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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
Rad: 06-038137- -00002-0000
Fec: 2006-09-29 17:45:20 Dep. 2020 NUECREACIONES
Tra 11 PATENTES II
Exp: 379 FASE NACIONAL II
Act 444 RESPUESTAREQUE
Folios: 17

Señora Jefe de la
DIVISION DE NUEVAS CREACIONES
Superintendencia de Industria y Comercio
E. S. D.

Trámite : **011**
Evento : **379**
Actuación: **444**

Referencia : Expediente No. **06.038.137**
Asunto : Solicitud de patente para MIMETICOS DE GLUCOCORTICOIDES, METODOS DE PREPARACIÓN, COMPOSICIONES FARMACÉUTICAS Y USOS DE LOS MISMOS
Solicitante : BOEHRINGER INGELHEIM PHARMACEUTICALS INC.

CONTESTACION OFICIO No. 8442

1. Yo, Emilio FERRERO, en mi condición de apoderado de la sociedad solicitante, BOEHRINGER INGELHEIM PHARMACEUTICALS INC., doy contestación al requerimiento efectuado por este Despacho mediante Oficio No. 8442 notificado por fijación en lista el 4 de agosto de 2006, para lo cual presento el siguiente documento:

- Copia del Reporte de Examen Preliminar Internacional de Patentabilidad de la invención de que trata el presente asunto, el cual no contiene anexos.

Se acompaña este documento con su correspondiente traducción al español.

2. De acuerdo con lo anterior, comedidamente solicito a Usted proseguir con el trámite de este asunto y ordenar la publicación de la solicitud de la patente identificada en la referencia.

Señora Jefe,

EMILIO FERRERO
T.P.A. No. 31.929

COLO 07612-841-012-3
SCT/SCT/
ID-000290/WPCL7612
Cns M-2006-00010849

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 9-269PCT_	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/US2004/031009	International filing date (day/month/year) 22.09.2004	Priority date (day/month/year) 24.09.2003

International Patent Classification (IPC) or national classification and IPC

A61K31/4745, A61K31/52, C07D471/04, C07D487/04, C07D495/04, C07D491/04, C07D406/10, C07D307/79, A61P5/44, A61P5/48, A61K31/478

Applicant

BOEHRINGER INGELHEIM PHARMACEUTICALS, INC.

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
02.02.2005	24.08.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Cortés, J Telephone No. +49 89 2399-

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US2004/031009

Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements* of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-500 as originally filed

   Claims, Numbers

   1-46 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US2004/031009

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 31-37

because:

☒ the said international application, or the said claims Nos. 31-37 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US2004/031009

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-46
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-46
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-30, 38-46
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (SEPARATE SHEET)

International application No. PCT/US2004/031009

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 31-37 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion with regard to the industrial applicability will be formulated for these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The following documents have been cited in the International Search Report:

D1: WO 03/059899 A1 (BOEHRINGER INGELHEIM PHARMACEUTICALS INC (US)) 24 July 2003 (2003-07-24)

Novelty (Article 33(2) PCT)

The present compounds differ from the compounds in D1 in the group R4. The present claim set is therefore novel.

Inventive Step (Article 33(3) PCT)

D1 discloses glucocorticoid ligands and could be regarded as the closest prior art.

The problem of the invention was the provision of new glucocorticoid ligands.

The present compounds are not suggested by D1. The present in invention is therefore based on an inventive step.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (SEPARATE SHEET)

International application No.
PCT/US2004/031009

Clarity (Article 6 PCT)

Many of the examples in the description are not encompassed by the claims (e.g. examples 1-73, 76, etc., p. 324, 1st compound, etc.)

Re Item VI
Certain documents cited

Reference is made to the following P-documents:

D2: WO 03/082280 A1 (BOEHRINGER INGELHEIM PHARMACEUTICALS INC (US)) 9 October 2003 (2003-10-09)

D3: WO 03/082787 A1 (BOEHRINGER INGELHEIM PHARMACEUTICALS INC (US)) 9 October 2003 (2003-10-09)

D4: WO 2004/063163 A1 (BOEHRINGER INGELHEIM PHARMACEUTICALS INC (US)) 29 July 2004 (2004-07-29)

The priority documents pertaining to the present application were not available at the time of establishing this report. Hence, it is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct, the P-documents cited in the international search report could become relevant to asses whether the present claims satisfy the criteria set forth in Article 33(1) PCT.

TRATADO DE COOPERACION DE PATENTES

PCT

TRADUCCION

REPORTE DE EXAMEN PRELIMINAR SOBRE PATENTABILIDAD

(Cápitulo II del Tratado de Cooperación de Patentes)

(Artículo PCT 36 y Regla 70)

Archivo de Referencia del Aplicante o Agente

9-289PCT

PARA ACCION COMPLEMENTARIA

Ver forma PCT/IPEA/416

Aplicación Internacional No

PCT/US2004/031009

Fecha de presentación Internacional *(día/mes/año)*

22.09.2004

Fecha de Prioridad *(día/mes/año)*

24.09.2003

Clasificación Internacional de Patente (IPC) o clasificación nacional e IPC

A62K31/4745, A61K31/52, CO7D471/04, CO7D487/04, CO7D495/04, CO7D491/04, CO7D405/10, CO7D307/79, AK61P5/44, A61P5/46, A61K31/475

Aplicante

BOEHRINGER INGELHEIM PHARMACEUTICALS, INC

1. Este reporte es el reporte de examen preliminar internacional, establecido por la Autoridad Internacional de Examen Preliminar bajo el Rtículo 35 y trasmitido al aplicante de acuerdo al Artículo 36.

2. Este REPORTE consiste de un total de 6 hojas, incluyendo esta hoja de portada.

3. Este reporte está también acompañado de ANEXOS que incluyen:

a. ☐ *(Enviado al aplicante y a la Oficina Internacional)* un total de ____ hojas como sigue.

☐ Hojas de descripción, reivindicaciones y/o figuras las cuales han sido enmendadas y son la base de este reporte y/o hojas que contienen rectificaciones autorizadas por esta Autoridad (ver Regla 70.16 y sección 607 de las Instrucciones Administrativas)

☐ Hojas que sustituyen hojas previas, pero que esta Autoridad considera que contienen una enmienda que va mas allá de la exposición presentada en la aplicación internacional, como se indica en el Item 4 de la Casilla I y en la Casilla suplementaria.

b. ☐ *(enviado solo a la Oficina Internacional)* un total de (indicar el tipo y número del trasportador (es) electrónico _____,) que contienen un listado de secuencia y/o tablas relacionadas con ella, en forma leíble por computador únicamente, como se indica en la Casilla Suplementaria relacionada con el Listado de Secuencia (ver Sección 802 de las Instrucciones Administrativas9

4. Este reporte contiene indicaciones relacionadas con los siguientes itemes

☒	Casilla No I	Base del Reporte
☐	Casilla No II	Prioridad
☒	Casilla No III	No establecimiento de opinión en relación a novedad, pasos de invención y aplicación industrial
☐	Casilla No IV	Carencia de unidad de la invención
☒	Casilla No V	Declaración razonada bajo Artículo 35 (2) con respecto a novedad, pasos de invención o aplicabilidad industrial; citas y explicaciones soportando tal declaración.

☒ Casilla No VI Ciertos documentos citados

☐ Casilla No VII Ciertos defectos en la aplicación internacional

☐ Casilla No VIII Ciertas Observaciones sobre la aplicación internacional

Fecha de Presentación de la Petición

02.02.2005

Fecha de Terminación de este Reporte

02.08.2005

Nombre y dirección de correo de la autoridad internacional de reporte preliminar

European Patent Office
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Oficial Autorizado

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REPORTE DE EXAMEN PRELIMINAR SOBRE PATENTABILIDAD

Aplicación Internacional No

PCT/US2004/031009

Casilla No I. Bases del Reporte

1. En relación al lenguaje, este reporte está basado en la aplicación internacional en el lenguaje en la cual fue presentada, a menos que se indique de otra manera en este item.

☐ Este reporte esta basado en una traducción del lenguaje original al siguiente lenguaje , el cual es el lenguaje de la traducción suministrada para el propósito de

☐ a búsqueda internacional (Reglas 12.3(a) y 23.1 (b))

☐ publicación de la aplicación internacional (Reglas 12.4)

☐ examen internacional preliminar (Reglas 55.2 y/o 55.3)

2. Con respecto a los elementos* de la aplicación internacional, este reporte esta basado en (*hojas de reemplazo que han sido suministradas a la Oficina receptora en respuesta a una invitación bajo el Artículo 14 son referidas en este reporte como "originalmente presentadas" y no son anexadas a este reporte)*

Descripción, páginas

1 – 500 como se presentaron originalmente

Reivindicaciones, Números

1 – 46 como se presentaron originalmente

3. ☐ Las enmiendas han resultado en la cancelación de

☐ La descripción, páginas

☐ las reivindicaciones, páginas

☐ los dibujos, hojas/figuras

☐ el listado de secuencias (*especificar)*

☐ cualquier tabla (s) relacionada con el listado de secuencias

4. ☐ Este reporte ha sido establecido como si (alguno de) las enmiendas anexas a este reporte y listadas abajo no hubieran sido realizadas puesto que se ha considerado que ellas van mas allá del descubrimiento como fue presentado, como se indica en la Casilla Suplementaria (Regla 70.2 (c))

☐ La descripción, páginas

☐ las reivindicaciones, páginas

☐ los dibujos, hojas/figuras

☐ el listado de secuencias (*especificar)*

☐ cualquier tabla (s) relacionada con el listado de secuencias.

* Si el item 4 aplica , algunas o todas esas hojas pueden ser marcadas "suplentes"

REPORTE DE EXAMEN PRELIMINAR SOBRE PATENTABILIDAD

Aplicación Internacional No

PCT/US2004/031009

Casilla No III. No establecimiento de Opinión en relación con novedad, paso inventivo y aplicabilidad industrial.

1. La pregunta de si la invención reivindicada es novedosa , incorpora un paso de invención (ser no obvio) o es industrialmente aplicable no ha sido examinada con respecto a

☐ la integridad de la aplicación internacional

☒ reivindicaciones No 31 - 37

Por qué

☒ la mencionada aplicación internacional, o las mencionadas reivindicaciones No 31 - 37 se relacionan al siguiente materia la cual no requieren de un examen preliminar internacional (especificar)

Ver hoja aparte

☐ la descripción, reivindicaciones o dibujos (*indicar abajo los elementos particulares)* o las reivindicaciones mencionadas Nos. Son tan poco claras que no es posible formar una opinión significativa (especificar)

☐ las reivindicaciones o las reivindicaciones mencionadas Nos. Son inadecuadamente soportadas no es posible formar una opinión significativa

☐ no se ha establecido un reporte de búsqueda internacional por las reivindicaciones mencionadas Nos.

☐ el listado de secuencia de nucleótido y/o amino ácido no cumple con el estándar establecido para ello en el Anexo C de las instrucciones administrativas en que

en la forma escrita

☐ no ha sido suministrado

☐ no cumple con el estándar

en la forma leíble por computador

☐ no ha sido suministrado

☐ no cumple con el estándar

☐ las tablas relacionadas al listado de secuencias de nucleótidos y/o amino ácidos, si están solo en una forma leíble por computador, no cumplen con lo requerimientos técnicos previstos en el Anexo C de las instrucciones administrativas.

☐ Ver hojas separadas para detalles adicionales

REPORTE DE EXAMEN PRELIMINAR SOBRE PATENTABILIDAD

Aplicación Internacional No

PCT/US2004/031009

Casilla No V. Declaración motivada bajo Artículo 35 (2) con respecto a novedad, pas inventivo o aplicabilidad industrial; citas y explicaciones soportando tal declaración.

1. Declaración

Novedad (N)

Si: Reivindicaciones 1- 46

No: Reivindicaciones

Paso Inventivo (IS)

Si: Reivindicaciones 1- 46

No: Reivindicaciones

Aplicación Industrial (IA)

Si: Reivindicaciones 1- 30, 38 - 46

No: Reivindicaciones

2. Citas y Explicaciones (Regla 70.7)

Ver hoja aparte

Casilla No VI. Ciertos documentos citados

1. Ciertos documentos publicados (Regla 70.10)

Y/o

2. Descubrimientos no escritos (Regla 70.9)

Ver hoja aparte

REPORTE DE EXAMEN PRELIMINAR SOBRE PATENTABILIDAD (HOJA SEPARADA)

Aplicación Internacional No

PCT/US2004/031009

Re Item III

No establecimiento de Opinión en relación con novedad, paso inventivo y aplicabilidad industrial.

Las reivindicaciones 31 –37 se relacionan con un objeto-materia considerada por esta Autoridad cubierta por las provisiones de la Regla PCT 67.1 (iv) .

Consecuentemente ninguna opinión en relación con la aplicabilidad industrial será formulada en estas reivindicaciones (Artículo PCT 34(4)(a)(i)).

Re Item V

Declaración motivada bajo Artículo 35 (2) con respecto a novedad, pas inventivo o aplicabilidad industrial; citas y explicaciones soportando tal declaración.

Los siguientes documentos han sido citados en el Reporte de Búsqueda Internacional

D1. WO 03/059899 A1 (BOEHRINGER INGELHEIM PHARMACEUTICALS, INC (US)) 24 de julio de 2003 (2003-07-24)

Novedad (Artículo PCT 33 (2))

Los compuestos presentes difieren de los compuestos en D1 en el grupo R4. El presente grupo de reivindicaciones es en consecuencia novedoso.

Paso de Invención (Artículo PCT 33 (3))

D1 descubre ligandos glucocorticoides y podrían ser considerados como el arte anterior mas próximo.

El problema de la invención fue la provisión de nuevos ligandos glucocorticoides.

Los compuestos presentes no son sugeridos por D1. La presente invención está en consecuencia basada en un paso de invención.

REPORTE DE EXAMEN PRELIMINAR SOBRE PATENTABILIDAD
(HOJA SEPARADA)

Aplicación Internacional No
PCT/US2004/031009

Claridad (Artículo PCT 6)

Muchos de los ejemplos en la descripción no están incluidos por las reivindicaciones (es decir, ejemplos 1 –73, 76, etc p.324 1er compuesto etc.)

Re Item VI

Ciertos documentos citados

Se hace referencia a los siguientes documentos-P

D2: WO 03/082280 A1 (BOEHRINGER INGELHEIM PHARMACEUTICALS, INC (US)) 9 de octubre de 2003 (2003-10-09)

D3: WO 03/082787 A1 (BOEHRINGER INGELHEIM PHARMACEUTICALS, INC (US)) 9 de octubre de 2003 (2003-10-09)

D4. WO 2004/063163 A1 (BOEHRINGER INGELHEIM PHARMACEUTICALS, INC (US)) 29 de julio de 2004 (2004-07-29)

Los documentos de prioridad referentes a la presente aplicación no estaban disponibles al momento de hacerse este reporte. Por lo tanto, esta basado en la presunción de que todas las reivindicaciones gozan de derechos de prioridad desde la fecha de presentación del documento de prioridad. Si mas tarde aparece que esto no es correcto, lo documentos-P citados en el reporte de búsqueda internacional podrían llegar a ser relevantes para determinar si las reivindicaciones presentes satisfacen los criterios establecidos en el Artículo PCT 33(1).

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2-(2,6-Dichloroquinolin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-[3-(2-Chloro-8-methylquinolin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

2-[3-(2,6-Dichloroquinolin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

4-(2,3-Dihydrobenzofuran-7-yl)-2-(2,6-dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(3-fluorophenyl)-4-methylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(4-fluorophenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-methyl-4-*m*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(2-methylquinolin-4-ylmethyl)pentan-2-ol;

4-Fluoro-2-(4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-quinolin-4-ylmethylbutyl)phenol;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(2-methylquinolin-4-ylmethyl)butyl]phenol;

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2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(7-methylquinolin-4-ylmethyl)pentan-2-ol;

2-[3-(2,6-Dimethylpyridin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-5-fluorophenol;

2-(5,7-Dimethylquinolin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-(2-methylquinolin-4-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(3-methyl-1*H*-indol-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-(2-trifluoromethylphenyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(7-fluoro-4-methylquinolin-8-yl)-4-methylpentan-2-ol;

4-(2,6-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

2-(3-Bromo-1*H*-indol-2-ylmethyl)-1,1,1-trifluoro-4-(3-fluorophenyl)-4-methylpentan-2-ol;

4-(3,4-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluoro-4-methylphenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-3-methylphenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluoro-4-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-2-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(3,4-Dimethylphenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(2,5-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-(2-methoxy-5-methylphenyl)-4-methylpentan-2-ol;

4-Methyl-2-[4,4,4-trifluoro-3-hydroxy-3-(1*H*-indol-2-ylmethyl)-1,1-dimethylbutyl]phenol;

4-(2,5-Dimethylphenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(2,5-Dimethoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-4-methylpentan-2-ol;

2-(2,4-Dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-(2-Amino-4-chloro-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-(2,4-Dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

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2-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

4-(5-Bromo-2-methoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Bromo-2-methoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

2-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-[5-(ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-methylpentan-2-ol;

2-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-phenylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-pyrrolidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-phenyl-2-(5-pyrrolidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4'-Methoxy-3'-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-2-carbonitrile;

2-(5-Diethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-[5-(isopropylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-4-methylpentan-2-ol;

1,1,1-Trifluoro-2-[5-(isopropylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-4-methyl-4-phenylpentan-2-ol;

2-(5-Diethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methyl-4-phenylpentan-2-ol;

4-(3-Bromophenyl)-1,1,1-trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-(5-pyrrolidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(3-pyrimidin-5-ylphenyl)pentan-2-ol;

2-[5-(2,6-Dimethylmorpholin-4-yl)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

2-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-methyl-4-phenylpentan-2-ol;

2-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-(3-fluorophenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(5-pyrrolidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Diethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(3-fluorophenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-2-[5-(isopropylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-4-methylpentan-2-ol;

3'-{3-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl}-4'-methoxybiphenyl-2-carbonitrile;

2-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methylpentan-2-ol;

3'-{3-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl}-4'-hydroxybiphenyl-2-carbonitrile;

4'-Hydroxy-3'-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-2-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Dimethylaminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-[5-(4-methylpiperazin-1-ylmethyl)-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl]pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(5-dimethylaminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)pentan-2-ol;

4-Chloro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)butyl]phenol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-pyrrolo[3,2-*c*]pyridine-6-carbonitrile;

2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridine-5-carbonitrile;

2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carboxylic acid methyl ester;

1-{2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}ethanone;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(6*H*-pyrrolo[2,3-g]quinoxalin-7-ylmethyl)pentan-2-ol;

2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carboxylic acid amide;

2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carboxylic acid;

{2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}morpholin-4-ylmethanone;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(5-hydroxymethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

2-(5-Aminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)butyl]phenol;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)butyl]phenol;

2-(6-Chloro-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(6-chloro-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(3-phenyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(3-phenyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

1-{2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}-2,2-dimethylpropan-1-one;

2-[5-(1-*tert*-Butyl-1-hydroxy-2,2-dimethylpropyl)-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl]-4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-ol;

1-{2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}propan-1-one;

1-{2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}-2-methylpropan-1-one;

1,1,1-Trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

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1,1,1-Trifluoro-4-(2-methoxy-5-thiophen-3-ylphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(4-methoxybiphenyl-3-yl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]phenol;

4-Thiophen-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]phenol;

3-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]biphenyl-4-ol;

1,1,1-Trifluoro-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(5-pyrimidin-5-yl-2,3-dihydrobenzofuran-7-yl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(5-phenoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-phenyl-2-(3-phenyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(3-phenyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(5-phenoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-phenyl-2-(3-phenyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(3-phenyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylmethylphenyl)-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-2-[5-(4-fluorophenyl)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-4-methylpentan-2-ol;

2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

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1,1,1-Trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-[3-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

2-[3-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-5-fluorophenol;

5-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol;

4-(5-Bromo-2-methoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-Bromo-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(3-[1,3]Dioxan-2-ylphenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(4-methoxybiphenyl-3-yl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-thiophen-3-ylphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylmethylphenyl)-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

3-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-4-ol;

4-Thiophen-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol;

4-Thiophen-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol;

4-Thiophen-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol;

4'-Methoxy-3'-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-2-carbonitrile;

4'-Methoxy-3'-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-3-carbonitrile;

1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(3-Chlorophenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]phenol;

1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylmethylphenyl)-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(3-pyridin-3-ylphenyl)-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(3-pyrimidin-5-ylphenyl)-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(3-pyridin-3-ylphenyl)-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(3-pyrimidin-5-ylphenyl)-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-pyridin-2-yl-1*H*-indol-2-ylmethyl)pentan-2-ol;

2-(5-Bromo-1*H*-indol-2-ylmethyl)-4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-2-(5-methanesulfinyl-1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

7-[3-(5-Bromo-1*H*-indol-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-2,3-dihydrobenzofuran-5-sulfonic acid amide;

7-[3-(5-Bromo-1*H*-indol-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-2,3-dihydrobenzofuran-5-sulfonic acid dimethylamide;

2-(1-Benzenesulfonyl-5-pyridin-3-yl-1*H*-indol-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol;

3-{2-[4-(5-Fluoro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}benzonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-pyridin-4-yl-1*H*-indol-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-pyridin-3-yl-1*H*-indol-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-pyrimidin-5-yl-1*H*-indol-2-ylmethyl)pentan-2-ol;

2-{2-[4-(5-Fluoro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}benzamide;

2-[5-(4-Dimethylaminophenyl)-1*H*-indol-2-ylmethyl]-1,1,1-trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-2-(7-fluoro-4-methyl-1*H*-indol-2-ylmethyl)-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol;

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2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile;

2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carbonitrile;

1,1,1-Trifluoro-2-(7-fluoro-1*H*-indol-2-ylmethyl)-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(4-methyl-1*H*-indol-2-ylmethyl)pentan-2-ol;

4-Methanesulfonyl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-trifluoromethyl-1*H*-indol-2-ylmethyl)butyl]phenol;

1,1,1-Trifluoro-2-(7-fluoro-5-methyl-1*H*-indol-2-ylmethyl)-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol;

7-Fluoro-2-[2-hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carboxylic acid methyl ester;

2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carboxylic acid methyl ester;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carboxylic acid;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carboxylic acid amide;

2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carboxylic acid amide;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carbonitrile;

2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carbonitrile;

2-(4-Ethyl-1*H*-indol-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-[3-(4-Ethyl-1*H*-indol-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(2-isopropyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(2-isopropyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(2-isopropyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)-4-methylpentan-2-ol;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-3-(2-isopropyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)-1,1-dimethylbutyl]phenol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)butyl]phenol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)butyl]phenol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(2-chloro-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-phenyl-2-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

4-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)butyl]benzonitrile;

1,1,1-Trifluoro-4-(2-methoxy-5-methylphenyl)-4-methyl-2-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-methylphenyl)-4-methyl-2-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methyl-2-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)butyl]phenol;

2-(5-Ethoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Bromo-2-methoxyphenyl)-2-(5-dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

4-(5-Bromo-2-methoxyphenyl)-1,1,1-trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-trifluoromethylphenyl)-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(4-methoxybiphenyl-3-yl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(2-methoxy-5-thiophen-3-ylphenyl)-4-methylpentan-2-ol;

2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methyl-4-phenylpentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(4-methoxybiphenyl-3-yl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methylpentan-2-ol;

4-Bromo-2-[3-(5-chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]phenol;

2-[3-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

2-[2-Hydroxy-4-(4-hydroxybiphenyl-3-yl)-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridin-5-ol;

1,1,1-Trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methyl-4-(5-phenyl-2,3-dihydrobenzofuran-7-yl)pentan-2-ol;

2-[2-Hydroxy-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridin-5-ol;

Trifluoromethanesulfonic acid 2-[4-(5-fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridin-5-yl ester;

2-[5-(2,6-Dimethylmorpholin-4-yl)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-methyl-4-phenylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-phenyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methyl-4-phenylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylmethylphenyl)-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylmethylphenyl)-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Diethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(5-methoxy-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-methoxy-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(5-chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(4-methoxy-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,5-dihydropyrrolo[3,2-*c*]pyridin-4-one;

2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,4-dihydropyrrolo[3,2-*b*]pyridin-5-one;

2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-5-hydroxy-1,6-dihydropyrrolo[2,3-*c*]pyridin-7-one;

2-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol;

2-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(2-methoxy-5-thiophen-3-ylphenyl)-4-methylpentan-2-ol;

2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile;

2-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methyl-4-(5-methylsulfanyl-2,3-dihydrobenzofuran-7-yl)pentan-2-ol;

4-(5-Bromo-2-methoxyphenyl)-2-(5-chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-naphthalen-1-ylphenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(2'-Chloro-4-methoxybiphenyl-3-yl)-1,1,1-trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methylpentan-2-ol;

4'-Methoxy-3'-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-2-carbonitrile;

4-(2'-Chloro-4-methoxybiphenyl-3-yl)-1,1,1-trifluoro-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-[3-(3-Dimethylaminomethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

1,1,1-Trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(3-Chloro-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(5-methylsulfanyl-2,3-dihydrobenzofuran-7-yl)-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol; and

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol,

or a tautomer, prodrug, solvate, or salt thereof.

