,44 – 1,29 (m, 2H); MS (ESI+) *m/z* 283(M+H)$^+$.

Paso B: El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-L-neopentilglicina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(2-(metilsulfonil)pirimidin-5–il)octahidrociclopenta[*c*]pirrol-4-amina del Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,34 (s, 2H), 7,79 (ddd, *J* = 3,5, 1,7, 0,7, 1H), 7,10 – 6,93 (m, 1H), 4,52 (td, *J* = 8,2, 4,7, 1H), 4,27 (qd, *J* = 7,1, 5,4, 1H), 3,90 (d, *J* = 11,1, 3H), 3,85 (dd, *J* = 8,1, 3,9, 1H), 3,77 (dd, *J* = 12,1, 7,6, 1H), 3,67 (dd, *J* = 11,8, 7,9, 1H), 3,42 (dd, *J* = 11,8, 4,1, 1H), 2,79 – 2,63 (m, 2H), 2,16 – 2,02 (m, 2H), 1,97 – 1,83 (m, 1H), 1,72 (dd, *J* = 14,3, 8,0, 1H), 1,68 – 1,56 (m, 1H), 1,49 (s, 9H), 1,44 – 1,30 (m, 1H), 0,99 (s, 9H); MS (ESI+) *m/z* 510(M+H)$^+$.

Ejemplo 266

(S)-2-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilcarbamoil)pirrolidin-1-carboxilato de tert-butilo

Se combinó ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico (53,1 mg, 0,247 mmol), y hexafluorofosfato(V) de 2-(3H-[1,2,3]triazolo[4,5-b]piridin-3–il)-1,1,3,3-tetrametilisouronio (94 mg, 0,247 mmol) en diclorometano (2 ml). Luego de 10 minutos, se agregó (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina (75 mg, 0,224 mmol) del Paso A de Ejemplo 254. Luego de agitar por 10 minutos más, se agregó *N*-etil-*N*-isopropilpropan-2-amina (0,098 ml, 0,561 mmol) y la mezcla de la reacción se agitó a temperatura ambiente durante la noche. La reacción se detuvo con Solución saturada de $NaHCO_3$, se extrajo con 2 ml de diclorometano, se lavó con HCl 0,1 N, y se concentró al vacío. El material crudo se purificó usando un cartucho de 12 g de gel de sílice con un gradiente de metanol al 1-5% (amoníaco 2 N)/diclorometano a lo largo de 20 minutos para dar el compuesto del título: ^{1}H NMR (501 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,29-8,30 (bs, 1H), 8,13 (d, *J* = 7,9 Hz, 1H), 7,83 (d, *J* = 7,8 Hz, 1H), 7,66-7,72 (m, 1H), 7,64 (t, *J* = 7,9 Hz, 1H), 4,29-4,32 (m, 1H), 4,06-4,10 (m, 1H), 3,68-3,71 (m, 1H), 3,46-3,51 (m, 1H), 3,34-3,42 (m, 1H), 3,26 (dd, *J* = 9,9, 7,4 Hz, 1H), 3,06-3,17 (m, 2H), 2,55-2,57 (m, 2H), 2,09 (d, *J* = 3,0 Hz, 1H), 1,88-1,98 (m, 3H), 1,80-1,88 (m, 1H), 1,59-1,68 (m, 1H), 1,55 (dd, *J* = 13,2, 8,7 Hz, 1H), 1,50 (s, 9H), 1,25-1,37 (m, 1H); MS (ESI+) *m/z* 532 $(M+H)^+$.

Ejemplo 267

(1R)-1-isopropil-3-oxo-3-[((3aS,4R,6aR)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]propilcarbamato de tert-butilo

El compuesto del título se preparó utilizando ácido (R)-3-(tert-butoxicarbonilamino)-4-metilpentanoico en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (501 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,29-8,31 (bs, 1H), 8,14 (d, *J* = 7,8 Hz, 1H), 7,83 (d, *J* = 7,8 Hz, 1H), 7,76-7,80 (bs, 1H), 7,65 (t, *J* = 7,9 Hz, 1H), 6,53-6,62 (m, 1H), 4,08-4,15 (m, 1H), 4,02-4,08 (m, 1H), 3,67 (dd, *J* = 10,1,

3,2 Hz, 1H), 3,28 (dd, *J* = 9,9, 7,9 Hz, 1H), 3,08-3,16 (m, 2H), 2,46-2,59 (m, 4H), 1,87-1,98 (m, 2H), 1,79-1,87 (m, 1H), 1,50-1,62 (m, 1H), 1,48 (s, 9H), 1,24-1,36 (m, 1H), 0,89-0,93 (m, 6H); MS (ESI+) *m/z* 548 $(M+H)^+$.

Ejemplo 268

(2S)-2-{[((3aS,4R,6aR)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]carbonil}piperidin-1-carboxilato de tert-butilo

El compuesto del título se preparó utilizando ácido (S)-1-(tert-butoxicarbonil)piperidin-2-carboxílico en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (501 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,29-8,30 (bs, 1H), 8,14 (d, *J* = 7,8 Hz, 1H), 7,83 (d, *J* = 7,9 Hz, 1H), 7,64 (t, *J* = 7,9 Hz, 1H), 7,39-7,43 (bs, 1H), 4,82-4,84 (m, 1H), 4,04-4,12 (m, 2H), 3,68 (dd, *J* = 10,1, 3,3 Hz, 1H), 3,28-3,32 (m, 1H), 3,23-3,28 (m, 1H), 3,08-3,16 (m, 2H), 2,48-2,58 (m, 2H), 2,16-2,21 (m, 1H), 1,89-1,96 (m, 1H), 1,78-1,85 (m, 1H), 1,49-1,63 (m, 5H), 1,47 (s, 9H), 1,32-1,39 (m, 1H), 1,23-1,32 (m, 1H); MS (ESI+) *m/z* 544 $(M+H)^+$.

Ejemplo 269

***N*-(*tert*-butoxicarbonil)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida**

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-L-fenilalanina en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso D de Ejemplo 252 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (500 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,28-8,32 (m, 1H), 8,11-8,17 (m, 1H), 7,82-7,93 (m, 2H), 7,63-7,69 (m, 1H), 7,21-7,29 (m, 4H), 7,16-7,21 (m, 1H), 7,07-7,15 (m, 1H), 4,65-4,70 (m, 1H), 4,0 (m, 1H), 3,52-3,62 (m, 1H), 3,26-3,31 (m, 1H), 3,12-3,21 (m, 2H), 3,03-3,11 (m, 2H), 2,42-2,48 (m, 1H), 2,31-2,36 (m, 1H), 1,81-1,88 (m, 1H), 1,69-1,77 (m, 1H), 1,37-1,48 (m, 1H), 1,42 (s, 9H), 1,16-1,26 (m, 1H); MS (ESI+) *m/z* 599 $(M+H)^+$.

Ejemplo 270

***N*-(*tert*-butoxicarbonil)-*N*-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida**

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-fenilalanina en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso D de Ejemplo 252 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,65 – 8,52 (m, 1H), 8,38 (s, 1H), 8,22 (d, *J* = 7,8, 1H), 7,93 (d, *J* = 7,8, 1H), 7,75 (t, *J* = 7,8, 1H), 7,39 – 7,23 (m, 5H), 5,40 – 5,29 (m, 1H), 4,30 – 4,14 (m, 1H), 3,84 – 3,72 (m, 1H), 3,65 – 3,45 (m, 1H), 3,13 (d, *J* = 5,4, 2H), 3,06 (s, 3H), 3,03 (dd, *J* = 9,7, 7,6, 1H), 2,89 (dd, *J* = 9,5, 7,5, 1H), 2,41 (dd, *J* = 13,4, 6,1, 1H), 2,39 – 2,30 (m, 1H), 1,95-1,80 (m, 1H), 1,74 (s, 1H), 1,55 – 1,40 (m, 1H), 1,36 (s, 5H), 1,25 (s, 4H), 1,22 – 1,15 (m, 1H); MS (ESI+) *m/z* 596 $(M+H)^+$.

Ejemplo 271

(S)-2-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilcarbamoil)pirrolidin-1-carboxilato de tert-butilo

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso D de Ejemplo 252 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,42-8,59 (m, 1H), 8,36-8,38 (bs, 1H), 8,16-8,22 (m, 1H), 7,92 (d, *J* = 7,3 Hz, 1H), 7,74 (t, *J* = 7,5 Hz, 1H), 4,31-4,55 (m, 1H), 4,09-4,31 (m, 1H), 3,73-3,90 (m, 1H), 3,48-3,68 (m, 1H), 3,27-3,48 (m, 1H), 3,06-3,25 (m, 2H), 2,85-3,03 (m, 1H), 2,42-2,65 (m, 2H), 1,72-2,22 (m, 5H), 1,60-1,72 (m, 1H), 1,53-1,57 (bs, 5H), 1,49-1,54 (bs, 4H), 1,4 (m, 1H), 1,13-1,26 (m, 1H); MS (ESI+) *m/z* 532 $(M+H)^+$,549 $(M+NH_4)^+$.

Ejemplo 272

(1R)-1-isopropil-3-oxo-3-[((3aR,4S,6aS)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]propilcarbamato de tert-butilo

El compuesto del título se preparó utilizando ácido (R)-3-(tert-butoxicarbonilamino)-4-metilpentanoico en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso D de Ejemplo 252 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (500 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,30-8,31 (bs, 1H), 8,14 (d, *J* = 7,8 Hz, 1H), 7,84 (d, *J* = 7,6 Hz, 1H), 7,76-7,85 (bs, 1H), 7,66 (t, *J* = 7,8 Hz, 1H), 6,50-6,69 (bs, 1H), 4,08-4,16 (m, 1H), 3,64-3,72 (m, 1H), 3,24-3,33 (m, 1H), 3,12 (d, *J* = 5,2 Hz, 2H), 2,42-2,63 (m, 4H), 1,89-2,00 (m, 2H), 1,79-1,89 (m, 1H), 1,49-1,63 (m, 1H), 1,48 (s, 9H), 1,23-1,33 (m, 2H), 0,88-0,95 (m, 6H); MS (ESI+) *m/z* 570 $(M+Na)^+$.

Ejemplo 273

metil((S)-3-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-valina en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso D de Ejemplo 252 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (500 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,30-8,32 (bs, 1H), 8,14 (d, *J* = 7,8 Hz, 1H), 7,84 (d, *J* = 7,8 Hz, 1H), 7,64 (t, *J* = 7,8 Hz, 1H), 7,58-7,69 (bs, 1H), 4,32 (d, *J* = 9,5 Hz, 1H), 4,03-4,12 (m, 1H), 3,68 (dd, *J* = 10,2, 3,3 Hz, 1H), 3,27-3,31 (m, 1H), 3,08-3,16 (m, 2H), 3,00 (s, 3H), 2,53-2,61 (m, 1H), 2,46-2,53 (m, 1H), 2,33-2,43 (m, 1H), 1,85-1,93 (m, 1H), 1,77-1,85 (m, 1H), 1,47-1,54 (m, 1H), 1,45 (s, 9H), 1,21-1,30 (m, 1H), 0,97 (d, *J* = 6,5 Hz, 3H), 0,86 (d, *J* = 6,7 Hz, 3H); MS (ESI+) *m/z* 570 $(M+Na)^+$.

Ejemplo 274

(2S)-2-{[((3aR,4S,6aS)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4-il)amino]carbonil}piperidin-1-carboxilato de tert-butilo

El compuesto del título se preparó utilizando ácido (S)-1-(tert-butoxicarbonil)piperidin-2-carboxílico en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso D de Ejemplo 252D en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37-8,38 (bs, 1H), 8,32 (d, *J* = 5,2 Hz, 1H), 8,19 (d, *J* = 7,9 Hz, 1H), 7,91 (d, *J* = 7,9 Hz, 1H), 7,71 (t, *J* = 7,8 Hz, 1H), 4,07-4,23 (m, 2H), 3,84 (dd, *J* = 9,9, 2,2 Hz, 1H), 3,46 (td, *J* = 12,9, 2,8 Hz, 1H), 3,16 (d, *J* = 9,2 Hz, 1H), 3,12 (dd, *J* = 9,5, 7,6 Hz, 1H), 2,90-2,94 (m, 1H), 2,41-2,57 (bs, 2H), 2,24-2,29 (m, 1H), 1,75-1,97 (m, 2H), 1,53-1,65 (m, 3H), 1,49-1,55 (m, 2H), 1,48 (s, 9H), 1,42-1,51 (m, 1H), 1,29-1,39 (m, 1H), 1,17-1,29 (m, 1H); MS (ESI+) *m/z* 563 $(M+H)^+$.

Ejemplo 275

(3S)-3-{[((3aR,4S,6aS)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4-il)amino]carbonil}-3,4-dihidroisoquinolin-2(1H)-carboxilato de tert-butilo

El compuesto del título se preparó utilizando ácido (S)-2-(tert-butoxicarbonil)-1,2,3,4-tetrahidroisoquinolin-3-carboxílico en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso D de Ejemplo 252 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (500 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,26-8,27 (bs, 1H), 8,08-8,10 (m, 1H), 7,81-7,84 (m, 1H), 7,62 (t, *J* = 7,8 Hz, 1H), 7,29-7,36 (m, 1H), 7,12-7,14 (m, 2H), 7,08-7,11 (m, 2H), 4,83-5,02 (m, 1H), 4,78 (d, *J* = 15,6 Hz, 1H), 4,67 (d, *J* = 15,6 Hz, 1H), 3,90-3,97 (m, 1H), 3,52 (dd, *J* = 10,1, 3,3 Hz, 1H), 3,30 (dd, *J* = 15,3, 4,8 Hz, 1H), 3,14 (dd, *J* = 9,9, 7,8 Hz, 1H), 3,11 (dd, *J* = 15,4, 6,3 Hz, 1H), 3,04-3,08 (m, 2H), 2,45-2,53 (m, 1H), 2,38-2,45 (m,

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1H), 1,64-1,75 (m, 2H), 1,50 (s, 9H), 1,35-1,46 (m, 1H), 1,15-1,25 (m, 1H); MS (ESI+) *m/z* 594 $(M+H)^+$,611 $(M+NH_4)^+$.

Ejemplo 276

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-L-neopentilglicina en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso D de Ejemplo 252D en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (500 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,29-8,30 (bs, 1H), 8,14 (d, *J* = 7,9 Hz, 1H), 7,83 (d, *J* = 7,9 Hz, 1H), 7,79-7,87 (bs, 1H), 7,64 (t, *J* = 7,8 Hz, 1H), 7,05-7,18 (bs, 1H), 4,46-4,51 (m, 1H), 4,06-4,14 (m, 1H), 3,67 (dd, *J* = 10,2, 2,8 Hz, 1H), 3,27 (dd, *J* = 10,1, 7,6 Hz, 1H), 3,07-3,15 (m, 2H), 2,50-2,59 (m, 2H), 2,08 (dd, *J* = 14,2, 4,6 Hz, 1H), 1,85-1,92 (m, 1H), 1,77-1,85 (m, 1H), 1,70 (dd, *J* = 14,2, 8,0 Hz, 1H), 1,48-1,54 (m, 1H), 1,47 (s, 9H), 1,21-1,30 (m, 1H), 0,96 (s, 9H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Ejemplo 277

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)hexan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-norleucina en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso D de Ejemplo 252 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,44 (d, *J* = 6,9 Hz, 1H), 8,36-8,38 (bs, 1H), 8,19 (d, *J* = 7,9 Hz, 1H), 7,91 (d, *J* = 7,6 Hz, 1H), 7,72 (t, *J* = 7,8 Hz, 1H), 5,0 (m, 0,7H), 4,6 (m, 0,3H), 4,18-4,24 (m, 1H), 3,83-3,86 (m, 1H), 3,13-3,19 (m, 1H), 3,08-3,13 (m, 1H), 2,97-3,10 (bs, 3H), 2,91 (dd, *J* = 9,4, 7,4 Hz, 1H), 2,44-2,59 (m, 2H), 1,98-2,19 (m, 1H), 1,84-1,98 (m, 1H), 1,72-1,85 (m, 2H), 1,47-1,60 (m, 1H), 1,44-1,46 (m, 9H), 1,22-1,34 (m, 1H), 1,15-1,34 (m, 4H), 0,76-

0,81 (m, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$,579.$(M+NH_4)^+$.

Ejemplo 278

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-norvalina en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso D de Ejemplo 252 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (500 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,30-8,31 (bs, 1H), 8,14 (d, *J* = 7,9 Hz, 1H), 7,84 (d, *J* = 7,8 Hz, 1H), 7,64 (t, *J* = 7,8 Hz, 1H), 7,49 (d, *J* = 5,6 Hz, 1H), 4,72-4,73 (m, 1H), 4,04-4,11 (m, 1H), 3,67 (dd, *J* = 10,1, 3,3 Hz, 1H), 3,26 (dd, *J* = 10,1, 7,7 Hz, 1H), 3,10-3,13 (m, 2H), 2,93 (s, 3H), 2,46-2,59 (m, 2H), 1,86-2,01 (m, 2H), 1,71-1,84 (m, 2H), 1,46-1,58 (m, 1H), 1,45 (s, 9H), 1,29-1,36 (m, 2H), 1,22-1,30 (m, 1H), 0,86 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 548 $(M+H)^+$.

Ejemplo 279

(S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de isopropilo

El compuesto del título se preparó utilizando ácido (S)-2-(isopropoxicarbonilamino)pentanoico del Paso A de Ejemplo 263 en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 256 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (501 MHz, piridin-d_5) δ ppm 8,08 (d, *J* = 8,2, 2H), 7,96 (d, *J* = 4,8, 1H), 7,82 (d, *J* = 8,3, 2H), 7,18 (d, *J* = 4,5, 2H), 5,01 (hept, *J* = 6,2, 1H), 4,45 (dd, *J* = 14,0, 7,7, 1H), 4,11 (dt, *J* = 13,0, 6,7, 1H), 3,67 (dd, *J* = 10,2, 3,0, 1H), 3,30 (dd, *J* = 10,2, 7,6, 1H), 3,16 – 3,07 (m, 2H), 2,57 (h, *J* = 9,3, 2H), 1,99 – 1,85 (m, 2H), 1,86 – 1,72 (m, 2H), 1,58 – 1,50 (m, 1H), 1,45 (ddd, *J* = 20,8, 11,7, 7,2, 2H), 1,26 (ddd, *J* = 13,1, 10,9, 6,6, 1H), 1,19 (d, *J* = 6,2, 3H), 1,16

(d, J = 6,2, 3H), 0,84 (t, J = 7,4, 3H); MS (ESI+) m/z 520 $(M+H)^+$.

Ejemplo 280

(S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de isopropilo

El compuesto del título se preparó utilizando N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida del Ejemplo 382 en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo y cloroformiato de isopropilo en lugar de cloruro de metansulfonilo en el procedimiento descrito en Ejemplo 242: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,22 – 8,15 (m, 1H), 7,65 (d, J = 8,0, 2H), 7,51 (d, J = 7,9, 2H), 7,39 – 7,34 (m, 1H), 5,11 – 5,02 (m, 1H), 4,74 – 4,64 (m, 1H), 4,48 – 4,40 (m, 1H), 3,57 (d, J = 13,7, 1H), 3,46 (d, J = 13,6, 1H), 2,90 – 2,82 (m, 1H), 2,62 – 2,49 (m, 2H), 2,44 – 2,38 (m, 1H), 2,34 – 2,28 (m, 1H), 2,24 (dd, J = 9,7, 6,3, 1H), 2,10 – 2,00 (m, 2H), 1,92 – 1,81 (m, 2H), 1,65 – 1,57 (m, 1H), 1,55 – 1,45 (m, 2H), 1,42 – 1,33 (m, 1H), 1,22 (d, J = 6,2, 3H), 1,15 (d, J = 6,2, 3H), 0,81 (t, J = 7,4, 3H); MS (ESI+) m/z 470 $(M+H)^+$.

Ejemplo 281

(3a*S*,4*R*,6a*R*)-*N*-neopentil-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina

Se combinó (3a*S*,4*R*,6a*R*)-2-(3-(Trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina (100 mg, 0,299 mmol) del Paso A de Ejemplo 254 y pivalaldehido (0,043 ml, 0,389 mmol) en diclorometano (1 ml). Se agregó ácido acético (0,3 ml). La reacción se agitó a temperatura ambiente por 20 minutos, luego se agregó PS-cianoborohidruro (147 mg, 0,359 mmol). La reacción se agitó a temperatura ambiente por 72 horas, luego se filtró. La mezcla de la reacción se lavó con $NaHCO_3$ 1 N y se concentró al vacío. El material crudo se purificó usando un cartucho de 12 g de gel de sílice con un gradiente de metanol al 0-4% (amoníaco 2 N)/diclorometano para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,40-8,41 (bs, 1H), 8,22-8,25 (m, 1H), 7,92-7,95 (m, 1H), 7,75 (t, J = 7,8 Hz, 1H), 3,42 (dd, J = 9,8, 3,1 Hz, 1H), 3,17 (dd, J = 9,6, 3,1 Hz, 1H), 3,06-3,10 (m, 1H), 2,96 (dd, J = 9,6, 7,7 Hz, 1H), 2,74-2,77 (m, 1H), 2,48-2,53 (m, 1H), 2,30 (d, J = 11,3 Hz, 1H), 2,22-2,27 (m, 1H), 2,22 (d, J = 7,9 Hz, 1H), 1,78-1,92 (m, 2H), 1,18-1,31 (m, 3H), 0,90 (s, 9H);

MS (ESI+) *m/z* 405 $(M+H)^+$.

Ejemplo 282

(3a*R*,4*S*,6a*S*)-*N*-neopentil-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso D de Ejemplo 252 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,40-8,41 (bs, 1H), 8,22-8,25 (m, 1H), 7,92-7,95 (m, 1H), 7,75 (t, *J* = 7,9 Hz, 1H), 3,42 (dd, *J* = 9,8, 3,1 Hz, 1H), 3,17 (dd, *J* = 9,6, 3,0 Hz, 1H), 3,05-3,09 (m, 1H), 2,96 (dd, *J* = 9,6, 7,7 Hz, 1H), 2,73-2,77 (m, 1H), 2,48-2,53 (m, 1H), 2,30 (d, *J* = 11,3 Hz, 1H), 2,22-2,27 (m, 1H), 2,21 (d, *J* = 11,0 Hz, 1H), 1,78-1,93 (m, 2H), 1,18-1,32 (m, 3H), 0,90 (s, 9H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Ejemplo 283

(3a*R*,4*S*,6a*S*)-*N*-isopropil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso A de Ejemplo 256 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,14-8,22 (m, 2H), 7,91-7,98 (m, 2H), 3,40 (dd, *J* = 9,7, 3,0 Hz, 1H), 3,16 (dd, *J* = 9,6, 3,3 Hz, 1H), 3,06 (dd, *J* = 9,7, 7,8 Hz, 1H), 2,99 (dd, *J* = 9,6, 7,7 Hz, 1H), 2,85-2,90 (m, 1H), 2,74 (hept, *J* = 6,2 Hz, 1H), 2,46-2,53 (m, 1H), 2,14-2,25 (m, 1H), 1,80-1,91 (m, 2H), 1,07-1,43 (m, 3H), 1,00 (d, *J* = 6,2 Hz, 3H), 0,96 (d, *J* = 6,1 Hz, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Ejemplo 284

(3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}-*N*-isopropiloctahidrociclopenta[*c*]pirrol-4-amina

Paso A: Se preparó (3aR,4S,6aS)-2-(2-cloro-4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo utilizando 2-cloro-cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro

000688
970.81

de 3-(trifluorometil)bencen-1-sulfonilo en el Paso C de Ejemplo 252: ^{1}H NMR (500 MHz, piridin-d_5) δ 8,33 (d, *J* = 8,0, 1H), 8,00 (s, 1H), 7,77 – 7,68 (m, 2H), 4,04 – 3,96 (m, 1H), 3,83 (d, *J* = 9,5, 1H), 3,48 (dd, *J* = 10,2, 7,5, 1H), 3,41 – 3,29 (m, 2H), 2,72 – 2,59 (m, 2H), 2,02 (td, *J* = 12,0, 6,4, 1H), 1,90 (qd, *J* = 7,1, 4,5, 1H), 1,64 (ddd, *J* = 16,1, 12,4, 8,8, 1H), 1,50 (s, 9H), 1,41 – 1,32 (m, 1H) ;MS (ESI+) *m/z* 486(M+NH$_4$)$^+$.

Paso B: Se preparó (3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4-amina utilizando (3aR,4S,6aS)-2-(2-cloro-4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo del Paso A en lugar de (3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo en el procedimiento descrito en el Paso D de Ejemplo 252: ^{1}H NMR (500 MHz, piridin-d_5) δ 8,34 (d, *J* = 8,2, 1H), 8,01 (s, 1H), 7,75 (d, *J* = 8,3, 1H), 3,55 (dd, *J* = 10,1, 3,1, 1H), 3,38 – 3,31 (m, 2H), 3,28 (dd, *J* = 9,9, 3,7, 1H), 3,10 (q, *J* = 6,1, 1H), 2,70 – 2,60 (m, 1H), 2,31 – 2,22 (m, 1H), 1,93 (ddd, *J* = 11,1, 8,2, 5,7, 1H), 1,87 – 1,76 (m, 1H), 1,74 – 1,49 (m, 2H), 1,37 – 1,24 (m, 2H); MS (ESI+) *m/z* 369(M+H)$^+$.

Paso C: El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina del Paso A en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37 (d, *J* = 8,2 Hz, 1H), 8,03 (d, *J* = 1,7 Hz, 1H), 7,77 (d, *J* = 9,0 Hz, 1H), 3,56 (dd, *J* = 10,0, 3,1 Hz, 1H), 3,41 (dd, *J* = 10,1, 7,8 Hz, 1H), 3,31-3,38 (m, 2H), 2,97 (q, *J* = 6,3 Hz, 1H), 2,78 (hept, *J* = 6,2 Hz, 1H), 2,58-2,63 (m, 1H), 2,30-2,35 (m, 1H), 1,87-1,96 (m, 2H), 1,05-1,67 (m, 1H), 1,21-1,37 (m, 2H), 1,01 (d, *J* = 6,2 Hz, 3H), 0,98 (d, *J* = 6,1 Hz, 3H); MS (ESI+) *m/z* 411 (M+H)$^+$.

Ejemplo 285

(3a*S*,4*R*,6a*R*)-*N*-(4-fluorobencil)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina

El compuesto del título se preparó utilizando 4-fluorobenzaldehido en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,39-8,40 (bs, 1H), 8,23 (d, *J* = 7,9 Hz, 1H), 7,94 (d, *J* = 7,9 Hz,

1H), 7,76 (t, *J* = 7,8 Hz, 1H), 7,41 (dd, *J* = 8,3, 5,5 Hz, 2H), 7,11-7,15 (m, 2H), 3,71 (d, *J* = 13,2 Hz, 1H), 3,67 (d, *J* = 13,2 Hz, 1H), 3,39 (dd, *J* = 9,8, 3,1 Hz, 1H), 3,16 (dd, *J* = 9,6, 3,0 Hz, 1H), 3,06 (dd, *J* = 9,8, 8,0 Hz, 1H), 2,96 (dd, *J* = 9,6, 7,6 Hz, 1H), 2,83-2,88 (m, 1H), 2,47-2,56 (m, 1H), 2,30-2,36 (m, 1H), 1,92-2,09 (m, 1H), 1,87-1,94 (m, 1H), 1,80-1,88 (m, 1H), 1,29-1,37 (m, 1H), 1,20-1,29 (m, 1H); MS (ESI+) *m/z* 443 $(M+H)^+$.

Ejemplo 286

(3a*R*,4*S*,6a*S*)-*N*-(4-fluorobencil)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso D de Ejemplo 252 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y 4-fluorobenzaldehido en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,39-8,40 (bs, 1H), 8,22-8,24 (m, 1H), 7,93-7,95 (m, 1H), 7,75 (t, *J* = 7,8 Hz, 1H), 7,41 (dd, *J* = 8,3, 5,5 Hz, 2H), 7,13 (t, *J* = 8,7 Hz, 2H), 3,71 (d, *J* = 13,3 Hz, 1H), 3,67 (d, *J* = 13,2 Hz, 1H), 3,39 (dd, *J* = 9,8, 3,1 Hz, 1H), 3,16 (dd, *J* = 9,6, 3,0 Hz, 1H), 3,06 (dd, *J* = 9,8, 8,0 Hz, 1H), 2,96 (dd, *J* = 9,6, 7,6 Hz, 1H), 2,85 (q, *J* = 6,1 Hz, 1H), 2,47-2,56 (m, 1H), 2,30-2,35 (m, 1H), 1,93-2,07 (m, 1H), 1,87-1,94 (m, 1H), 1,79-1,87 (m, 1H), 1,29-1,38 (m, 1H), 1,20-1,29 (m, 1H); MS (ESI+) *m/z* 443 $(M+H)^+$.

Ejemplo 287

(3a*R*,4*S*,6a*S*)-*N*-(4-fluorobencil)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4-amina

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina (0,83 g, 3,84 mmol) del Paso A de Ejemplo 33 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y 4-fluorobenzaldehido en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,79-7,80 (bs, 1H), 7,58-7,61 (m, 1H), 7,60 (s, 1H), 7,44-7,49 (m, 1H), 7,39-7,44 (m, 2H), 7,12 (t, *J* = 8,6 Hz, 2H), 3,71-3,79 (m, 2H), 3,55-3,56 (bs, 2H), 2,96 (q, *J* = 5,1 Hz, 1H), 2,57-2,63 (m, 1H), 2,51 (dd, *J* = 8,8, 3,2 Hz, 1H), 2,39-2,43 (m, 1H), 2,31-2,39 (m, 3H), 1,91-1,98 (m,

2H), 1,72-1,93 (m, 1H), 1,34-1,48 (m, 2H); MS (ESI+) *m/z* 393 $(M+H)^+$.

Ejemplo 288

(3a*R*,4*S*,6a*S*)-*N*-etil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina

Se combinó (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina (120 mg, 0,359 mmol) del Paso A de Ejemplo 256, yodoetano (0,287 ml, 3,59 mmol), y trietilamina (0,750 ml, 5,38 mmol) en tetrahidrofurano (1 ml). La reacción se agitó a 65 °C por 3 días, y luego el solvente se eliminó al vacío. El residuo se diluyó con diclorometano (5 ml), y la adición de bicarbonato de sodio acuoso saturado dio los productos como un sólido. Este material se purificó usando un cartucho de 12 g de gel de sílice con un gradiente de 0-5% metanol (amoníaco 2 N)/diclorometano a lo largo de 20 minutos para dar dos productos. El segundo producto se purificó adicionalmente sobre una placa de cromatografía de capa fina preparativa de 4 x0,25 mm eluyendo con metanol al 6% (amoníaco 2 N)/diclorometano para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,17-8,19 (m, 2H), 7,93-7,95 (m, 2H), 3,38 (dd, *J* = 9,8, 3,1 Hz, 1H), 3,15 (dd, *J* = 9,6, 3,2 Hz, 1H), 3,06 (dd, *J* = 9,8, 8,0 Hz, 1H), 2,96 (dd, *J* = 9,6, 7,7 Hz, 1H), 2,78 (q, *J* = 6,1 Hz, 1H), 2,44-2,58 (m, 4H), 2,25-2,33 (m, 1H), 1,85-1,92 (m, 1H), 1,75-1,85 (m, 1H), 1,16-1,34 (m, 2H), 1,05 (t, *J* = 7,1 Hz, 3H); MS (ESI+) *m/z* 363 $(M+H)^+$.

Ejemplo 289

(3a*R*,4*S*,6a*S*)-*N*,*N*-dietil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina

El primer producto del Ejemplo 288 se purificó sobre una placa de cromatografía de capa fina preparativa de 2 x0,25 mm eluyendo con acetona para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,18-8,20 (m, 2H), 7,94-7,97 (m, 2H), 3,43 (dd, *J* = 9,6, 2,6 Hz, 1H), 3,22 (dd, *J* = 9,5, 2,6 Hz, 1H), 2,98 (dd, *J* = 9,6, 7,8 Hz, 1H), 2,88 (dd, *J* = 9,5, 7,4 Hz, 1H), 2,70-2,75 (m, 1H), 2,30-2,50 (m, 5H), 2,22-2,29 (m, 1H), 1,75-1,81 (m, 1H), 1,62-1,68 (m, 1H), 1,25-1,34 (m, 1H), 1,16-1,25 (m, 1H), 0,92 (t, *J* = 7,0 Hz, 6H); MS (ESI+) *m/z* 391 $(M+H)^+$.

Ejemplo 290

(3a*R*,4*S*,6a*S*)-*N*-propil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina

El compuesto del título se preparó utilizando 1-yodopropano en lugar de yodoetano en el procedimiento descrito en Ejemplo 288: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,17-8,19 (m, 2H), 7,93-7,95 (m, 2H), 3,39 (dd, *J* = 9,8, 3,1 Hz, 1H), 3,16 (dd, *J* = 9,6, 3,2 Hz, 1H), 3,07 (dd, *J* = 9,8, 8,0 Hz, 1H), 2,98 (dd, *J* = 9,6, 7,7 Hz, 1H), 2,77 (q, *J* = 5,9 Hz, 1H), 2,50-2,58 (m, 1H), 2,39-2,51 (m, 2H), 2,24-2,30 (m, 1H), 1,77-1,92 (m, 2H), 1,36-1,50 (m, 2H), 1,16-1,57 (m, 1H), 1,19-1,34 (m, 2H), 0,88 (t, *J* = 7,4 Hz, 3H); MS (ESI+) *m/z* 377 $(M+H)^+$.

Ejemplo 291

(3a*R*,4*S*,6a*S*)-*N*,*N*-dipropil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina

El compuesto del título se preparó como se describe en Ejemplo 290 siguiendo los procedimientos descritos en Ejemplos 288 y 289: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,18-8,20 (m, 2H), 7,93-7,95 (m, 2H), 3,48 (dd, *J* = 9,5, 2,3 Hz, 1H), 3,23 (dd, *J* = 9,5, 2,8 Hz, 1H), 2,99 (dd, *J* = 9,4, 7,7 Hz, 1H), 2,92 (dd, *J* = 9,3, 7,8 Hz, 1H), 2,74-2,80 (m, 1H), 2,37-2,48 (m, 1H), 2,19-2,35 (m, 5H), 1,78-1,84 (m, 1H), 1,61-1,66 (m, 1H), 1,16-1,39 (m, 6H), 0,84 (t, *J* = 7,3 Hz, 6H); MS (ESI+) *m/z* 419 $(M+H)^+$.

Ejemplo 292

(3a*R*,4*S*,6a*S*)-*N*-(ciclopropilmetil)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina

El compuesto del título se preparó utilizando (bromometil)ciclopropano en lugar de yodoetano en el procedimiento descrito en Ejemplo 288: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,17-8,19 (m, 2H), 7,93-7,95 (m, 2H), 3,38 (dd, *J* = 9,8, 3,2 Hz, 1H), 3,16 (dd, *J* = 9,6, 3,2 Hz, 1H), 3,07 (dd, *J* = 9,8, 8,0 Hz, 1H), 2,98 (dd, *J* = 9,6, 7,6 Hz, 1H), 2,79-2,84 (m, 1H), 2,51-2,58 (m, 1H), 2,36-2,50 (m, 2H), 2,26-2,32 (m, 1H), 1,85-1,93 (m, 1H), 1,78-1,85 (m, 1H), 1,35-1,78 (m, 1H), 1,22-1,33 (m, 2H), 0,89-0,98 (m, 1H), 0,36-0,44 (m, 2H), 0,11-0,13 (m, 2H); MS (ESI+) *m/z* 389 $(M+H)^+$.

Ejemplo 293

(3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}-*N*-etiloctahidrociclopenta[*c*]pirrol-4-amina

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4-amina del Paso B de Ejemplo 284 en lugar de (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 288: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37 (d, *J* = 8,2 Hz, 1H), 8,03 (s, 1H), 7,78 (dd, *J* = 8,3, 1,7 Hz, 1H), 3,54 (dd, *J* = 10,0, 3,5 Hz, 1H), 3,43 (dd, *J* = 10,0, 8,0 Hz, 1H), 3,27-3,36 (m, 2H), 2,86 (q, *J* = 5,9 Hz, 1H), 2,59-2,65 (m, 1H), 2,47-2,58 (m, 2H), 2,35-2,41 (m, 1H), 1,82-1,95 (m, 2H), 1,04-1,73 (m, 1H), 1,25-1,40 (m, 2H), 1,05 (t, *J* = 7,1 Hz, 3H); MS (ESI+) *m/z* 397 $(M+H)^+$.

Ejemplo 294

(3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}-*N*,*N*-dietiloctahidrociclopenta[*c*]pirrol-4-amina

El compuesto del título se preparó como se describe en Ejemplo 293 siguiendo los procedimientos descritos en Ejemplos 288 y 289: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,38 (d, *J* = 8,2 Hz, 1H), 8,04 (d, *J* = 1,7 Hz, 1H), 7,77-7,79 (m, 1H), 3,57 (dd, *J* = 9,9, 2,7 Hz, 1H), 3,34-3,41 (m, 2H), 3,29 (dd, *J* = 9,9, 7,3 Hz, 1H), 2,81-2,87 (m, 1H), 2,33-2,57 (m, 6H), 1,80-1,86 (m, 1H), 1,68-1,74 (m, 1H), 1,22-1,43 (m, 2H), 0,94 (t, *J* = 7,1 Hz, 6H); MS (ESI+) *m/z* 442 $(M+NH_4)^+$.

Ejemplo 295

(3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}-*N*-[5-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4-amina

(3a*R*,4*S*,6a*S*)-2-{[2-Cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4-amina (70 mg, 0,190 mmol) del Paso B de Ejemplo 284, 2-bromo-5-(trifluorometil)piridina (42,9 mg, 0,190 mmol), y trietilamina (0,079 ml, 0,569 mmol) se combinaron en etanol (0,6 ml). La reacción se calentó a 86 °C por 5 días y el solvente se evaporó al vacío. El material resultante se purificó usando un cartucho de 12 g de gel de sílice con un gradiente de metanol al 0-0,8% (amoníaco 2 N)/diclorometano a lo largo de 20 minutos para dar producto crudo. Se purificó adicionalmente cargándolo en una placa de cromatografía de capa fina preparativa de 2×0,25 mm y se eluyó con

acetona al 30%/hexanos para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,50-8,52 (bs, 1H), 8,40 (d, *J* = 8,2 Hz, 1H), 8,03 (s, 1H), 7,96-7,98 (m, 1H), 7,75-7,78 (m, 1H), 7,54-7,59 (m, 1H), 6,59 (d, *J* = 8,8 Hz, 1H), 4,30-4,42 (m, 1H), 3,89 (dd, *J* = 10,2, 2,7 Hz, 1H), 3,57 (dd, *J* = 10,2, 7,0 Hz, 1H), 3,43 (dd, *J* = 9,9, 6,7 Hz, 1H), 3,39 (dd, *J* = 10,0, 2,9 Hz, 1H), 2,68 (d, *J* = 3,5 Hz, 2H), 2,13-2,20 (m, 1H), 1,90-1,97 (m, 1H), 1,59-1,66 (m, 1H), 1,40-1,48 (m, 1H); MS (ESI+) *m/z* 514 $(M+H)^+$.

Ejemplo 296

(S)-1-(etil((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4,4-dimetilpentanoico del Paso A de Ejemplo 247 en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-*N*-etil-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 288 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,11 (d, *J* = 8,3, 2H), 7,83 (d, *J* = 8,4, 2H), 5,44 – 4,96 (m, 2H), 4,20 – 3,97 (m, 1H), 3,57 – 3,39 (m, 2H), 3,38 – 3,23 (m, 2H), 3,19 (d, *J* = 4,1, 2H), 2,89 (s, 3H), 2,85 – 2,73 (m, 1H), 2,72 – 2,59 (m, 1H), 2,25 – 2,08 (m, 1H), 1,97 – 1,73 (m, 3H), 1,52 (s, 9H), 1,35 – 1,21 (m, 1H), 1,17 (t, *J* = 7,0, 3H), 0,97 (s, 9H); MS (ESI+) *m/z* 604$(M+H)^+$.

Ejemplo 297

(S)-4,4-dimetil-1-oxo-1-(propil((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)pentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4,4-dimetilpentanoico del Paso A de Ejemplo 247 en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-*N*-propil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 290 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,11 (d, *J* = 8,2,

2H), 7,83 (d, *J* = 8,4, 2H), 5,37 – 5,09 (m, 1H), 4,15 – 3,99 (m, 1H), 3,54 (dd, *J* = 10,1, 3,2, 1H), 3,48 – 3,35 (m, 1H), 3,29 (dt, *J* = 9,1, 8,7, 1H), 3,18 (dd, *J* = 9,1, 4,5, 3H), 2,90 (s, 3H), 2,86 – 2,77 (m, 1H), 2,74 – 2,64 (m, 1H), 2,24 – 2,09 (m, 1H), 1,96 – 1,86 (m, 2H), 1,85 – 1,75 (m, 1H), 1,59 (dt, *J* = 15,2, 7,5, 3H), 1,52 (s, 9H), 1,34 – 1,22 (m, 1H), 0,98 (s, 9H), 0,90 (t, *J* = 7,3, 3H); MS (ESI+) *m/z* 618(M+H)$^+$.

Ejemplo 298

(S)-1-((ciclopropilmetil)((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4,4-dimetilpentanoico del Paso A de Ejemplo 247 en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-*N*-(ciclopropilmetil)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 292 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,11 (d, *J* = 8,2, 2H), 7,83 (d, *J* = 8,3, 2H), 5,39 – 5,07 (m, 1H), 4,12 – 3,95 (m, 1H), 3,58 (dd, *J* = 9,9, 3,4, 1H), 3,44 – 3,24 (m, 3H), 3,20 (d, *J* = 4,7, 2H), 3,11 – 2,96 (m, 1H), 2,88 (s, 3H), 2,80 – 2,65 (m, 1H), 2,32 – 2,16 (m, 1H), 2,13 – 2,00 (m, 1H), 1,99 – 1,90 (m, 1H), 1,90 – 1,80 (m, 1H), 1,51 (m, 10H), 1,31 (ddd, *J* = 20,7, 12,5, 7,9, 1H), 1,03 – 0,92 (m, 10H), 0,55 (tt, *J* = 14,1, 7,5, 2H), 0,47 – 0,36 (m, 1H), 0,32 – 0,22 (m, 1H); MS (ESI+) *m/z* 630(M+H)$^+$.

Ejemplo 299

2-nitro-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)bencenosulfonamida

Se combinó (3a*R*,4*S*,6a*S*)-2-(4-(Trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina (300 mg, 0,897 mmol) del Paso A de Ejemplo 256 y trietilamina (0,313 ml, 2,243 mmol) en diclorometano (20 ml). Se agregó cloruro de 2-nitrobencen-1-sulfonilo (258 mg, 1,166 mmol) en diclorometano (5 ml) por goteo. La mezcla de la reacción se agitó a temperatura ambiente por 16 horas. La reacción se detuvo con agua, y la capa

orgánica se separó y se concentró. El material crudo resultante se trituró con éter dietílico al 50%/hexano, se recogió mediante filtración, se lavó con agua luego hexano para dar un sólido. El sólido crudo se purificó usando un cartucho de 12 g de gel de sílice con un gradiente de acetato de etilo al 10-100%/hexano a lo largo de 20 minutos para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,69 (s, 1H), 8,31 (dd, *J* = 6,0, 3,3, 1H), 8,12 (d, *J* = 8,2, 2H), 7,92 (dd, *J* = 8,6, 2,1, 3H), 7,67 (dd, *J* = 5,9, 3,3, 2H), 4,94 (s, 2H), 3,84 (dd, *J* = 15,0, 6,2, 1H), 3,58 (dd, *J* = 10,0, 2,4, 1H), 3,17 (dd, *J* = 9,7, 2,7, 1H), 2,94 (dd, *J* = 10,0, 7,7, 1H), 2,87 (dd, *J* = 9,6, 7,7, 1H), 2,71 (td, *J* = 9,3, 2,4, 1H), 2,60 – 2,50 (m, 1H), 1,94 – 1,80 (m, 2H), 1,71 – 1,58 (m, 1H), 1,23 (tt, *J* = 10,5, 6,5, 1H); MS (ESI+) *m/z* 518(M+H)$^+$.

Ejemplo 300

N-metil-2-nitro-N-((3aR,4S,6aS)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)bencenosulfonamida

Se combinó 2-nitro-*N*-((3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4–il)bencenosulfonamida (250 mg, 0,481 mmol) del Ejemplo 299 y sulfato de dimetilo (0,138 ml, 1,444 mmol) se combinaron en *N,N*-dimetilformamida (3 ml) a 0 °C y se agregó 1,8-diazabiciclo[5,4,0]undec-7-eno (0,145 ml, 0,962 mmol) por goteo. La mezcla de la reacción se agitó por 0,5 horas, se agregó agua, y el precipitado se recogió mediante filtración. El material crudo resultante se purificó usando un cartucho de 12 g de gel de sílice eluyendo con un gradiente de acetato de etilo al 0-60%/hexano a lo largo de 20 minutos para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,15 (dd, *J* = 12,1, 4,7, 3H), 7,94 (d, *J* = 8,3, 2H), 7,88 (dd, *J* = 7,7, 1,3, 1H), 7,68 (dtd, *J* = 19,1, 7,5, 1,3, 2H), 4,29 (dt, *J* = 10,8, 7,0, 1H), 3,63 (dd, *J* = 9,9, 1,5, 1H), 3,21 (dd, *J* = 9,7, 2,3, 1H), 2,90 (s, 3H), 2,89 – 2,81 (m, 2H), 2,58 – 2,39 (m, 2H), 1,83 – 1,72 (m, 1H), 1,68 – 1,58 (m, 1H), 1,50 (qd, *J* = 11,8, 7,3, 1H), 1,21 (ddd, *J* = 19,4, 12,4, 7,1, 1H); MS (ESI+) *m/z* 551(M+NH_4)$^+$.

Ejemplo 301

(3aR,4S,6aS)-N-metil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4-amina

Se agregó 2-mercaptoetanol (0,056 ml, 0,793 mmol) por goteo a una

mezcla de *N*-metil-2-nitro-*N*-((3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4–il)bencenosulfonamida (235 mg, 0,440 mmol) del Ejemplo 300 y 1,8-diazabiciclo[5,4,0]undec-7-eno (0,166 ml, 1,101 mmol) en *N*,*N*-dimetilformamida (1ml) a temperatura ambiente. La mezcla de la reacción se agitó por 30 minutos, y se agregó Solución 1 N de $NaHCO_3$, La mezcla se extrajo con diclorometano, y la capa orgánica separada se concentró. El material crudo resultante se purificó usando un cartucho SF15-12g (Analogix®, Burlington, Wisconsin) con un gradiente de metanol al 0-5,5% (NH_3 2 N)/diclorometano a lo largo de 20 minutos para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,17 (d, *J* = 8,1, 2H), 7,94 (d, *J* = 8,2, 2H), 4,93 – 4,86 (m, 1H), 3,34 (dd, *J* = 9,8, 3,3, 1H), 3,14 (dd, *J* = 9,7, 3,2, 1H), 3,06 (dd, *J* = 9,7, 8,2, 1H), 2,65 (q, *J* = 5,7, 1H), 2,57 – 2,46 (m, 1H), 2,29 (s, 3H), 2,25 (ddd, *J* = 8,6, 5,0, 2,5, 1H), 1,86 (ddd, *J* = 12,0, 8,6, 6,1, 1H), 1,80 – 1,72 (m, 1H), 1,61 – 1,32 (m, 1H), 1,32 – 1,19 (m, 2H); MS (ESI+) *m/z* 349(M+H)$^+$.

Ejemplo 302

(S)-4,4-dimetil-1-(metil((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4,4-dimetilpentanoico del Paso A de Ejemplo 247 en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-*N*-metil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 301 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,11 (d, *J* = 8,2, 2H), 7,83 (d, *J* = 8,3, 2H), 5,37 – 5,10 (m, 1H), 4,73 – 4,53 (m, 1H), 3,57 (d, *J* = 9,1, 1H), 3,24 (dd, *J* = 16,5, 7,2, 2H), 3,16 (dd, *J* = 9,9, 3,4, 1H), 2,94 (s, 3H), 2,88 (s, 3H), 2,64 – 2,51 (m, 2H), 2,25 – 2,09 (m, 1H), 1,89 – 1,78 (m, 1H), 1,77 – 1,54 (m, 3H), 1,52 (s, 9H), 1,26 (dt, *J* = 17,5, 7,1, 1H), 0,96 (s, 9H); MS (ESI+) *m/z* 590(M+H)$^+$.

Ejemplo 303

(2*S*)-2-(1,1-dioxidoisotiazolidin-2–il)-4-metil-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}pentanamida

Paso A: Se agregó (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-Benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida (265 mg, 0,611 mmol) del Ejemplo 220 Paso D y etanol (20 ml) a Pd(OH)#2 al 20% sobre carbono, húmedo (53,0 mg, 0,377 mmol) en una botella de presión de 50 ml y se agitó por 48 horas bajo 30 psi de hidrógeno a 50 °C. La mezcla se filtró a través de una membrana de nylon y el solvente se eliminó al vacío para dar (2*S*)-2-(1,1-dioxidoisotiazolidin-2–il)-4-metil-*N*-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]pentanamida: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,89 (dd, *J* = 6,6, 18,9, 1H), 4,55 - 4,50 (m, 1H), 4,42 - 4,31 (m, 1H), 3,99 - 3,91 (m, 1H), 3,44 - 3,39 (m, 1H), 3,34 (dd, *J* = 2,8, 11,4, 0,5H), 3,29 - 3,25 (m, 2H), 3,21 (dd, *J* = 5,4, 13,2, 1H), 3,13 (dd, *J* = 7,7, 11,2, 0,5H), 2,99 (td, *J* = 7,5, 10,8, 1H), 2,79 (dd, *J* = 3,3, 10,9, 0,5H), 2,73 (dd, *J* = 3,3, 10,9, 0,5H), 2,69 - 2,55 (m, 2H), 2,31 - 2,16 (m, 2H), 2,12 - 2,00 (m, 1H), 1,94 - 1,78 (m, 4H), 1,69 (dddd, *J* = 5,2, 11,0, 16,7, 19,8, 2H), 1,49 - 1,29 (m, 1H), 0,88 (t, *J* = 6,5, 3H), 0,83 (t, *J* = 6,4, 3H); MS (ESI+) *m/z* 344(M+H)$^+$

Paso B: Se disolvió (2*S*)-2-(1,1-dioxidoisotiazolidin-2–il)-4-metil-*N*-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]pentanamida (204 mg, 0,594 mmol) y 3-(trifluorometil)benzaldehido (0,158 ml, 1,188 mmol) en diclorometano (3 ml). Se agregó ácido acético (1 ml). La reacción se agitó a temperatura ambiente por 20 min, luego se agregó PS-cianoborohidruro (487 mg, 1,188 mmol). La reacción se agitó a temperatura ambiente durante la noche, luego se filtró, y el solvente se eliminó al vacío. El material crudo se purificó mediante cromatografía sobre gel de sílice usando metanol al 1-10% (amoníaco 2 N)/diclorometano para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,79 (d, *J* = 7,0, 1H), 7,75 (d, *J* = 10,3, 1H), 7,61 - 7,54 (m, 2H), 7,44 (t, *J* = 7,7, 1H), 4,52 (dd, *J* = 6,6, 8,9, 1H), 4,38 (dq, *J* = 6,4, 12,6, 1H), 3,94 (dd, *J* = 7,3, 16,2, 1H), 3,57 (dd, *J* = 9,1, 13,5, 1H), 3,50 - 3,37 (m, 2H), 3,31 - 3,19 (m, 2H), 2,79 (ddd, *J* = 3,0, 9,1, 19,0, 1H), 2,62 - 2,54 (m, 1H), 2,54 - 2,45 (m, 1H), 2,43 - 2,36 (m, 1H), 2,31 - 2,16 (m, 4H), 2,13 - 2,03 (m, 1H), 1,94 - 1,78 (m, 3H), 1,77 - 1,59 (m, 2H), 1,39 (dt, *J* = 6,5, 19,8, 1H), 0,88 (d, *J* = 6,6, 3H), 0,82 (dd, *J* = 2,3, 6,5, 3H); MS (ESI+) *m/z*

502(M+H)$^+$.

Ejemplo 304

2-isopropil-3-metil-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida

El compuesto del título se preparó utilizando *N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-isopropil-3-metilbutanamida del Ejemplo 235 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,12-8,14 (m, 1H), 7,75-7,76 (bs, 1H), 7,55-7,63 (m, 2H), 7,44 (t, *J* = 7,8 Hz, 1H), 4,42-4,48 (m, 1H), 3,62 (d, *J* = 13,5 Hz, 1H), 3,46 (d, *J* = 13,5 Hz, 1H), 2,86 (dd, *J* = 9,0, 2,4 Hz, 1H), 2,50-2,57 (m, 2H), 2,44-2,49 (m, 1H), 2,25-2,31 (m, 2H), 2,06-2,15 (m, 3H), 1,83-1,90 (m, 2H), 1,58-1,65 (m, 1H), 1,35-1,42 (m, 1H), 1,14 (d, *J* = 6,7 Hz, 3H), 1,13 (d, *J* = 6,6 Hz, 3H), 0,98 (d, *J* = 6,8 Hz, 6H); MS (ESI+) *m/z* 411 (M+H)$^+$.

Ejemplo 305

2-isopropil-3-metil-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida

El compuesto del título se preparó utilizando *N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-isopropil-3-metilbutanamida del Ejemplo 229 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,12-8,14 (m, 1H), 7,75-7,77 (bs, 1H), 7,58-7,63 (m, 1H), 7,42-7,47 (m, 1H), 4,42-4,48 (m, 1H), 3,62 (d, *J* = 13,5 Hz, 1H), 3,46 (d, *J* = 13,5 Hz, 1H), 2,85 (dd, *J* = 8,9, 2,5 Hz, 1H), 2,50-2,58 (m, 2H), 2,45-2,49 (m, 1H), 2,28 (d, *J* = 6,6 Hz, 2H), 2,06-2,16 (m, 4H), 1,84-1,90 (m, 2H), 1,58-1,66 (m, 1H), 1,35-1,42 (m, 1H), 1,14 (d, *J* = 6,6 Hz, 3H), 1,13 (d, *J* = 6,6 Hz, 3H), 0,98 (d, *J* = 6,8 Hz, 6H); MS (ESI-) *m/z* 409 (M-H)-.

Ejemplo 306

(S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–ilcarbamato de

tert-butilo del Ejemplo 221 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,64 (d, *J* = 7,2 Hz, 1H), 7,96-7,99 (m, 1H), 7,72-7,77 (m, 1H), 7,55-7,63 (m, 2H), 7,44 (t, *J* = 7,7 Hz, 1H), 4,66-4,75 (m, 1H), 4,35-4,44 (m, 1H), 3,59 (d, *J* = 13,5 Hz, 1H), 3,46 (d, *J* = 13,6 Hz, 1H), 2,81-2,84 (m, 1H), 2,44-2,59 (m, 3H), 2,22-2,31 (m, 2H), 2,14 (s, 3H, OAc), 1,96-2,07 (m, 1H), 1,79-1,91 (m, 4H), 1,55-1,70 (m, 1H), 1,50 (s, 9H), 1,27-1,41 (m, 1H), 0,82-0,89 (m, 6H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Ejemplo 307

metil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 222 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,27-8,34 (m, 1H), 7,75-7,76 (bs, 1H), 7,52-7,63 (m, 2H), 7,42-7,47 (m, 1H), 5,1 (m, 0,7H), 4,7 (0,3H), 4,35-4,41 (m, 1H), 3,59 (d, *J* = 13,5 Hz, 1H), 3,45-3,49 (m, 1H), 3,04-3,13 (m, 3H), 2,82-2,85 (m, 1H), 2,42-2,54 (m, 3H), 2,22-2,31 (m, 2H), 1,98-2,11 (m, 1H), 1,80-2,11 (m, 1H), 1,79-1,87 (m, 2H), 1,53-1,62 (m, 2H), 1,46-1,48 (m, 9H), 1,33-1,38 (m, 1H), 0,88 (d, *J* = 6,4 Hz, 3H), 0,85 (d, *J* = 6,6 Hz, 3H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Ejemplo 308

metil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 222 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida y 4-(trifluorometil)benzaldehido en lugar de 3-

(trifluorometil)benzaldehido en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,31-8,36 (bs, 1H), 7,64-7,66 (m, 2H), 7,50-7,53 (m, 2H), 5,1 (m, 0,7H) 4,7 (0,3H), 4,38-4,43 (m, 1H), 3,57 (d, *J* = 13,7 Hz, 1H), 3,45-3,49 (m, 1H), 3,04-3,12 (m, 3H), 2,84-2,87 (m, 1H), 2,51-2,56 (m, 2H), 2,35-2,42 (m, 1H), 2,30-2,35 (m, 1H), 2,20-2,24 (m, 1H), 2,05-2,10 (m, 1H), 1,81-1,93 (m, 3H), 1,55-1,61 (m, 2H), 1,46-1,48 (m, 9H), 1,35-1,40 (m, 1H), 0,88 (d, *J* = 6,3 Hz, 3H), 0,85 (d, *J* = 6,6 Hz, 3H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Ejemplo 309

(S)-1-((3aR,4S,6aS)-2-(4-fluorobencil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 222 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida y 4-fluorobenzaldehido en lugar de 3-(trifluorometil)benzaldehido en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,30-8,32 (m, 1H), 7,35-7,38 (m, 2H), 7,12 (t, *J* = 8,6 Hz, 2H), 5,1 (m, 0,7H) 4,7 (0,3H), 4,37-4,41 (m, 1H), 3,50 (d, *J* = 13,1 Hz, 1H), 3,40 (d, *J* = 13,1 Hz, 1H), 3,04-3,11 (m, 3H), 2,81-2,84 (m, 1H), 2,47-2,53 (m, 2H), 2,29-2,39 (m, 2H), 2,19-2,23 (m, 1H), 2,02-2,11 (m, 1H), 1,79-1,94 (m, 3H), 1,53-1,62 (m, 2H), 1,46-1,48 (m, 9H), 1,34-1,39 (m, 1H), 0,89 (d, *J* = 6,4 Hz, 3H), 0,85 (d, *J* = 6,6 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 310

etil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(etil)carbamato de tert-butilo del Ejemplo 223 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,14-8,17 (m, 1H), 7,74-7,77 (m, 1H), 7,55-7,61 (m, 2H), 7,41-7,46 (m, 1H), 5,1 (m, 0,7H) 4,7 (0,3H), 4,32-4,42 (m, 1H), 3,59 (d, *J* = 13,4

Hz, 1H), 3,38-3,53 (m, 3H), 2,78-2,87 (m, 1H), 2,44-2,54 (m, 2H), 2,36-2,44 (m, 1H), 2,28-2,35 (m, 1H), 2,20-2,27 (m, 1H), 2,01-2,13 (m, 1H), 1,91-2,01 (m, 1H), 1,79-1,88 (m, 1H), 1,71-1,79 (m, 1H), 1,62-1,71 (m, 1H), 1,53-1,62 (m, 1H), 1,48 (s, 9H), 1,33-1,42 (m, 1H), 1,17-1,33 (m, 3H), 0,83-0,97 (m, 6H); MS (ESI+) *m/z* 526 $(M+H)^+$.