More preferred compounds of Formula (IA) include:

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(4,6-Dimethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-pyrrolo[3,2-*c*]pyridine-6-carbonitrile;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridine-5-carbonitrile;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*c*]pyridine-4-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-thieno[2,3-*d*]pyridazin-2-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(2-methyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*d*]pyridazin-2-ylmethyl)pentan-2-ol;

2-(4,6-Dimethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(4,6-dimethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile;

2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(7-fluoro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5,7-Dichloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5-trifluoromethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(5-methoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-methoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(5-methoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(7-fluoro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-trifluoromethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(5-chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(5-methyl-2,3-dihydrobenzofuran-7-yl)-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-pyrrolo[2,3-*b*]pyridin-1-ylmethylpentan-2-ol;

2-Benzo[*b*]thiophen-2-ylmethyl-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-thieno[2,3-*c*]pyridin-2-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-[4-((Z)propenyl)-3-vinylpyrazol-1-ylmethyl]pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,4-dimethyl-1-thieno[2,3-*c*]pyridin-2-ylpentan-2-ol;

4-(5-Fluoro-2-methylphenyl)-2,4-dimethyl-1-thieno[2,3-*c*]pyridin-2-ylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(5-methyl-2,3-dihydrobenzofuran-7-yl)-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(3-Dimethylaminomethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-pyrrolo[3,2-*c*]pyridin-1-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-furo[3,2-*c*]pyridin-2-ylmethyl-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

1,1-Difluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-thieno[3,2-*c*]pyridin-2-ylmethylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-thieno[3,2-*c*]pyridin-2-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-thieno[3,2-*c*]pyridin-2-ylmethylpentan-2-ol;

2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carboxylic acid dimethylamide;

{2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-6-yl}morpholin-4-ylmethanone;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carboxylic acid dimethylamide;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carboxylic acid dimethylamide;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-6-yl}morpholin-4-ylmethanone;

2-[4-(2,3-Dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carboxylic acid amide;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carboxylic acid amide;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-nitro-1*H*-indol-2-ylmethyl)butyl]phenol;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carbonitrile;

2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carbonitrile;

N-{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}acetamide;

1,1,1-Trifluoro-4-(4-fluoro-2-methoxyphenyl)-2-(7-fluoro-4-methyl-1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-(7-fluoro-4-methyl-1*H*-indol-2-ylmethyl)-3-hydroxy-1,1-dimethylbutyl]phenol;

2-[4-(3-[1,3]Dioxolan-2-ylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid-2-trimethylsilanylethyl ester;

2-[4-(4-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}piperidin-1-ylmethanone;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid methylamide;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}pyrrolidin-1-ylmethanone;

1-{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}piperidin-4-one;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid (2-hydroxyethyl)amide;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}(4-hydroxypiperidin-1-yl)methanone;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}(3-hydroxypyrrolidin-1-yl)methanone;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid cyanomethylamide;

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({2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}amino)acetic acid methyl ester;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid carbamoylmethylamide;

4-({2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}amino)butyric acid methyl ester;

({2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}amino)acetic acid;

4-({2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}amino)butyric acid;

2-[4-(3-Dimethylaminomethylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-trifluoromethyl-1*H*-indol-2-ylmethyl)butyl]phenol;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid amide;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid dimethylamide;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid cyanomethylamide;

{2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}pyrrolidin-1-ylmethanone;

{2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}morpholin-4-ylmethanone;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid amide;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}morpholin-4-ylmethanone;

2-(4-Benzo[1,3]dioxol-4-yl-2-hydroxy-4-methyl-2-trifluoromethylpentyl)-4-methyl-1*H*-indole-6-carbonitrile;

1,1,1-Trifluoro-4-methyl-4-phenyl-2-quinolin-4-ylmethylhexan-2-ol;

2-[2-Hydroxy-4-methyl-4-(5-methylsulfanyl-2,3-dihydrobenzofuran-7-yl)-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

7-(4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-quinolin-4-ylmethylbutyl)-2,3-dihydrobenzofuran-5-carbonitrile;

2-[2-Hydroxy-4-(2-hydroxy-5-methylphenyl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-methylsulfanyl-1*H*-indol-2-ylmethyl)pentan-2-ol;

2-[2-Hydroxy-4-(5-methanesulfonyl-2-methoxyphenyl)-4-methyl-2-trifluoromethyl-pentyl]-1*H*-indole-3-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-phenyl-1*H*-indol-2-ylmethyl)pentan-2-ol;

2-[4-(5-*tert*-Butyl-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethyl-pentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(2-hydroxy-5-isopropylphenyl)-4-methyl-2-trifluoromethyl-pentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(2-hydroxy-3,5-dimethylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(5-hydroxy-2,4-dimethylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

2-[4-(5-*tert*-Butyl-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(5-isopropyl-2-methoxyphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(2-methoxy-5-methylphenyl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*o*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*m*-tolylpentan-2-ol;

1;1,1-Trifluoro-4-(2-fluorophenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(2-fluorophenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorophenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

3-(4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-quinolin-4-ylmethylbutyl)phenol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-(2-trifluoromethylphenyl)pentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-(4-trifluoromethylphenyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-(4-trifluoromethylphenyl)pentan-2-ol;

4-(3-Chlorophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

4-(3-Chlorophenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(4-Dimethylaminophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

4-Biphenyl-3-yl-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(3-Bromophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

4-(2-Difluoromethoxy-5-fluorophenyl)-1,1,1 -trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

4-Biphenyl-3-yl-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

4-(4-Dimethylaminophenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,6-dihydropyrrolo[2,3-*c*]pyridin-5-one;

2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-6-methyl-1,6-dihydropyrrolo[2,3-*c*]pyridin-5-one;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-methoxy-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

2-[4-(3-Dimethylaminomethylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-pyridin-2-ylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-pyridin-4-yl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*o*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*m*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-pyridin-4-ylmethylpentan-2-ol;

4-Fluoro-2-[4,4,4-trifluoro-3-(2-fluoropyridin-4-ylmethyl)-3-hydroxy-1,1-dimethylbutyl]phenol;

2-[3-(2-Bromopyridin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

2-(6,8-Dimethylquinolin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

4-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]pyridine-2-carbonitrile;

2,6-Dichloro-4-[4-(5-fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]nicotinonitrile;

2,6-Dichloro-4-[4-(5-fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]nicotinonitrile;

2-(2,6-Dichloroquinolin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-[3-(2-Chloro-8-methylquinolin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

2-[3-(2,6-Dichloroquinolin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

4-(2,3-Dihydrobenzofuran-7-yl)-2-(2,6-dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(3-fluorophenyl)-4-methylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(4-fluorophenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-methyl-4-*m*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(2-methylquinolin-4-ylmethyl)pentan-2-ol;

4-Fluoro-2-(4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-quinolin-4-ylmethylbutyl)phenol;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(2-methylquinolin-4-ylmethyl)butyl]phenol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(7-methylquinolin-4-ylmethyl)pentan-2-ol;

2-[3-(2,6-Dimethylpyridin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-5-fluorophenol;

1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-(2-methylquinolin-4-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(3-methyl-1*H*-indol-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-(2-trifluoromethylphenyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(7-fluoro-4-methylquinolin-8-yl)-4-methylpentan-2-ol;

4-(2,6-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

2-(3-Bromo-1*H*-indol-2-ylmethyl)-1,1,1-trifluoro-4-(3-fluorophenyl)-4-methylpentan-2-ol;

4-(3,4-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluoro-4-methylphenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-3-methylphenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluoro-4-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-2-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(3,4-Dimethylphenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(2,5-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-(2-methoxy-5-methylphenyl)-4-methylpentan-2-ol;

4-Methyl-2-[4,4,4-trifluoro-3-hydroxy-3-(1*H*-indol-2-ylmethyl)-1,1-dimethylbutyl]phenol;

4-(2,5-Dimethylphenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(2,5-Dimethoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-(2-trifluoromethylphenyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-4-methylpentan-2-ol;

2-(2,4-Dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-(2-Amino-4-chloro-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol; and

2-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol,

or a tautomer, prodrug, solvate, or salt thereof.

Most preferred compounds of Formula (IA) include:

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(4,6-Dimethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-pyrrolo[3,2-*c*]pyridine-6-carbonitrile;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridine-5-carbonitrile;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*c*]pyridine-4-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-thieno[2,3-*d*]pyridazin-2-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*d*]pyridazin-2-ylmethyl)pentan-2-ol;

2-(4,6-Dimethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(4,6-dimethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile;

2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(7-fluoro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5,7-Dichloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5-trifluoromethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(5-methoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-methoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(5-methoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(7-fluoro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-trifluoromethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(5-chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(5-methyl-2,3-dihydrobenzofuran-7-yl)-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-thieno[2,3-*c*]pyridin-2-ylmethylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,4-dimethyl-1-thieno[2,3-*c*]pyridin-2-ylpentan-2-ol;

4-(5-Fluoro-2-methylphenyl)-2,4-dimethyl-1-thieno[2,3-*c*]pyridin-2-ylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(5-methyl-2,3-dihydrobenzofuran-7-yl)-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

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4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(3-Dimethylaminomethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-furo[3,2-*c*]pyridin-2-ylmethyl-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

1,1-Difluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-thieno[3,2-*c*]pyridin-2-ylmethylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-thieno[3,2-*c*]pyridin-2-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-thieno[3,2-*c*]pyridin-2-ylmethylpentan-2-ol;

2-[4-(2,3-Dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-nitro-1*H*-indol-2-ylmethyl)butyl]phenol;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carbonitrile;

2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carbonitrile;

N-{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}acetamide;

1,1,1-Trifluoro-4-(4-fluoro-2-methoxyphenyl)-2-(7-fluoro-4-methyl-1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-(7-fluoro-4-methyl-1*H*-indol-2-ylmethyl)-3-hydroxy-1,1-dimethylbutyl]phenol;

2-[4-(3-[1,3]Dioxolan-2-ylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile;

2-[4-(4-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}piperidin-1-ylmethanone;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid methylamide;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}pyrrolidin-1-ylmethanone;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid (2-hydroxyethyl)amide;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}(3-hydroxypyrrolidin-1-yl)methanone;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid cyanomethylamide;

({2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}amino)acetic acid methyl ester;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid carbamoylmethylamide;

4-({2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}amino)butyric acid methyl ester;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-trifluoromethyl-1*H*-indol-2-ylmethyl)butyl]phenol;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid amide;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid dimethylamide;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid cyanomethylamide;

{2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}pyrrolidin-1-ylmethanone;

{2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}morpholin-4-ylmethanone;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid amide;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}morpholin-4-ylmethanone;

2-(4-Benzo[1,3]dioxol-4-yl-2-hydroxy-4-methyl-2-trifluoromethylpentyl)-4-methyl-1*H*-indole-6-carbonitrile;

1,1,1-Trifluoro-4-methyl-4-phenyl-2-quinolin-4-ylmethylhexan-2-ol;

2-[2-Hydroxy-4-methyl-4-(5-methylsulfanyl-2,3-dihydrobenzofuran-7-yl)-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

7-(4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-quinolin-4-ylmethylbutyl)-2,3-dihydrobenzofuran-5-carbonitrile;

2-[2-Hydroxy-4-(2-hydroxy-5-methylphenyl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-methylsulfanyl-1*H*-indol-2-ylmethyl)pentan-2-ol;

2-[2-Hydroxy-4-(5-methanesulfonyl-2-methoxyphenyl)-4-methyl-2-trifluoromethyl-pentyl]-1*H*-indole-3-carbonitrile;

2-[4-(5-*tert*-Butyl-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethyl-pentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(2-hydroxy-5-isopropylphenyl)-4-methyl-2-trifluoromethyl-pentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(2-hydroxy-3,5-dimethylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(5-hydroxy-2,4-dimethylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

2-[4-(5-*tert*-Butyl-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(5-isopropyl-2-methoxyphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*o*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*m*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-(2-fluorophenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(2-fluorophenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorophenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

3-(4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-quinolin-4-ylmethylbutyl)phenol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-(2-trifluoromethylphenyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-(4-trifluoromethylphenyl)pentan-2-ol;

4-(3-Chlorophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

4-(3-Chlorophenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-Biphenyl-3-yl-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(3-Bromophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

4-(2-Difluoromethoxy-5-fluorophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

4-(4-Dimethylaminophenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-6-methyl-1,6-dihydropyrrolo[2,3-*c*]pyridin-5-one;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-methoxy-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

2-[4-(3-Dimethylaminomethylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-pyridin-2-ylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*o*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*m*-tolylpentan-2-ol;

4-Fluoro-2-[4,4,4-trifluoro-3-(2-fluoropyridin-4-ylmethyl)-3-hydroxy-1,1-dimethylbutyl]phenol;

2-[3-(2-Bromopyridin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

2-(6,8-Dimethylquinolin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

4-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]pyridine-2-carbonitrile;

2,6-Dichloro-4-[4-(5-fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]nicotinonitrile;

2,6-Dichloro-4-[4-(5-fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]nicotinonitrile;

2-[3-(2,6-Dichloroquinolin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

4-(2,3-Dihydrobenzofuran-7-yl)-2-(2,6-dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(3-fluorophenyl)-4-methylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(4-fluorophenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-methyl-4-*m*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(2-methylquinolin-4-ylmethyl)pentan-2-ol;

4-Fluoro-2-(4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-quinolin-4-ylmethylbutyl)phenol;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(2-methylquinolin-4-ylmethyl)butyl]phenol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(7-methylquinolin-4-ylmethyl)pentan-2-ol;

2-[3-(2,6-Dimethylpyridin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-5-fluorophenol;

1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-(2-methylquinolin-4-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(3-methyl-1*H*-indol-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-(2-trifluoromethylphenyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(7-fluoro-4-methylquinolin-8-yl)-4-methylpentan-2-ol;

4-(2,6-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

2-(3-Bromo-1*H*-indol-2-ylmethyl)-1,1,1-trifluoro-4-(3-fluorophenyl)-4-methylpentan-2-ol;

4-(3,4-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluoro-4-methylphenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-3-methylphenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluoro-4-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-2-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(3,4-Dimethylphenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(2,5-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-(2-methoxy-5-methylphenyl)-4-methylpentan-2-ol;

4-Methyl-2-[4,4,4-trifluoro-3-hydroxy-3-(1*H*-indol-2-ylmethyl)-1,1-dimethylbutyl]phenol;

4-(2,5-Dimethylphenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(2,5-Dimethoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-(2-trifluoromethylphenyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-4-methylpentan-2-ol;

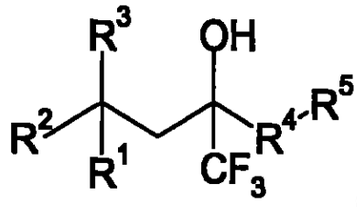
2-(2,4-Dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-(2-Amino-4-chloro-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol; and

2-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol,

or a tautomer, prodrug, solvate, or salt thereof.

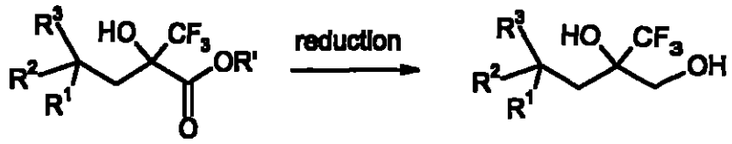
The invention also provides a method of making a compound of Formula (IA)



(IA)

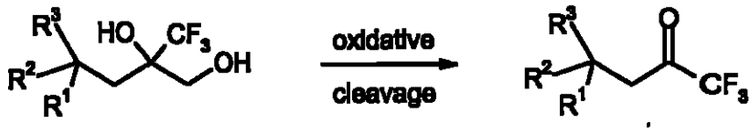
where R^1, R^2, R^3, R^4, and R^5 are as defined above, the method comprising:

(a) reacting an ester of Formula (II) with a suitable reducing agent in a suitable solvent to form a diol of Formula (III)



II III ;

(b) reacting the diol of Formula (III) under suitable oxidative cleavage conditions to form a ketone of Formula (IV)

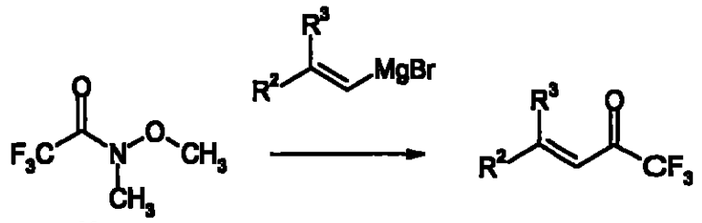


III IV ; and

(c) reacting the ketone of Formula (IV) with a suitable organometallic reagent R^5R^4M where M is Li or MgX and X is Cl, Br, or I, in a suitable solvent to form the compound of Formula (IA)

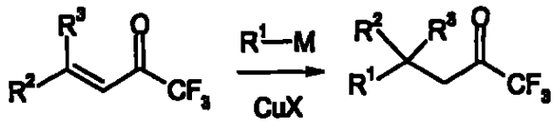
IV IA ; or

(a') reacting the trifluoroacetamide of Formula (X) with a vinyl magnesium bromide bearing R^2 and R^3 in a suitable solvent to provide the trifluoromethylenone of Formula (XI)



X XI ;

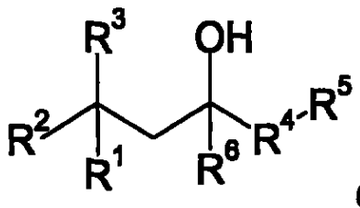
(b') reacting the trifluoromethylenone of Formula (XI) with a suitable organocopper reagent generated from an organometallic reagent R^5R^4M where M is Li or MgX and a copper salt CuX, where X is Cl, Br, or I, in a suitable solvent to form the ketone of Formula (IV)



XI IV ; and

performing step (c) as set forth above.

The instant invention is also directed to compounds of Formula (IB)



(IB)

wherein:

R^1 is an aryl or heteroaryl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_5 alkoxy, C_2-C_5 alkenyloxy, C_2-C_5 alkynyloxy, aryloxy, acyl, C_1-C_5 alkoxycarbonyl, C_1-C_5 alkanoyloxy, C_1-C_5 alkanoyl, aroyl, aminocarbonyl, C_1-C_5 alkylaminocarbonyl, C_1-C_5 dialkylaminocarbonyl, aminocarbonyloxy, C_1-C_5 alkylaminocarbonyloxy, C_1-C_5 dialkylaminocarbonyloxy, C_1-C_5 alkanoylamino, C_1-C_5 alkoxycarbonylamino, C_1-C_5 alkylsulfonylamino, aminosulfonyl, C_1-C_5 alkylaminosulfonyl, C_1-C_5 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, trifluoromethoxy, nitro, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl; or C_1-C_5 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with one to three substituent groups selected from methyl, methoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl;

R^2 and R^3 are each independently C_1-C_5 alkyl;

R^4 is C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^4 is independently C_1-C_3 alkyl, hydroxy, halogen, or oxo;

R^5 is a heteroaryl group optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_5 alkoxy, C_2-C_5 alkenyloxy, C_2-C_5 alkynyloxy, aryloxy, acyl, C_1-C_5 alkoxycarbonyl, C_1-C_5 alkanoyloxy, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, aminocarbonyloxy, C_1-C_5 alkylaminocarbonyloxy, C_1-C_5 dialkylaminocarbonyloxy, C_1-C_5 alkanoylamino, C_1-C_5 alkoxycarbonylamino, C_1-C_5 alkylsulfonylamino, C_1-C_5 alkylaminosulfonyl, C_1-C_5 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, nitro, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl; or C_1-C_5 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^5 is optionally independently substituted with one to three substituent groups selected from C_1-C_3 alkyl, C_1-C_3 alkoxy, halogen,

hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl, or trifluoromethyl; and

R^6 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, carbocycle, heterocyclyl, aryl, heteroaryl, carbocycle-C_1-C_8 alkyl, carboxy, alkoxycarbonyl, aryl-C_1-C_8 alkyl, aryl-C_1-C_8 haloalkyl, heterocyclyl-C_1-C_8 alkyl, heteroaryl-C_1-C_8 alkyl, carbocycle-C_2-C_8 alkenyl, aryl-C_2-C_8 alkenyl, heterocyclyl-C_2-C_8 alkenyl, or heteroaryl-C_2-C_8 alkenyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, C_3-C_8 cycloalkyl, phenyl, C_1-C_5 alkoxy, phenoxy, C_1-C_5 alkanoyl, aroyl, C_1-C_5 alkoxycarbonyl, C_1-C_5 alkanoyloxy, aminocarbonyloxy, C_1-C_5 alkylaminocarbonyloxy, C_1-C_5 dialkylaminocarbonyloxy, aminocarbonyl, C_1-C_5 alkylaminocarbonyl, C_1-C_5 dialkylaminocarbonyl, C_1-C_5 alkanoylamino, C_1-C_5 alkoxycarbonylamino, C_1-C_5 alkylsulfonylamino, C_1-C_5 alkylaminosulfonyl, C_1-C_5 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, oxo, trifluoromethyl, nitro, amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl; or C_1-C_5 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein R^6 cannot be trifluoromethyl,

or a tautomer, prodrug, solvate, or salt thereof.

Another aspect of the invention includes compounds of Formula (IB), wherein:

R^1 is thienyl, phenyl, naphthyl, dihydrobenzofuranyl, benzofuranyl, chromanyl, dihydroindolyl, indolyl, dihydrobenzothienyl, benzothienyl, benzodioxolanyl, benzoxazolyl, benzisoxazolyl, benzpyrazolyl, benzimidazolyl, thienyl, quinolinyl,

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pyridinyl, pyrimidinyl, or pyrazinyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_1-C_3 alkanoyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with a substituent group selected from methyl, methoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl;

R^2 and R^3 are each independently C_1-C_3 alkyl;

R^4 is CH_2;

R^5 is an imidazolyl, pyridyl, indolyl, azaindolyl, diazaindolyl, benzofuranyl, furanopyridinyl, furanopyrimidinyl, benzothienyl, thienopyridinyl, thienopyrimidinyl, benzoxazolyl, oxazolopyridinyl, benzothiazolyl, thiazolopyridinyl, benzimidazolyl, imidazolopyridinyl, imidazolopyrimidinyl, imidazolopyridazinyl, imidazolopyrazinyl, quinolinyl, or isoquinolinyl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, phenyl, C_1-C_3 alkoxy, methoxycarbonyl, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, heterocyclylcarbonyl, hydroxy, fluoro, chloro, bromo, cyano, trifluoromethyl, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^5 is optionally independently substituted with a substituent group selected from methyl, methoxy, fluoro, chloro, bromo,

trifluoromethyl, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl; and

R^6 is C_1-C_3 alkyl, C_2-C_3 alkenyl, C_3-C_6 cycloalkyl, phenyl, C_3-C_6 cycloalkyl-C_1-C_3 alkyl, phenyl-C_1-C_3 alkyl, phenyl-C_1-C_3 haloalkyl, C_3-C_6 cycloalkyl-C_2-C_3 alkenyl, phenyl-C_2-C_3 alkenyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, halogen, hydroxy, oxo, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

or a tautomer, prodrug, solvate, or salt thereof.

Yet another aspect of the invention includes compounds of Formula (IB), wherein:

R^1 is thienyl, phenyl, naphthyl, pyridyl, chromanyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one or two substituent groups,

wherein each substituent group of R^1 is independently methyl, ethyl, methoxy, ethoxy, fluoro, chloro, bromo, hydroxy, trifluoromethyl, cyano, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone;

R^2 and R^3 are each methyl;

R^4 is CH_3;

R^5 is a pyridyl, indolyl, azaindolyl, diazaindolyl, benzofuranyl, furanopyridinyl, thienopyridinyl, benzoxazolyl, benzimidazolyl, quinolinyl, or isoquinolinyl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently methyl, phenyl, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminoaminocarbonyl, morpholinylcarbonyl, hydroxy, fluoro, chloro, bromo, cyano, or trifluoromethyl; and

R^6 is C_1-C_3 alkyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkylmethyl-, or benzyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently methyl, methoxy, fluoro, chloro, bromo, cyano, trifluoromethyl, or hydroxy,

or a tautomer, prodrug, solvate, or salt thereof.

Yet another aspect of the invention includes compounds of Formula (IB), wherein:

R^1 is phenyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_1-C_3 alkanoyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone; and

R^2 and R^3 are each independently C_1-C_3 alkyl,

or a tautomer, prodrug, solvate, or salt thereof.

Yet another aspect of the invention includes compounds of Formula (IB), wherein:

R^1 is thienyl, phenyl, naphthyl, pyridyl, chromanyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one or two substituent groups,

wherein each substituent group of R^1 is independently methyl, ethyl, methoxy, ethoxy, fluoro, chloro, bromo, hydroxy, trifluoromethyl, cyano, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone;

R^2 and R^3 are each methyl;

R^4 is CH_2;

R^5 is a pyridyl, indolyl, azaindolyl, diazaindolyl, benzofuranyl, furanopyridinyl, thienopyridinyl, benzoxazolyl, benzimidazolyl, quinolinyl, or isoquinolinyl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently methyl, phenyl, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminoaminocarbonyl, morpholinylcarbonyl, pyridinyl, hydroxy, fluoro, chloro, bromo, cyano, or trifluoromethyl; and

R^6 is C_1-C_3 alkyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkylmethyl-, or benzyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently methyl, methoxy, fluoro, chloro, bromo, cyano, trifluoromethyl, or hydroxy,

or a tautomer, prodrug, solvate, or salt thereof.

In the above aspects of the invention of the compounds of Formula (IB), it is preferred that R^6 is not hydrogen.

Representative compounds of Formula (IB) according to the invention are appended hereto as Table IB, where column A is the compound name according to standard nomenclature and column B is the corresponding chemical structure.