Ejemplo 311

(S)-1-((3aS,4R,6aR)-2-(3-fluoro-4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida del Ejemplo 151 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida y 3-fluoro-4-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,33-8,42 (m, 1H), 7,31-7,35 (m, 1H), 7,24-7,29 (m, 1H), 5,1 (m, 0,7H) 4,7 (0,3H), 4,35-4,42 (m, 1H), 3,51-3,56 (m, 1H), 3,41-3,45 (m, 1H), 3,04-3,12 (m, 3H), 2,77-2,97 (m, 1H), 2,47-2,52 (m, 2H), 2,29-2,35 (m, 2H), 2,19-2,22 (m, 1H), 2,06-2,15 (m, 1H), 1,83-1,89 (m, 3H), 1,53-1,66 (m, 2H), 1,47 (s, 9H), 1,32-1,41 (m, 2H), 0,88-0,90 (m, 3H), 0,85 (d, *J* = 6,6 Hz, 3H); MS (ESI+) *m/z* 530 $(M+H)^+$.

Ejemplo 312

(S)-1-((3aS,4R,6aR)-2-(4-fluoro-3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida del Ejemplo 151 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida y 4-fluoro-3-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,32-8,39 (m, 1H), 7,62-7,75 (m, 1H), 7,20-7,27 (m, 2H), 5,1 (m, 0,7H) 4,7 (0,3H), 4,29-4,47 (m, 1H), 3,49-3,54 (m, 1H), 3,38-3,43

(m, 1H), 3,04-3,12 (m, 3H), 2,74-2,89 (m, 1H), 2,47-2,51 (m, 2H), 2,19-2,38 (m, 3H), 2,05-2,15 (m, 1H), 1,84 (dd, *J* = 9,0, 5,2 Hz, 3H), 1,54-1,65 (m, 2H), 1,46 (s, 9H), 1,26-1,42 (m, 1H), 0,89 (d, *J* = 6,4 Hz, 3H), 0,85 (d, *J* = 6,6 Hz, 3H); MS (ESI+) *m/z* 530 $(M+H)^+$.

Ejemplo 313

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

Paso A: Se preparó metil((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-norvalina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,26 – 8,15 (m, 1H), 7,43 (d, *J* = 7,4, 2H), 7,36 (t, *J* = 7,5, 2H), 7,27 (t, *J* = 7,3, 1H), 5,07 – 5,00 (m, 1H), 4,72 – 4,58 (m, 1H), 4,46 – 4,31 (m, 1H), 3,59 (d, *J* = 13,1, 1H), 3,44 (d, *J* = 13,1, 1H), 3,12 – 2,99 (m, 3H), 2,83 (d, *J* = 8,9, 1H), 2,53 – 2,44 (m, 2H), 2,44 – 2,37 (m, 1H), 2,33 (d, *J* = 7,9, 1H), 2,26 – 2,19 (m, 1H), 2,14 – 1,95 (m, 2H), 1,79 (ddt, *J* = 7,1, 5,2, 4,2, 2H), 1,62 – 1,51 (m, 1H), 1,46 (s, 9H), 1,40 – 1,24 (m, 2H), 0,83 (t, *J* = 6,7, 3H); MS (ESI+) *m/z* 430$(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,24-8,26 (m, 1H), 7,75-7,76 (bs, 1H), 7,54-7,62 (m, 2H), 7,44 (t, *J* = 7,7 Hz, 1H), 5,1 (m, 0,7H), 4,7 (0,3H), 4,33-4,44 (m, 1H), 3,59 (d, *J* = 13,5 Hz, 1H), 3,45-3,48 (m, 1H), 3,02-3,10 (m, 3H), 2,82-2,85 (m, 1H), 2,46-2,54 (m, 2H), 2,40-2,43 (m, 1H), 2,28-2,32 (m, 1H), 2,21-2,25 (m, 1H), 1,99-2,04 (m, 2H), 1,76-1,86 (m, 2H), 1,48-1,63 (m, 1H), 1,46 (s, 9H), 1,20-1,41 (m, 3H), 0,80-0,86 (m, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Ejemplo 314

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A de Ejemplo 313 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida y 4-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,25-8,29 (bs, 1H), 7,64-7,66 (m, 2H), 7,50-7,52 (m, 2H), 5,1 (m, 0,7H), 4,7 (0,3H), 4,37-4,43 (m, 1H), 3,55-3,59 (m, 1H), 3,45-3,48 (m, 1H), 3,02-3,11 (m, 3H), 2,84-2,87 (m, 1H), 2,45-2,54 (m, 2H), 2,30-2,39 (m, 2H), 2,20-2,23 (m, 1H), 2,02-2,15 (m, 2H), 1,77-1,87 (m, 2H), 1,52-1,59 (m, 1H), 1,46-1,47 (m, 9H), 1,28-1,39 (m, 3H), 0,81-0,85 (m, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Ejemplo 315

(S)-1-((3aR,4S,6aS)-2-(4-fluorobencil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A de Ejemplo 313 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida y 4-fluorobenzaldehido en lugar de 3-(trifluorometil)benzaldehido en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,23-8,27 (m, 1H), 7,34-7,38 (m, 2H), 7,12 (t, *J* = 8,5 Hz, 2H), 5,1 (m, 0,7H), 4,7 (0,3H), 4,33-4,45 (m, 1H), 3,50 (d, *J* = 13,1 Hz, 1H), 3,38-3,41 (m, 1H), 3,02-3,11 (m, 3H), 2,81-2,84 (m, 1H), 2,44-2,53 (m, 2H), 2,29-2,39 (m, 2H), 2,19-2,23 (m, 1H), 2,02-2,04 (m, 2H), 1,81-1,84 (m, 2H), 1,55-1,59 (m, 1H), 1,46-1,47 (m, 9H), 1,28-1,38 (m, 3H), 0,81-0,85 (m, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Ejemplo 316

metil((S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxobutan-2–il(metil)carbamato de tert-butilo del Ejemplo 232 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 7,69-7,70 (bs, 1H), 7,49-7,57 (m, 2H), 7,32-7,41 (m, 2H), 4,31-4,35 (m, 1H), 4,19-4,29 (m, 1H), 3,57 (d, *J* = 13,5 Hz, 1H), 3,50 (d, *J* = 13,6 Hz, 1H), 3,00 (s, 3H), 2,76 (d, *J* = 6,4 Hz, 1H), 2,50-2,56 (m, 1H), 2,38-2,46 (m, 3H), 2,28-2,37 (m, 2H), 2,06 (dq, *J* = 12,2, 6,1 Hz, 1H), 1,82-1,90 (m, 1H), 1,52-1,62 (m, 1H), 1,46 (s, 9H), 1,35-1,44 (m, 1H), 1,00 (d, *J* = 6,5 Hz, 3H), 0,87 (d, *J* = 6,7 Hz, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Ejemplo 317

metil((S)-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 233 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida y 4-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 7,58-7,61 (m, 2H), 7,45-7,48 (m, 2H), 7,18-7,28 (m, 1H), 4,70-4,75 (m, 1H), 4,22-4,30 (m, 1H), 3,48-3,59 (m, 2H), 2,94 (s, 3H), 2,78-2,81 (m, 1H), 2,52-2,57 (m, 1H), 2,34-2,47 (m, 3H), 2,27-2,32 (m, 1H), 2,04-2,12 (m, 1H), 1,93-2,03 (m, 1H), 1,82-1,91 (m, 1H), 1,71-1,81 (m, 1H), 1,49-1,67 (m, 1H), 1,46-1,47 (m, 9H), 1,37-1,46 (m, 1H), 1,26-1,36 (m, 2H), 0,87 (t, *J* = 7,4 Hz, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Ejemplo 318

(S)-1-((3aS,4R,6aR)-2-(4-fluorobencil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 233 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida y 4-fluorobenzaldehido en lugar de 3-(trifluorometil)benzaldehido en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 7,28-7,32 (m, 2H), 7,16-7,21 (m, 1H), 7,02 (t, *J* = 8,6 Hz, 2H), 4,69-4,77 (m, 1H), 4,21-4,28 (m, 1H), 3,49 (d, *J* = 13,2 Hz, 1H), 3,43 (d, *J* = 13,2 Hz, 1H), 2,94 (s, 3H), 2,76-2,78 (m, 1H), 2,48-2,55 (m, 1H), 2,33-2,46 (m, 3H), 2,25-2,32 (m, 1H), 2,04-2,14 (m, 1H), 1,94-2,03 (m, 1H), 1,82-1,91 (m, 1H), 1,70-1,81 (m, 1H), 1,49-1,58 (m, 1H), 1,46-1,48 (m, 9H), 1,37-1,44 (m, 1H), 1,28-1,36 (m, 2H), 0,87 (t, *J* = 7,4 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Ejemplo 319

(2*S*)-4-metil-2-morfolin-4–il-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida

Paso A: Se agregó (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-Benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida (0,400 g, 1,001 mmol) del Paso B de Ejemplo 249 y etanol (40 ml) a Pd(OH)#2 al 20% sobre carbono, húmedo (0,080 g, 0,570 mmol) en una botella de presión de acero inoxidable de 250 ml y se agitó por 16 horas bajo 30 psi de hidrógeno a 55 °C. La mezcla se filtró a través de una membrana de nylon y el solvente se eliminó al vacío para dar (*S*)-4-metil-2-morfolino-*N*-((3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il)pentanamida: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,46 (d, *J* = 6,9, 1H), 4,46 - 4,38 (m, 1H), 3,74 (s, 4H), 3,45 (dd, *J* = 2,0, 11,3, 1H), 3,31 - 3,21 (m, 2H), 3,10 (dd, *J* = 7,0, 11,0, 1H), 2,89 (dd, *J* = 2,3, 11,0, 1H), 2,83 - 2,77 (m, 2H), 2,76 - 2,67 (m, 4H), 2,09 (td, *J* = 6,0, 11,8, 1H), 1,95 - 1,87 (m, 1H), 1,84 (dq, *J* = 6,0, 9,7, 2H), 1,71 - 1,57 (m, 2H), 1,49 (ddt, *J* = 6,3, 9,1, 12,5, 1H), 0,94 (dd, *J* = 6,3, 11,2, 6H); MS (ESI+) *m/z* 310$(M+H)^+$

Paso B: Se combinó (*S*)-4-metil-2-morfolino-*N*-((3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il)pentanamida (191mg, 0,617 mmol), trietilamina

(0,129 ml, 0,926 mmol), y cloruro de 3-(trifluorometil)bencen-1-sulfonilo (0,109 ml, 0,679 mmol) en diclorometano (0,5 ml). La reacción se agitó a temperatura ambiente por 3 horas. El material crudo se purificó mediante cromatografía sobre gel de sílice usando metanol al 1-10% (amoníaco 2 N)/diclorometano para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,44 (d, *J* = 6,2, 1H), 8,38 (s, 1H), 8,19 (d, *J* = 7,9, 1H), 7,92 (d, *J* = 7,8, 1H), 7,72 (t, *J* = 7,9, 1H), 4,27 - 4,20 (m, 1H), 3,90 (dd, *J* = 2,3, 10,0, 1H), 3,76 - 3,67 (m, 4H), 3,20 (ddd, *J* = 3,9, 9,4, 10,9, 3H), 2,97 (dd, *J* = 7,1, 9,6, 1H), 2,78 - 2,72 (m, 2H), 2,72 - 2,67 (m, 2H), 2,62 - 2,53 (m, 2H), 1,94 (dt, *J* = 6,2, 12,1, 1H), 1,89 - 1,77 (m, 3H), 1,64 - 1,54 (m, 2H), 1,30 (ddt, *J* = 6,5, 9,3, 12,8, 1H), 0,92 (d, *J* = 4,4, 3H), 0,91 (d, *J* = 4,4, 3H); MS (ESI+) *m/z* 518(M+H)$^+$.

Ejemplo 320

(2*S*)-4-metil-2-pirrolidin-1–il-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida

El compuesto del título se preparó utilizando (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-pirrolidin-1–ilpentanamida del Ejemplo 250 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37-8,39 (m, 1H), 8,17-8,20 (m, 1H), 8,12-8,15 (m, 1H), 7,89-7,92 (m, 1H), 7,71 (t, *J* = 7,8 Hz, 1H), 4,23-4,29 (m, 1H), 3,86 (dd, *J* = 9,9, 2,4 Hz; 1H), 3,16-3,20 (m, 2H), 3,13-3,15 (m, 1H), 2,97 (dd, *J* = 9,6, 6,8 Hz, 1H), 2,65-2,69 (m, 2H), 2,55-2,61 (m, 4H), 1,90-2,00 (m, 1H), 1,76-1,90 (m, 3H), 1,54-1,62 (m, 6H), 1,25-1,34 (m, 1H), 0,98 (d, *J* = 6,3 Hz, 3H), 0,91 (d, *J* = 6,3 Hz, 3H); MS (ESI+) *m/z* 502 (M+H)$^+$.

Ejemplo 321

(2*S*)-4-metil-2-piperidin-1–il-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida

El compuesto del título se preparó utilizando (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-piperidin-1–ilpentanamida del Ejemplo 251 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,38-8,39 (bs, 1H), 8,18-8,20 (m, 2H), 7,90-7,92 (m, 1H), 7,71 (t, *J* = 7,8 Hz, 1H), 4,20-4,26 (m, 1H), 3,87 (dd, *J* = 9,9, 2,1

Hz, 1H), 3,16-3,20 (m, 3H), 2,97 (dd, *J* = 9,5, 6,3 Hz, 1H), 2,56-2,64 (m, 6H), 1,80-1,97 (m, 4H), 1,46-1,59 (m, 6H), 1,23-1,37 (m, 3H), 0,93 (d, *J* = 6,6 Hz, 3H), 0,92 (d, *J* = 6,7 Hz, 3H); MS (ESI+) *m/z* 516 $(M+H)^+$.

Ejemplo 322

metil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 222 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,48-8,50 (m, 1H), 8,36-8,37 (bs, 1H), 8,19 (d, *J* = 7,9 Hz, 1H), 7,91 (d, *J* = 7,9 Hz, 1H), 7,72 (t, *J* = 7,8 Hz, 1H), 5,13 (m, 0,7H), 4,78 (m, 0,3H), 4,15-4,29 (m, 1H), 3,84 (dd, *J* = 9,9, 2,1 Hz, 1H), 3,13-3,16 (m, 1H), 3,02-3,12 (m, 4H), 2,91 (dd, *J* = 9,6, 6,9 Hz, 1H), 2,48-2,52 (m, 2H), 1,74-1,90 (m, 4H), 1,49-1,67 (m, 2H), 1,44-1,46 (m, 9H), 1,16-1,29 (m, 1H), 0,89 (d, *J* = 6,4 Hz, 3H), 0,84 (d, *J* = 6,4 Hz, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Ejemplo 323

etil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(etil)carbamato de tert-butilo del Ejemplo 223 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37-8,40 (m, 2H), 8,19 (d, *J* = 7,9 Hz, 1H), 7,91 (d, *J* = 7,9 Hz, 1H), 7,72 (t, *J* = 7,9 Hz, 1H), 5,0 (m, 0,7H), 4,7 (m, 0,3H), 4,16-4,27 (m, 1H), 3,83-3,86 (m, 1H), 3,43-3,49 (m, 2H), 3,09-3,18 (m, 2H), 2,90-2,94 (m, 1H), 2,43-2,58 (m, 2H), 1,90-2,02 (m, 2H), 1,71-1,84 (m, 2H), 1,62-1,67 (m, 1H), 1,34-1,59 (m, 10H), 1,21-1,31 (m, 4H), 0,88-0,91 (m, 6H); MS (ESI+) *m/z* 576 $(M+H)^+$.

Ejemplo 324

metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida del Ejemplo 151 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (501 MHz, piridin-d_5, temperatura 60 °C) δ ppm 8,08-8,11 (m, 2H), 7,99-8,03 (bs, 1H), 7,84-7,87 (m, 2H), 4,95 (m, 0,7H), 4,4 (m, 0,3H), 4,11-4,17 (m, 1H), 3,70-3,74 (m, 1H), 3,15-3,21 (m, 1H), 3,13 (dd, *J* = 9,8, 2,8 Hz, 1H), 3,03 (dd, *J* = 9,7, 7,3 Hz, 1H), 3,00 (s, 3H), 2,50-2,54 (m, 2H), 1,89-1,97 (m, 1H), 1,72-1,89 (m, 3H), 1,50-1,61 (m, 2H), 1,45 (s, 9H), 1,28 (ddt, *J* = 9,5, 12,9, 6,5 Hz, 1H), 0,89 (d, *J* = 6,8 Hz, 3H), 0,85 (d, *J* = 6,5 Hz, 3H); MS (DCI+) *m/z* 562 $(M+H)^+$,579 $(M+NH_4)^+$.

Ejemplo 325

metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida del Ejemplo 151 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (501 MHz, piridin-d_5, temperatura 60 °C) δ ppm 8,32-8,33 (bs, 1H), 8,15 (d, *J* = 8,1 Hz, 1H), 7,97-8,01 (m, 1H), 7,87 (d, *J* = 7,7 Hz, 1H), 7,68 (t, *J* = 7,9 Hz, 1H), 4,95 (m, 0,7H), 4,4 (m, 0,3H), 4,11-4,15 (m, 1H), 3,71-3,75 (m, 1H), 3,12-3,18 (m, 2H), 3,00-3,04 (m, 1H), 2,99 (s, 3H), 2,48-2,52 (m, 2H), 1,90-1,96 (m, 1H), 1,73-1,86 (m, 3H), 1,50-1,60 (m, 2H), 1,46 (s, 9H), 1,24-1,30 (m, 1H), 0,88 (d, *J* = 6,6 Hz, 3H), 0,85 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 579 $(M+NH_4)^+$.

Ejemplo 326

(S)-1-((3aS,4R,6aR)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida del Ejemplo 151 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-fluorobencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,51-8,58 (m, 1H), 7,97-7,99 (m, 2H), 7,29-7,35 (m, 2H), 5,13 (m, 0,7H), 4,8 (m, 0,3H), 4,20-4,23 (m, 1H), 3,70-3,81 (m, 1H), 3,00-3,11 (m, 5H), 2,86-2,91 (m, 1H), 2,42-2,53 (m, 2H), 1,75-1,96 (m, 4H), 1,49-1,62 (m, 2H), 1,41-1,50 (bs, 9H), 1,23-1,39 (m, 1H), 0,81-0,88 (m, 6H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Ejemplo 327

(S)-1-((3aS,4R,6aR)-2-(4-fluoro-3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida del Ejemplo 151 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y 4-fluoro-cloruro de 3-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (501 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,28 (dd, *J* = 6,6, 2,3 Hz, 1H), 8,16-8,20 (m, 1H), 7,54-7,59 (m, 1H), 7,44 (t, *J* = 9,4 Hz, 1H), 4,79-4,84 (m, 1H), 4,08 (p, *J* = 6,9 Hz, 1H), 3,67 (dd, *J* = 10,1, 3,3 Hz, 1H), 3,25 (dd, *J* = 10,1, 7,7 Hz, 1H), 3,09-3,17 (m, 2H), 2,94 (s, 3H), 2,53-2,61 (m, 1H), 2,46-2,53 (m, 1H), 1,91-1,98 (m, 1H), 1,79-1,87 (m, 2H), 1,73 (ddd, *J* = 14,1, 9,1, 5,1 Hz, 1H), 1,56-1,64 (m, 1H), 1,48-1,56 (m, 1H), 1,46 (s, 9H), 1,26-1,33 (m, 1H), 0,89 (d, *J* = 6,6 Hz, 3H), 0,87 (d, *J* = 6,6 Hz, 3H); MS (ESI+) *m/z* 580 $(M+H)^+$.

Ejemplo 328

metil((S)-1-oxo-1-((3aR,4R,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aR,4R,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 240 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,04-8,07 (m, 2H), 7,80-7,83 (m, 2H), 7,54-7,57 (m, 1H), 4,79 (dd, *J* = 9,4, 6,0 Hz, 1H), 4,29 (dq, *J* = 9,8, 7,0 Hz, 1H), 3,49 (dd, *J* = 10,3, 4,7 Hz, 1H), 3,21 (dd, *J* = 9,9, 7,8 Hz, 1H), 3,07-3,13 (m, 2H), 3,01 (s, 3H), 2,92-3,01 (m, 1H), 2,46-2,54 (m, 1H), 1,95-2,07 (m, 1H), 1,75-1,85 (m, 1H), 1,68-1,77 (m, 1H), 1,55-1,66 (m, 2H), 1,54 (s, 9H), 1,25-1,39 (m, 3H), 0,87 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 548 $(M+H)^+$.

Ejemplo 329

metil((S)-4-metil-1-oxo-1-((3aR,4R,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aR,4R,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 241 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,04-8,07 (m, 2H), 7,80-7,83 (m, 2H), 7,54-7,61 (m, 1H), 4,90 (dd, *J* = 9,2, 6,0 Hz, 1H), 4,26-4,34 (m, 1H), 3,49 (dd, *J* = 10,3, 4,7 Hz, 1H), 3,21 (dd, *J* = 9,9, 7,8 Hz, 1H), 3,06-3,14 (m, 2H), 3,02 (s, 3H), 2,94-3,01 (m, 1H), 2,47-2,55 (m, 1H), 1,87 (ddd, *J* = 14,2, 8,5, 5,6 Hz, 1H), 1,69-1,83 (m, 2H), 1,57-1,67 (m, 3H), 1,54 (s, 9H), 1,27-1,39 (m, 1H), 0,90 (d, *J* = 6,9 Hz, 3H), 0,89 (d, *J* = 6,9 Hz, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Ejemplo 330

(S)-1-((3aS,4R,6aR)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 233 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-fluorobencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 7,90-7,97 (m, 2H), 7,38-7,48 (bs, 1H), 7,18-7,24 (m, 2H), 7,18-7,23 (m, 1H), 4,65-4,75 (m, 1H), 4,03-4,13 (m, 1H), 3,58 (dd, *J* = 10,1, 3,4 Hz, 1H), 3,22 (dd, *J* = 10,1, 7,8 Hz, 1H), 3,03-3,13 (m, 2H), 2,94 (s, 3H), 2,51-2,60 (m, 1H), 2,43-2,51 (m, 1H), 1,89-2,01 (m, 2H), 1,80-1,86 (m, 1H), 1,69-1,81 (m, 1H), 1,47-1,62 (m, 1H), 1,45 (s, 9H), 1,23-1,38 (m, 3H), 0,86 (t, *J* = 7,3 Hz, 2H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Ejemplo 331

metil((S)-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 233 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,05-8,08 (m, 2H), 7,79-7,83 (m, 2H), 7,43-7,48 (bs, 1H), 4,68-4,72 (m, 1H), 4,01-4,11 (m, 1H), 3,65 (dd, *J* = 10,2, 3,3 Hz, 1H), 3,26 (dd, *J* = 10,1, 7,7 Hz, 1H), 3,07-3,18 (m, 2H), 2,94 (s, 3H), 2,45-2,58 (m, 2H), 1,89-2,00 (m, 2H), 1,70-1,86 (m, 2H), 1,46-1,57 (m, 1H), 1,45 (s, 9H), 1,31 (dt, *J* = 15,2, 7,6 Hz, 2H), 1,23-1,37 (m, 1H), 0,85 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 565 $(M+NH_4)^+$.

Ejemplo 332

metil((2S,3S)-3-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando (2S,3S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 224 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,66 (d, *J* = 6,0 Hz, 1H), 8,39-8,40 (m, 1H), 8,21 (d, *J* = 7,9 Hz, 1H), 7,92 (d, *J* = 7,6 Hz, 1H), 7,72 (t, *J* = 7,9 Hz, 1H), 4,67 (d, *J* = 11,1 Hz, 1H), 4,15-4,25 (m, 1H), 4,15-4,23 (m, 1H), 3,89 (d, *J* = 9,9 Hz, 1H), 3,09-3,26 (m, 5H), 2,88-3,08 (m, 1H), 2,46-2,55 (m, 2H), 2,17-2,31 (m, 1H), 1,74-1,94 (m, 2H), 1,42-1,55 (m, 1H), 1,48 (s, 9H), 1,18-1,30 (m, 1H), 1,00-1,12 (m, 1H), 0,94 (d, *J* = 6,3 Hz, 3H), 0,80 (t, *J* = 7,0 Hz, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Ejemplo 333

metil((2S,3S)-3-metil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando (2S,3S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 224 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,68 (d, *J* = 6,3 Hz, 1H), 8,12-8,17 (m, 2H), 7,87-7,95 (m, 2H), 4,68 (d, *J* = 11,0 Hz, 1H), 4,16-4,24 (m, 1H), 3,87 (d, *J* = 9,8 Hz, 1H), 3,09-3,24 (m, 5H), 2,89-3,08 (m, 1H), 2,50-2,58 (m, 2H), 2,22-2,27 (m, 1H), 1,77-1,85 (m, 2H), 1,51-1,66 (m, 1H), 1,48 (s, 9H), 1,34-1,49 (m, 1H), 1,19-1,31 (m, 1H), 0,98-1,13 (m, 1H), 0,95 (d, *J* = 6,1 Hz, 3H), 0,80 (t, *J* = 6,9 Hz, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Ejemplo 334

metil((2S,3S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

Paso A: Se preparó (2S,3S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-isoleucina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 16 Paso E en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,43 (d, *J* = 6,4, 1H), 7,41 (d, *J* = 7,2, 2H), 7,36 (t, *J* = 7,5, 2H), 7,27 (t, *J* = 7,2, 1H), 4,70 (d, *J* = 11,1, 1H), 4,36 (d, *J* = 4,4, 2H), 3,56 (d, *J* = 13,0, 1H), 3,40 (d, *J* = 13,1, 1H), 3,24 (s, 1H), 3,13 (s, 3H), 2,72 (d, *J* = 8,6, 1H), 2,47 (s, 2H), 2,37 – 2,18 (m, 4H), 2,13 (dd, *J* = 11,7, 5,6, 1H), 1,91 – 1,76 (m, 1H), 1,65 (dd, *J* = 11,4, 6,8, 1H), 1,48 (s, 9H), 1,11 – 0,95 (m, 4H), 0,80 (t, *J* = 7,1, 3H); MS (ESI+) *m/z* 444 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (2S,3S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Paso A en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,68 (d, *J* = 7,2 Hz, 1H), 8,35-8,40 (m, 1H), 8,15 (d, *J* = 7,8 Hz, 1H), 7,91 (d, *J* = 7,6 Hz, 1H), 7,72 (t, *J* = 7,8 Hz, 1H), 4,68 (d, *J* = 11,3 Hz, 1H), 4,13-4,25 (m, 1H), 3,74-3,88 (m, 1H), 3,15-3,25 (m, 1H), 3,11-3,16 (bs, 3H), 2,95-3,05 (m, 1H), 2,83-2,94 (m, 1H), 2,38-2,61 (m, 2H), 2,17-2,32 (m, 1H), 1,88-2,03 (m, 1H), 1,76-1,88 (m, 1H), 1,52-1,66 (m, 1H), 1,44-1,53 (bs, 9H), 1,33-1,46 (m, 1H), 1,21-1,33 (m, 1H), 0,96-1,12 (m, 1H), 0,94 (d, *J* = 6,4 Hz, 3H), 0,79 (t, *J* = 7,2 Hz, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Ejemplo 335

metil((2S,3S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando (2S,3S)-1-((3aS,4R,6aR)-2-

benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Paso A de Ejemplo 334 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,66-8,72 (m, 1H), 8,05-8,13 (m, 2H), 7,88-7,91 (m, 2H), 4,69 (d, *J* = 11,3 Hz, 1H), 4,15-4,22 (m, 1H), 3,73-3,87 (m, 1H), 3,16-3,23 (m, 1H), 3,11-3,18 (bs, 3H), 3,00 (t, *J* = 8,3 Hz, 1H), 2,90 (t, *J* = 8,4 Hz, 1H), 2,42-2,56 (m, 2H), 2,21-2,28 (m, 1H), 1,88-2,03 (m, 1H), 1,73-1,88 (m, 1H), 1,52-1,66 (m, 1H), 1,48 (s, 9H), 1,34-1,46 (m, 1H), 1,21-1,34 (m, 1H), 0,98-1,13 (m, 1H), 0,94 (d, *J* = 6,3 Hz, 3H), 0,76-0,81 (m, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Ejemplo 336

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 247 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,36-8,38 (bs, 1H), 8,30-8,37 (m, 1H), 8,19 (d, *J* = 7,8 Hz, 1H), 7,91 (d, *J* = 7,8 Hz, 1H), 7,72 (t, *J* = 7,8 Hz, 1H), 5,4 (m, 0,7H), 4,7 (m, 0,3H), 4,16-4,20 (m, 1H), 3,86 (d, *J* = 9,8 Hz, 1H), 3,13-3,18 (m, 1H), 3,08-3,13 (m, 1H), 2,96-3,08 (bs, 3H), 2,90-2,93 (m, 1H), 2,41-2,56 (m, 2H), 2,13-2,37 (m, 1H), 1,81-1,92 (m, 1H), 1,72-1,81 (m, 1H), 1,60-1,72 (m, 1H), 1,47-1,60 (m, 1H), 1,41-1,50 (bs, 9H), 1,19-1,33 (m, 1H), 0,87-0,99 (bs, 9H); MS (ESI+) *m/z* 576 $(M+H)^+$,593 $(M+NH_4)^+$.

Ejemplo 337

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–

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il(metil)carbamato de tert-butilo del Ejemplo 247 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,35-8,38 (m, 1H), 8,12-8,15 (m, 2H), 7,89-7,91 (m, 2H), 5,11-5,19 (m, 1H), 4,15-4,19 (m, 1H), 3,83-3,86 (m, 1H), 3,13-3,17 (m, 1H), 3,09-3,14 (m, 1H), 2,97-3,09 (bs, 3H), 2,92-2,96 (m, 1H), 2,43-2,57 (m, 2H), 2,15-2,38 (m, 1H), 1,81-1,91 (m, 1H), 1,72-1,81 (m, 1H), 1,61-1,72 (m, 1H), 1,48-1,60 (m, 1H), 1,40-1,51 (bs, 9H), 1,20-1,36 (m, 1H), 0,89-0,99 (bs, 9H); MS (ESI+) *m/z* 576 $(M+H)^+$.

Ejemplo 338

(S)-4,4-dimetil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 248 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,29-8,30 (bs, 1H), 8,13 (d, *J* = 7,9 Hz, 1H), 7,83 (d, *J* = 8,6 Hz, 1H), 7,64 (t, *J* = 7,8 Hz, 1H), 7,29 (d, *J* = 3,9 Hz, 1H), 4,82-4,87 (bs, 1H), 4,05 (p, *J* = 6,7 Hz, 1H), 3,63 (dd, *J* = 10,2, 3,3 Hz, 1H), 3,25 (dd, *J* = 10,1, 7,8 Hz, 1H), 3,07-3,17 (m, 2H), 2,91 (s, 3H), 2,51-2,59 (m, 1H), 2,43-2,50 (m, 1H), 2,15 (dd, *J* = 14,3, 5,6 Hz, 1H), 1,92 (dq, *J* = 12,2, 6,1 Hz, 1H), 1,77-1,85 (m, 1H), 1,61 (dd, *J* = 14,3, 7,2 Hz, 1H), 1,47-1,55 (m, 1H), 1,46 (s, 9H), 1,23-1,36 (m, 1H), 0,93 (s, 9H); MS (ESI+) *m/z* 576 $(M+H)^+$.

Ejemplo 339

(S)-4,4-dimetil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 248 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-

2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,05-8,08 (m, 2H), 7,79-7,82 (m, 2H), 7,28-7,32 (m, 1H), 4,79-4,91 (m, 1H), 4,05 (p, *J* = 6,7 Hz, 1H), 3,62 (dd, *J* = 10,2, 3,4 Hz, 1H), 3,26 (dd, *J* = 10,2, 7,8 Hz, 1H), 3,09-3,17 (m, 2H), 2,92 (s, 3H), 2,51-2,62 (m, 1H), 2,43-2,51 (m, 1H), 2,15 (dd, *J* = 14,3, 5,6 Hz, 1H), 1,88-1,98 (m, 1H), 1,76-1,86 (m, 1H), 1,62 (dd, *J* = 14,3, 7,0 Hz, 1H), 1,47-1,56 (m, 1H), 1,46 (s, 9H), 1,29 (ddt, *J* = 9,0, 13,0, 6,5 Hz, 1H), 0,94 (s, 9H); MS (ESI+) *m/z* 576 $(M+H)^+$.

Ejemplo 340

metil((S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxobutan-2–il(metil)carbamato de tert-butilo del Ejemplo 232 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (501 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,29-8,30 (bs, 1H), 8,13 (d, *J* = 7,8 Hz, 1H), 7,83 (d, *J* = 7,7 Hz, 1H), 7,64 (t, *J* = 7,8 Hz, 1H), 7,59-7,68 (m, 1H), 4,32 (d, *J* = 10,4 Hz, 1H), 4,07 (p, *J* = 6,6 Hz, 1H), 3,64 (dd, *J* = 10,2, 3,3 Hz, 1H), 3,23 (t, *J* = 9,0 Hz, 1H), 3,07-3,15 (m, 2H), 3,00 (s, 3H), 2,49-2,59 (m, 1H), 2,42-2,49 (m, 1H), 2,31-2,42 (m, 1H), 1,90-1,97 (m, 1H), 1,79-1,86 (m, 1H), 1,47-1,59 (m, 1H), 1,45 (s, 9H), 1,24-1,33 (m, 1H), 0,97 (d, *J* = 6,5 Hz, 3H), 0,86 (d, *J* = 6,7 Hz, 3H); MS (ESI+) *m/z* 548 $(M+H)^+$.

Ejemplo 341

(S)-3,3-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–ilcarbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3,3-dimetil-1-oxobutan-2–ilcarbamato de tert-butilo del Ejemplo 225 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-

benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,86 (d, *J* = 6,7 Hz, 1H), 8,11-8,18 (m, 2H), 7,89-7,92 (m, 2H), 7,71 (d, *J* = 9,5 Hz, 1H), 4,56 (d, *J* = 9,8 Hz, 1H), 4,20 (p, *J* = 6,4 Hz, 1H), 3,79 (dd, *J* = 10,0, 3,0 Hz, 1H), 3,24 (dd, *J* = 9,9, 7,7 Hz, 1H), 3,14 (d, *J* = 3,2 Hz, 1H), 3,02 (dd, *J* = 9,7, 7,3 Hz, 1H), 2,55-2,65 (m, 2H), 1,76-1,84 (m, 2H), 1,44-1,56 (m, 1H), 1,48 (s, 9H), 1,19-1,27 (m, 1H), 1,16 (s, 9H); MS (ESI+) *m/z* 548 $(M+H)^+$,565 $(M+NH_4)^+$.

Ejemplo 342

(S)-3,3-dimetil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrocíclopenta[c]pirrol-4–ilamino)butan-2–ilcarbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3,3-dimetil-1-oxobutan-2–ilcarbamato de tert-butilo del Ejemplo 234 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,89 (d, *J* = 7,4, 1H), 8,10 (d, *J* = 8,1, 2H), 7,90 (d, *J* = 8,3, 2H), 7,73 (s, 1H), 4,55 (d, *J* = 9,8, 1H), 4,27 – 4,16 (m, 1H), 3,70 (dd, *J* = 9,8, 2,2, 1H), 3,14 (dd, *J* = 9,8, 2,5, 1H), 2,98 – 2,92 (m, 1H), 2,91 – 2,85 (m, 1H), 2,53 – 2,39 (m, 2H), 1,99 (td, *J* = 11,5, 5,7, 1H), 1,83 (td, *J* = 12,4, 7,2, 1H), 1,60 (dt, *J* = 12,3, 8,2, 1H), 1,48 (s, 9H), 1,34 – 1,25 (m, 1H), 1,15 (s, 9H); MS (ESI+) *m/z* 548 $(M+H)^+$, 565 $(M+NH_4)^+$.

Ejemplo 343

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)hexan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxohexan-2–il(metil)carbamato de tert-butilo del Ejemplo 227 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de

4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,06-8,09 (m, 2H), 7,79-7,82 (m, 2H), 7,40 (d, *J* = 5,6 Hz, 1H), 4,68-4,72 (m, 1H), 4,07 (p, *J* = 6,8 Hz, 1H), 3,65 (dd, *J* = 10,2, 3,4 Hz, 1H), 3,28 (dd, *J* = 10,2, 7,7 Hz, 1H), 3,09-3,17 (m, 2H), 2,94 (s, 3H), 2,54-2,59 (m, 1H), 2,47-2,53 (m, 1H), 1,97-2,07 (m, 1H), 1,87-1,96 (m, 1H), 1,72-1,86 (m, 2H), 1,47-1,56 (m, 1H), 1,46 (s, 9H), 1,23-1,35 (m, 1H), 1,27-1,30 (m, 4H), 0,80-0,84 (m, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$,579 $(M+NH_4)^+$,620 $(M+CH_3CN+NH_4)^+$.

Ejemplo 344

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo del Ejemplo 226 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,06-8,08 (m, 1H), 8,06 (d, *J* = -0,9 Hz, 1H), 7,79-7,82 (m, 2H), 7,73-7,77 (m, 1H), 7,00-7,05 (m, 1H), 4,47 (td, *J* = 8,2, 4,7 Hz, 1H), 4,04-4,11 (m, 1H), 3,65 (dd, *J* = 10,2, 3,0 Hz, 1H), 3,29 (dd, *J* = 10,2, 7,3 Hz, 1H), 3,15 (dd, *J* = 10,0, 6,9 Hz, 1H), 3,11 (dd, *J* = 9,9, 3,4 Hz, 1H), 2,51-2,59 (m, 2H), 2,08 (dd, *J* = 14,2, 4,6 Hz, 1H), 1,84-1,93 (m, 1H), 1,75-1,83 (m, 1H), 1,69 (dd, *J* = 14,2, 8,0 Hz, 1H), 1,48-1,56 (m, 1H), 1,47 (s, 9H), 1,22-1,33 (m, 1H), 0,96 (s, 9H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Ejemplo 345

(2*S*)-4-metil-2-pirrolidin-1–il-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)benzoil]octahidrociclopenta[*c*]pirrol-4–il}pentanamida

El compuesto del título se preparó utilizando (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-pirrolidin-1–ilpentanamida del Ejemplo 250 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y 3-(trifluorometil)cloruro de benzoilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos

en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,41 – 8,17 (m, 1H), 8,14 – 8,05 (m, 1H), 8,01 – 7,78 (m, 1H), 7,76 – 7,66 (m, 1H), 7,53 (t, J = 7,6, 1H), 4,51 – 4,29 (m, 1H), 4,20 – 4,00 (m, 1H), 3,89 (ddd, J = 12,0, 6,6, 1,5, 1H), 3,74 (tdd, J = 8,3, 5,2, 2,8, 1H), 3,67 – 3,45 (m, 1H), 3,32 – 3,13 (m, 2H), 2,87 – 2,57 (m, 6H), 2,23 – 2,02 (m, 1H), 1,96 – 1,78 (m, 2H), 1,73 – 1,55 (m, 6H), 1,47 – 1,24 (m, 1H), 1,04 – 0,79 (m, 6H); MS (ESI+) m/z 466 $(M+H)^+$.

Ejemplo 346

(2*S*)-4-metil-*N*-[(3a*S*,4*R*,6a*R*)-2-(metilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-2-pirrolidin-1–ilpentanamida

El compuesto del título se preparó utilizando (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-pirrolidin-1–ilpentanamida del Ejemplo 250 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de metansulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,24-8,26 (m, 1H), 4,35 (p, J = 6,8 Hz, 1H), 3,79 (dd, J = 9,9, 2,6 Hz, 1H), 3,50 (dd, J = 9,9, 7,0 Hz, 1H), 3,35 (dd, J = 9,6, 7,0 Hz, 1H), 3,17-3,21 (m, 2H), 3,04 (s, 3H), 2,67-2,75 (m, 4H), 2,60-2,63 (m, 2H), 1,99-2,07 (m, 1H), 1,78-1,95 (m, 3H), 1,58-1,68 (m, 6H), 1,32-1,39 (m, 1H), 0,99 (d, J = 6,2 Hz, 3H), 0,92 (d, J = 6,3 Hz, 3H); MS (ESI+) m/z 372 $(M+H)^+$.

Ejemplo 347

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-(ciclopropilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-pirrolidin-1–ilpentanamida

El compuesto del título se preparó utilizando (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-pirrolidin-1–ilpentanamida del Ejemplo 250 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de ciclopropansulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en los procedimientos descritos en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,14 (d, J = 7,3 Hz, 1H), 4,33-4,40 (m, 1H), 3,82 (dd, J = 9,9, 2,6 Hz, 1H), 3,57 (dd, J = 9,9, 7,0 Hz, 1H), 3,41 (dd, J = 9,6, 7,0 Hz, 1H), 3,22 (dd, J = 9,6, 3,2 Hz, 1H), 3,16 (dd, J = 9,2, 5,1 Hz, 1H), 2,60-2,70 (m, 7H), 2,04 (dq, J = 11,9, 5,9 Hz, 1H), 1,79-1,97 (m, 3H), 1,56-1,67 (m, 6H), 1,33-1,40 (m, 1H), 1,16-1,23 (m, 2H), 0,99 (d, J = 6,3 Hz, 3H), 0,92 (d, J = 6,4 Hz, 3H), 0,86-0,92 (m, 2H); MS (ESI+) m/z 398 $(M+H)^+$.

Ejemplo 348

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida

Se combinó (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo (60 mg, 0,135 mmol) del Ejemplo 222 con cloruro de hidrógeno 4 N en 1,4-dioxano (0,698 ml, 2,79 mmol). La reacción se agitó a temperatura ambiente por 16 horas y luego se concentró. El material se purificó usando un cartucho de 12 g de gel de sílice con un gradiente de metanol al 1-10% (amoníaco 2 N)/diclorometano a lo largo de 20 minutos para dar el compuesto del título: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,16-8,19 (m, 1H), 7,44-7,46 (m, 2H), 7,37 (t, *J* = 7,5 Hz, 2H), 7,28 (t, *J* = 7,3 Hz, 1H), 4,42-4,48 (m, 1H), 3,61 (d, *J* = 13,1 Hz, 1H), 3,46 (d, *J* = 13,1 Hz, 1H), 3,22 (dd, *J* = 8,2, 5,8 Hz, 1H), 2,87 (d, *J* = 10,3 Hz, 1H), 2,51-2,61 (m, 2H), 2,44 (dd, *J* = 8,8, 7,1 Hz, 1H), 2,43 (s, 3H), 2,37 (dd, *J* = 9,0, 2,0 Hz, 1H), 2,25-2,29 (m, 1H), 2,09-2,17 (m, 1H), 1,95-2,07 (m, 1H), 1,82-1,95 (m, 2H), 1,72 (ddd, *J* = 13,5, 7,8, 5,8 Hz, 1H), 1,55-1,64 (m, 2H), 1,38-1,45 (m, 1H), 0,92 (d, *J* = 6,6 Hz, 3H), 0,86 (d, *J* = 6,6 Hz, 3H); MS (ESI+) *m/z* 344 $(M+H)^+$.

Ejemplo 349

metil((S)-4-metil-1-((3aS,4R,6aR)-octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(tert-butiloxicarbonil)-N^2-metil-L-leucinamida del Ejemplo 151 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida en el procedimiento descrito en Ejemplo 319 Paso A: ^{1}H NMR (500 MHz, piridin-d_5) δ 8,47 – 8,30 (m, 1H), 5,15 (dd, *J* = 6,4, 5,1, 1H), 4,82 – 4,77 (m, 1H), 4,40 – 4,21 (m, 1H), 3,25 – 3,04 (m, 4H), 3,03 – 2,92 (m, 1H), 2,88 (dd, *J* = 10,8, 7,1, 1H), 2,69 (d, *J* = 10,2, 1H), 2,56 – 2,44 (m, 2H), 2,04 (td, *J* = 11,6, 5,8, 1H), 1,93 – 1,78 (m, 3H), 1,64 – 1,53 (m, 2H), 1,47 (s, 9H), 1,34 (ddt, *J* = 11,0, 7,1, 5,5, 1H), 0,89 (d, *J* = 6,3, 3H), 0,85 (d, *J* = 6,5, 3H); MS (ESI+) *m/z* 354 $(M+H)^+$.

Ejemplo 350

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]piperidin-2-carboxamida

El compuesto del título se preparó utilizando (2S)-2-({[(3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–il]amino}carbonil)piperidin-1-carboxilato de tert-butilo del Ejemplo 231 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,67-7,70 (m, 1H), 7,42-7,44 (m, 2H), 7,36 (t, *J* = 7,5 Hz, 2H), 7,27 (t, *J* = 7,3 Hz, 1H), 4,34-4,40 (m, 1H), 3,59 (d, *J* = 13,1 Hz, 1H), 3,41 (d, *J* = 13,1 Hz, 1H), 3,32 (dd, *J* = 10,3, 3,2 Hz, 1H), 2,99-3,02 (m, 1H), 2,83 (dd, *J* = 8,9, 2,5 Hz, 1H), 2,54-2,61 (m, 1H), 2,46-2,54 (m, 1H), 2,40-2,58 (m, 1H), 2,39-2,47 (m, 1H), 2,33-2,39 (m, 2H), 2,21 (dd, *J* = 8,9, 7,2 Hz, 1H), 2,02-2,10 (m, 2H), 1,77-1,84 (m, 1H), 1,64-1,74 (m, 1H), 1,47-1,64 (m, 2H), 1,34-1,45 (m, 2H), 1,25-1,34 (m, 2H); MS (ESI+) *m/z* 328 $(M+H)^+$.

Ejemplo 351

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-valinamida

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxobutan-2–il(metil)carbamato de tert-butilo del Ejemplo 232 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,10-8,12 (m, 1H), 7,43-7,45 (m, 2H), 7,37 (t, *J* = 7,5 Hz, 2H), 7,28 (t, *J* = 7,3 Hz, 1H), 4,44-4,50 (m, 1H), 3,62 (d, *J* = 13,1 Hz, 1H), 3,44 (d, *J* = 13,1 Hz, 1H), 2,85-2,90 (m, 2H), 2,47-2,57 (m, 2H), 2,43 (dd, *J* = 8,8, 7,0 Hz, 1H), 2,40 (s, 3H), 2,36 (dd, *J* = 8,9, 2,7 Hz, 1H), 2,26 (dd, *J* = 8,9, 6,8 Hz, 1H), 2,07-2,16 (m, 2H), 1,91-2,06 (m, 1H), 1,81-1,89 (m, 1H), 1,59 (dq, *J* = 12,1, 7,6 Hz, 1H), 1,38-1,45 (m, 1H), 1,06 (d, *J* = 6,9 Hz, 3H), 1,05 (d, *J* = 6,9 Hz, 3H); MS (ESI+) *m/z* 330 $(M+H)^+$.

Ejemplo 352

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 233 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,11-8,14 (m, 1H), 7,43-7,45 (m, 2H), 7,37 (t, *J* = 7,5 Hz, 2H), 7,28 (t, *J* = 7,3 Hz, 1H), 4,42-4,48 (m, 1H), 3,61 (d, *J* = 13,1 Hz, 1H), 3,44 (d, *J* = 13,1 Hz, 1H), 3,16 (t, *J* = 6,5 Hz, 1H), 2,86 (dd, *J* = 8,9, 2,6 Hz, 1H), 2,47-2,57 (m, 2H), 2,42 (dd, *J* = 8,9, 7,2 Hz, 1H), 2,40 (s, 3H), 2,36 (dd, *J* = 8,9, 2,7 Hz, 1H), 2,26 (dd, *J* = 8,9, 7,0 Hz, 1H), 2,12 (dq, *J* = 11,9, 6,0 Hz, 2H), 1,77-1,89 (m, 2H), 1,65-1,73 (m, 1H), 1,54-1,64 (m, 1H), 1,37-1,54 (m, 3H), 0,84 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 330 $(M+H)^+$.

Ejemplo 353

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-isoleucinamida

El compuesto del título se preparó utilizando (2S,3S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 224 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,10-8,14 (m, 1H), 7,44-7,46 (m, 2H), 7,37 (t, *J* = 7,5 Hz, 2H), 7,26-7,30 (m, 1H), 4,42-4,50 (m, 1H), 3,61 (d, *J* = 13,1 Hz, 1H), 3,46 (d, *J* = 13,1 Hz, 1H), 2,97 (d, *J* = 6,0 Hz, 1H), 2,87 (d, *J* = 10,2 Hz, 1H), 2,50-2,57 (m, 2H), 2,41-2,45 (m, 1H), 2,41 (s, 3H), 2,35-2,39 (m, 1H), 2,24-2,29 (m, 1H), 2,07-2,16 (m, 1H), 1,89-2,09 (m, 1H), 1,73-1,92 (m, 3H), 1,55-1,68 (m, 1H), 1,26-1,46 (m, 2H), 1,03 (d, *J* = 6,7 Hz, 3H), 0,86 (t, *J* = 7,4 Hz, 3H); MS (ESI+) *m/z* 344 $(M+H)^+$.

Ejemplo 354

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-isoleucinamida

El compuesto del título se preparó utilizando (2S,3S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Paso A de Ejemplo 334 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,11-8,14 (m, 1H), 7,43-7,46 (m, 2H), 7,37 (t, *J* = 7,5 Hz, 2H), 7,25-7,30 (m, 1H), 4,44-4,51 (m, 1H), 3,62 (d, *J* = 13,1 Hz, 1H), 3,44 (d, *J* = 13,1 Hz, 1H), 2,96 (d, *J* = 6,0 Hz, 1H), 2,87 (dd, *J* = 8,9, 2,1 Hz, 1H), 2,47-2,61 (m, 2H), 2,43 (dd, *J* = 8,8, 7,0 Hz, 1H), 2,40 (s, 3H), 2,36 (dd, *J* = 8,9, 2,4 Hz, 1H), 2,26 (dd, *J* = 8,9, 6,6 Hz, 1H), 2,07-2,16 (m, 1H), 1,88-2,02 (m, 1H), 1,73-1,91 (m, 3H), 1,60 (dq, *J* = 12,1, 7,5 Hz, 1H), 1,25-1,46 (m, 2H), 1,03 (d, *J* = 6,8 Hz, 3H), 0,86 (t, *J* = 7,4 Hz, 3H); MS (ESI+) *m/z* 344 $(M+H)^+$.

Ejemplo 355

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2,4-dimetil-L-leucinamida

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 247 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,21-8,24 (m, 1H), 7,43-7,46 (m, 2H), 7,37 (t, *J* = 7,4 Hz, 2H), 7,24-7,30 (m, 1H), 4,42-4,47 (m, 1H), 3,61 (d, *J* = 13,0 Hz, 1H), 3,46 (d, *J* = 13,1 Hz, 1H), 3,19-3,22 (m, 1H), 2,88 (d, *J* = 10,0 Hz, 1H), 2,52 (d, *J* = 4,7 Hz, 2H), 2,40-2,46 (m, 1H), 2,41 (s, 3H), 2,37 (dd, *J* = 9,0, 2,4 Hz, 1H), 2,26 (dd, *J* = 8,7, 6,2 Hz, 1H), 2,07-2,18 (m, 1H), 1,93 (dd, *J* = 14,1, 5,1 Hz, 1H), 1,80-1,89 (m, 1H), 1,58-1,82 (m, 1H), 1,55-1,65 (m, 1H), 1,51 (dd, *J* = 14,0, 6,6 Hz, 1H), 1,34-1,46 (m, 1H), 0,98 (s, 9H); MS (ESI+) *m/z* 358 $(M+H)^+$.

Ejemplo 356

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-L-valinamida

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3,3-dimetil-1-oxobutan-2–ilcarbamato de tert-butilo del Ejemplo 234 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,09-8,12 (m, 1H), 7,42-7,44 (m, 2H), 7,37 (t, *J* = 7,3 Hz, 2H), 7,25-7,32 (m, 1H), 4,38-4,44 (m, 1H), 3,58 (d, *J* = 13,0 Hz, 1H), 3,44 (d, *J* = 13,1 Hz, 1H), 3,26 (s, 1H), 2,78 (dd, *J* = 8,9, 2,5 Hz, 1H), 2,44-2,52 (m, 2H), 2,38-2,42 (m, 1H), 2,33 (dd, *J* = 9,0, 2,7 Hz, 1H), 2,23-2,27 (m, 1H), 2,07-2,16 (m, 2H), 1,91-2,26 (m, 1H), 1,80-1,88 (m, 1H), 1,55-1,62 (m, 1H), 1,36-1,43 (m, 1H), 1,14 (s, 9H); MS (ESI+) *m/z* 330 $(M+H)^+$.

Ejemplo 357

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-L-valinamida

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3,3-dimetil-1-oxobutan-2–ilcarbamato de tert-butilo del Ejemplo 225 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,07-8,10 (m, 1H), 7,43-7,45 (m, 2H), 7,37 (t, *J* = 7,4 Hz, 2H), 7,25-7,31 (m, 1H), 4,42 (t, *J* = 5,0 Hz, 1H), 3,61 (d, *J* = 13,1 Hz, 1H), 3,44 (d, *J* = 13,1 Hz, 1H), 3,26 (s, 1H), 2,84-2,87 (m, 1H), 2,44-2,55 (m, 2H), 2,41-2,44 (m, 1H), 2,33-2,36 (m, 1H), 2,24-2,27 (m, 1H), 1,96-2,20 (m, 1H), 2,03-2,12 (m, 2H), 1,79-1,86 (m, 1H), 1,51-1,59 (m, 1H), 1,35-1,41 (m, 1H), 1,14 (s, 9H); MS (ESI+) *m/z* 330 $(M+H)^+$.

Ejemplo 358

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2,4-dimetil-L-leucinamida

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–

il(metil)carbamato de tert-butilo del Ejemplo 248 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,21-8,24 (m, 1H), 7,43-7,45 (m, 2H), 7,37 (t, *J* = 7,4 Hz, 2H), 7,27 (t, *J* = 7,3 Hz, 1H), 4,42-4,48 (m, 1H), 3,61 (d, *J* = 13,1 Hz, 1H), 3,45 (d, *J* = 13,1 Hz, 1H), 3,19 (t, *J* = 5,8 Hz, 1H), 2,88 (d, *J* = 10,3 Hz, 1H), 2,50-2,55 (m, 2H), 2,42 (dd, *J* = 9,0, 7,1 Hz, 1H), 2,40 (s, 3H), 2,36 (dd, *J* = 8,6, 2,6 Hz, 1H), 2,23-2,27 (m, 1H), 2,12 (dq, *J* = 11,9, 5,9 Hz, 1H), 1,93 (dd, *J* = 14,0, 5,2 Hz, 1H), 1,80-1,90 (m, 2H), 1,68-1,93 (m, 1H), 1,55-1,64 (m, 1H), 1,51 (dd, *J* = 14,0, 6,6 Hz, 1H), 1,36-1,45 (m, 1H), 0,98 (s, 9H); MS (ESI+) *m/z* 358 $(M+H)^+$.

Ejemplo 359

N^1-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando (S)-1-((3aS,4S,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 238 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37-8,42 (m, 1H), 7,51-7,53 (m, 2H), 7,36-7,41 (m, 2H), 7,31 (t, *J* = 7,4 Hz, 1H), 4,52-4,57 (m, 1H), 3,73 (d, *J* = 12,7 Hz, 1H), 3,30 (d, *J* = 12,8 Hz, 1H), 3,19 (t, *J* = 6,2 Hz, 1H), 2,77-2,82 (m, 1H), 2,67-2,73 (m, 1H), 2,39-2,47 (m, 3H), 2,40 (s, 3H), 2,18 (dd, *J* = 9,5, 7,1 Hz, 1H), 2,07-2,15 (m, 1H), 1,85-1,91 (m, 1H), 1,79-1,83 (m, 1H), 1,63-1,78 (m, 2H), 1,54-1,62 (m, 1H), 1,42-1,52 (m, 2H), 1,23-1,31 (m, 1H), 0,86 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 330 $(M+H)^+$.

Ejemplo 360

N^1-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida

El compuesto del título se preparó utilizando (S)-1-((3aS,4S,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 239 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H

NMR (500 MHz, piridin-d_5) δ ppm 8,47 (d, J = 7,3 Hz, 1H), 7,51-7,53 (m, 2H), 7,39 (t, J = 7,5 Hz, 2H), 7,31 (t, J = 7,3 Hz, 1H), 4,52-4,58 (m, 1H), 3,77 (d, J = 12,8 Hz, 1H), 3,29 (d, J = 12,8 Hz, 1H), 3,27 (dd, J = 8,2, 5,7 Hz, 1H), 2,82 (dd, J = 9,5, 2,3 Hz, 1H), 2,71-2,76 (m, 1H), 2,42-2,49 (m, 1H), 2,41 (s, 3H), 2,37-2,42 (m, 1H), 2,22 (dd, J = 9,4, 7,2 Hz, 1H), 2,15 (t, J = 8,3 Hz, 1H), 1,83-1,96 (m, 2H), 1,72-1,80 (m, 1H), 1,54-1,72 (m, 3H), 1,28 (dq, J = 12,9, 6,4 Hz, 1H), 0,92 (d, J = 6,6 Hz, 3H), 0,90 (d, J = 6,6 Hz, 3H); MS (ESI+) *m/z* 344 $(M+H)^+$.