Preferred compounds of Formula (IB) include the following:

2-Cyclopropyl-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[3,2-*c*]pyridin-2-yl)pentan-2-ol;

2-Cyclopropyl-4-(5-fluoro-2-methylphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-cyclopropyl-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

2-Cyclopropyl-4-(5-fluoro-2-methylphenyl)-4-methyl-1-(1*H*-pyrrolo[3,2-*c*]pyridin-2-yl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-cyclopropyl-4-methyl-1-(1*H*-pyrrolo[3,2-*c*]pyridin-2-yl)pentan-2-ol;

4-(5-Fluoro-2-methoxyphenyl)-2,4-dimethyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

5-(5-Fluoro-2-methoxyphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methoxyphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

2-Cyclohexyl-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

2-Cyclopentyl-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

5-(5-Fluoro-2-methoxyphenyl)-5-methyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

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2-(5-Fluoro-2-methoxyphenyl)-2,6-dimethyl-4-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)heptan-4-ol;

2-(5-Fluoro-2-methoxyphenyl)-2,5,5-trimethyl-4-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)heptan-4-ol;

1,1-Difluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1-Cyclohexyl-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

5-(5-Fluoro-2-methylphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

2-Cyclobutyl-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

2-(5-Fluoro-2-methoxyphenyl)-2,6,6-trimethyl-4-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)heptan-4-ol;

5-(5-Fluoro-2-methoxyphenyl)-5-methyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hex-1-en-3-ol;

5-(5-Fluoro-2-methoxyphenyl)-5-methyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hex-1-yn-3-ol;

1-Fluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2,2-Difluoro-5-(5-fluoro-2-methoxyphenyl)-5-methyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

2-Fluoro-5-(5-fluoro-2-methoxyphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

2-Fluoro-5-(5-fluoro-2-methoxyphenyl)-5-methyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methoxyphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hex-1-en-3-ol;

1,1,1-Trifluoro-5-(5-fluoro-2-methoxyphenyl)-5-methyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

4-(5-Fluoro-2-methoxyphenyl)-4-methyl-2-phenyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-thieno[2,3-*c*]pyridin-2-ylmethylhexan-3-ol;

1,1-Difluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

5-(5-Fluoro-2-methoxyphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methoxyphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

2-(1-Fluorocyclopropyl)-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

2-(1-Fluorocyclopropyl)-4-(4-fluorophenyl)-4-methyl-1-quinolin-4-ylpentan-2-ol;

2-[4,4-Difluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]-4-fluorophenol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,5-dimethyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1-Difluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Bromo-1*H*-indol-2-ylmethyl)-1,1-difluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol; and

2-[2-Difluoromethyl-2-hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentyl]-4-methyl-1*H*-indole-6-carbonitrile,

or a tautomer, prodrug, solvate, or salt thereof.

More preferred compounds of Formula (*IB*) include:

2-Cyclopropyl-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[3,2-*c*]pyridin-2-yl)pentan-2-ol;

2-Cyclopropyl-4-(5-fluoro-2-methylphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-cyclopropyl-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

2-Cyclopropyl-4-(5-fluoro-2-methylphenyl)-4-methyl-1-(1*H*-pyrrolo[3,2-*c*]pyridin-2-yl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-cyclopropyl-4-methyl-1-(1*H*-pyrrolo[3,2-*c*]pyridin-2-yl)pentan-2-ol;

4-(5-Fluoro-2-methoxyphenyl)-2,4-dimethyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

5-(5-Fluoro-2-methoxyphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methoxyphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

2-Cyclopentyl-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

5-(5-Fluoro-2-methoxyphenyl)-5-methyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

2-(5-Fluoro-2-methoxyphenyl)-2,6-dimethyl-4-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)heptan-4-ol;

2-(5-Fluoro-2-methoxyphenyl)-2,5,5-trimethyl-4-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)heptan-4-ol;

1,1-Difluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1-Cyclohexyl-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

5-(5-Fluoro-2-methylphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

1,1-Difluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

5-(5-Fluoro-2-methoxyphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methoxyphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

2-(1-Fluorocyclopropyl)-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

2-(1-Fluorocyclopropyl)-4-(4-fluorophenyl)-4-methyl-1-quinolin-4-ylpentan-2-ol;

2-[4,4-Difluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]-4-fluorophenol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,5-dimethyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1-Difluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Bromo-1*H*-indol-2-ylmethyl)-1,1-difluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol; and

2-[2-Difluoromethyl-2-hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentyl]-4-methyl-1*H*-indole-6-carbonitrile,

or a tautomer, prodrug, solvate, or salt thereof.

Most preferred compounds of Formula (IB) include:

2-Cyclopropyl-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[3,2-*c*]pyridin-2-yl)pentan-2-ol;

2-Cyclopropyl-4-(5-fluoro-2-methylphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-cyclopropyl-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

2-Cyclopropyl-4-(5-fluoro-2-methylphenyl)-4-methyl-1-(1*H*-pyrrolo[3,2-*c*]pyridin-2-yl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-cyclopropyl-4-methyl-1-(1*H*-pyrrolo[3,2-*c*]pyridin-2-yl)pentan-2-ol;

5-(5-Fluoro-2-methoxyphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methoxyphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

2-Cyclopentyl-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

2-(5-Fluoro-2-methoxyphenyl)-2,5,5-trimethyl-4-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)heptan-4-ol;

1,1-Difluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

5-(5-Fluoro-2-methylphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

1,1-Difluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

5-(5-Fluoro-2-methoxyphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methoxyphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

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2-(1-Fluorocyclopropyl)-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

2-(1-Fluorocyclopropyl)-4-(4-fluorophenyl)-4-methyl-1-quinolin-4-ylpentan-2-ol;

2-[4,4-Difluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]-4-fluorophenol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

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5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

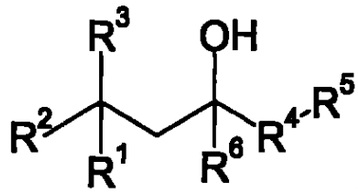
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Bromo-1*H*-indol-2-ylmethyl)-1,1-difluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol; and

2-[2-Difluoromethyl-2-hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentyl]-4-methyl-1*H*-indole-6-carbonitrile,

or a tautomer, prodrug, solvate, or salt thereof.

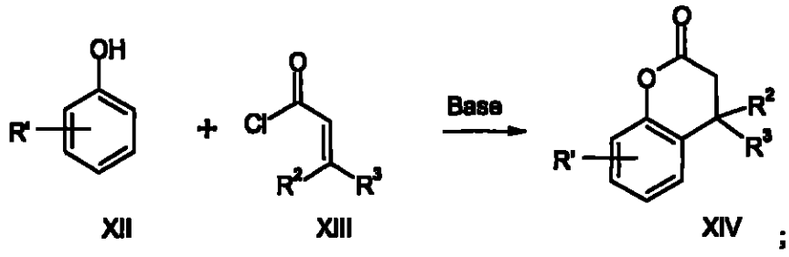
The invention further provides methods of making a compound of Formula (IB). One method of making a compound of Formula (IB)



(IB)

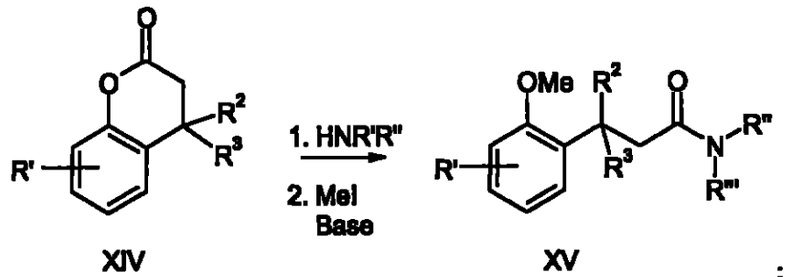
where R^1 is an optionally substituted 2-methoxyphenyl group and R^2, R^3, R^4, R^5, and R^6 are as defined above, the method comprising:

(a) reacting an optionally substituted phenol of Formula (XXII) with an acryloyl chloride of Formula (XIII) in the presence of a suitable base, followed by cyclization of the intermediate ester by treatment with a suitable Lewis acid to form a lactone of Formula (XIV)



XII XIII XIV ;

(b) reacting the lactone of Formula (XIV) with a suitable amine HNR'R", followed by treatment of the intermediate phenol with methyl iodide in the presence of a suitable base to form an amide of Formula (XV)

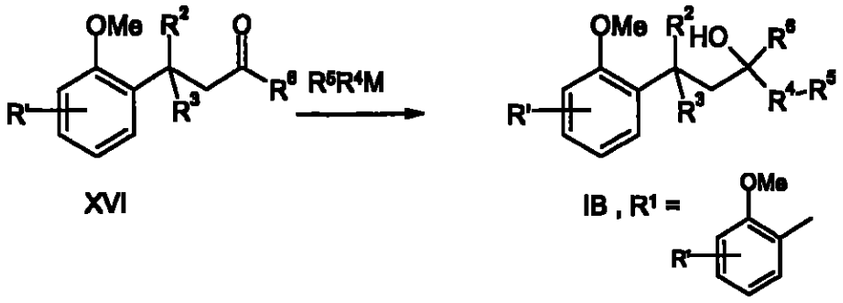


XIV XV ;

(c) reacting the amide of Formula (XV) with a suitable organometallic reagent R^6M, where M is Li or MgX and X is Cl, Br, or I, in a suitable solvent to form a ketone of Formula (XVI)

XV XVI ;

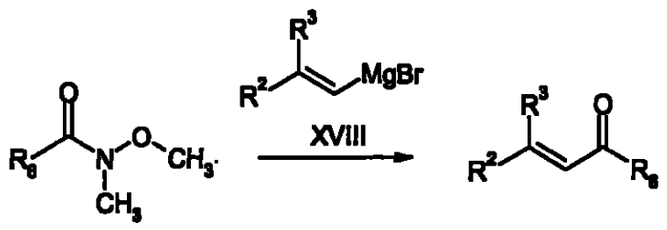
(d) reacting the ketone of Formula (XVI) with a suitable organometallic reagent R^5R^4M where M is Li or MgX and X is Cl, Br, or I, in a suitable solvent to form the compound of Formula (IB)



XVI IB , R^1 =

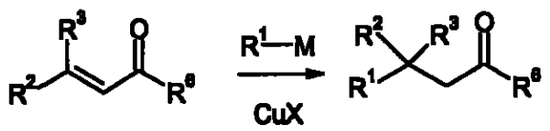
A second method for making a compound of Formula (IB) comprises:

(a') reacting an amide of Formula (XVII) with a vinyl magnesium bromide bearing R^2 and R^3 of Formula (XVIII) in a suitable solvent to provide an enone of Formula (XIX)



XVII XIX ;

(b') reacting the enone of Formula (XIX) with a suitable organocopper reagent generated from an organometallic reagent R^1M, where M is Li or MgX, and a copper salt CuX, where X is Cl, Br, or I, in a suitable solvent to form a ketone of Formula (XX)

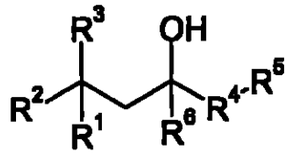


XIX XX ; and

(c') reacting the ketone of Formula (XX) with a suitable organometallic reagent R^5R^4M, where M is Li or MgX, and X is Cl, Br, or I, in a suitable solvent to form the compound of Formula (IB)

XX IB

The instant invention is directed to compounds of Formula (IC)



(IC)

wherein:

R^1 is an aryl or heteroaryl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_5 alkoxy, C_2-C_5 alkenyloxy, C_2-C_5 alkynyloxy, aryloxy, acyl, C_1-C_5 alkoxycarbonyl, C_1-C_5 alkanoyloxy, C_1-C_5 alkanoyl, aroyl, aminocarbonyl, C_1-C_5 alkylaminocarbonyl, C_1-C_5 dialkylaminocarbonyl, aminocarbonyloxy, C_1-C_5 alkylaminocarbonyloxy, C_1-C_5 dialkylaminocarbonyloxy, C_1-C_5 alkanoylamino, C_1-C_5 alkoxycarbonylamino, C_1-C_5 alkylsulfonylamino, aminosulfonyl, C_1-C_5 alkylaminosulfonyl, C_1-C_5 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, trifluoromethoxy, nitro, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl; or C_1-C_5 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with one to three substituent groups selected from methyl, methoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl; or ureido

wherein either nitrogen atom is optionally independently substituted with C_1-C_3 alkyl;

R^2 and R^3 are each independently C_1-C_3 alkyl;

R^4 is C_1-C_3 alkyl, C_2-C_3 alkenyl, or C_2-C_3 alkynyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^4 is independently C_1-C_3 alkyl, hydroxy, halogen, or oxo;

R^5 is a heteroaryl group fused with a saturated or partially saturated carbocyclic ring optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_2-C_3 alkynyloxy, aryloxy, acyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, aminocarbonyloxy, C_1-C_3 alkylaminocarbonyloxy, C_1-C_3 dialkylaminocarbonyloxy, C_1-C_3 alkanoylamino, C_1-C_3 alkoxycarbonylamino, C_1-C_3 alkylsulfonylamino, C_1-C_3 alkylaminosulfonyl, C_1-C_3 dialkylaminosulfonyl, halogen, hydroxy, oxo, carboxy, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, nitro, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_3 alkyl; or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^5 is optionally independently substituted with one to three substituent groups selected from C_1-C_3 alkyl, C_1-C_3 alkoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_3 alkyl, or trifluoromethyl, and

R^6 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, carbocycle, heterocyclyl, aryl, heteroaryl, carbocycle-C_1-C_8 alkyl, carboxy, trifluoromethyl, alkoxycarbonyl, aryl-C_1-C_8 alkyl, aryl-C_1-C_8 haloalkyl, heterocyclyl-C_1-C_8 alkyl, heteroaryl-C_1-C_8 alkyl, carbocycle-C_2-C_8 alkenyl, aryl-C_2-C_8 alkenyl, heterocyclyl-C_2-C_8 alkenyl, or heteroaryl-C_2-C_8 alkenyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, C_3-C_8 cycloalkyl, phenyl, C_1-C_5 alkoxy, phenoxy, C_1-C_5 alkanoyl, aroyl, C_1-C_5 alkoxycarbonyl, C_1-C_5 alkanoyloxy, aminocarbonyloxy, C_1-C_5 alkylaminocarbonyloxy, C_1-C_5 dialkylaminocarbonyloxy, aminocarbonyl, C_1-C_5 alkylaminocarbonyl, C_1-C_5 dialkylaminocarbonyl, C_1-C_5 alkanoylamino, C_1-C_5 alkoxycarbonylamino, C_1-C_5 alkylsulfonylamino, C_1-C_5 alkylaminosulfonyl, C_1-C_5 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, oxo, trifluoromethyl, nitro, amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl; or C_1-C_5 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

or a tautomer, prodrug, solvate, or salt thereof.

Another aspect of the invention includes compounds of Formula (IC), wherein:

R^1 is thienyl, phenyl, naphthyl, dihydrobenzofuranyl, benzofuranyl, chromanyl, dihydroindolyl, indolyl, dihydrobenzothienyl, benzothienyl, benzodioxolanyl, benzoxazolyl, benzisoxazolyl, benzpyrazolyl, benzimidazolyl, thienyl, quinolinyl, pyridinyl, pyrimidinyl, or pyrazinyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_1-C_3 alkanoyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with a substituent group selected from methyl, methoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl;

R^2 and R^3 are each independently C_1-C_3 alkyl;

R^4 is CH_2;

R^5 is a N-linked heteroaryl with a fused 5-7 membered saturated carbocyclic ring optionally and independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, phenyl, C_1-C_3 alkoxy, methoxycarbonyl, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, heterocyclylcarbonyl, fluoro, chloro, bromo, cyano, trifluoromethyl, hydroxyl, oxo, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^5 is optionally independently substituted with a substituent group selected from methyl, methoxy, fluoro, chloro, bromo, trifluoromethyl, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl; and

R^6 is C_1-C_3 alkyl, C_2-C_3 alkenyl, C_3-C_6 cycloalkyl, trifluoromethyl, phenyl, C_3-C_6 cycloalkyl-C_1-C_3 alkyl, phenyl-C_1-C_3 alkyl, phenyl-C_1-C_3 haloalkyl, C_3-C_6 cycloalkyl-C_2-C_3 alkenyl, phenyl-C_2-C_3 alkenyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3

dialkylaminocarbonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

or a tautomer, prodrug, solvate, or salt thereof.

Yet another aspect of the invention includes compounds of Formula (IC), wherein:

R^1 is thienyl, phenyl, naphthyl, pyridyl, chromanyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one or two substituent groups,

wherein each substituent group of R^1 is independently methyl, ethyl, methoxy, ethoxy, fluoro, chloro, bromo, hydroxy, trifluoromethyl, cyano, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone;

R^2 and R^3 are each methyl;

R^4 is CH_3;

R^5 is a N-linked pyrrole, pyrazole, or imidazole fused to a 5-7 membered saturated carbocyclic ring optionally and independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently methyl, phenyl, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminoaminocarbonyl, morpholinylcarbonyl, fluoro, chloro, bromo, cyano, hydroxy, oxo, or trifluoromethyl; and

R^6 is C_1-C_3 alkyl, C_3-C_6 cycloalkyl, trifluoromethyl, C_3-C_6 cycloalkylmethyl-, or benzyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently methyl, methoxy, fluoro, chloro, bromo, cyano, trifluoromethyl, or hydroxy,

or a tautomer, prodrug, solvate, or salt thereof.

Another aspect of the invention includes compounds of Formula (IC), wherein:

R^1 is thienyl, phenyl, naphthyl, dihydrobenzofuranyl, benzofuranyl, chromanyl, dihydroindolyl, indolyl, dihydrobenzothienyl, benzothienyl, benzodioxolanyl, benzoxazolyl, benzisoxazolyl, benzpyrazolyl, benzimidazolyl, thienyl, quinolinyl, pyridinyl, pyrimidinyl, or pyrazinyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_1-C_3 alkanoyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, aryl, heteroaryl, heterocyclyl, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with a substituent group selected from methyl, methoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl;

R^2 and R^3 are each independently C_1-C_3 alkyl;

R^4 is CH_2;

R^5 is a N-linked heteroaryl with a fused 5-7 membered saturated carbocyclic ring optionally and independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, phenyl, C_1-C_3 alkoxy, methoxycarbonyl, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, heterocyclylcarbonyl, fluoro, chloro, bromo, cyano,

trifluoromethyl, hydroxyl, oxo, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^5 is optionally independently substituted with a substituent group selected from methyl, methoxy, fluoro, chloro, bromo, trifluoromethyl, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl; and

R^6 is C_1-C_3 alkyl, C_2-C_3 alkenyl, C_3-C_6 cycloalkyl, trifluoromethyl, phenyl, C_3-C_6 cycloalkyl-C_1-C_3 alkyl, phenyl-C_1-C_3 alkyl, phenyl-C_1-C_3 haloalkyl, C_3-C_6 cycloalkyl-C_2-C_3 alkenyl, phenyl-C_2-C_3 alkenyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

or a tautomer, prodrug, solvate, or salt thereof.

Yet another aspect of the invention includes compounds of Formula (IC), wherein:

R^1 is thienyl, phenyl, naphthyl, pyridyl, chromanyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one or two substituent groups,

wherein each substituent group of R^1 is independently methyl, ethyl, methoxy, ethoxy, fluoro, chloro, bromo, hydroxy, trifluoromethyl, pyridinyl, pyrimidinyl, pyrazinyl, cyano, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone;

wherein each substituent group of R^1 is optionally independently substituted with a substituent group selected from cyano or halogen;

R^2 and R^3 are each methyl;

R^4 is CH_3;

R^5 is a N-linked pyrrole, pyrazole, or imidazole fused to a 5-7 membered saturated carbocyclic ring optionally and independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently methyl, phenyl, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminoaminocarbonyl, morpholinylcarbonyl, fluoro, chloro, bromo, cyano, hydroxy, oxo, or trifluoromethyl; and

R^6 is C_1-C_3 alkyl, C_3-C_6 cycloalkyl, trifluoromethyl, C_3-C_6 cycloalkylmethyl-, or benzyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently methyl, methoxy, fluoro, chloro, bromo, cyano, trifluoromethyl, or hydroxy,

or a tautomer, prodrug, solvate, or salt thereof.

Representative compounds of Formula (IC) according to the invention are appended hereto as Table IC, where column A is the compound name according to standard nomenclature and column B is the corresponding chemical structure.

Preferred compounds of Formula (IC) include the following:

1-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl-1,5,6,7-tetrahydroindol-4-one;

1-[4-(2,3-Dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[2-Hydroxy-4-methyl-4-(5-pyrimidin-5-yl-2,3-dihydrobenzofuran-7-yl)-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[2-Hydroxy-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[2-Hydroxy-4-(2-hydroxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[2-Hydroxy-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[2-Hydroxy-4-(2-hydroxy-5-pyridin-3-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one; and

1-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one,

or a tautomer, prodrug, solvate, or salt thereof.

More preferred compounds of Formula (IC) include the following:

1-[2-Hydroxy-4-methyl-4-(5-pyrimidin-5-yl-2,3-dihydrobenzofuran-7-yl)-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[2-Hydroxy-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[2-Hydroxy-4-(2-hydroxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[2-Hydroxy-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one; and

1-[2-Hydroxy-4-(2-hydroxy-5-pyridin-3-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one,

or a tautomer, prodrug, solvate, or salt thereof.

The most preferred compounds of Formula (IC) include the following:

1-[2-Hydroxy-4-methyl-4-(5-pyrimidin-5-yl-2,3-dihydrobenzofuran-7-yl)-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[2-Hydroxy-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

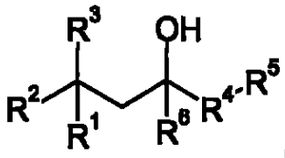
1-[2-Hydroxy-4-(2-hydroxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[2-Hydroxy-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one; and

1-[2-Hydroxy-4-(2-hydroxy-5-pyridin-3-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one,

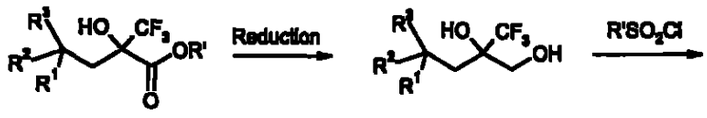
or a tautomer, prodrug, solvate, or salt thereof.

The invention further provides methods of making a compound of Formula (IC)

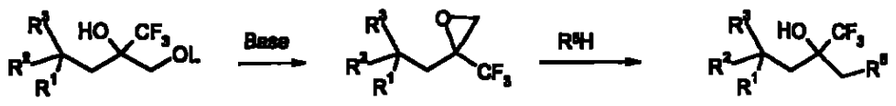


(IC).

One synthetic sequence for making a compound of Formula (IC) is shown below.

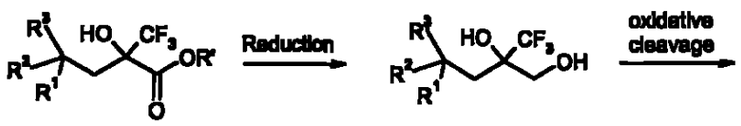


II III

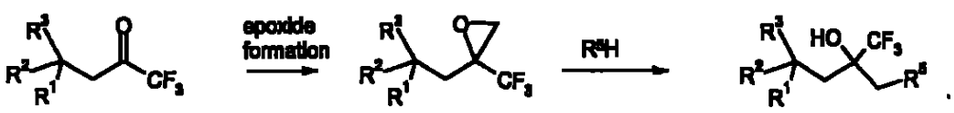


IV V I ($R^4 = -CH_2-$)

A second method of making a compound of Formula (IC) is shown below.

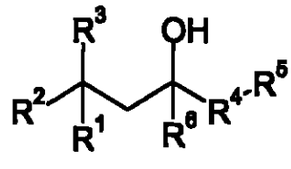


II III



IV V I ($R^4 = -CH_2-$)

The instant invention is also directed to compounds of Formula (ID)



(ID)

wherein:

R^1 is an aryl or heteroaryl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_5 alkoxy, C_2-C_5 alkenyloxy, C_2-C_5 alkynyloxy, aryloxy, acyl, C_1-C_5 alkoxycarbonyl, C_1-C_5 alkanoyloxy, C_1-C_5 alkanoyl, aroyl, aminocarbonyl, C_1-C_5 alkylaminocarbonyl, C_1-C_5 dialkylaminocarbonyl, aminocarbonyloxy, C_1-C_5 alkylaminocarbonyloxy, C_1-C_5 dialkylaminocarbonyloxy, C_1-C_5 alkanoylamino, C_1-C_5 alkoxycarbonylamino, C_1-C_5 alkylsulfonylamino, aminosulfonyl, C_1-C_5 alkylaminosulfonyl, C_1-C_5 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, trifluoromethoxy, nitro, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl; or C_1-C_5 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with one to three substituent groups selected from methyl, methoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl;

R^2 and R^3 are each independently C_1-C_5 alkyl, wherein one or both are independently substituted with hydroxy, C1-C5 alkoxy, C_1-C_5 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone, amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl;

R^4 is C_1-C_3 alkyl, C_2-C_3 alkenyl, or C_2-C_3 alkynyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^4 is independently C_1-C_3 alkyl, hydroxy, halogen, or oxo;

R^5 is a heteroaryl group optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_2-C_3 alkynyloxy, aryloxy, acyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, aminocarbonyloxy, C_1-C_3 alkylaminocarbonyloxy, C_1-C_3 dialkylaminocarbonyloxy, C_1-C_3 alkanoylamino, C_1-C_3 alkoxycarbonylamino, C_1-C_3 alkylsulfonylamino, C_1-C_3 alkylaminosulfonyl, C_1-C_3 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, nitro, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_3 alkyl; or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^5 is optionally independently substituted with one to three substituent groups selected from C_1-C_3 alkyl, C_1-C_3 alkoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_3 alkyl, or trifluoromethyl; and

R^6 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, carbocycle, heterocyclyl, aryl, heteroaryl, trifluoromethyl, carbocycle-C_1-C_8 alkyl, carboxy, alkoxycarbonyl, aryl-C_1-C_8 alkyl, aryl-C_1-C_8 haloalkyl, heterocyclyl-C_1-C_8 alkyl, heteroaryl-C_1-C_8 alkyl, carbocycle-

C_2-C_8 alkenyl, aryl-C_2-C_8 alkenyl, heterocyclyl-C_2-C_8 alkenyl, or heteroaryl-C_2-C_8 alkenyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, C_3-C_8 cycloalkyl, phenyl, C_1-C_5 alkoxy, phenoxy, C_1-C_5 alkanoyl, aroyl, C_1-C_5 alkoxycarbonyl, C_1-C_5 alkanoyloxy, aminocarbonyloxy, C_1-C_5 alkylaminocarbonyloxy, C_1-C_5 dialkylaminocarbonyloxy, aminocarbonyl, C_1-C_5 alkylaminocarbonyl, C_1-C_5 dialkylaminocarbonyl, C_1-C_5 alkanoylamino, C_1-C_5 alkoxycarbonylamino, C_1-C_5 alkylsulfonylamino, C_1-C_5 alkylaminosulfonyl, C_1-C_5 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, oxo, trifluoromethyl, nitro, amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl; or C_1-C_5 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

or a tautomer, prodrug, solvate, or salt thereof.