Ejemplo 361

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-L-leucinamida

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo del Ejemplo 226 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,27-8,30 (m, 1H), 7,43-7,45 (m, 2H), 7,37 (t, J = 7,4 Hz, 2H), 7,25-7,29 (m, 1H), 4,36-4,42 (m, 1H), 3,58-3,61 (m, 2H), 3,45 (d, J = 13,1 Hz, 1H), 2,86 (dd, J = 9,0, 2,4 Hz, 1H), 2,45-2,54 (m, 2H), 2,39 (dd, J = 9,0, 7,2 Hz, 1H), 2,36 (dd, J = 9,1, 2,5 Hz, 1H), 2,24 (dd, J = 8,8, 6,9 Hz, 1H), 2,18 (dd, J = 14,0, 4,3 Hz, 1H), 2,01-2,23 (m, 2H), 2,07-2,14 (m, 1H), 1,79-1,87 (m, 1H), 1,56 (dq, J = 12,0, 7,7 Hz, 1H), 1,44 (dd, J = 14,0, 7,5 Hz, 1H), 1,35-1,44 (m, 1H), 0,98 (s, 9H); MS (ESI+) *m/z* 344 $(M+H)^+$.

Ejemplo 362

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norleucinamida

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxohexan-2–il(metil)carbamato de tert-butilo del Ejemplo 227 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,07-8,10 (m, 1H), 7,43-7,46 (m, 2H), 7,37 (t, J = 7,5 Hz, 2H), 7,28 (t, J = 7,4 Hz, 1H), 4,42-4,47 (m, 1H), 3,61 (d, J = 13,1 Hz, 1H), 3,46 (d, J = 13,1 Hz, 1H), 3,15 (t, J = 6,5 Hz, 1H), 2,87 (dd, J = 9,0, 2,5 Hz, 1H),

2,47-2,58 (m, 2H), 2,40-2,44 (m, 1H), 2,41 (s, 3H), 2,37 (dd, *J* = 8,9, 2,6 Hz, 1H), 2,26 (dd, *J* = 8,9, 6,8 Hz, 1H), 2,08-2,17 (m, 1H), 1,93-2,16 (m, 1H), 1,80-1,89 (m, 2H), 1,67-1,75 (m, 1H), 1,59 (dq, *J* = 12,0, 7,6 Hz, 1H), 1,38-1,50 (m, 3H), 1,20-1,28 (m, 2H), 0,81 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 344 $(M+H)^+$.

Ejemplo 363

N^1-[(3a*R*,4*R*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando (S)-1-((3aR,4R,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 240 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,26 (d, *J* = 7,8 Hz, 1H), 7,50-7,52 (m, 2H), 7,39 (t, *J* = 7,5 Hz, 2H), 7,32 (t, *J* = 7,3 Hz, 1H), 4,51-4,57 (m, 1H), 3,57 (d, *J* = 12,7 Hz, 1H), 3,42 (d, *J* = 12,7 Hz, 1H), 3,13-3,16 (m, 1H), 2,75-2,78 (m, 1H), 2,63-2,70 (m, 1H), 2,45-2,49 (m, 1H), 2,39-2,47 (m, 1H), 2,39 (s, 3H), 2,14 (dd, *J* = 8,9, 7,6 Hz, 1H), 2,09 (dd, *J* = 9,5, 7,2 Hz, 1H), 1,82-2,27 (m, 1H), 1,83-1,91 (m, 1H), 1,63-1,81 (m, 3H), 1,54-1,63 (m, 1H), 1,39-1,54 (m, 2H), 1,25-1,33 (m, 1H), 0,86 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 330 $(M+H)^+$.

Ejemplo 364

N^1-[(3a*R*,4*R*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida

El compuesto del título se preparó utilizando (S)-1-((3aR,4R,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 241 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,24-8,27 (m, 1H), 7,50-7,52 (m, 2H), 7,40 (t, *J* = 7,5 Hz, 2H), 7,32 (t, *J* = 7,4 Hz, 1H), 4,50-4,56 (m, 1H), 3,54 (d, *J* = 12,7 Hz, 1H), 3,45 (d, *J* = 12,7 Hz, 1H), 3,20 (dd, *J* = 8,2, 5,7 Hz, 1H), 2,76-2,78 (m, 1H), 2,64-2,71 (m, 1H), 2,46-2,49 (m, 1H), 2,41-2,47 (m, 1H), 2,39 (s, 3H), 2,16 (t, *J* = 8,2 Hz, 1H), 2,06-2,12 (m, 1H), 1,78-2,09 (m, 1H), 1,82-1,93 (m, 2H), 1,63-1,76 (m, 2H), 1,55-1,63 (m, 1H), 1,48-1,56 (m, 1H), 1,25-1,35 (m, 1H), 0,93 (d, *J* = 6,5 Hz,

3H), 0,88 (d, *J* = 6,6 Hz, 3H); MS (ESI+) *m/z* 344 $(M+H)^+$.

Ejemplo 365

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A de Ejemplo 313 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,08-8,10 (m, 1H), 7,43-7,46 (m, 2H), 7,37 (t, *J* = 7,4 Hz, 2H), 7,28 (t, *J* = 7,3 Hz, 1H), 4,41-4,46 (m, 1H), 3,61 (d, *J* = 13,1 Hz, 1H), 3,45 (d, *J* = 13,1 Hz, 1H), 3,15 (t, *J* = 6,5 Hz, 1H), 2,86 (dd, *J* = 9,0, 2,5 Hz, 1H), 2,47-2,57 (m, 2H), 2,40-2,44 (m, 1H), 2,40 (s, 3H), 2,37 (dd, *J* = 9,0, 2,3 Hz, 1H), 2,24-2,27 (m, 1H), 2,07-2,16 (m, 1H), 1,90-2,10 (m, 1H), 1,77-1,88 (m, 2H), 1,63-1,73 (m, 1H), 1,54-1,63 (m, 1H), 1,36-1,53 (m, 3H), 0,84 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 330 $(M+H)^+$.

Ejemplo 366

N^2-etil-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando etil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 310 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,23-8,26 (m, 1H), 7,76-7,77 (bs, 1H), 7,55-7,63 (m, 2H), 7,45 (t, *J* = 7,7 Hz, 1H), 4,41-4,45 (m, 1H), 3,61 (d, *J* = 13,5 Hz, 1H), 3,48 (d, *J* = 13,5 Hz, 1H), 3,33 (dd, *J* = 8,2, 5,8 Hz, 1H), 2,86 (dd, *J* = 9,0, 2,3 Hz, 1H), 2,70-2,78 (m, 1H), 2,60-2,64 (m, 1H), 2,53-2,55 (m, 2H), 2,43-2,47 (m, 1H), 2,33 (dd, *J* = 9,0, 2,4 Hz, 1H), 2,28 (dd, *J* = 8,8, 6,3 Hz, 1H), 2,08-2,12 (m, 1H), 1,80-2,05 (m, 1H), 1,82-1,95 (m, 2H), 1,72 (ddd, *J* = 13,5, 7,8, 5,8 Hz, 1H), 1,56-1,63 (m, 2H), 1,39-1,45 (m, 1H), 1,08 (t, *J* = 7,1 Hz, 3H), 0,92 (d, *J* = 6,6 Hz, 3H), 0,86 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 367

N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-valinamida

Paso A: Se preparó metil((S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxobutan-2–il(metil)carbamato de tert-butilo del Ejemplo 232 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida y 4-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,59 (d, *J* = 8,0, 2H), 7,46 (d, *J* = 7,9, 2H), 4,35 (d, *J* = 9,6, 1H), 4,30 – 4,23 (m, 1H), 3,55 (d, *J* = 13,7, 1H), 3,48 (d, *J* = 13,7, 1H), 3,01 (s, 3H), 2,77 (dd, *J* = 8,9, 2,1, 1H), 2,57 – 2,48 (m, 1H), 2,42 (ddd, *J* = 10,7, 9,3, 6,0, 2H), 2,36 (dd, *J* = 14,0, 5,7, 2H), 2,30 – 2,25 (m, 1H), 2,12 – 2,03 (m, 2H), 1,87 (td, *J* = 12,9, 6,3, 1H), 1,57 (dt, *J* = 14,8, 7,9, 1H), 1,45 (s, 9H), 1,43 – 1,35 (m, 1H), 1,01 (d, *J* = 6,5, 3H), 0,87 (d, *J* = 6,7, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,13-8,16 (m, 1H), 7,65-7,67 (m, 2H), 7,51-7,54 (m, 2H), 4,45-4,51 (m, 1H), 3,60 (d, *J* = 13,7 Hz, 1H), 3,47 (d, *J* = 13,7 Hz, 1H), 2,90 (d, *J* = 13,1 Hz, 1H), 2,88-2,90 (m, 1H), 2,48-2,59 (m, 2H), 2,40 (s, 3H), 2,33-2,40 (m, 2H), 2,24 (dd, *J* = 8,9, 7,0 Hz, 1H), 2,08-2,16 (m, 2H), 1,94-2,10 (m, 1H), 1,85-1,93 (m, 1H), 1,60 (dq, *J* = 12,0, 7,7 Hz, 1H), 1,43 (ddt, *J* = 8,9, 12,4, 6,2 Hz, 1H), 1,06 (t, *J* = 6,9 Hz, 6H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Ejemplo 368

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]piperidin-2-carboxamida

Paso A: Se preparó (2S)-2-({[(3aS,4R,6aR)-2-(4-flurobencil)octahidrociclopenta[c]pirrol-4–il]amino}carbonil)piperidin-1-carboxilato

de tert-butilo utilizando (2S)-2-({[(3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–il]amino}carbonil)piperidin-1-carboxilato de tert-butilo del Ejemplo 231 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida y 4-fluorobenzaldehido en lugar de 3-(trifluorometil)benzaldehido en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,37 (d, *J* = 7,2, 2H), 7,30 (t, *J* = 7,5, 2H), 7,21 (t, *J* = 7,3, 2H), 4,87 (d, *J* = 3,9, 1H), 4,32 – 4,23 (m, 1H), 4,10 (d, *J* = 12,8, 1H), 3,58 (d, *J* = 13,2, 1H), 3,47 (d, *J* = 13,2, 1H), 3,29 (td, *J* = 12,8, 2,9, 1H), 2,83 – 2,76 (m, 1H), 2,52 (td, *J* = 8,1, 3,4, 1H), 2,48 – 2,41 (m, 2H), 2,36 (dd, *J* = 9,0, 3,1, 1H), 2,33 – 2,28 (m, 1H), 2,24 (dd, *J* = 11,7, 1,6, 1H), 2,07 (dq, *J* = 12,2, 6,1, 1H), 1,87 – 1,78 (m, 1H), 1,69 – 1,59 (m, 1H), 1,59 – 1,49 (m, 3H), 1,48 (s, 9H), 1,45 – 1,29 (m, 3H); MS (ESI+) *m/z* 428 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (2S)-2-({[(3aS,4R,6aR)-2-(4-flurobencil)octahidrociclopenta[c]pirrol-4–il]amino}carbonil)piperidin-1-carboxilato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,68-7,70 (m, 1H), 7,35 (dd, *J* = 8,3, 5,6 Hz, 2H), 7,10-7,14 (m, 2H), 4,34-4,40 (m, 1H), 3,51 (d, *J* = 13,1 Hz, 1H), 3,36 (d, *J* = 13,1 Hz, 1H), 3,32 (dd, *J* = 10,4, 3,2 Hz, 1H), 2,98-3,02 (m, 1H), 2,82 (dd, *J* = 9,0, 2,6 Hz, 1H), 2,54-2,61 (m, 1H), 2,48-2,54 (m, 1H), 2,39-2,46 (m, 1H), 2,33-2,45 (m, 1H), 2,29-2,35 (m, 2H), 2,16-2,22 (m, 1H), 2,01-2,10 (m, 2H), 1,78-1,87 (m, 1H), 1,65-1,74 (m, 1H), 1,56-1,64 (m, 1H), 1,47-1,56 (m, 1H), 1,34-1,44 (m, 2H), 1,26-1,34 (m, 2H); MS (ESI+) *m/z* 346 $(M+H)^+$.

Ejemplo 369

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-*N*^{2}-metil-L-valinamida

Paso A: Se preparó metil((S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-fluorobencil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxobutan-2–il(metil)carbamato de tert-butilo del Ejemplo 232 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida y 4-fluorobenzaldehido en lugar de 3-

(trifluorometil)benzaldehido en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,43 (s, 1H), 7,30 (dd, *J* = 8,3, 5,7, 2H), 7,03 (t, *J* = 8,8, 2H), 4,35 (d, *J* = 9,5, 1H), 4,25 (s, 1H), 3,49 (d, *J* = 13,2, 1H), 3,41 (d, *J* = 13,2, 1H), 3,01 (s, 3H), 2,75 (dd, *J* = 8,9, 2,3, 1H), 2,57 – 2,48 (m, 1H), 2,45 – 2,31 (m, 4H), 2,27 (dd, *J* = 8,8, 7,4, 1H), 2,11 – 2,03 (m, 1H), 1,85 (dt, *J* = 20,7, 6,5, 1H), 1,56 (dt, *J* = 15,2, 7,3, 1H), 1,46 (s, 9H), 1,43 – 1,35 (m, 1H), 1,01 (d, *J* = 6,5, 3H), 0,87 (d, *J* = 6,7, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-fluorobencil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,11-8,14 (m, 1H), 7,37 (dd, *J* = 8,3, 5,6 Hz, 2H), 7,11-7,15 (m, 2H), 4,43-4,49 (m, 1H), 3,54 (d, *J* = 13,1 Hz, 1H), 3,39 (d, *J* = 13,1 Hz, 1H), 2,90 (d, *J* = 5,8 Hz, 1H), 2,86 (dd, *J* = 9,0, 2,6 Hz, 1H), 2,47-2,56 (m, 2H), 2,40 (s, 3H), 2,38 (dd, *J* = 9,0, 7,0 Hz, 1H), 2,34 (dd, *J* = 9,0, 2,6 Hz, 1H), 2,23 (dd, *J* = 8,9, 7,0 Hz, 1H), 2,07-2,16 (m, 2H), 1,93-2,04 (m, 1H), 1,83-1,92 (m, 1H), 1,59 (dq, *J* = 12,1, 7,7 Hz, 1H), 1,41 (ddt, *J* = 8,9, 12,4, 6,2 Hz, 1H), 1,06 (t, *J* = 6,8 Hz, 6H); MS (ESI+) *m/z* 348 $(M+H)^+$.

Ejemplo 370

(2*S*)-*N*-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}piperidin-2-carboxamida

Paso A: Se preparó (2S)-2-({[(3aS,4R,6aR)-2-(4-(triflurometil)bencil)octahidrociclopenta[c]pirrol-4–il]amino}carbonil)piperidin-1-carboxilato de tert-butilo utilizando (2S)-2-({[(3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–il]amino}carbonil)piperidin-1-carboxilato de tert-butilo del Ejemplo 231 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida y 4-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,59 (d, *J* = 8,1, 2H), 7,47 (d, *J* = 8,0, 2H), 7,27 – 7,20 (m, 1H), 4,87 (d, *J* = 3,7, 1H), 4,32 – 4,23 (m, 1H), 3,57 (d, *J* = 13,7, 1H), 3,49 (d, *J* = 13,8, 1H), 3,29 (td, *J* = 12,8, 3,0, 1H), 2,81 (dd, *J* = 8,7, 2,0, 1H), 2,59 –

2,50 (m, 1H), 2,46 (ddd, *J* = 12,1, 7,0, 2,8, 1H), 2,43 – 2,38 (m, 1H), 2,36 (dd, *J* = 9,0, 2,9, 1H), 2,32 – 2,27 (m, 1H), 2,27 – 2,20 (m, 1H), 2,11 – 2,03 (m, 2H), 1,86 (ddd, *J* = 12,7, 8,1, 6,3, 1H), 1,70 – 1,60 (m, 1H), 1,59 – 1,49 (m, 4H), 1,47 (s, 9H), 1,45 – 1,29 (m, 2H); MS (ESI+) *m/z* 496 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (2S)-2-({[(3aS,4R,6aR)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–il]amino}carbonil)piperidin-1-carboxilato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,71 (d, *J* = 7,5 Hz, 1H), 7,64-7,66 (m, 2H), 7,49-7,52 (m, 2H), 4,36-4,41 (m, 1H), 3,57 (d, *J* = 13,7 Hz, 1H), 3,43 (d, *J* = 13,7 Hz, 1H), 3,33 (dd, *J* = 10,3, 3,2 Hz, 1H), 2,98-3,03 (m, 1H), 2,85 (dd, *J* = 9,0, 2,5 Hz, 1H), 2,50-2,60 (m, 2H), 2,36-2,58 (m, 1H), 2,41-2,46 (m, 1H), 2,34 (d, *J* = 7,6 Hz, 1H), 2,31-2,33 (m, 1H), 2,20 (dd, *J* = 8,9, 7,2 Hz, 1H), 2,02-2,10 (m, 2H), 1,81-1,88 (m, 1H), 1,66-1,71 (m, 1H), 1,50-1,63 (m, 2H), 1,35-1,42 (m, 2H), 1,24-1,34 (m, 2H); MS (ESI+) *m/z* 396 $(M+H)^+$.

Ejemplo 371

N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 317 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,14-8,17 (m, 1H), 7,64-7,67 (m, 2H), 7,51-7,54 (m, 2H), 4,43-4,49 (m, 1H), 3,59 (d, *J* = 13,7 Hz, 1H), 3,47 (d, *J* = 13,7 Hz, 1H), 3,16 (t, *J* = 6,5 Hz, 1H), 2,88 (dd, *J* = 9,0, 2,6 Hz, 1H), 2,44-2,58 (m, 2H), 2,40 (s, 3H), 2,34-2,39 (m, 2H), 2,24 (t, *J* = 8,0 Hz, 1H), 2,12 (dq, *J* = 11,8, 5,9 Hz, 1H), 1,95-2,18 (m, 1H), 1,85-1,93 (m, 1H), 1,76-1,85 (m, 1H), 1,66-1,73 (m, 1H), 1,56-1,64 (m, 1H), 1,39-1,53 (m, 3H), 0,84 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Ejemplo 372

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-(4-fluorobencil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 318 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,12-8,15 (m, 1H), 7,35-7,39 (m, 2H), 7,11-7,15 (m, 2H), 4,41-4,47 (m, 1H), 3,53 (d, *J* = 13,1 Hz, 1H), 3,39 (d, *J* = 13,1 Hz, 1H), 3,16 (t, *J* = 6,5 Hz, 1H), 2,85 (dd, *J* = 9,0, 2,6 Hz, 1H), 2,46-2,59 (m, 2H), 2,40 (s, 3H), 2,38 (dd, *J* = 8,9, 6,8 Hz, 1H), 2,34 (dd, *J* = 8,9, 2,8 Hz, 1H), 2,23 (dd, *J* = 8,9, 7,1 Hz, 1H), 2,07-2,16 (m, 1H), 1,91-2,12 (m, 1H), 1,84-1,91 (m, 1H), 1,76-1,83 (m, 1H), 1,66-1,73 (m, 1H), 1,54-1,63 (m, 1H), 1,36-1,54 (m, 3H), 0,84 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 348 $(M+H)^+$.

Ejemplo 373

N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-valinamida

El compuesto del título se preparó utilizando metil((S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo del Ejemplo 316 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,13 (d, *J* = 7,6, 1H), 7,76 (s, 1H), 7,61 (d, *J* = 7,6, 1H), 7,56 (s, 1H), 7,45 (t, *J* = 7,7, 1H), 4,52 – 4,36 (m, 1H), 3,62 (d, *J* = 13,6, 1H), 3,46 (d, *J* = 13,6, 1H), 2,92 – 2,79 (m, 2H), 2,59 – 2,46 (m, 2H), 2,43 (d, *J* = 8,8, 1H), 2,40 (s, 3H), 2,33 (dd, *J* = 9,0, 2,5, 1H), 2,28 – 2,22 (m, 1H), 2,15 – 2,05 (m, 2H), 2,04 – 1,93 (m, 1H), 1,86 (td, *J* = 12,9, 6,4, 1H), 1,59 (dt, *J* = 14,9, 7,7, 1H), 1,44 – 1,36 (m, 1H), 1,05 (t, *J* = 7,0, 6H); MS (ESI+) *m/z* 398 $(M+H)^+$.

C00734

Ejemplo 374

N^1-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-(3-fluoro-4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 311 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,20-8,22 (m, 1H), 7,58-7,61 (m, 1H), 7,32-7,36 (m, 1H), 7,27-7,29 (m, 1H), 4,43-4,48 (m, 1H), 3,55-3,62 (m, 1H), 3,45 (d, *J* = 14,1 Hz, 1H), 3,22 (dd, *J* = 8,2, 5,8 Hz, 1H), 2,91 (dd, *J* = 9,0, 2,5 Hz, 1H), 2,48-2,60 (m, 2H), 2,42 (s, 3H), 2,35-2,39 (m, 2H), 2,23 (dd, *J* = 8,9, 7,1 Hz, 1H), 2,07-2,16 (m, 1H), 1,91-2,11 (m, 1H), 1,84-1,95 (m, 2H), 1,71 (ddd, *J* = 13,5, 7,8, 5,8 Hz, 1H), 1,56-1,65 (m, 2H), 1,39-1,46 (m, 1H), 0,91 (d, *J* = 6,6 Hz, 3H), 0,85 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Ejemplo 375

N^1-{(3a*S*,4*R*,6a*R*)-2-[4-fluoro-3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-(4-fluoro-3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 312 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,18-8,21 (m, 1H), 7,68-7,71 (m, 1H), 7,57-7,60 (m, 1H), 7,22-7,28 (m, 1H), 4,42-4,46 (m, 1H), 3,55 (d, *J* = 13,5 Hz, 1H), 3,43 (d, *J* = 13,4 Hz, 1H), 3,21 (dd, *J* = 8,2, 5,8 Hz, 1H), 2,88 (dd, *J* = 9,0, 2,6 Hz, 1H), 2,48-2,60 (m, 2H), 2,42 (s, 3H), 2,37-2,42 (m, 1H), 2,34 (dd, *J* = 8,8, 2,4 Hz, 1H), 2,21-2,28 (m, 1H), 2,06-2,14 (m, 1H), 1,90-2,08 (m, 1H), 1,83-1,94 (m, 2H), 1,71 (ddd, *J* = 13,5, 7,8, 5,8 Hz, 1H), 1,55-1,64 (m, 2H), 1,38-1,45 (m, 1H), 0,91 (d, *J* = 6,5 Hz, 3H), 0,85 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

600235
9707.61

Ejemplo 376

N^2-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 313 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,09-8,12 (m, 1H), 7,76-7,77 (bs, 1H), 7,60-7,63 (m, 1H), 7,55-7,58 (m, 1H), 7,45 (t, *J* = 7,7 Hz, 1H), 4,40-4,44 (m, 1H), 3,61 (d, *J* = 13,5 Hz, 1H), 3,47 (d, *J* = 13,5 Hz, 1H), 3,15 (t, *J* = 6,5 Hz, 1H), 2,87 (dd, *J* = 9,0, 2,6 Hz, 1H), 2,47-2,57 (m, 2H), 2,40-2,44 (m, 1H), 2,40 (s, 3H), 2,33 (dd, *J* = 9,0, 2,7 Hz, 1H), 2,23-2,27 (m, 1H), 2,05-2,12 (m, 1H), 1,93-2,10 (m, 1H), 1,83-1,90 (m, 1H), 1,76-1,83 (m, 1H), 1,64-1,73 (m, 1H), 1,54-1,63 (m, 1H), 1,36-1,53 (m, 3H), 0,84 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Ejemplo 377

N^2-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 314 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,12-8,15 (m, 1H), 7,64-7,67 (m, 2H), 7,51-7,54 (m, 2H), 4,42-4,47 (m, 1H), 3,57-3,61 (m, 1H), 3,48 (d, *J* = 13,7 Hz, 1H), 3,16 (t, *J* = 6,5 Hz, 1H), 2,89 (dd, *J* = 9,0, 2,5 Hz, 1H), 2,48-2,58 (m, 2H), 2,41 (s, 3H), 2,34-2,41 (m, 2H), 2,24 (dd, *J* = 8,9, 7,0 Hz, 1H), 2,03-2,18 (m, 1H), 1,94-2,26 (m, 1H), 1,77-1,95 (m, 2H), 1,66-1,73 (m, 1H), 1,55-1,64 (m, 1H), 1,38-1,55 (m, 3H), 0,84 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Ejemplo 378

N^1-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-(4-

fluorobencil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 315 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,12-8,15 (m, 1H), 7,64-7,67 (m, 2H), 7,51-7,54 (m, 2H), 4,42-4,47 (m, 1H), 3,57-3,61 (m, 1H), 3,48 (d, *J* = 13,7 Hz, 1H), 3,16 (t, *J* = 6,5 Hz, 1H), 2,89 (dd, *J* = 9,0, 2,5 Hz, 1H), 2,48-2,58 (m, 2H), 2,41 (s, 3H), 2,34-2,41 (m, 2H), 2,24 (dd, *J* = 8,9, 7,0 Hz, 1H), 2,03-2,18 (m, 1H), 1,94-2,26 (m, 1H), 1,77-1,95 (m, 2H), 1,66-1,73 (m, 1H), 1,55-1,64 (m, 1H), 1,38-1,55 (m, 3H), 0,84 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Ejemplo 379

N^2-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando metil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 307 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,18-8,20 (m, 1H), 7,76-7,77 (bs, 1H), 7,60-7,64 (m, 1H), 7,54-7,59 (m, 1H), 7,45 (t, *J* = 7,7 Hz, 1H), 4,40-4,47 (m, 1H), 3,61 (d, *J* = 13,5 Hz, 1H), 3,47 (d, *J* = 13,5 Hz, 1H), 3,22 (dd, *J* = 8,2, 5,8 Hz, 1H), 2,87 (d, *J* = 10,4 Hz, 1H), 2,49-2,57 (m, 2H), 2,40-2,46 (m, 1H), 2,42 (s, 3H), 2,33 (dd, *J* = 8,9, 2,5 Hz, 1H), 2,26 (dd, *J* = 8,9, 6,5 Hz, 1H), 2,01-2,16 (m, 1H), 1,92-2,12 (m, 1H), 1,83-1,97 (m, 2H), 1,71 (ddd, *J* = 13,5, 7,7, 5,8 Hz, 1H), 1,55-1,64 (m, 2H), 1,37-1,44 (m, 1H), 0,91 (d, *J* = 6,6 Hz, 3H), 0,85 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 412 $(M+H)^+$.

Ejemplo 380

N^2-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando metil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 308 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-

2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,19-8,22 (m, 1H), 7,64-7,67 (m, 2H), 7,51-7,54 (m, 2H), 4,43-4,48 (m, 1H), 3,59 (d, *J* = 13,7 Hz, 1H), 3,48 (d, *J* = 13,7 Hz, 1H), 3,23 (dd, *J* = 8,2, 5,8 Hz, 1H), 2,90 (dd, *J* = 9,0, 2,4 Hz, 1H), 2,49-2,58 (m, 2H), 2,43 (s, 3H), 2,38-2,42 (m, 1H), 2,37 (dd, *J* = 19,2, 2,5 Hz, 1H), 2,24 (dd, *J* = 8,9, 6,8 Hz, 1H), 2,09-2,17 (m, 1H), 1,95-2,13 (m, 1H), 1,83-1,97 (m, 2H), 1,72 (ddd, *J* = 13,5, 7,8, 5,8 Hz, 1H), 1,56-1,65 (m, 2H), 1,39-1,46 (m, 1H), 0,91 (d, *J* = 6,6 Hz, 3H), 0,85 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 412 $(M+H)^+$.

Ejemplo 381

N^1-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-(4-fluorobencil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 309 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,17-8,20 (m, 1H), 7,37 (dd, *J* = 8,2, 5,6 Hz, 2H), 7,11-7,15 (m, 2H), 4,41-4,47 (m, 1H), 3,52 (d, *J* = 13,1 Hz, 1H), 3,40 (d, *J* = 13,1 Hz, 1H), 3,22 (dd, *J* = 8,2, 5,8 Hz, 1H), 2,86 (dd, *J* = 9,0, 2,4 Hz, 1H), 2,46-2,57 (m, 2H), 2,42 (s, 3H), 2,34-2,41 (m, 2H), 2,24 (dd, *J* = 8,9, 6,7 Hz, 1H), 2,05-2,18 (m, 1H), 1,98-2,11 (m, 1H), 1,83-1,97 (m, 2H), 1,71 (ddd, *J* = 13,5, 7,8, 5,8 Hz, 1H), 1,55-1,64 (m, 2H), 1,41 (ddt, *J* = 8,9, 12,3, 6,2 Hz, 1H), 0,91 (d, *J* = 6,6 Hz, 3H), 0,85 (d, *J* = 6,6 Hz, 3H); MS (ESI+) *m/z* 362 $(M+H)^+$.

Ejemplo 382

N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida

Paso A: Se preparó ((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando *N*-(*tert*-butoxicarbonil)-L-norvalina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,61 – 8,53 (m, 1H), 7,92 (d, *J* = 8,2, 1H), 7,43 (d, *J* = 7,4, 2H), 7,35 (d, *J* = 7,6, 2H), 7,27 (t, *J* = 7,2, 1H), 4,64 (dd, *J* = 14,4, 7,8, 1H), 4,47 – 4,35 (m, 1H), 3,59 (d, *J* = 13,1, 1H), 3,43 (d, *J* = 13,2, 1H), 2,83 (dd, *J* = 4,7, 4,1, 1H), 2,60 –

2,48 (m, 2H), 2,47 – 2,40 (m, 1H), 2,32 (dd, *J* = 5,0, 3,9, 1H), 2,27 – 2,20 (m, 1H), 2,11 – 1,97 (m, 2H), 1,91 – 1,76 (m, 2H), 1,63 – 1,42 (m, 12H), 1,40 – 1,29 (m, 1H), 0,81 (t, *J* = 7,3, 3H); MS (ESI+) *m/z* 416 $(M+H)^+$.

Paso B: Se preparó ((*S*)-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando ((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida y 4-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido en los procedimientos descritos en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,60 (d, *J* = 7,0, 1H), 7,93 (d, *J* = 8,3, 1H), 7,65 (d, *J* = 8,1, 2H), 7,51 (d, *J* = 7,9, 2H), 4,64 (dd, *J* = 13,0, 6,5, 1H), 4,47 – 4,37 (m, 1H), 3,57 (d, *J* = 13,7, 1H), 3,45 (d, *J* = 13,7, 1H), 2,86 (d, *J* = 8,3, 1H), 2,55 (dd, *J* = 14,1, 9,2, 2H), 2,43 – 2,36 (m, 1H), 2,31 (d, *J* = 7,8, 1H), 2,26 – 2,20 (m, 1H), 2,14 (s, 1H), 2,04 (dd, *J* = 12,1, 6,0, 2H), 1,90 – 1,80 (m, 2H), 1,59 (s, 1H), 1,49 (d, *J* = 11,3, 10H), 1,37 (s, 1H), 0,81 (t, *J* = 7,3, 3H); MS (ESI+) *m/z* 484 $(M+H)^+$.

Paso C: El compuesto del título se preparó utilizando ((S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso B en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,19-8,22 (m, 1H), 7,64-7,67 (m, 2H), 7,50-7,53 (m, 2H), 4,37-4,43 (m, 1H), 3,53-3,58 (m, 2H), 3,46 (d, *J* = 13,7 Hz, 1H), 2,86 (dd, *J* = 9,0, 2,6 Hz, 1H), 2,49-2,57 (m, 1H), 2,43-2,49 (m, 1H), 2,33-2,36 (m, 2H), 2,19-2,25 (m, 1H), 2,11-2,20 (m, 2H), 2,06-2,14 (m, 1H), 1,91-2,01 (m, 1H), 1,82-1,90 (m, 1H), 1,62-1,69 (m, 1H), 1,38-1,58 (m, 4H), 0,84 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 384 $(M+H)^+$.

Ejemplo 383

N^2-etil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando etil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–

ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 323 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37-8,39 (m, 1H), 8,32-8,37 (m, 1H), 8,19-8,21 (m, 1H), 7,90-7,93 (m, 1H), 7,73 (t, *J* = 7,9 Hz, 1H), 4,23-4,29 (m, 1H), 3,86 (d, *J* = 11,2 Hz, 1H), 3,31 (t, *J* = 6,9 Hz, 1H), 3,18 (dd, *J* = 9,7, 2,1 Hz, 1H), 3,16 (dd, *J* = 9,9, 7,5 Hz, 1H), 2,96 (dd, *J* = 9,5, 6,5 Hz, 1H), 2,68-2,75 (m, 1H), 2,51-2,63 (m, 3H), 1,90-2,12 (m, 1H), 1,91-1,99 (m, 1H), 1,80-1,91 (m, 2H), 1,66-1,72 (m, 1H), 1,52-1,60 (m, 2H), 1,26-1,34 (m, 1H), 1,06 (t, *J* = 7,1 Hz, 3H), 0,92 (d, *J* = 6,6 Hz, 3H), 0,85 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Ejemplo 384

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando metil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 322 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,38-8,39 (bs, 1H), 8,29-8,31 (m, 1H), 8,19-8,21 (m, 1H), 7,91-7,93 (m, 1H), 7,73 (t, *J* = 7,8 Hz, 1H), 4,24-4,29 (m, 1H), 3,87 (dd, *J* = 9,9, 2,2 Hz, 1H), 3,17-3,22 (m, 2H), 3,15 (dd, *J* = 9,8, 7,4 Hz, 1H), 2,95 (dd, *J* = 9,6, 6,7 Hz, 1H), 2,49-2,60 (m, 2H), 2,39 (s, 3H), 1,93-2,10 (m, 1H), 1,91-1,99 (m, 1H), 1,80-1,91 (m, 2H), 1,68 (ddd, *J* = 13,5, 7,8, 5,8 Hz, 1H), 1,53-1,59 (m, 2H), 1,25-1,33 (m, 1H), 0,91 (d, *J* = 6,6 Hz, 3H), 0,85 (d, *J* = 6,6 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 385

***N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida**

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida del Ejemplo 269 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–

il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,38-8,39 (bs, 1H), 8,19-8,22 (m, 2H), 7,91-7,94 (m, 1H), 7,74 (t, *J* = 7,8 Hz, 1H), 7,29-7,35 (m, 4H), 7,24-7,29 (m, 1H), 4,92-4,95 (m, 1H), 4,16-4,23 (m, 1H), 3,80 (dd, *J* = 7,6, 5,7 Hz, 1H), 3,77 (dd, *J* = 9,8, 2,7 Hz, 1H), 3,32 (dd, *J* = 13,2, 5,7 Hz, 1H), 3,15 (dd, *J* = 9,6, 2,9 Hz, 1H), 2,99-3,03 (m, 2H), 2,89 (dd, *J* = 9,6, 7,6 Hz, 1H), 2,41-2,47 (m, 1H), 2,32-2,37 (m, 1H), 1,98-2,15 (m, 1H), 1,83-1,89 (m, 1H), 1,71-1,77 (m, 1H), 1,35-1,43 (m, 1H), 1,17-1,26 (m, 1H); MS (ESI+) *m/z* 482 $(M+H)^+$.

Ejemplo 386

***N*-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida**

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida del Ejemplo 270 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,39-8,40 (bs, 1H), 8,25 (d, *J* = 5,1 Hz, 1H), 7,94-7,96 (m, 1H), 7,79 (t, *J* = 7,8 Hz, 1H), 7,31-7,33 (m, 4H), 7,24-7,28 (m, 1H), 4,17-4,24 (m, 1H), 3,73 (dd, *J* = 9,9, 2,8 Hz, 1H), 3,45 (t, *J* = 6,8 Hz, 1H), 3,13-3,20 (m, 2H), 3,01-3,10 (m, 2H), 2,91 (dd, *J* = 9,6, 7,6 Hz, 1H), 2,39-2,50 (m, 1H), 2,36 (s, 3H), 2,28-2,37 (m, 1H), 2,0 (m, 1H), 1,89-2,26 (m, 1H), 1,84-1,92 (m, 1H), 1,72-1,79 (m, 1H), 1,40-1,48 (m, 1H), 1,18-1,26 (m, 1H); MS (ESI+) *m/z* 496 $(M+H)^+$.

Ejemplo 387

***N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-prolinamida**

El compuesto del título se preparó utilizando (S)-2-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilcarbamoil)pirrolidin-1-carboxilato de tert-butilo del Ejemplo 271 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,35-8,38 (m, 1H), 8,17-8,19 (m, 2H), 7,90-7,92 (m, 1H), 7,72 (t, *J* = 7,9 Hz, 1H), 4,13-4,19 (m, 1H), 3,86 (dd, *J* = 8,6, 5,8 Hz, 1H),

3,79 (dd, *J* = 9,9, 2,6 Hz, 1H), 3,16 (dd, *J* = 9,6, 2,9 Hz, 1H), 3,02 (dd, *J* = 9,9, 7,8 Hz, 1H), 2,66-3,18 (m, 1H), 2,79-2,91 (m, 3H), 2,48-2,55 (m, 1H), 2,40-2,45 (m, 1H), 1,99-2,10 (m, 2H), 1,76-1,92 (m, 2H), 1,55-1,65 (m, 1H), 1,48-1,56 (m, 1H), 1,39-1,48 (m, 1H), 1,21-1,29 (m, 1H); MS (ESI+) *m/z* 432 $(M+H)^+$.

Ejemplo 388

(3*R*)-3-amino-4-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida

El compuesto del título se preparó utilizando (1R)-1-isopropil-3-oxo-3-[((3aR,4S,6aS)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]propilcarbamato de tert-butilo del Ejemplo 272 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,74-8,76 (bs, 2H), 8,37-8,38 (bs, 1H), 8,19 (d, *J* = 7,9 Hz, 1H), 7,91 (d, *J* = 7,9 Hz, 1H), 7,72 (t, *J* = 7,8 Hz, 1H), 4,23-4,28 (m, 1H), 3,85 (dd, *J* = 9,9, 2,4 Hz, 1H), 3,14-3,19 (m, 2H), 3,12 (dd, *J* = 9,9, 7,6 Hz, 1H), 2,94 (dd, *J* = 9,6, 6,8 Hz, 1H), 2,50-2,55 (m, 2H), 2,43 (dd, *J* = 14,4, 3,2 Hz, 1H), 2,27 (dd, *J* = 14,4, 9,9 Hz, 1H), 1,92-1,99 (m, 1H), 1,80-1,88 (m, 1H), 1,65-1,90 (m, 1H), 1,50-1,61 (m, 2H), 1,25-1,32 (m, 1H), 0,85 (d, *J* = 6,9 Hz, 3H), 0,83 (d, *J* = 6,9 Hz, 3H); MS (ESI-) *m/z* 446 $(M-H)^-$.

Ejemplo 389

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida

El compuesto del título se preparó utilizando metil((S)-3-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo del Ejemplo 273 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,39-8,40 (bs, 1H), 8,24 (d, *J* = 6,9 Hz, 1H), 8,21 (d, *J* = 7,8 Hz, 1H), 7,91-7,93 (m, 1H), 7,73 (t, *J* = 7,8 Hz, 1H), 4,24-4,28 (m, 1H), 3,86 (dd, *J* = 9,9, 2,4 Hz, 1H), 3,18 (dd, *J* = 9,7, 2,4 Hz, 1H), 3,15 (dd, *J* = 9,9, 7,5 Hz, 1H), 2,96 (dd, *J* = 9,6, 6,9 Hz, 1H), 2,88 (d, *J* = 5,9 Hz, 1H), 2,51-2,56 (m, 2H), 2,38 (s, 3H), 2,04-2,14 (m, 1H), 1,88-2,12 (m, 1H), 1,90-1,98 (m, 1H), 1,80-1,88 (m, 1H), 1,51-1,58 (m, 1H), 1,29 (ddt, *J* = 9,6, 12,8, 6,4 Hz, 1H), 1,04 (d, *J* = 6,9

Hz, 3H), 1,01-1,05 (m, 6H), 1,02 (d, *J* = 6,9 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Ejemplo 390

(2*S*)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)piperidin-2-carboxamida

El compuesto del título se preparó utilizando (2S)-2-{[((3aR,4S,6aS)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]carbonil}piperidin-1-carboxilato de tert-butilo del Ejemplo 274 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,35-8,36 (bs, 1H), 8,17-8,19 (m, 1H), 7,90-7,92 (m, 1H), 7,78-7,80 (m, 1H), 7,73 (t, *J* = 7,8 Hz, 1H), 4,16-4,23 (m, 1H), 3,79 (dd, *J* = 9,8, 2,6 Hz, 1H), 3,32 (dd, *J* = 10,3, 3,2 Hz, 1H), 3,15 (dd, *J* = 9,6, 2,9 Hz, 1H), 3,02 (dd, *J* = 9,8, 7,7 Hz, 1H), 2,96-3,00 (m, 1H), 2,89 (dd, *J* = 9,6, 7,4 Hz, 1H), 2,49-2,59 (m, 2H), 2,42-2,49 (m, 1H), 2,18-2,71 (m, 1H), 2,01-2,05 (m, 1H), 1,87-1,95 (m, 1H), 1,75-1,83 (m, 1H), 1,65-1,71 (m, 1H), 1,54-1,61 (m, 1H), 1,44-1,52 (m, 1H), 1,35-1,43 (m, 1H), 1,19-1,35 (m, 3H); MS (ESI+) *m/z* 446 $(M+H)^+$.

Ejemplo 391

(3*S*)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-1,2,3,4-tetrahidroisoquinolin-3-carboxamida

El compuesto del título se preparó utilizando (3S)-3-{[((3aR,4S,6aS)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]carbonil}-3,4-dihidroisoquinolin-2(1H)-carboxilato de tert-butilo del Ejemplo 275 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (501 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,30-8,31 (bs, 1H), 8,13-8,16 (m, 1H), 7,83-7,85 (m, 1H), 7,68-7,71 (m, 1H), 7,65 (t, *J* = 7,9 Hz, 1H), 7,08-7,12 (m, 3H), 6,97-7,00 (m, 1H), 4,05-4,15 (m, 2H), 3,94-3,98 (m, 1H), 3,66 (dd, *J* = 10,3, 3,4 Hz, 1H), 3,63 (dd, *J* = 9,8, 5,2 Hz, 1H), 3,21-3,26 (m, 1H), 3,11-3,18 (m, 3H), 2,99-3,06 (m, 1H), 2,54-2,58 (m, 1H), 2,47-2,52 (m, 1H), 1,96 (m, 1H), 1,87-1,94 (m, 1H), 1,78-1,85 (m, 1H), 1,45-1,54 (m, 1H), 1,23-1,31 (m, 1H); MS (ESI-) *m/z* 492 $(M-H)^-$.

Ejemplo 392

4-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando (S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo del Ejemplo 276 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (501 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,30-8,31 (bs, 1H), 8,13-8,16 (m, 1H), 7,82-7,85 (m, 2H), 7,65 (t, *J* = 7,9 Hz, 1H), 4,03-4,10 (m, 1H), 3,69 (dd, *J* = 10,1, 3,4 Hz, 1H), 3,48 (dd, *J* = 7,5, 4,0 Hz, 1H), 3,23-3,27 (m, 1H), 3,11-3,13 (m, 2H), 2,54-2,59 (m, 1H), 2,46-2,51 (m, 1H), 2,07 (dd, *J* = 14,1, 4,0 Hz, 1H), 2,0 (m, 1H), 1,89-1,96 (m, 1H), 1,78-1,87 (m, 1H), 1,65-1,92 (m, 1H), 1,46-1,55 (m, 1H), 1,34 (dd, *J* = 14,1, 7,6 Hz, 1H), 1,23-1,32 (m, 1H), 0,96 (s, 9H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 393

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norleucinamida

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)hexan-2–il)carbamato de tert-butilo del Ejemplo 277 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,38-8,39 (bs, 1H), 8,19-8,23 (m, 2H), 7,91-7,93 (m, 1H), 7,73 (t, *J* = 7,8 Hz, 1H), 4,24-4,29 (m, 1H), 3,87 (dd, *J* = 9,9, 2,3 Hz, 1H), 3,18 (dd, *J* = 9,8, 2,3 Hz, 1H), 3,11-3,16 (m, 2H), 2,94 (dd, *J* = 9,6, 6,8 Hz, 1H), 2,53-2,66 (m, 2H), 2,39 (s, 3H), 1,98-2,19 (m, 1H), 1,91-1,99 (m, 1H), 1,78-1,88 (m, 2H), 1,65-1,73 (m, 1H), 1,50-1,59 (m, 1H), 1,35-1,48 (m, 2H), 1,20-1,33 (m, 3H), 0,81 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 394

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 278 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,38-8,39 (bs, 1H), 8,19-8,21 (m, 2H), 7,90-7,93 (m, 1H), 7,72 (t, *J* = 7,9 Hz, 1H), 4,22-4,29 (m, 1H), 3,87 (dd, *J* = 9,9, 2,5 Hz, 1H), 3,18 (dd, *J* = 9,6, 2,4 Hz, 1H), 3,10-3,15 (m, 2H), 2,94 (dd, *J* = 9,6, 7,0 Hz, 1H), 2,49-2,57 (m, 2H), 2,37 (s, 3H), 1,92-2,22 (m, 1H), 1,89-1,99 (m, 1H), 1,74-1,87 (m, 2H), 1,62-1,70 (m, 1H), 1,40-1,58 (m, 3H), 1,25-1,32 (m, 1H), 0,84 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Ejemplo 395

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

Paso A: Se preparó metil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 222 en lugar de (S)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,08 (d, *J* = 8,2, 2H), 7,82 (d, *J* = 8,2, 2H), 7,51 (d, *J* = 2,1, 1H), 4,83 (s, 1H), 4,12 – 4,04 (m, 1H), 3,67 (dd, *J* = 10,2, 3,4, 1H), 3,27 (dd, *J* = 10,2, 7,8, 1H), 3,14 – 3,09 (m, 2H), 2,94 (s, 3H), 2,63 – 2,46 (m, 2H), 1,95 – 1,68 (m, 4H), 1,60 (td, *J* = 13,4, 6,8, 1H), 1,54 – 1,47 (m, 1H), 1,46 (s, 9H), 1,27 (ddt, *J* = 13,3, 9,3, 6,7, 1H), 0,89 (dd, *J* = 10,7, 6,6, 6H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-4-metil-1-

oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,32-8,34 (m, 1H), 8,13-8,16 (m, 2H), 7,90-7,92 (m, 2H), 4,23-4,30 (m, 1H), 3,86 (dd, *J* = 9,9, 2,4 Hz, 1H), 3,22 (dd, *J* = 8,2, 5,9 Hz, 1H), 3,18 (dd, *J* = 9,8, 2,4 Hz, 1H), 3,15 (dd, *J* = 10,0, 7,6 Hz, 1H), 2,97 (dd, *J* = 9,6, 6,8 Hz, 1H), 2,53-2,60 (m, 2H), 2,41 (s, 3H), 2,0 (m, 1H), 1,91-1,99 (m, 1H), 1,80-1,91 (m, 2H), 1,69 (ddd, *J* = 13,5, 7,7, 5,9 Hz, 1H), 1,52-1,60 (m, 2H), 1,26-1,35 (m, 1H), 0,91 (d, *J* = 6,6 Hz, 3H), 0,85 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 396

***N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-prolinamida**

El compuesto del título se preparó utilizando (S)-2-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilcarbamoil)pirrolidin-1-carboxilato de tert-butilo del Ejemplo 266 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,36-8,37 (bs, 1H), 8,17-8,19 (m, 2H), 7,90-7,92 (m, 1H), 7,72 (t, *J* = 7,8 Hz, 1H), 4,13-4,19 (m, 1H), 3,81-3,85 (m, 2H), 3,17 (dd, *J* = 9,6, 2,9 Hz, 1H), 3,05 (dd, *J* = 9,9, 7,8 Hz, 1H), 2,80-2,91 (m, 3H), 2,50-2,55 (m, 1H), 2,39-2,45 (m, 1H), 1,97-2,09 (m, 2H), 1,96 (m, 1H), 1,84-1,91 (m, 1H), 1,76-1,82 (m, 1H), 1,56-1,65 (m, 1H), 1,48-1,56 (m, 1H), 1,40-1,48 (m, 1H), 1,21-1,29 (m, 1H); MS (ESI+) *m/z* 432 $(M+H)^+$.

Ejemplo 397

(3*R*)-3-amino-4-metil-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida

El compuesto del título se preparó utilizando (1R)-1-isopropil-3-oxo-3-[((3aS,4R,6aR)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]propilcarbamato de tert-butilo del Ejemplo 267 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H

NMR (500 MHz, piridin-d_5) δ ppm 8,37-8,38 (bs, 1H), 8,20 (d, J = 7,9 Hz, 1H), 7,90-7,92 (m, 1H), 7,72 (t, J = 7,8 Hz, 1H), 4,22-4,27 (m, 1H), 3,86 (dd, J = 9,9, 2,4 Hz, 1H), 3,12-3,18 (m, 3H), 2,95 (dd, J = 9,6, 6,8 Hz, 1H), 2,51-2,56 (m, 2H), 2,45 (dd, J = 14,4, 3,2 Hz, 1H), 2,27 (dd, J = 14,4, 9,9 Hz, 1H), 1,90-1,98 (m, 1H), 1,79-1,88 (m, 1H), 1,63-1,83 (m, 3H), 1,49-1,62 (m, 2H), 1,24-1,32 (m, 1H), 0,80-0,95 (m, 6H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Ejemplo 398

(2*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)piperidin-2-carboxamida

El compuesto del título se preparó utilizando (2S)-2-{[((3aS,4R,6aR)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]carbonil}piperidin-1-carboxilato de tert-butilo del Ejemplo 268 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,35-8,36 (bs, 1H), 8,17 (d, J = 7,9 Hz, 1H), 7,90-7,92 (m, 1H), 7,78-7,80 (m, 1H), 7,72 (t, J = 7,8 Hz, 1H), 4,16-4,23 (m, 1H), 3,83 (dd, J = 9,9, 2,7 Hz, 1H), 3,30 (dd, J = 10,3, 3,2 Hz, 1H), 3,16 (dd, J = 9,6, 2,8 Hz, 1H), 3,04 (dd, J = 9,8, 7,8 Hz, 1H), 2,95-3,00 (m, 1H), 2,89 (dd, J = 9,6, 7,4 Hz, 1H), 2,49-2,59 (m, 2H), 2,41-2,49 (m, 1H), 2,29-2,51 (m, 1H), 1,96-2,04 (m, 1H), 1,86-1,92 (m, 1H), 1,77-1,83 (m, 1H), 1,64-1,70 (m, 1H), 1,52-1,61 (m, 1H), 1,43-1,53 (m, 1H), 1,34-1,43 (m, 1H), 1,20-1,34 (m, 3H); MS (ESI+) *m/z* 446 $(M+H)^+$.

Ejemplo 399

(2*S*)-*N*-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}piperidin-2-carboxamida

Paso A: Se preparó (2S)-2-{[((3aS,4R,6aR)-2-{[4-fluorofenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]carbonil}piperidin-1-carboxilato de tert-butilo utilizando (2S)-2-({[(3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–il]amino}carbonil)piperidin-1-carboxilato de tert-butilo del Ejemplo 231 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-fluorobencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-

d_5) δ ppm 7,98 – 7,91 (m, 2H), 7,47 – 7,40 (m, 1H), 7,22 (dd, *J* = 12,0, 5,3, 2H), 4,88 – 4,80 (m, 1H), 4,13 – 4,05 (m, 2H), 3,61 (dd, *J* = 10,1, 3,3, 1H), 3,30 (td, *J* = 12,8, 3,2, 1H), 3,23 (dd, *J* = 10,0, 7,8, 1H), 3,07 (dd, *J* = 8,6, 5,3, 2H), 2,60 – 2,46 (m, 2H), 2,19 (dd, *J* = 12,5, 1,1, 1H), 1,97 – 1,89 (m, 1H), 1,85 – 1,77 (m, 1H), 1,66 – 1,49 (m, 5H), 1,47 (s, 9H), 1,31 (dtdd, *J* = 13,3, 6,8, 6,0, 3,1, 2H); MS (ESI+) *m/z* 513 $(M+NH_4)^+$.

Paso B: El compuesto del título se preparó utilizando (2S)-2-{[((3aS,4R,6aR)-2-{[4-fluorofenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]carbonil}piperidin-1-carboxilato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,96-7,99 (m, 2H), 7,78 (d, *J* = 7,0 Hz, 1H), 7,30-7,34 (m, 2H), 4,20 (p, *J* = 7,0 Hz, 1H), 3,75 (dd, *J* = 9,9, 2,9 Hz, 1H), 3,30 (dd, *J* = 10,3, 3,2 Hz, 1H), 3,11 (dd, *J* = 9,6, 2,9 Hz, 1H), 2,96-3,03 (m, 2H), 2,87 (dd, *J* = 9,6, 7,4 Hz, 1H), 2,48-2,60 (m, 2H), 2,42-2,49 (m, 1H), 2,28-2,46 (m, 1H), 2,00-2,05 (m, 1H), 1,86-1,92 (m, 1H), 1,76-1,83 (m, 1H), 1,66-1,71 (m, 1H), 1,44-1,62 (m, 2H), 1,24-1,41 (m, 4H); MS (ESI+) *m/z* 396 $(M+H)^+$.

Ejemplo 400

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-valinamida

Paso A: Se preparó metil((S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxobutan-2–il(metil)carbamato de tert-butilo del Ejemplo 232 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-fluorobencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,97 – 7,89 (m, 2H), 7,74 – 7,63 (m, 1H), 7,25 – 7,18 (m, 2H), 4,34 (d, *J* = 10,1, 1H), 4,08 (dt, *J* = 13,5, 6,7, 1H), 3,57 (dd, *J* = 10,1, 3,3, 1H), 3,22 – 3,16 (m, 1H), 3,07 (d, *J* = 5,5, 2H), 3,01 (s, 3H), 2,57 – 2,50 (m, 1H), 2,50 – 2,43 (m, 1H), 2,38 (qd, *J* = 13,2, 6,6, 1H), 1,94 (td, *J* = 12,2, 6,5, 1H), 1,86 – 1,77 (m, 1H), 1,54 (ddd, *J* = 16,4, 12,6, 7,7, 1H), 1,45 (s, 9H), 1,34 – 1,24 (m, 1H), 0,98 (d, *J* = 6,5, 3H), 0,86 (d, *J* = 6,7, 3H) ; MS (ESI+) *m/z* 498

$(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,13-8,31 (m, 1H), 7,99-8,02 (m, 2H), 7,30-7,34 (m, 2H), 4,24-4,29 (m, 1H), 3,78 (dd, *J* = 9,9, 2,5 Hz, 1H), 3,11-3,14 (m, 2H), 2,94 (dd, *J* = 9,6, 6,9 Hz, 1H), 2,87 (d, *J* = 5,8 Hz, 1H), 2,47-2,58 (m, 2H), 2,37 (s, 3H), 2,05-2,14 (m, 1H), 1,92-2,08 (m, 1H), 1,91-1,98 (m, 1H), 1,80-1,87 (m, 1H), 1,51-1,59 (m, 1H), 1,25-1,35 (m, 1H), 0,98-1,08 (m, 6H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Ejemplo 401

(2*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)piperidin-2-carboxamida

Paso A: Se preparó (2S)-2-{[((3aS,4R,6aR)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]carbonil}piperidin-1-carboxilato de tert-butilo se preparó utilizando (2S)-2-({[(3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–il]amino}carbonil)piperidin-1-carboxilato de tert-butilo del Ejemplo 231 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,08 (d, *J* = 8,1, 2H), 7,82 (d, *J* = 8,2, 2H), 7,46 (d, *J* = 5,2, 1H), 4,84 (d, *J* = 3,3, 1H), 4,09 (dt, *J* = 13,3, 6,6, 2H), 3,68 (dd, *J* = 10,2, 3,3, 1H), 3,34 – 3,24 (m, 2H), 3,12 (d, *J* = 5,5, 2H), 2,61 – 2,48 (m, 2H), 2,22 – 2,15 (m, 1H), 1,93 (dt, *J* = 11,8, 6,6, 1H), 1,81 (dtd, *J* = 12,7, 7,6, 4,8, 1H), 1,65 – 1,49 (m, 5H), 1,47 (s, 9H), 1,40 – 1,24 (m, 2H); MS (ESI+) *m/z* 563 $(M+NH_4)^+$.

Paso B: El compuesto del título se preparó utilizando (2S)-2-{[((3aS,4R,6aR)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]carbonil}piperidin-1-carboxilato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H

NMR (500 MHz, piridin-d_5) δ ppm 8,10-8,13 (m, 2H), 7,89-7,92 (m, 2H), 7,79 (d, J = 7,0 Hz, 1H), 4,17-4,22 (m, 1H), 3,82 (dd, J = 9,9, 2,8 Hz, 1H), 3,30 (dd, J = 10,3, 3,2 Hz, 1H), 3,16 (dd, J = 9,6, 2,9 Hz, 1H), 3,03-3,07 (m, 1H), 2,96-2,99 (m, 1H), 2,92 (dd, J = 9,6, 7,4 Hz, 1H), 2,50-2,59 (m, 2H), 2,43-2,50 (m, 1H), 2,27-2,53 (m, 1H), 2,00-2,04 (m, 1H), 1,86-1,92 (m, 1H), 1,76-1,83 (m, 1H), 1,64-1,70 (m, 1H), 1,53-1,63 (m, 1H), 1,43-1,53 (m, 1H), 1,35-1,43 (m, 1H), 1,20-1,35 (m, 3H); MS (ESI+) *m/z* 446 $(M+H)^+$.