Another aspect of the invention includes compounds of Formula (ID), wherein:

R^1 is thienyl, phenyl, naphthyl, dihydrobenzofuranyl, benzofuranyl, chromanyl, dihydroindolyl, indolyl, dihydrobenzothienyl, benzothienyl, benzodioxolanyl, benzoxazolyl, benzisoxazolyl, benzpyrazolyl, benzimidazolyl, thienyl, quinolinyl, pyridinyl, pyrimidinyl, or pyrazinyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_1-C_3 alkanoyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with a substituent group selected from methyl, methoxy, halogen, hydroxy, oxo, cyano,

heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl;

R^2 and R^3 are each independently C_1-C_3 alkyl, wherein one or both are independently substituted with hydroxy, C_1-C_3 alkoxy;

R^4 is CH_2;

R^5 is an imidazolyl, pyridyl, indolyl, azaindolyl, diazaindolyl, benzofuranyl, furanopyridinyl, furanopyrimidinyl, benzothienyl, thienopyridinyl, thienopyrimidinyl, benzoxazolyl, oxazolopyridinyl, benzothiazolyl, thiazolopyridinyl, benzimidazolyl, imidazolopyridinyl, imidazolopyrimidinyl, imidazolopyridazinyl, imidazolopyrazinyl, quinolinyl, or isoquinolinyl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, phenyl, C_1-C_3 alkoxy, methoxycarbonyl, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, heterocyclylcarbonyl, fluoro, chloro, bromo, cyano, trifluoromethyl, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^5 is optionally independently substituted with a substituent group selected from methyl, methoxy, fluoro, chloro, bromo, trifluoromethyl, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl; and

R^6 is C_1-C_3 alkyl, C_2-C_3 alkenyl, C_3-C_6 cycloalkyl, trifluoromethyl, phenyl, C_3-C_6 cycloalkyl-C_1-C_3 alkyl, phenyl-C_1-C_3 alkyl, phenyl-C_1-C_3 haloalkyl, C_3-C_6 cycloalkyl-C_2-C_3 alkenyl, phenyl-C_2-C_3 alkenyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

or a tautomer, prodrug, solvate, or salt thereof.

Yet another aspect of the invention includes compounds of Formula (ID), wherein:

R^1 is thienyl, phenyl, naphthyl, pyridyl, chromanyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one or two substituent groups,

wherein each substituent group of R^1 is independently methyl, ethyl, methoxy, ethoxy, fluoro, chloro, bromo, hydroxy, trifluoromethyl, cyano, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone;

R^2 and R^3 are each methyl wherein one or both are independently substituted with hydroxy or methoxy;

R^4 is CH_2;

R^5 is a pyridyl, indolyl, azaindolyl, benzofuranyl, furanopyridinyl, thienopyridinyl, benzoxazolyl, benzimidazolyl, quinolinyl, or isoquinolinyl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently methyl, phenyl, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminoaminocarbonyl, morpholinylcarbonyl, fluoro, chloro, bromo, cyano, or trifluoromethyl; and

R^6 is C_1-C_3 alkyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkylmethyl-, trifluoromethyl, or benzyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently methyl, methoxy, fluoro, chloro, bromo, cyano, trifluoromethyl, or hydroxy,

or a tautomer, prodrug, solvate, or salt thereof.

Yet another aspect of the invention includes compounds of Formula (ID), wherein:

R^1 is phenyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_1-C_3 alkanoyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone; and

R^2 and R^3 are each independently C_1-C_3 alkyl each optionally independently substituted with hydroxy, C_1-C_3 alkoxy,

or a tautomer, prodrug, solvate, or salt thereof.

Representative compounds of Formula (ID) according to the invention are appended hereto as Table ID, where column A is the compound name according to standard nomenclature and column B is the corresponding chemical structure.

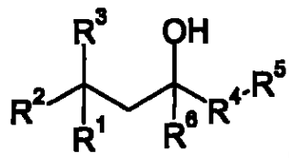
Preferred compounds of Formula (ID) include the following:

1,1,1-Trifluoro-5-methoxy-4-methyl-4-phenyl-2-quinolin-4-ylmethylpentan-2-ol; and

5,5,5-Trifluoro-2-methyl-2-phenyl-4-quinolin-4-ylmethylpentane-1,4-diol,

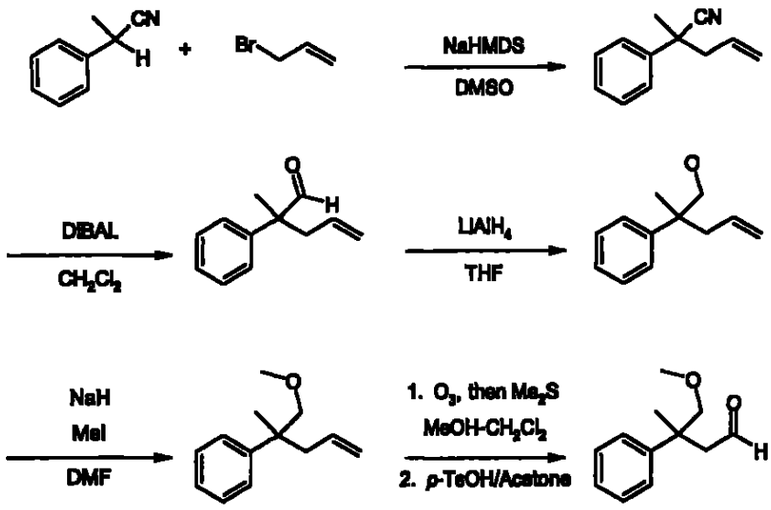
or a tautomer, prodrug, solvate, or salt thereof.

The invention further provides methods of making a compound of Formula (ID).



(ID)

One method of making a compounds of Formula (ID) is via the intermediate aldehyde which is shown below.



In another aspect of the invention, the compounds according to the invention are formulated into pharmaceutical compositions comprising an effective amount, preferably a pharmaceutically effective amount, of a compound according to the invention or a tautomer, prodrug, solvate, or salt thereof, and a pharmaceutically acceptable excipient or carrier.

The invention also provides a method of modulating the glucocorticoid receptor function in a patient, the method comprising administering to the patient an effective amount of a compound according to the invention or a tautomer, prodrug, solvate, or salt thereof.

The invention further provides a method of treating a disease-state or condition mediated by the glucocorticoid receptor function in a patient in need of such treatment, the method comprising

administering to the patient an effective amount of a pharmaceutically acceptable compound according to the invention or a tautomer, prodrug, solvate, or salt thereof.

In addition, the invention also provides a method of treating a disease-state or condition selected from: type II diabetes, obesity, cardiovascular diseases, hypertension, arteriosclerosis, neurological diseases, adrenal and pituitary tumors, and glaucoma, in a patient in need of such treatment, the method comprising administering to the patient an effective amount of a pharmaceutically acceptable compound according to the invention or a tautomer, prodrug, solvate, or salt thereof.

The invention provides a method of treating a disease characterized by inflammatory, allergic, or proliferative processes, in a patient in need of such treatment, the method comprising administering to the patient an effective amount of a pharmaceutically acceptable compound according to the invention or a tautomer, prodrug, solvate, or salt thereof. In a preferred embodiment of the invention, the disease characterized by inflammatory, allergic, or proliferative processes is selected from: (i) lung diseases; (ii) rheumatic diseases or autoimmune diseases or joint diseases; (iii) allergic diseases; (iv) vasculitis diseases; (v) dermatological diseases; (vi) renal diseases; (vii) hepatic diseases; (viii) gastrointestinal diseases; (ix) proctological diseases; (x) eye diseases; (xi) diseases of the ear, nose, and throat (ENT) area; (xii) neurological diseases; (xiii) blood diseases; (xiv) tumor diseases; (xv) endocrine diseases; (xvi) organ and tissue transplantations and graft-versus-host diseases; (xvii) severe states of shock; (xviii) substitution therapy; and (xix) pain of inflammatory genesis. In another preferred embodiment of the invention, the disease characterized by inflammatory, allergic, or proliferative processes is selected from: type I diabetes, osteoarthritis, Guillain-Barre syndrome, restenosis following percutaneous transluminal coronary angioplasty, Alzheimer disease, acute and chronic pain, atherosclerosis, reperfusion injury, bone resorption diseases, congestive heart failure, myocardial infarction, thermal injury, multiple organ injury secondary to trauma, acute purulent meningitis, necrotizing enterocolitis, and syndromes associated with hemodialysis, leukopheresis, and granulocyte transfusion.

The invention further provides methods of treating the disease-states or conditions mentioned above, in a patient in need of such treatment, the methods comprising sequentially or

simultaneously administering to the patient: (a) an effective amount of a pharmaceutically acceptable compound according to the invention or a tautomer, prodrug, solvate, or salt thereof; and (b) a pharmaceutically acceptable glucocorticoid.

The invention further provides a method of assaying the glucocorticoid receptor function in a sample, comprising: (a) contacting the sample with a selected amount of a compound according to the invention or a tautomer, prodrug, solvate, or salt thereof; and (b) detecting the amount of the compound according to the invention or a tautomer, prodrug, solvate, or salt thereof bound to glucocorticoid receptors in the sample. In a preferred embodiment of the invention, the compound according to the invention or a tautomer, prodrug, solvate, or salt thereof is labeled with a detectable marker selected from: a radiolabel, fluorescent tag, a chemiluminescent tag, a chromophore, and a spin label.

The invention also provides a method of imaging the glucocorticoid receptor distribution in a sample or patient, the method comprising: (a) contacting the sample or administering to a patient a compound according to the invention or a tautomer, prodrug, solvate, or salt thereof having a detectable marker; (b) detecting the spatial distribution and amount of the compound according to the invention or a tautomer, prodrug, solvate, or salt thereof having a detectable marker bound to glucocorticoid receptors in the sample or patient using an imaging means to obtain an image; and (c) displaying an image of the spatial distribution and amount of the compound according to the invention or a tautomer, prodrug, solvate, or salt thereof having a detectable marker bound to glucocorticoid receptors in the sample. In a preferred embodiment of the invention, the imaging means is selected from: radioscintigraphy, nuclear magnetic resonance imaging (MRI), computed tomography (CT scan), or positron emission tomography (PET).

The invention also provides a kit for the *in vitro* diagnostic determination of the glucocorticoid receptor function in a sample, comprising: (a) a diagnostically effective amount of a compound according to the invention or a tautomer, prodrug, solvate, or salt thereof; and (b) instructions for use of the diagnostic kit.

It is preferred that the compounds of Formula (IA), (IB), (IC), and (ID) exclude the compounds disclosed in U. S. Patent Application Pub. No. 2004/0023999.

Brief Description of the Tables

Table IA lists representative compounds of Formula (IA);

Table IB lists representative compounds of Formula (IB);

Table IC lists representative compounds of Formula (IC); and

Table ID lists representative compounds of Formula (ID).

Detailed Description of the Invention

Definition of Terms and Conventions Used

Terms not specifically defined herein should be given the meanings that would be given to them by one of skill in the art in light of the disclosure and the context. As used in the specification and appended claims, however, unless specified to the contrary, the following terms have the meaning indicated and the following conventions are adhered to.

A. Chemical Nomenclature, Terms, and Conventions

In the groups, radicals, or moieties defined below, the number of carbon atoms is often specified preceding the group, for example, C_1-C_{10} alkyl means an alkyl group or radical having 1 to 10 carbon atoms. The term "lower" applied to any carbon-containing group means a group containing from 1 to 8 carbon atoms, as appropriate to the group (i.e., a cyclic group must have at least 3 atoms to constitute a ring). In general, for groups comprising two or more subgroups, the last named group is the radical attachment point, for example, "alkylaryl" means a monovalent radical of the formula Alk-Ar-, while "arylalkyl" means a monovalent radical of the formula Ar-Alk- (where Alk is an alkyl group and Ar is an aryl group). Furthermore, the use of a term designating a monovalent radical where a divalent radical is appropriate shall be construed to designate the respective divalent radical and vice versa. Unless otherwise specified, conventional definitions of terms control and conventional stable atom valences are presumed and achieved in all formulas and groups.

The terms "alkyl" or "alkyl group" mean a branched or straight-chain saturated aliphatic hydrocarbon monovalent radical. This term is exemplified by groups such as methyl, ethyl, *n*-propyl, 1-methylethyl (isopropyl), *n*-butyl, *n*-pentyl, 1,1-dimethylethyl (*tert*-butyl), and the like. It may be abbreviated "Alk".

The terms "alkenyl" or "alkenyl group" mean a branched or straight-chain aliphatic hydrocarbon monovalent radical containing at least one carbon-carbon double bond. This term is exemplified by groups such as ethenyl, propenyl, *n*-butenyl, isobutenyl, 3-methylbut-2-enyl, *n*-pentenyl, heptenyl, octenyl, decenyl, and the like.

The terms "alkynyl" or "alkynyl group" mean a branched or straight-chain aliphatic hydrocarbon monovalent radical containing at least one carbon-carbon triple bond. This term is exemplified by groups such as ethynyl, propynyl, *n*-butynyl, 2-butynyl, 3-methylbutynyl, *n*-pentynyl, heptynyl, octynyl, decynyl, and the like.

The terms "alkylene" or "alkylene group" mean a branched or straight-chain saturated aliphatic hydrocarbon divalent radical having the specified number of carbon atoms. This term is exemplified by groups such as methylene, ethylene, propylene, *n*-butylene, and the like, and may alternatively and equivalently be denoted herein as -(alkyl)-.

The terms "alkenylene" or "alkenylene group" mean a branched or straight-chain aliphatic hydrocarbon divalent radical having the specified number of carbon atoms and at least one carbon-carbon double bond. This term is exemplified by groups such as ethenylene, propenylene, *n*-butenylene, and the like, and may alternatively and equivalently be denoted herein as -(alkylenyl)-.

The terms "alkynylene" or "alkynylene group" mean a branched or straight-chain aliphatic hydrocarbon divalent radical containing at least one carbon-carbon triple bond. This term is exemplified by groups such as ethynylene, propynylene, *n*-butynylene, 2-butynylene, 3-methylbutynylene, *n*-pentynylene, heptynylene, octynylene, decynylene, and the like, and may alternatively and equivalently be denoted herein as -(alkynyl)-.

The terms "alkoxy" or "alkoxy group" mean a monovalent radical of the formula AlkO-, where Alk is an alkyl group. This term is exemplified by groups such as methoxy, ethoxy, propoxy, isopropoxy, butoxy, *sec*-butoxy, *tert*-butoxy, pentoxy, and the like.

The terms "aryloxy", "aryloxy group", mean a monovalent radical of the formula ArO-, where Ar is aryl. This term is exemplified by groups such as phenoxy, naphthoxy, and the like.

The term "oxo" means a double-bonded divalent oxygen radical of the formula (=O), for example, one example of an alkyl group substituted by an "oxo" would be a group of the formula Alk-C(O)-Alk, wherein each Alk is an alkyl.

The terms "alkylcarbonyl", "alkylcarbonyl group", "alkanoyl", or "alkanoyl group" mean a monovalent radical of the formula AlkC(O)-, where Alk is alkyl or hydrogen.

The terms "arylcarbonyl", "arylcarbonyl group", "aroyl" or "aroyl group" mean a monovalent radical of the formula ArC(O)-, where Ar is aryl.

The terms "acyl" or "acyl group" mean a monovalent radical of the formula RC(O)-, where R is a substituent selected from hydrogen or an organic substituent. Exemplary substituents include alkyl, aryl, arylalkyl, cycloalkyl, heterocyclyl, heteroaryl, heteroarylalkyl, and the like. As such, the terms comprise alkylcarbonyl groups and arylcarbonyl groups.

The terms "acylamino" or "acylamino group" mean a monovalent radical of the formula RC(O)N(R)-, where each R is a substituent selected from hydrogen or a substituent group.

The terms "alkoxycarbonyl" or "alkoxycarbonyl group" mean a monovalent radical of the formula AlkO-C(O)-, where Alk is alkyl. Exemplary alkoxycarbonyl groups include methoxycarbonyl, ethoxycarbonyl, *tert*-butyloxycarbonyl, and the like.

The terms "alkylaminocarbonyloxy" or "alkylaminocarbonyloxy group" mean a monovalent radical of the formula $R_2NC(O)O$-, where each R is independently hydrogen or lower alkyl.

The term "alkoxycarbonylamino" or "alkoxycarbonylamino group" mean a monovalent radical of the formula ROC(O)NH-, where R is lower alkyl.

The terms "alkylcarbonylamino" or "alkylcarbonylamino group" or "alkanoylamino" or "alkanoylamino groups" mean a monovalent radical of the formula AlkC(O)NH-, where Alk is alkyl. Exemplary alkylcarbonylamino groups include acetamido ($CH_3C(O)NH$-).

The terms "alkylaminocarbonyloxy" or "alkylaminocarbonyloxy group" mean a monovalent radical of the formula AlkNHC(O)O-, where Alk is alkyl.

The terms "amino" or "amino group" mean an $-NH_2$ group.

The terms "alkylamino" or "alkylamino group" mean a monovalent radical of the formula (Alk)NH-, where Alk is alkyl. Exemplary alkylamino groups include methylamino, ethylamino, propylamino, butylamino, *tert*-butylamino, and the like.

The terms "dialkylamino" or "dialkylamino group" mean a monovalent radical of the formula (Alk)(Alk)N-, where each Alk is independently alkyl. Exemplary dialkylamino groups include dimethylamino, methylethylamino, diethylamino, dipropylamino, ethylpropylamino, and the like.

The terms "substituted amino" or "substituted amino group" mean a monovalent radical of the formula $-NR_2$, where each R is independently a substituent selected from hydrogen or the specified substituents (but where both Rs cannot be hydrogen). Exemplary substituents include alkyl, alkanoyl, aryl, arylalkyl, cycloalkyl, heterocyclyl, heteroaryl, heteroarylalkyl, and the like.

The terms "alkoxycarbonylamino" or "alkoxycarbonylamino group" mean a monovalent radical of the formula AlkOC(O)NH-, where Alk is alkyl.

The terms "ureido" or "ureido group" mean a monovalent radical of the formula $R_2NC(O)NH$-, where each R is independently hydrogen or alkyl.

The terms "halogen" or "halogen group" mean a fluoro, chloro, bromo, or iodo group.

The term "halo" means one or more hydrogen atoms of the group are replaced by halogen groups.

The terms "haloalkyl" or "haloalkyl group" mean a branched or straight-chain saturated aliphatic hydrocarbon monovalent radical, wherein one or more hydrogen atoms thereof are each independently replaced with halogen atoms. This term is exemplified by groups such as chloromethyl, 1,2-dibromoethyl, 1,1,1-trifluoropropyl, 2-iodobutyl, 1-chloro-2-bromo-3-fluoropentyl, and the like.

The terms "sulfanyl", "sulfanyl group", "thioether", or "thioether group" mean a divalent radical of the formula -S-.

The terms "alkylthio" or "alkylthio group" mean a monovalent radical of the formula AlkS-, where Alk is alkyl. Exemplary groups include methylthio, ethylthio, *n*-propylthio, isopropylthio, *n*-butylthio, and the like.

The terms "sulfonyl" or "sulfonyl group" mean a divalent radical of the formula $-SO_2-$.

The terms "sulfonylamino" or "sulfonylamino group" mean a divalent radical of the formula $-SO_2NR-$, where R is a hydrogen or a substituent group.

The terms "aminosulfonyl" or "aminosulfonyl group" mean a monovalent radical of the formula NR_2SO_2-, where R is each independently a hydrogen or a substituent group.

The terms "carbocycle" or "carbocyclic group" mean a stable aliphatic 3- to 15-membered monocyclic or polycyclic monovalent or divalent radical consisting solely of carbon and hydrogen atoms which may comprise one or more fused or bridged ring(s), preferably a 5- to 7-

membered monocyclic or 7- to 10-membered bicyclic ring. Unless otherwise specified, the carbocycle may be attached at any carbon atom which results in a stable structure and, if substituted, may be substituted at any suitable carbon atom which results in a stable structure. The term comprises cycloalkyl (including spiro cycloalkyl), cycloalkylene, cycloalkenyl, cycloalkenylene, cycloalkynyl, and cycloalkynylene, and the like.

The terms "cycloalkyl" or "cycloalkyl group" mean a stable aliphatic saturated 3- to 15-membered monocyclic or polycyclic monovalent radical consisting solely of carbon and hydrogen atoms which may comprise one or more fused or bridged ring(s), preferably a 5- to 7-membered monocyclic or 7- to 10-membered bicyclic ring. Unless otherwise specified, the cycloalkyl ring may be attached at any carbon atom which results in a stable structure and, if substituted, may be substituted at any suitable carbon atom which results in a stable structure. Exemplary cycloalkyl groups include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, cyclononyl, cyclodecyl, norbornanyl, adamantyl, tetrahydronaphthyl (tetralin), 1-decalinyl, bicyclo[2.2.2]octanyl, 1-methylcyclopropyl, 2-methylcyclopentyl, 2-methylcyclooctyl, and the like.

The terms "cycloalkenyl" or "cycloalkenyl group" mean a stable aliphatic 3- to 15-membered monocyclic or polycyclic monovalent radical having at least one carbon-carbon double bond and consisting solely of carbon and hydrogen atoms which may comprise one or more fused or bridged ring(s), preferably a 5- to 7-membered monocyclic or 7- to 10-membered bicyclic ring. Unless otherwise specified, the cycloalkenyl ring may be attached at any carbon atom which results in a stable structure and, if substituted, may be substituted at any suitable carbon atom which results in a stable structure. Exemplary cycloalkenyl groups include cyclopentenyl, cyclohexenyl, cycloheptenyl, cyclooctenyl, cyclononenyl, cyclodecenyl, norbornenyl, 2-methylcyclopentenyl, 2-methylcyclooctenyl, and the like.

The terms "cycloalkynyl" or "cycloalkynyl group" mean a stable aliphatic 8- to 15-membered monocyclic or polycyclic monovalent radical having at least one carbon-carbon triple bond and consisting solely of carbon and hydrogen atoms which may comprise one or more fused or bridged ring(s), preferably a 8- to 10-membered monocyclic or 12- to 15-membered bicyclic ring. Unless otherwise specified, the cycloalkynyl ring may be attached at any carbon atom

which results in a stable structure and, if substituted, may be substituted at any suitable carbon atom which results in a stable structure. Exemplary cycloalkynyl groups include, cyclooctynyl, cyclononynyl, cyclodecynyl, 2-methylcyclooctynyl, and the like.

The terms "cycloalkylene" or "cycloalkylene group" mean a stable saturated aliphatic 3- to 15-membered monocyclic or polycyclic divalent radical consisting solely of carbon and hydrogen atoms which may comprise one or more fused or bridged ring(s), preferably a 5- to 7-membered monocyclic or 7- to 10-membered bicyclic ring. Unless otherwise specified, the cycloalkyl ring may be attached at any carbon atom which results in a stable structure and, if substituted, may be substituted at any suitable carbon atom which results in a stable structure. Exemplary cycloalkylene groups include cyclopentylene, and the like.

The terms "cycloalkenylene" or "cycloalkenylene group" mean a stable aliphatic 5- to 15-membered monocyclic or polycyclic divalent radical having at least one carbon-carbon double bond and consisting solely of carbon and hydrogen atoms which may comprise one or more fused or bridged ring(s), preferably a 5- to 7-membered monocyclic or 7- to 10-membered bicyclic ring. Unless otherwise specified, the cycloalkenylene ring may be attached at any carbon atom which results in a stable structure and, if substituted, may be substituted at any suitable carbon atom which results in a stable structure. Exemplary cycloalkenylene groups include cyclopentenylene, cyclohexenylene, cycloheptenylene, cyclooctenylene, cyclononenylene, cyclodecenylene, norbornenylene, 2-methylcyclopentenylene, 2-methylcyclooctenylene, and the like.