Ejemplo 402

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida

Paso A: Se preparó metil((S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxobutan-2–il(metil)carbamato de tert-butilo del Ejemplo 232 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,07 (d, J = 8,2, 2H), 7,82 (d, J = 8,2, 2H), 7,72 (s, 1H), 4,34 (d, J = 10,4, 1H), 4,09 (dd, J = 13,6, 6,7, 1H), 3,64 (dd, J = 10,2, 3,3, 1H), 3,26 – 3,19 (m, 1H), 3,15 – 3,07 (m, 2H), 3,01 (s, 3H), 2,58 – 2,51 (m, 1H), 2,50 – 2,44 (m, 1H), 2,38 (qd, J = 13,2, 6,6, 1H), 1,93 (td, J = 12,1, 6,5, 1H), 1,82 (td, J = 12,7, 7,5, 1H), 1,53 (ddd, J = 15,6, 12,6, 8,3, 1H), 1,45 (s, 9H), 1,29 (ddd, J = 15,9, 13,2, 6,7, 1H), 0,97 (d, J = 6,5, 3H), 0,86 (d, J = 6,7, 3H); MS (ESI+) *m/z* 548 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,22-8,25 (m, 1H), 8,13-8,15 (m, 2H), 7,89-7,92 (m, 2H), 4,23-4,29 (m, 1H), 3,86 (dd, J = 9,9, 2,6 Hz, 1H), 3,13-3,20 (m, 2H), 2,98 (dd, J = 9,6, 7,0 Hz, 1H), 2,87 (d, J = 5,8 Hz, 1H), 2,50-2,59 (m, 2H), 2,37 (s, 3H),

2,05-2,13 (m, 1H), 1,93-2,11 (m, 1H), 1,90-1,98 (m, 1H), 1,80-1,87 (m, 1H), 1,51-1,58 (m, 1H), 1,26-1,34 (m, 1H), 1,04 (d, *J* = 6,9 Hz, 3H), 1,02 (d, *J* = 6,9 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Ejemplo 403

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 330 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,23 (d, *J* = 7,2 Hz, 1H), 7,98-8,01 (m, 2H), 7,30-7,34 (m, 2H), 4,26 (p, *J* = 6,8 Hz, 1H), 3,77 (dd, *J* = 9,9, 2,7 Hz, 1H), 3,09-3,15 (m, 3H), 2,93 (dd, *J* = 9,6, 7,1 Hz, 1H), 2,47-2,58 (m, 2H), 2,38 (s, 3H), 1,92-2,21 (m, 1H), 1,91-1,99 (m, 1H), 1,75-1,87 (m, 2H), 1,64-1,71 (m, 1H), 1,51-1,60 (m, 1H), 1,38-1,51 (m, 2H), 1,25-1,35 (m, 1H), 0,84 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Ejemplo 404

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 331 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,24-8,26 (m, 1H), 8,12-8,15 (m, 2H), 7,89-7,92 (m, 2H), 4,26 (p, *J* = 6,9 Hz, 1H), 3,85 (dd, *J* = 9,9, 2,7 Hz, 1H), 3,18 (dd, *J* = 9,6, 2,7 Hz, 1H), 3,15 (dd, *J* = 7,7, 3,9 Hz, 1H), 3,13 (d, *J* = 7,0 Hz, 1H), 2,97 (dd, *J* = 9,6, 7,2 Hz, 1H), 2,51-2,61 (m, 2H), 2,38 (s, 3H), 1,95-2,31 (m, 1H), 1,92-1,98 (m, 1H), 1,75-1,87 (m, 2H), 1,64-1,72 (m, 1H), 1,51-1,59 (m, 1H), 1,39-1,52 (m, 2H), 1,30 (ddt, *J* = 9,7, 13,0, 6,5 Hz, 1H), 0,84 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Ejemplo 405

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 259 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,20-8,23 (m, 1H), 8,13-8,15 (m, 2H), 7,89-7,92 (m, 2H), 4,22-4,29 (m, 1H), 3,85 (dd, *J* = 9,9, 2,7 Hz, 1H), 3,18 (dd, *J* = 9,7, 2,7 Hz, 1H), 3,11-3,16 (m, 2H), 2,96 (dd, *J* = 9,6, 7,1 Hz, 1H), 2,50-2,61 (m, 2H), 2,38 (s, 3H), 1,98-2,07 (m, 1H), 1,90-1,98 (m, 1H), 1,75-1,87 (m, 2H), 1,63-1,70 (m, 1H), 1,41-1,58 (m, 3H), 1,26-1,33 (m, 1H), 0,84 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Ejemplo 406

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida

El compuesto del título se preparó utilizando metil((S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo del Ejemplo 340 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,39-8,40 (bs, 1H), 8,24 (d, *J* = 7,2 Hz, 1H), 8,18-8,22 (m, 1H), 7,90-7,92 (m, 1H), 7,72 (t, *J* = 7,8 Hz, 1H), 4,24-4,30 (m, 1H), 3,86 (dd, *J* = 9,9, 2,3 Hz, 1H), 3,14-3,20 (m, 2H), 2,96 (dd, *J* = 9,7, 7,1 Hz, 1H), 2,86 (d, *J* = 5,8 Hz, 1H), 2,50-2,57 (m, 2H), 2,37 (s, 3H), 2,04-2,13 (m, 1H), 1,88-2,08 (m, 1H), 1,89-1,98 (m, 1H), 1,80-1,89 (m, 1H), 1,50-1,59 (m, 1H), 1,25-1,34 (m, 1H), 1,03 (d, *J* = 6,9 Hz, 3H), 1,01 (d, *J* = 7,0 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Ejemplo 407

N^1-((3a*S*,4*R*,6a*R*)-2-{[4-fluoro-3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-metil-L-leucinamida

El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-(4-fluoro-3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 327 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,35 (dd, *J* = 6,5, 1,9 Hz, 1H), 8,31 (d, *J* = 7,3 Hz, 1H), 8,26 (ddd, *J* = 8,5, 4,7, 2,4 Hz, 1H), 7,53-7,58 (m, 1H), 4,24-4,30 (m, 1H), 3,88 (dd, *J* = 9,9, 2,5 Hz, 1H), 3,16-3,20 (m, 3H), 3,00 (dd, *J* = 9,6, 7,2 Hz, 1H), 2,53-2,62 (m, 2H), 2,38 (s, 3H), 1,82-2,01 (m, 4H), 1,67 (ddd, *J* = 13,5, 7,8, 5,7 Hz, 1H), 1,53-1,59 (m, 2H), 1,32 (ddt, *J* = 9,7, 12,9, 6,5 Hz, 1H), 0,89 (d, *J* = 6,6 Hz, 3H), 0,84 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 480 $(M+H)^+$.

Ejemplo 408

3-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida

El compuesto del título se preparó utilizando (S)-3,3-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–ilcarbamato de tert-butilo del Ejemplo 341 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,25 (d, *J* = 6,7 Hz, 1H), 8,12-8,16 (m, 2H), 7,90-7,92 (m, 2H), 4,18-4,24 (m, 1H), 3,82 (dd, *J* = 10,0, 2,3 Hz, 1H), 3,24 (s, 1H), 3,13-3,18 (m, 2H), 2,98 (dd, *J* = 9,5, 6,5 Hz, 1H), 2,49-2,60 (m, 2H), 1,93-2,29 (m, 2H), 1,85-1,95 (m, 1H), 1,77-1,85 (m, 1H), 1,47-1,55 (m, 1H), 1,22-1,31 (m, 1H), 1,12 (s, 9H); MS (ESI-) *m/z* 446 $(M-H)^-$.

Ejemplo 409

3-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida

El compuesto del título se preparó utilizando (S)-3,3-dimetil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–

ilamino)butan-2–ilcarbamato de tert-butilo del Ejemplo 342 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,23 (d, J = 6,7 Hz, 1H), 8,12-8,14 (m, 2H), 7,89-7,91 (m, 2H), 4,18-4,25 (m, 1H), 3,80 (dd, J = 9,9, 2,7 Hz, 1H), 3,24 (s, 1H), 3,16 (dd, J = 9,7, 2,8 Hz, 1H), 3,10 (dd, J = 9,9, 7,5 Hz, 1H), 2,95 (dd, J = 9,6, 7,2 Hz, 1H), 2,45-2,55 (m, 2H), 1,96-2,22 (m, 2H), 1,88-1,96 (m, 1H), 1,78-1,85 (m, 1H), 1,49-1,57 (m, 1H), 1,20-1,32 (m, 1H), 1,11 (s, 9H).

Ejemplo 410

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-isoleucinamida

El compuesto del título se preparó utilizando metil((2S,3S)-3-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 332 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,39-8,40 (bs, 1H), 8,24 (d, J = 7,2 Hz, 1H), 8,19-8,22 (m, 1H), 7,91-7,93 (m, 1H), 7,73 (d, J = 7,9 Hz, 1H), 4,24-4,30 (m, 1H), 3,87 (dd, J = 9,9, 2,3 Hz, 1H), 3,13-3,20 (m, 2H), 2,95 (d, J = 6,3 Hz, 2H), 2,50-2,58 (m, 2H), 2,38 (s, 3H), 1,89-2,02 (m, 1H), 1,90-1,98 (m, 1H), 1,79-1,89 (m, 2H), 1,72-1,82 (m, 1H), 1,51-1,59 (m, 1H), 1,23-1,40 (m, 2H), 1,00 (d, J = 6,8 Hz, 3H), 0,86 (t, J = 7,4 Hz, 3H); MS (ESI+) m/z 462 $(M+H)^+$.

Ejemplo 411

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-isoleucinamida

El compuesto del título se preparó utilizando metil((2S,3S)-3-metil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 333 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,24-8,26 (m, 1H), 8,13-8,16 (m, 2H), 7,90-7,92

(m, 2H), 4,23-4,30 (m, 1H), 3,86 (dd, *J* = 9,9, 2,5 Hz, 1H), 3,19 (dd, *J* = 9,6, 2,4 Hz, 1H), 3,15 (dd, *J* = 9,8, 7,6 Hz, 1H), 2,97 (dd, *J* = 9,4, 6,9 Hz, 1H), 2,95 (d, *J* = 6,0 Hz, 1H), 2,52-2,60 (m, 2H), 2,39 (s, 3H), 1,92-2,04 (m, 1H), 1,91-1,97 (m, 1H), 1,80-1,88 (m, 2H), 1,72-1,80 (m, 1H), 1,51-1,60 (m, 1H), 1,25-1,36 (m, 2H), 1,01 (d, *J* = 6,9 Hz, 3H), 0,86 (t, *J* = 7,4 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 412

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-isoleucinamida

El compuesto del título se preparó utilizando metil((2S,3S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 334 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,23-8,26 (m, 1H), 8,12-8,16 (m, 2H), 7,89-7,91 (m, 2H), 4,24-4,29 (m, 1H), 3,86 (dd, *J* = 9,9, 2,5 Hz, 1H), 3,15-3,20 (m, 2H), 2,98 (dd, *J* = 9,6, 6,9 Hz, 1H), 2,94 (d, *J* = 6,1 Hz, 1H), 2,50-2,62 (m, 2H), 2,38 (s, 3H), 1,91-2,04 (m, 1H), 1,91-1,98 (m, 1H), 1,80-1,88 (m, 2H), 1,72-1,80 (m, 1H), 1,51-1,59 (m, 1H), 1,24-1,35 (m, 2H), 1,00 (d, *J* = 6,8 Hz, 3H), 0,85 (t, *J* = 7,4 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 413

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-isoleucinamida

El compuesto del título se preparó utilizando metil((2S,3S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 335 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,38-8,39 (bs, 1H), 8,24 (d, *J* = 7,0 Hz, 1H), 8,19-8,22 (m, 1H), 7,90-7,92 (m, 1H), 7,72 (t, *J* = 7,8 Hz, 1H), 4,23-4,30 (m, 1H), 3,86 (dd, *J* = 9,9, 2,2 Hz, 1H), 3,14-3,20 (m, 2H), 2,97 (dd, *J* = 9,6, 6,6 Hz, 1H), 2,93 (d, *J* = 6,1 Hz, 1H), 2,55 (t, *J* = 4,5 Hz, 2H), 2,37 (s, 3H), 1,92-2,10 (m, 1H), 1,91-1,99

(m, 1H), 1,80-1,89 (m, 2H), 1,71-1,81 (m, 1H), 1,51-1,59 (m, 1H), 1,24-1,40 (m, 2H), 0,99 (d, *J* = 6,8 Hz, 3H), 0,84 (t, *J* = 7,4 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 414

N^2,4-dimetil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando (S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo del Ejemplo 336 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,38-8,40 (m, 1H), 8,34 (d, *J* = 6,9 Hz, 1H), 8,20-8,22 (m, 1H), 7,90-7,93 (m, 1H), 7,73 (d, *J* = 7,9 Hz, 1H), 4,23-4,28 (m, 1H), 3,89 (dd, *J* = 9,9, 2,1 Hz, 1H), 3,16-3,21 (m, 2H), 3,15 (dd, *J* = 9,8, 7,4 Hz, 1H), 2,93-2,97 (m, 1H), 2,50-2,58 (m, 2H), 2,38 (s, 3H), 2,00-2,06 (m, 1H), 1,90-1,99 (m, 1H), 1,90 (dd, *J* = 14,1, 5,1 Hz, 1H), 1,79-1,87 (m, 1H), 1,51-1,60 (m, 1H), 1,48 (dd, *J* = 14,0, 6,5 Hz, 1H), 1,25-1,32 (m, 1H), 0,97 (s, 9H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Ejemplo 415

N^2,4-dimetil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando (S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo del Ejemplo 337 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37-8,40 (m, 1H), 8,14-8,16 (m, 2H), 7,90-7,92 (m, 2H), 4,23-4,27 (m, 1H), 3,87 (dd, *J* = 9,9, 2,2 Hz, 1H), 3,22 (t, *J* = 5,9 Hz, 1H), 3,18 (dd, *J* = 9,7, 2,1 Hz, 1H), 3,15 (dd, *J* = 9,9, 7,5 Hz, 1H), 2,95-2,99 (m, 1H), 2,55-2,58 (m, 2H), 2,40 (s, 3H), 1,91-1,98 (m, 1H), 1,92 (dd, *J* = 14,0, 5,1 Hz, 2H), 1,80-1,86 (m, 1H), 1,52-1,61 (m, 1H), 1,50 (dd, *J* = 14,0, 6,4 Hz, 1H), 1,25-1,34 (m, 1H), 0,97 (s, 9H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Ejemplo 416

N^2,4-dimetil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando (S)-4,4-dimetil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo del Ejemplo 338 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37-8,39 (bs, 1H), 8,33-8,36 (m, 1H), 8,18-8,21 (m, 1H), 7,91 (d, *J* = 7,0 Hz, 1H), 7,72 (t, *J* = 7,8 Hz, 1H), 4,23-4,29 (m, 1H), 3,88 (dd, *J* = 9,9, 2,1 Hz, 1H), 3,12-3,20 (m, 3H), 2,94 (dd, *J* = 9,6, 6,6 Hz, 1H), 2,54 (t, *J* = 4,6 Hz, 2H), 2,37 (s, 3H), 1,92-2,00 (m, 1H), 1,75-2,14 (m, 1H), 1,90 (dd, *J* = 14,0, 5,2 Hz, 1H), 1,80-1,87 (m, 1H), 1,51-1,59 (m, 1H), 1,49 (dd, *J* = 14,0, 6,6 Hz, 1H), 1,24-1,33 (m, 1H), 0,96 (s, 9H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Ejemplo 417

N^2,4-dimetil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando (S)-4,4-dimetil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo del Ejemplo 339 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,36-8,38 (m, 1H), 8,13-8,15 (m, 2H), 7,89-7,91 (m, 2H), 4,22-4,29 (m, 1H), 3,87 (d, *J* = 10,4 Hz, 1H), 3,16-3,20 (m, 2H), 3,14 (dd, *J* = 9,9, 7,5 Hz, 1H), 2,96 (dd, *J* = 9,6, 6,8 Hz, 1H), 2,54-2,59 (m, 2H), 2,38 (s, 3H), 1,91-1,99 (m, 1H), 1,95 (m, 1H), 1,91 (dd, *J* = 14,0, 5,2 Hz, 1H), 1,79-1,87 (m, 1H), 1,52-1,60 (m, 1H), 1,50 (dd, *J* = 14,0, 6,6 Hz, 1H), 1,26-1,33 (m, 1H), 0,96 (s, 9H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Ejemplo 418

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norleucinamida

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)hexan-2–il)carbamato de tert-butilo del Ejemplo 343 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el prócedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,21-8,24 (m, 1H), 8,13-8,15 (m, 2H), 7,90-7,92 (m, 2H), 4,23-4,30 (m, 1H), 3,86 (dd, *J* = 9,9, 2,5 Hz, 1H), 3,18 (dd, *J* = 9,6, 2,6 Hz, 1H), 3,12-3,16 (m, 2H), 2,96 (dd, *J* = 9,6, 7,0 Hz, 1H), 2,54-2,61 (m, 2H), 2,40 (s, 3H), 1,94-2,28 (m, 1H), 1,91-1,98 (m, 1H), 1,78-1,87 (m, 2H), 1,65-1,73 (m, 1H), 1,51-1,59 (m, 1H), 1,36-1,50 (m, 2H), 1,27-1,34 (m, 1H), 1,24 (h, *J* = 7,4 Hz, 2H), 0,81 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 419

4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando (S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butiló del Ejemplo 344 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,39-8,41 (m, 1H), 8,13-8,15 (m, 2H), 7,90-7,92 (m, 2H), 4,18-4,24 (m, 1H), 3,85 (dd, *J* = 9,9, 2,6 Hz, 1H), 3,59 (dd, *J* = 7,4, 4,3 Hz, 1H), 3,16 (dd, *J* = 9,6, 2,8 Hz, 1H), 3,10 (dd, *J* = 9,9, 7,4 Hz, 1H), 2,95 (dd, *J* = 9,6, 7,1 Hz, 1H), 2,48-2,58 (m, 2H), 2,16 (dd, *J* = 14,0, 4,3 Hz, 1H), 2,06-2,22 (m, 1H), 1,88-1,95 (m, 1H), 1,78-1,83 (m, 1H), 1,47-1,55 (m, 1H), 1,43 (dd, *J* = 13,9, 7,4 Hz, 1H), 1,23-1,31 (m, 1H), 0,98 (s, 9H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 420

N^2-metil-N^1-((3a*R*,4*R*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4R,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 328 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,52 (d, J = 7,9 Hz, 1H), 8,10-8,15 (m, 2H), 7,88-7,91 (m, 2H), 4,44-4,50 (m, 1H), 3,63 (dd, J = 9,5, 2,8 Hz, 1H), 3,23-3,26 (m, 1H), 3,14-3,19 (m, 1H), 2,98 (dd, J = 25,4, 9,3 Hz, 3H), 2,49-2,56 (m, 1H), 2,48 (s, 3H), 1,86-1,92 (m, 1H), 1,90 (m, 1H), 1,75-1,83 (m, 1H), 1,69-1,75 (m, 2H), 1,59-1,68 (m, 1H), 1,44-1,59 (m, 2H), 1,33-1,39 (m, 1H), 0,88 (t, J = 7,3 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Ejemplo 421

N^2-metil-N^1-((3a*R*,4*R*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando metil((S)-4-metil-1-oxo-1-((3aR,4R,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 329 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,60-8,65 (m, 1H), 8,12-8,14 (m, 2H), 7,88-7,91 (m, 2H), 4,45-4,50 (m, 1H), 3,63-3,66 (m, 1H), 3,33-3,37 (m, 1H), 3,15 (dd, J = 9,6, 3,0 Hz, 1H), 2,95-3,05 (m, 3H), 2,51 (s, 3H), 2,46-2,52 (m, 1H), 1,91-1,97 (m, 2H), 1,78-1,83 (m, 1H), 1,72-1,75 (m, 3H), 1,63 (dq, J = 13,0, 8,2 Hz, 1H), 1,34-1,39 (m, 1H), 0,94 (d, J = 6,5 Hz, 3H), 0,88 (d, J = 6,5 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 422

N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

Paso A: Se preparó ((S)-1-oxo-1-((3aR,4S,6aS)-2-(4-

(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando ((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 382 Paso A en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,13 (d, *J* = 8,1, 2H), 7,96 (d, *J* = 8,0, 1H), 7,90 (d, *J* = 8,3, 2H), 4,60 (dd, *J* = 14,5, 8,2, 1H), 4,27 – 4,18 (m, 1H), 3,81 (dd, *J* = 9,8, 1,5, 1H), 3,21 – 3,10 (m, 2H), 2,99 – 2,92 (m, 1H), 2,61 – 2,50 (m, 2H), 2,00 (dd, *J* = 14,3, 5,4, 1H), 1,84 (ddd, *J* = 13,4, 11,2, 6,8, 3H), 1,55 – 1,44 (m, 13H), 1,25 (d, *J* = 8,9, 1H), 0,81 (t, *J* = 7,3, 3H); MS (ESI+) *m/z* 551 $(M+NH_4)^+$.

Paso B: El compuesto del título se preparó utilizando ((S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,28 (d, *J* = 7,0 Hz, 1H), 8,11-8,15 (m, 2H), 7,89-7,92 (m, 2H), 4,17-4,24 (m, 1H), 3,82 (dd, *J* = 9,9, 2,8 Hz, 1H), 3,52 (dd, *J* = 7,9, 4,9 Hz, 1H), 3,16 (dd, *J* = 9,6, 2,9 Hz, 1H), 3,09 (dd, *J* = 9,9, 7,7 Hz, 1H), 2,94 (dd, *J* = 9,6, 7,3 Hz, 1H), 2,46-2,57 (m, 2H), 2,07-2,18 (m, 2H), 1,88-1,96 (m, 2H), 1,77-1,84 (m, 1H), 1,63 (dddd, *J* = 13,1, 8,0, 10,1, 5,1 Hz, 1H), 1,40-1,53 (m, 3H), 1,23-1,32 (m, 1H), 0,85 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 434 $(M+H)^+$.

Ejemplo 423

N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

Paso A: Se preparó (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–ilcarbamato de tert-butilo utilizando *N*-(*tert*-butoxicarbonil)-L-norvalina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 16 Paso E en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo

221: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,58 (d, *J* = 7,2, 1H), 7,91 (d, *J* = 8,3, 1H), 7,42 (d, *J* = 7,3, 2H), 7,36 (t, *J* = 7,4, 2H), 7,27 (t, *J* = 7,2, 1H), 4,64 (dd, *J* = 14,4, 7,7, 1H), 4,45 – 4,35 (m, 1H), 3,56 (d, *J* = 13,1, 1H), 3,40 (d, *J* = 13,2, 1H), 2,74 (d, *J* = 8,9, 1H), 2,52 – 2,43 (m, 2H), 2,39 – 2,27 (m, 2H), 2,26 – 2,19 (m, 1H), 2,14 (dq, *J* = 12,0, 6,0, 1H), 2,02 (dt, *J* = 13,9, 6,7, 1H), 1,85 (td, *J* = 13,8, 8,2, 2H), 1,65 (td, *J* = 14,3, 7,3, 1H), 1,49 (d, *J* = 8,5, 11H), 1,44 – 1,32 (m, 1H), 0,86 – 0,76 (m, 3H); MS (ESI+) *m/z* 416 $(M+H)^+$.

Paso B: Se preparó ((S)-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–ilcarbamato de tert-butilo del Paso A en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,79 (d, *J* = 6,8, 1H), 8,11 (d, *J* = 8,1, 2H), 7,98 (d, *J* = 8,1, 1H), 7,90 (d, *J* = 8,3, 2H), 4,59 (dd, *J* = 14,4, 7,8, 1H), 4,28 – 4,20 (m, 1H), 3,78 (d, *J* = 9,7, 1H), 3,14 (d, *J* = 9,6, 1H), 3,05 – 2,98 (m, 1H), 2,93 – 2,86 (m, 1H), 2,50 (d, *J* = 2,3, 2H), 2,02 – 1,92 (m, 2H), 1,88 – 1,77 (m, 2H), 1,63 – 1,53 (m, 1H), 1,53 – 1,38 (m, 11H), 1,33 – 1,22 (m, 1H), 0,79 (t, *J* = 7,4, 3H); MS (ESI+) *m/z* 551 $(M+NH_4)^+$.

Paso C: El compuesto del título se preparó utilizando ((S)-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso B en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,27 (d, *J* = 7,2 Hz, 1H), 8,10-8,14 (m, 2H), 7,89-7,91 (m, 2H), 4,18-4,24 (m, 1H), 3,83 (dd, *J* = 9,9, 2,9 Hz, 1H), 3,51 (dd, *J* = 7,9, 4,9 Hz, 1H), 3,16 (dd, *J* = 9,6, 2,9 Hz, 1H), 3,08 (dd, *J* = 9,9, 7,7 Hz, 1H), 2,93 (dd, *J* = 9,6, 7,4 Hz, 1H), 2,45-2,56 (m, 2H), 2,03-2,23 (m, 2H), 1,88-1,95 (m, 2H), 1,77-1,84 (m, 1H), 1,64 (dddd, *J* = 13,1, 8,1, 10,1, 5,1 Hz, 1H), 1,38-1,54 (m, 3H), 1,24-1,32 (m, 1H), 0,84 (t, *J* = 7,3 Hz, 3H); MS (ESI-) *m/z* 432 $(M-H)^-$.

Ejemplo 424

N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

Paso A: Se preparó ((S)-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando ((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 382 Paso A en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida en el procedimiento descrito en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,70 (d, *J* = 6,9, 1H), 8,37 (s, 1H), 8,18 (d, *J* = 7,8, 1H), 7,95 (d, *J* = 8,0, 1H), 7,91 (d, *J* = 7,8, 1H), 7,72 (t, *J* = 7,9, 1H), 4,59 (dd, *J* = 14,1, 7,8, 1H), 4,23 (dt, *J* = 13,0, 6,5, 1H), 3,82 (dd, *J* = 9,7, 1,4, 1H), 3,18 – 3,07 (m, 2H), 2,98 – 2,90 (m, 1H), 2,62 – 2,48 (m, 2H), 2,00 (ddd, *J* = 15,3, 11,0, 6,5, 1H), 1,91 – 1,74 (m, 3H), 1,57 – 1,39 (m, 12H), 1,23 (ddd, *J* = 16,9, 12,6, 6,1, 1H), 0,81 (t, *J* = 7,3, 3H); MS (ESI+) *m/z* 551 $(M+NH_4)^+$.

Paso B: El compuesto del título se preparó utilizando ((S)-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,36-8,37 (bs, 1H), 8,26 (d, *J* = 6,9 Hz, 1H), 8,17-8,20 (m, 1H), 7,90-7,92 (m, 1H), 7,70-7,74 (m, 1H), 4,18-4,24 (m, 1H), 3,83 (dd, *J* = 9,8, 2,7 Hz, 1H), 3,52 (dd, *J* = 7,9, 4,9 Hz, 1H), 3,16 (dd, *J* = 9,6, 2,8 Hz, 1H), 3,07 (dd, *J* = 9,9, 7,5 Hz, 1H), 2,91 (dd, *J* = 9,6, 7,3 Hz, 1H), 2,44-2,54 (m, 2H), 1,95-2,28 (m, 2H), 1,86-1,99 (m, 2H), 1,77-1,84 (m, 1H), 1,59-1,66 (m, 1H), 1,39-1,54 (m, 3H), 1,22-1,32 (m, 1H), 0,84 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 434 $(M+H)^+$.

Ejemplo 425

N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

Paso A: Se preparó ((S)-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando (S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–ilcarbamato de tert-butilo del Ejemplo 423 Paso A en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida en el procedimiento descrito en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,77 (d, *J* = 6,9, 1H), 8,35 (s, 1H), 8,16 (d, *J* = 7,7, 1H), 7,96 (d, *J* = 8,2, 1H), 7,90 (d, *J* = 8,0, 1H), 7,72 (t, *J* = 7,9, 1H), 4,58 (dd, *J* = 14,4, 8,0, 1H), 4,30 – 4,20 (m, 1H), 3,84 – 3,75 (m, 1H), 3,15 (d, *J* = 9,4, 1H), 3,04 – 2,95 (m, 1H), 2,91 – 2,79 (m, 1H), 2,47 (dd, *J* = 2,3, 1,2, 2H), 2,03 – 1,91 (m, 2H), 1,88 – 1,76 (m, 2H), 1,64 – 1,53 (m, 1H), 1,53 – 1,40 (m, 11H), 1,33 – 1,19 (m, 1H), 0,79 (t, *J* = 7,3, 3H); MS (ESI+) *m/z* 551 $(M+NH_4)^+$.

Paso B: El compuesto del título se preparó utilizando ((S)-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,35-8,37 (m, 1H), 8,27 (d, *J* = 7,0 Hz, 1H), 8,17-8,19 (m, 1H), 7,90-7,92 (m, 1H), 7,72 (t, *J* = 7,8 Hz, 1H), 4,18-4,25 (m, 1H), 3,84 (dd, *J* = 9,9, 2,7 Hz, 1H), 3,51 (dd, *J* = 7,9, 4,9 Hz, 1H), 3,17 (dd, *J* = 9,6, 2,8 Hz, 1H), 3,07 (dd, *J* = 9,9, 7,6 Hz, 1H), 2,91 (dd, *J* = 9,6, 7,3 Hz, 1H), 2,43-2,54 (m, 2H), 1,96-2,32 (m, 2H), 1,87-1,95 (m, 2H), 1,78-1,84 (m, 1H), 1,59-1,67 (m, 1H), 1,37-1,53 (m, 3H), 1,23-1,32 (m, 1H), 0,83 (t, *J* = 7,3 Hz, 3H); MS (ESI-) *m/z* 432 $(M-H)^-$.

Ejemplo 426

3-ciclohexil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-alaninamida

Paso A: Se preparó (S)-3-ciclohexil-1-oxo-1-((3aR,4S,6aS)-2-(4-

(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)propan-2–ilcarbamato de tert-butilo utilizando ácido (S)-2-(tert-butoxicarbonilamino)-3-ciclohexilpropanoico en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 256 Paso A en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,76 (s, 1H), 8,13 (d, *J* = 8,1, 2H), 8,01 (d, *J* = 8,3, 1H), 7,90 (d, *J* = 8,3, 2H), 4,74 – 4,65 (m, 1H), 4,31 – 4,19 (m, 1H), 3,85 – 3,78 (m, 1H), 3,21 – 3,10 (m, 2H), 3,01 – 2,93 (m, 1H), 2,64 – 2,51 (m, 2H), 1,96 – 1,74 (m, 6H), 1,69 – 1,60 (m, 1H), 1,60 – 1,45 (m, 13H), 1,32 – 1,18 (m, 1H), 1,16 – 0,96 (m, 3H), 0,94 – 0,81 (m, 1H), 0,79 – 0,67 (m, 1H); MS (ESI+) *m/z* 605 $(M+NH_4)^+$.

Paso B: El compuesto del título se preparó utilizando (S)-3-ciclohexil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)propan-2–ilcarbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,35 (d, *J* = 7,0 Hz, 1H), 8,12-8,15 (m, 2H), 7,90-7,92 (m, 2H), 4,20-4,26 (m, 1H), 3,83 (dd, *J* = 9,9, 2,7 Hz, 1H), 3,63 (dd, *J* = 9,2, 4,7 Hz, 1H), 3,17 (dd, *J* = 9,7, 2,8 Hz, 1H), 3,10 (dd, *J* = 9,8, 7,6 Hz, 1H), 2,96 (dd, *J* = 9,6, 7,2 Hz, 1H), 2,46-2,61 (m, 2H), 1,97-2,47 (m, 2H), 1,86-1,96 (m, 2H), 1,78-1,86 (m, 1H), 1,72-1,78 (m, 1H), 1,65-1,71 (m, 1H), 1,47-1,62 (m, 6H), 1,22-1,33 (m, 1H), 0,99-1,23 (m, 3H), 0,91 (qd, *J* = 12,5, 3,4 Hz, 1H), 0,79 (qd, *J* = 12,0, 3,4 Hz, 1H); MS (ESI+) *m/z* 488 $(M+H)^+$.

Ejemplo 427

3-ciclohexil-*N*^{2}-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-alaninamida

Paso A: Se preparó (S)-3-ciclohexil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)propan-2–il(metil)carbamato de tert-butilo utilizando ácido (S)-2-(tert-butoxicarbonil(metil)amino)-3-ciclohexilpropanoico en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-2-(4-

(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 256 Paso A en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,51 (d, *J* = 6,9, 1H), 8,13 (d, *J* = 8,2, 2H), 7,90 (d, *J* = 8,3, 2H), 5,23 – 5,14 (m, 0,4H), 4,89 – 4,79 (m, 0,6H), 4,28 – 4,15 (m, 1H), 3,83 (d, *J* = 10,6, 1H), 3,17 – 3,01 (m, 5H), 2,94 (dd, *J* = 9,4, 7,2, 1H), 2,57 – 2,48 (m, 2H), 1,99 – 1,74 (m, 5H), 1,67 (d, *J* = 13,1, 1H), 1,62 – 1,48 (m, 4H), 1,45 (s, 9H), 1,34 – 1,20 (m, 2H), 1,18 – 1,00 (m, 3H), 0,98 – 0,85 (m, 1H), 0,81 – 0,66 (m, 1H); MS (ESI+) *m/z* 602 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (S)-3-ciclohexil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)propan-2–il(metil)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,30 (d, *J* = 7,2 Hz, 1H), 8,13-8,16 (m, 2H), 7,89-7,93 (m, 2H), 4,24-4,32 (m, 1H), 3,86 (dd, *J* = 9,9, 2,3 Hz, 1H), 3,25 (dd, *J* = 7,8, 5,6 Hz, 1H), 3,13-3,21 (m, 2H), 2,98 (dd, *J* = 9,5, 6,8 Hz, 1H), 2,47-2,63 (m, 2H), 2,41 (s, 3H), 1,95-2,23 (m, 1H), 1,91-1,99 (m, 1H), 1,79-1,90 (m, 1H), 1,66-1,78 (m, 3H), 1,51-1,62 (m, 6H), 1,26-1,35 (m, 1H), 1,00-1,23 (m, 3H), 0,76-0,93 (m, 2H); MS (ESI+) *m/z* 502 $(M+H)^+$.

Ejemplo 428

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-5-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-4-metil-L-leucinamida

Paso A: Se preparó (S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(2-cloro-5-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo del Ejemplo 226 en lugar de (S)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 2-cloro-5-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,56 (d, *J* = 1,9, 1H), 8,14 (d, *J* = 8,7, 1H), 7,80

(dd, *J* = 8,3, 1,9, 1H), 7,73 (d, *J* = 8,3, 1H), 4,92 (s, 1H), 4,70 (td, *J* = 8,3, 5,1, 1H), 4,34 – 4,25 (m, 1H), 3,91 (dd, *J* = 10,1, 2,9, 1H), 3,54 (dd, *J* = 10,2, 7,7, 1H), 3,36 (dd, *J* = 9,9, 7,5, 1H), 3,27 (dd, *J* = 10,0, 3,3, 1H), 2,72 – 2,57 (m, 2H), 2,13 (dd, *J* = 14,1, 4,8, 1H), 1,94 (qd, *J* = 6,4, 1,2, 1H), 1,86 – 1,77 (m, 2H), 1,60 – 1,52 (m, 1H), 1,49 (s, 9H), 1,35 – 1,25 (m, 1H), 0,96 (s, 9H); MS (ESI+) *m/z* 596 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(2-cloro-5-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,56 (d, *J* = 2,2 Hz, 1H), 8,41 (d, *J* = 7,0 Hz, 1H), 7,80 (dd, *J* = 8,3, 2,2 Hz, 1H), 7,74 (d, *J* = 8,3 Hz, 1H), 4,25-4,32 (m, 1H), 3,94 (dd, *J* = 10,2, 2,6 Hz, 1H), 3,58 (dd, *J* = 7,4, 4,3 Hz, 1H), 3,49 (dd, *J* = 10,1, 7,2 Hz, 1H), 3,34 (dd, *J* = 9,9, 7,0 Hz, 1H), 3,30 (dd, *J* = 9,9, 3,1 Hz, 1H), 2,58-2,66 (m, 2H), 1,87-2,45 (m, 2H), 2,14 (dd, *J* = 14,0, 4,4 Hz, 1H), 1,96-2,04 (m, 1H), 1,82-1,88 (m, 1H), 1,52-1,60 (m, 1H), 1,41 (dd, *J* = 13,9, 7,5 Hz, 1H), 1,30-1,38 (m, 1H), 0,97 (s, 9H); MS (ESI-) *m/z* 494 $(M-H)^-$.

Ejemplo 429

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-4-metil-L-leucinamida

Paso A: Se preparó (S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(2-cloro-4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo del Ejemplo 226 en lugar de (S)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y 2-cloro-cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,33 (d, *J* = 8,2, 1H), 8,14 (d, *J* = 8,7, 1H), 7,99 (s, 1H), 7,75 – 7,71 (m, 1H), 4,95 (s, 1H), 4,71 (td, *J* = 8,3, 4,9, 1H), 4,33 – 4,25 (m, 1H), 3,92 (dd, *J* = 10,2, 2,9, 1H), 3,53 (dd, *J* = 10,2, 7,7, 1H), 3,38 (dd, *J* = 9,9, 7,4, 1H), 3,30 (dd, *J* = 10,0, 3,3, 1H), 2,72 – 2,58 (m, 2H), 2,14 (dd, *J* = 14,1, 4,7,

1H), 1,93 (dt, *J* = 18,2, 6,2, 1H), 1,86 – 1,77 (m, 2H), 1,57 (ddd, *J* = 16,4, 12,5, 8,6, 1H), 1,50 (s, 9H), 1,31 (ddd, *J* = 16,0, 13,2, 6,7, 1H), 0,97 (s, 9H); MS (ESI+) *m/z* 596 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(2-cloro-4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,44 (d, *J* = 7,0 Hz, 1H), 8,35 (d, *J* = 8,2 Hz, 1H), 7,99 (d, *J* = 1,7 Hz, 1H), 7,74 (dd, *J* = 8,2, 1,7 Hz, 1H), 4,25-4,32 (m, 1H), 3,94 (dd, *J* = 10,1, 2,8 Hz, 1H), 3,59 (dd, *J* = 7,4, 4,4 Hz, 1H), 3,49 (dd, *J* = 10,2, 7,3 Hz, 1H), 3,31-3,39 (m, 2H), 2,58-2,67 (m, 2H), 1,86-2,48 (m, 2H), 2,15 (dd, *J* = 14,0, 4,4 Hz, 1H), 1,97-2,05 (m, 1H), 1,82-1,88 (m, 1H), 1,53-1,61 (m, 1H), 1,42 (dd, *J* = 14,0, 7,4 Hz, 1H), 1,31-1,39 (m, 1H), 0,98 (s, 9H); MS (ESI-) *m/z* 494 $(M-H)^-$.

Ejemplo 430

***N*-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalanínamida**

El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida del Ejemplo 258 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,15-8,20 (m, 3H), 7,92-7,96 (m, 2H), 7,29-7,34 (m, 4H), 7,24-7,28 (m, 1H), 3,75 (dd, *J* = 9,9, 2,9 Hz, 1H), 3,43 (t, *J* = 6,8 Hz, 1H), 3,13-3,20 (m, 3H), 3,04-3,10 (m, 3H), 2,95 (dd, *J* = 9,6, 7,6 Hz, 1H), 2,43-2,52 (m, 1H), 2,34 (s, 3H), 1,75-2,16 (m, 1H), 1,84-1,91 (m, 1H), 1,70-1,79 (m, 1H), 1,37-1,47 (m, 1H), 1,19-1,28 (m, 1H); MS (ESI+) *m/z* 496 $(M+H)^+$,554 $(M+CH_3CN+NH_4)^+$.

Ejemplo 431

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2,4-dimetil-L-leucinamida

Paso A: Se preparó (S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(2-cloro-4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 247 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 2-cloro-4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,40 (d, *J* = 6,9, 1H), 8,34 (d, *J* = 8,1, 1H), 7,99 (d, *J* = 1,1, 1H), 7,76 – 7,67 (m, 1H), 5,19 – 5,10 (m, 1H), 4,31 – 4,20 (m, 1H), 3,93 (dd, *J* = 10,2, 2,0, 1H), 3,53 – 3,44 (m, 1H), 3,39 – 3,28 (m, 2H), 3,01 (s, 3H), 2,67 – 2,53 (m, 2H), 2,22 – 2,11 (m, 1H), 2,00 – 1,88 (m, 1H), 1,85 – 1,74 (m, 1H), 1,70 – 1,60 (m, 1H), 1,60 – 1,49 (m, 1H), 1,44 (d, *J* = 11,0, 9H), 1,37 – 1,25 (m, 1H), 0,91 (d, *J* = 8,9, 9H); MS (ESI+) *m/z* 610 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(2-cloro-4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,34-8,37 (m, 2H), 7,99 (d, *J* = 1,7 Hz, 1H), 7,72-7,75 (m, 1H), 4,30-4,35 (m, 1H), 3,96 (dd, *J* = 10,2, 2,3 Hz, 1H), 3,53 (dd, *J* = 10,1, 7,2 Hz, 1H), 3,39 (dd, *J* = 10,0, 7,1 Hz, 1H), 3,35 (dd, *J* = 9,9, 2,9 Hz, 1H), 3,17 (dd, *J* = 6,5, 5,1 Hz, 1H), 2,64-2,70 (m, 2H), 2,38 (s, 3H), 2,03 (dtd, *J* = 12,5, 6,3, 4,2 Hz, 1H), 1,89 (dd, *J* = 14,0, 5,2 Hz, 1H), 1,83-1,92 (m, 1H), 1,67-2,06 (m, 1H), 1,56-1,66 (m, 1H), 1,47 (dd, *J* = 14,0, 6,6 Hz, 1H), 1,32-1,43 (m, 1H), 0,96 (s, 9H); MS (ESI+) *m/z* 510 $(M+H)^+$.

Ejemplo 432

***N*-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-*N*-metil-L-fenilalaninamida**

Paso A: *N*-(*tert*-Butoxicarbonil)-*N*-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-L-fenilalanina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 284 Paso B en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,69 – 8,55 (m, 1H), 8,37 (d, *J* = 8,2, 1H), 8,01 (d, *J* = 1,1, 1H), 7,76 (dd, *J* = 8,3, 1,0, 1H), 7,28 (d, *J* = 15,4, 4H), 7,23 (d, *J* = 1,3, 1H), 5,38 – 5,26 (m, 1H), 4,38 – 4,20 (m, 1H), 3,95 – 3,80 (m, 1H), 3,65 – 3,48 (m, 1H), 3,48 – 3,40 (m, 1H), 3,37 – 3,25 (m, 2H), 3,15 – 3,07 (m, 1H), 3,05 (s, 3H), 2,59 – 2,48 (m, 1H), 2,48 – 2,39 (m, 1H), 2,06 – 1,86 (m, 1H), 1,83 – 1,70 (m, 1H), 1,61 – 1,43 (m, 1H), 1,39 – 1,20 (m, 10H); MS (ESI+) *m/z* 630 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando *N*-(*tert*-butoxicarbonil)-*N*-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,37 (d, *J* = 8,2, 1H), 8,20 (d, *J* = 7,3, 1H), 8,01 (d, *J* = 1,2, 1H), 7,76 (dd, *J* = 8,3, 1,1, 1H), 7,35 – 7,23 (m, 5H), 4,34 – 4,24 (m, 1H), 3,85 (dd, *J* = 10,2, 3,0, 1H), 3,49 – 3,27 (m, 4H), 3,17 (dd, *J* = 13,3, 6,8, 1H), 3,05 (dd, *J* = 13,3, 6,8, 1H), 2,61 – 2,50 (m, 1H), 2,49 – 2,39 (m, 1H), 2,34 (s, 3H), 2,10 – 2,01 (m, 1H), 1,96 (dtd, *J* = 10,8, 6,5, 4,4, 1H), 1,83 – 1,72 (m, 1H), 1,53 – 1,41 (m, 1H), 1,31 (ddt, *J* = 13,2, 9,6, 6,7, 1H); MS (ESI+) *m/z* 530 $(M+H)^+$.

Ejemplo 433

***N*^{1}-ciclopropil-*N*^{2},4-dimetil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida**

Paso A: Se preparó (3a*R*,4*S*,6a*S*)-*N*-Ciclopropil-2-(4-

(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina utilizando (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 256 Paso A en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y (1-etoxiciclopropoxi)trimetilsilano en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,19 (d, *J* = 8,1, 2H), 7,94 (d, *J* = 8,3, 2H), 3,44 (dd, *J* = 9,8, 2,9, 1H), 3,17 (dd, *J* = 9,6, 3,2, 1H), 3,06 (dd, *J* = 9,8, 7,9, 1H), 2,96 (dd, *J* = 9,6, 7,7, 1H), 2,88 (dd, *J* = 13,2, 5,8, 1H), 2,56 – 2,46 (m, 1H), 2,28 (ddd, *J* = 12,1, 9,0, 2,9, 1H), 2,20 – 2,07 (m, 1H), 1,99 (dq, *J* = 6,3, 4,0, 1H), 1,89 – 1,79 (m, 2H), 1,37 – 1,18 (m, 2H), 0,42 – 0,25 (m, 4H); MS (ESI+) *m/z* 375 $(M+H)^+$.

Paso B: Se preparó (S)-1-(ciclopropil((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo se preparó utilizando ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4,4-dimetilpentanoico en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-*N*-ciclopropil-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Paso A en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,12 – 8,07 (m, 2H), 7,86 – 7,80 (m, 2H), 5,85 – 5,57 (m, 1H), 3,93 (s, 1H), 3,56 (dd, *J* = 10,0, 3,2, 1H), 3,19 (dd, *J* = 10,0, 3,4, 2H), 3,13 (dd, *J* = 16,7, 9,1, 1H), 2,98 – 2,88 (m, 4H), 2,76 (ddd, *J* = 11,0, 7,1, 4,2, 1H), 2,72 – 2,64 (m, 1H), 2,15 (ddd, *J* = 18,3, 11,1, 7,7, 1H), 2,05 – 1,97 (m, 1H), 1,97 – 1,88 (m, 1H), 1,80 – 1,71 (m, 1H), 1,68 – 1,56 (m, 1H), 1,49 (s, 9H), 1,35 – 1,20 (m, 1H), 1,05 (dtd, *J* = 10,0, 6,8, 5,0, 1H), 0,99 (s, 9H), 0,88 (dddd, *J* = 9,6, 8,1, 6,7, 3,3, 2H), 0,79 – 0,70 (m, 1H); MS (ESI+) *m/z* 616 $(M+H)^+$.

Paso C: El compuesto del título se preparó utilizando (S)-1-(ciclopropil((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Paso B en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,08-8,11 (m, 2H), 7,81-7,85

(m, 2H), 4,00 (dd, *J* = 8,3, 4,1 Hz, 1H), 3,91-3,97 (m, 2H), 3,51 (dd, *J* = 9,6, 2,8 Hz, 1H), 3,08-3,24 (m, 4H), 2,66-2,77 (m, 1H), 2,60-2,66 (m, 1H), 2,30 (s, 3H), 2,11 (qd, *J* = 11,1, 7,6 Hz, 1H), 1,89-2,02 (m, 1H), 1,79-1,86 (m, 1H), 1,59 (dd, *J* = 14,1, 4,0 Hz, 1H), 1,45 (dd, *J* = 14,2, 8,1 Hz, 1H), 1,27 (tt, *J* = 11,9, 7,5 Hz, 1H), 1,02 (s, 9H), 0,73-0,97 (m, 4H); MS (ESI+) *m/z* 516 $(M+H)^+$.

Ejemplo 434

N^1-etil-N^2,4-dimetil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando (S)-1-(etil((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 296 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,08-8,11 (m, 2H), 7,82-7,85 (m, 2H), 4,18-4,25 (m, 1H), 3,66 (d, *J* = 9,9 Hz, 1H), 3,17-3,54 (m, 4H), 2,84-3,15 (m, 2H), 2,52-2,82 (m, 2H), 2,22-2,50 (m, 3H), 1,87-2,19 (m, 2H), 1,67-1,85 (m, 2H), 1,61 (dd, *J* = 14,2, 3,8 Hz, 1H), 1,48 (dd, *J* = 14,2, 8,2 Hz, 1H), 1,27-1,40 (m, 1H), 1,17 (t, *J* = 7,0 Hz, 3H), 1,04 (s, 9H); MS (ESI+) *m/z* 505 $(M+H)^+$.

Ejemplo 435

N^2,4-dimetil-N^1-propil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando (S)-4,4-dimetil-1-oxo-1-(propil((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)pentan-2–il(metil)carbamato de tert-butilo del Ejemplo 297 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,08-8,11 (m, 2H), 7,82-7,85 (m, 2H), 4,18-4,30 (m, 1H), 3,64-3,75 (m, 2H), 2,97-3,36 (m, 5H), 2,18-2,88 (m, 5H), 1,72-2,14 (m, 4H), 1,55-1,71 (m, 3H), 1,48 (dd, *J* = 14,3, 8,3 Hz, 1H), 1,28-1,34 (m, 1H), 1,04-1,06 (m, 9H), 0,87 (t, *J* = 7,4 Hz, 3H); MS (ESI+) *m/z* 518 $(M+H)^+$.

Ejemplo 436

N^1-(ciclopropilmetil)-N^2,4-dimetil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando (S)-1-((ciclopropilmetil)((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 298 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,08-8,11 (m, 2H), 7,82-7,85 (m, 2H), 4,13-4,26 (m, 1H), 3,51-3,78 (m, 2H), 3,20-3,35 (m, 3H), 2,82-3,18 (m, 2H), 2,52-2,81 (m, 2H), 2,29-2,50 (m, 3H), 1,77-2,10 (m, 3H), 1,70-2,15 (m, 1H), 1,65 (dd, *J* = 14,2, 3,8 Hz, 1H), 1,48 (dd, *J* = 14,3, 8,2 Hz, 1H), 1,27-1,40 (m, 1H), 1,05 (s, 10H), 0,43-0,72 (m, 2H), 0,31-0,35 (m, 2H); MS (ESI+) *m/z* 530 $(M+H)^+$.

Ejemplo 437

N^1,N^2,4-trimetil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando (S)-4,4-dimetil-1-(metil((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 302 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,08-8,11 (m, 2H), 7,82-7,85 (m, 2H), 4,14-4,96 (m, 1H), 3,62 (dd, *J* = 9,9, 1,8 Hz, 2H), 3,00-3,30 (m, 3H), 2,89 (s, 3H), 2,49-2,65 (m, 2H), 2,25-2,47 (m, 3H), 1,59-2,10 (m, 5H), 1,46 (dd, *J* = 14,2, 7,6 Hz, 1H), 1,22-1,41 (m, 1H), 1,01-1,03 (m, 9H); MS (ESI+) *m/z* 5490 $(M+H)^+$.

Ejemplo 438

N^1,N^2-dimetil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

Paso A: Se preparó metil((S)-1-(metil((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)-1-oxopentan-2–

il)carbamato de tert-butilo utilizando ácido (S)-2-(tert-butoxicarbonil(metil)amino)pentanoico en lugar de ácido (S)-1-(tert-butoxicarbonil)pirrolidin-2-carboxílico y (3a*R*,4*S*,6a*S*)-*N*-metil-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 301 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 266: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,11 (d, *J* = 8,3, 2H), 7,83 (d, *J* = 8,3, 2H), 4,69 – 4,57 (m, 1H), 3,59 (dd, *J* = 9,9, 1,2, 1H), 3,29 – 3,18 (m, 2H), 3,16 (dd, *J* = 9,8, 3,3, 1H), 2,88 (s, 3H), 2,86 (s, 3H), 2,61 – 2,50 (m, 2H), 1,91 – 1,56 (m, 6H), 1,51 (s, 10H), 1,40 – 1,21 (m, 3H), 0,91 (t, *J* = 7,4, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-1-(metil((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)-1-oxopentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (400 MHz, piridin-d_5, temperatura 90 °C) δ ppm 8,08-8,11 (m, 2H), 7,82-7,85 (m, 2H), 4,48-4,67 (bs, 1H), 3,61 (dd, *J* = 10,0, 2,0 Hz, 1H), 3,41-3,56 (m, 1H), 2,93-3,34 (m, 4H), 2,86 (s, 3H), 2,50-2,62 (m, 2H), 2,22-2,49 (m, 3H), 1,80-1,95 (m, 1H), 1,39-1,79 (m, 6H), 1,23-1,38 (m, 1H), 0,89 (t, *J* = 7,2 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 439

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-*N*^{1},*N*^{2},4-trimetil-L-leucinamida

Paso A: Se disolvió (3aR,4S,6aS)-2-(2-cloro-4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo (62 mg, 0,132 mmol) del Ejemplo 284 Paso A en 1,2-dimetoxietano (1,0 ml) y se agregó hidruro de litio y aluminio (10,04 mg, 0,264 mmol) por porciones. La reacción se agitó a 70 °C durante la noche, luego se detuvo con sulfato de sodio húmedo. El material crudo se aplicó a un cartucho de 4 g de gel de sílice y se purificó con un gradiente de metanol al 1-10% (amoníaco 2 N)/diclorometano a lo largo de 20 minutos para dar (3a*R*,4*S*,6a*S*)-2-(2-cloro-4-(trifluorometil)fenilsulfonil)-*N*-metiloctahidrociclopenta[*c*]pirrol-4-amina: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm

8,46 (s, 1H), 8,34 (d, *J* = 8,2, 1H), 7,99 (s, 1H), 4,92 (s, 3H), 4,32 (dt, *J* = 13,7, 7,0, 1H), 3,89 (dd, *J* = 10,2, 3,0, 1H), 3,49 (dd, *J* = 10,2, 7,5, 1H), 3,41 – 3,30 (m, 2H), 2,70 – 2,59 (m, 2H), 2,48 (dt, *J* = 4,4, 2,2, 1H), 2,01 (td, *J* = 11,8, 6,6, 1H), 1,95 – 1,83 (m, 1H), 1,59 (ddd, *J* = 16,1, 10,8, 7,7, 1H), 1,37 (dt, *J* = 22,2, 6,5, 1H); MS (APCI+) *m/z* 383 $(M+H)^+$.

Paso B: Se preparó (S)-1-(((3aR,4S,6aS)-2-(2-cloro-4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)(metil)amino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo utilizando ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4,4-dimetilpentanoico en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(2-cloro-4-(trifluorometil)fenilsulfonil)-*N*-metiloctahidrociclopenta[*c*]pirrol-4-amina del Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: MS (ESI+) *m/z* 625 $(M+H)^+$.

Paso C: El compuesto del título se preparó utilizando (S)-1-(((3aR,4S,6aS)-2-(2-cloro-4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)(metil)amino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Paso B en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,30 (d, *J* = 8,2, 1H), 7,90 (s, 1H), 7,69 (d, *J* = 8,1, 1H), 3,80 - 3,72 (m, *J* = 7,3, 1H), 3,68 (d, *J* = 9,8, 1H), 3,50 - 3,27 (m, 3H), 2,94 (s, 3H), 2,74 - 2,58 (m, *J* = 5,3, 11,8, 2H), 2,38 (s, 3H), 1,99 - 1,87 (m, *J* = 8,2, 18,8, 1H), 1,85 - 1,64 (m, 4H), 1,53 (dd, *J* = 7,0, 14,1, 1H), 1,47 - 1,33 (m, 1H), 0,99 (s, 9H). ; MS (ESI+) *m/z* 525 $(M+H)^+$.

Ejemplo 440

4-metil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando (S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(5-(trifluorometil)piridin-2–il)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo del Ejemplo 262 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,62 (d, *J* = 2,4 Hz, 1H), 8,48-8,50 (m, 1H), 7,67 (dd, *J* = 8,9, 2,5 Hz, 1H), 6,38 (d, *J* = 8,9 Hz, 1H), 4,35-4,41 (m, 1H), 3,80-3,83 (m,

1H), 3,65 (dd, *J* = 7,5, 4,4 Hz, 1H), 3,60-3,66 (m, 1H), 3,54-3,60 (m, 1H), 3,30-3,34 (m, 1H), 2,68-2,79 (m, 2H), 2,20 (dd, *J* = 14,0, 4,4 Hz, 1H), 1,73-2,56 (m, 2H), 2,10-2,17 (m, 1H), 1,89-1,97 (m, 1H), 1,68 (dq, *J* = 12,7, 8,1 Hz, 1H), 1,47 (dd, *J* = 14,0, 7,5 Hz, 1H), 1,35-1,42 (m, 1H), 1,01 (s, 9H); MS (ESI+) *m/z* 399 $(M+H)^+$.

Ejemplo 441

4-metil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando (S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(6-(trifluorometil)piridin-2–il)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo del Ejemplo 264 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,43-8,46 (m, 1H), 7,51 (t, *J* = 7,9 Hz, 1H), 6,98 (d, *J* = 7,2 Hz, 1H), 6,50 (d, *J* = 8,5 Hz, 1H), 4,32-4,38 (m, 1H), 3,71 (dd, *J* = 10,9, 2,9 Hz, 1H), 3,64 (dd, *J* = 7,5, 4,3 Hz, 1H), 3,46-3,60 (m, 2H), 3,27 (dd, *J* = 10,9, 3,5 Hz, 1H), 2,65-2,74 (m, 2H), 2,19 (dd, *J* = 13,9, 4,3 Hz, 1H), 1,71-2,58 (m, 2H), 2,06-2,15 (m, 1H), 1,87-1,97 (m, 1H), 1,65 (dq, *J* = 12,7, 8,0 Hz, 1H), 1,46 (dd, *J* = 14,0, 7,5 Hz, 1H), 1,32-1,39 (m, 1H), 1,01 (s, 9H); MS (ESI+) *m/z* 399 $(M+H)^+$.

Ejemplo 442

4-metil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[2-(metilsulfonil)pirimidin-5–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando (S)-4,4-dimetil-1-((3aR,4S,6aS)-2-(2-(metilsulfonil)pirimidin-5–il)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–ilcarbamato de tert-butilo del Ejemplo 265 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,45 (s, 2H), 8,43 (d, *J* = 7,3 Hz, 1H), 4,95 (s, 3H), 4,39 (p, *J* = 7,0 Hz, 1H), 3,97 (dd, *J* = 11,9, 3,3 Hz, 1H), 3,76 (dd, *J* = 12,0, 7,7 Hz, 1H), 3,70 (dd, *J* = 11,6, 8,1 Hz, 1H), 3,62 (dd, *J* = 7,5, 4,2 Hz, 1H), 3,44 (dd, *J* = 11,7, 4,5 Hz, 1H), 2,65-2,75 (m, 2H), 2,18 (dd, *J* = 14,0, 4,3 Hz, 1H), 2,09-2,16 (m, 1H), 2,02-2,19 (m, 2H), 1,86-1,94 (m, 1H), 1,65 (dq, *J* = 12,7, 8,2 Hz, 1H), 1,45 (dd, *J* = 14,0, 7,5 Hz, 1H), 1,33-1,42 (m, 1H), 1,00 (s, 9H); MS (ESI+) *m/z* 411 $(M+H)^+$.