The terms "cycloalkynylene" or "cycloalkynylene group" mean a stable aliphatic 8- to 15-membered monocyclic or polycyclic divalent radical having at least one carbon-carbon triple bond and consisting solely of carbon and hydrogen atoms which may comprise one or more fused or bridged ring(s), preferably a 8- to 10-membered monocyclic or 12- to 15-membered bicyclic ring. Unless otherwise specified, the cycloalkynylene ring may be attached at any carbon atom which results in a stable structure and, if substituted, may be substituted at any suitable carbon atom which results in a stable structure. Exemplary cycloalkynylene groups include cyclooctynylene, cyclononynylene, cyclodecynylene, 2-methylcyclooctynylene, and the like.

The terms "aryl" or "aryl group" mean an aromatic carbocyclic monovalent or divalent radical of from 6 to 14 carbon atoms having a single ring (e.g., phenyl or phenylene) or multiple condensed rings (e.g., naphthyl or anthranyl). Unless otherwise specified, the aryl ring may be attached at any suitable carbon atom which results in a stable structure and, if substituted, may be substituted at any suitable carbon atom which results in a stable structure. Exemplary aryl groups include phenyl, naphthyl, anthryl, phenanthryl, indanyl, indenyl, biphenyl, and the like. It may be abbreviated "Ar".

The terms "heteroaryl" or "heteroaryl group" mean a stable aromatic 5- to 14-membered, monocyclic or polycyclic monovalent or divalent radical which may comprise one or more fused or bridged ring(s), preferably a 5- to 7-membered monocyclic or 7- to 10-membered bicyclic radical, having from one to four heteroatoms in the ring(s) independently selected from nitrogen, oxygen, and sulfur, wherein any sulfur heteroatoms may optionally be oxidized and any nitrogen heteroatom may optionally be oxidized or be quaternized. Unless otherwise specified, the heteroaryl ring may be attached at any suitable heteroatom or carbon atom which results in a stable structure and, if substituted, may be substituted at any suitable heteroatom or carbon atom which results in a stable structure. Exemplary and preferred heteroaryls include furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, tetrazolyl, thiadiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, indolizinyl, azaindolizinyl, indolyl, azaindolyl, diazaindolyl, dihydroindolyl, dihydroazaindoyl, isoindolyl, azaisoindolyl, benzofuranyl, furanopyridinyl, furanopyrimidinyl, furanopyrazinyl, furanopyridazinyl, dihydrobenzofuranyl, dihydrofuranopyridinyl, dihydrofuranopyrimidinyl, benzodioxolanyl, benzothienyl, thienopyridinyl, thienopyrimidinyl, thienopyrazinyl, thienopyridazinyl, dihydrobenzothienyl, dihydrothienopyridinyl, dihydrothienopyrimidinyl, indazolyl, azaindazolyl, diazaindazolyl, benzimidazolyl, imidazopyridinyl, benzthiazolyl, thiazolopyridinyl, thiazolopyrimidinyl, benzoxazolyl, oxazolopyridinyl, oxazolopyrimidinyl, benzisoxazolyl, purinyl, chromanyl, azachromanyl, quinolizinyl, quinolinyl, dihydroquinolinyl, tetrahydroquinolinyl, isoquinolinyl, dihydroisoquinolinyl, tetrahydroisoquinolinyl, cinnolinyl, azacinnolinyl, phthalazinyl, azaphthalazinyl, quinazolinyl, azaquinazolinyl, quinoxalinyl, azaquinoxalinyl, naphthyridinyl,

dihydronaphthyridinyl, tetrahydronaphthyridinyl, pteridinyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl, and phenoxazinyl, and the like.

The terms "heterocycle", "heterocycle group", "heterocyclyl", or "heterocyclyl group" mean a stable non-aromatic 5- to 14-membered monocyclic or polycyclic, monovalent or divalent, ring which may comprise one or more fused or bridged ring(s), preferably a 5- to 7-membered monocyclic or 7- to 10-membered bicyclic ring, having from one to three heteroatoms in the ring(s) independently selected from nitrogen, oxygen, and sulfur, wherein any sulfur heteroatoms may optionally be oxidized and any nitrogen heteroatom may optionally be oxidized or be quaternized. Unless otherwise specified, the heterocyclyl ring may be attached at any suitable heteroatom or carbon atom which results in a stable structure and, if substituted, may be substituted at any suitable heteroatom or carbon atom which results in a stable structure. Exemplary and preferred heterocycles include pyrrolinyl, pyrrolidinyl, pyrazolinyl, pyrazolidinyl, piperidinyl, morpholinyl, thiomorpholinyl, piperazinyl, tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrofuranyl, hexahydropyrimidinyl, hexahydropyridazinyl, and the like.

The term "compounds of Formula (I)" and equivalent expressions are mean to embrace compounds of Formula (IA), compounds of Formula (IB), compounds of Formula (IC), and compounds of Formula (ID), either individually, in some combination, or all of them, as the context permits.

The term "compounds of the invention" and equivalent expressions are meant to embrace compounds of Formula (I) as herein described, including the tautomers, the prodrugs, the salts, particularly the pharmaceutically acceptable salts, and the solvates and hydrates thereof, where the context so permits. In general and preferably, the compounds of the invention and the formulas designating the compounds of the invention are understood to only include the stable compounds thereof and exclude unstable compounds, even if an unstable compound might be considered to be literally embraced by the compound formula. Similarly, reference to intermediates, whether or not they themselves are claimed, is meant to embrace their salts and solvates, where the context so permits. For the sake of clarity, particular instances when the

context so permits are sometimes indicated in the text, but these instances are purely illustrative and it is not intended to exclude other instances when the context so permits.

The terms "optional" or "optionally" mean that the subsequently described event or circumstances may or may not occur, and that the description includes instances where the event or circumstance occurs and instances in which it does not. For example, "optionally substituted aryl" means that the aryl radical may or may not be substituted and that the description includes both substituted aryl radicals and aryl radicals having no substitution.

The terms "stable compound" or "stable structure" mean a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic or diagnostic agent. For example, a compound which would have a "dangling valency" or is a carbanion is not a compound contemplated by the invention.

The term "substituted" means that any one or more hydrogens on an atom of a group or moiety, whether specifically designated or not, is replaced with a selection from the indicated group of substituents, provided that the atom's normal valency is not exceeded and that the substitution results in a stable compound. If a bond to a substituent is shown to cross the bond connecting two atoms in a ring, then such substituent may be bonded to any atom on the ring. When a substituent is listed without indicating the atom via which such substituent is bonded to the rest of the compound, then such substituent may be bonded via any atom in such substituent. For example, when the substituent is piperazinyl, piperidinyl, or tetrazolyl, unless specified otherwise, such piperazinyl, piperidinyl, or tetrazolyl group may be bonded to the rest of the compound of the invention via any atom in such piperazinyl, piperidinyl, or tetrazolyl group. Generally, when any substituent or group occurs more than one time in any constituent or compound, its definition on each occurrence is independent of its definition at every other occurrence. Thus, for example, if a group is shown to be substituted with 0 to 2 R^5, then such group is optionally substituted with up to two R^5 groups and R^5 at each occurrence is selected independently from the defined list of possible R^5. Such combinations of substituents and/or variables, however, are permissible only if such combinations result in stable compounds.

In a specific embodiment, the term "about" or "approximately" means within 20%, preferably within 10%, and more preferably within 5% of a given value or range.

The yield of each of the reactions described herein is expressed as a percentage of the theoretical yield.

B. Salt, Prodrug, Derivative, and Solvate Terms and Conventions

The terms "prodrug" or "prodrug derivative" mean a covalently-bonded derivative or carrier of the parent compound or active drug substance which undergoes at least some biotransformation prior to exhibiting its pharmacological effect(s). In general, such prodrugs have metabolically cleavable groups and are rapidly transformed in vivo to yield the parent compound, for example, by hydrolysis in blood, and generally include esters and amide analogs of the parent compounds. The prodrug is formulated with the objectives of improved chemical stability, improved patient acceptance and compliance, improved bioavailability, prolonged duration of action, improved organ selectivity, improved formulation (e.g., increased hydrosolubility), and/or decreased side effects (e.g., toxicity). In general, prodrugs themselves have weak or no biological activity and are stable under ordinary conditions. Prodrugs can be readily prepared from the parent compounds using methods known in the art, such as those described in A Textbook of Drug Design and Development, Krogsgaard-Larsen and H. Bundgaard (eds.), Gordon & Breach, 1991, particularly Chapter 5: "Design and Applications of Prodrugs"; Design of Prodrugs, H. Bundgaard (ed.), Elsevier, 1985; Prodrugs: Topical and Ocular Drug Delivery, K.B. Sloan (ed.), Marcel Dekker, 1998; Methods in Enzymology, K. Widder *et al.* (eds.), Vol. 42, Academic Press, 1985, particularly pp. 309-396; Burger's Medicinal Chemistry and Drug Discovery, 5th Ed., M. Wolff (ed.), John Wiley & Sons, 1995, particularly Vol. 1 and pp. 172-178 and pp. 949-982; Pro-Drugs as Novel Delivery Systems, T. Higuchi and V. Stella (eds.), Am. Chem. Soc., 1975; Bioreversible Carriers in Drug Design, E.B. Roche (ed.), Elsevier, 1987, each of which is incorporated herein by reference in their entireties.

The term "pharmaceutically acceptable prodrug" as used herein means a prodrug of a compound of the invention which is, 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, as well as the zwitterionic forms, where possible.

The term "salt" means an ionic form of the parent compound or the product of the reaction between the parent compound with a suitable acid or base to make the acid salt or base salt of the parent compound. Salts of the compounds of the present invention can be synthesized from the parent compounds which contain a basic or acidic moiety by conventional chemical methods. Generally, the salts are prepared by reacting the free base or acid parent compound with stoichiometric amounts or with an excess of the desired salt-forming inorganic or organic acid or base in a suitable solvent or various combinations of solvents.

The term "pharmaceutically acceptable salt" means a salt of a compound of the invention which is, 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, generally water or oil-soluble or dispersible, and effective for their intended use. The term includes pharmaceutically-acceptable acid addition salts and pharmaceutically-acceptable base addition salts. As the compounds of the present invention are useful in both free base and salt form, in practice, the use of the salt form amounts to use of the base form. Lists of suitable salts are found in, e.g., S.M. Birge *et al.*, J. Pharm. Sci., 1977, 66, pp. 1-19, which is hereby incorporated by reference in its entirety.

The term "pharmaceutically-acceptable acid addition salt" means those salts which retain the biological effectiveness and properties of the free bases and which are not biologically or otherwise undesirable, formed with inorganic acids such as hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid, sulfamic acid, nitric acid, phosphoric acid, and the like, and organic acids such as acetic acid, trichloroacetic acid, trifluoroacetic acid, adipic acid, alginic acid, ascorbic acid, aspartic acid, benzenesulfonic acid, benzoic acid, 2-acetoxybenzoic acid, butyric acid, camphoric acid, camphorsulfonic acid, cinnamic acid, citric acid, digluconic acid, ethanesulfonic acid, glutamic acid, glycolic acid, glycerophosphoric acid, hemisulfic acid, heptanoic acid, hexanoic acid, formic acid, fumaric acid, 2-hydroxyethanesulfonic acid (isethionic acid), lactic acid, maleic acid, hydroxymaleic acid, malic acid, malonic acid, mandelic acid, mesitylenesulfonic acid, methanesulfonic acid, naphthalenesulfonic acid,

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nicotinic acid, 2-naphthalenesulfonic acid, oxalic acid, pamoic acid, pectinic acid, phenylacetic acid, 3-phenylpropionic acid, picric acid, pivalic acid, propionic acid, pyruvic acid, pyruvic acid, salicylic acid, stearic acid, succinic acid, sulfanilic acid, tartaric acid, *p*-toluenesulfonic acid, undecanoic acid, and the like.

The term "pharmaceutically-acceptable base addition salt" means those salts which retain the biological effectiveness and properties of the free acids and which are not biologically or otherwise undesirable, formed with inorganic bases such as ammonia or hydroxide, carbonate, or bicarbonate of ammonium or a metal cation such as sodium, potassium, lithium, calcium, magnesium, iron, zinc, copper, manganese, aluminum, and the like. Particularly preferred are the ammonium, potassium, sodium, calcium, and magnesium salts. Salts derived from pharmaceutically-acceptable organic nontoxic bases include salts of primary, secondary, and tertiary amines, quaternary amine compounds, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion-exchange resins, such as methylamine, dimethylamine, trimethylamine, ethylamine, diethylamine, triethylamine, isopropylamine, tripropylamine, tributylamine, ethanolamine, diethanolamine, 2-dimethylaminoethanol, 2-diethylaminoethanol, dicyclohexylamine, lysine, arginine, histidine, caffeine, hydrabamine, choline, betaine, ethylenediamine, glucosamine, methylglucamine, theobromine, purines, piperazine, piperidine, *N*-ethylpiperidine, tetramethylammonium compounds, tetraethylammonium compounds, pyridine, *N,N*-dimethylaniline, *N*-methylpiperidine, *N*-methylmorpholine, dicyclohexylamine, dibenzylamine, *N,N*-dibenzylphenethylamine, 1-ephenamine, *N,N'*-dibenzylethylenediamine, polyamine resins, and the like. Particularly preferred organic nontoxic bases are isopropylamine, diethylamine, ethanolamine, trimethylamine, dicyclohexylamine, choline, and caffeine.

The term "solvate" means a physical association of a compound with one or more solvent molecules or a complex of variable stoichiometry formed by a solute (for example, a compound of Formula (I)) and a solvent, for example, water, ethanol, or acetic acid. This physical association may involve varying degrees of ionic and covalent bonding, including hydrogen bonding. In certain instances, the solvate will be capable of isolation, for example, when one or more solvent molecules are incorporated in the crystal lattice of the crystalline solid. In general, the solvents selected do not interfere with the biological activity of the solute. Solvates

encompasses both solution-phase and isolatable solvates. Representative solvates include hydrates, ethanolates, methanolates, and the like.

The term "hydrate" means a solvate wherein the solvent molecule(s) is/are H_2O.

The compounds of the present invention as discussed below include the free base or acid thereof, their salts, solvates, and prodrugs and may include oxidized sulfur atoms or quaternized nitrogen atoms in their structure, although not explicitly stated or shown, particularly the pharmaceutically acceptable forms thereof. Such forms, particularly the pharmaceutically acceptable forms, are intended to be embraced by the appended claims.

C. Isomer Terms and Conventions

The term "isomers" means compounds having the same number and kind of atoms, and hence the same molecular weight, but differing with respect to the arrangement or configuration of the atoms in space. The term includes stereoisomers and geometric isomers.

The terms "stereoisomer" or "optical isomer" mean a stable isomer that has at least one chiral atom or restricted rotation giving rise to perpendicular dissymmetric planes (e.g., certain biphenyls, allenes, and spiro compounds) and can rotate plane-polarized light. Because asymmetric centers and other chemical structure exist in the compounds of the invention which may give rise to stereoisomerism, the invention contemplates stereoisomers and mixtures thereof. The compounds of the invention and their salts include asymmetric carbon atoms and may therefore exist as single stereoisomers, racemates, and as mixtures of enantiomers and diastereomers. Typically, such compounds will be prepared as a racemic mixture. If desired, however, such compounds can be prepared or isolated as pure stereoisomers, i.e., as individual enantiomers or diastereomers, or as stereoisomer-enriched mixtures. As discussed in more detail below, individual stereoisomers of compounds are prepared by synthesis from optically active starting materials containing the desired chiral centers or by preparation of mixtures of enantiomeric products followed by separation or resolution, such as conversion to a mixture of diastereomers followed by separation or recrystallization, chromatographic techniques, use of chiral resolving agents, or direct separation of the enantiomers on chiral chromatographic

columns. Starting compounds of particular stereochemistry are either commercially available or are made by the methods described below and resolved by techniques well-known in the art.

The term "enantiomers" means a pair of stereoisomers that are non-superimposable mirror images of each other.

The terms "diastereoisomers" or "diastereomers" mean optical isomers which are not mirror images of each other.

The terms "racemic mixture" or "racemate" mean a mixture containing equal parts of individual enantiomers.

The term "non-racemic mixture" means a mixture containing unequal parts of individual enantiomers.

The term "geometrical isomer" means a stable isomer which results from restricted freedom of rotation about double bonds (e.g., *cis*-2-butene and *trans*-2-butene) or in a cyclic structure (e.g., *cis*-1,3-dichlorocyclobutane and *trans*-1,3-dichlorocyclobutane). Because carbon-carbon double (olefinic) bonds, C=N double bonds, cyclic structures, and the like may be present in the compounds of the invention, the invention contemplates each of the various stable geometric isomers and mixtures thereof resulting from the arrangement of substituents around these double bonds and in these cyclic structures. The substituents and the isomers are designated using the *cis/trans* convention or using the *E* or *Z* system, wherein the term "*E*" means higher order substituents on opposite sides of the double bond, and the term "*Z*" means higher order substituents on the same side of the double bond. A thorough discussion of *E* and *Z* isomerism is provided in J. March, Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, 4th ed., John Wiley & Sons, 1992, which is hereby incorporated by reference in its entirety. Several of the following examples represent single *E* isomers, single *Z* isomers, and mixtures of *E/Z* isomers. Determination of the *E* and *Z* isomers can be done by analytical methods such as x-ray crystallography, ^{1}H-NMR, and ^{13}C-NMR.

Some of the compounds of the invention can exist in more than one tautomeric form. As mentioned above, the compounds of the invention include all such tautomers.

It is well-known in the art that the biological and pharmacological activity of a compound is sensitive to the stereochemistry of the compound. Thus, for example, enantiomers often exhibit strikingly different biological activity including differences in pharmacokinetic properties, including metabolism, protein binding, and the like, and pharmacological properties, including the type of activity displayed, the degree of activity, toxicity, and the like. Thus, one skilled in the art will appreciate that one enantiomer may be more active or may exhibit beneficial effects when enriched relative to the other enantiomer or when separated from the other enantiomer. Additionally, one skilled in the art would know how to separate, enrich, or selectively prepare the enantiomers of the compounds of the invention from this disclosure and the knowledge of the prior art.

Thus, although the racemic form of drug may be used, it is often less effective than administering an equal amount of enantiomerically pure drug; indeed, in some cases, one enantiomer may be pharmacologically inactive and would merely serve as a simple diluent. For example, although ibuprofen had been previously administered as a racemate, it has been shown that only the *S*-isomer of ibuprofen is effective as an anti-inflammatory agent (in the case of ibuprofen, however, although the *R*-isomer is inactive, it is converted in vivo to the *S*-isomer, thus, the rapidity of action of the racemic form of the drug is less than that of the pure *S*-isomer). Furthermore, the pharmacological activities of enantiomers may have distinct biological activity. For example, *S*-penicillamine is a therapeutic agent for chronic arthritis, while *R*-penicillamine is toxic. Indeed, some purified enantiomers have advantages over the racemates, as it has been reported that purified individual isomers have faster transdermal penetration rates compared to the racemic mixture. See U.S. Patent Nos. 5,114,946 and 4,818,541.

Thus, if one enantiomer is pharmacologically more active, less toxic, or has a preferred disposition in the body than the other enantiomer, it would be therapeutically more beneficial to administer that enantiomer preferentially. In this way, the patient undergoing treatment would

be exposed to a lower total dose of the drug and to a lower dose of an enantiomer that is possibly toxic or an inhibitor of the other enantiomer.

Preparation of pure enantiomers or mixtures of desired enantiomeric excess (ee) or enantiomeric purity are accomplished by one or more of the many methods of (a) separation or resolution of enantiomers, or (b) enantioselective synthesis known to those of skill in the art, or a combination thereof. These resolution methods generally rely on chiral recognition and include, for example, chromatography using chiral stationary phases, enantioselective host-guest complexation, resolution or synthesis using chiral auxiliaries, enantioselective synthesis, enzymatic and nonenzymatic kinetic resolution, or spontaneous enantioselective crystallization. Such methods are disclosed generally in Chiral Separation Techniques: A Practical Approach (2nd Ed.), G. Subramanian (ed.), Wiley-VCH, 2000; T.E. Beesley and R.P.W. Scott, Chiral Chromatography, John Wiley & Sons, 1999; and Satinder Ahuja, Chiral Separations by Chromatography, Am. Chem. Soc., 2000. Furthermore, there are equally well-known methods for the quantitation of enantiomeric excess or purity, for example, GC, HPLC, CE, or NMR, and assignment of absolute configuration and conformation, for example, CD/ORD, X-ray crystallography, or NMR.

In general, all tautomeric forms and isomeric forms and mixtures, whether individual geometric isomers or stereoisomers or racemic or non-racemic mixtures, of a chemical structure or compound is intended, unless the specific stereochemistry or isomeric form is specifically indicated in the compound name or structure. Generally, one enantiomer is preferred, when a racemic mixtures is resolved.

D. Pharmaceutical Administration and Diagnostic and Treatment Terms and Conventions

The term "patient" includes both human and non-human mammals.

The term "effective amount" means an amount of a compound according to the invention which, in the context of which it is administered or used, is sufficient to achieve the desired effect or result. Depending on the context, the term effective amount may include or be synonymous with a pharmaceutically effective amount or a diagnostically effective amount.

The terms "pharmaceutically effective amount" or "therapeutically effective amount" means an amount of a compound according to the invention which, when administered to a patient in need thereof, is sufficient to effect treatment for disease-states, conditions, or disorders for which the compounds have utility. Such an amount would be sufficient to elicit the biological or medical response of a tissue, system, or patient that is sought by a researcher or clinician. The amount of a compound of according to the invention which constitutes a therapeutically effective amount will vary depending on such factors as the compound and its biological activity, the composition used for administration, the time of administration, the route of administration, the rate of excretion of the compound, the duration of treatment, the type of disease-state or disorder being treated and its severity, drugs used in combination with or coincidentally with the compounds of the invention, and the age, body weight, general health, sex, and diet of the patient. Such a therapeutically effective amount can be determined routinely by one of ordinary skill in the art having regard to their own knowledge, the prior art, and this disclosure.

The term "diagnostically effective amount" means an amount of a compound according to the invention which, when used in a diagnostic method, apparatus, or assay, is sufficient to achieve the desired diagnostic effect or the desired biological activity necessary for the diagnostic method, apparatus, or assay. Such an amount would be sufficient to elicit the biological or medical response in a diagnostic method, apparatus, or assay, which may include a biological or medical response in a patient or in a in vitro or in vivo tissue or system, that is sought by a researcher or clinician. The amount of a compound according to the invention which constitutes a diagnostically effective amount will vary depending on such factors as the compound and its biological activity, the diagnostic method, apparatus, or assay used, the composition used for administration, the time of administration, the route of administration, the rate of excretion of the compound, the duration of administration, drugs and other compounds used in combination with or coincidentally with the compounds of the invention, and, if a patient is the subject of the diagnostic administration, the age, body weight, general health, sex, and diet of the patient. Such a diagnostically effective amount can be determined routinely by one of ordinary skill in the art having regard to their own knowledge, the prior art, and this disclosure.

The term "modulate" means the ability of a compound to alter the function of the glucocorticoid receptor by, for example, binding to and stimulating or inhibiting the glucocorticoid receptor functional responses.

The term "modulator" in the context of describing compounds according to the invention means a compound that modulates the glucocorticoid receptor function. As such, modulators include, but are not limited to, agonists, partial agonists, antagonists, and partial antagonists.

The term "agonist" in the context of describing compounds according to the invention means a compound that, when bound to the glucocorticoid receptor, enhances or increases the glucocorticoid receptor function. As such, agonists include partial agonists and full agonists.

The term "full agonist" in the context of describing compounds according to the invention means a compound that evokes the maximal stimulatory response from the glucocorticoid receptor, even when there are spare (unoccupied) glucocorticoid receptors present.

The term "partial agonist" in the context of describing compounds according to the invention means a compound that is unable to evoke the maximal stimulatory response from the glucocorticoid receptor, even at concentrations sufficient to saturate the glucocorticoid receptors present.

The term "antagonist" in the context of describing compounds according to the invention means a compound that directly or indirectly inhibits or suppresses the glucocorticoid receptor function. As such, antagonists include partial antagonists and full antagonists.

The term "full antagonist" in the context of describing compounds according to the invention means a compound that evokes the maximal inhibitory response from the glucocorticoid receptor, even when there are spare (unoccupied) glucocorticoid receptors present.

The term "partial antagonist" in the context of describing compounds according to the invention means a compound that is unable to evoke the maximal inhibitory response from the

glucocorticoid receptor, even at concentrations sufficient to saturate the glucocorticoid receptors present.

The terms "treating" or "treatment" mean the treatment of a disease-state in a patient, and include:

(i) preventing the disease-state from occurring in a patient, in particular, when such patient is genetically or otherwise predisposed to the disease-state but has not yet been diagnosed as having it;

(ii) inhibiting or ameliorating the disease-state in a patient, i.e., arresting or slowing its development; or

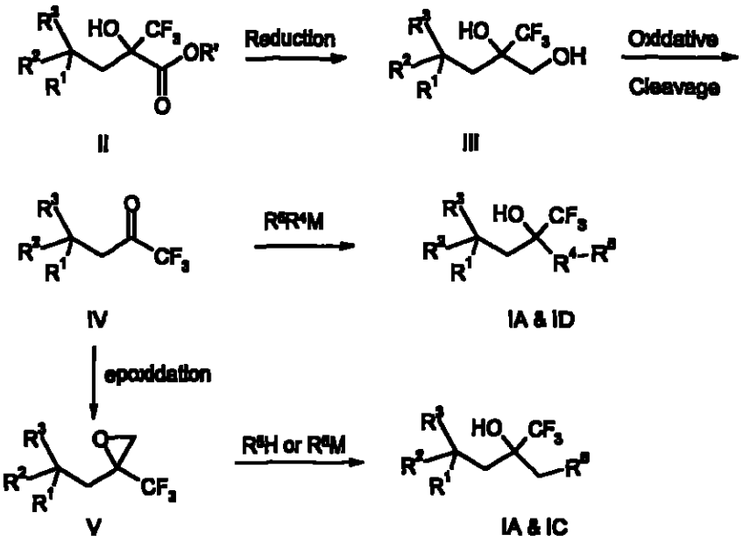
(iii) relieving the disease-state in a patient, i.e., causing regression or cure of the disease-state.