Ejemplo 443

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida

Paso A: Se preparó metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida del Ejemplo 151 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 3-fluorobencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: MS (APCI+) *m/z* 512 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,38 (d, *J* = 6,6 Hz, 1H), 7,84 (dt, *J* = 8,2, 2,0 Hz, 1H), 7,77 (d, *J* = 7,8 Hz, 1H), 7,53 (td, *J* = 8,0, 5,5 Hz, 1H), 7,38 (td, *J* = 8,4, 2,4 Hz, 1H), 4,23-4,29 (m, 1H), 3,81 (dd, *J* = 9,9, 2,3 Hz, 1H), 3,25 (dd, *J* = 8,1, 5,9 Hz, 1H), 3,11-3,16 (m, 2H), 2,94 (dd, *J* = 9,6, 6,7 Hz, 1H), 2,53-2,56 (m, 2H), 2,42 (s, 3H), 1,92-2,00 (m, 1H), 1,79-1,92 (m, 2H), 1,9 (m, 1H), 1,68-1,74 (m, 1H), 1,52-1,62 (m, 2H), 1,24-1,36 (m, 1H), 0,90 (d, *J* = 6,6 Hz, 3H), 0,85 (d, *J* = 6,5 Hz, 3H); MS (ESI-) *m/z* 410 $(M-H)^-$.

Ejemplo 444

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida

Paso A: Se preparó metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida del Ejemplo 151 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-fluorobencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo

319: MS (APCI+) *m/z* 512 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,30 (d, *J* = 7,2 Hz, 1H), 7,98-8,01 (m, 2H), 7,30-7,35 (m, 2H), 4,25-4,29 (m, 1H), 3,79 (dd, *J* = 9,9, 2,6 Hz, 1H), 3,19 (dd, *J* = 8,2, 5,8 Hz, 1H), 3,14 (d, *J* = 2,9 Hz, 1H), 3,10-3,12 (m, 1H), 2,93 (dd, *J* = 9,6, 6,9 Hz, 1H), 2,52-2,58 (m, 2H), 2,39 (s, 3H), 1,92-2,00 (m, 1H), 1,78-2,08 (m, 1H), 1,80-1,92 (m, 2H), 1,68 (ddd, *J* = 13,5, 7,7, 5,8 Hz, 1H), 1,58 (dd, *J* = 8,1, 6,4 Hz, 1H), 1,52-1,58 (m, 1H), 1,26-1,35 (m, 1H), 0,90 (d, *J* = 6,6 Hz, 3H), 0,84 (d, *J* = 6,6 Hz, 3H); MS (ESI+) *m/z* 412 $(M+H)^+$.

Ejemplo 445

***N*^{1}-{(3a*S*,4*R*,6a*R*)-2-[(3,4-difluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-*N*^{2}-metil-L-leucinamida**

Paso A: Se preparó metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(3,4-difluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando *N*^{1}-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*^{2}-(*tert*-butiloxicarbonil)-*N*^{2}-metil-L-leucinamida del Ejemplo 151 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 3,4-difluorobencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: MS (APCI+) *m/z* 530 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(3,4-difluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,30 (d, *J* = 7,3 Hz, 1H), 8,00 (ddd, *J* = 9,6, 7,3, 2,2 Hz, 1H), 7,76-7,79 (m, 1H), 7,35-7,49 (m, 1H), 4,24-4,30 (m, 1H), 3,82 (dd, *J* = 9,9, 2,6 Hz, 1H), 3,19 (dd, *J* = 7,5, 5,0 Hz, 1H), 3,13-3,17 (m, 2H), 2,98 (dd, *J* = 9,6, 7,1 Hz, 1H), 2,52-2,62 (m, 2H), 2,39 (s, 3H), 1,86-2,18 (m, 1H), 1,94-2,02 (m,

1H), 1,79-1,92 (m, 2H), 1,63-1,74 (m, 1H), 1,53-1,62 (m, 2H), 1,28-1,40 (m, 1H), 0,90 (d, *J* = 6,7 Hz, 3H), 0,84 (d, *J* = 6,6 Hz, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Ejemplo 446

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3,5-difluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida

Paso A: Se preparó metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(3,5-difluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida del Ejemplo 151 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 3,5-difluorobencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: MS (APCI+) *m/z* 530 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(3,5-difluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,32 (d, *J* = 7,2 Hz, 1H), 7,66-7,69 (m, 2H), 7,33-7,42 (m, 1H), 4,24-4,30 (m, 1H), 3,84 (dd, *J* = 9,9, 2,5 Hz, 1H), 3,16-3,21 (m, 3H), 3,00 (dd, *J* = 9,7, 7,0 Hz, 1H), 2,48-2,60 (m, 2H), 2,39 (s, 3H), 1,89-2,25 (m, 1H), 1,93-2,01 (m, 1H), 1,81-1,92 (m, 2H), 1,68 (ddd, *J* = 13,6, 7,8, 5,8 Hz, 1H), 1,52-1,63 (m, 2H), 1,31 (ddt, *J* = 9,7, 12,9, 6,4 Hz, 1H), 0,90 (d, *J* = 6,6 Hz, 3H), 0,84 (d, *J* = 6,6 Hz, 3H); MS (ESI+) *m/z* 430 $(M+H)^+$.

Ejemplo 447

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-clorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida

Paso A: Se preparó metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-clorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida del Ejemplo 151 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-clorobencen-1-sulfonilo en lugar de cloruro

de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: MS (APCI+) *m/z* 530 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-clorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,29-8,31 (m, 1H), 7,91-7,93 (m, 2H), 7,57-7,59 (m, 2H), 4,24-4,31 (m, 1H), 3,80 (dd, *J* = 9,9, 2,5 Hz, 1H), 3,19 (dd, *J* = 8,2, 5,8 Hz, 1H), 3,13 (dd, *J* = 9,4, 2,7 Hz, 1H), 3,11 (dd, *J* = 9,5, 7,2 Hz, 1H), 2,92 (dd, *J* = 9,6, 7,0 Hz, 1H), 2,52-2,59 (m, 2H), 2,39 (s, 3H), 1,90-2,16 (m, 1H), 1,92-2,00 (m, 1H), 1,80-1,91 (m, 2H), 1,68 (ddd, *J* = 13,5, 7,8, 5,8 Hz, 1H), 1,52-1,62 (m, 2H), 1,27-1,34 (m, 1H), 0,90 (d, *J* = 6,6 Hz, 3H), 0,85 (d, *J* = 6,5 Hz, 3H); MS (ESI-) *m/z* 426 $(M-H)^-$.

Ejemplo 448

N^2-metil-N^1-[(3a*S*,4*R*,6a*R*)-2-(fenilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-L-leucinamida

Paso A: Se preparó metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida del Ejemplo 151 en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de bencensulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: MS (APCI+) *m/z* 494 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-clorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,28 (d, *J* = 7,0 Hz, 1H), 7,97-8,00 (m, 2H), 7,52-7,58 (m, 3H), 4,24-4,31 (m, 1H), 3,79 (dd, *J* = 9,9, 2,4 Hz, 1H), 3,19 (dd, *J* = 8,2, 5,8 Hz, 1H), 3,08-3,15 (m, 2H), 2,91 (dd, *J* = 9,6, 6,7 Hz, 1H), 2,48-2,52 (m, 2H),

2,39 (s, 3H), 1,77-2,03 (m, 4H), 1,68 (ddd, *J* = 13,5, 7,8, 5,8 Hz, 1H), 1,49-1,60 (m, 2H), 1,24-1,33 (m, 1H), 0,90 (d, *J* = 6,6 Hz, 3H), 0,84 (d, *J* = 6,5 Hz, 3H); MS (ESI-) *m/z* 392 $(M-H)^-$.

Ejemplo 449

N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

Paso A: Se preparó (S)-1-((3aS,4R,6aR)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida del Ejemplo 151 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida y 4-(trifluorometil)benzaldehido en lugar de 3-(trifluorometil)benzaldehido en el procedimiento descrito en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,36 – 8,27 (m, 1H), 7,65 (d, *J* = 8,1, 2H), 7,50 (d, *J* = 7,6, 2H), 5,14 (m, 0,4H), 4,78 (m, 0,6H), 4,45 – 4,31 (m, 1H), 3,62 – 3,51 (m, 1H), 3,45 (ddd, *J* = 7,5, 5,3, 3,5, 1H), 3,05 (s, 3H), 2,90 – 2,73 (m, 1H), 2,55 – 2,41 (m, 2H), 2,31 (d, *J* = 5,7, 2H), 2,23 – 2,17 (m, 1H), 2,10 (dt, *J* = 11,5, 5,8, 1H), 1,94 – 1,75 (m, 3H), 1,65 – 1,51 (m, 2H), 1,46 (s, 9H), 1,42 – 1,34 (m, 1H), 0,88 (d, *J* = 6,3, 3H), 0,84 (d, *J* = 6,6, 3H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,19-8,21 (m, 1H), 7,64-7,67 (m, 2H), 7,51-7,53 (m, 2H), 4,44-4,50 (m, 1H), 3,57-3,61 (m, 1H), 3,47 (d, *J* = 13,6 Hz, 1H), 3,22 (dd, *J* = 8,2, 5,8 Hz, 1H), 2,89 (dd, *J* = 9,0, 2,6 Hz, 1H), 2,48-2,58 (m, 2H), 2,42 (s, 3H), 2,34-2,40 (m, 2H), 2,24 (dd, *J* = 8,9, 7,0 Hz, 1H), 2,09-2,17 (m, 1H), 1,92-2,08 (m, 1H), 1,84-1,94 (m, 2H), 1,71 (ddd, *J* = 13,5, 7,8, 5,8 Hz, 1H), 1,56-1,65 (m, 2H), 1,39-1,47 (m, 1H), 0,91 (d, *J* = 6,5 Hz, 3H), 0,85 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 412 $(M+H)^+$.

Ejemplo 450

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida

Paso A: Se preparó (S)-1-((3aS,4R,6aR)-2-(4-fluorobencil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo utilizando N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida del Ejemplo 151 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida y 4-fluorobenzaldehido en lugar de 3-(trifluorometil)benzaldehido en el procedimiento descrito en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,30 (d, *J* = 6,2, 1H), 7,39 – 7,32 (m, 2H), 7,12 (t, *J* = 8,8, 2H), 5,18 – 5,11 (m, 1H), 4,44 – 4,33 (m, 1H), 3,54 – 3,46 (m, 1H), 3,38 (t, *J* = 13,8, 1H), 3,05 (s, 3H), 2,87 – 2,71 (m, 1H), 2,53 – 2,41 (m, 2H), 2,31 (d, *J* = 6,3, 2H), 2,23 – 2,17 (m, 1H), 2,13 – 2,06 (m, 1H), 1,83 (dd, *J* = 9,0, 5,2, 3H), 1,64 – 1,52 (m, 2H), 1,46 (s, 9H), 1,42 – 1,33 (m, 1H), 0,88 (d, *J* = 6,4, 3H), 0,84 (d, *J* = 6,5, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-(4-fluorobencil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,23-8,25 (m, 1H), 7,37 (dd, *J* = 8,3, 5,4 Hz, 2H), 7,13 (t, *J* = 8,6 Hz, 2H), 4,43-4,48 (m, 1H), 3,53 (d, *J* = 13,1 Hz, 1H), 3,40 (d, *J* = 13,1 Hz, 1H), 3,24 (dd, *J* = 8,1, 5,9 Hz, 1H), 2,85 (dd, *J* = 9,1, 2,6 Hz, 1H), 2,48-2,56 (m, 2H), 2,42 (s, 3H), 2,39 (dd, *J* = 8,8, 7,1 Hz, 1H), 2,34 (dd, *J* = 9,0, 2,3 Hz, 1H), 2,24 (dd, *J* = 8,9, 6,9 Hz, 1H), 2,13 (dq, *J* = 11,9, 6,0 Hz, 1H), 1,62-2,52 (m, 1H), 1,85-1,94 (m, 2H), 1,72 (ddd, *J* = 13,5, 7,7, 5,8 Hz, 1H), 1,56-1,65 (m, 2H), 1,38-1,45 (m, 1H), 0,91 (d, *J* = 6,6 Hz, 3H), 0,86 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 362 $(M+H)^+$.

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Ejemplo 451

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida

Paso A: Se preparó metil((S)-3-metil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo utilizando (*S*)-2-(*tert*-butoxicarbonil(metil)amino)-ácido 3-metilbutanoico en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 256 Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,08 (d, *J* = 8,1, 2H), 7,81 (d, *J* = 8,3, 2H), 7,58 – 7,53 (m, 1H), 4,31 (d, *J* = 10,6, 1H), 4,11 – 4,02 (m, 1H), 3,66 (dd, *J* = 10,2, 3,3, 1H), 3,31 (dd, *J* = 10,2, 7,8, 1H), 3,19 – 3,09 (m, 2H), 3,00 (s, 3H), 2,63 – 2,47 (m, 2H), 2,43 – 2,33 (m, 1H), 1,94 – 1,75 (m, 2H), 1,55 – 1,47 (m, 1H), 1,45 (s, 9H), 1,28 (ddd, *J* = 13,0, 8,9, 6,2, 1H), 0,98 (d, *J* = 6,5, 3H), 0,86 (d, *J* = 6,7, 3H).

Paso B: El compuesto del título se preparó utilizando metil((S)-3-metil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,25-8,27 (m, 1H), 8,13-8,16 (m, 2H), 7,90-7,92 (m, 2H), 4,23-4,30 (m, 1H), 3,85 (dd, *J* = 9,9, 2,6 Hz, 1H), 3,13-3,20 (m, 2H), 2,97 (dd, *J* = 9,6, 7,0 Hz, 1H), 2,88 (d, *J* = 5,9 Hz, 1H), 2,48-2,62 (m, 2H), 2,39 (s, 3H), 2,05-2,13 (m, 1H), 1,94-2,09 (m, 1H), 1,90-1,97 (m, 1H), 1,80-1,87 (m, 1H), 1,51-1,59 (m, 1H), 1,30 (ddt, *J* = 9,7, 12,9, 6,4 Hz, 1H), 1,02-1,05 (m, 6H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Ejemplo 452

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-valinamida

Paso A: Se preparó (S)-1-((3aR,4S,6aS)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxobutan-2–il(metil)carbamato de tert-butilo utilizando ácido (S)-2-(tert-butoxicarbonil(metil)amino)-3-metilbutanoico en lugar de *N*-(*tert*-butoxicarbonil)-L-

leucina y (3a*R*,4*S*,6a*S*)-2-(4-fluorofenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 261 Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,94 (dd, *J* = 8,6, 5,3, 2H), 7,20 (t, *J* = 8,7, 2H), 4,31 (d, *J* = 11,2, 1H), 4,07 (dt, *J* = 13,3, 6,8, 1H), 3,59 (dd, *J* = 9,9, 3,7, 1H), 3,27 (dd, *J* = 10,1, 7,8, 1H), 3,15 – 3,03 (m, 2H), 2,99 (s, 3H), 2,61 – 2,46 (m, 2H), 2,38 (dq, *J* = 17,5, 6,8, 1H), 1,94 – 1,75 (m, 2H), 1,51 (dd, *J* = 14,6, 6,6, 1H), 1,45 (s, 9H), 1,33 – 1,21 (m, 1H), 0,98 (d, *J* = 6,5, 3H), 0,86 (d, *J* = 6,7, 3H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxobutan-2–il(metil)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,26 (d, *J* = 6,7 Hz, 1H), 7,99-8,02 (m, 2H), 7,31-7,35 (m, 2H), 4,24-4,31 (m, 1H), 3,78 (dd, *J* = 9,9, 2,5 Hz, 1H), 3,09-3,14 (m, 2H), 2,93 (dd, *J* = 9,6, 6,8 Hz, 1H), 2,89 (d, *J* = 5,9 Hz, 1H), 2,48-2,58 (m, 2H), 2,39 (s, 3H), 2,05-2,13 (m, 1H), 1,92-2,12 (m, 1H), 1,90-1,98 (m, 1H), 1,80-1,87 (m, 1H), 1,52-1,59 (m, 1H), 1,24-1,34 (m, 1H), 1,04 (d, *J* = 7,2 Hz, 3H), 1,03 (d, *J* = 7,2 Hz, 3H); MS (ESI-) *m/z* 396 $(M-H)^-$.

Ejemplo 453

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-4-metil-L-leucinamida

Paso A: Se preparó (S)-1-((3aR,4S,6aS)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo utilizando ácido (S)-2-(tert-butoxicarbonilamino)-4,4-dimetilpentanoico en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(4-fluorofenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 261 Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,70 (d, *J* = 7,0, 1H), 8,14 (d, *J* = 8,7, 1H), 7,99 (dd, *J* = 8,6, 5,2, 2H), 7,32 (t, *J* = 8,6, 2H), 4,75 – 4,65 (m, 1H), 4,27 – 4,18 (m, 1H), 3,74 (dd, *J* = 9,9, 2,7, 1H), 3,10 (ddd, *J* = 13,9, 9,6, 5,4, 2H), 2,92 (dd, *J* = 9,4, 7,7, 1H), 2,61 – 2,47 (m, 2H), 2,15

(dd, *J* = 14,2, 4,7, 1H), 1,89 – 1,73 (m, 3H), 1,56 – 1,45 (m, 10H), 1,28 – 1,18 (m, 1H), 0,98 (s, 9H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,38-8,40 (m, 1H), 7,98-8,01 (m, 2H), 7,31-7,38 (m, 2H), 4,20-4,23 (m, 1H), 3,77 (dd, *J* = 9,8, 2,6 Hz, 1H), 3,59 (dd, *J* = 7,4, 4,3 Hz, 1H), 3,11 (dd, *J* = 9,6, 2,7 Hz, 1H), 3,06 (dd, *J* = 9,9, 7,3 Hz, 1H), 2,91 (dd, *J* = 9,6, 7,0 Hz, 1H), 2,46-2,58 (m, 2H), 2,16 (dd, *J* = 14,0, 4,3 Hz, 1H), 1,98-2,31 (m, 2H), 1,88-1,96 (m, 1H), 1,77-1,85 (m, 1H), 1,47-1,57 (m, 1H), 1,43 (dd, *J* = 14,0, 7,6 Hz, 1H), 1,23-1,32 (m, 1H), 0,99 (s, 9H); MS (ESI-) *m/z* 410 $(M-H)^-$.

Ejemplo 454

***N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-*N*^{2}-metil-L-norleucinamida**

Paso A: Se preparó (S)-1-((3aR,4S,6aS)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxohexan-2–il(metil)carbamato de tert-butilo utilizando ácido (S)-2-(tert-butoxicarbonil(metil)amino)hexanoico en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(4-fluorofenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 261 Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,45 (d, *J* = 6,8, 1H), 7,99 (dd, *J* = 8,7, 5,2, 2H), 7,32 (t, *J* = 8,7, 2H), 4,94 (s, 3H), 4,28 – 4,15 (m, 1H), 3,75 (d, *J* = 10,4, 1H), 3,07 (dd, *J* = 20,0, 10,4, 4H), 2,89 (dd, *J* = 9,5, 7,2, 1H), 2,57 – 2,46 (m, 2H), 2,13 – 1,98 (m, 1H), 1,93 – 1,68 (m, 3H), 1,45 (s, 9H), 1,26 (d, *J* = 6,0, 5H), 0,78 (s, 3H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxohexan-2–il(metil)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H

NMR (500 MHz, piridin-d_5) δ ppm 8,20-8,22 (m, 1H), 7,99-8,02 (m, 2H), 7,31-7,38 (m, 2H), 4,24-4,30 (m, 1H), 3,78 (dd, *J* = 9,9, 2,5 Hz, 1H), 3,08-3,16 (m, 3H), 2,88-2,94 (m, 1H), 2,52-2,59 (m, 2H), 2,40 (s, 3H), 1,92-1,98 (m, 1H), 1,60-2,28 (m, 1H), 1,78-1,87 (m, 2H), 1,65-1,73 (m, 1H), 1,52-1,59 (m, 1H), 1,36-1,50 (m, 2H), 1,27-1,35 (m, 1H), 1,24 (h, *J* = 7,4 Hz, 2H), 0,81 (t, *J* = 7,3 Hz, 3H); MS (ESI-) *m/z* 410 $(M-H)^-$.

Ejemplo 455

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida

Paso A: Se preparó (S)-1-((3aR,4S,6aS)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo utilizando ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4-metilpentanoico en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(4-fluorofenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 261 Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,94 (dd, *J* = 8,1, 5,2, 2H), 7,44 – 7,37 (m, 1H), 7,20 (t, *J* = 8,5, 2H), 4,85 – 4,77 (m, 1H), 4,12 – 4,03 (m, 1H), 3,61 – 3,55 (m, 1H), 3,27 – 3,21 (m, 1H), 3,13 – 3,02 (m, 2H), 2,93 (s, 3H), 2,59 – 2,44 (m, 2H), 1,83 (ddd, *J* = 37,1, 15,2, 5,0, 4H), 1,50 (d, *J* = 0,6, 2H), 1,46 (d, *J* = 0,8, 9H), 1,33 – 1,22 (m, 1H), 0,89 (t, *J* = 7,2, 6H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,29-8,31 (m, 1H), 7,99-8,02 (m, 2H), 7,31-7,35 (m, 2H), 4,24-4,30 (m, 1H), 3,79 (dd, *J* = 9,9, 2,4 Hz, 1H), 3,21 (dd, *J* = 8,2, 5,9 Hz, 1H), 3,09-3,14 (m, 2H), 2,93 (dd, *J* = 9,6, 6,7 Hz, 1H), 2,53-2,59 (m, 2H), 2,40 (s, 3H), 1,89-2,27 (m, 1H), 1,91-1,99 (m, 1H), 1,79-1,91 (m, 2H), 1,69 (ddd, *J* = 13,5, 7,7, 5,8 Hz, 1H), 1,53-1,59 (m, 2H), 1,25-1,35 (m, 1H), 0,91 (d, *J* = 6,6 Hz, 3H), 0,85 (d, *J* = 6,6 Hz, 3H); MS (ESI-) *m/z* 410 $(M-H)^-$.

Ejemplo 456

N^2-metil-N^1-((3a*S*,4*S*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

Paso A: Se preparó metil((S)-1-oxo-1-((3aS,4S,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando (S)-1-((3aS,4S,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 238 en lugar de (S)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: MS (ESI+) *m/z* 548 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aS,4S,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,52 (d, *J* = 6,8 Hz, 1H), 8,12-8,14 (m, 2H), 7,90-7,92 (m, 2H), 4,47 (p, *J* = 7,6 Hz, 1H), 3,64 (dd, *J* = 9,5, 2,9 Hz, 1H), 3,24 (dd, *J* = 7,3, 5,4 Hz, 1H), 3,16 (dd, *J* = 9,7, 3,1 Hz, 1H), 2,96-3,05 (m, 3H), 2,51 (s, 3H), 2,45-2,54 (m, 1H), 1,79-2,31 (m, 1H), 1,86-1,94 (m, 1H), 1,69-1,75 (m, 3H), 1,47-1,65 (m, 3H), 1,34-1,40 (m, 1H), 0,90 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Ejemplo 457

N^2-metil-N^1-((3a*S*,4*S*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

Paso A: Se preparó metil((S)-4-metil-1-oxo-1-((3aS,4S,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando (S)-1-((3aS,4S,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 239 en lugar de (S)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro

de 4-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,99 – 8,92 (m, 1H), 8,12 (d, *J* = 8,0, 2H), 7,91 (d, *J* = 8,2, 2H), 5,33 – 5,24 (m, 1H), 4,44 – 4,28 (m, 1H), 3,65 (dd, *J* = 10,0, 2,8, 1H), 3,19 – 3,09 (m, 4H), 3,03 – 2,81 (m, 3H), 2,50 – 2,42 (m, 1H), 2,05 – 1,92 (m, 2H), 1,73 – 1,55 (m, 4H), 1,50 (s, 9H), 1,35 – 1,25 (m, 1H), 0,97 (d, *J* = 6,6, 3H), 0,89 – 0,79 (m, 3H); MS (ESI+) *m/z* 562 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-4-metil-1-oxo-1-((3aS,4S,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,61 (d, *J* = 6,9 Hz, 1H), 8,12-8,14 (m, 2H), 7,90-7,92 (m, 2H), 4,48 (s, 1H), 3,65 (dd, *J* = 9,6, 3,1 Hz, 1H), 3,29-3,33 (m, 1H), 3,16 (dd, *J* = 9,6, 3,1 Hz, 1H), 3,01-3,06 (m, 1H), 2,98-3,03 (m, 1H), 2,94-2,98 (m, 1H), 2,52 (s, 3H), 2,46-2,52 (m, 1H), 1,90-1,99 (m, 1H), 1,77-1,84 (m, 1H), 1,28-2,16 (m, 1H), 1,67-1,76 (m, 2H), 1,57-1,66 (m, 2H), 1,34-1,40 (m, 1H), 0,97 (d, *J* = 6,6 Hz, 3H), 0,90 (d, *J* = 6,6 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 458

N^1-{(3a*R*,4*S*,6a*S*)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida

Paso A: Se preparó (S)-1-((3aR,4S,6aS)-2-(3,3-bis(4-fluorofenil)propil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 313 Paso A en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida y 3,3-bis(4-fluorofenil)propanal en lugar de 3-(trifluorometil)benzaldehído en el procedimiento descrito en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,35 – 8,19 (m, 1H), 7,42 – 7,31 (m, 4H), 7,18 – 7,06 (m, 4H), 4,92-4,88 (m, 1H), 4,52 – 4,42 (m, 1H), 4,28 (dd, *J* = 10,0, 5,3, 1H), 3,15 – 3,02 (m, 3H), 2,92 (dd, *J* = 4,9, 4,1, 1H), 2,48 (dd, *J* = 7,1, 5,7, 2H), 2,41 – 2,35 (m, 1H), 2,33 – 2,27 (m, 2H), 2,26 – 2,17 (m, 3H), 2,15 – 2,08 (m, 2H), 2,08 – 1,99 (m,

2H), 1,93 – 1,75 (m, 2H), 1,62 – 1,50 (m, 1H), 1,48 (d, *J* = 7,3, 9H), 1,37 – 1,28 (m, 2H), 0,88 – 0,80 (m, 3H); MS (ESI+) *m/z* 570 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-(3,3-bis(4-fluorofenil)propil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,12-8,15 (m, 1H), 7,34-7,42 (m, 4H), 7,11-7,17 (m, 4H), 4,48-4,54 (m, 1H), 4,28 (t, *J* = 7,6 Hz, 1H), 3,18 (t, *J* = 6,5 Hz, 1H), 2,93 (dd, *J* = 9,0, 2,2 Hz, 1H), 2,49-2,57 (m, 1H), 2,43-2,49 (m, 1H), 2,42 (s, 3H), 2,28-2,33 (m, 2H), 2,18-2,28 (m, 3H), 2,08-2,28 (m, 3H), 1,95-2,15 (m, 1H), 1,89-2,00 (m, 1H), 1,79-1,87 (m, 1H), 1,67-1,75 (m, 1H), 1,43-1,61 (m, 4H), 0,85 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 470 $(M+H)^+$.

Ejemplo 459

2,2-bis(4-fluorofenil)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]acetamida

Paso A: Se agregó *N*-((3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-2,2-bis(4-fluorofenil)acetamida (150 mg, 0,336 mmol) del Ejemplo 228 y etanol (20 ml) a Pd(OH)#2 al 20% sobre carbono, húmedo (30,0 mg, 0,214 mmol) en una botella de presión de 50 ml y se agitó por 2 horas a bajo 30 psi de hidrógeno a 50 °C. La mezcla se filtró y el solvente se eliminó al vacío para dar 2,2-bis(4-fluorofenil)-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,09 (d, *J* = 7,1, 1H), 7,60 – 7,55 (m, 4H), 7,13 (q, *J* = 8,2, 4H), 5,26 (s, 1H), 4,36 – 4,27 (m, 1H), 3,06 (dd, *J* = 10,9, 2,7, 1H), 2,92 (dd, *J* = 10,9, 7,0, 1H), 2,81 (dd, *J* = 10,7, 7,0, 1H), 2,59 (dd, *J* = 10,8, 2,8, 1H), 2,52 – 2,41 (m, 2H), 2,33 – 2,25 (m, 1H), 2,06 – 1,96 (m, 1H), 1,83 (td, *J* = 12,7, 6,9, 1H), 1,65 – 1,52 (m, 1H), 1,26 (ddt, *J* = 12,3, 8,7, 6,1, 1H); MS (ESI+) *m/z* 357$(M+H)^+$.

Paso B: Se disolvió 2,2-Bis(4-fluorofenil)-*N*-[(3a*R*,4*S*,6a*S*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida (30 mg, 0,084 mmol) y ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4-metilpentanoico (22,71 mg, 0,093 mmol) en diclorometano (0,5 ml) y luego se trató con hidrato de 1-hidroxibenzotriazol (14,18 mg, 0,093 mmol). Luego de 10 minutos, se agregó N^1-((etilimino)metilen)-N^3,N^3-dimetilpropan-1,3-diamina (0,016 ml, 0,093 mmol), y la mezcla de la reacción se

agitó a temperatura ambiente durante la noche seguido por detención con agua. El material en la capa orgánica se purificó con un cartucho de 4 g de gel de sílice eluyendo con metanol al 1-10% (amoníaco 2 N)/diclorometano para dar (S)-1-((3aR,4S,6aS)-4-(2,2-bis(4-fluorofenil)acetamido)hexahidrociclopenta[c]pirrol-2(1H)–il)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,25 (s, 1H), 7,46 (td, J = 8,5, 5,5, 4H), 7,08 – 6,96 (m, 4H), 5,08 (s, 2H), 4,29 – 4,18 (m, 1H), 3,80 (s, 2H), 3,69 (s, 1H), 3,43 (dd, J = 11,7, 3,5, 1H), 2,93 (s, 3H), 2,63 (s, 2H), 2,10 (td, J = 12,9, 6,9, 1H), 1,91 – 1,69 (m, 3H), 1,63 (dt, J = 13,2, 6,5, 2H), 1,51 (s, 9H), 1,40 – 1,26 (m, 1H), 0,97 (d, J = 6,5, 3H), 0,92 (d, J = 6,6, 3H); MS (ESI+) *m/z* 584(M+H)$^+$.

Paso C: El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-4-(2,2-bis(4-fluorofenil)acetamido)hexahidrociclopenta[c]pirrol-2(1H)–il)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Paso B en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,36 – 8,22 (m, 1H), 7,46 (td, J = 8,4, 5,5, 4H), 7,03 (td, J = 8,7, 3,4, 4H), 5,10 (s, 1H), 4,34 – 4,23 (m, 1H), 3,77 – 3,66 (m, 2H), 3,63 – 3,52 (m, 2H), 3,47 – 3,37 (m, 2H), 2,67 – 2,56 (m, 2H), 2,38 (s, 3H), 2,14 – 2,02 (m, 1H), 1,99 – 1,82 (m, 2H), 1,70 – 1,57 (m, 1H), 1,49 (t, J = 6,7, 2H), 1,36 (dt, J = 15,6, 6,5, 1H), 0,91 (dd, J = 8,7, 6,8, 6H); MS (ESI+) *m/z* 484(M+H)$^+$.

Ejemplo 460

2,2-bis(4-fluorofenil)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-metil-L-norvalil)octahidrociclopenta[*c*]pirrol-4–il]acetamida

El compuesto del título se preparó utilizando ácido (S)-2-(tert-butoxicarbonil(metil)amino)pentanoico en lugar de ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4-metilpentanoico en el procedimiento descrito en Ejemplo 459: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,35 – 8,24 (m, 1H), 7,50 – 7,40 (m, 4H), 7,07 – 6,98 (m, 4H), 5,10 (s, 1H), 4,31 – 4,21 (m, 1H), 3,75 – 3,64 (m, 2H), 3,61 – 3,51 (m, 2H), 3,41 – 3,31 (m, 1H), 2,66 – 2,54 (m, 2H), 2,37 (s, 3H), 2,14 – 2,02 (m, 1H), 1,92 – 1,83 (m, 1H), 1,71 – 1,40 (m, 6H), 1,33 (dd, J = 12,9, 8,1, 1H), 0,87 (t, J = 7,2, 3H); MS (ESI+) *m/z* 470(M+H)$^+$.

Ejemplo 461

***N*-[(3a*R*,4*S*,6a*S*)-2-(*N*,4-dimetil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-2,2-bis(4-fluorofenil)acetamida**

El compuesto del título se preparó utilizando ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4,4-dimetilpentanoico en lugar de ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4-metilpentanoico en el procedimiento descrito en Ejemplo 459: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,36 – 8,25 (m, 1H), 7,49 – 7,40 (m, 4H), 7,03 (ddd, *J* = 8,8, 6,3, 3,9, 4H), 5,10 (s, 1H), 4,35 – 4,20 (m, 1H), 3,77 – 3,66 (m, 2H), 3,63 – 3,51 (m, 2H), 3,49 – 3,38 (m, 1H), 2,68 – 2,54 (m, 2H), 2,36 (s, 3H), 2,16 – 2,00 (m, 1H), 1,95 – 1,78 (m, 2H), 1,71 (dd, *J* = 14,1, 4,9, 1H), 1,66 – 1,56 (m, 1H), 1,53 – 1,43 (m, 1H), 1,41 – 1,27 (m, 1H), 0,99 (s, 9H). ; MS (ESI+) *m/z* 498(M+H)$^+$.

Ejemplo 462

2,2-bis(4-fluorofenil)-*N*-[(3a*R*,4*S*,6a*S*)-2-(4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]acetamida

El compuesto del título se preparó utilizando ácido (S)-2-(tert-butoxicarbonilamino)-4,4-dimetilpentanoico en lugar de ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4-metilpentanoico en el procedimiento descrito en Ejemplo 459: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,37 – 8,15 (m, 1H), 7,46 (td, *J* = 8,6, 5,6, 4H), 7,09 – 6,96 (m, 4H), 5,09 (s, 1H), 4,32 – 4,18 (m, 1H), 3,76 – 3,63 (m, 4H), 3,62 – 3,51 (m, 2H), 3,51 – 3,32 (m, 1H), 2,68 – 2,52 (m, 2H), 2,12 – 1,99 (m, 1H), 1,93 – 1,77 (m, 2H), 1,62 (td, *J* = 15,7, 7,8, 1H), 1,44 (dd, *J* = 14,1, 7,5, 1H), 1,39 – 1,23 (m, 1H), 0,99 (s, 9H); MS (ESI+) *m/z* 498(M+H)$^+$.

Ejemplo 463

(S)-1-((3aR,4S,6aS)-4-((S)-2-(tert-butoxicarbonilamino)-4,4-dimetilpentanamido)hexahidrociclopenta[c]pirrol-2(1H)–il)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo del Ejemplo 226 en lugar de *N*-((3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-2,2-bis(4-fluorofenil)acetamida (150 mg, 0,336 mmol) y ácido (S)-2-(tert-butoxicarbonilamino)-4,4-dimetilpentanoico en lugar de ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4-metilpentanoico en el

procedimiento descrito en Ejemplo 459 Pasos A y B: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,76 (d, *J* = 5,2, 1H), 7,02 (d, *J* = 4,7, 1H), 6,97 – 6,86 (m, 1H), 4,78 (td, *J* = 8,7, 4,5, 1H), 4,49 (td, *J* = 8,2, 4,6, 1H), 4,25 – 4,14 (m, 1H), 3,84 – 3,76 (m, 2H), 3,54 – 3,35 (m, 1H), 2,73 – 2,59 (m, 2H), 2,07 (ddd, *J* = 20,0, 13,7, 5,6, 2H), 1,94 – 1,81 (m, 2H), 1,69 (ddd, *J* = 11,1, 7,4, 3,2, 2H), 1,64 – 1,55 (m, 1H), 1,48 (s, 9H), 1,48 (s, 9H), 1,38 – 1,27 (m, 1H), 1,02 (s, 9H), 0,97 (s, 9H); MS (ESI+) *m/z* 581(M+H)$^+$.

Ejemplo 464

4-metil-*N*^{1}-[(3a*R*,4*S*,6a*S*)-2-(4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-L-leucinamida

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-4-((S)-2-(tert-butoxicarbonilamino)-4,4-dimetilpentanamido)hexahidrociclopenta[c]pirrol-2(1H)–il)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo del Ejemplo 463 en lugar de (S)-1-((3aR,4S,6aS)-4-(2,2-bis(4-fluorofenil)acetamido)hexahidrociclopenta[c]pirrol-2(1H)–il)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 459 Paso C: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,88 – 7,76 (m, 1H), 4,22 – 4,14 (m, 1H), 3,78 – 3,66 (m, 6H), 3,61 (dddd, *J* = 9,1, 4,5, 2,1, 0,7, 2H), 3,50 (dd, *J* = 7,5, 4,1, 2H), 2,70 – 2,60 (m, 1H), 2,60 – 2,51 (m, 1H), 2,11 – 2,00 (m, 2H), 1,96 – 1,83 (m, 2H), 1,66 – 1,53 (m, 1H), 1,45 (dd, *J* = 14,1, 7,4, 1H), 1,36 (dd, *J* = 14,1, 7,5, 2H), 1,00 (s, 9H), 0,97 (s, 9H); MS (ESI+) *m/z* 381(M+H)$^+$.

Ejemplo 465

4-metil-*N*^{1}-[(3a*R*,4*S*,6a*S*)-2-L-fenilalaniloctahidrociclopenta[*c*]pirrol-4–il]-L-leucinamida

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo del Ejemplo 226 en lugar de *N*-((3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-2,2-bis(4-fluorofenil)acetamida y ácido (S)-2-(tert-butoxicarbonilamino)-3-fenilpropanoico en lugar de ácido (S)-2-(tert-butoxicarbonil(metil)amino)-4-metilpentanoico en el procedimiento descrito en Ejemplo 459: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,84 – 7,68 (m, 1H), 7,34 – 7,24 (m, 3H), 7,18 (t, *J* = 6,8, 2H), 4,08 (dt, *J* = 14,3, 7,0, 1H), 3,81 – 3,67 (m, 6H), 3,53 – 3,46 (m, 4H), 3,10 (dd, *J* = 13,2, 7,0, 1H), 2,88 (dd, *J* = 13,2, 6,8, 1H), 2,53 (td, *J*

= 14,0, 7,9, 1H), 2,41 (dt, *J* = 14,4, 7,0, 1H), 2,10 – 2,04 (m, 1H), 1,98 (ddd, *J* = 19,6, 7,2, 5,1, 1H), 1,80 (dt, *J* = 13,0, 7,8, 1H), 1,53 (dq, *J* = 12,8, 8,1, 1H), 1,35 (dd, *J* = 14,1, 7,6, 1H), 1,25 – 1,05 (m, 1H), 0,97 (s, 9H); MS (ESI+) *m/z* 401(M+H)$^+$.

Ejemplo 466

(3a*R*,4*S*,6a*S*)-*N*-benzhidril-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4-amina

Se combinó (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina (60 mg, 0,211 mmol), del Ejemplo 156 Paso A con (bromometilen)dibenceno (62,6 mg, 0,253 mmol) y carbonato de potasio (87 mg, 0,633 mmol) en *N*,*N*-dimetilformamida (1 ml). La reacción se agitó a temperatura ambiente por 72 horas. La reacción se detuvo con agua y se extrajo con éter dietílico. Los extractos de éter se lavaron con agua (3×1 ml) y el solvente se eliminó. El material crudo se purificó usando un cartucho de 12 g de gel de sílice eluyendo con un gradiente de metanol al 0-3% (amoníaco 2 N)/diclorometano para dar (3a*R*,4*S*,6a*S*)-*N*-benzhidril-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,71 (s, 1H), 7,64 – 7,59 (m, 4H), 7,52 (d, *J* = 7,7, 1H), 7,44 (t, *J* = 7,7, 1H), 7,33 (td, *J* = 7,6, 4,7, 4H), 7,25 – 7,21 (m, 4H), 5,09 (s, 1H), 3,51 (q, *J* = 13,5, 2H), 3,02 (dd, *J* = 12,9, 5,5, 1H), 2,63 – 2,54 (m, 1H), 2,51 (dd, *J* = 8,8, 2,8, 1H), 2,47 – 2,41 (m, 1H), 2,37 (t, *J* = 8,0, 1H), 2,32 – 2,25 (m, 2H), 1,98 (td, *J* = 11,4, 5,6, 1H), 1,89 (ddd, *J* = 12,7, 10,4, 5,8, 1H), 1,45 (ddd, *J* = 14,7, 11,9, 8,1, 1H), 1,32 – 1,23 (m, 1H); MS (ESI+) *m/z* 451(M+H)$^+$.

Ejemplo 467

(3a*S*,4*R*,6a*R*)-*N*-benzhidril-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina

El compuesto del título se preparó utilizando (3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 254 Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 466: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,35-8,36 (bs, 1H), 8,17-8,19 (m, 1H), 7,92-7,95 (m, 1H), 7,75 (t, *J* = 7,8 Hz, 1H), 7,61-7,64 (m, 2H),

7,57-7,60 (m, 2H), 7,32-7,38 (m, 4H), 7,22-7,26 (m, 2H), 5,02 (s, 1H), 3,33 (dd, *J* = 9,7, 3,1 Hz, 1H), 3,07 (dd, *J* = 9,6, 3,0 Hz, 1H), 3,03 (dd, *J* = 9,8, 7,9 Hz, 1H), 2,90-2,95 (m, 2H), 2,48-2,57 (m, 1H), 2,39-2,45 (m, 1H), 2,17-2,48 (m, 1H), 1,80-1,88 (m, 2H), 1,31-1,39 (m, 1H), 1,04-1,12 (m, 1H); MS (ESI+) *m/z* 501 $(M+H)^+$.

Ejemplo 468

(3a*R*,4*S*,6a*S*)-*N*-benzhidril-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 252 Paso D en lugar de (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 466: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,35-8,36 (bs, 1H), 8,17-8,19 (m, 1H), 7,92-7,95 (m, 1H), 7,74 (t, *J* = 7,8 Hz, 1H), 7,61-7,64 (m, 2H), 7,57-7,60 (m, 2H), 7,31-7,39 (m, 4H), 7,22-7,27 (m, 2H), 5,01-5,06 (m, 1H), 3,33 (dd, *J* = 9,8, 3,1 Hz, 1H), 3,07 (dd, *J* = 9,6, 2,9 Hz, 1H), 3,03 (dd, *J* = 9,5, 8,2 Hz, 1H), 2,90-2,94 (m, 2H), 2,49-2,55 (m, 1H), 2,38-2,45 (m, 1H), 2,28-2,38 (m, 1H), 1,80-1,88 (m, 2H), 1,31-1,39 (m, 1H), 1,04-1,12 (m, 1H); MS (ESI+) *m/z* 501 $(M+H)^+$.

Ejemplo 469

N^1-[(3a*S*,4*R*,6a*R*)-2-benzhidriloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida

Paso A: Se preparó (S)-1-((3aS,4R,6aR)-2-benzhidriloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo utilizando metil((S)-4-metil-1-((3aS,4R,6aR)-octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il)carbamato de tert-butilo del Ejemplo 349 en lugar de (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 466: MS (APCI+) *m/z* 520 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (S)-1-((3aS,4R,6aR)-2-benzhidriloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H

NMR (500 MHz, piridin-d_5) δ ppm 8,16-8,18 (m, 1H), 7,63-7,65 (m, 2H), 7,56-7,62 (m, 2H), 7,27-7,37 (m, 4H), 7,13-7,20 (m, 2H), 4,47-4,54 (m, 1H), 4,21 (s, 1H), 3,20 (dd, *J* = 8,2, 5,9 Hz, 1H), 2,78-2,85 (m, 1H), 2,48-2,59 (m, 2H), 2,39 (s, 3H), 2,34-2,38 (m, 2H), 2,20-2,28 (m, 2H), 1,87-2,07 (m, 1H), 1,81-1,94 (m, 2H), 1,60-1,71 (m, 2H), 1,52-1,59 (m, 1H), 1,44-1,52 (m, 1H), 0,89 (d, *J* = 6,6 Hz, 3H), 0,83 (d, *J* = 6,5 Hz, 3H); MS (ESI+) *m/z* 420 $(M+H)^+$.

Ejemplo 470

4-metil-*N*^{2}-propil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 419 en lugar de (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y 1-yodopropano en lugar de yodoetano en el procedimiento descrito en Ejemplo 288: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,31-8,34 (m, 1H), 8,14-8,16 (m, 2H), 7,90-7,92 (m, 2H), 4,22-4,27 (m, 1H), 3,86 (d, *J* = 11,3 Hz, 1H), 3,28 (t, *J* = 5,7 Hz, 1H), 3,15-3,20 (m, 2H), 2,98 (dd, *J* = 9,5, 6,5 Hz, 1H), 2,52-2,62 (m, 4H), 1,92-2,00 (m, 1H), 1,89 (dd, *J* = 14,1, 4,8 Hz, 1H), 1,81-1,88 (m, 1H), 1,65-1,86 (m, 1H), 1,53-1,62 (m, 1H), 1,40-1,54 (m, 3H), 1,27-1,38 (m, 1H), 0,99 (s, 9H), 0,89 (t, *J* = 7,4 Hz, 3H); MS (ESI+) *m/z* 504 $(M+H)^+$.

Ejemplo 471

N^2-(ciclopropilmetil)-4-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 419 en lugar de (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y (bromometil)ciclopropano en lugar de yodoetano en el procedimiento descrito en Ejemplo 288: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,29-8,31 (m, 1H), 8,13-8,15 (m, 2H), 7,89-7,91 (m, 2H), 4,21-4,26 (m, 1H), 3,87 (dd, *J* = 9,9, 2,3 Hz, 1H), 3,31 (dd, *J* = 7,0, 4,5 Hz, 1H), 3,18 (dd, *J* = 9,8, 2,1 Hz, 1H), 3,16 (dd, *J* = 9,8, 7,5 Hz, 1H), 2,97 (dd, *J* = 9,6, 6,7 Hz, 1H), 2,49-2,59 (m, 4H), 1,90-2,04 (m, 1H), 1,92-1,98 (m, 1H), 1,90 (dd, *J* = 14,1, 4,5 Hz, 1H), 1,80-1,87 (m, 1H), 1,53-1,61 (m, 1H), 1,50

(dd, *J* = 14,1, 7,1 Hz, 1H), 1,26-1,34 (m, 1H), 0,99 (s, 9H), 0,92-1,03 (m, 1H), 0,39-0,47 (m, 2H), 0,13-0,19 (m, 2H); MS (ESI+) *m/z* 516 $(M+H)^+$.

Ejemplo 472

N^2-(ciclobutilmetil)-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 419 en lugar de (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y (bromometil)ciclobutano en lugar de yodoetano en el procedimiento descrito en Ejemplo 288: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,28-8,30 (m, 1H), 8,14-8,16 (m, 2H), 7,89-7,92 (m, 2H), 4,23-4,27 (m, 1H), 3,88 (dd, *J* = 9,9, 2,2 Hz, 1H), 3,27 (dd, *J* = 7,0, 4,6 Hz, 1H), 3,16-3,20 (m, 2H), 2,98 (dd, *J* = 9,5, 6,5 Hz, 1H), 2,58-2,69 (m, 4H), 2,36-2,47 (m, 1H), 1,94-2,03 (m, 3H), 1,88 (dd, *J* = 14,0, 4,6 Hz, 1H), 1,74-1,88 (m, 3H), 1,62-1,73 (m, 2H), 1,53-1,62 (m, 1H), 1,48 (dd, *J* = 14,1, 7,1 Hz, 1H), 1,32 (ddt, *J* = 9,6, 12,8, 6,4 Hz, 1H), 0,99 (s, 9H); MS (ESI+) *m/z* 530 $(M+H)^+$.

Ejemplo 473

N^2-isobutil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 419 en lugar de (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y 1-yodo-2-metilpropano en lugar de yodoetano en el procedimiento descrito en Ejemplo 288: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,26-8,28 (m, 1H), 8,14-8,16 (m, 2H), 7,89-7,92 (m, 2H), 4,22-4,28 (m, 1H), 3,86 (dd, *J* = 10,0, 2,4 Hz, 1H), 3,25 (dd, *J* = 7,1, 4,6 Hz, 1H), 3,16-3,21 (m, 2H), 2,99 (dd, *J* = 9,6, 6,8 Hz, 1H), 2,54-2,60 (m, 2H), 2,38-2,46 (m, 2H), 1,96 (dq, *J* = 11,8, 5,9 Hz, 1H), 1,87 (dd, *J* = 14,1, 4,7 Hz, 1H), 1,80-1,88 (m, 1H), 1,63-1,77 (m, 1H), 1,62-1,70 (m, 1H), 1,53-1,61 (m, 1H), 1,50 (dd, *J* = 14,0, 7,2 Hz, 1H), 1,28-1,35 (m, 1H), 0,99 (s, 9H), 0,92 (d, *J* = 6,7 Hz, 3H), 0,90 (d, *J* = 6,7 Hz, 3H); MS (ESI+) *m/z* 518 $(M+H)^+$.

Ejemplo 474

N^2-(ciclopentilmetil)-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 419 en lugar de (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y (iodometil)ciclopentano en lugar de yodoetano en el procedimiento descrito en Ejemplo 288: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,30-8,32 (m, 1H), 8,13-8,16 (m, 2H), 7,89-7,92 (m, 2H), 4,22-4,27 (m, 1H), 3,87 (dd, *J* = 9,9, 2,2 Hz, 1H), 3,28 (dd, *J* = 7,1, 4,5 Hz, 1H), 3,15-3,22 (m, 2H), 2,96-3,01 (m, 1H), 2,46-2,60 (m, 4H), 1,82-2,01 (m, 4H), 1,20-2,29 (m, 1H), 1,67-1,79 (m, 2H), 1,42-1,63 (m, 6H), 1,13-1,36 (m, 3H), 1,00 (s, 9H); MS (ESI+) *m/z* 544 $(M+H)^+$.

Ejemplo 475

N^2-(ciclohexilmetil)-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 419 en lugar de (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y (bromometil)ciclohexano en lugar de yodoetano en el procedimiento descrito en Ejemplo 288: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,27-8,29 (m, 1H), 8,14-8,16 (m, 2H), 7,89-7,92 (m, 2H), 4,23-4,28 (m, 1H), 3,88 (dd, *J* = 9,9, 2,2 Hz, 1H), 3,25 (dd, *J* = 7,1, 4,5 Hz, 1H), 3,16-3,21 (m, 2H), 2,99 (dd, *J* = 9,6, 6,5 Hz, 1H), 2,59-2,61 (m, 2H), 2,47 (dd, *J* = 11,1, 6,7 Hz, 1H), 2,43 (dd, *J* = 11,2, 6,2 Hz, 1H), 1,98 (dq, *J* = 11,8, 5,9 Hz, 1H), 1,89 (dd, *J* = 14,2, 4,4 Hz, 1H), 1,82-1,89 (m, 1H), 1,71-1,82 (m, 2H), 1,58-1,79 (m, 1H), 1,56-1,67 (m, 4H), 1,52 (dd, *J* = 14,0, 7,2 Hz, 1H), 1,28-1,41 (m, 2H), 1,05-1,22 (m, 3H), 1,00 (s, 9H), 0,86-0,98 (m, 2H); MS (ESI+) *m/z* 558 $(M+H)^+$.

Ejemplo 476

N^2-butil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-

(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 419 en lugar de (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y 1-yodobutano en lugar de yodoetano en el procedimiento descrito en Ejemplo 288: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,32-8,34 (m, 1H), 8,14-8,16 (m, 2H), 7,90-7,92 (m, 2H), 4,24-4,29 (m, 1H), 3,87 (dd, *J* = 9,9, 2,1 Hz, 1H), 3,29 (dd, *J* = 6,8, 4,8 Hz, 1H), 3,15-3,21 (m, 2H), 2,99 (dd, *J* = 9,5, 6,4 Hz, 1H), 2,55-2,66 (m, 4H), 1,94-2,01 (m, 1H), 1,90 (dd, *J* = 14,0, 4,9 Hz, 1H), 1,82-1,89 (m, 1H), 1,64-1,88 (m, 1H), 1,54-1,63 (m, 1H), 1,51 (dd, *J* = 14,0, 6,9 Hz, 1H), 1,39-1,47 (m, 2H), 1,26-1,38 (m, 3H), 0,99 (s, 9H), 0,84 (t, *J* = 7,3 Hz, 3H); MS (ESI-) *m/z* 516 $(M-H)^-$.

Ejemplo 477

N^2-etil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 419 en lugar de (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 288: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,35-8,38 (m, 1H), 8,14-8,16 (m, 2H), 7,90-7,92 (m, 2H), 4,22-4,27 (m, 1H), 3,86 (dd, *J* = 10,0, 2,2 Hz, 1H), 3,30 (t, *J* = 5,8 Hz, 1H), 3,14-3,20 (m, 2H), 2,98 (dd, *J* = 9,5, 6,4 Hz, 1H), 2,65-2,72 (m, 1H), 2,57-2,63 (m, 1H), 2,56-2,60 (m, 2H), 1,92-1,99 (m, 1H), 1,90 (dd, *J* = 14,0, 5,0 Hz, 1H), 1,79-1,88 (m, 1H), 1,62-1,94 (m, 1H), 1,52-1,63 (m, 1H), 1,50 (dd, *J* = 14,0, 6,6 Hz, 1H), 1,26-1,40 (m, 1H), 1,06 (t, *J* = 7,1 Hz, 3H), 0,98 (s, 9H); MS (ESI+) *m/z* 490 $(M+H)^+$.

Ejemplo 478

N^2-(ciclopropilmetil)-4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 440 en lugar de (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y (bromometil)ciclopropano en lugar de yodoetano en el procedimiento descrito en Ejemplo 288: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,62-8,63 (bs, 1H), 8,38-8,41

(m, 1H), 7,68 (dd, *J* = 8,9, 2,5 Hz, 1H), 6,40 (d, *J* = 8,9 Hz, 1H), 4,38-4,44 (m, 1H), 3,82-3,86 (m, 1H), 3,66-3,70 (m, 1H), 3,56-3,61 (m, 1H), 3,29-3,41 (m, 2H), 2,75-2,78 (m, 2H), 2,57 (dd, *J* = 6,7, 2,1 Hz, 2H), 2,12-2,21 (m, 1H), 1,92-2,00 (m, 1H), 1,95 (dd, *J* = 14,0, 4,5 Hz, 1H), 1,71 (dq, *J* = 12,7, 8,1 Hz, 1H), 1,54 (dd, *J* = 14,1, 7,0 Hz, 1H), 1,38-1,48 (m, 1H), 1,02 (s, 9H), 0,96-1,05 (m, 1H), 0,45-0,48 (m, 2H), 0,16-0,24 (m, 2H); MS (ESI+) *m/z* 453 $(M+H)^+$.

Ejemplo 479

N^2-(ciclopropilmetil)-4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluorometil)piridin-2-il]octahidrociclopenta[*c*]pirrol-4-il}-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluorometil)piridin-2-il]octahidrociclopenta[*c*]pirrol-4-il}-L-leucinamida del Ejemplo 441 en lugar de (3a*R*,4*S*,6a*S*)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y (bromometil)ciclopropano en lugar de yodoetano en el procedimiento descrito en Ejemplo 288: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,34-8,36 (m, 1H), 7,51 (t, *J* = 7,9 Hz, 1H), 6,98 (d, *J* = 7,2 Hz, 1H), 6,52 (d, *J* = 8,5 Hz, 1H), 4,35-4,41 (m, 1H), 3,73 (dd, *J* = 10,9, 2,9 Hz, 1H), 3,60-3,65 (m, 1H), 3,52 (dd, *J* = 10,7, 7,3 Hz, 1H), 3,36 (dd, *J* = 7,1, 4,5 Hz, 1H), 3,29 (dd, *J* = 10,9, 3,6 Hz, 1H), 2,69-2,77 (m, 2H), 2,55 (dd, *J* = 6,7, 2,8 Hz, 2H), 2,10-2,16 (m, 1H), 1,94 (dd, *J* = 14,1, 4,5 Hz, 1H), 1,89-1,96 (m, 1H), 1,74-2,09 (m, 1H), 1,69 (dq, *J* = 12,7, 7,9 Hz, 1H), 1,53 (dd, *J* = 14,1, 7,0 Hz, 1H), 1,31-1,42 (m, 1H), 1,02 (s, 9H), 0,95-1,05 (m, 1H), 0,42-0,51 (m, 2H), 0,15-0,25 (m, 2H); MS (ESI+) *m/z* 453 $(M+H)^+$.

Ejemplo 480

N^2-isopropil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-il)-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-il)-L-leucinamida del Ejemplo 419 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,26-8,29 (m, 1H), 8,13-8,16 (m, 2H), 7,89-7,91 (m, 2H), 4,21-4,26 (m, 1H), 3,85 (dd, *J* = 9,9, 2,3 Hz, 1H), 3,36 (dd, *J* = 7,5, 4,1 Hz, 1H), 3,15-3,20 (m, 2H), 2,98 (dd, *J* = 9,6, 6,7 Hz, 1H), 2,83 (hept, *J* = 6,2 Hz, 1H), 2,51-2,62

(m, 2H), 1,91-1,97 (m, 1H), 1,79-1,88 (m, 2H), 1,63-1,81 (m, 1H), 1,51-1,59 (m, 1H), 1,47 (dd, *J* = 14,1, 7,5 Hz, 1H), 1,31 (ddt, *J* = 9,6, 12,8, 6,4 Hz, 1H), 1,03 (dd, *J* = 6,2, 2,7 Hz, 6H), 0,98 (s, 9H); MS (ESI+) *m/z* 504 $(M+H)^+$.