General Synthetic Methods for Making Compounds of Formula (IA), Formula (IB), Formula (IC), and Formula (ID)

The invention also provides processes for making compounds of Formula (IA), Formula (IB), Formula (IC), and Formula (ID). In all schemes, unless specified otherwise, R^1 to R^5 in the formulas below shall have the meaning of R^1 to R^5 in the Formula (I) of the invention described hereinabove; and where appropriate, R^1 to R^6 in the formulas below shall have the meaning of R^1 to R^6 in the Formula (IB), Formula (IC), or Formula (ID) of the invention described hereinabove. Intermediates used in the preparation of compounds of the invention are either commercially available or readily prepared by methods known to those skilled in the art.

Optimum reaction conditions and reaction times may vary depending on the particular reactants used. Unless otherwise specified, solvents, temperatures, pressures, and other reaction conditions may be readily selected by one of ordinary skill in the art. Specific procedures are provided in the Experimental Examples section. Typically, reaction progress may be monitored by thin layer chromatography (TLC), if desired, and intermediates and products may be purified by chromatography on silica gel and/or by recrystallization.

Compounds of Formula (IA), Formula (IC), and Formula (ID) may be prepared by the method outlined in Scheme I.



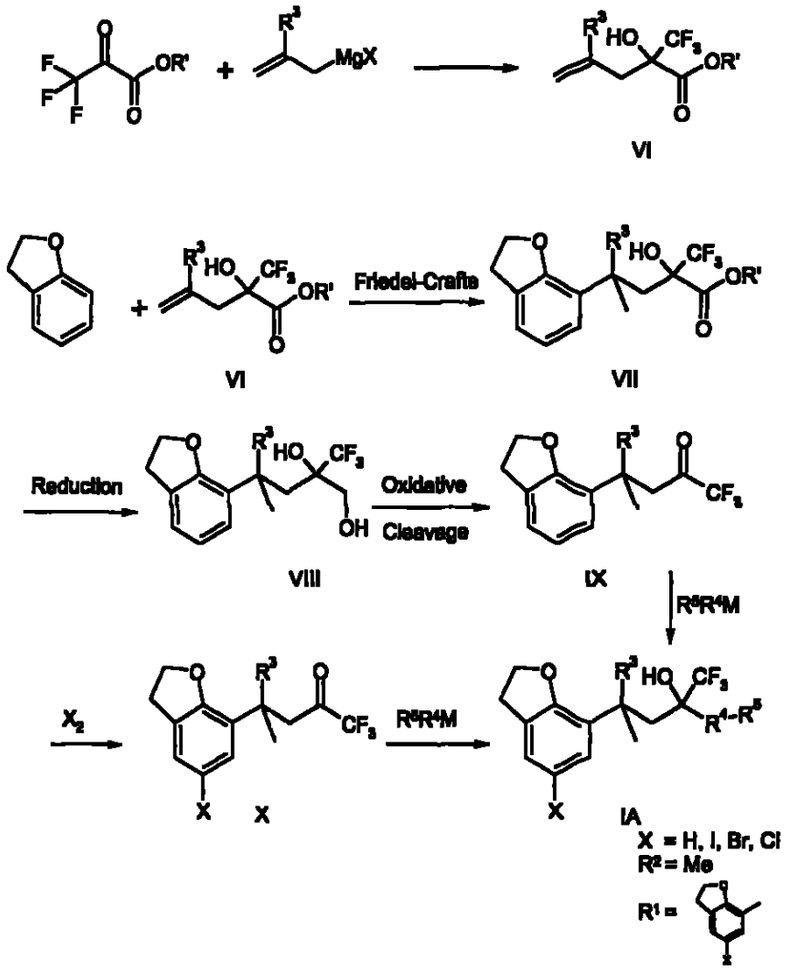
Scheme I

As illustrated in Scheme I, an ester intermediate of Formula (II), where R' is Me or Et, is reduced with a suitable reducing agent, such as lithium aluminum hydride, in a suitable solvent, such as THF or diethyl ether, to produce the 1,2-diol of Formula (III). Oxidative cleavage of 1,2-diols is well-known in the art and may be achieved with periodic acid or lead tetraacetate, for example, in a suitable solvent, such as methanol, to provide ketone (IV). Reaction of ketone (IV) with a suitable organometallic reagent R^5R^4M, such as a Grignard reagent (M is MgBr or MgCl) or an organolithium reagent (M is Li), in a suitable solvent such as THF or diethyl ether provides the desired compound of Formula (I). Such organolithium reagents or Grignard reagents are well-known in the art, for example, Grignard reagents are easily prepared by reacting the corresponding halides (R^5R^4X, where X is Br or Cl) with magnesium metal in a suitable solvent, such as diethyl ether or THF, under anhydrous conditions. The aforementioned organolithium reagents are readily prepared by reacting the R^5R^4H, where R^5 is heteroaryl, with alkyl lithium reagents such lithium diisopropylamide (LDA) in a suitable solvent, such as diethyl ether or THF, under anhydrous conditions.

Alternatively, ketone (IV) is reacted with a suitable reagent to provide epoxide (V). Reaction of epoxide (V) with the desired R^5H or R^5M (M is Na or Li), provides the desired product of Formula (I). The reaction may take place by heating R^5H and epoxide (V) in a suitable solvent such as DMF, heating R^5H and epoxide (V) together in a solvent in the presence of a suitable

base such as sodium ethoxide in ethanol, or by reacting R^5M and epoxide (V) in suitable solvents such as DMF or DMSO. Such organometallic reagents could be generated by treating R^5H with NaH, LiH, or other reagents or methods known by one of ordinary skill in the art, in suitable solvents such as THF, DMF, or DMSO.

Scheme II outlines another approach that may be used to obtain compounds of Formula (IA).



Scheme II

In Scheme II, ethyl trifluoropyruvate is reacted with a substituted allyl Grignard to provide olefin (VI). Reaction of olefin (VI) with 2,3-dihydrobenzofuran in the presence of a suitable Lewis acid such as $AlCl_3$, well-known in the art as the "Friedel-Crafts alkylation", gives ester

197.
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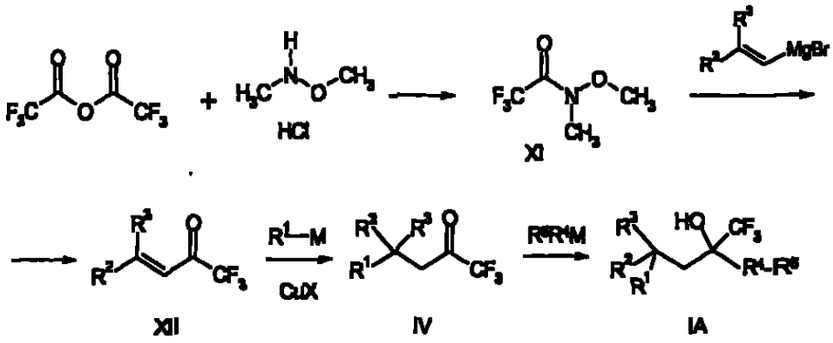
(VII). Reduction of ester (VII) with a suitable reducing agent such as lithium aluminum hydride (LAH) in a solvent such as THF provides 1,2-diol (VIII). Oxidative cleavage of 1,2-diol (VIII) may be achieved with sodium periodate or lead tetraacetate, for instance, in a suitable solvent, such as methanol, to provide ketone (IX). Reaction of ketone (IX) with a suitable halogen (Cl_2, Br_2, or I_2) or halogenating reagents such as *N*-bromosuccinimide (NBS), affords ketone (X). Treatment of ketones (IX) or (X) with a suitable organometallic reagent R^5R^4M, where M is Li or MgX and X is Cl, Br, or I, provides the desired compound of Formula (I), where R^1 is an optionally substituted 2,3-dihydrobenzofuranyl group and R^1 is a methyl group.

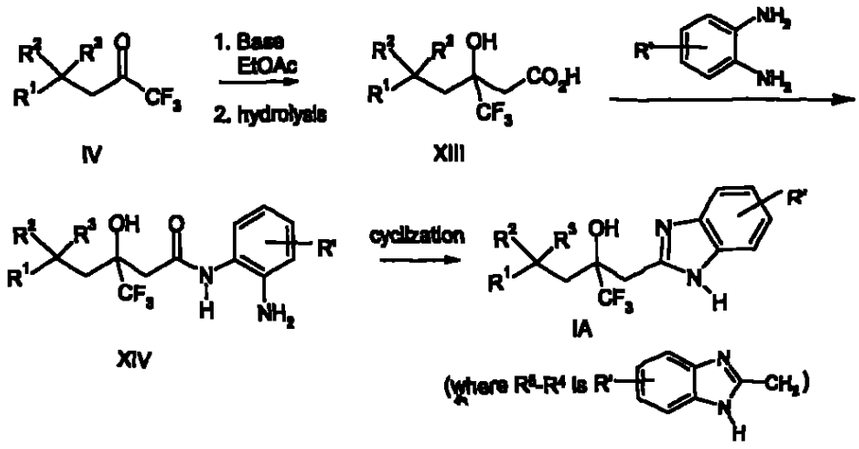
Compounds of Formula (IA) may also be prepared by the method outlined in Scheme III.



Scheme III

In this approach, trifluoroacetic anhydride and *N,O*-dimethylhydroxylamine hydrochloride are coupled under basic conditions to afford trifluoroacetamide (XI) (Weinreb amide). Weinreb amide (XI) is reacted with a vinyl magnesium bromide bearing R^2 and R^3 to afford trifluoromethylenone intermediate (XII). Trifluoromethylenone intermediate (XII) is treated with an organocopper reagent, derived from a Grignard or organolithium reagent by treating with a copper salt, to afford 1,4-addition product (IV). This trifluoroketone intermediate (IV) is reacted with an organometallic reagent R^4R^5M (as described in Scheme I) to afford the desired compound of Formula (IA).

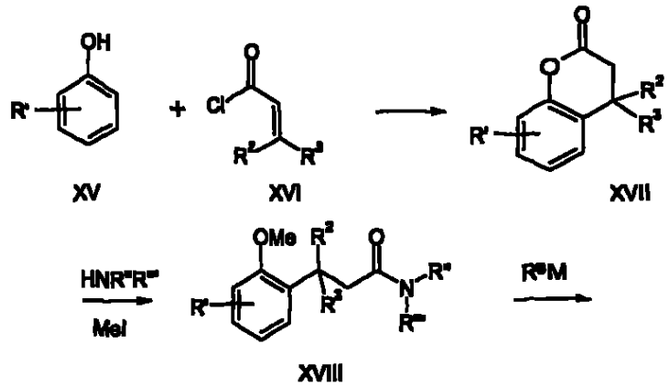
Compounds of Formula (IA) where R^4-R^5 is an optionally substituted benzimidazol-2-ylmethyl group may be prepared by the procedure outlined in Scheme IV.

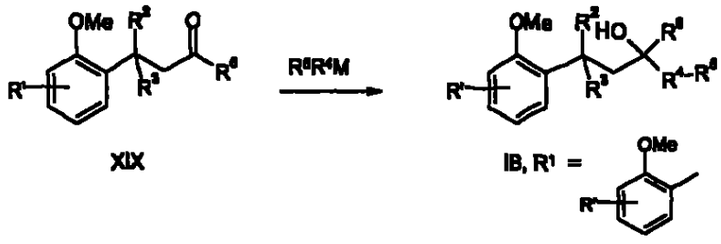


Scheme IV

As illustrated in Scheme IV, trifluoromethylketone (IV) is reacted with ethyl acetate in the presence of a strong base such as lithium diisopropylamide (LDA) in a suitable solvent such as THF. The intermediate ester is hydrolyzed, for example, by treatment with aqueous base, to provide carboxylic acid intermediate (XIII). This carboxylic acid intermediate (XIII) is then coupled with an optionally substituted phenylenediamine under standard coupling conditions known in the art, for example, by treatment with 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (EDC) in the presence of 1-hydroxybenzotriazole in a suitable solvent such as *N,N*-dimethylformamide (DMF), to provide compound (XIV). Ring closure by methods known in the art, for example, acid catalyzed ring closure by treatment with polyphosphoric acid, provides the desired compound of Formula (IA).

Compounds of Formula (IB) may be prepared by the procedure illustrated in Scheme V.

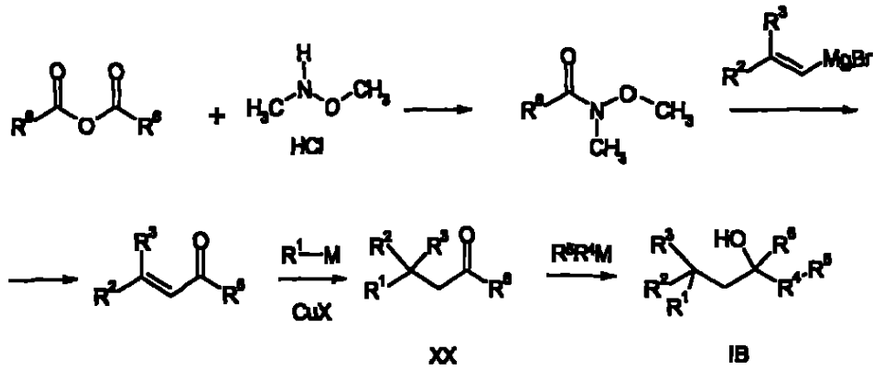




Scheme V

In Scheme V, substituted phenol (XV) is reacted with an acryloyl chloride bearing R^2 and R^3 (XVI) in the presence of a suitable base, such as triethylamine, to provide an intermediate ester which is cyclized by treatment with a Lewis acid, such as aluminum trichloride, in a suitable solvent, such as carbon disulfide, to provide lactone (XVII). Lactone (XVII) is treated with a suitable amine $HNR''R'''$, such as morpholine, such that in the resulting amide (XVIII), $-NR''R'''$ will function as a leaving group in the subsequent reactions. The intermediate phenol that forms is protected, for example, by reaction with methyl iodide in the presence of a suitable base such as potassium hydroxide to form protected phenol (XVIII), in this case having a methoxy group. Amide (XVIII) is then reacted with an organometallic reagent (R^6M), such as a Grignard reagent (M is MgBr or MgCl) or an organolithium reagent (M is Li), in a suitable solvent, such as THF or diethyl ether, to provide the ketone (XIX). Reaction of the ketone (XIX) with R^5R^4M as described in the last step in Scheme I provides the desired compound of Formula (IB) where R^1 is an optionally substituted methoxyphenyl group.

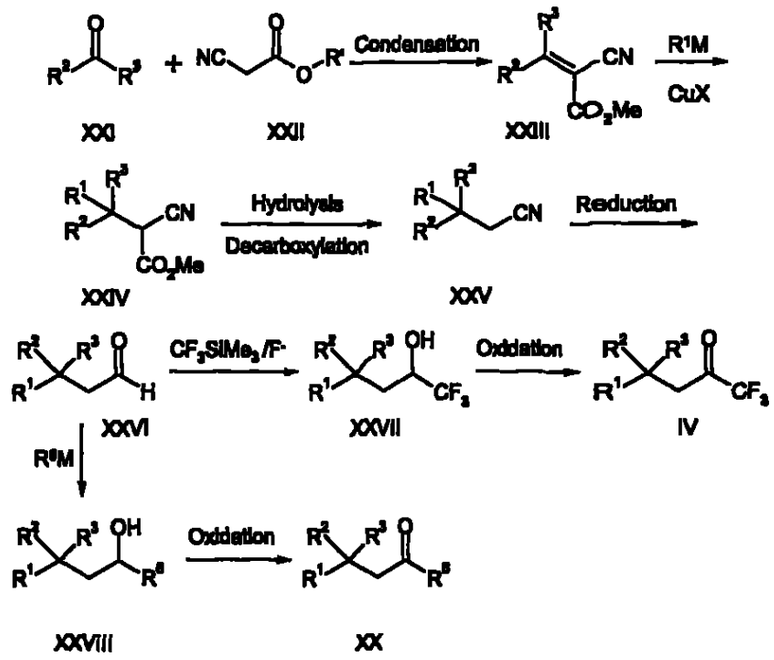
In a more general procedure, suitable for a variety of R^1, one may use a method analogous to that described in Scheme III. As illustrated in Scheme VI, using a Weinreb amide bearing R^6 one may employ the method described in Scheme III to prepare the desired ketone (XX) and compound of Formula (IB).



XX IB

Scheme VI

An alternative method to prepare intermediate (IV) in Schemes I, III, and IV, as well as ketone (XX) in Scheme VI, is illustrated in Scheme VII.



XXI XXII XXIII XXIV XXV XXVI XXVII IV XXVIII XX

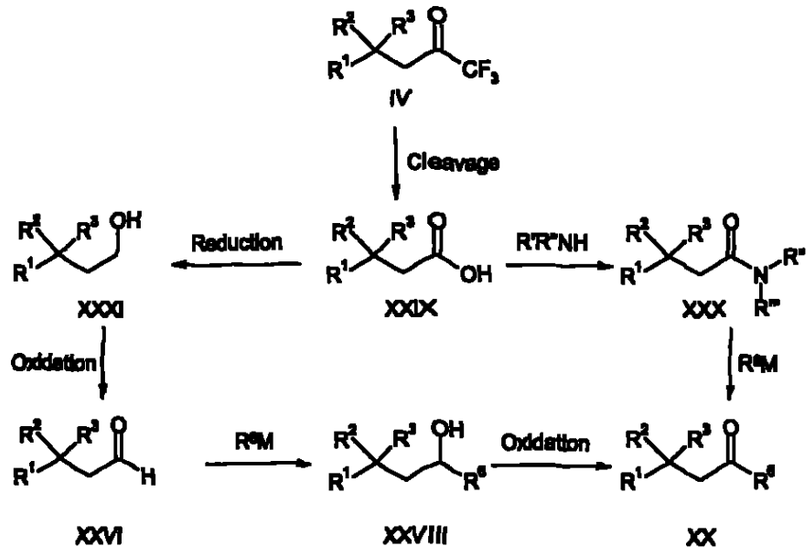
Scheme VII

As illustrated in Scheme VII, a ketone bearing R^1 and R^2 (XXI) is condensed with cyanoacetic acid ester (XXII), where R' is Me or Et, in a reaction known in the art as a Knoevenagel condensation to provide olefin (XXIII). Reaction of olefin (XXIII) with a suitable organometallic reagent such as R^1M, where M is MgBr, MgCl, or Li, in the presence of a

copper salt, such as CuI, affords ester (XXIV). Hydrolysis of ester (XXIV) followed by the concomitant decarboxylation of resulting acid in the presence of suitable reagent, such as sodium chloride, and in a suitable solvent mixture, such as DMSO and water, gives the corresponding nitrile (XXV). Reduction of nitrile (XXV), for example, by treatment with a suitable reducing agent, such as diisobutylaluminum hydride (DIBAL), in a suitable solvent such as dichloromethane, furnishes aldehyde (XXVI). Treatment of aldehyde (XXVI) with trimethyl(trifluoromethyl)silane in the presence of a suitable fluoride source, such as tetrabutylammonium fluoride, provides alcohol (XXVII). Oxidation of alcohol (XXVII) by methods known in the art, such as treatment with the Dess-Martin periodinane reagent, in a suitable solvent, such as dichloromethane, gives ketone (IV).

Alternatively, aldehyde (XXVI) is treated with a suitable organometallic reagent R^6M, such as a Grignard reagent (M is MgBr or MgCl) or an organolithium reagent (M is Li), in a suitable solvent such as THF or diethyl ether to provide alcohol (XXVIII). Subsequent oxidation of alcohol (XXVIII) by a method well-known in the art provides ketone (XX).

Additionally, ketone (XX) in Scheme VII may be prepared from ketone (IV) as depicted in Scheme VIII.

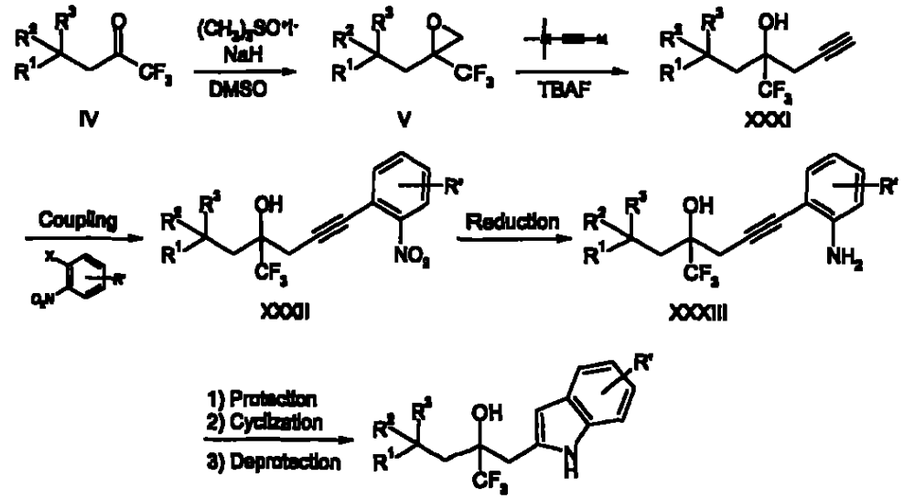


Scheme VIII

In Scheme VIII, ketone (IV) is cleaved in the presence of a suitable base, such as NaOH, and in a suitable solvent mixture, such as a mixture of water and ethanol, to provide acid (XXIX). Acid (XXIX) is treated with a suitable amine HNR"R"', such as morpholine, such that -NR"R"' will function as a leaving group in the subsequent reaction. The resulting amide (XXX), is then reacted with an organometallic reagent (R^6M), such as a Grignard reagent (M is MgBr or MgCl) or an organolithium reagent (M is Li), in a suitable solvent, such as THF or diethyl ether, to provide ketone (XX). Alternatively, acid (XXIX) is treated with a suitable reducing agent such as lithium aluminum hydride (LAH) in a solvent such as THF to give alcohol (XXXI). Oxidation of alcohol (XXXI) according to methods known by one of ordinary skills in the art, such as treatment with the Dess-Martin periodinane reagent, in a suitable solvent, such as dichloromethane, gives aldehyde (XXVI).

As previouly illustrated in Scheme VII, reaction of aldehyde (XXVI) with a suitable organometallic reagent R^6M (M is MgBr, MgCl, or Li), in a solvent such as THF or diethyl ether affords alcohol (XXVIII), which is oxidized to alcohol (XXVIII) by a method, such as Swern oxidation or treatment with the Dess-Martin periodinane, provides ketone (XX).

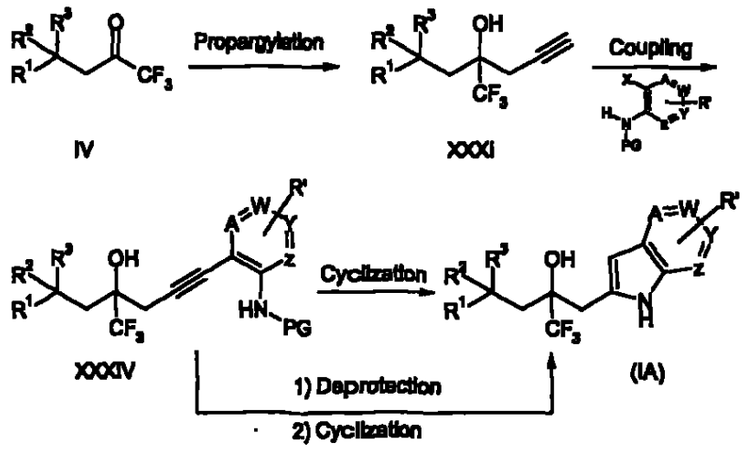
Compounds of Formula (IA) where R^4-R^5 is an optionally substituted indol-2-ylmethyl group may be synthesized by the procedure outlined in Scheme IX.



Scheme IX

As depicted in Scheme IX, reaction of ketone (IV) with sulfur ylide in a suitable solvent, such as DMSO, provides epoxide (V). Opening of epoxide (V) with a suitable acetylide reagent, such as lithium trimethylsilylacetylide (M is Li) in a suitable solvent, such as DMSO, followed by deprotection with a suitable fluoride source in a suitable solvent, affords alkyne (XXXI). Treatment of alkyne (XXXI) with a suitable coupling partner, such as optionally substituted aniline or nitrobenzene (X is OTf, I, or Br) in the presence of suitable catalysts, base and solvent (e.g., dichlorobis(triphenylphosphine)palladium (II), CuI, triethylamine, and DMF) provides alkyne (XXXII). Reduction of intermediate (XXXII) with a suitable metal reducing agent, such as iron, in a suitable solvent, such as acetic acid, affords aniline (XXXIII). Protection of aniline (XXXIII) with a suitable protecting group, such as trifluoroacetyl is well-known in the art and may be achieved by treatment with trifluoroacetic anhydride in a suitable solvent, such as dichloromethane. The resulting intermediate is cyclized with a suitable base, such as 1,1,3,3-tetramethyl guanidine, in a suitable solvent, such as methanol, provides the trifluoroacetyl-protected indole, which undergoes an *in situ* deprotection of the acyl group to afford compound of Formula (IA).