Ejemplo 481

N^2-isopropil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

El compuesto del título se preparó utilizando N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida del Ejemplo 422 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,31-8,34 (m, 1H), 8,13-8,15 (m, 2H), 7,89-7,91 (m, 2H), 4,21-4,27 (m, 1H), 3,84 (dd, *J* = 9,9, 2,7 Hz, 1H), 3,31-3,34 (m, 1H), 3,18 (dd, *J* = 9,8, 2,8 Hz, 1H), 3,16 (dd, *J* = 10,2, 7,9 Hz, 1H), 2,98 (dd, *J* = 9,6, 7,0 Hz, 1H), 2,83 (hept, *J* = 6,1 Hz, 1H), 2,46-2,60 (m, 2H), 1,94 (dq, *J* = 11,8, 5,9 Hz, 1H), 1,77-1,87 (m, 2H), 1,59-1,69 (m, 1H), 1,37-1,59 (m, 4H), 1,27-1,35 (m, 1H), 1,05 (d, *J* = 6,3 Hz, 3H), 1,03 (d, *J* = 6,3 Hz, 3H), 0,85 (t, *J* = 7,4 Hz, 3H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Ejemplo 482

N^2-isopropil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

El compuesto del título se preparó utilizando N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida del Ejemplo 423 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,26-8,28 (m, 1H), 8,11-8,14 (m, 2H), 7,88-7,91 (m, 2H), 4,23 (p, *J* = 6,9 Hz, 1H), 3,85 (dd, *J* = 9,9, 2,9 Hz, 1H), 3,30 (dd, *J* = 7,5, 5,5 Hz, 1H), 3,18 (dd, *J* = 9,7, 3,0 Hz, 1H), 3,14 (dd, *J* = 9,9, 7,7 Hz, 1H), 2,97 (dd, *J* = 9,6, 7,3 Hz, 1H), 2,81 (p, *J* = 6,2 Hz, 1H), 2,49-2,61 (m, 2H), 1,90-1,99 (m, 1H), 1,81-1,92 (m, 1H), 1,81-1,88 (m, 1H), 1,74-1,81 (m, 1H), 1,59-1,68 (m, 1H), 1,37-1,58 (m, 3H),

1,27-1,36 (m, 1H), 1,02 (dd, *J* = 6,2, 1,5 Hz, 6H), 0,85 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Ejemplo 483

N^2-isopropil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

El compuesto del título se preparó utilizando N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida del Ejemplo 424 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,38-8,39 (bs, 1H), 8,26-8,28 (m, 1H), 8,20 (d, *J* = 7,9 Hz, 1H), 7,90-7,92 (m, 1H), 7,72 (t, *J* = 7,8 Hz, 1H), 4,20-4,27 (m, 1H), 3,85 (dd, *J* = 9,9, 2,5 Hz, 1H), 3,29 (dd, *J* = 7,6, 5,5 Hz, 1H), 3,18 (dd, *J* = 20,2, 2,5 Hz, 1H), 3,14-3,18 (m, 1H), 2,96 (dd, *J* = 9,6, 7,0 Hz, 1H), 2,77-2,83 (m, 1H), 2,51-2,57 (m, 2H), 1,89-1,99 (m, 1H), 1,82-1,93 (m, 1H), 1,80-1,88 (m, 1H), 1,73-1,81 (m, 1H), 1,56-1,67 (m, 1H), 1,36-1,56 (m, 3H), 1,25-1,35 (m, 1H), 1,02 (dd, *J* = 9,4, 6,2 Hz, 6H), 0,85 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Ejemplo 484

N^2-isopropil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

El compuesto del título se preparó utilizando N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida del Ejemplo 425 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37-8,38 (bs, 1H), 8,26-8,28 (m, 1H), 8,17-8,20 (m, 1H), 7,90-7,92 (m, 1H), 7,71 (t, *J* = 7,8 Hz, 1H), 4,21-4,27 (m, 1H), 3,86 (dd, *J* = 9,9, 2,7 Hz, 1H), 3,29 (dd, *J* = 7,5, 5,5 Hz, 1H), 3,18 (dd, *J* = 9,6, 2,8 Hz, 1H), 3,14 (dd, *J* = 9,9, 7,5 Hz, 1H), 2,95 (dd, *J* = 9,6, 7,2 Hz, 1H), 2,76-2,84 (m, 1H), 2,47-2,58 (m, 2H), 1,91-1,98 (m, 1H), 1,82-1,93 (m, 1H), 1,81-1,89 (m, 1H), 1,73-1,81 (m, 1H), 1,57-1,66 (m, 1H), 1,36-1,57 (m, 3H), 1,25-1,35 (m, 1H), 1,02 (dd, *J* = 6,2, 2,0 Hz, 6H),

0,84 (t, *J* = 7,3 Hz, 3H).

Ejemplo 485

3-ciclohexil-*N*^{2}-isopropil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-alaninamida

El compuesto del título se preparó utilizando 3-ciclohexil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-alaninamida del Ejemplo 426 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,32 (d, *J* = 7,2 Hz, 1H), 8,13-8,16 (m, 2H), 7,89-7,95 (m, 2H), 4,22-4,30 (m, 1H), 3,85 (dd, *J* = 10,0, 2,3 Hz, 1H), 3,41 (dd, *J* = 8,5, 5,2 Hz, 1H), 3,15-3,21 (m, 2H), 2,99 (dd, *J* = 9,6, 6,7 Hz, 1H), 2,85 (p, *J* = 6,2 Hz, 1H), 2,56-2,61 (m, 2H), 1,83-2,11 (m, 1H), 1,90-2,00 (m, 1H), 1,79-1,89 (m, 1H), 1,66-1,78 (m, 3H), 1,46-1,65 (m, 6H), 1,25-1,37 (m, 1H), 1,08-1,25 (m, 3H), 1,06 (d, *J* = 6,3 Hz, 3H), 1,04 (d, *J* = 6,3 Hz, 3H), 0,75-1,00 (m, 2H); MS (ESI+) *m/z* 530 $(M+H)^+$.

Ejemplo 486

***N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-5-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-*N*^{2}-isopropil-4-metil-L-leucinamida**

El compuesto del título se preparó utilizando *N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-5-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-4-metil-L-leucinamida del Ejemplo 428 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,57 (d, *J* = 2,2 Hz, 1H), 8,32-8,35 (m, 1H), 7,81 (dd, *J* = 8,3, 2,2 Hz, 1H), 7,75 (d, *J* = 8,3 Hz, 1H), 4,29-4,35 (m, 1H), 3,93 (dd, *J* = 10,2, 2,2 Hz, 1H), 3,56 (dd, *J* = 10,1, 6,6 Hz, 1H), 3,35-3,41 (m, 2H), 3,32 (dd, *J* = 10,0, 2,6 Hz, 1H), 2,83 (hept, *J* = 6,2 Hz, 1H), 2,66-2,68 (m, 2H), 2,01-2,08 (m, 1H), 1,86-1,93 (m, 1H), 1,84 (dd, *J* = 14,2, 4,3 Hz, 1H), 1,66-1,81 (m, 1H), 1,56-1,66 (m, 1H), 1,46 (dd, *J* = 14,1, 7,4 Hz, 1H), 1,35-1,42 (m, 1H), 1,03 (d, *J* = 6,1 Hz, 3H), 1,02 (d, *J* = 6,1 Hz, 3H), 0,98 (s, 9H); MS (ESI+) *m/z* 538 $(M+H)^+$.

Ejemplo 487

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-isopropil-4-metil-L-leucinamida

El compuesto del título se preparó utilizando N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-4-metil-L-leucinamida del Ejemplo 429 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (501 MHz, piridin-d_5) δ ppm 8,35 (d, *J* = 8,2 Hz, 1H), 8,29-8,32 (m, 1H), 7,99 (s, 1H), 7,73 (d, *J* = 9,1 Hz, 1H), 4,29-4,35 (m, 1H), 3,95 (dd, *J* = 10,2, 2,4 Hz, 1H), 3,54 (dd, *J* = 10,1, 6,9 Hz, 1H), 3,40 (dd, *J* = 10,0, 6,5 Hz, 1H), 3,33-3,36 (m, 2H), 2,82 (dq, *J* = 12,4, 6,2 Hz, 1H), 2,65-2,68 (m, 2H), 2,00-2,07 (m, 1H), 1,85-1,92 (m, 1H), 1,84 (dd, *J* = 14,1, 4,2 Hz, 1H), 1,65-1,82 (m, 1H), 1,55-1,65 (m, 1H), 1,46 (dd, *J* = 14,1, 7,6 Hz, 1H), 1,34-1,43 (m, 1H), 1,03 (d, *J* = 6,1 Hz, 3H), 1,02 (d, *J* = 6,3 Hz, 3H), 0,98 (s, 9H); MS (ESI+) *m/z* 538 $(M+H)^+$.

Ejemplo 488

N^2-isopropil-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropil-4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-4-metil-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-[(3a*R*,4*S*,6a*S*)-2-(4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-L-leucinamida del Ejemplo 464 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,77 – 7,66 (m, 1H), 4,30 – 4,18 (m, 1H), 3,80 – 3,72 (m, 3H), 3,72 – 3,61 (m, 3H), 3,60 – 3,45 (m, 1H), 3,32 (dd, *J* = 7,3, 4,2, 1H), 2,87 – 2,77 (m, 2H), 2,76 – 2,68 (m, 1H), 2,68 – 2,60 (m, 1H), 2,17 – 2,05 (m, 1H), 2,02 – 1,90 (m, 1H), 1,82 (dd, *J* = 14,2, 4,2, 1H), 1,64 (dd, *J* = 14,2, 4,2, 2H), 1,46 (ddd, *J* = 27,5, 14,2, 7,7, 3H), 1,12 – 0,92 (m, 30H); MS (ESI+) *m/z* 465 $(M+H)^+$.

Ejemplo 489

N^2-isopropil-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropil-L-fenilalanil)octahidrociclopenta[*c*]pirrol-4–il]-4-metil-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-[(3a*R*,4*S*,6a*S*)-2-L-

fenilalaniloctahidrociclopenta[*c*]pirrol-4–il]-L-leucinamida del Ejemplo 465 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,74 – 7,61 (m, 1H), 7,36 – 7,23 (m, 4H), 7,22 – 7,15 (m, 2H), 4,19 – 4,02 (m, 2H), 3,77 (dd, *J* = 11,9, 3,7, 5H), 3,56 – 3,48 (m, 1H), 3,32 (dd, *J* = 7,3, 4,3, 1H), 3,05 – 2,94 (m, 2H), 2,92 – 2,76 (m, 2H), 2,66 – 2,50 (m, 1H), 2,48 – 2,35 (m, 1H), 2,06 – 1,92 (m, 1H), 1,83 (dd, *J* = 14,2, 4,3, 2H), 1,55 (dq, *J* = 12,8, 8,0, 1H), 1,42 (dd, *J* = 14,2, 7,3, 1H), 1,08 – 1,00 (m, 12H), 0,99 (s, 9H); MS (ESI+) *m/z* 485 $(M+H)^+$.

Ejemplo 490

N^2-isopropil-4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 440 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,62-8,63 (bs, 1H), 8,34-8,36 (m, 1H), 7,68 (dd, *J* = 8,9, 2,5 Hz, 1H), 6,40 (d, *J* = 8,9 Hz, 1H), 4,39-4,44 (m, 1H), 3,82-3,85 (m, 1H), 3,67-3,71 (m, 1H), 3,57-3,61 (m, 1H), 3,29-3,44 (m, 2H), 2,88 (hept, *J* = 6,2 Hz, 1H), 2,74-2,76 (m, 2H), 2,13-2,20 (m, 1H), 1,64-2,00 (m, 4H), 1,51 (dd, *J* = 14,1, 7,6 Hz, 1H), 1,39-1,46 (m, 1H), 1,08 (d, *J* = 6,3 Hz, 3H), 1,07 (d, *J* = 6,3 Hz, 3H), 1,01 (s, 9H); MS (ESI+) *m/z* 441 $(M+H)^+$.

Ejemplo 491

N^2-isopropil-4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 441 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,31-8,34 (m, 1H), 7,51 (t, *J* = 7,9 Hz, 1H), 6,98 (d, *J* = 7,2 Hz, 1H), 6,52 (d, *J* = 8,6 Hz, 1H), 4,36-4,41 (m, 1H), 3,73 (dd, *J* = 10,9, 3,0 Hz, 1H),

3,63 (dd, *J* = 10,9, 7,0 Hz, 1H), 3,53 (dd, *J* = 10,8, 7,4 Hz, 1H), 3,40 (dd, *J* = 7,5, 4,0 Hz, 1H), 3,29 (dd, *J* = 10,9, 3,6 Hz, 1H), 2,88 (p, *J* = 6,2 Hz, 1H), 2,74 (dd, *J* = 5,6, 2,8 Hz, 2H), 2,09-2,16 (m, 1H), 1,89-1,98 (m, 1H), 1,90 (dd, *J* = 14,1, 4,0 Hz, 1H), 1,69-1,85 (m, 1H), 1,63-1,73 (m, 1H), 1,50 (dd, *J* = 14,1, 7,6 Hz, 1H), 1,36-1,43 (m, 1H), 1,07 (d, *J* = 6,3 Hz, 3H), 1,07 (d, *J* = 6,1 Hz, 3H), 1,01 (s, 9H); MS (ESI+) *m/z* 441 $(M+H)^+$.

Ejemplo 492

2,2-bis(4-fluorofenil)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropil-4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]acetamida

El compuesto del título se preparó utilizando 2,2-bis(4-fluorofenil)-*N*-[(3a*R*,4*S*,6a*S*)-2-(4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]acetamida del Ejemplo 462 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,35 – 8,23 (m, 1H), 7,49 – 7,41 (m, 4H), 7,07 – 6,99 (m, 4H), 5,10 (s, 1H), 4,37 – 4,19 (m, 1H), 3,78 – 3,70 (m, 2H), 3,66-3,41 (m 4H), 2,84 – 2,71 (m, 1H), 2,69 – 2,54 (m, 2H), 2,14 – 2,00 (m, 1H), 1,95 – 1,80 (m, 1H), 1,63 (ddd, *J* = 12,4, 9,1, 6,0, 2H), 1,48 (dd, *J* = 14,2, 8,0, 1H), 1,42 – 1,29 (m, 1H), 1,08 – 0,95 (m, 15H); MS (ESI+) *m/z* 526 $(M+H)^+$.

Ejemplo 493

N^2-isopropil-4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[2-(metilsulfonil)pirimidin-5–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[2-(metilsulfonil)pirimidin-5–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 442 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,45 (s, 2H), 8,31-8,33 (m, 1H), 4,95 (s, 3H), 4,40-4,46 (m, 1H), 3,97 (dd, *J* = 11,8, 2,8 Hz, 1H), 3,80 (dd, *J* = 11,9, 7,6 Hz, 1H), 3,73 (dd, *J* = 11,6, 8,1 Hz, 1H), 3,45 (dd, *J* = 11,7, 4,1 Hz, 1H), 3,40 (dd, *J* = 7,5, 4,0 Hz, 1H), 2,86 (hept, *J* = 6,2 Hz, 1H), 2,70-2,78 (m, 2H), 2,13-2,19 (m, 1H), 1,89-1,98 (m, 1H), 1,89 (dd, *J* = 14,2, 4,1 Hz, 1H), 1,65-1,81 (m, 1H), 1,63-1,72 (m, 1H), 1,49 (dd, *J* = 14,1, 7,6 Hz, 1H), 1,38-1,45 (m, 1H), 1,06 (d, *J* = 6,1 Hz, 3H), 1,05 (d, *J* = 6,1 Hz,

3H), 1,00 (s, 9H); MS (ESI+) *m/z* 450 $(M+H)^+$.

Ejemplo 494

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-isopropil-L-norvalinamida

Paso A: N^1-{(3a*R*,4*S*,6a*S*)-2-Benciloctahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida se preparó utilizando ((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 382 Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,17 (d, *J* = 7,3, 1H), 7,43 (d, *J* = 7,4, 2H), 7,36 (t, *J* = 7,6, 2H), 7,27 (t, *J* = 7,3, 1H), 4,42 – 4,35 (m, 1H), 3,59 (d, *J* = 13,2, 1H), 3,53 (dd, *J* = 7,9, 4,9, 1H), 3,44 (d, *J* = 13,1, 1H), 2,84 (dd, *J* = 8,9, 2,4, 1H), 2,54 – 2,42 (m, 2H), 2,41 – 2,33 (m, 2H), 2,23 (dd, *J* = 8,7, 7,3, 1H), 2,10 (dt, *J* = 17,7, 5,8, 3H), 1,98 – 1,90 (m, 1H), 1,82 (dt, *J* = 20,2, 6,2, 1H), 1,69 – 1,61 (m, 1H), 1,58 – 1,34 (m, 4H), 0,84 (t, *J* = 7,3, 3H); MS (ESI+) *m/z* 316 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando N^1-{(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida del Paso A en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,17-8,19 (m, 1H), 7,43-7,46 (m, 2H), 7,37 (t, *J* = 7,5 Hz, 2H), 7,28 (t, *J* = 7,3 Hz, 1H), 4,39-4,44 (m, 1H), 3,61 (d, *J* = 13,1 Hz, 1H), 3,46 (d, *J* = 13,1 Hz, 1H), 3,32 (dd, *J* = 7,6, 5,5 Hz, 1H), 2,81-2,86 (m, 2H), 2,48-2,59 (m, 2H), 2,45 (dd, *J* = 8,7, 7,2 Hz, 1H), 2,36 (dd, *J* = 9,0, 2,7 Hz, 1H), 2,28 (dd, *J* = 8,9, 6,8 Hz, 1H), 2,12 (dq, *J* = 12,0, 6,0 Hz, 1H), 1,84-1,99 (m, 1H), 1,77-1,89 (m, 2H), 1,40-1,67 (m, 5H), 1,05 (d, *J* = 6,1 Hz, 3H), 1,04 (d, *J* = 6,0 Hz, 3H), 0,85 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 358 $(M+H)^+$.

Ejemplo 495

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-isopropil-L-norvalinamida

Paso A: Se preparó ((S)-1-oxo-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando *N*-(*tert*-butoxicarbonil)-L-norvalina en lugar de *N*-(*tert*-butoxicarbonil)-L-

leucina y (3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 16 Paso D en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,58 (d, *J* = 7,2, 1H), 7,91 (d, *J* = 8,3, 1H), 7,42 (d, *J* = 7,3, 2H), 7,36 (t, *J* = 7,4, 2H), 7,27 (t, *J* = 7,2, 1H), 4,64 (dd, *J* = 14,4, 7,7, 1H), 4,45 – 4,34 (m, 1H), 3,56 (d, *J* = 13,1, 1H), 3,40 (d, *J* = 13,2, 1H), 2,74 (d, *J* = 8,9, 1H), 2,48 (d, *J* = 0,7, 2H), 2,39 – 2,27 (m, 2H), 2,26 – 2,19 (m, 1H), 2,14 (dq, *J* = 12,0, 6,0, 1H), 2,07 – 1,96 (m, 1H), 1,85 (td, *J* = 13,8, 8,2, 2H), 1,65 (td, *J* = 14,3, 7,3, 1H), 1,49 (d, *J* = 8,5, 11H), 1,45 – 1,33 (m, 1H), 0,81 (t, *J* = 7,3, 3H); MS (ESI+) *m/z* 416 $(M+H)^+$.

Paso B: Se preparó N^1-{(3a*S*,4*R*,6a*R*)-2-Benciloctahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida se preparó utilizando ((*S*)-1-oxo-1-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,19 (d, *J* = 7,4, 1H), 7,43 (d, *J* = 7,3, 2H), 7,36 (t, *J* = 7,6, 2H), 7,27 (t, *J* = 7,3, 1H), 4,43 – 4,35 (m, 1H), 3,59 (d, *J* = 13,1, 1H), 3,53 (dd, *J* = 7,9, 5,0, 1H), 3,43 (d, *J* = 13,2, 1H), 2,83 (dd, *J* = 8,9, 2,4, 1H), 2,55 – 2,48 (m, 1H), 2,44 (ddd, *J* = 9,2, 6,0, 3,6, 1H), 2,41 – 2,33 (m, 2H), 2,23 (dd, *J* = 8,8, 7,3, 1H), 2,10 (td, *J* = 11,8, 5,9, 3H), 1,98 – 1,89 (m, 1H), 1,83 (dt, *J* = 20,4, 6,2, 1H), 1,70 – 1,60 (m, 1H), 1,58 – 1,33 (m, 4H), 0,84 (t, *J* = 7,3, 3H); MS (ESI+) *m/z* 316 $(M+H)^+$.

Paso C: El compuesto del título se preparó utilizando N^1-{(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida del Paso B en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,18-8,20 (m, 1H), 7,43-7,45 (m, 2H), 7,37 (t, *J* = 7,5 Hz, 2H), 7,28 (t, *J* = 7,3 Hz, 1H), 4,40-4,46 (m, 1H), 3,60 (d, *J* = 13,1 Hz, 1H), 3,44 (d, *J* = 13,1 Hz, 1H), 3,32 (dd, *J* = 7,5, 5,5 Hz, 1H), 2,80-2,86 (m, 2H), 2,46-2,59 (m, 2H), 2,43 (dd, *J* = 8,8, 7,2 Hz, 1H), 2,35 (dd, *J* = 8,9, 2,9 Hz, 1H), 2,27 (dd, *J* = 8,9, 7,1 Hz, 1H), 2,12 (dq, *J* = 12,0, 6,0 Hz, 1H), 1,86-2,04 (m, 1H), 1,77-1,90 (m, 2H), 1,55-1,70 (m, 2H), 1,38-1,55 (m, 3H), 1,05 (d, *J* = 6,9 Hz, 3H), 1,04 (d, *J* = 6,6 Hz, 3H), 0,85 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 358 $(M+H)^+$.

Ejemplo 496

N^2-isopropil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

Paso A: Se preparó ((*S*)-4-metil-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina de 252 Paso D en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,75 (d, *J* = 13,1, 1H), 8,37 (s, 1H), 8,18 (d, *J* = 7,7, 1H), 8,00 (d, *J* = 8,4, 1H), 7,91 (d, *J* = 7,9, 1H), 7,71 (t, *J* = 7,9, 1H), 4,70 – 4,59 (m, 1H), 4,29 – 4,18 (m, 1H), 3,82 (dd, *J* = 10,1, 2,4, 1H), 3,15 (dd, *J* = 9,9, 7,6, 2H), 2,99 – 2,89 (m, 1H), 2,62 – 2,44 (m, 2H), 1,93 – 1,70 (m, 5H), 1,55 – 1,44 (m, 10H), 1,30 – 1,16 (m, 1H), 0,86 (d, *J* = 5,9, 3H), 0,83 (d, *J* = 5,9, 3H). ; MS (ESI-) *m/z* 545 (M-H)$^-$.

Paso B: Se preparó N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(Trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida utilizando ((*S*)-4-metil-1-oxo-1-((3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,44 – 8,32 (m, 2H), 8,19 (d, *J* = 7,9, 1H), 7,91 (d, *J* = 7,9, 1H), 7,79 – 7,66 (m, 1H), 4,72 – 4,38 (m, 3H), 4,29 – 4,15 (m, 1H), 3,84 (dd, *J* = 9,9, 2,4, 1H), 3,60 (dd, *J* = 9,3, 4,5, 1H), 3,06 (dt, *J* = 21,7, 10,8, 1H), 2,92 (dd, *J* = 9,6, 7,2, 1H), 2,57 – 2,45 (m, 2H), 1,98 – 1,76 (m, 4H), 1,61 – 1,43 (m, 2H), 1,26 (ddt, *J* = 13,2, 9,9, 6,5, 1H), 0,90 (d, *J* = 6,4, 3H), 0,84 (d, *J* = 6,3, 3H); MS (ESI-) *m/z* 448 (M-H)$^-$.

Paso C: El compuesto del título se preparó utilizando N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Paso B en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,38 (s, 1H), 8,30-8,33 (m, 1H), 8,20 (d, *J* = 7,9 Hz, 1H), 7,90-

7,93 (m, 1H), 7,72 (t, *J* = 7,8 Hz, 1H), 4,20-4,26 (m, 1H), 3,86 (dd, *J* = 9,9, 2,3 Hz, 1H), 3,35 (dd, *J* = 8,9, 5,1 Hz, 1H), 3,14-3,20 (m, 2H), 2,97 (dd, *J* = 9,6, 6,8 Hz, 1H), 2,83 (hept, *J* = 6,2 Hz, 1H), 2,52-2,56 (m, 2H), 2,07-2,81 (m, 1H), 1,78-2,01 (m, 3H), 1,64 (ddd, *J* = 13,6, 8,4, 5,2 Hz, 1H), 1,47-1,59 (m, 2H), 1,25-1,36 (m, 1H), 1,04 (d, *J* = 6,3 Hz, 3H), 1,02 (d, *J* = 6,1 Hz, 3H), 0,91 (d, *J* = 6,7 Hz, 3H), 0,85 (d, *J* = 6,6 Hz, 3H); MS (ESI-) *m/z* 488 $(M-H)^-$.

Ejemplo 497

N^2,N^2-dimetil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 384 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y formaldehido en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,37 (s, 1H), 8,26 (d, *J* = 7,0, 1H), 8,19 (d, *J* = 7,9, 1H), 7,91 (d, *J* = 7,9, 1H), 7,72 (t, *J* = 7,9, 1H), 4,24 (dt, *J* = 13,3, 6,5, 1H), 3,85 (dd, *J* = 10,0, 2,0, 1H), 3,20 – 3,11 (m, 3H), 2,94 (dd, *J* = 9,6, 7,1, 1H), 2,59 – 2,48 (m, 2H), 2,33 (s, 6H), 1,96 (dt, *J* = 12,3, 6,3, 1H), 1,81 (tdd, *J* = 14,4, 11,4, 6,9, 3H), 1,56 (ddt, *J* = 18,7, 13,2, 8,6, 2H), 1,28 (ddt, *J* = 13,0, 9,8, 6,4, 1H), 0,93 (d, *J* = 6,5, 3H), 0,90 (d, *J* = 6,4, 3H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Ejemplo 498

(3*R*)-3-(dimetilamino)-4-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida

El compuesto del título se preparó utilizando (3*R*)-3-amino-4-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida del Ejemplo 388 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y formaldehido en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,47-8,49 (m, 1H), 8,37-8,38 (bs, 1H), 8,20 (d, *J* = 7,9 Hz, 1H), 7,91 (d, *J* = 7,9 Hz, 1H), 7,71 (t, *J* = 7,8 Hz, 1H), 4,24 (p, *J* = 6,4 Hz, 1H), 3,85 (dd, *J* = 9,9, 2,4 Hz, 1H), 3,13-3,18 (m, 2H), 2,95-3,01 (m, 2H), 2,48-2,55 (m, 3H), 2,23 (s, 6H), 2,20 (dd, *J* = 15,1, 5,8 Hz, 1H), 1,95 (dq, *J* = 11,8, 5,9 Hz, 1H), 1,80-1,88 (m, 1H), 1,63-1,73 (m, 1H), 1,51-1,59 (m, 1H), 1,29 (ddt, *J* = 9,4, 12,7, 6,4 Hz,

1H), 0,98 (d, *J* = 6,6 Hz, 3H), 0,92 (d, *J* = 6,6 Hz, 3H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Ejemplo 499

N^2-ciclopropil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 419 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y (1-etoxiciclopropoxi)trimetilsilano en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,54-8,56 (m, 1H), 8,14-8,16 (m, 2H), 7,89-7,92 (m, 2H), 4,27-4,31 (m, 1H), 3,89 (dd, *J* = 9,9, 2,6 Hz, 1H), 3,44 (t, *J* = 6,0 Hz, 1H), 3,15-3,21 (m, 2H), 2,99 (dd, *J* = 9,6, 6,9 Hz, 1H), 2,53-2,66 (m, 2H), 2,24-2,28 (m, 1H), 1,94-2,00 (m, 1H), 1,81-1,90 (m, 3H), 1,56-1,64 (m, 1H), 1,51 (dd, *J* = 13,9, 6,6 Hz, 1H), 1,31 (ddt, *J* = 9,7, 12,8, 6,4 Hz, 1H), 0,96 (s, 9H), 0,46-0,51 (m, 1H), 0,30-0,45 (m, 3H); MS (ESI+) *m/z* 502 $(M+H)^+$.

Ejemplo 500

N^2,N^2-diciclopropil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 419 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y (1-etoxiciclopropoxi)trimetilsilano en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,13-8,15 (m, 2H), 7,88-7,90 (m, 2H), 7,83-7,85 (m, 1H), 4,21 (dq, *J* = 9,1, 6,2 Hz, 1H), 3,89 (dd, *J* = 9,9, 2,2 Hz, 1H), 3,53 (dd, *J* = 9,1, 1,8 Hz, 1H), 3,16 (dd, *J* = 9,9, 7,4 Hz, 2H), 2,96 (dd, *J* = 9,6, 6,7 Hz, 1H), 2,62 (dd, *J* = 13,6, 9,3 Hz, 1H), 2,46-2,57 (m, 2H), 2,23-2,28 (m, 2H), 1,88-1,94 (m, 1H), 1,76-1,82 (m, 1H), 1,65 (dd, *J* = 13,6, 1,9 Hz, 1H), 1,48-1,58 (m, 1H), 1,23-1,32 (m, 1H), 1,00 (s, 9H), 0,44-0,56 (m, 8H); MS (ESI+) *m/z* 542 $(M+H)^+$.

Ejemplo 501

N^2-ciclopentil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 419 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y ciclopentanona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,34-8,36 (m, 1H), 8,13-8,16 (m, 2H), 7,89-7,91 (m, 2H), 4,23-4,29 (m, 1H), 3,88 (dd, *J* = 10,0, 2,1 Hz, 1H), 3,34 (dd, *J* = 7,4, 4,3 Hz, 1H), 3,10-3,22 (m, 3H), 2,96-3,00 (m, 1H), 2,56-2,58 (m, 2H), 1,90-2,02 (m, 1H), 1,81-1,89 (m, 2H), 1,70-1,84 (m, 1H), 1,55-1,75 (m, 5H), 1,36-1,54 (m, 5H), 1,24-1,35 (m, 1H), 0,99 (s, 9H); MS (ESI+) *m/z* 530 $(M+H)^+$.

Ejemplo 502

N^2-ciclohexil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 419 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y ciclohexanona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,25-8,27 (m, 1H), 8,13-8,16 (m, 2H), 7,89-7,91 (m, 2H), 4,22-4,28 (m, 1H), 3,86 (dd, *J* = 9,9, 2,1 Hz, 1H), 3,42 (dd, *J* = 7,6, 3,8 Hz, 1H), 3,12-3,22 (m, 2H), 2,99 (dd, *J* = 9,6, 6,4 Hz, 1H), 2,55-2,65 (m, 2H), 2,47-2,53 (m, 1H), 1,91-2,01 (m, 1H), 1,78-1,91 (m, 4H), 1,65-1,76 (m, 1H), 1,60-1,67 (m, 2H), 1,54-1,60 (m, 1H), 1,45-1,52 (m, 2H), 1,28-1,37 (m, 1H), 1,03-1,25 (m, 5H), 1,00 (s, 9H); MS (ESI+) *m/z* 544 $(M+H)^+$.

Ejemplo 503

N^2-(1-etilpropil)-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 419 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-

(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y pentan-3-ona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,25-8,27 (m, 1H), 8,13-8,16 (m, 2H), 7,89-7,92 (m, 2H), 4,21-4,27 (m, 1H), 3,85 (d, *J* = 11,2 Hz, 1H), 3,40 (dd, *J* = 7,0, 4,7 Hz, 1H), 3,18 (dd, *J* = 10,2, 2,7 Hz, 2H), 2,97-3,02 (m, 1H), 2,55-2,59 (m, 2H), 2,45 (p, *J* = 5,7 Hz, 1H), 1,96 (dt, *J* = 11,8, 5,9 Hz, 1H), 1,86 (dd, *J* = 14,1, 4,5 Hz, 1H), 1,78-1,89 (m, 1H), 1,53-1,81 (m, 1H), 1,26-1,63 (m, 7H), 1,00 (s, 9H), 0,92 (t, *J* = 7,4 Hz, 3H), 0,84 (t, *J* = 7,4 Hz, 3H); MS (ESI+) *m/z* 532 $(M+H)^+$.

Ejemplo 504

N^2-ciclobutil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 419 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y ciclobutanona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (501 MHz, piridin-d_5) δ ppm 8,30-8,33 (m, 1H), 8,13-8,16 (m, 2H), 7,89-7,91 (m, 2H), 4,21-4,27 (m, 1H), 3,88 (dd, *J* = 10,0, 2,0 Hz, 1H), 3,31 (t, *J* = 6,5 Hz, 2H), 3,15-3,20 (m, 2H), 2,96-2,99 (m, 1H), 2,56-2,59 (m, 2H), 2,08-2,21 (m, 2H), 2,01-2,16 (m, 1H), 1,92-1,99 (m, 1H), 1,88 (dd, *J* = 14,1, 5,3 Hz, 1H), 1,82-1,86 (m, 2H), 1,70-1,78 (m, 1H), 1,48-1,64 (m, 4H), 1,27-1,34 (m, 1H), 0,98 (s, 9H); MS (ESI+) *m/z* 516 $(M+H)^+$.

Ejemplo 505

4-metil-N^2-neopentil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 419 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,20-8,22 (m, 1H), 8,14-8,16 (m, 2H), 7,89-7,92 (m, 2H), 4,21-4,28 (m, 1H), 3,86 (dd, *J* = 10,0, 2,8 Hz, 1H), 3,23 (dd, *J* = 7,9, 4,0 Hz, 1H), 3,17-3,21 (m, 2H), 3,00 (dd, *J* = 9,7, 7,2 Hz, 1H), 2,52-2,58 (m, 2H), 2,39 (d, *J* = 11,1 Hz, 1H), 2,31 (d, *J* = 11,1 Hz, 1H), 1,94-

2,01 (m, 1H), 1,87 (dd, *J* = 14,1, 4,2 Hz, 1H), 1,83-1,89 (m, 2H), 1,52-1,61 (m, 1H), 1,50 (dd, *J* = 14,0, 7,8 Hz, 1H), 1,29-1,36 (m, 1H), 0,99 (s, 9H), 0,92 (s, 9H); MS (ESI+) *m/z* 532 $(M+H)^+$.

Ejemplo 506

N^2-ciclopentil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

El compuesto del título se preparó utilizando N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida del Ejemplo 422 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y ciclopentanona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,30-8,33 (m, 1H), 8,12-8,15 (m, 2H), 7,88-7,91 (m, 2H), 4,21-4,29 (m, 1H), 3,86 (d, *J* = 11,3 Hz, 1H), 3,27 (t, *J* = 6,5 Hz, 1H), 3,12-3,21 (m, 3H), 2,96-3,01 (m, 1H), 2,50-2,64 (m, 2H), 1,89-2,18 (m, 2H), 1,24-1,90 (m, 15H), 0,86 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 502 $(M+H)^+$.

Ejemplo 507

N^2-ciclohexil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

El compuesto del título se preparó utilizando N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida del Ejemplo 422 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y ciclohexanona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,25-8,27 (m, 1H), 8,12-8,15 (m, 2H), 7,89-7,92 (m, 2H), 4,20-4,28 (m, 1H), 3,84 (dd, *J* = 10,0, 2,4 Hz, 1H), 3,35 (dd, *J* = 7,6, 5,4 Hz, 1H), 3,14-3,21 (m, 2H), 2,96-3,01 (m, 1H), 2,51-2,65 (m, 2H), 2,40-2,51 (m, 1H), 1,75-2,01 (m, 6H), 1,44-1,67 (m, 7H), 1,26-1,38 (m, 1H), 1,04-1,24 (m, 5H), 0,87 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 516 $(M+H)^+$.

Ejemplo 508

N^2-ciclopentil-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-ciclopentil-4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-4-metil-L-leucinamida

El compuesto del título se preparó utilizando 4-metil-N^1-[(3a*R*,4*S*,6a*S*)-2-(4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-L-leucinamida del Ejemplo 464 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y ciclopentanona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,73 (d, *J* = 5,6, 1H), 4,31 – 4,20 (m, 1H), 3,83 – 3,71 (m, 2H), 3,72-3,49 (m, 3H), 3,31 (dd, *J* = 7,2, 4,4, 1H), 3,19 – 3,07 (m, 2H), 2,78 – 2,63 (m, 2H), 2,12 (dt, *J* = 12,6, 6,4, 1H), 1,96 (tt, *J* = 5,7, 5,0, 1H), 1,86 – 1,59 (m, 12H), 1,57 – 1,33 (m, 12H), 1,04 (s, 9H), 0,99 (s, 9H); MS (ESI+) *m/z* 517 $(M+H)^+$.

Ejemplo 509

N^2,N^2-dimetil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 164 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y formaldehido en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,17-8,20 (m, 1H), 7,76-7,77 (bs, 1H), 7,63-7,65 (m, 2H), 7,50 (t, *J* = 7,7 Hz, 1H), 4,48-4,54 (m, 1H), 3,74 (d, *J* = 13,1 Hz, 1H), 3,30 (d, *J* = 13,1 Hz, 1H), 3,05 (dd, *J* = 9,0, 5,0 Hz, 1H), 2,74-2,78 (m, 1H), 2,68-2,74 (m, 1H), 2,42-2,47 (m, 1H), 2,33 (s, 7H), 2,21 (dd, *J* = 9,4, 7,2 Hz, 1H), 2,14 (dd, *J* = 9,0, 7,5 Hz, 1H), 1,76-1,89 (m, 3H), 1,67-1,74 (m, 1H), 1,53-1,61 (m, 2H), 1,21-1,28 (m, 1H), 0,96 (d, *J* = 6,6 Hz, 3H), 0,94 (d, *J* = 6,7 Hz, 3H); MS (ESI-) *m/z* 424 $(M-H)^-$.

Ejemplo 510

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-N^2-neopentil-L-leucinamida

El compuesto del título se preparó utilizando N^1-{(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida del Ejemplo 165 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-

d_5) δ ppm 8,15-8,17 (m, 1H), 7,43-7,46 (m, 2H), 7,37 (t, *J* = 7,5 Hz, 2H), 7,28 (t, *J* = 7,3 Hz, 1H), 4,39-4,45 (m, 1H), 3,61 (d, *J* = 13,1 Hz, 1H), 3,46 (d, *J* = 13,1 Hz, 1H), 3,27 (dd, *J* = 7,9, 6,0 Hz, 1H), 2,85 (dd, *J* = 8,9, 2,0 Hz, 1H), 2,52-2,58 (m, 2H), 2,46-2,52 (m, 2H), 2,45 (s, 3H), 2,43 (d, *J* = 13,8 Hz, 1H), 2,29-2,36 (m, 2H), 2,12 (dq, *J* = 12,2, 6,1 Hz, 1H), 1,82-2,02 (m, 3H), 1,53-1,63 (m, 2H), 1,37-1,47 (m, 1H), 0,95 (d, *J* = 6,6 Hz, 3H), 0,94 (d, *J* = 6,6 Hz, 3H), 0,90 (s, 9H); MS (ESI+) *m/z* 414 $(M+H)^+$.

Ejemplo 511

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(3,3-dimetilbutil)-N^2-metil-L-leucinamida

El compuesto del título se preparó utilizando N^1-{(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida del Ejemplo 165 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y 3,3-dimetilbutanal en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,04-8,06 (m, 1H), 7,43-7,46 (m, 2H), 7,37 (t, *J* = 7,5 Hz, 2H), 7,28 (t, *J* = 7,4 Hz, 1H), 4,42-4,48 (m, 1H), 3,63 (d, *J* = 13,1 Hz, 1H), 3,46 (d, *J* = 13,1 Hz, 1H), 3,33 (dd, *J* = 8,2, 5,3 Hz, 1H), 2,89-2,92 (m, 1H), 2,55-2,66 (m, 4H), 2,44-2,48 (m, 1H), 2,39 (s, 3H), 2,36-2,39 (m, 1H), 2,27 (dd, *J* = 8,8, 6,1 Hz, 1H), 2,12 (dq, *J* = 11,9, 6,0 Hz, 1H), 1,83-1,99 (m, 3H), 1,56-1,63 (m, 2H), 1,40-1,48 (m, 3H), 0,95 (d, *J* = 6,3 Hz, 6H), 0,89 (s, 9H); MS (ESI+) *m/z* 428 $(M+H)^+$.

Ejemplo 512

N^2,N^2-dimetil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida

El compuesto del título se preparó utilizando N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida del Ejemplo 184 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y formaldehido en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,38-8,39 (bs, 1H), 8,18-8,25 (m, 2H), 7,90-7,92 (m, 1H), 7,72 (t, *J* = 7,8 Hz, 1H), 4,20-4,25 (m, 1H), 3,88 (d, *J* = 10,8 Hz, 1H), 3,18 (dd, *J* = 9,8, 2,5 Hz, 1H), 3,11-3,18 (m, 2H), 2,95-2,98 (m, 1H), 2,51-2,60 (m, 2H), 2,32 (s, 6H), 1,90-1,97 (m, 1H), 1,75-1,86 (m, 3H), 1,49-1,60 (m, 2H), 1,24-1,32 (m, 1H),

0,90 (d, J = 6,4 Hz, 3H), 0,90 (d, J = 6,4 Hz, 3H); MS (ESI+) m/z 476 $(M+H)^+$.

Ejemplo 513

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(4-fluorobencil)-N^2-metil-L-leucinamida

El compuesto del título se preparó utilizando N^1-{(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida del Ejemplo 165 en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y 4-fluorobenzaldehido en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,25-8,27 (m, 1H), 7,36-7,46 (m, 6H), 7,28 (t, J = 7,3 Hz, 1H), 7,13-7,17 (m, 2H), 4,45-4,50 (m, 1H), 3,86 (d, J = 13,7 Hz, 1H), 3,76 (d, J = 13,7 Hz, 1H), 3,63 (d, J = 13,1 Hz, 1H), 3,47 (d, J = 13,1 Hz, 1H), 3,41 (dd, J = 7,7, 6,2 Hz, 1H), 2,91 (dd, J = 9,0, 2,7 Hz, 1H), 2,53-2,64 (m, 2H), 2,49 (dd, J = 8,8, 7,0 Hz, 1H), 2,34-2,39 (m, 1H), 2,36 (s, 3H), 2,30 (dd, J = 8,9, 6,9 Hz, 1H), 2,10-2,22 (m, 1H), 1,84-1,94 (m, 3H), 1,67-1,76 (m, 1H), 1,59-1,67 (m, 1H), 1,39-1,46 (m, 1H), 0,93 (d, J = 6,8 Hz, 3H), 0,91 (d, J = 6,6 Hz, 3H); MS (ESI+) m/z 452 $(M+H)^+$.

Ejemplo 514

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-(metilsulfonil)piperidin-2-carboxamida

El compuesto del título se preparó utilizando (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]piperidin-2-carboxamida del Ejemplo 350 en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo en el procedimiento descrito en Ejemplo 242 Paso A: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,54 (d, J = 7,2, 1H), 7,43 (d, J = 7,2, 2H), 7,37 (dd, J = 10,2, 4,7, 2H), 7,28 (t, J = 7,2, 1H), 4,89 (d, J = 3,1, 1H), 4,40 – 4,31 (m, 1H), 3,90 – 3,77 (m, 2H), 3,57 (d, J = 13,1, 1H), 3,45 (d, J = 13,1, 1H), 3,15 (s, 3H), 2,79 (dd, J = 9,0, 2,1, 1H), 2,54 – 2,41 (m, 2H), 2,40 – 2,31 (m, 2H), 2,24 (dd, J = 8,8, 6,9, 1H), 2,20 – 2,14 (m, 1H), 2,09 (dq, J = 12,0, 6,0, 1H), 1,88 – 1,78 (m, 1H), 1,67 – 1,53 (m, 4H), 1,51 – 1,34 (m, 3H); MS (ESI+) m/z 406 $(M+H)^+$.

Ejemplo 515

(3*R*)-4-metil-3-[(metilsulfonil)amino]-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida

El compuesto del título se preparó utilizando (3*R*)-3-amino-4-metil-*N*-

((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida del Ejemplo 388 en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo en el procedimiento descrito en Ejemplo 242 Paso A: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,77 (d, *J* = 6,6, 1H), 8,42 – 8,34 (m, 2H), 8,20 (d, *J* = 7,8, 1H), 7,91 (d, *J* = 7,8, 1H), 7,72 (t, *J* = 7,9, 1H), 4,21 (dq, *J* = 13,4, 6,1, 2H), 3,85 (dd, *J* = 9,9, 1,7, 1H), 3,23 (s, 3H), 3,17 (dd, *J* = 9,6, 1,9, 1H), 3,11 (dd, *J* = 9,8, 7,3, 1H), 2,93 (dd, *J* = 9,5, 7,1, 1H), 2,76 – 2,65 (m, 2H), 2,56 – 2,45 (m, 2H), 2,11 (dq, *J* = 13,5, 6,8, 1H), 1,95 (td, *J* = 12,2, 6,3, 1H), 1,83 (dt, *J* = 12,5, 6,4, 1H), 1,55 (ddd, *J* = 15,9, 12,3, 9,1, 1H), 1,28 (ddd, *J* = 12,8, 9,4, 6,3, 1H), 1,02 (d, *J* = 6,8, 3H), 0,97 (d, *J* = 6,8, 3H); MS (ESI+) *m/z* 524 $(M+H)^+$.

Ejemplo 516

N^2-(metilsulfonil)-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

Paso A: Se preparó (S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo utilizando (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 156 Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,67 (d, *J* = 7,2, 1H), 7,96 (d, *J* = 8,4, 1H), 7,75 (s, 1H), 7,61 (s, 1H), 7,56 (s, 1H), 7,45 (dd, *J* = 14,3, 6,7, 1H), 4,75 – 4,66 (m, 1H), 4,45 – 4,36 (m, 1H), 3,59 (d, *J* = 13,5, 1H), 3,46 (d, *J* = 13,6, 1H), 2,81 (dd, *J* = 9,1, 2,3, 1H), 2,62 – 2,56 (m, 1H), 2,56 – 2,49 (m, 1H), 2,49 – 2,43 (m, 1H), 2,27 (d, *J* = 5,3, 2H), 2,03 (td, *J* = 11,6, 5,7, 1H), 1,94 – 1,78 (m, 4H), 1,65 – 1,56 (m, 1H), 1,50 (s, 9H), 1,35 (dt, *J* = 13,6, 5,7, 1H), 0,86 (dd, *J* = 11,2, 5,7, 6H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Paso B: Se preparó N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(Trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida utilizando (S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,31 (d, *J* = 7,5, 1H), 7,76 (s, 1H), 7,62 (d, *J* =

7,9, 1H), 7,56 (s, 1H), 7,46 (t, *J* = 7,7, 1H), 4,44 – 4,33 (m, 1H), 3,63 – 3,56 (m, 2H), 3,47 (d, *J* = 13,5, 1H), 2,83 (dd, *J* = 9,0, 2,3, 1H), 2,58 – 2,46 (m, 2H), 2,44 – 2,39 (m, 1H), 2,32 (dd, *J* = 9,0, 2,6, 1H), 2,28 – 2,23 (m, 1H), 2,08 (td, *J* = 11,9, 5,9, 2H), 1,95 – 1,81 (m, 4H), 1,62 – 1,51 (m, 2H), 1,43 – 1,34 (m, 1H), 0,90 (d, *J* = 6,3, 3H), 0,85 (d, *J* = 6,2, 3H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Paso C: El compuesto del título se preparó utilizando *N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Paso B en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo en el procedimiento descrito en Ejemplo 242 Paso A: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,36 (d, *J* = 8,9, 1H), 9,24 (d, *J* = 7,3, 1H), 7,78 (s, 1H), 7,62 (d, *J* = 8,2, 2H), 7,46 (t, *J* = 7,7, 1H), 4,48 (qd, *J* = 13,1, 7,5, 2H), 3,62 (d, *J* = 13,5, 1H), 3,50 (d, *J* = 13,5, 1H), 3,20 (s, 3H), 2,86 (dd, *J* = 9,1, 2,9, 1H), 2,64 (dt, *J* = 8,4, 6,1, 1H), 2,60 – 2,53 (m, 1H), 2,49 (dd, *J* = 8,8, 7,5, 1H), 2,34 – 2,27 (m, 2H), 2,15 – 2,09 (m, 1H), 2,04 – 1,95 (m, 1H), 1,90 (ddd, *J* = 14,5, 9,2, 4,2, 2H), 1,78 (ddd, *J* = 13,9, 8,5, 5,7, 1H), 1,65 (dt, *J* = 19,1, 7,2, 1H), 1,41 (dq, *J* = 13,9, 6,1, 1H), 0,83 (d, *J* = 6,7, 3H), 0,81 (d, *J* = 6,6, 3H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Ejemplo 517

N^2-(metilsulfonil)-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida

Paso A: Se preparó (R)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo utilizando (3a*R*,4*S*,6a*S*)-2-(3-(trifluorometil)bencil)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 156 Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina y *N*-(*tert*-butoxicarbonil)-D-leucina en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,70 (d, *J* = 7,4, 1H), 7,95 (d, *J* = 8,4, 1H), 7,73 (s, 1H), 7,59 (s, 1H), 7,56 (s, 1H), 7,45 (t, *J* = 7,7, 1H), 4,72 (br s, 1H), 4,40 (br s, 1H), 3,57 (d, *J* = 13,4, 1H), 3,42 (d, *J* = 13,6, 1H), 2,73 (d, *J* = 9,0, 1H), 2,50 (s, 2H), 2,39 – 2,32 (m, 1H), 2,25 (dd, *J* = 12,9, 7,0, 2H), 2,11 (dq, *J* = 12,3, 6,2, 1H), 1,94 – 1,78 (m, 4H), 1,66 (dq, *J* = 21,9, 7,3, 1H), 1,50 (s, 9H), 1,39 (d, *J* = 7,0, 1H), 0,86 (dd, *J* = 10,2, 5,6, 6H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Paso B: *N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[3-

(Trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida se preparó utilizando (R)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,33 (d, *J* = 7,6, 1H), 7,75 (s, 1H), 7,62 (s, 1H), 7,56 (s, 1H), 7,46 (t, *J* = 7,7, 1H), 4,43 – 4,34 (m, 1H), 3,64 – 3,56 (m, 2H), 3,46 (d, *J* = 13,5, 1H), 2,82 (dd, *J* = 9,0, 2,5, 1H), 2,59 – 2,45 (m, 2H), 2,44 – 2,39 (m, 1H), 2,31 (dd, *J* = 9,0, 2,8, 1H), 2,25 (dd, *J* = 8,8, 7,1, 1H), 2,09 (td, *J* = 11,9, 5,9, 2H), 1,88 (tdd, *J* = 13,5, 8,9, 6,0, 4H), 1,57 (tt, *J* = 18,0, 6,6, 2H), 1,44 – 1,34 (m, 1H), 0,90 (d, *J* = 6,4, 3H), 0,85 (d, *J* = 6,3, 3H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Paso C: El compuesto del título se preparó utilizando *N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Paso B en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo en el procedimiento descrito en Ejemplo 242 Paso A: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,35 (d, *J* = 8,5, 1H), 9,24 (d, *J* = 7,2, 1H), 7,76 (s, 1H), 7,63 – 7,56 (m, 2H), 7,45 (dd, *J* = 14,6, 7,0, 1H), 4,47 (dt, *J* = 13,0, 8,2, 2H), 3,59 (d, *J* = 13,6, 1H), 3,48 (d, *J* = 13,5, 1H), 3,18 (s, 3H), 2,85 (dd, *J* = 9,1, 2,5, 1H), 2,63 – 2,49 (m, 2H), 2,39 (dd, *J* = 9,0, 7,1, 1H), 2,33 (dd, *J* = 9,0, 2,6, 1H), 2,29 – 2,22 (m, 1H), 2,15 (dt, *J* = 12,2, 6,1, 1H), 2,04 – 1,95 (m, 1H), 1,94 – 1,84 (m, 2H), 1,81 – 1,66 (m, 2H), 1,43 (dt, *J* = 21,0, 6,4, 1H), 0,85 – 0,79 (m, 6H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Ejemplo 518

N^2-etil-N^2-(metilsulfonil)-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando *N*^{2}-etil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 366 en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo en el procedimiento descrito en Ejemplo 242 Paso A: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,83 (d, *J* = 7,3, 1H), 7,77 (s, 1H), 7,63 – 7,55 (m, 2H), 7,45 (t, *J* = 7,7, 1H), 4,71 (t, *J* = 6,9, 1H), 4,43 – 4,34 (m, 1H), 3,93 (td, *J* = 13,9, 6,8, 1H), 3,63 – 3,45 (m, 3H), 3,15 (d, *J* = 5,3, 3H), 2,89 – 2,81 (m, 1H), 2,54 (ddd, *J* = 29,4, 12,7, 9,2, 2H), 2,46 – 2,42 (m, 1H), 2,39 – 2,30 (m, 1H), 2,24 (dd, *J* = 17,4, 8,7, 1H), 2,08 (ddt, *J* = 17,6, 11,7,

5,8, 1H), 1,90 – 1,75 (m, 4H), 1,68 – 1,53 (m, 1H), 1,40 (dd, *J* = 12,7, 6,4, 1H), 1,36 – 1,30 (m, 3H), 0,85 (d, *J* = 5,4, 3H), 0,82 (t, *J* = 5,3, 3H); MS (ESI+) *m/z* 502 $(M+H)^+$.

Ejemplo 519

4-metil-*N*^{2}-(metilsulfonil)-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

Paso A: Se preparó (S)-1-((3aR,4S,6aS)-2-[4-trifluorometil)bencil]octahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo del Ejemplo 226 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida en el procedimiento descrito en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,60 (d, *J* = 7,5, 1H), 8,12 (d, *J* = 8,9, 1H), 7,65 (d, *J* = 8,0, 2H), 7,51 (d, *J* = 8,0, 2H), 4,75 (td, *J* = 8,4, 5,1, 1H), 4,45 – 4,37 (m, 1H), 3,56 (d, *J* = 13,8, 1H), 3,46 (d, *J* = 13,7, 1H), 2,86 (dd, *J* = 9,0, 2,2, 1H), 2,62 – 2,46 (m, 2H), 2,42 – 2,36 (m, 1H), 2,30 (dd, *J* = 8,7, 2,2, 1H), 2,26 – 2,20 (m, 1H), 2,19 – 2,12 (m, 1H), 2,04 (td, *J* = 11,7, 5,7, 1H), 1,89 – 1,80 (m, 2H), 1,64 – 1,53 (m, 1H), 1,51 (s, 9H), 1,36 (dt, *J* = 21,2, 7,3, 1H), 0,98 (s, 9H); MS (ESI+) *m/z* 512 $(M+H)^+$.

Paso B: Se preparó 4-Metil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida utilizando (S)-1-((3aR,4S,6aS)-2-[4-trifluorometil)bencil]octahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,31 (d, *J* = 7,7, 1H), 7,65 (d, *J* = 8,0, 2H), 7,52 (d, *J* = 7,9, 2H), 4,45 – 4,31 (m, 1H), 3,62 – 3,53 (m, 2H), 3,47 (d, *J* = 13,9, 1H), 2,89 (d, *J* = 8,4, 1H), 2,58 – 2,43 (m, 2H), 2,35 (t, *J* = 7,6, 2H), 2,25 – 2,15 (m, 3H), 2,10 (dt, *J* = 11,7, 6,7, 2H), 1,87 (td, *J* = 13,1, 6,6, 1H), 1,57 (dt, *J* = 14,8, 7,7, 1H), 1,48 – 1,36 (m, 2H), 0,98 (s, 9H); MS (ESI+) *m/z* 412 $(M+H)^+$.

Paso C: El compuesto del título se preparó utilizando 4-metil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Paso B en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo

en el procedimiento descrito en Ejemplo 242 Paso A: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,55 (d, *J* = 9,7, 1H), 9,30 (d, *J* = 7,3, 1H), 7,66 (d, *J* = 8,1, 2H), 7,54 (d, *J* = 8,0, 2H), 4,57 – 4,51 (m, 1H), 4,51 – 4,44 (m, 1H), 3,60 (d, *J* = 13,8, 1H), 3,50 (d, *J* = 13,8, 1H), 3,18 (s, 3H), 2,92 (dd, *J* = 9,0, 2,5, 1H), 2,67 – 2,61 (m, 1H), 2,58 – 2,50 (m, 1H), 2,43 (dd, *J* = 8,9, 7,3, 1H), 2,36 (dd, *J* = 9,0, 2,6, 1H), 2,25 (dd, *J* = 8,7, 7,5, 1H), 2,17 – 2,10 (m, 1H), 2,03 (dd, *J* = 14,1, 5,4, 1H), 1,95 – 1,85 (m, 2H), 1,64 (dtd, *J* = 12,2, 8,1, 5,8, 1H), 1,46 – 1,37 (m, 1H), 0,96 (s, 9H); MS (ESI+) *m/z* 490 $(M+H)^+$.

Ejemplo 520

3-metil-*N*^{2}-(metilsulfonil)-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-valinamida

Paso A: Se preparó (S)-1-((3aR,4S,6aS)-2-[4-(trifluorometil)bencil]octahidrociclopenta[c]pirrol-4–ilamino)-3,3-dimetil-1-oxobutan-2–ilcarbamato de tert-butilo utilizando (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3,3-dimetil-1-oxobutan-2–ilcarbamato de tert-butilo del Ejemplo 225 en lugar de (2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida en el procedimiento descrito en Ejemplo 303: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,72 (d, *J* = 9,7, 1H), 7,66 (d, *J* = 8,1, 2H), 7,52 (d, *J* = 8,0, 2H), 7,37 (d, *J* = 3,1, 1H), 4,61 (d, *J* = 9,8, 1H), 4,46 – 4,39 (m, 1H), 3,60 (d, *J* = 13,7, 1H), 3,46 (d, *J* = 13,7, 1H), 2,89 (dd, *J* = 9,1, 2,5, 1H), 2,63 – 2,57 (m, 1H), 2,57 – 2,50 (m, 1H), 2,46 – 2,41 (m, 1H), 2,35 – 2,29 (m, 1H), 2,28 – 2,22 (m, 1H), 1,99 (dq, *J* = 11,8, 5,7, 1H), 1,84 (td, *J* = 12,7, 6,2, 1H), 1,57 – 1,49 (m, 1H), 1,48 (s, 9H), 1,40 – 1,31 (m, 1H), 1,18 (s, 9H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Paso B: Se preparó 3-Metil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-valinamida utilizando (S)-1-((3aR,4S,6aS)-2-[4-(trifluorometil)bencil]octahidrociclopenta[c]pirrol-4–ilamino)-3,3-dimetil-1-oxobutan-2–ilcarbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,15 – 8,06 (m, 1H), 7,66 (d, *J* = 8,1, 2H), 7,52 (d, *J* = 8,0, 2H), 4,47 – 4,40 (m, 1H), 3,59 (d, *J* = 13,6, 1H), 3,46 (d, *J* = 13,8, 1H), 3,27 (s, 1H), 2,89 – 2,85 (m, 1H), 2,56 – 2,50 (m, 2H), 2,41 – 2,36 (m, 1H), 2,35 –

2,32 (m, 1H), 2,26 – 2,21 (m, 1H), 2,19 – 2,12 (m, 2H), 2,11 – 2,02 (m, 1H), 1,90 – 1,82 (m, 1H), 1,60 – 1,52 (m, 1H), 1,43 – 1,35 (m, 1H), 1,14 (s, 9H); MS (ESI+) *m/z* 398 $(M+H)^+$.