Additionally, compounds of Formula (IA) where R^4-R^5 is an optionally substituted azaindol-2-ylmethyl group may be prepared by the procedure illustrated in Scheme X.



Scheme X

Ketone (IV) is treated with a suitable propargylating reagent, such as propargyl aluminum sesquibromide, in a suitable solvent, such as THF, to furnish alkyne (XXXI). Reaction of homopropargyl alcohol (XXXI) with a suitable coupling partner, such as optionally substituted

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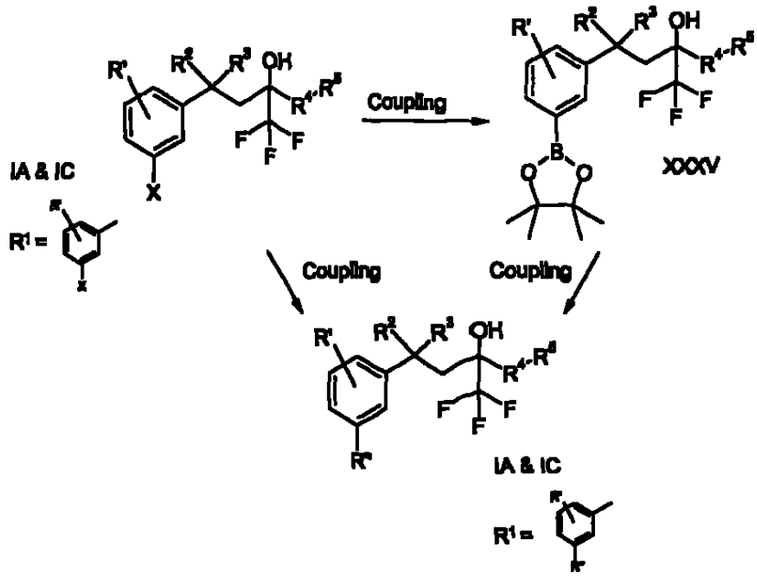
and protected amino pyridines, optionally substituted and protected amino pyrimidines or optionally substituted and protected amino pyridazines, wherein one or two atoms selected from A, W, Y, and Z are nitrogens and the remaining atoms are carbons, X is I or Br and PG is H or BOC (*tert*-butoxycarboyl), in the presence of suitable catalysts, base and solvent (e.g., dichlorobis(triphenylphosphine)palladium (II), CuI, triethylamine, and DMF) provides alkyne (XXXIV). Alkyne (XXXIV), where PG is H, is converted to the corresponding optionally protected azaindole or diazaindole of Formula (IA) by treatment with the suitable base such as potassium *tert*-butoxide, in a suitable solvent, such as *N*-methyl pyrrolidinone (NMP). In addition, alkyne (XXXIV) containing a *N*-BOC group is cyclized with a suitable base, such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), in a suitable solvent mixture, such as a mixture of water and methanol, to give the desired product of Formula (IA). Alternatively, the *N*-BOC protecting group of alkyne (XXXIV) may be removed by treatment with a suitable acid, such as HCl, in a suitable solvent, such as ethyl acetate, to provide the corresponding amine salt, which is cyclized in the presence of potassium *tert*-butoxide in NMP to provide the compound of Formula (IA).

Moreover, compounds of Formula (I) where R^1 is an optionally substituted aryl group may be converted by the sequence illustrated in Scheme XI to compounds of Formula (I) where R^1 is further optionally functionalized.



Scheme XI

As outlined in Scheme XI, compounds of Formula (I) where R^1 is an optionally substituted aryl group in which one of the substituents is a suitable coupling group, such as Cl, Br, I, or OTf, may be treated with a suitable coupling partner, such as a boronic acid or a boronic ester, in a suitable solvent or a mixture of solvents, such as a mixture of DME, methanol, and DMF, in the presence of a suitable catalyst, such as tetrakis(triphenylphosphine)palladium (0), with an appropriate base, such as potassium carbonate, at a suitable temperature and under an appropriate atmospheric environment, such as argon, to give compounds of Formula (I) where R^1 is further optionally functionalized. Alternatively, compounds of Formula (I) where R^1 is an optionally substituted aryl group containing a suitable group, such as Cl, Br, I, or OTf, is converted to its corresponding boronic ester (XXXV) by reacting with an appropriate coupling partner, such as bis(pinacolato)diboron, under a suitable condition, such as heating at 100°C in DME with potassium carbonate and in the presence of [1,1'-bis(diphenylphosphino)ferrocene]dichloropalladium (II). Subsequently, the boronic ester of formula (XXXV) may be converted to compounds of Formula (I) where R^1 is optionally functionalized by treating with a suitable aryl halide, and under a suitable, previously indicated, coupling condition. The choice between the two described methods depends on the commercial or synthetic availability of the coupling partner, which is up to the discretion of one skilled in the art.

As illustrated in Scheme XII, compounds of Formula (IA) where R^4R^5 is a cyano-substituted azaindol-2-ylmethyl or a cyano-substituted indol-2-ylmethyl may be converted to a compound of Formula (IA) where R^4R^5 is optionally functionalized.

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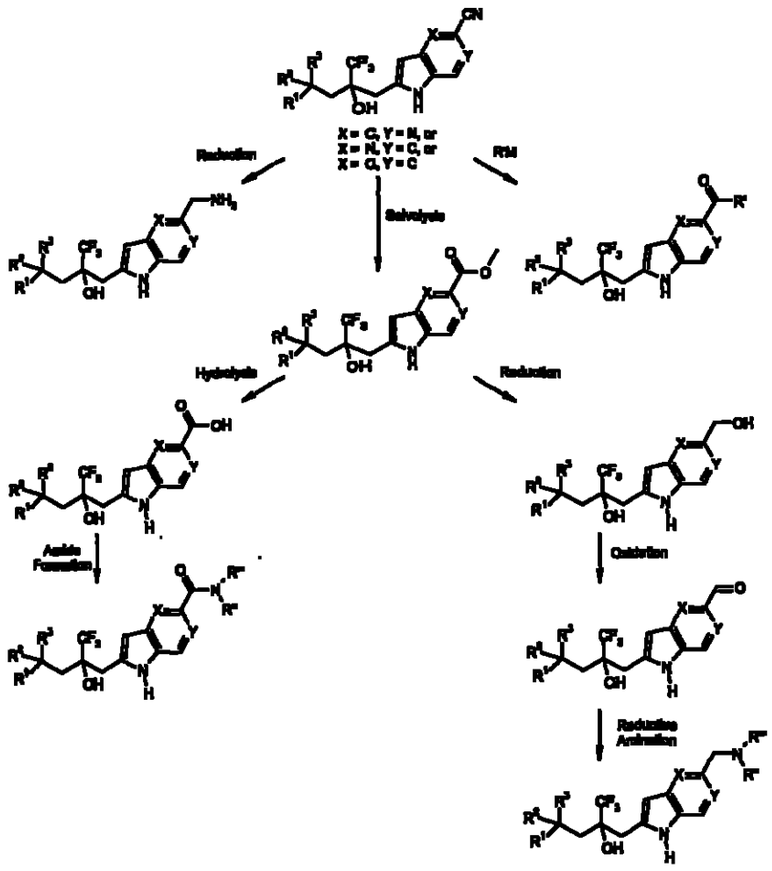

Scheme XII

Compounds of Formula (IA) where R^4R^5 is a cyano-substituted azaindol-2-ylmethyl (X is a nitrogen and Y is a carbon, or X is a carbon and Y is a nitrogen) or a cyano-substituted indol-2-ylmethyl (X and Y are carbons), may be converted to the corresponding ketone by treatment with a suitable organometallic reagent such as R'M, where M is MgI, MgBr, MgCl, or Li, and R' is alkyl, cycloalkyl, aryl, heteroaryl, or heterocyclyl. Reduction of the cyano group with a suitable reducing agent, such as borane•methyl sulfide complex, in a suitable solvent such as THF, gives a compound of Formula (IA) bearing a 1° amine moiety. Moreover, the compound of Formula (IA) bearing a cyano group may be treated with an alcohol, such as methanol, in the presence of an acid catalyst, such as HCl, to afford the corresponding ester. The resulting ester may be hydrolyzed by treatment with a suitable base, such as lithium hydroxide, in a suitable mixture of solvents, such as a mixture of THF, water, and methanol, to provide a compound of

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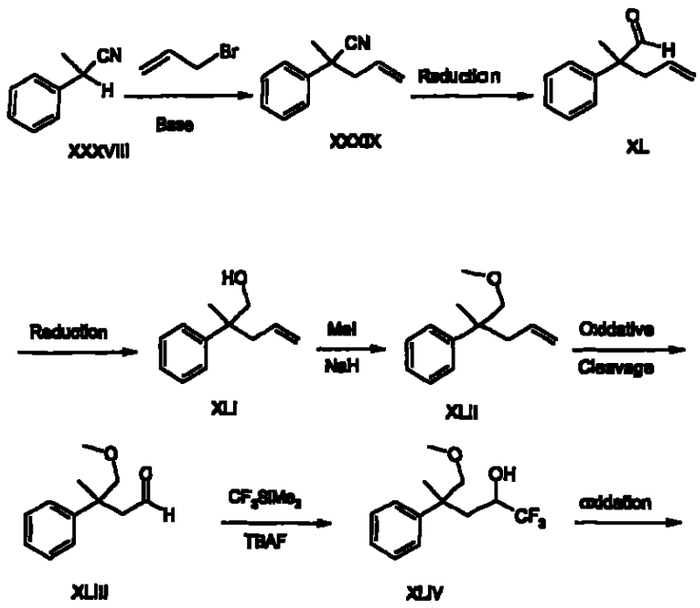
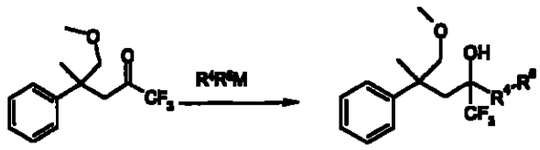
Formula (IA) containing a carboxylic acid moiety. The resulting carboxylic acid of Formula (IA) can be converted to an amide using standard peptide coupling conditions known to one skilled in the art. This transformation may be affected by treatment with a suitable amine HNR"R"' and a suitable activating reagent, such as 1,3-dicyclohexylcarbodiimide (DCC), in the presence of a suitable base, such as *N,N*-diisopropylethyl amine, in an appropriate solvent, such as DMF or acetonitrile. Alternatively, the compound of Formula (IA) bearing an ester group may be reduced by treatment with a suitable reducing agent, such as lithium aluminum hydride (LAH), in a suitable solvent such as THF, to furnish the corresponding alcohol. Oxidation of the resulting alcohol with a suitable oxidizing agent, such as manganese (IV) oxide, in a suitable solvent, such as acetone, gives the desired compound of Formula (IA) containing an aldehyde group. Such aldehyde may be converted to the corresponding amine by a method well-known in the art as reductive amination. This functional group inter conversion may be performed by reaction of an aldehyde with a suitable amine HNR"R"' in the presence of a suitable reducing agent, such as sodium triacetoxyborohydride, and an appropriate acid catalyst, such as acetic acid, in a suitable solvent, such as 1,2-dichloroethane.

Compounds of Formula (ID) may be prepared according to the procedure shown in Scheme XIII.





XLV (ID)

Scheme XIII

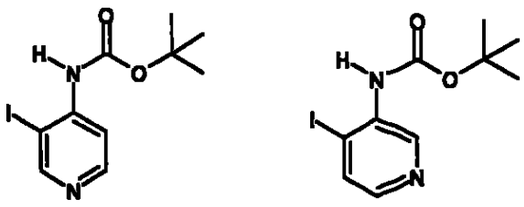
In Scheme XIII, nitrile (XXXVIII) is treated with allyl bromide in the presence of a suitable base, such as sodium bis(trimethylsilyl)amide (NaHMDS), in a suitable solvent, such as DMSO, to provide the corresponding nitrile (XXXIX). Reduction of the nitrile (XXXIX) with a suitable reducing agent, such as DIBAL, in an appropriate solvent, such as dichloromethane, affords aldehyde (XL). Aldehyde (XL) is further reduced by reacting with a suitable reducing agent, such as lithium aluminum hydride (LAH), in a suitable solvent, such as THF, to give alcohol (XLI). Reaction of alcohol (XLI) with methyl iodide, in the presence of a suitable base, such as sodium hydride (NaH), in an appropriate solvent such as DMF, provides ether (XLII). Ether (XLII) is converted to aldehyde (XLIII) by oxidative cleavage methods well-known in the art, such as treatment with ozone. Reaction of aldehyde (XLIII) with a suitable nucleophilic trifluoromethylating reagent, such as trimethyl(trifluoromethyl)silane, in the presence of a fluoride source, such as tetrabutylammonium fluoride (TBAF), provides alcohol (XLIV). Subsequent oxidation of alcohol (XLIV) with a suitable oxidizing reagent, such as Dess-Martin periodinane reagent, provides trifluoromethyl ketone (XLV). Reaction of ketone (XLV) with a suitable organometallic reagent R^5R^4M, where M is Li or MgX, and X is Cl, Br, or I, in a suitable solvent, such as THF, furnishes the compound of Formula (ID).

In order that this invention may be more fully understood, the following Examples are set forth. These Examples are for the purpose of illustrating embodiments of this invention, and are not to be construed as limiting the scope of the invention in any way since, as recognized by one skilled in the art, particular reagents or conditions could be modified as needed for individual compounds. Thus, while the Examples illustrate the synthesis of certain compounds of the invention or intermediates that may be used to synthesize compounds according to the invention, all of the compounds disclosed herein may be made by one or more methods disclosed herein, as one of skill in the art would appreciate. Starting materials used are either

commercially available or easily prepared from commercially available materials by those skilled in the art.

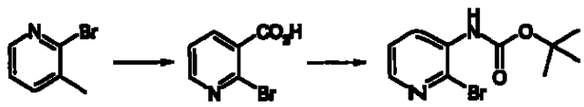
Experimental Examples

Example 1: Syntheses of (3-Iodopyridin-4-yl)carbamic acid *tert*-butyl ester and (4-Iodopyridin-3-yl)carbamic acid *tert*-butyl ester



The title products were prepared according to the procedure described by T.A. Kelly *et al.*, J. Org. Chem., 1995, 60, p. 1875.

Example 2: Synthesis of (2-Bromopyridin-3-yl)carbamic acid *tert*-butyl ester



2-bromo-3-methylpyridine (25.0 mL, 213 mmol) was added to a solution of potassium permanganate (87.7 g, 555 mmol) in 800 mL of water and the mixture was stirred under reflux. After 5 hours, 600 mL of water was distilled off and the remaining suspension was filtered. The residue was washed with two 50 mL portions of hot water and the combined filtrates were acidified with concentrated HCl. The white precipitate was filtered and dried in a vacuum oven to give 26.8 g of 2-bromonicotinic acid (62% yield).

Diphenylphosphorylazide was added to a solution of 2-bromonicotinic acid (15.0 g, 74.0 mmol) and triethylamine (11.4 mL, 81.4 mmol) in 140 mL of anhydrous *tert*-butanol. The reaction mixture was stirred under reflux for 2 hours, cooled to room temperature, and concentrated *in vacuo*. The residue was dissolved in 150 mL of ethyl acetate and washed with three 50 mL portions of water, three 50 mL portions of saturated aqueous sodium bicarbonate, and with two 50 mL portions of brine. The organic layer was dried over magnesium sulfate ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue crystallized upon standing to give 15.3 g of the title product (76% yield).

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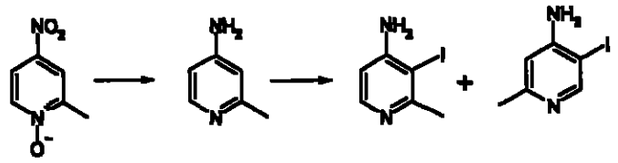
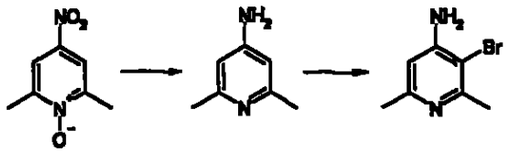
Example 3: Synthesis of 4-Amino-3-iodo-2-methylpyridine and 4-Amino-3-iodo-6-methylpyridine



A solution of 2-methyl-4-nitropyridine-*N*-oxide (3.80 g, 24.6 mmol) in 100 mL of acetic acid was slowly heated with iron powder (6.89 g, 124 mmol) in a large flask (caution: the reaction becomes very exothermic upon turning brown). The resulting slurry was heated for 2 hours at 80°C. Excess acetic acid was removed *in vacuo*, the residue was taken up in 20% aqueous sodium hydroxide solution, and 100 mL of chloroform ($CHCl_3$) was added and the mixture filtered through CELITE® filter aid. The aqueous phase was extracted with two 200 mL portions of chloroform. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude product (2.2 g, 83% yield) was used without further purification.

A solution of KI (1.96 g, 11.9 mmol) and I_2 (1.87 g, 7.36 mmol) in 10 mL of water was added to a refluxing solution of the 2-methylpyridin-4-ylamine (1.00 g, 9.25 mmol) and sodium carbonate (683 mg, 6.44 mmol) in 5 mL of water. The mixture was heated at reflux for 2 hours, cooled to room temperature, and treated with 20 mL of ethyl acetate (EtOAc). Phases were separated and the aqueous layer was extracted with three 20 mL portions of ethyl acetate. The combined organic layers were washed with a saturated aqueous sodium thiosulfate ($Na_2S_2O_3$) solution, dried over magnesium sulfate, and concentrated *in vacuo*. Flash chromatography (30% ethyl acetate in hexanes to 100% ethyl acetate, gradient) of the resulting residue yielded 4-amino-3-iodo-6-methylpyridine (first eluting: 226 mg, 11% yield) and 4-amino-3-iodo-2-methylpyridine (second eluting: 116 mg; 5% yield).

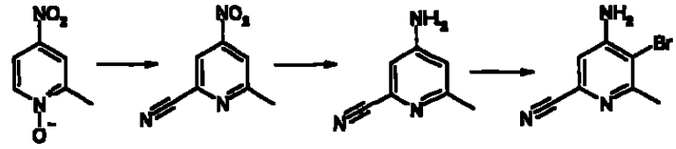
Example 4: Synthesis of 4-Amino-3-bromo-2,6-dimethylpyridine



A solution of 4-nitro-2,6-dimethylpyridine-*N*-oxide (11.0 g, 65.4 mmol) in 50 mL of acetic acid was treated with iron powder (21.8 g, 390 mmol) in small portions while the mixture was rapidly stirred and gradually heated to 50°C (caution: the reaction becomes very exothermic at this temperature). After the exotherm ceased, the mixture was heated for an additional hour at 80°C. The resulting solidified mixture was treated with 50 mL of water and the suspension was filtered through CELITE® filter aid. The filtrate was treated with *ca.* 200 mL of 6 N sodium hydroxide solution until the pH of the solution was basic (>12). The resulting green suspension was extracted with three 300 mL portions of chloroform. The extracts were combined, dried over magnesium sulfate, filtered, and concentrated *in vacuo* to give yellowish crystals (5.70 g, 71% yield).

A solution of 2,6-dimethylpyridin-4-ylamine (2.00 g, 16.4 mmol) in 5 mL of acetic acid was treated dropwise with a solution of bromine (0.84 mL, 16.3 mmol) in 2 mL of acetic acid at room temperature in a water bath over a period of 10 minutes. After 1 hour, the resulting slurry was treated with 40 mL of 20% sodium hydroxide solution and extracted with three 100 mL portions of dichloromethane (CH_2Cl_2). The combined extracts were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The resulting solid (starting material-desired product-dibromo byproduct (1:3:1)) was dissolved in 100 mL of hot hexanes and hot filtered to remove the insoluble starting material. The filtrate was allowed to cool to room temperature, which gave the title product as fine white needles (1.30 g, 40% yield).

Example 5: Synthesis of 4-Amino-3-bromo-6-cyano-2-methylpyridine



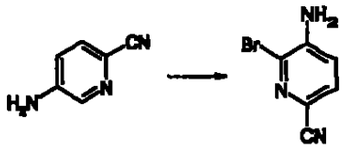
4-Nitropicoline-*N*-oxide (10.0 g, 64.9 mmol) and dimethylsulfate (6.39 mL, 64.5 mmol) were heated at 70°C for 6 hours under a nitrogen gas (N_2) atmosphere. The dark brown mixture, which solidified upon cooling to room temperature was dissolved in 20 mL of water, cooled to

-10°C while vigorously stirring, and treated dropwise with a solution of KCN (5.04 g, 77.4 mmol) in 20 mL of water. The mixture was warmed to room temperature overnight. The resulting black heterogeneous mixture was dissolved in 50 mL of ethyl acetate and 50 mL of water. The phases were separated and the aqueous layer was extracted with two 50 mL portions of ethyl acetate. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Flash chromatography (20% to 50% ethyl acetate in hexanes, gradient) afforded the product as a brown solid (2.80 g, 27% yield).

2-Cyano-6-methyl-4-nitropyridine (1.9 g, 11.6 mmol) in a mixture of 50 mL of ethanol and 15 mL of saturated aqueous ammonium chloride (NH_4Cl) solution was heated with indium powder (7.00 g, 60.9 mmol) to 60°C for 3 days. 20 mL of water was then added, and the slurry was filtered through CELITE® filter aid and the pad was washed with methanol. The filtrate was concentrated *in vacuo* to remove volatile organics and extracted with three 20 mL portions of dichloromethane. The combined extracts were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Chromatography on SiO_2 (30% ethyl acetate in hexanes to 100% ethyl acetate, gradient) gave the product as a tan solid (580 mg, 27% yield).

4-Amino-6-methylpyridine-2-carbonitrile was converted to the title product in 57% yield according to the procedure described for the preparation of 4-amino-3-bromo-2,6-dimethylpyridine.

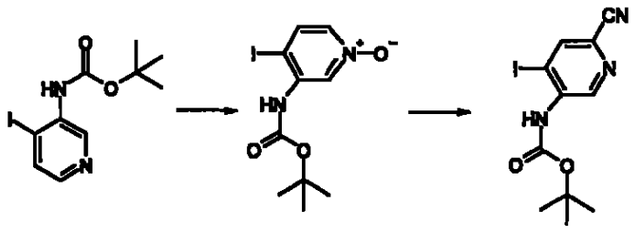
Example 6: Synthesis of 5-Amino-6-bromopyridine-2-carbonitrile



5-Aminopyridine-2-carbonitrile (2.38 g, 20 mmol) was dissolved in 6 mL of glacial acetic acid. A solution of bromine (1 mL, 20 mmol) in 2.5 mL of glacial acetic acid was added dropwise over a period of 30 minutes while the room temperature was maintained with a water bath. The resulting slurry was stirred for 1 hour at room temperature, treated with 50 mL of aqueous 20% sodium hydroxide solution and extracted with three 160 mL portions of dichloromethane. The combined organic layers were dried over sodium sulfate (Na_2SO_4), filtered, and concentrated *in*

vacuo. The residue was purified by crystallization from ethyl acetate-hexanes to give 5-amino-6-bromopyridine-2-carbonitrile (1.42 g, 35% yield).

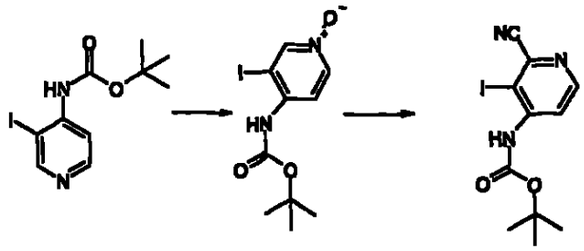
Example 7: Synthesis of (6-Cyano-4-iodopyridin-3-yl)carbamic acid *tert*-butyl ester



(4-Iodopyridin-3-yl)carbamic acid *tert*-butyl ester (3.2 g, 10 mmol) was dissolved in 100 mL of dimethoxyethane at room temperature. *m*-Chloroperoxybenzoic acid (77% by weight, 3.36 g, 15 mmol) was added and the reaction was stirred overnight at room temperature. The mixture was concentrated *in vacuo*, redissolved in 400 mL of ethyl acetate, and washed with two 200 mL portions of saturated sodium bicarbonate ($NaHCO_3$) solution. The phases were separated and the aqueous layer was extracted with two 100 mL portions of ethyl acetate. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Crystallization from ethyl acetate-hexanes gave (4-iodo-1-oxypyridin-3-yl)carbamic acid *tert*-butyl ester (2.65 g, 79% yield).

A mixture of (4-iodo-1-oxypyridin-3-yl)carbamic acid *tert*-butyl ester (2.65 g, 7.6 mmol), trimethylsilyl cyanide (4 mL, 30 mmol), triethylamine (2.6 mL, 18.9 mmol), and 40 mL of anhydrous acetonitrile was heated at 90°C for 2.5 hours. The mixture was concentrated *in vacuo*, diluted with 500 mL of dichloromethane, and treated with saturated aqueous sodium carbonate (Na_2CO_3) solution until the aqueous layer was basic. After phases were separated, the organic layer was washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. Chromatography on SiO_2 (2:98 to 8:92 ethyl acetate-hexanes, gradient) gave (6-cyano-4-iodopyridin-3-yl)carbamic acid *tert*-butyl ester (185 mg, 7% yield).