Paso C: El compuesto del título se preparó utilizando 3-metil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-valinamida del Paso B en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo en el procedimiento descrito en Ejemplo 242 Paso A: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,28 (d, *J* = 10,4, 1H), 9,13 (d, *J* = 7,4, 1H), 7,67 (d, *J* = 8,1, 2H), 7,55 (d, *J* = 8,1, 2H), 4,54 – 4,46 (m, 1H), 4,19 (d, *J* = 10,4, 1H), 3,64 (d, *J* = 13,7, 1H), 3,50 (d, *J* = 13,7, 1H), 3,13 (s, 3H), 2,92 (dd, *J* = 9,0, 2,4, 1H), 2,67 – 2,52 (m, 2H), 2,46 (dd, *J* = 8,8, 7,1, 1H), 2,37 (dd, *J* = 9,0, 2,5, 1H), 2,30 – 2,23 (m, 1H), 2,09 (dq, *J* = 11,7, 5,8, 1H), 1,94 – 1,83 (m, 1H), 1,62 – 1,53 (m, 1H), 1,45 – 1,37 (m, 1H), 1,18 (s, 9H); MS (ESI+) *m/z* 476 $(M+H)^+$.

Ejemplo 521

N^2-(metilsulfonil)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida

El compuesto del título se preparó utilizando *N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida del Ejemplo 382 en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo en el procedimiento descrito en Ejemplo 242 Paso A: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,42 (d, *J* = 9,2, 1H), 9,10 (d, *J* = 7,4, 1H), 7,66 (d, *J* = 8,0, 2H), 7,53 (d, *J* = 8,0, 2H), 4,50 – 4,39 (m, 2H), 3,60 (d, *J* = 13,7, 1H), 3,49 (d, *J* = 13,7, 1H), 3,19 (s, 3H), 2,89 (dd, *J* = 9,1, 2,4, 1H), 2,65 – 2,58 (m, 1H), 2,58 – 2,51 (m, 1H), 2,46 – 2,40 (m, 1H), 2,35 (dd, *J* = 9,0, 2,5, 1H), 2,28 – 2,23 (m, 1H), 2,13 (dt, *J* = 11,9, 6,0, 1H), 1,98 (tt, *J* = 13,2, 6,5, 1H), 1,94 – 1,83 (m, 2H), 1,63 (dt, *J* = 19,4, 7,6, 1H), 1,58 – 1,47 (m, 2H), 1,42 (dt, *J* = 14,6, 6,3, 1H), 0,77 (t, *J* = 7,4, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 522

N^2-(isopropilsulfonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando *N*^{1}-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 170 Paso B en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo y cloruro de propan-2-sulfonilo en lugar de cloruro de metansulfonilo en el procedimiento

descrito en Ejemplo 242 Paso A: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,34 (d, *J* = 9,2, 1H), 9,12 (d, *J* = 7,4, 1H), 7,75 (d, *J* = 12,2, 2H), 7,61 (d, *J* = 7,5, 1H), 7,45 (t, *J* = 7,8, 1H), 4,50 – 4,41 (m, 2H), 3,58 (d, *J* = 13,5, 1H), 3,51 (d, *J* = 13,4, 1H), 3,38 – 3,31 (m, 1H), 2,89 (d, *J* = 9,6, 1H), 2,56 (qd, *J* = 5,6, 1,6, 2H), 2,41 – 2,34 (m, 2H), 2,25 (dd, *J* = 8,7, 6,7, 1H), 2,19 – 2,12 (m, 1H), 2,06 – 1,97 (m, 1H), 1,95 – 1,86 (m, 3H), 1,79 – 1,66 (m, 2H), 1,46 (d, *J* = 6,8, 6H), 0,82 (d, *J* = 6,5, 1H); MS (ESI+) *m/z* 504 $(M+H)^+$.

Ejemplo 523

N^2-(fenilsulfonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 170 Paso B en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo y cloruro de bencensulfonilo en lugar de cloruro de metansulfonilo en el procedimiento descrito en Ejemplo 242 Paso A: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 10,09 – 9,90 (m, 1H), 8,77 (d, *J* = 7,3, 1H), 8,18 (dd, *J* = 8,0, 1,5, 2H), 7,78 (s, 1H), 7,62 (d, *J* = 7,9, 1H), 7,51 – 7,34 (m, 5H), 4,36 (dd, *J* = 9,4, 5,5, 1H), 4,16 – 4,08 (m, 1H), 3,59 (d, *J* = 13,5, 1H), 3,49 (d, *J* = 13,6, 1H), 2,60 (dd, *J* = 9,1, 3,0, 1H), 2,51 – 2,42 (m, 1H), 2,33 (dd, *J* = 8,9, 7,6, 1H), 2,27 (dd, *J* = 11,1, 6,5, 2H), 2,24 – 2,17 (m, 1H), 2,05 (td, *J* = 12,1, 5,9, 1H), 1,98 (dd, *J* = 13,8, 6,7, 1H), 1,88 – 1,79 (m, 2H), 1,72 (ddd, *J* = 13,7, 8,6, 5,4, 1H), 1,58 (dt, *J* = 19,1, 7,0, 1H), 1,36 (dt, *J* = 20,4, 6,2, 1H), 0,81 (d, *J* = 6,7, 3H), 0,77 (d, *J* = 6,5, 3H); MS (ESI+) *m/z* 538 $(M+H)^+$.

Ejemplo 524

N^2-(ciclopentilsulfonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida

El compuesto del título se preparó utilizando N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 170 Paso B en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo y cloruro de ciclopentansulfonilo en lugar de cloruro de metansulfonilo en el procedimiento descrito en Ejemplo 242 Paso A: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,30 (d, *J* = 9,6, 1H), 9,12 (d, *J* = 7,5, 1H), 7,76 (d, *J* = 15,6, 2H), 7,45 (dd, *J* = 17,4, 9,7, 2H), 4,53 – 4,44 (m, 2H), 3,59 (d, *J* = 13,4, 1H), 3,53 (d, *J* = 13,7, 1H), 2,91 (d, *J* = 8,0, 1H), 2,60 – 2,54 (m, 2H), 2,39 (t, *J* = 9,0, 2H), 2,34 – 2,10 (m, 6H), 2,08 – 1,99 (m,

2H), 1,96 – 1,85 (m, 3H), 1,79 – 1,63 (m, 3H), 1,49 – 1,35 (m, 3H), 0,82 (d, *J* = 6,6, 6H); MS (ESI+) *m/z* 530 $(M+H)^+$.

Ejemplo 525

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de isopropilo

El compuesto del título se preparó utilizando 4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida del Ejemplo 519 Paso B en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo y cloroformiato de isopropilo en lugar de cloruro de metansulfonilo en el procedimiento descrito en Ejemplo 242 Paso A: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,38 (d, *J* = 9,0, 1H), 7,65 (d, *J* = 8,1, 2H), 7,51 (d, *J* = 8,0, 2H), 5,08 (dt, *J* = 12,8, 6,5, 1H), 4,81 (td, *J* = 8,5, 5,3, 1H), 4,46 – 4,38 (m, 1H), 3,57 (d, *J* = 13,7, 1H), 3,46 (d, *J* = 13,8, 1H), 2,88 (dd, *J* = 8,8, 1,7, 1H), 2,63 – 2,54 (m, 1H), 2,49 (tt, *J* = 4,3, 3,3, 1H), 2,43 – 2,36 (m, 1H), 2,31 (dd, *J* = 8,9, 2,5, 1H), 2,25 – 2,21 (m, 1H), 2,21 – 2,17 (m, 1H), 2,16 (d, *J* = 4,8, 1H), 2,10 – 1,99 (m, 1H), 1,90 – 1,77 (m, 2H), 1,59 (ddd, *J* = 14,7, 12,6, 7,8, 1H), 1,41 – 1,32 (m, 1H), 1,23 (d, *J* = 6,2, 3H), 1,14 (d, *J* = 6,2, 3H), 0,98 (s, 9H); MS (ESI+) *m/z* 498 $(M+H)^+$.

Ejemplo 526

(S)-3,3-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–ilcarbamato de isopropilo

El compuesto del título se preparó utilizando 3-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-valinamida del Ejemplo 520 Paso B en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo y cloroformiato de isopropilo en lugar de cloruro de metansulfonilo en el procedimiento descrito en Ejemplo 242 Paso A: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,84 (d, *J* = 7,3, 1H), 8,05 (d, *J* = 9,6, 1H), 7,66 (d, *J* = 8,1, 2H), 7,52 (d, *J* = 8,0, 2H), 5,06 (dt, *J* = 12,6, 6,3, 1H), 4,67 (d, *J* = 9,8, 1H), 4,44 (p, *J* = 7,3, 1H), 3,61 (d, *J* = 13,8, 1H), 3,47 (d, *J* = 13,7, 1H), 2,89 (dd, *J* = 9,0, 2,5, 1H), 2,66 – 2,58 (m, 1H), 2,57 – 2,50 (m, 1H), 2,49 – 2,41 (m, 1H), 2,29 (dt, *J* = 15,8, 7,5, 2H), 2,00 (td, *J* = 11,5, 5,3, 1H), 1,85 (dt, *J* = 20,3, 6,6, 1H), 1,54 (dt, *J* = 15,1, 7,3, 1H), 1,41 – 1,30 (m, 1H), 1,24 (d, *J* = 6,2, 3H), 1,19 (s, 9H), 1,12 (d, *J* = 6,0, 3H); MS (ESI+) *m/z* 484 $(M+H)^+$.

Ejemplo 527

(S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de ciclopentilo

El compuesto del título se preparó utilizando *N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida del Ejemplo 382 en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo y cloroformiato de ciclopentilo en lugar de cloruro de metansulfonilo en el procedimiento descrito en Ejemplo 242 Paso A: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,76 (d, *J* = 1,7, 1H), 8,22 (d, *J* = 8,4, 1H), 7,65 (d, *J* = 8,1, 2H), 7,51 (d, *J* = 7,9, 2H), 5,32 – 5,24 (m, 1H), 4,71 (dd, *J* = 14,3, 7,9, 1H), 4,49 – 4,39 (m, 1H), 3,57 (d, *J* = 13,7, 1H), 3,46 (d, *J* = 14,0, 1H), 2,87 (dd, *J* = 8,8, 1,7, 1H), 2,63 – 2,50 (m, 2H), 2,41 (dd, *J* = 8,6, 7,5, 1H), 2,31 (dd, *J* = 8,0, 1,8, 1H), 2,27 – 2,20 (m, 1H), 2,12 – 1,98 (m, 2H), 1,93 – 1,82 (m, 2H), 1,81 – 1,73 (m, 2H), 1,73 – 1,65 (m, 2H), 1,65 – 1,55 (m, 3H), 1,54 – 1,45 (m, 2H), 1,45 – 1,31 (m, 3H), 0,81 (t, *J* = 7,4, 3H); MS (ESI+) *m/z* 496 $(M+H)^+$.

Ejemplo 528

***N*^{2}-(2,2-dimetilpropanoil)-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida**

El compuesto del título se preparó utilizando *N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida del Ejemplo 382 en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo y cloruro de pivaloilo en lugar de cloruro de metansulfonilo en el procedimiento descrito en Ejemplo 242 Paso A: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,70 (d, *J* = 7,6, 1H), 7,72 (d, *J* = 7,9, 1H), 7,65 (d, *J* = 8,0, 2H), 7,51 (d, *J* = 8,0, 2H), 4,45 – 4,36 (m, 1H), 3,57 (d, *J* = 13,9, 1H), 3,47 (d, *J* = 13,8, 1H), 2,85 (dd, *J* = 9,1, 2,0, 1H), 2,60 – 2,51 (m, 2H), 2,42 (dd, *J* = 8,8, 6,9, 1H), 2,32 (dd, *J* = 8,9, 2,0, 1H), 2,28 – 2,23 (m, 1H), 2,06 (dq, *J* = 12,1, 6,0, 1H), 1,97 (dq, *J* = 9,4, 6,4, 1H), 1,90 – 1,75 (m, 2H), 1,59 (dt, *J* = 14,2, 7,3, 1H), 1,51 – 1,37 (m, 3H), 1,36 (s, 1H), 1,31 (s, 9H), 0,79 (t, *J* = 7,4, 3H); MS (ESI+) *m/z* 468 $(M+H)^+$.

Ejemplo 529

(S)-1-((3aR,4S,6aS)-2-(3-cloro-4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 313 Paso A en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y 3-cloro-cloruro de 4-fluorobencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: ^{1}H NMR (300 MHz, $CDCl_3$) ppm 7,88 (dd, *J* = 6,7, 2,2 Hz, 1H), 7,70 (ddd, *J* = 8,6, 4,4, 2,2 Hz, 1H), 7,26-7,33 (m, 1H), 5,73-6,40 (m, 1H), 4,43 (d, *J* = 4,3 Hz, 1H), 3,85-3,95 (m, 1H), 3,40-3,52 (m, 1H), 3,09 (dd, *J* = 9,6, 3,2 Hz, 1H), 3,05 (dd, *J* = 10,1, 8,3 Hz, 1H), 2,97 (dd, *J* = 9,6, 7,4 Hz, 1H), 2,73 (s, 3H), 2,63-2,76 (m, 2H), 2,32-2,42 (m, 1H), 1,76-2,09 (m, 3H), 1,58-1,72 (m, 1H), 1,46 (s, 9H), 1,19-1,34 (m, 3H), 0,94 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 532 $(M+H)^+$.

Ejemplo 530

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(piridin-3–ilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 313 Paso A en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de piridin-3-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 9,01-9,04 (bs, 1H), 8,80-8,85 (bs, 1H), 8,09 (ddd, *J* = 8,0, 2,2, 1,7 Hz, 1H), 7,49 (dd, *J* = 8,0, 4,8 Hz, 1H), 5,78-6,33 (m, 1H), 4,32-4,52 (m, 1H), 3,84-3,95 (m, 1H), 3,40-3,52 (m, 1H), 3,05-3,15 (m, 2H), 3,02 (dd, *J* = 9,7, 7,4 Hz, 1H), 2,73 (s, 3H), 2,61-2,75 (m, 1H), 2,33-2,50 (m, 1H), 1,77-2,07 (m, 3H), 1,53-1,71 (m, 2H), 1,46 (s, 9H), 1,18-1,32 (m, 3H), 0,94 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 481 $(M+H)^+$.

Ejemplo 531

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(tiofen-2–ilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 313 Paso A en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de tiofen-2-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: ^{1}H NMR (300 MHz, $CDCl_3$) δ ppm 7,62 (dd, *J* = 5,0, 1,3 Hz, 1H), 7,56 (dd, *J* = 3,7, 1,3 Hz, 1H), 7,16 (dd, *J* = 5,0, 3,7 Hz, 1H), 5,75-6,30 (m, 1H), 4,33-4,53 (m, 1H), 3,88-3,97 (m, 1H), 3,37 (dd, *J* = 10,2, 3,6 Hz, 1H), 3,04-3,20 (m, 3H), 2,73 (s, 3H), 2,63-2,75 (m, 1H), 2,36-2,50 (m, 1H), 1,77-2,10 (m, 3H), 1,55-1,71 (m, 1H), 1,46 (s, 9H), 1,35-1,55 (m, 2H), 1,19-1,32 (m, 2H), 0,94 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 486 $(M+H)^+$.

Ejemplo 532

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometoxi)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

Paso A: Se preparó metil((S)-1-oxo-1-((3aR,4S,6aS)-2-{[4-(trifluorometoxi)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 313 Paso A en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-(trifluorometoxi)bencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: MS (APCI+) *m/z* 564 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-{[4-(trifluorometoxi)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-

2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,99-10,02 (m, 1H), 8,05-8,07 (m, 2H), 7,50-7,52 (m, 2H), 4,55-4,59 (m, 1H), 4,26-4,36 (m, 1H), 3,73 (dd, *J* = 9,9, 2,8 Hz, 1H), 3,18 (dd, *J* = 9,6, 2,9 Hz, 1H), 3,11 (dd, *J* = 9,9, 7,9 Hz, 1H), 2,92 (s, 3H), 2,88-2,94 (m, 1H), 2,73-2,86 (m, 1H), 2,62-2,68 (m, 1H), 2,19-2,40 (m, 2H), 1,97-2,07 (m, 2H), 1,77-1,87 (m, 1H), 1,51-1,75 (m, 2H), 1,31-1,38 (m, 1H), 0,85 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 464 $(M+H)^+$.

Ejemplo 533

N^2-metil-N^1-[(3a*R*,4*S*,6a*S*)-2-(tien-2–ilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-L-norvalinamida

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(tiofen-2–ilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 531 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 10,02-10,04 (m, 1H), 7,86 (d, *J* = 5,4 Hz, 1H), 7,76 (d, *J* = 4,2 Hz, 1H), 7,18-7,22 (m, 1H), 6,93-6,93 (m, 1H), 4,65 (dd, *J* = 9,1, 4,8 Hz, 1H), 4,28-4,36 (m, 1H), 3,72 (dd, *J* = 10,0, 3,0 Hz, 1H), 3,24 (dd, *J* = 10,0, 8,0 Hz, 1H), 3,19 (dd, *J* = 9,7, 3,1 Hz, 1H), 3,04 (dd, *J* = 9,7, 7,7 Hz, 1H), 2,94 (s, 3H), 2,78-2,84 (m, 1H), 2,66-2,72 (m, 1H), 2,35-2,42 (m, 1H), 2,22-2,30 (m, 1H), 1,98-2,11 (m, 2H), 1,81-1,89 (m, 1H), 1,6 6-1,77 (m, 1H), 1,54-1,66 (m, 1H), 1,31-1,38 (m, 1H), 0,86 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 386 $(M+H)^+$.

Ejemplo 534

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-cloro-4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando (S)-1-((3aR,4S,6aS)-2-(3-cloro-4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo del Ejemplo 529 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 10,05-10,07 (m, 1H), 8,19 (dd, *J* = 6,8, 2,2 Hz, 1H), 7,89 (ddd, *J* = 8,6, 4,4, 2,2 Hz, 1H), 7,44 (t, *J* = 8,7 Hz, 1H), 4,66 (dd, *J* = 9,1,

4,8 Hz, 1H), 4,27-4,36 (m, 1H), 3,72 (dd, *J* = 9,9, 2,9 Hz, 1H), 3,06-3,18 (m, 2H), 2,94 (s, 3H), 2,90-2,93 (m, 1H), 2,80-2,85 (m, 1H), 2,67-2,73 (m, 1H), 2,35-2,42 (m, 1H), 2,22-2,30 (m, 1H), 1,99-2,10 (m, 2H), 1,82-1,90 (m, 1H), 1,66-1,76 (m, 1H), 1,53-1,65 (m, 1H), 1,33-1,40 (m, 1H), 0,85 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 432 $(M+H)^+$.

Ejemplo 535

N^2-metil-N^1-[(3a*R*,4*S*,6a*S*)-2-(piridin-3–ilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-L-norvalinamida

El compuesto del título se preparó utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(piridin-3–ilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 530 en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 10,18-10,21 (m, 1H), 9,34 (d, *J* = 2,3 Hz, 1H), 8,92 (dd, *J* = 4,8, 1,6 Hz, 1H), 8,25 (ddd, *J* = 8,0, 2,4, 1,6 Hz, 1H), 7,50 (dd, *J* = 8,0, 4,8 Hz, 1H), 4,73 (dd, *J* = 9,3, 4,6 Hz, 1H), 4,30 (p, *J* = 6,3 Hz, 1H), 3,71 (dd, *J* = 10,0, 2,9 Hz, 1H), 3,08-3,21 (m, 2H), 2,87-3,07 (m, 4H), 2,78-2,83 (m, 1H), 2,64-2,70 (m, 1H), 2,40-2,47 (m, 1H), 2,26-2,34 (m, 1H), 1,98-2,17 (m, 2H), 1,78-1,92 (m, 1H), 1,55-1,77 (m, 2H), 1,29-1,36 (m, 1H), 0,84 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 381 $(M+H)^+$.

Ejemplo 536

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-cianofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida

Paso A: Se preparó metil((S)-1-oxo-1-((3aR,4S,6aS)-2-[(4-cianofenil)sulfonil]octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 313 Paso A en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida y cloruro de 4-cianobencen-1-sulfonilo en lugar de cloruro de 3-(trifluorometil)bencen-1-sulfonilo en el procedimiento descrito en Ejemplo 319: MS (APCI+) *m/z* 505 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando metil((S)-1-oxo-1-

((3aR,4S,6aS)-2-[(4-cianofenil)sulfonil]octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Paso A en lugar de (S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo en el procedimiento descrito en Ejemplo 348: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 10,09-10,11 (m, 1H), 8,05-8,07 (m, 2H), 7,94-7,96 (m, 2H), 4,68 (dd, J = 9,2, 4,6 Hz, 1H), 4,26-4,35 (m, 1H), 3,71 (dd, J = 10,0, 3,0 Hz, 1H), 3,14-3,18 (m, 2H), 2,93-2,99 (m, 1H), 2,95 (s, 3H), 2,80-2,86 (m, 1H), 2,67-2,73 (m, 1H), 2,36-2,43 (m, 1H), 2,23-2,31 (m, 1H), 1,99-2,14 (m, 2H), 1,83-1,90 (m, 1H), 1,65-1,75 (m, 1H), 1,55-1,65 (m, 1H), 1,31-1,40 (m, 1H), 0,85 (t, J = 7,3 Hz, 3H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Ejemplo 537

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-metoxifenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida

Paso A: Se preparó metil((S)-1-((3aR,4S,6aS)-octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il)carbamato de tert-butilo utilizando metil((S)-1-oxo-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo del Ejemplo 313 Paso A en lugar de (*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-4-metil-2-morfolinopentanamida en el procedimiento descrito en Ejemplo 319 Paso A: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,44 – 8,32 (m, 1H), 4,76 – 4,57 (m, 1H), 4,41 – 4,26 (m, 1H), 3,30 (dd, J = 11,1, 1,6, 1H), 3,17 – 2,95 (m, 5H), 2,78 (d, J = 9,8, 1H), 2,60 (s, 2H), 2,11 – 1,93 (m, 2H), 1,91 – 1,71 (m, 2H), 1,62 – 1,53 (m, 1H), 1,46 (s, 9H), 1,40 – 1,24 (m, 4H), 0,84 (t, J = 6;0, 3H); MS (ESI+) *m/z* 340 $(M+H)^+$.

Paso B: El compuesto del título se preparó combinando metil((S)-1-((3aR,4S,6aS)-octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il)carbamato de tert-butilo (0,075 g, 0,221 mmol) del Paso A con cloruro de 4-metoxibencen-1-sulfonilo (0,050 g, 0,243 mmol) y diisopropiletilamina (0,042 ml, 0,243 mmol) en diclorometano (5 ml). La reacción se agitó a temperatura ambiente durante la noche y los volátiles se eliminaron al vacío. A la mezcla resultante se agregó HCl 4 N/dioxano (5 ml), y la mezcla de reacción resultante se agitó a temperatura ambiente por 30 minutos. Los volátiles se eliminaron al vacío, y el material crudo se purificó mediante HPLC de fase inversa preparativa (columna Fenomenex® Luna® C8(2) 5 µm 100Å AXIA, 30×75 mm, gradiente 10-95% de acetonitrilo en

ácido trifluoroacético acuoso 0,1%, velocidad de flujo 50 ml/minuto) para dar el compuesto del título como la sal de ácido trifluoroacético: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,83 (d, *J* = 6,7 Hz, 1H), 7,94-7,97 (m, 2H), 7,09-7,13 (m, 2H), 4,39 (t, *J* = 6,8 Hz, 1H), 4,32 (p, *J* = 6,5 Hz, 1H), 3,73 (s, 3H), 3,69-3,76 (m, 1H), 3,04-3,19 (m, 2H), 2,87-2,95 (m, 1H), 2,90 (s, 3H), 2,64-2,71 (m, 1H), 2,56-2,64 (m, 1H), 2,07-2,19 (m, 2H), 1,96-2,04 (m, 1H), 1,86-1,96 (m, 1H), 1,62-1,71 (m, 1H), 1,47-1,61 (m, 2H), 1,29-1,39 (m, 1H), 0,80 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 410 $(M+H)^+$.

Ejemplo 538

N^1-((3a*R*,4*S*,6a*S*)-2-{[3,5-bis(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando cloruro de 3,5-bis(trifluorometil)fenil-1-sulfonilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,73 (d, *J* = 6,7 Hz, 1H), 8,84 (s, 1H), 8,63 (s, 2H), 8,46-8,47 (bs, 1H), 4,47 (t, *J* = 6,7 Hz, 1H), 4,26-4,34 (m, 1H), 3,87 (dd, *J* = 10,0, 2,6 Hz, 1H), 3,20-3,29 (m, 2H), 3,03 (dd, *J* = 9,5, 7,7 Hz, 1H), 2,96 (s, 3H), 2,69-2,77 (m, 1H), 2,60-2,69 (m, 1H), 2,04-2,17 (m, 2H), 1,90-2,05 (m, 2H), 1,66-1,74 (m, 1H), 1,43-1,61 (m, 2H), 1,27-1,37 (m, 1H), 0,78 (t, *J* = 7,3 Hz, 3H).

Ejemplo 539

N^1-{(3a*R*,4*S*,6a*S*)-2-[(2-cloro-4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando cloruro de 2-cloro-4-fluorofenil-1-sulfonilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,84-9,86 (m, 1H), 8,22 (dd, *J* = 8,9, 6,0 Hz, 1H), 7,45 (dd, *J* = 8,5, 2,4 Hz, 1H), 7,19-7,23 (m, 1H), 4,46 (t, *J* = 6,8 Hz, 1H), 4,30-4,39 (m, 1H), 3,81 (dd, *J* = 10,1, 3,0 Hz, 1H), 3,48 (dd, *J* = 10,1, 7,7 Hz, 1H), 3,23-3,35 (m, 2H), 2,94 (s, 3H), 2,75-2,82 (m, 1H), 2,67-2,75 (m, 1H), 2,02-2,19 (m, 3H), 1,92-1,99 (m, 1H), 1,73 (dq, *J* = 12,5, 8,1 Hz, 1H), 1,47-1,62 (m, 2H), 1,39 (ddt, *J* = 9,1, 13,0, 6,5 Hz, 1H), 0,80 (t, *J* = 7,3 Hz, 3H); MS (ESI-) *m/z* 430 $(M-H)^-$.

Ejemplo 540

N^2-metil-N^1-[(3a*R*,4*S*,6a*S*)-2-(1-naftilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-L-norvalinamida

El compuesto del título se preparó utilizando cloruro de 1-naftil-1-sulfonilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,74-9,78 (m, 1H), 9,25 (d, *J* = 8,7 Hz, 1H), 8,43 (d, *J* = 7,3 Hz, 1H), 8,12 (d, *J* = 8,2 Hz, 1H), 7,98 (d, *J* = 8,2 Hz, 1H), 7,69 (t, *J* = 7,8 Hz, 1H), 7,54-7,57 (m, 1H), 4,38 (t, *J* = 6,8 Hz, 1H), 4,26-4,32 (m, 1H), 3,83 (dd, *J* = 9,9, 2,7 Hz, 1H), 3,29 (dd, *J* = 9,9, 7,8 Hz, 1H), 3,22 (dd, *J* = 9,7, 2,7 Hz, 1H), 3,08 (dd, *J* = 9,6, 7,5 Hz, 1H), 2,89 (s, 3H), 2,59-2,66 (m, 1H), 2,50-2,59 (m, 1H), 2,02-2,15 (m, 2H), 1,80-2,00 (m, 2H), 1,57-1,67 (m, 1H), 1,45-1,55 (m, 2H), 1,23-1,30 (m, 1H), 0,78 (t, *J* = 7,3 Hz, 3H); MS (ESI-) *m/z* 428 $(M-H)^-$.

Ejemplo 541

N^1-((3a*R*,4*S*,6a*S*)-2-{[4-bromo-3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando cloruro de 4-bromo-3-(trifluorometil)fenil-1-sulfonilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,81-9,83 (m, 1H), 8,32 (d, *J* = 2,0 Hz, 1H), 8,04 (dd, *J* = 8,3, 2,0 Hz, 1H), 8,01 (d, *J* = 8,3 Hz, 1H), 6,60-8,44 (bs, 1H), 4,33-4,38 (m, 1H), 4,26-4,33 (m, 1H), 3,82 (dd, *J* = 9,9, 2,6 Hz, 1H), 3,21 (dd, *J* = 9,8, 2,7 Hz, 1H), 3,18 (dd, *J* = 9,8, 7,9 Hz, 1H), 2,96 (dd, *J* = 9,6, 7,5 Hz, 1H), 2,89 (s, 3H), 2,69-2,76 (m, 1H), 2,61-2,69 (m, 1H), 2,05-2,17 (m, 2H), 1,97-2,05 (m, 1H), 1,89-1,97 (m, 1H), 1,64-1,72 (m, 1H), 1,45-1,59 (m, 2H), 1,34 (ddt, *J* = 9,3, 13,0, 6,5 Hz, 1H), 0,79 (t, *J* = 7,3 Hz, 3H); MS (ESI-) *m/z* 524 $(M-H)^-$.

Ejemplo 542

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3,4-diclorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando cloruro de 3,4-diclorofenil-1-sulfonilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,84-9,86 (m, 1H), 7,41-8,78 (bs, 1H), 7,82 (dd, *J* = 8,3, 2,1 Hz, 1H), 7,69 (d, *J* = 8,3 Hz, 1H), 7,58-

7,59 (bs, 1H), 4,45 (t, *J* = 6,8 Hz, 1H), 4,30 (p, *J* = 6,7 Hz, 1H), 3,76 (dd, *J* = 9,9, 2,7 Hz, 1H), 3,16 (dd, *J* = 9,9, 2,9 Hz, 1H), 3,14 (dd, *J* = 10,0, 8,0 Hz, 1H), 2,94 (s, 3H), 2,89-2,95 (m, 1H), 2,70-2,75 (m, 1H), 2,62-2,69 (m, 1H), 2,06-2,18 (m, 2H), 1,97-2,04 (m, 1H), 1,90-1,96 (m, 1H), 1,65-1,73 (m, 1H), 1,46-1,62 (m, 2H), 1,30-1,37 (m, 1H), 0,80 (t, *J* = 7,3 Hz, 3H); MS (ESI-) *m/z* 446 $(M-H)^-$.

Ejemplo 543

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-*tert*-butilfenil)sulfonil]octahidrociclopenta[*c*]pirrol-4-il}-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando cloruro de 4-*tert*-butilfenil-sulfonilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,85 (d, *J* = 6,8 Hz, 1H), 7,96-7,99 (m, 2H), 7,58-7,66 (m, 2H), 4,43 (t, *J* = 6,8 Hz, 1H), 4,27-4,33 (m, 1H), 3,78 (dd, *J* = 9,8, 2,5 Hz, 1H), 3,20 (dd, *J* = 9,6, 2,6 Hz, 1H), 3,11 (dd, *J* = 9,8, 7,7 Hz, 1H), 2,93 (s, 3H), 2,90 (dd, *J* = 9,5, 7,6 Hz, 1H), 2,47-2,62 (m, 2H), 2,08-2,18 (m, 2H), 1,93-2,01 (m, 1H), 1,85-1,92 (m, 1H), 1,60-1,68 (m, 1H), 1,48-1,59 (m, 2H), 1,28-1,39 (m, 1H), 1,26 (s, 9H), 0,81 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 436 $(M+H)^+$.

Ejemplo 544

N^1-[(3a*R*,4*S*,6a*S*)-2-(1,1'-bifenil-4-ilsulfonil)octahidrociclopenta[*c*]pirrol-4-il]-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando cloruro de 1,1'-bifenil-4-sulfonilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,86-9,88 (m, 1H), 8,07-8,09 (m, 2H), 7,86-7,88 (m, 2H), 7,71-7,75 (m, 2H), 7,48-7,53 (m, 2H), 7,41-7,47 (m, 1H), 4,44 (t, *J* = 6,8 Hz, 1H), 4,29-4,36 (m, 1H), 3,78 (dd, *J* = 9,9, 2,7 Hz, 1H), 3,21 (dd, *J* = 9,7, 2,7 Hz, 1H), 3,15 (dd, *J* = 9,8, 7,9 Hz, 1H), 2,95 (dd, *J* = 9,5, 7,7 Hz, 1H), 2,93 (s, 3H), 2,64-2,71 (m, 1H), 2,56-2,64 (m, 1H), 2,06-2,19 (m, 2H), 1,97-2,04 (m, 1H), 1,88-1,97 (m, 1H), 1,62-1,73 (m, 1H), 1,48-1,62 (m, 2H), 1,30-1,40 (m, 1H), 0,80 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 456 $(M+H)^+$.

Ejemplo 545

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3,4-dimetoxifenil)sulfonil]octahidrociclopenta[*c*]pirrol-4-il}-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando cloruro de 3,4-dimetoxifenil-

sulfonilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,86 (d, J = 6,9 Hz, 1H), 7,66 (dd, J = 8,4, 2,0 Hz, 1H), 7,55 (d, J = 2,0 Hz, 1H), 7,08 (d, J = 8,4 Hz, 1H), 4,38-4,43 (m, 1H), 4,31-4,38 (m, 1H), 3,81 (s, 3H), 3,78 (dd, J = 10,2, 2,8 Hz, 1H), 3,76 (s, 3H), 3,17-3,23 (m, 2H), 3,00 (dd, J = 9,6, 7,5 Hz, 1H), 2,91 (s, 3H), 2,68-2,75 (m, 1H), 2,60-2,68 (m, 1H), 2,06-2,18 (m, 2H), 1,98-2,06 (m, 1H), 1,88-1,98 (m, 1H), 1,64-1,73 (m, 1H), 1,49-1,59 (m, 2H), 1,33-1,40 (m, 1H), 0,79 (t, J = 7,3 Hz, 3H); MS (ESI-) *m/z* 438 $(M-H)^-$.

Ejemplo 546

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-cianofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando cloruro de 3-cianofenil-sulfonilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,86-9,88 (m, 1H), 8,56 (s, 1H), 8,18 (d, J = 8,0 Hz, 1H), 7,96 (d, J = 7,8 Hz, 1H), 7,66 (t, J = 7,8 Hz, 1H), 4,39-4,44 (m, 1H), 4,23-4,32 (m, 1H), 3,77 (dd, J = 10,0, 2,7 Hz, 1H), 3,18 (dd, J = 9,8, 2,9 Hz, 1H), 3,14 (dd, J = 9,9, 7,8 Hz, 1H), 2,93-2,96 (m, 1H), 2,91 (s, 3H), 2,65-2,72 (m, 1H), 2,58-2,65 (m, 1H), 2,04-2,18 (m, 2H), 1,95-2,03 (m, 1H), 1,87-1,95 (m, 1H), 1,68 (dq, J = 12,3, 8,1 Hz, 1H), 1,45-1,59 (m, 2H), 1,27-1,38 (m, 1H), 0,79 (t, J = 7,3 Hz, 3H); MS (ESI+) *m/z* 405 $(M+H)^+$.

Ejemplo 547

N^1-[(3a*R*,4*S*,6a*S*)-2-(2-furilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando cloruro de 2-furilsulfonilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,88-9,90 (m, 1H), 7,86-7,87 (m, 1H), 7,26-7,28 (m, 1H), 6,58 (dd, J = 3,4, 1,8 Hz, 1H), 4,42 (t, J = 6,8 Hz, 1H), 4,24-4,33 (m, 1H), 3,79 (dd, J = 10,3, 3,2 Hz, 1H), 3,46 (dd, J = 10,3, 7,8 Hz, 1H), 3,20-3,32 (m, 2H), 2,92 (s, 3H), 2,67-2,75 (m, 1H), 2,60-2,68 (m, 1H), 2,06-2,20 (m, 2H), 1,97-2,05 (m, 1H), 1,88-1,95 (m, 1H), 1,71 (dq, J = 12,5, 8,0 Hz, 1H), 1,46-1,62 (m, 2H), 1,30 (ddt, J = 8,9, 13,0, 6,5 Hz, 1H), 0,81 (t, J = 7,3 Hz, 3H); MS (ESI+) *m/z* 370 $(M+H)^+$.

Ejemplo 548

N^1-{(3a*R*,4*S*,6a*S*)-2-[(2,3-diclorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando cloruro de 2,3-diclorofenilsulfonilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,84-9,86 (m, 1H), 8,14 (dd, *J* = 7,9, 1,5 Hz, 1H), 7,68 (dd, *J* = 8,0, 1,5 Hz, 1H), 7,34 (t, *J* = 8,0 Hz, 1H), 4,49 (t, *J* = 6,8 Hz, 1H), 4,32-4,38 (m, 1H), 3,84-3,90 (m, 1H), 3,51 (dd, *J* = 10,2, 7,7 Hz, 1H), 3,26-3,41 (m, 2H), 2,95 (s, 3H), 2,76-2,82 (m, 1H), 2,68-2,75 (m, 1H), 2,09-2,19 (m, 2H), 2,01-2,09 (m, 1H), 1,90-2,00 (m, 1H), 1,73 (dq, *J* = 12,5, 8,1 Hz, 1H), 1,46-1,64 (m, 2H), 1,35-1,42 (m, 1H), 0,80 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Ejemplo 549

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)bencil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

El compuesto del título se preparó utilizando cloruro de 4-(trifluorometil)bencil-sulfonilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,72-9,74 (m, 1H), 7,79-7,81 (m, 2H), 7,68-7,70 (m, 2H), 4,75-4,75 (bs, 2H), 4,51 (dd, *J* = 8,3, 6,3 Hz, 1H), 4,33 (p, *J* = 6,7 Hz, 1H), 3,78 (dd, *J* = 10,1, 3,1 Hz, 1H), 3,62 (dd, *J* = 10,2, 7,5 Hz, 1H), 3,45 (dd, *J* = 9,9, 7,5 Hz, 1H), 3,23 (dd, *J* = 9,9, 3,7 Hz, 1H), 2,90 (s, 3H), 2,68-2,85 (m, 2H), 2,02-2,15 (m, 3H), 1,91-1,98 (m, 1H), 1,75 (dq, *J* = 12,4, 8,1 Hz, 1H), 1,43-1,64 (m, 2H), 1,30-1,39 (m, 1H), 0,81 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 550

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[2-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida

El compuesto del título se preparó utilizando cloruro de 2-(trifluorometil)fenil-sulfonilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,81-9,83 (m, 1H), 8,26 (d, *J* = 7,9 Hz, 1H), 7,93 (d, *J* = 7,8 Hz, 1H), 7,73 (t, *J* = 7,7 Hz,

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1H), 7,67 (t, *J* = 7,7 Hz, 1H), 4,50 (t, *J* = 6,8 Hz, 1H), 4,31 (p, *J* = 6,7 Hz, 1H), 3,83 (dd, *J* = 10,1, 2,9 Hz, 1H), 3,36 (dd, *J* = 10,1, 7,7 Hz, 1H), 3,29 (dd, *J* = 9,9, 3,1 Hz, 1H), 3,18 (dd, *J* = 9,9, 7,5 Hz, 1H), 2,95 (s, 3H), 2,75-2,80 (m, 1H), 2,65-2,73 (m, 1H), 2,14 (q, *J* = 7,5 Hz, 2H), 1,99-2,06 (m, 1H), 1,91-1,98 (m, 1H), 1,68-1,76 (m, 1H), 1,47-1,65 (m, 2H), 1,36 (ddt, *J* = 9,2, 12,9, 6,5 Hz, 1H), 0,80 (t, *J* = 7,3 Hz, 3H); MS (ESI+) *m/z* 448 $(M+H)^+$.

Ejemplo 551

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-bromofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando cloruro de 2-(trifluorometil)fenil-sulfonilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,78-9,80 (m, 1H), 8,26 (t, *J* = 1,8 Hz, 1H), 7,90 (dt, *J* = 7,8, 1,2 Hz, 1H), 7,78 (ddd, *J* = 8,0, 1,9, 1,0 Hz, 1H), 7,43 (t, *J* = 7,9 Hz, 1H), 4,42 (dd, *J* = 7,9, 5,8 Hz, 1H), 4,29 (p, *J* = 6,7 Hz, 1H), 3,75 (dd, *J* = 9,9, 2,7 Hz, 1H), 3,15 (dd, *J* = 9,7, 2,8 Hz, 1H), 3,10 (dd, *J* = 9,9, 7,7 Hz, 1H), 2,92 (s, 3H), 2,88 (dd, *J* = 9,6, 7,5 Hz, 1H), 2,62-2,68 (m, 1H), 2,55-2,61 (m, 1H), 2,04-2,20 (m, 2H), 1,86-2,03 (m, 2H), 1,63-1,70 (m, 1H), 1,48-1,60 (m, 2H), 1,31 (ddt, *J* = 9,2, 12,9, 6,5 Hz, 1H), 0,80 (t, *J* = 7,3 Hz, 3H); MS (ESI-) *m/z* 456 $(M-H)^-$.

Ejemplo 552

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando cloruro de 2-cloro-4-(trifluorometil)fenilsulfonilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 10,09-10,11 (m, 1H), 8,33 (d, *J* = 8,2 Hz, 1H), 7,99-8,00 (bs, 1H), 7,73-7,75 (m, 1H), 4,66-4,70 (m, 1H), 4,35-4,44 (m, 1H), 3,85 (dd, *J* = 10,3, 3,2 Hz, 1H), 3,55 (d, *J* = 8,7 Hz, 1H), 3,30-3,42 (m, 2H), 2,95 (s, 3H), 2,88-2,95 (m, 1H), 2,75-2,86 (m, 1H), 2,35-2,41 (m, 1H), 2,22-2,30 (m, 1H), 1,99-2,19 (m, 2H), 1,89-1,95 (m, 1H), 1,54-1,77 (m, 2H), 1,39-1,47 (m, 1H), 0,85 (t, *J* = 7,3 Hz, 3H); MS (ESI-) *m/z* 480 $(M-H)^-$.

Ejemplo 553

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-5-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-metil-L-norvalinamida

El compuesto del título se preparó utilizando cloruro de 2-cloro-5-(trifluorometil)fenilsulfonilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 10,09-10,12 (m, 1H), 8,54 (d, *J* = 2,2 Hz, 1H), 7,82 (dd, *J* = 8,3, 2,2 Hz, 1H), 7,76 (d, *J* = 8,3 Hz, 1H), 4,73 (dd, *J* = 9,1, 4,6 Hz, 1H), 4,35-4,43 (m, 1H), 3,84 (dd, *J* = 10,2, 3,2 Hz, 1H), 3,56 (dd, *J* = 10,2, 7,8 Hz, 1H), 3,29-3,40 (m, 2H), 2,96 (s, 3H), 2,89-3,00 (m, 1H), 2,76-2,88 (m, 1H), 2,35-2,44 (m, 1H), 2,21-2,33 (m, 1H), 2,05-2,19 (m, 2H), 1,88-1,98 (m, 1H), 1,66-1,79 (m, 1H), 1,53-1,66 (m, 1H), 1,38-1,48 (m, 1H), 0,85 (t, *J* = 7,3 Hz, 3H); MS (ESI-) *m/z* 480 $(M-H)^-$.

Ejemplo 554

N^2-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)benzoil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida

El compuesto del título se preparó utilizando 3-(trifluorometil)cloruro de benzoilo en lugar de cloruro de 4-metoxibencen-1-sulfonilo en el procedimiento descrito en Ejemplo 537: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 7,98 (s, 1H), 7,80 (d, *J* = 7,7, 1H), 7,65 (d, *J* = 7,9, 1H), 7,52 – 7,40 (m, 3H), 4,34 – 4,19 (m, 1H), 3,88 – 3,74 (m, 3H), 3,66 (d, *J* = 8,2, 1H), 3,44 (s, 1H), 2,85 – 2,52 (m, 5H), 2,51 – 2,38 (m, 0H), 2,11 (dt, *J* = 12,6, 6,2, 1H), 1,91 (dddd, *J* = 22,0, 15,6, 10,7, 4,6, 3H), 1,72 (dq, *J* = 12,8, 8,0, 1H), 1,57 – 1,17 (m, 4H), 0,83 (t, *J* = 7,3, 3H); MS (ESI+) *m/z* 412 $(M+H)^+$.

Ejemplo 555

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*-isopropil-3-(trifluorometil)bencenosulfonamida**

Paso A: Se preparó (3a*R*,4*S*,6a*S*)-2-Bencil-*N*-isopropiloctahidrociclopenta[*c*]pirrol-4-amina utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 33 Paso A en lugar de (3a*S*,4*R*,6a*R*)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[*c*]pirrol-4-amina y acetona en lugar de pivalaldehido en el procedimiento descrito en Ejemplo 281: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 7,48 (d, *J* = 7,5, 2H), 7,39 (t, *J* = 7,5, 2H), 7,29 (t,

J = 7,3, 1H), 3,61 – 3,51 (m, 2H), 3,05 (dd, *J* = 12,1, 5,4, 1H), 2,87 – 2,78 (m, 1H), 2,61 – 2,51 (m, 2H), 2,43 – 2,36 (m, 2H), 2,35 – 2,30 (m, 1H), 2,28 – 2,21 (m, 1H), 2,00 – 1,93 (m, 1H), 1,93 – 1,87 (m, 1H), 1,42 – 1,28 (m, 3H), 1,05 – 0,98 (m, 6H); MS (ESI+) *m/z* 259 $(M+H)^+$.

Paso B: El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-bencil-*N*-isopropiloctahidrociclopenta[*c*]pirrol-4-amina del Paso A en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo y cloruro de 3-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de metansulfonilo en el procedimiento descrito en Ejemplo 242: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,43 (s, 1H), 8,30 – 8,21 (m, 1H), 7,84 (d, *J* = 7,6, 1H), 7,66 – 7,59 (m, 1H), 7,40 (ddd, *J* = 12,7, 8,4, 2,6, 4H), 7,32 – 7,27 (m, 1H), 3,82 – 3,70 (m, 2H), 3,51 (d, *J* = 2,0, 2H), 2,82 – 2,74 (m, 1H), 2,67 – 2,62 (m, 1H), 2,52 – 2,43 (m, 3H), 2,09 – 2,04 (m, 1H), 1,99 – 1,95 (m, 1H), 1,91 – 1,79 (m, 2H), 1,75 – 1,65 (m, 1H), 1,26 (dd, *J* = 6,8, 2,6, 6H); MS (ESI+) *m/z* 467 $(M+H)^+$.

Ejemplo 556

***N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida**

El compuesto del título se preparó utilizando (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 33 Paso A en lugar de (S)-2-amino-4-metilpentanoato de tert-butilo y cloruro de 3-(trifluorometil)bencen-1-sulfonilo en lugar de cloruro de metansulfonilo en el procedimiento descrito en Ejemplo 242 Paso A: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 9,49 (d, *J* = 7,2, 1H), 8,43 (s, 1H), 8,30 (d, *J* = 7,9, 1H), 7,81 (d, *J* = 7,9, 1H), 7,60 (d, *J* = 7,9, 1H), 7,37 (dd, *J* = 9,6, 3,8, 4H), 7,33 – 7,26 (m, 1H), 3,83 – 3,75 (m, 1H), 3,50 (d, *J* = 13,1, 1H), 3,44 (d, *J* = 13,1, 1H), 2,61 (dd, *J* = 9,2, 2,0, 1H), 2,56 – 2,43 (m, 2H), 2,35 (dd, *J* = 9,1, 2,1, 1H), 2,21 – 2,13 (m, 2H), 1,99 (td, *J* = 11,7, 5,8, 1H), 1,82 (ddd, *J* = 12,5, 10,2, 5,6, 1H), 1,63 – 1,53 (m, 1H), 1,29 (ddt, *J* = 12,7, 10,0, 6,4, 1H); MS (ESI+) *m/z* 442 $(M+NH_4)^+$.

Ejemplo 557

***N*-isopropil-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida**

El compuesto del título se preparó utilizando *N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*-isopropil-3-

(trifluorometil)bencenosulfonamida del Ejemplo 555 en lugar de *N*-((3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-2,2-bis(4-fluorofenil)acetamida en el procedimiento descrito en Ejemplo 459: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,30 (s, 1H), 8,17 (d, *J* = 7,8, 1H), 7,79 (d, *J* = 8,1, 1H), 7,61 (t, *J* = 7,8, 1H), 3,90 – 3,80 (m, 2H), 3,77 – 3,67 (m, 4H), 3,39 (dd, *J* = 9,0, 4,2, 1H), 3,10 – 3,01 (m, 1H), 2,82 – 2,70 (m, 1H), 2,39 (s, 3H), 2,13 – 2,01 (m, 1H), 2,02 – 1,83 (m, 3H), 1,51 (t, *J* = 6,7, 2H), 1,29 (d, *J* = 6,8, 5H), 1,23 (d, *J* = 6,8, 3H), 0,97 – 0,89 (m, 6H); MS (ESI+) *m/z* 504 $(M+H)^+$.

Ejemplo 558

***N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida**

El compuesto del título se preparó utilizando *N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida del Ejemplo 556 en lugar de *N*-((3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-2,2-bis(4-fluorofenil)acetamida en el procedimiento descrito en Ejemplo 459: ^{1}H NMR (400 MHz, piridin-d_5) δ ppm 8,88 (qt, *J* = 7,3, 2,9, 1H), 8,35 (s, 1H), 8,24 (d, *J* = 7,9, 1H), 7,79 (d, *J* = 7,9, 1H), 7,59 (t, *J* = 8,0, 1H), 3,79 – 3,70 (m, 3H), 3,68 – 3,53 (m, 2H), 3,37 (ddd, *J* = 8,4, 7,7, 2,4, 1H), 2,77 – 2,62 (m, 2H), 2,37 (s, 3H), 2,06 – 1,87 (m, 3H), 1,75 – 1,63 (m, 1H), 1,53 – 1,44 (m, 2H), 1,38 – 1,24 (m, 1H), 0,92 (dd, *J* = 8,8, 6,7, 7H); MS (ESI+) *m/z* 462 $(M+H)^+$.

Ejemplo 559

***N*-ciclopropil-*N*-[(3a*S**,4*S**,6a*R**)-[2-(*N*-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida**

El compuesto del título se preparó utilizando *N*-[(3a*S**,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*-ciclopropil-3-(trifluorometil)bencenosulfonamida del Ejemplo 199 en lugar de *N*-((3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il)-2,2-bis(4-fluorofenil)acetamida en el procedimiento descrito en Ejemplo 459: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,50 (s, 1H), 8,39 – 8,31 (m, 1H), 7,96 (dd, *J* = 20,3, 7,8, 1H), 7,82 – 7,71 (m, 1H), 4,20 (dd, *J* = 13,1, 5,0, 0,5H), 4,12 (dt, *J* = 13,2, 6,7, 0,5H), 4,04 – 3,98 (m, 0,5H), 3,97 – 3,80 (m, 1,5H), 3,72 (ddd, *J* = 22,3, 16,1, 9,9, 1H), 3,60 (dt, *J* = 8,6, 7,6, 0,5H), 3,53 – 3,38 (m, 2H), 3,29 – 3,21 (m, 0,5H), 2,72 – 2,65 (m, 0,5H), 2,63 – 2,52 (m, 0,5H), 2,48 (s, 0,5H), 2,42 (d, *J* = 4,6, 2H), 2,39 (s, 0,5H), 2,15 – 1,97 (m, 3H), 1,92

– 1,82 (m, 1H), 1,75 – 1,68 (m, 1H), 1,67 – 1,34 (m, 5H), 1,04 (d, *J* = 6,6, 1H), 0,99 – 0,94 (m, 3H), 0,91 (dt, *J* = 14,0, 5,1, 3H), 0,85 – 0,71 (m, 1,5H), 0,69 – 0,59 (m, 0,5H); MS (ESI+) *m/z* 502 $(M+H)^+$.

Ejemplo 560

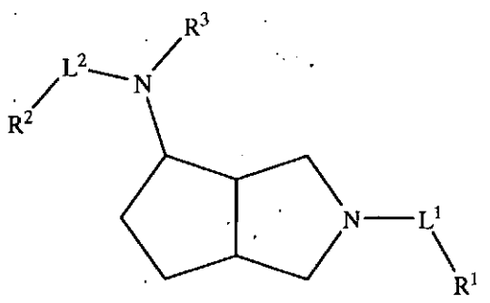
4-fluoro-*N*-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}benzamida

El compuesto del título se preparó utilizando ácido 4-fluorobenzoico en lugar de *N*-(*tert*-butoxicarbonil)-L-leucina y (3a*R*,4*S*,6a*S*)-2-(6-(trifluorometil)piridin-2–il)octahidrociclopenta[*c*]pirrol-4-amina del Ejemplo 264 Paso A en lugar de (3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4-amina en el procedimiento descrito en Ejemplo 221: ^{1}H NMR (500 MHz, piridin-d_5) δ ppm 8,90 (d, *J* = 6,9, 1H), 8,27 – 8,21 (m, 2H), 7,55 – 7,50 (m, 1H), 7,20 – 7,14 (m, 2H), 6,99 (d, *J* = 7,2, 1H), 6,53 (d, *J* = 8,6, 1H), 4,61 – 4,54 (m, 1H), 3,80 (dd, *J* = 11,0, 3,7, 1H), 3,63 (dd, *J* = 10,9, 8,2, 1H), 3,51 (dd, *J* = 10,8, 8,4, 1H), 3,30 (dd, *J* = 10,9, 4,6, 1H), 2,88 – 2,81 (m, 1H), 2,76 – 2,67 (m, 1H), 2,23 (ddd, *J* = 19,5, 7,1, 4,7, 1H), 1,93 (dtd, *J* = 12,7, 8,0, 4,6, 1H), 1,81 (ddd, *J* = 16,4, 12,7, 8,1, 1H), 1,40 (dt, *J* = 13,2, 7,6, 1H); MS (ESI+) *m/z* 394 $(M+H)^+$.

A la luz de la descripción detallada precedente serán evidentes para aquellos capacitados en el arte muchas variaciones de la invención. Todas tales variaciones obvias se encuentran dentro del espectro de las reivindicaciones adjuntas.

REIVINDICACIONES

1. Un compuesto de fórmula (I),



(I),

o una sal, prodroga, sal de una prodroga aceptables farmacéuticamente, o una combinación de las mismas, donde

L^1 es C(O), $S(O)_2$, $SO_2N(R^4)$, C(O)O o $-(CR^aR^b)_m-$;

R^1 es alquilo, G^1, $-CH(G^1)_2$, $-(CR^aR^b)_m-G^1$, $-(CR^aR^b)_m-CH(G^1)_2$, $-(CR^eR^f)_n-N(R^5)_2$, $-(CR^eR^f)_n-N(R^5)-C(O)O$(alquilo), $-(CR^eR^f)_n-N(R^5)-C(O)$(alquilo), o $-(CR^eR^f)_n-N(R^5)-SO_2R^6$; o

L^1-R^1 tomados juntos son hidrógeno, alquilo, hidroxialquilo, G^1, o $-CH(G^1)_2$;

L^2 es $-(CR^cR^d)_p-$, C(O), $C(O)N(R^4)$, $S(O)_2$, $SO_2N(R^5)$, o C(O)O;

R^2 es alquilo, G^2, $-C(R^c)(G^2)(G^3)$, $-(CR^cR^d)_p-G^2$, $-(CR^cR^d)_p-CH(G^2)(G^3)$, $-(CR^gR^h)_q-N(R^5)-C(O)O$(alquilo), $-(CR^gR^h)_q-N(R^5)-C(O)O-G^2$, $-(CR^gR^h)_q-N(R^5)-C(O)$(alquilo), $-(CR^gR^h)_q-N(R^5)-SO_2R^6$, $-(CR^gR^h)_q-N(R^4)(R^5)$, $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)$-(alquilo), o $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-G^2$; o

L^2-R^2 tomados juntos son alquilo, G^2, o $-C(R^c)(G^2)(G^3)$;

m y p, en cada caso, son cada uno en forma independiente 1, 2, 3, 4, 5, o 6;

n y q, en cada caso, son cada uno en forma independiente 1, 2, 3, 4, o 5;

R^a, R^b, R^c, y R^d, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, arilalquilo, halógeno, haloalquilo o OR^7; o

R^a y R^b, o R^c y R^d, junto con el átomo de carbono al cual se encuentran unidos, forman opcionalmente un anillo C_{3-6} cicloalquilo;

R^e, R^f, R^g, y R^h, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, halógeno, haloalquilo, OR^7, cicloalquilalquilo, heteroarilo, arilalquilo, o heteroarilalquilo; donde los grupos arilo, cicloalquilo y heteroarilo de arilo, cicloalquilo y heteroarilo cada uno en forma independiente no se sustituye o se sustituye con 1, 2, 3, 4, o 5 sustituyentes seleccionados en forma independiente

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entre el grupo que consiste en alquilo y haloalquilo;

G^1, G^2, y G^3 en cada caso, son cada uno en forma independiente arilo, cicloalquilo, cicloalquenilo, heteroarilo, o heterociclo; donde G^1, G^2, y G^3 en cada caso cada uno en forma independiente no se sustituye o se sustituye con 1, 2, 3, 4, o 5 sustituyentes seleccionados entre el grupo que consiste en alquilo, alquenilo, alquinilo, ciano, haloalquilo, halógeno, nitro, oxo, fenilo, $N(R^7)_2$, $N(R^7)C(O)R^7$, OR^7, $C(O)R^7$, $C(O)OR^7$, $C(O)N(R^7)_2$, SO_2R^8, y $SO_2N(R^7)_2$; y donde G^1 no es quinolina, quinazolindiona, o piridopirimidindiona;

R^3 es hidrógeno, alquilo, haloalquilo, cicloalquilo, o cicloalquilalquilo;

R^4, R^5, y R^7, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, arilo, arilalquilo, cicloalquilo, cicloalquilalquilo, o haloalquilo; donde dichos arilo, el arilo de arialquilo y cicloalquilo no se sustituyen o se sustituyen en forma independiente con 1, 2 3, 4, o 5 sustituyentes seleccionados en forma independiente entre el grupo que consiste en alquilo, haloalquilo, y halógeno;

R^6 es alquilo, arilo, cicloalquilo, cicloalquenilo, heteroarilo, o heterociclo; donde dichos arilo, heteroarilo y heterociclo no se sustituyen o se sustituyen en forma independiente con 1, 2 3, 4, o 5 sustituyentes seleccionados en forma independiente entre el grupo que consiste en alquilo, haloalquilo, y halógeno;

R^8 es alquilo o haloalquilo;

con la condición de que L^1-R^1 y L^2-R^2 no son ambos alquilo al mismo tiempo;

y con la condición de que cuando L^1-R^1 es alquilo, L^2-R^2 no es $C(O)N(R^4)$, donde R^4 es alquilo;

y con la condición adicional de que el compuesto no es:

N-(2-tritiloctahidrociclopenta[*c*]pirrol-4–il)acetamida;

N-(octahidrociclopenta[*c*]pirrol-4–il)acetamida

N-metil-*N*-(2-tritiloctahidrociclopenta[*c*]pirrol-4–il)acetamida;

N-metil-*N*-(octahidrociclopenta[*c*]pirrol-4–il)acetamida;

6-(2-(2-(3-fluoro-6-metoxi-1,5-naftiridin-4–il)etil)octahidrociclopenta[*c*]pirrol-4–ilamino)metil-2*H*-pirido[3,2-*b*][1,4]tiazin-3(4*H*)-ona;

2-(2-(3-fluoro-6-metoxi-1,5-naftiridin-4–il)etil)octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo;

octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo 2-bencilo; o octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo.

2. El compuesto de acuerdo con la reivindicación 1, donde

L^1 es $-(CR^aR^b)_m-$;

R^a y R^b son cada uno hidrógeno;

m es 1;

R^1 es G^1; donde G^1 es arilo;

L^2 es C(O);

R^2 es $-(CR^cR^d)_p-G^2$; donde G^2 es arilo;

p es 1;

R^c y R^d, junto con el átomo de carbono al cual se encuentran unidos forman un anillo C_{3-6} cicloalquilo; y

R^3 es hidrógeno.

3. El compuesto de acuerdo con la reivindicación 1, donde

L^1-R^1 juntos son alquilo; o

L^1 es $-(CR^aR^b)_m-$ o C(O);

R^1 es G^1; donde G^1 es arilo, cicloalquilo, o heteroarilo;

L^2 es C(O);

R^2 es $-(CR^cR^d)_p-G^2$; donde G^2 es arilo y p es 1 o 2;

R^a, R^b, R^c, y R^d, en cada caso son en forma independiente hidrógeno, alquilo, o arilalquilo; y

R^3 es hidrógeno o alquilo.

4. El compuesto de acuerdo con la reivindicación 1, donde

L^1 es $-(CR^aR^b)_m-$;

R^a y R^b en cada caso son cada uno hidrógeno;

m es 1 o 2;

R^1 es G^1; donde G^1 es arilo;

L^2 es $C(O)N(R^4)$, donde R^4 es alquilo;

R^2 es G^2, donde G^2 es arilo; y

R^3 es hidrógeno.

5. El compuesto de acuerdo con la reivindicación 1, donde

L^1 es $-(CR^aR^b)_m-$, C(O) o $S(O)_2$;

R^a y R^b en cada caso son cada uno hidrógeno;

m es 1;

R^1 es alquilo o G^1; donde G^1 es arilo o cicloalquilo;

L^2 es C(O);

R^2 es $-(CR^cR^d)_p-G^2$; donde

R^c y R^d en cada caso son en forma independiente hidrógeno, alquilo o OR^7;

p es 1;

G^2 es cicloalquilo o heterociclo; donde dicho cicloalquilo o heterociclo no se sustituye o se sustituye con 1, 2, 3, 4, o 5 sustituyentes seleccionados en forma independiente entre el grupo que consiste en alquilo, haloalquilo, halógeno, oxo y $C(O)OR^7$;

R^7 es hidrógeno; y

R^3 es hidrógeno.

6. El compuesto de acuerdo con la reivindicación 1, donde

L^1 es $-(CR^aR^b)_m-$;

R^a y R^b en cada caso son cada uno hidrógeno;

m es 1;

R^1 es G^1; donde G^1 es arilo;

L^2-R^2 juntos son cicloalquilo; y

R^3 es hidrógeno o cicloalquilo.

7. El compuesto de acuerdo con la reivindicación 1, donde

L^1 es $-(CR^aR^b)_m-$;

R^a y R^b en cada caso son cada uno hidrógeno;

m es 1;

R^1 es G^1; donde G^1 es arilo;

L^2 es C(O);

R^2 es $-C(R^c)(G^2)(G^3)$, o $-(CR^cR^d)_p-CH(G^2)(G^3)$; donde G^2 es arilo y G^3 es arilo o cicloalquilo;

R^c y R^d son cada uno hidrógeno; y

R^3 es hidrógeno.

8. El compuesto de acuerdo con la reivindicación 1, donde

L^1-R^1 juntos son hidrógeno o $-CH(G^1)_2$, donde cada G^1 es arilo o heteroarilo;

o

L^1 es $-(CR^aR^b)_m-$, C(O), o $S(O)_2$;

R^1 es G^1, $-CH(G^1)_2$, $-(CR^aR^b)_m-G^1$, $-(CR^aR^b)_m-CH(G^1)_2$, $-(CR^eR^f)_n-N(R^5)_2$; donde cada G^1 es arilo o heteroarilo;

R^a y R^b son cada uno hidrógeno;

R^e y R^f en cada caso, son cada uno en forma independiente hidrógeno o alquilo;

R^5 en cada caso, es en forma independiente hidrógeno o alquilo;

L^2 es C(O);

R^2 es $-C(R^c)(G^2)(G^3)$; donde G^2 y G^3 son cada uno cicloalquilo;

R^c hidrógeno o OR^7, donde R^7 es hidrógeno; y

R^3 es hidrógeno.

9. El compuesto de acuerdo con la reivindicación 1, donde

L^1 es $-(CR^aR^b)_m-$ o $S(O)_2$;

R^a y R^b en cada caso son cada uno hidrógeno;

m es 1;

R^1 es G^1; donde G^1 es arilo;

L^2 es C(O); y

R^2 es alquilo o G^2, donde G^2 es cicloalquilo o heterociclo; y

R^3 es hidrógeno.

10. El compuesto de acuerdo con la reivindicación 1, donde

L^1 es $-(CR^aR^b)_m-$, C(O) o $S(O)_2$;

R^a y R^b en cada caso son cada uno hidrógeno;

m, en cada caso, es 1 o 2;

R^1 es G^1, $-(CR^aR^b)_m-G^1$, o $-CH(G^1)_2$, donde G^1, en cada caso, es en forma independiente arilo o heteroarilo;

L^2 es C(O);

R^2 es $-(CR^gR^h)_q-N(R^5)-C(O)O$(alquilo), $-(CR^gR^h)_q-N(R^5)-C(O)O-G^2$, $-(CR^gR^h)_q-N(R^5)-C(O)$(alquilo), $-(CR^gR^h)_q-N(R^5)-SO_2-R^6$, $-(CR^gR^h)_q-N(R^4)(R^5)$, $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-$(alquilo), o $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-G^2$;

q es 1 o 2;

R^g y R^h, en cada caso, son cada uno en forma independiente

hidrógeno, alquilo, arilalquilo, o cicloalquilalquilo;

R^4 y R^5 en cada caso, son cada uno en forma independiente hidrógeno, alquilo, arilalquilo, cicloalquilo o cicloalquilalquilo;

R^6 es alquilo, arilo, o cicloalquilo;

G^2 es arilo o cicloalquilo; y

R^3 es hidrógeno, alquilo, cicloalquiló o cicloalquilalquilo.

11. El compuesto de acuerdo con la reivindicación 1, donde

L^1-R^1 juntos son hidrógeno o hidroxialquilo; o

L^1 es $-(CR^aR^b)_m-$, C(O) o $S(O)_2$;

R^1 es G^1, $-(CR^aR^b)_m-G^1$ o $-CH(G^1)_2$, donde cada G^1 es arilo o heteroarilo;

R^a y R^b, en cada caso, son cada uno en forma independiente hidrógeno o alquilo;

L^2 es $S(O)_2$;

R^2 es G^2, donde G^2 es arilo o heteroarilo; o

R^3 es hidrógeno, alquilo o cicloalquilo.

12. El compuesto de acuerdo con la reivindicación 1, donde

L^1 es $-(CR^aR^b)_m-$;

R^a y R^b son cada uno hidrógeno;

R^1 es $-CH(G^1)_2$, donde cada G^1 es arilo;

L^2 es C(O);

R^2 es $-(CR^cR^d)_p-G^2$; donde G^2 es arilo;

p es 1;

R^c y R^d, en cada caso, son cada uno en forma independiente hidrógeno o alquilo; y

R^3 es hidrógeno.

13. El compuesto de acuerdo con la reivindicación 1, donde

L^1 es C(O), $S(O)_2$ o $-(CR^aR^b)_m-$;

R^a y R^b, en cada caso, son en forma independiente hidrógeno o alquilo;

m es 1;

R^1 es G^1 o $-(CR^aR^b)_m-G^1$, donde G^1 es arilo o heteroarilo;

L^2 es $-(CR^cR^d)_p-$;

R^c y R^d son cada uno hidrógeno;

p es 1;

R^2 es G^2, donde G^2 es arilo, cicloalquilo o heteroarilo; o

L^2-R^2 tomados juntos son alquilo, G^2, o -$C(R^c)(G^2)(G^3)$, donde G^2 y G^3 son cada uno arilo o heteroarilo y R^c es hidrógeno; y

R^3 es hidrógeno o alquilo.

14. El compuesto de acuerdo con la reivindicación 1, donde

L^1 es C(O);

R^1 es $-(CR^eR^f)_n$-$N(R^5)_2$;

n es 1 o 2;

R^e y R^f en cada caso son cada uno en forma independiente hidrógeno o alquilo;

R^5 en cada caso es en forma independiente hidrógeno o alquilo;

L^2 es C(O) o $S(O)_2$;

R^2 es G^2 o -$C(R^c)(G^2)(G^3)$, donde G^2 y G^3 son cada uno arilo o heteroarilo y R^c es hidrógeno; y

R^3 es hidrógeno, alquilo, o cicloalquilo.

15. El compuesto de acuerdo con la reivindicación 1, donde

L^1 es C(O);

R^1 es $-(CR^eR^f)_n$-$N(R^5)_2$ o $-(CR^eR^f)_n$-$N(R^5)C(O)O$(alquil);

n es 1 o 2;

R^e y R^f en cada caso son cada uno en forma independiente hidrógeno, alquilo, o arilalquilo;

R^5 en cada caso es en forma independiente hidrógeno, alquilo o cicloalquilo;

L^2 es C(O);

R^2 es $-(CR^gR^h)_qN(R^4)(R^5)$ o $-(CR^gR^h)_q$-$N(R^5)C(O)O$(alquil);

q es 1 o 2;

R^4 es hidrógeno o alquilo;

R^g y R^h en cada caso son cada uno en forma independiente hidrógeno o alquilo; y

R^3 es hidrógeno.

16. El compuesto de la reivindicación 1, donde

L^1-R^1 tomados juntos son hidrógeno; G^1 o $CH(G^1)_2$, donde G^1 es arilo o

heteroarilo;

L^2 es C(O);

R^2 es $-(CR^gR^h)_qN(R^4)(R^5)$ o $-(CR^gR^h)_q-N(R^5)C(O)O$(alquil);

q es 1 o 2;

R^4 es hidrógeno, alquilo, o cicloalquilalquilo;

R^5 es hidrógeno o alquilo;

R^g y R^h en cada caso son cada uno en forma independiente hidrógeno o alquilo; y

R^3 es hidrógeno.

17. El compuesto de la reivindicación 1, donde

L^1-R^1 tomados juntos son G^1, donde G^1 es arilo o heteroarilo;

L^2 es C(O);

R^2 es G^2, donde G^2 es arilo o heteroarilo; y

R^3 es hidrógeno o alquilo.

18. El compuesto de acuerdo con la reivindicación 1 o una sal aceptable farmacéuticamente del mismo, seleccionado a partir del grupo que consiste en:

N-[(3a*S**,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclopentancarboxamida;

N-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclopentancarboxamida;

N-[(3a*R**,4*R**,6a*S**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclohexil-2-fenilacetamida;

N-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclohexil-2-fenilacetamida;

N-[(3a*R**,4*R**,6a*S**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*R**,4*S**,6a*S**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*S**,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclopentil-2-fenilacetamida;

N-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclopentil-2-fenilacetamida;

N-[(3a*S**,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-

fenilciclohexanocarboxamida;

N-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclohexanocarboxamida;

N-[(3a*S**,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida;

(2*S*)-2-(3-benzoilfenil)-*N*-[(3a*S**,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]propanamida;

(2*S*)-2-(3-benzoilfenil)-*N*-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]propanamida;

N-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclopentil-2-fenilacetamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilpropanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-propilpentanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]cicloheptancarboxamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(4-isobutilfenil)propanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclohexanocarboxamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,3-difenilpropanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-metil-3-fenilpropanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-metil-2-fenilpropanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclopropancarboxamida;

2-bencil-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetilbutanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetil-2-fenilbutanamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetil-2-fenilbutanamida;

(2*R*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetil-2-fenilbutanamida;

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclopentil-2-fenilacetamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

(2*R*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida;

(2*R*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilpropanamida;

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilpropanamida;

(2*S*)-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(4-isobutilfenil)propanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclopropil-2-fenilacetamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-ciclobutil-2-

fenilacetamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(4-clorofenil)-3-metilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-etil-2-fenilpentanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(4-hidroxifenil)-3-metilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclohexanocarboxamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-metil-2-fenilpropanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-fenilciclopropancarboxamida;

2-bencil-*N*-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,3-difenilpropanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-metil-3-fenilpropanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3,3-dimetil-2-fenilbutanamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(2-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[4-fluoro-3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-fluoro-4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

N-{(3a*S*,4*S*,6a*R*)-2-[3,5-bis(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-

4–il}-2,2-diciclohexilacetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[2-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-metilbencil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(4-metilbencil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometoxi)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

N-{(3a*S*,4*S*,6a*R*)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida;

N-{(3a*S*,4*S*,6a*R*)-2-[6,6-bis(4-fluorofenil)hexil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida;

N-{(3a*S*,4*S*,6a*R*)-2-[3-(3-clorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(3-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(3-fenilpropil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-((3a*S*,4*S*,6a*R*)-2-{3-[4-(trifluorometil)fenil]propil}octahidrociclopenta[*c*]pirrol-4–il)acetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(piridin-4–ilmetil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*S*,6a*R*)-2-(piridin-3–ilmetil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-

(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

N-{(3a*S*,4*R*,6a*R*)-2-[3,5-bis(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida;

N-{(3a*S*,4*R*,6a*R*)-2-[6,6-bis(4-fluorofenil)hexil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida;

2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-2-(3,3-difenilpropil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

N-{(3a*S*,4*R*,6a*R*)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida;

N-{(3a*S*,4*R*,6a*R*)-2-[4,4-bis(4-fluorofenil)butil]octahidrociclopenta[*c*]pirrol-4–il}-2,2-diciclohexilacetamida;

3-metil-2-fenil-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(ciclohexilmetil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

3-metil-*N*-[(3a*R*,4*S*,6a*S*)-2-metiloctahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(2-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(3-clorobencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(3-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

3-metil-2-fenil-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(3-metoxibencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

3-metil-*N*-[(3a*R*,4*S*,6a*S*)-2-(3-metilbencil)octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida;

3-metil-*N*-[(3a*R*,4*S*,6a*S*)-2-(2-metilbencil)octahidrociclopenta[*c*]pirrol-4–il]-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(2,6-dimetilbencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(2-metoxibencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(4-*tert*-butilbencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(4-metoxibencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(3-cianobencil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

3-metil-2-fenil-*N*-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

3-metil-2-fenil-*N*-{(3a*R*,4*S*,6a*S*)-2-[2-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[4-fluoro-3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[3-fluoro-4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

3-metil-2-fenil-*N*-[(3a*R*,4*S*,6a*S*)-2-(tien-2–ilmetil)octahidrociclopenta[*c*]pirrol-4–il]butanamida;

3-metil-2-fenil-*N*-[(3a*R*,4*S*,6a*S*)-2-(piridin-4–ilmetil)octahidrociclopenta[*c*]pirrol-4–il]butanamida;

3-metil-2-fenil-*N*-[(3a*R*,4*S*,6a*S*)-2-(2-feniletil)octahidrociclopenta[*c*]pirrol-4–il]butanamida;

3-metil-2-fenil-*N*-[(3a*R*,4*S*,6a*S*)-2-(3-fenilpropil)octahidrociclopenta[*c*]pirrol-4–il]butanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[3-(4-*tert*-butilfenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[6,6-bis(4-fluorofenil)hexil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

3-metil-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(2-metilfenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-2-fenilbutanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[3-(3-clorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-3-

metil-2-fenilbutanamida;

3-metil-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(3-metilfenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-2-fenilbutanamida;

3-metil-2-fenil-*N*-((3a*R*,4*S*,6a*S*)-2-{3-[3-(trifluorometil)fenil]propil}octahidrociclopenta[*c*]pirrol-4–il)butanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[3-(3-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

3-metil-2-fenil-*N*-[(3a*R*,4*S*,6a*S*)-2-(4-fenilbutil)octahidrociclopenta[*c*]pirrol-4–il]butanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[3-(3-cloro-5-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

3-metil-2-fenil-*N*-((3a*R*,4*S*,6a*S*)-2-{3-[4-(trifluorometil)fenil]propil}octahidrociclopenta[*c*]pirrol-4–il)butanamida;

N-[(3a*R*,4*S*,6a*S*)-2-(3,3-difenilpropil)octahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[4,4-bis(4-fluorofenil)butil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

N-{(3a*R*,4*S*,6a*S*)-2-[5,5-bis(4-fluorofenil)pentil]octahidrociclopenta[*c*]pirrol-4–il}-3-metil-2-fenilbutanamida;

N-[(3a*S*,4*S*,6a*R*)-2-benzhidriloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida;

N-[(3a*S*,4*R*,6a*R*)-2-benzhidriloctahidrociclopenta[*c*]pirrol-4–il]-2,2-diciclohexilacetamida;

3-metil-2-fenil-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

3,3-dimetil-2-fenil-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

2,2-diciclohexil-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2-etil-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

2-propil-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}pentanamida;

N-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}ciclohexanocarboxamida;

N-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}cicloheptancarboxamida;

N-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}ciclopentancarboxamida;

6,6-bis(4-fluorofenil)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}hexanamida;

3,3-difenil-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}propanamida;

5,5-bis(4-fluorofenil)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}pentanamida;

3,3-bis(4-fluorofenil)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[c]pirrol-4–il}propanamida;

4,4-bis(4-fluorofenil)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

2,2-difenil-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-bis(4-fluorofenil)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^2-(*tert*-butiloxicarbonil)-N^2-metil-N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

6,6-bis(4-fluorofenil)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}hexanamida;

3,3-difenil-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}propanamida;

5,5-bis(4-fluorofenil)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-

(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}pentanamida;

3,3-bis(4-fluorofenil)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}propanamida;

4,4-bis(4-fluorofenil)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

2,2-difenil-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-bis(4-fluorofenil)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

3,3-dimetil-2-fenil-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(*tert*-butiloxicarbonil)-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^2-(*tert*-butiloxicarbonil)-N^2-metil-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(*tert*-butiloxicarbonil)-N^2-metil-L-leucinamida;

2,2-diciclohexil-2-hidroxi-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

N^2-(*tert*-butiloxicarbonil)-N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

2,2-diciclohexil-2-hidroxi-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

N^2-(*tert*-butiloxicarbonil)-N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

2,2-diciclohexil-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-{(3a*R*,4*R*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-{(3a*R**,4*R**,6a*S**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^2-metil-N^1-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^2-metil-N^1-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida;

N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[c]pirrol-4–il}-L-leucinamida;

N^2-metil-N^2-(metilsulfonil)-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-N^2-(metilsulfonil)-L-leucinamida;

N^2-metil-N^2-(metilsulfonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(metilsulfonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(metilsulfonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^2-(ciclopropilsulfonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(isobutilsulfonil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(ciclopropilsulfonil)-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-acetil-N^2-metil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-

(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(2,2-dimetilpropanoil)-N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(2,2-dimetilpropanoil)-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

(S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de isobutilo;

(S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de ciclopentilo;

N^2-[(*tert*-butilamino)carbonil]-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-[(ciclopentilamino)carbonil]-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

3-(trifluorometil)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida;

3-(trifluorometil)-*N*-{(3a*S**,4*R**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida;

3-(trifluorometil)-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida;

3-(trifluorometil)-*N*-{(3a*R*,4*R*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida;

3-(trifluorometil)-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida;

N-{(3a*S*,4*R*,6a*R*)-2-[6,6-bis(4-fluorofenil)hexil]octahidrociclopenta[*c*]pirrol-4–il}-3-(trifluorometil)bencenosulfonamida;

N-{(3a*S*,4*R*,6a*R*)-2-[3,5-bis(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-3-(trifluorometil)bencenosulfonamida;

N-{(3a*S*,4*R*,6a*R*)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-3-(trifluorometil)bencenosulfonamida;

N-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-3-(trifluorometil)bencenosulfonamida;

N-[(3a*S*,4*S*,6a*R*)-2-(4-hidroxibutil)octahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida;

(3a*S**,4*S**,6a*R**)-*N*,*N*-diciclopropil-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4-amina;

(3a*S**,4*R**,6a*R**)-2-bencil-*N*-ciclopropiloctahidrociclopenta[*c*]pirrol-4-amina;

(3a*S**,4*S**,6a*R**)-2-bencil-*N*-ciclopropiloctahidrociclopenta[*c*]pirrol-4-amina;

N-[(3a*S**,4*S**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*-ciclopropil-3-(trifluorometil)bencenosulfonamida;

N-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*-ciclopropil-3-(trifluorometil)bencenosulfonamida;

N-ciclopropil-*N*-[(3a*S**,4*S**,6a*R**)-octahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida;

N-{(3a*S**,4*S**,6a*R**)-2-[6,6-bis(4-fluorofenil)hexil]octahidrociclopenta[*c*]pirrol-4–il}-*N*-ciclopropil-3-(trifluorometil)bencenosulfonamida;

N-{(3a*S**,4*S**,6a*R**)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-*N*-ciclopropil-3-(trifluorometil)bencenosulfonamida;

N-ciclopropil-3-(trifluorometil)-*N*-{(3a*S**,4*S**,6a*R**)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}bencenosulfonamida;

2,2-diciclohexil-*N*-((3a*S*,4*S*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)acetamida;

2,2-diciclohexil-*N*-{(3a*S*,4*S*,6a*R*)-2-[(2-feniletil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

2,2-diciclohexil-*N*-((3a*S*,4*S*,6a*R*)-2-{[2-(1-

naftil)etil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)acetamida;

2,2-diciclohexil-*N*-((3a*S*,4*S*,6a*R*)-2-{[3-(trifluorometil)bencil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)acetamida;

2,2-diciclohexil-*N*-((3a*S*,4*S*,6a*R*)-2-{[2-(4-fluorofenil)etil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)acetamida;

(2*S*)-2-fenil-*N*-{(3a*R*,4*R*,6a*S*)-2-[(1*S*)-1-feniletil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

(2*S*)-2-fenil-*N*-{(3a*R*,4*S*,6a*S*)-2-[(1*S*)-1-feniletil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

(2*S*)-2-fenil-*N*-{(3a*S*,4*S*,6a*R*)-2-[(1*S*)-1-feniletil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

(2*S*)-2-fenil-*N*-{(3a*S*,4*R*,6a*R*)-2-[(1*S*)-1-feniletil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*,3-dimetil-2-fenilbutanamida;

N-[(3a*S**,4*R**,6a*R**)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*,3-dimetil-2-fenilbutanamida;

(3a*R**,4*S**,6a*S**)-*N*-bencil-2-(3-metil-2-fenilbutanoil)octahidrociclopenta[*c*]pirrol-4-amina;

2,2-diciclohexil-*N*-[(3a*S*,4*R*,6a*R*)-2-(*N*,*N*-dimetil-D-leucil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

N-[(3a*R*,4*S*,6a*S*)-2-benzoiloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-2-fenilbutanamida;

N'-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*-isopropil-*N*-fenilurea;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-(1,1-dioxidoisotiazolidin-2–il)-4-metilpentanamida;

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–ilcarbamato de tert-butilo;

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(etil)carbamato de tert-butilo;

(2S,3S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3,3-dimetil-1-oxobutan-2–ilcarbamato de tert-butilo;

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo;

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxohexan-2–il(metil)carbamato de tert-butilo;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2,2-bis(4-fluorofenil)acetamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-isopropil-3-metilbutanamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metilbutanamida;

(2S)-2-({[(3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–il]amino}carbonil)piperidin-1-carboxilato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3-metil-1-oxobutan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-3,3-dimetil-1-oxobutan-2–ilcarbamato de tert-butilo;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-2-isopropil-3-metilbutanamida;

N-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metilbutanamida;

2-ciclohexil-2-hidroxi-*N*-{(3a*S*,4*S*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}acetamida;

(S)-1-((3aS,4S,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aS,4S,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aR,4R,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-1-

oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aR,4R,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

S-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(metilsulfonil)-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-(metilsulfonil)-L-leucinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-neopentil-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-neopentil-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-neopentil-L-norvalinamida;

(S)-1-((3aR,4S,6aS)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-benciloctahidrociclopenta[c]pirrol-4–ilamino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-morfolin-4–ilpentanamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-pirrolidin-1–ilpentanamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-piperidin-1–ilpentanamida;

N^2-neopentil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-neopentil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-neopentil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-neopentil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-neopentil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

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N^2-neopentil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N-(*tert*-butoxicarbonil)-*N*-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida;

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

N^2-neopentil-*N*^{1}-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-*N*^{2}-neopentil-L-leucinamida;

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(5-(trifluorometil)piridin-2–il)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo;

(S)-1-oxo-1-((3aR,4S,6aS)-2-(5-(trifluorometil)piridin-2–il)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de isopropilo;

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(6-(trifluorometil)piridin-2–il)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo;

(S)-4,4-dimetil-1-((3aR,4S,6aS)-2-(2-(metilsulfonil)pirimidin-5–il)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–ilcarbamato de tert-butilo;

(S)-2-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilcarbamoil)pirrolidin-1-carboxilato de tert-butilo;

(1R)-1-isopropil-3-oxo-3-[((3aS,4R,6aR)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]propilcarbamato de tert-butilo;

(2S)-2-{[((3aS,4R,6aR)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]carbonil}piperidin-1-carboxilato de tert-butilo;

N-(*tert*-butoxicarbonil)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida;

N-(*tert*-butoxicarbonil)-*N*-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida;

(S)-2-((3aR,4S,6aS)-2-(3-

(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilcarbamoil)pirrolidin-1-carboxilato de tert-butilo;

(1R)-1-isopropil-3-oxo-3-[((3aR,4S,6aS)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]propilcarbamato de tert-butilo;

metil((S)-3-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo;

(2S)-2-{[((3aR,4S,6aS)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]carbonil}piperidin-1-carboxilato de tert-butilo;

(3S)-3-{[((3aR,4S,6aS)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[c]pirrol-4–il)amino]carbonil}-3,4-dihidroisoquinolin-2(1H)-carboxilato de tert-butilo;

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo;

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)hexan-2–il)carbamato de tert-butilo;

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

(S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de isopropilo;

(S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de isopropilo;

(3a*S*,4*R*,6a*R*)-*N*-neopentil-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*-neopentil-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*-isopropil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}-*N*-isopropiloctahidrociclopenta[*c*]pirrol-4-amina;

(3a*S*,4*R*,6a*R*)-*N*-(4-fluorobencil)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*-(4-fluorobencil)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*-(4-fluorobencil)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*-etil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*,*N*-dietil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*-propil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*,*N*-dipropil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*-(ciclopropilmetil)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}-*N*-etiloctahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}-*N*,*N*-dietiloctahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}-*N*-[5-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4-amina;

(S)-1-(etil((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-4,4-dimetil-1-oxo-1-(propil((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)pentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((ciclopropilmetil)((3aR,4S,6aS)-2-(4-

(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)-4,4-dimetil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

2-nitro-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)bencenosulfonamida;

N-metil-2-nitro-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)bencenosulfonamida;

(3a*R*,4*S*,6a*S*)-*N*-metil-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(S)-4,4-dimetil-1-(metil((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–il)amino)-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(2*S*)-2-(1,1-dioxidoisotiazolidin-2–il)-4-metil-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}pentanamida;

2-isopropil-3-metil-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

2-isopropil-3-metil-*N*-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}butanamida;

(S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo;

metil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

(S)-1-((3aR,4S,6aS)-2-(4-fluorobencil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

etil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-(3-fluoro-4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–

il(metil)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-(4-fluoro-3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

(S)-1-((3aR,4S,6aS)-2-(4-fluorobencil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo;

metil((S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo;

metil((S)-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-(4-fluorobencil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(2*S*)-4-metil-2-morfolin-4–il-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida;

(2*S*)-4-metil-2-pirrolidin-1–il-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida;

(2*S*)-4-metil-2-piperidin-1–il-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida;

metil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

etil((S)-4-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-

(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((S)-4-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-(4-fluoro-3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-4-metil-1-oxopentan-2–il(metil)carbamato de tert-butilo;

metil((S)-1-oxo-1-((3aR,4R,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((S)-4-metil-1-oxo-1-((3aR,4R,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

(S)-1-((3aS,4R,6aR)-2-(4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo;

metil((S)-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((2S,3S)-3-metil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((2S,3S)-3-metil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((2S,3S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((2S,3S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo;

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo;

(S)-4,4-dimetil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo;

(S)-4,4-dimetil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il(metil)carbamato de tert-butilo;

metil((S)-3-metil-1-oxo-1-((3aS,4R,6aR)-2-(3-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–il)carbamato de tert-butilo;

(S)-3,3-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–ilcarbamato de tert-butilo;

(S)-3,3-dimetil-1-oxo-1-((3aS,4R,6aR)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–ilcarbamato de tert-butilo;

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)hexan-2–il)carbamato de tert-butilo;

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)fenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de tert-butilo;

(2*S*)-4-metil-2-pirrolidin-1–il-*N*-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)benzoil]octahidrociclopenta[*c*]pirrol-4–il}pentanamida;

(2*S*)-4-metil-*N*-[(3a*S*,4*R*,6a*R*)-2-(metilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-2-pirrolidin-1–ilpentanamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-(ciclopropilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-4-metil-2-pirrolidin-1–ilpentanamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida;

metil((S)-4-metil-1-((3aS,4R,6aR)-octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il)carbamato de tert-butilo;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]piperidin-2-carboxamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-valinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-isoleucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-isoleucinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2,4-dimetil-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-L-valinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-metil-L-valinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2,4-dimetil-L-leucinamida;

N^1-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida;

N^1-[(3a*S*,4*S*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-4-metil-L-leucinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norleucinamida;

N^1-[(3a*R*,4*R*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida;

N^1-[(3a*R*,4*R*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-

leucinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida;

N^2-etil-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-valinamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]piperidin-2-carboxamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-valinamida;

(2*S*)-*N*-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}piperidin-2-carboxamida;

N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida;

N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-valinamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[3-fluoro-4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[4-fluoro-3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida;

N^2-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida;

N^2-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida;

N^2-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida;

N^2-etil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida;

N-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida;

N-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-prolinamida;

(3*R*)-3-amino-4-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida;

(2*S*)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)piperidin-2-carboxamida;

(3*S*)-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-1,2,3,4-tetrahidroisoquinolin-3-carboxamida;

4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norleucinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-metil-N^1-((3a*R*;4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-prolinamida;

(3*R*)-3-amino-4-metil-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida;

(2*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)piperidin-2-carboxamida;

(2*S*)-*N*-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}piperidin-2-carboxamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-valinamida;

(2*S*)-*N*-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)piperidin-2-carboxamida;

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-metil-N^1-((3a*S*;4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida;

N^1-((3a*S*,4*R*,6a*R*)-2-{[4-fluoro-3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-metil-L-leucinamida;

3-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida;

3-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-isoleucinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-isoleucinamida;

N^2-metil-N^1-((3a*S*;4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-isoleucinamida;

N^2-metil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-

(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-isoleucinamida;

N^2,4-dimetil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2,4-dimetil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2,4-dimetil-*N*^{1}-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2,4-dimetil-*N*^{1}-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norleucinamida;

4-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-metil-*N*^{1}-((3a*R*,4*R*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-metil-*N*^{1}-((3a*R*,4*R*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

3-ciclohexil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-alaninamida;

3-ciclohexil-*N*^{2}-metil-*N*^{1}-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-alaninamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-5-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-4-metil-L-leucinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-4-metil-L-leucinamida;

N-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-fenilalaninamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2,4-dimetil-L-leucinamida;

N-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-*N*-metil-L-fenilalaninamida;

N^1-ciclopropil-N^2,4-dimetil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^1-etil-N^2,4-dimetil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2,4-dimetil-N^1-propil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^1-(ciclopropilmetil)-N^2,4-dimetil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^1,N^2,4-trimetil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^1,N^2-dimetil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^1,N^2,4-trimetil-L-leucinamida;

4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[2-(metilsulfonil)pirimidin-5–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3,4-difluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(3,5-difluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida;

N^1-{(3a*S*,4*R*,6a*R*)-2-[(4-clorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida;

N^2-metil-N^1-[(3a*S*,4*R*,6a*R*)-2-(fenilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-L-leucinamida;

N^2-metil-N^1-{(3a*S*,4*R*,6a*R*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-(4-fluorobencil)octahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-valinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-valinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-4-metil-L-leucinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norleucinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-leucinamida;

N^2-metil-N^1-((3a*S*,4*S*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-metil-N^1-((3a*S*,4*S*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[3,3-bis(4-fluorofenil)propil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

2,2-bis(4-fluorofenil)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

2,2-bis(4-fluorofenil)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-metil-L-norvalil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

N-[(3a*R*,4*S*,6a*S*)-2-(*N*,4-dimetil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-2,2-

bis(4-fluorofenil)acetamida;

2,2-bis(4-fluorofenil)-*N*-[(3a*R*,4*S*,6a*S*)-2-(4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

(S)-1-((3aR,4S,6aS)-4-((S)-2-(tert-butoxicarbonilamino)-4,4-dimetilpentanamido)hexahidrociclopenta[c]pirrol-2(1H)–il)-4,4-dimetil-1-oxopentan-2–ilcarbamato de tert-butilo;

4-metil-N^1-[(3a*R*,4*S*,6a*S*)-2-(4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-L-leucinamida;

4-metil-N^1-[(3a*R*,4*S*,6a*S*)-2-L-fenilalaniloctahidrociclopenta[*c*]pirrol-4–il]-L-leucinamida;

(3a*R*,4*S*,6a*S*)-*N*-benzhidril-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4-amina;

(3a*S*,4*R*,6a*R*)-*N*-benzhidril-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

(3a*R*,4*S*,6a*S*)-*N*-benzhidril-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4-amina;

N^1-[(3a*S*,4*R*,6a*R*)-2-benzhidriloctahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-leucinamida;

4-metil-N^2-propil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-(ciclopropilmetil)-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-(ciclobutilmetil)-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-isobutil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-(ciclopentilmetil)-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-(ciclohexilmetil)-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-butil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-etil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-

(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-(ciclopropilmetil)-4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(ciclopropilmetil)-4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-isopropil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-isopropil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-isopropil-N^1-((3a*S*,4*R*,6a*R*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-isopropil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-isopropil-N^1-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

3-ciclohexil-N^2-isopropil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-alaninamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-5-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-isopropil-4-metil-L-leucinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-isopropil-4-metil-L-leucinamida;

N^2-isopropil-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropil-4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-4-metil-L-leucinamida;

N^2-isopropil-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropil-L-fenilalanil)octahidrociclopenta[*c*]pirrol-4–il]-4-metil-L-leucinamida;

N^2-isopropil-4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[5-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-isopropil-4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

2,2-bis(4-fluorofenil)-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-isopropil-4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]acetamida;

N^2-isopropil-4-metil-N^1-{(3a*R*,4*S*,6a*S*)-2-[2-(metilsulfonil)pirimidin-5–il]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-isopropil-L-norvalinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-N^2-isopropil-L-norvalinamida;

N^2-isopropil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2,N^2-dimetil-N^1-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

(3*R*)-3-(dimetilamino)-4-metil-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida;

N^2-ciclopropil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2,N^2-diciclopropil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-ciclopentil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-ciclohexil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-(1-etilpropil)-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-ciclobutil-4-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

4-metil-N^2-neopentil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^2-ciclopentil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-ciclohexil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-ciclopentil-N^1-[(3a*R*,4*S*,6a*S*)-2-(*N*-ciclopentil-4-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-4-metil-L-leucinamida;

N^2,N^2-dimetil-N^1-{(3a*S*,4*S*,6a*R*)-2-[3-

(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*^{2}-metil-*N*^{2}-neopentil-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*^{2}-(3,3-dimetilbutil)-*N*^{2}-metil-L-leucinamida;

N^2,*N*^{2}-dimetil-*N*^{1}-((3a*S*,4*R*,6a*R*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-leucinamida;

N^1-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*^{2}-(4-fluorobencil)-*N*^{2}-metil-L-leucinamida;

(2*S*)-*N*-[(3a*S*,4*R*,6a*R*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-1-(metilsulfonil)piperidin-2-carboxamida;

(3*R*)-4-metil-3-[(metilsulfonil)amino]-*N*-((3a*R*,4*S*,6a*S*)-2-{[3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)pentanamida;

N^2-(metilsulfonil)-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(metilsulfonil)-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-D-leucinamida;

N^2-etil-*N*^{2}-(metilsulfonil)-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

4-metil-*N*^{2}-(metilsulfonil)-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

3-metil-*N*^{2}-(metilsulfonil)-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-valinamida;

N^2-(metilsulfonil)-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida;

N^2-(isopropilsulfonil)-*N*^{1}-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(fenilsulfonil)-*N*^{1}-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

N^2-(ciclopentilsulfonil)-*N*^{1}-{(3a*S*,4*R*,6a*R*)-2-[3-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-leucinamida;

(S)-4,4-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato

de isopropilo;

(S)-3,3-dimetil-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)butan-2–ilcarbamato de isopropilo;

(S)-1-oxo-1-((3aR,4S,6aS)-2-(4-(trifluorometil)bencil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–ilcarbamato de ciclopentilo;

N^2-(2,2-dimetilpropanoil)-N^1-{(3a*R*,4*S*,6a*S*)-2-[4-(trifluorometil)bencil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida;

(S)-1-((3aR,4S,6aS)-2-(3-cloro-4-fluorofenilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)-1-oxopentan-2–il(metil)carbamato de tert-butilo;

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(piridin-3–ilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

metil((S)-1-oxo-1-((3aR,4S,6aS)-2-(tiofen-2–ilsulfonil)octahidrociclopenta[c]pirrol-4–ilamino)pentan-2–il)carbamato de tert-butilo;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometoxi)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-metil-N^1-[(3a*R*,4*S*,6a*S*)-2-(tien-2–ilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-cloro-4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

N^2-metil-N^1-[(3a*R*,4*S*,6a*S*)-2-(piridin-3–ilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-cianofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-metoxifenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[3,5-bis(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-metil-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(2-cloro-4-fluorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

N^2-metil-N^1-[(3a*R*,4*S*,6a*S*)-2-(1-naftilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-L-norvalinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[4-bromo-3-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-metil-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3,4-diclorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(4-*tert*-butilfenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-(1,1'-bifenil-4–ilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3,4-dimetoxifenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-cianofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

N^1-[(3a*R*,4*S*,6a*S*)-2-(2-furilsulfonil)octahidrociclopenta[*c*]pirrol-4–il]-N^2-metil-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(2,3-diclorofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[4-(trifluorometil)bencil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^2-metil-N^1-((3a*R*,4*S*,6a*S*)-2-{[2-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-L-norvalinamida;

N^1-{(3a*R*,4*S*,6a*S*)-2-[(3-bromofenil)sulfonil]octahidrociclopenta[*c*]pirrol-4–il}-N^2-metil-L-norvalinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-4-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-metil-L-norvalinamida;

N^1-((3a*R*,4*S*,6a*S*)-2-{[2-cloro-5-(trifluorometil)fenil]sulfonil}octahidrociclopenta[*c*]pirrol-4–il)-N^2-metil-L-norvalinamida;

N^2-metil-*N*^{1}-{(3a*R*,4*S*,6a*S*)-2-[3-(trifluorometil)benzoil]octahidrociclopenta[*c*]pirrol-4–il}-L-norvalinamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-*N*-isopropil-3-(trifluorometil)bencenosulfonamida;

N-[(3a*R*,4*S*,6a*S*)-2-benciloctahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida;

N-isopropil-*N*-[(3a*R*,4*S*,6a*S*)-2-(*N*-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida;

N-[(3a*R*,4*S*,6a*S*)-2-(*N*-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida;

N-ciclopropil-*N*-[(3a*S**,4*S**,6a*R**)-[2-(*N*-metil-L-leucil)octahidrociclopenta[*c*]pirrol-4–il]-3-(trifluorometil)bencenosulfonamida; y

4-fluoro-*N*-{(3a*R*,4*S*,6a*S*)-2-[6-(trifluorometil)piridin-2–il]octahidrociclopenta[*c*]pirrol-4–il}benzamida.

19. Una composición farmacéutica, que comprende una cantidad terapéuticamente eficaz de un compuesto de la fórmula (I) de acuerdo con la reivindicación 1, o una sal farmacéuticamente aceptable del mismo, en combinación con un vehículo farmacéuticamente aceptable.

20. Un método de tratamiento del dolor en un sujeto que lo necesita, que comprende: administrarle al sujeto una cantidad terapéuticamente adecuada de un compuesto de la fórmula (I), o una sal farmacéuticamente aceptable del mismo, en donde el dolor es dolor agudo, dolor crónico, dolor neuropático, dolor inflamatorio, dolor visceral, dolor de cáncer, alodinia, fibromialgia, ciática, dolor de espalda y dolor de cabeza incluyendo migraña, o combinaciones de los mismos.

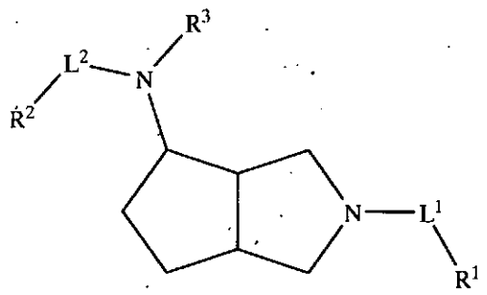
21. Un método de tratamiento de trastornos del sistema nervioso central en un sujeto que lo necesita, que comprende el paso de: administrar una cantidad terapéuticamente adecuada de un compuesto de la fórmula (I), o una sal farmacéuticamente aceptable del mismo, en donde los trastornos del sistema nervioso central incluyen accidente cerebrovascular, epilepsia, depresión maníaca, trastornos bipolares, depresión, ansiedad, esquizofrenia, migraña y psicosis; trastornos degenerativos neurales incluyendo mal de Alzheimer, demencia relacionada con SIDA, mal de Parkinson, neuropatía causada por lesión de la cabeza y demencia causada por trastornos cerebrovasculares; trastornos del

tracto urinario inferior incluyendo vejiga superactiva, prostatis, prostadinia, cistitis intersticial e hiperplasia prostática benigna; trastornos causados por estrés psicogénico incluyendo asma bronquial, angina inestable e inflamación de colon hipersensible; trastornos cardiovasculares incluyendo hipertensión, aterosclerosis, insuficiencia cardíaca y arritmias cardíacas; síntomas de abstinencia por adicción a drogas, incluyendo síntomas de abstinencia por adicción a etanol; trastornos de la piel incluyendo pruritis y dermatitis alérgica, enfermedad de intestino inflamatorio; cáncer; diabetes; y esterilidad y disfunción sexual, o combinaciones de los mismos.

NUEVAS OCTAHIDROCICLOPENTA[C]PIRROL-4-AMINAS SUSTITUIDAS COMO BLOQUEANTES DE LOS CANALES DE CALCIO

RESUMEN

Inhibidores que contienen compuestos de la fórmula (I)



(I)

en donde L^1, L^2, R^1, R^2 y R^3 son como se definen en la memoria descriptiva. La presente solicitud también se relaciona con composiciones que comprenden dichos compuestos, y métodos de tratamiento de condiciones y trastornos usando tales compuestos y composiciones.

000885

Industria y Comercio
SUPERINTENDENCIA

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

PATENTE DE INVENCION ___ PCT __X__ MODELO DE UTILIDAD ___ DISEÑO INDUSTRIAL ___

(21) Nº de solicitud: (22) Fecha de solicitud:
(51) Clasificación Internacional :

(71)Solicitante(s) **ABBOTT LABORATORIES**

(72) Inventor(es) **ANDREW STEWART, XENIA SEARLE, DARIA DARCZAK, MING YEUNG, STANLEY DIDOMENICO**

(74) Apoderado: **DRA. MARGARITA CASTELLANOS ABONDANO**

(30) Prioridad	(31)	**No. Prioridad**	32) **Fecha**	(33)	**País**
		61/117.995	**26/11/2008**		**US**

(85) Fecha inicio fase nacional:
(86) Datos relativos a la presentación de la solicitud PCT
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Nº publicación: **WO 2010/062927 A2**

(54) Titulo: **NUEVAS OCTAHIDROCICLOPENTA[C]PIRROL-4-AMINAS SUSTITUIDAS COMO BLOQUEANTES DE LOS CANALES DE CALCIO**

Industria y Comercio
SUPERINTENDENCIA

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

000886

(21) Nº de solicitud:

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(30) Prioridad (31) Nº Prioridad 32) Fecha (33) País
61/117.995 26/11/2008 US

(51) Int. Cl.:

(71)Solicitante(s) ABBOTT LABORATORIES

(72) Inventor(es) ANDREW STEWART
XENIA SEARLE
DARIA DARCZAK
Y OTROS

(74) Apoderado: MARGARITA CASTELLANOS ABONDANO

(85) Fecha limite inicio fase nacional:
(86) Datos relativos a la presentación de la solicitud PCT
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Nº de solicitud PCT/US2009/065847

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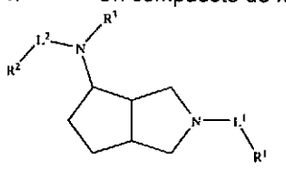
(54) Titulo: **NUEVAS OCTAHIDROCICLOPENTA[C]PIRROL-4-AMINAS SUSTITUIDAS COMO BLOQUEANTES DE LOS CANALES DE CALCIO**

Reivindicación(es):

1. Un compuesto de fórmula (I),



(I),

o una sal, prodroga, sal de una prodroga aceptables farmacéuticamente, o una combinación de las mismas, donde
L^1 es C(O), $S(O)_2$, $SO_2N(R^4)$, C(O)O o $-(CR^aR^b)_m-$;
R^1 es alquilo, G^1, $-CH(G^1)_2$, $-(CR^aR^b)_m-G^1$, $-(CR^aR^b)_m-CH(G^1)_2$, $-(CR^eR^f)_n-N(R^5)_2$, $-(CR^eR^f)_n-N(R^5)-C(O)O(alquilo)$, $-(CR^eR^f)_n-N(R^5)-C(O)(alquilo)$, o $-(CR^eR^f)_n-N(R^5)-SO_2R^6$; o
L^1-R^1 tomados juntos son hidrógeno, alquilo, hidroxialquilo, G^1, o $-CH(G^1)_2$;
L^2 es $-(CR^cR^d)_p-$, C(O), $C(O)N(R^4)$, $S(O)_2$, $SO_2N(R^5)$, o C(O)O;
R^2 es alquilo, G^2, $-C(R^c)(G^2)(G^3)$, $-(CR^cR^d)_p-G^2$, $-(CR^cR^d)_p-CH(G^2)(G^3)$, $-(CR^gR^h)_q-N(R^5)-C(O)O(alquilo)$, $-(CR^gR^h)_q-N(R^5)-C(O)O-G^2$, $-(CR^gR^h)_q-N(R^5)-C(O)(alquilo)$, $-(CR^gR^h)_q-N(R^5)-SO_2R^6$, $-(CR^gR^h)_q-N(R^4)(R^5)$, $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-(alquilo)$, o $-(CR^gR^h)_q-N(R^5)-C(O)N(R^5)-G^2$; o
L^2-R^2 tomados juntos son alquilo, G^2, o $-C(R^c)(G^2)(G^3)$;
m y p, en cada caso, son cada uno en forma independiente 1, 2, 3, 4, 5, o 6;
n y q, en cada caso, son cada uno en forma independiente 1, 2, 3, 4, o 5;
R^a, R^b, R^c, y R^d, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, arilalquilo, halógeno, haloalquilo o OR^7; o
R^a y R^b, o R^c y R^d, junto con el átomo de carbono al cual se encuentran unidos, forman opcionalmente un anillo C_{3-6} cicloalquilo;
R^e, R^f, R^g, y R^h, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, halógeno, haloalquilo, OR^7, cicloalquilalquilo, heteroarilo, arilalquilo, o heteroarilalquilo; donde los grupos arilo, cicloalquilo y heteroarilo de arilo, cicloalquilo y heteroarilo cada uno en forma independiente no se sustituye o se sustituye con 1, 2, 3, 4, o 5 sustituyentes seleccionados en forma independiente entre el grupo que consiste en alquilo y haloalquilo;
G^1, G^2, y G^3 en cada caso, son cada uno en forma independiente arilo, cicloalquilo, cicloalquenilo, heteroarilo, o heterociclo; donde G^1, G^2, y G^3 en cada caso cada uno en forma independiente no se sustituye o se sustituye con 1, 2, 3, 4, o 5 sustituyentes seleccionados entre el grupo que consiste en alquilo, alquenilo, alquinilo, ciano, haloalquilo, halógeno, nitro, oxo, fenilo, $N(R^7)_2$, $N(R^7)C(O)R^7$, OR^7, $C(O)R^7$, $C(O)OR^7$, $C(O)N(R^7)_2$, SO_2R^8, y $SO_2N(R^7)_2$; y donde G^1 no es quinolina, quinazolindiona, o piridopirimidindiona;
R^3 es hidrógeno, alquilo, haloalquilo, cicloalquilo, o cicloalquilalquilo;
R^4, R^5, y R^7, en cada caso, son cada uno en forma independiente hidrógeno, alquilo, arilo, arilalquilo, cicloalquilo, cicloalquilalquilo, o haloalquilo; donde dichos arilo, el arilo de arialquilo y cicloalquilo no se sustituyen o se sustituyen en forma independiente con 1, 2 3, 4, o 5 sustituyentes seleccionados en forma independiente entre el grupo que consiste en alquilo, haloalquilo, y halógeno;
R^6 es alquilo, arilo, cicloalquilo, cicloalquenilo, heteroarilo, o heterociclo; donde dichos arilo, heteroarilo y heterociclo no se sustituyen o se sustituyen en forma independiente con 1, 2 3, 4, o 5 sustituyentes seleccionados en forma independiente entre el grupo que consiste en alquilo, haloalquilo, y halógeno;
R^8 es alquilo o haloalquilo;
con la condición de que L^1-R^1 y L^2-R^2 no son ambos alquilo al mismo tiempo;
y con la condición de que cuando L^1-R^1 es alquilo, L^2-R^2 no es $C(O)N(R^4)$, donde R^4 es alquilo;
y con la condición adicional de que el compuesto no es:
N-(2-tritiloctahidrociclopenta[c]pirrol-4–il)acetamida;
N-(octahidrociclopenta[*c*]pirrol-4–il)acetamida
N-metil-*N*-(2-tritiloctahidrociclopenta[*c*]pirrol-4–il)acetamida;
N-metil-*N*-(octahidrociclopenta[*c*]pirrol-4–il)acetamida;
6-(2-(2-(3-fluoro-6-metoxi-1,5-naftiridin-4–il)etil)octahidrociclopenta[*c*]pirrol-4–ilamino)metil-2*H*-pirido[3,2-*b*][1,4]tiazin-3(4*H*)-ona;
2-(2-(3-fluoro-6-metoxi-1,5-naftiridin-4–il)etil)octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo;
octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo 2-bencilo; o
octahidrociclopenta[c]pirrol-4–ilcarbamato de tert-butilo.

2. . El compuesto de acuerdo con la reivindicación 1, donde
L^1 es $-(CR^aR^b)_m-$;

...

Industria y Comercio
SUPERINTENDENCIA

Bogotá,
2020

Doctor(a)
CASTELLANOS MARGARITA
Apoderado(a) y/o Representante de
ABBOTT LABORATORIES

REFERENCIA	Radicación No.	11 65858
	Solicitud internacional	PCT/US2009/065847
	Fecha inicio fase nacional	25/06/2012
	Trámite	11
	Evento	378
	Actuación	430
	Oficio No.	010970

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. Con respecto al resumen y de conformidad con lo dispuesto en el artículo 31 D. 486 en el cual se establece que el resumen consiste en una síntesis de la divulgación técnica contenida en la solicitud de patente, debe adecuar el resumen a los dispuesto en dicha norma, teniendo en cuenta que el extracto permitirá precisar el objeto de la invención, sus elementos característicos y el campo de aplicación.

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, conforme a lo establecido por el artículo 26 literal k) de la Decisión 486 de la Comisión de la Comunidad Andina. Cuando se trate de documentos otorgados en el extranjero, estos deberán legalizarse de conformidad con lo dispuesto por los artículos 259 y 260 del Código de Procedimiento Civil. Cuando se trate de las declaraciones a que hace referencia la Regla 4.17 ii) del Tratado de Cooperación en Materia de Patentes PCT., el alcance de las tales declaraciones se determinará según indiquen claramente una cesión de derechos del inventor al solicitante o su causante, de conformidad con lo dispuesto en el numeral 5.2.15 del Capítulo Quinto, Título X de la Circular Única de Superintendencia de Industria y Comercio.

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.

Continua en la página siguiente...

Radicación No.:11 65858

CARLOS DANIEL LEMUS GIRALDO
Profesional Universitario 2044-09 (P) con asignación de funciones
de la Dirección de Nuevas Creaciones.

El anterior requerimiento fue notificado por fijación en lista de fecha_____.
adpall: 15 JUL. 2011

Industria y Comercio
SUPERINTENDENCIA

Bogotá,
2020

Doctor(a)
CASTELLANOS MARGARITA
Apoderado(a) y/o Representante de
ABBOTT LABORATORIES

REFERENCIA	Radicación No.	11 65858
	Solicitud internacional	PCT/US2009/065847
	Fecha inicio fase nacional	25/06/2012
	Trámite	11
	Evento	378
	Actuación	430
	Oficio No.	010971

Teniendo en cuenta que el capítulo reivindicatorio presentado excede de diez reivindicaciones, es necesario que cancele la tasa establecida por cada reivindicación adicional presentada, de conformidad con lo dispuesto en la resolución de tasas vigente para la fecha de presentación de la solicitud, so pena de que no sean tenidas en cuenta dentro del presente trámite administrativo.

En consecuencia, con fundamento en lo previsto por el artículo 12 del Código Contencioso Administrativo, se le requiere para que dentro del término de dos (2) meses siguientes a la fecha de notificación del presente oficio atienda el requerimiento aquí señalado. Lo anterior, con el alcance que para tal efecto establece el artículo 13 de la misma codificación, respecto de las reivindicaciones adicionales.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del titulo primero de la Circular Única N° 10 de 2001.

CARLOS DANIEL LEMUS GIRALDO
Profesional Universitario 2044-09 (P) con asignación de funciones
de la Dirección de Nuevas Creaciones.

El anterior requerimiento fue notificado por fijación en lista de fecha_____.
adpa11 15 JUL. 2011

Industria y Comercio
SUPERINTENDENCIA

Bogotá,
2020

Doctor(a)
CASTELLANOS MARGARITA
Apoderado(a) y/o Representante de
ABBOTT LABORATORIES

REFERENCIA	Radicación No.	11 65858
	Solicitud internacional	PCT/US2009/065847
	Fecha inicio fase nacional	25/06/2012
	Trámite	11
	Evento	378
	Actuación	430
	Oficio No.	010971

Teniendo en cuenta que el capítulo reivindicatorio presentado excede de diez reivindicaciones, es necesario que cancele la tasa establecida por cada reivindicación adicional presentada, de conformidad con lo dispuesto en la resolución de tasas vigente para la fecha de presentación de la solicitud, so pena de que no sean tenidas en cuenta dentro del presente trámite administrativo.

En consecuencia, con fundamento en lo previsto por el artículo 12 del Código Contencioso Administrativo, se le requiere para que dentro del término de dos (2) meses siguientes a la fecha de notificación del presente oficio atienda el requerimiento aquí señalado. Lo anterior, con el alcance que para tal efecto establece el artículo 13 de la misma codificación, respecto de las reivindicaciones adicionales.

Notifíquese el presente oficio conforma a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del titulo primero de la Circular Única Nº 10 de 2001.

CARLOS DANIEL LEMUS GIRALDO
Profesional Universitario 2044-09 (P) con asignación de funciones
de la Dirección de Nuevas Creaciones.

El anterior requerimiento fue notificado por fijación en lista de fecha 15 JUL. 2011.
adpa11