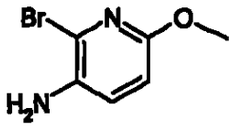
Example 8: Synthesis of (2-Cyano-3-iodopyridin-4-yl)carbamic acid *tert*-butyl ester



(3-Iodopyridin-4-yl)carbamic acid *tert*-butyl ester (3.2 g, 10 mmol) was dissolved in 100 mL of dimethoxyethane at room temperature. *m*-Chloroperoxybenzoic acid (77% by weight, 3.36 g, 15 mmol) was added and the reaction was stirred overnight at room temperature. After removing the solvent *in vacuo*, the residue was dissolved in 400 mL of ethyl acetate and washed with two 200 mL portions of saturated aqueous sodium bicarbonate solution. The phases were separated and the aqueous layer was extracted with two 100 mL portions of ethyl acetate. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Crystallization from ethyl acetate-hexanes gave (3-iodo-1-oxypyridin-4-yl)carbamic acid *tert*-butyl ester (1.95 g, 58% yield).

A mixture of (3-iodo-1-oxypyridin-4-yl)carbamic acid *tert*-butyl ester (1.95 g, 5.79 mmol), trimethylsilyl cyanide (3 mL, 23 mmol), and triethylamine (2 mL, 14.5 mmol) in 30 mL of anhydrous acetonitrile was heated to reflux at 90°C for 2.5 hours. The solvent was then removed *in vacuo*. The residue was diluted with 500 mL of dichloromethane and treated with saturated aqueous sodium carbonate solution until the aqueous layer was basic. The phases were separated and the organic layer was washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo*. Chromatography on SiO_2 (2:98 to 8:92 ethyl acetate-hexanes, gradient) gave (2-cyano-3-iodopyridin-4-yl)carbamic acid *tert*-butyl ester (1.22 g, 61% yield).

Example 9: Synthesis of 5-amino-6-bromo-2-methoxypyridine



A stirred mixture of 2-methoxy-5-aminopyridine (10 g, 0.081 mol, 1.0 equiv) and sodium acetate (6.6 g, 0.081 mol, 1.0 equiv) in 60 mL of acetic acid was treated dropwise with bromine (12.9 g, 0.081 mol, 1.0 equiv). After 20 minutes, the reaction mixture was poured into 1000

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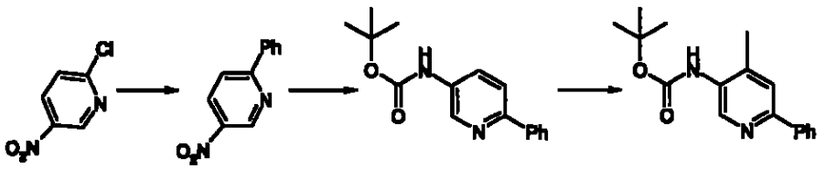
mL of 10% aqueous sodium hydroxide solution and extracted with three 250 mL portions of ethyl acetate. The combined organic layers were dried over magnesium sulfate, filtered, and evaporated to dryness. Chromatography on SiO_2 (20% hexanes in dichloromethane) gave 5-amino-6-bromo-2-methoxypyridine (6.5 g, 40% yield) as a purple solid.

Example 10: Synthesis of (4-Iodo-6-phenylpyridin-3-yl)carbamic acid *tert*-butyl ester



A mixture of $Pd(PPh_3)_4$ (354 mg, 1.58 mmol), 2-chloro-5-nitropyridine (5.00 g, 31.5 mmol), and phenylboronic acid (4.61 g, 37.8 mmol) was degassed and filled with nitrogen gas three times. The mixture was treated with 40 mL of DME and aqueous 2 M potassium carbonate (80.0 mmol) solution and heated to reflux. After 4 hours, the reaction mixture was cooled to room temperature and diluted with 100 mL of ethyl acetate and 50 mL of water. The phases were separated and the aqueous layer was extracted with three 100 mL portions of ethyl acetate. The combined organic layers were washed with 100 mL of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Chromatography on SiO_2 (0% to 50% ethyl acetate in hexanes, gradient) give 4.60 g of 5-nitro-2-phenylpyridine (73% yield).

A solution of 5-nitro-2-phenylpyridine (4.60 g, 23.0 mmol) and BOC anhydride (15.0 g, 68.9 mmol) in a mixture of 25 mL of methanol and 25 mL of ethyl acetate was treated with palladium (10% on carbon, 500 mg). The resulting mixture was shaken under 50 psi of hydrogen gas (H_2) at room temperature. After 18 hours, the mixture was diluted with 20 mL of dichloromethane, filtered through a pad of CELITE® filter aid, and concentrated *in vacuo*. The resulting solid was triturated with ethyl acetate, filtered, and dried to give 5.54 g of (6-phenylpyridin-3-yl)carbamic acid *tert*-butyl ester as white solid (89% yield).

A solution of (6-phenylpyridin-3-yl)carbamic acid *tert*-butyl ester (5.54 g, 20.5 mmol) and TMEDA (6.49 mL, 43.0 mmol) in 100 mL of anhydrous diethyl ether was treated with *n*-BuLi at -78°C. After 15 minutes at -78°C, the mixture was warmed to -10°C and stirred for an additional 3 hours. The reaction mixture was then cooled to -78°C and a solution of iodine in a

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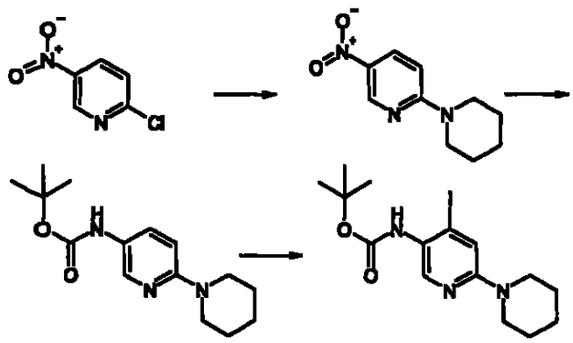
mixture of 10 mL of THF and 100 mL of diethyl ether was added dropwise. After 2 hours at -78°C, the mixture was allowed to warm to 0°C and was quenched with 400 mL of saturated aqueous ammonium chloride solution. The organic layer was washed with five 100 mL portions of saturated aqueous sodium thiosulfate. The combined aqueous layers extracted with three 200 mL portions of ethyl acetate. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Chromatography on SiO_2 (0% to 70% ethyl acetate in hexanes, gradient) afforded 900 mg of the title product as yellow oil that solidified over time (11% yield).

Example 11: Synthesis of (4'-Iodo-3,4,5,6-tetrahydro-2*H*-[1,2']bipyridinyl-5'-yl)carbamic acid *tert*-butyl ester



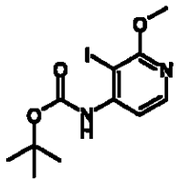
2-Chloro-5-nitropyridine (10 g, 63.3 mmol) was dissolved in 150 mL of THF. 20 mL of piperidine was then added and the resulting mixture was stirred for 18 hours at room temperature. The reaction mixture with copious precipitate was then diluted with 200 mL of water and 100 mL of diethyl ether. The layers were thoroughly mixed and separated. The organic layer was dried over sodium sulfate and concentrated *in vacuo*. The bright yellow solid was redissolved in 35 mL of dichloromethane and, with vigorous stirring, hexanes were added until the product began to precipitate. The bright yellow solid was collected by filtration and dried to afford 12.5 g of 5'-nitro-3,4,5,6-tetrahydro-2*H*-[1,2']bipyridinyl.

5'-Nitro-3,4,5,6-tetrahydro-2*H*-[1,2']bipyridinyl (12.5 g, 60.4 mmol) was suspended in 125 mL of methanol in a Parr shaker bottle and 16 g of di-*tert*-butyldicarbonate was added, followed by 500 mg of platinum oxide. The resulting mixture was shaken under 55 psi of hydrogen gas for 2 hours, followed by stirring under argon overnight. After 16 hours, the mixture was filtered

through a pad of diatomaceous earth and concentrated *in vacuo*. The crude residue was triturated with hexanes and filtered. Chromatography on silica gel (100% dichloromethane to 30% ethyl acetate in dichloromethane, gradient) provided 6.9 g (41.2% yield) of (3,4,5,6-tetrahydro-2*H*-[1,2']bipyridinyl-5'-yl)carbamic acid *tert*-butyl ester as a white solid.

The title product was prepared from (3,4,5,6-tetrahydro-2*H*-[1,2']bipyridinyl-5'-yl)carbamic acid *tert*-butyl ester in the same manner as described in the preparation of (4-iodo-6-phenylpyridin-3-yl)carbamic acid *tert*-butyl ester.

Example 12: Synthesis of 4-[(*tert*-Butoxycarbonyl)amino]-3-iodo-2-methoxypyridine



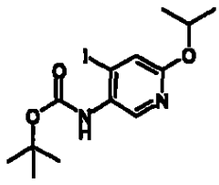
4-Amino-2-chloropyridine (15 g, 117 mmol, 1.0 equiv) was dissolved in 100 mL of THF. A solution of sodium methoxide in methanol (1.0 M, 234 mL, 234 mmol, 2.0 equiv) was added and the resulting solution was refluxed for 16 hours. The reaction mixture was poured into 500 mL of a rapidly stirring saturated sodium bicarbonate solution. 500 mL of ethyl acetate was added and the layers were separated. The organic layer was dried over sodium sulfate, decanted, and concentrated *in vacuo*. Chromatography on SiO_2 (30% ethyl acetate in hexanes) provided the titled compound as a yellow solid (2.1 g).

4-amino-2-methoxypyridine (2.1 g, 16.9 mmol, 1.0 equiv) was dissolved in 35 mL of ethyl acetate. BOC anhydride (5.4 g, 25.4 mmol, 1.5 equiv) was added and the resulting solution was refluxed for 3 hours. The reaction was cooled and concentrated *in vacuo*. The residue was triturated with 100 mL of hexanes to give an off-white precipitate that was collected and dried under vacuum to give the titled product (1.8 g).

A solution of 4-[(*tert*-butoxycarbonyl)amino]-2-methoxypyridine (1.8 g, 8.03 mmol, 1.0 equiv) in 100 mL of anhydrous diethyl ether was treated with 2.79 mL of *N,N,N',N'*-tetramethylethylenediamine (18.5 mmol, 2.3 equiv) under an inert atmosphere. The resulting solution was cooled to -78°C, treated with *n*-BuLi (2.5 M, 7.2 mL, 18.0 mmol, 2.24 equiv) and

warmed to -7°C. The reaction was stirred at -7°C to 0°C for 3 hours, cooled to -78°C and treated with a solution of iodine (3.05 g, 12 mmol) in 30 mL of anhydrous THF. The resulting mixture was stirred to room temperature for 16 hours. 200 mL of saturated ammonium chloride solution and 100 mL of diethyl ether were added. The phases were separated and the organic layer was washed with 100 mL of sodium thiosulfate (10% aqueous solution), dried over sodium sulfate, decanted, and concentrated *in vacuo*. Chromatography on SiO_2 (100% dichloromethane to 5% methanol in dichloromethane, gradient) provided the title product (650 mg, 23% yield) as a white wax.

Example 13: Synthesis of 5-[(*tert*-Butoxycarbonyl)amino]-4-iodo-2-(isopropoxy)pyridine



A mixture of 2-chloro-5-nitropyridine (15 g, 95 mmol) and 28 mL of isopropyl alcohol (366 mmol) in 100 mL of anhydrous THF was stirred until the solids dissolved. The resulting solution was cooled in an ice bath and treated dropwise with potassium *tert*-butoxide (1 M in THF, 115 mL, 115 mmol) over 45 minutes. The reaction was quenched with 75 mL of saturated aqueous ammonium chloride solution and diluted with 100 mL of ethyl acetate. The phases were separated and the organic layer was dried over magnesium sulfate, filtered, and concentrated *in vacuo*. This residue was triturated with hexanes and stirred at room temperature overnight. The mixture was filtered and the filtrate was concentrated *in vacuo* to yield 15.7 g of dark orange oil that was used in the next step without further purification.

5-nitro-2-isopropoxypyridine (15.7 g, 86 mmol) was dissolved in 125 mL of methanol and transferred to a Parr bottle. Palladium (10% on carbon, 1.57 g) and BOC anhydride (28.2 g, 129 mmol) were added. The resulting mixture was shaken on a Parr shaker under 50 psi of hydrogen gas overnight. The mixture was treated with 5 g of CELITE® filter aid, filtered through a pad of CELITE® filter aid and concentrated *in vacuo*. Chromatography on SiO_2 (hexanes-ethyl acetate (9:1)) yielded a pink solid (16.1 g). This solid was dissolved in dichloromethane, treated with hexanes, and filtered to give 13.7 g of the title product as a white solid.

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A solution of 13.7 g of 5-[(*tert*-butoxycarbonyl)amino]-2-(isopropoxy)pyridine (54.3 mmol) and 18.1 mL of *N,N,N',N'*-tetramethylethylenediamine (120 mmol) in 200 mL of anhydrous diethyl ether was cooled to -78°C and treated with *n*-BuLi (2.5 M in hexanes, 48 mL, 120 mmol) under an inert atmosphere. The mixture was placed in a -8°C bath for 1 hour and allowed to slowly warm to room temperature. After 40 minutes, the flask was cooled to -8°C and stirred for 4 hours. The mixture was then cooled to -78°C, treated with a solution of iodine (19.0 g, 75 mmol) in 100 mL of anhydrous THF, and the resulting mixture was stirred for 16 hours while allowing the bath to warm to 0°C. The reaction mixture was poured into a rapidly stirring aqueous saturated ammonium chloride solution (200 mL) and diluted with 100 mL of water and 300 mL of diethyl ether. The phases were separated and the aqueous layer was extracted with 400 mL of diethyl ether. The combined organic layers were washed with two 300 mL portions of sodium thiosulfate (10% aqueous solution), dried over sodium sulfate, decanted, and concentrated *in vacuo*. Chromatography on SiO_2 (10% to 50% ethyl acetate in hexanes gradient) gave the title product as an oil, which solidified on standing (15 g, 63% yield).

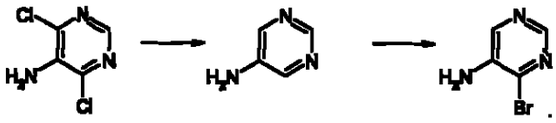
Example 14: Synthesis of 4-Amino-6-bromopyridazine and 4-Amino-5-bromopyridazine

50 mL of ammonia was condensed in a 100 mL 3-neck flask equipped with dry ice condenser. After the addition of a crystal of $Fe(NO_3)_3$, potassium (468 mg, 12.0 mmol) was added in small pieces at -78°C. The cooling bath was removed and the intense dark blue mixture was brought to a gentle reflux until a light gray slurry was obtained. After cooling to -78°C, 0.35 mL (4.80 mmol) of pyridazine was added and the mixture was stirred for 10 minutes. Solid $KMnO_4$ (1.50 g, 9.50 mmol) was added in small portions, the cooling bath was removed, and the mixture was stirred for 10 minutes. The reaction was carefully quenched with 2 g of solid ammonium chloride. 30 mL of methanol was added and the ammonia was left to evaporate in the hood. The black mixture was filtered through CELITE® filter aid, the filtrate was concentrated *in vacuo*, and the resulting black solid was purified on SiO_2 (100% CH_2Cl_2 to 10%

MeOH in CH_2Cl_2, gradient) to yield pyridazin-4-ylamine as a brownish solid (380 mg; 83% yield).

Bromination of pyridazin-4-ylamine was performed in the same manner as for the preparation of 4-amino-3-bromo-2,6-dimethylpyridine. Chromatography on SiO_2 (20% ethyl acetate in hexanes to 100% ethyl acetate, gradient, followed by 2% methanol in ethyl acetate) yielded 4-amino-3-bromopyridazine (first eluting: 15% yield) and 4-amino-5-bromopyridazine (second eluting: 5% yield) as tan solids.

Example 15: Synthesis of 5-Amino-4-bromopyrimidine



A solution of 5-amino-4,6-dichloropyrimidine (5.0 g, 30.5 mmol) in 250 mL of diethyl ether was treated with sodium hydroxide solution (20.0 g, 0.50 mol, in 60 mL of water) and palladium (10% on carbon, 400 mg). The mixture was shaken at room temperature on a Parr shaker under 50 psi of hydrogen gas for 20 hours. The mixture was filtered through CELITE® filter aid. The phases were separated and the aqueous layer was extracted with three 100 mL portions of ethyl acetate. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Crystallization of the crude from ethyl acetate gave pyrimidin-5-ylamine as white crystalline solid (2.8 g; 95% yield).

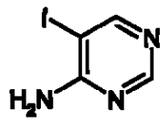
Bromination of pyrimidin-5-ylamine was performed in the same manner as for the preparation of 4-amino-3-bromo-2,6-dimethylpyridine. The resulting crude product (300 mg, 35% yield) was deemed pure and used without further purification.

Alternatively, 5-amino-4-bromopyrimidine can be synthesized according to the following procedure: A solution of 4,6-dichloro-5-aminopyrimidine (21 g, 128 mmol) in 250 mL of MeOH was sequentially treated with ammonium formate (45 g, 714 mmol) and palladium (10% on charcoal, 1 g, 0.943 mmol) at 0°C. The mixture was stirred overnight at room temperature and was filtered through CELITE® filter aid. The filtrate was concentrated to give a yellow solid. 100 mL of water and 250 mL of ethyl acetate were added. The organic phase was

separated and the aqueous layer was extracted with eight 250 mL portions of ethyl acetate. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated *in vacuo* to yield off-white crystals (8.1 g, 67%).

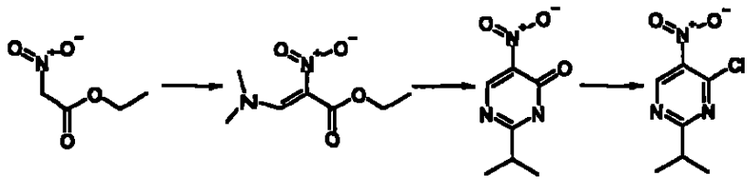
A stirred solution of 5-aminopyrimidine (3.0 g, 31.5 mmol) in 150 mL of dichloromethane and 30 mL of methanol was cooled to 0°C. Benzyltrimethylammonium tribromide (13.5 g, 34.7 mmol) was added in portions over a period of 10 minutes. Stirring was continued at 0°C for 15 minutes and at room temperature for 90 minutes. The reaction mixture was treated with aqueous sodium bicarbonate solution until the solution was pH 8. The organic layer was separated and aqueous layer was extracted with three 30 mL portions of ethyl acetate. The combined organic extracts were dried over sodium sulfate, filtered, and concentrated *in vacuo*. An off-white solid (2.8 g; 51%) was obtained, which was used without further purification.

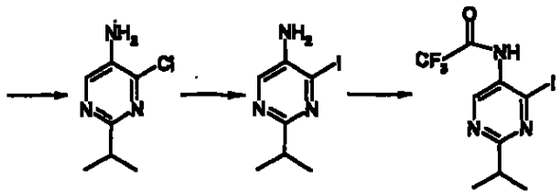
Example 16: Synthesis of 4-Amino-5-iodopyrimidine



A solution of 4-aminopyrimidine (0.970 g, 10.3 mmol) in 20 mL of acetic acid was treated with iodine monochloride (1.67 g, 10.3 mmol, 1.01 equiv), which gave a copious precipitate of the *N*-iodo intermediate. The resulting mixture was refluxed for 3 hours under argon and cooled to about 10°C with water bath. A precipitate formed that was collected and dried to provide the title compound as a yellowish solid (1.4 g, 62% yield).

Example 17: Synthesis of 2,2,2-Trifluoro-N-(4-iodo-2-isopropylpyrimidin-5-yl)acetamide





Ethylnitroacetate (11.7 mL, 105 mmol) was added slowly to a stirred solution of dimethyl formamide dimethyl acetal (29.2 mL, 220 mmol). The resulting reddish mixture was kept at room temperature for 2 hours, heated in an oil bath at 100°C for 90 minutes, and cooled to room temperature. The mixture was concentrated *in vacuo* to remove volatile organics and the resulting residue was heated at 60°C for 1 hour. A reddish orange liquid was obtained (18 g, ~100% yield), which was used in the next step without purification.

To a stirred solution of 3-dimethylamino-2-nitroacrylic acid ethyl ester (3.8 g, 20 mmol) in 50 mL of anhydrous ethanol was added isopropyl amidine hydrochloride (3.1 g, 25 mmol) followed by triethylamine (2.5 mL, 25 mmol). The resulting mixture was heated at 90°C for 6 hours. After cooling to room temperature, the mixture was concentrated *in vacuo* and the crude was purified on SiO_2 (3% methanol in dichloromethane) to give 3.1 g of a brownish oil (84% yield).

A suspension of 2-isopropyl-5-nitro-3*H*-pyrimidin-4-one (1.55 g, 8.5 mmol) and triethylamine (1.4 mL, 10 mmol) in 10 mL of dichloromethane was cooled in an ice bath. A solution of phosphorus oxychloride (1.9 mL, 20 mmol) in 5 mL of dichloromethane was added slowly over a period of 5 minutes, and the resulting mixture was stirred for 90 minutes. The resulting mixture was diluted with dichloromethane, quenched with ice, sequentially washed with a saturated sodium bicarbonate solution and water, dried over sodium sulfate, filtered, and concentrated *in vacuo* to give 0.7 g of brownish oil (41% yield), which was used without further purification.

A stirred solution of 4-chloro-2-isopropyl-5-nitropyrimidine (0.7 g, 3.5 mmol) in 10 mL of absolute alcohol and 5 mL of glacial acetic acid was treated with iron powder and the mixture was heated at 90°C for 20 minutes. After cooling to room temperature, the reaction mixture was diluted with 200 mL of dichloromethane, sequentially washed with a saturated sodium

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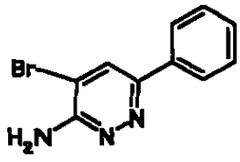
bicarbonate solution and water, dried over sodium sulfate, filtered, and concentrated *in vacuo* to give 450 mg of light brownish oil, which was used without further purification (75% yield).

A stirred mixture of 4-chloro-2-isopropylpyrimidin-5-ylamine (450 mg, 2.6 mmol) in 10 mL of a solution of HI (40% aqueous) was treated with NaI (1.97 g, 13.1 mmol). The resulting mixture was stirred at room temperature for 2 hours and poured onto dichloromethane. The phases were separated. The organic layer was washed with aqueous sodium carbonate solution, aqueous sodium bisulfite solution, and water, dried over sodium sulfate, filtered, and concentrated *in vacuo* to give 600 mg of brownish oil, which was used without further purification (87% yield).

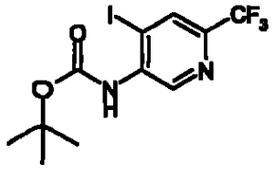
A stirred solution of 4-iodo-2-isopropylpyrimidin-5-ylamine (600 mg, 2.28 mmol) in 4 mL of anhydrous dichloromethane was treated with a solution of trifluoroacetic anhydride (0.43 mL, 3 mmol) in 2 mL of dichloromethane at room temperature. After 15 minutes, the mixture was concentrated *in vacuo* to give 0.8 g of brownish oil which solidified upon standing and was used without purification (quantitative yield).

Example 18: Synthesis of 4-Bromo-6-phenylpyridazin-3-ylamine



4-Bromo-6-phenylpyridazin-3-ylamine was prepared according to the procedure described in M. Bourotte, N. Pellegrini, M. Schmitt, and J.-J. Bourguignon, Syn. Lett., 2003, 10, pp. 1482-1484.

Example 19: Synthesis of (4-Iodo-6-trifluoromethylpyridin-3-yl)carbamic acid *tert*-butyl ester



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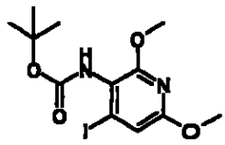
A solution of 6-trifluoromethylnicotinic acid (1.0 g, 5.23 mmol), diphenylphosphorylazide (1.36 mL, 6.3 mmol), and triethylamine (1.83 mL, 13.1 mmol) in 15 mL of anhydrous *tert*-butanol was heated at reflux under nitrogen gas for 5 hours. The reaction was cooled to room temperature and concentrated *in vacuo*. 150 mL of water was added and the mixture was extracted with two 150 mL portions of ethyl acetate. The combined organic layers were washed with 150 mL of water, 150 mL of saturated aqueous sodium bicarbonate solution, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude mixture was purified on SiO_2 (10% ethyl acetate in hexanes) to yield the title product (0.90 g, 66% yield).

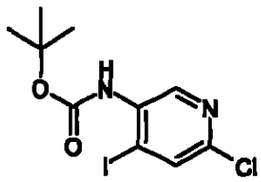
A solution of (6-trifluoromethylpyridin-3-yl)carbamic acid *tert*-butyl ester (0.90 g, 3.43 mmol) and *N,N,N',N'*-tetramethylethylenediamine (1.29 mL, 8.55 mmol) in 25 mL of anhydrous diethyl ether was cooled to -78°C under an argon atmosphere. The resulting mixture was treated dropwise with *n*-BuLi (2.5 M in hexanes, 3.42 mL, 8.55 mmol) over 5 minutes, and the mixture was allowed to warm to -10°C. After 30 minutes, the mixture was cooled to -78°C and a solution of I_2 (1.14 g, 4.5 mmol) in 5 mL of anhydrous THF was added rapidly. The resulting mixture was warmed to room temperature, stirred for 1 hour, and quenched with 50 mL of water. The organic layer was dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude mixture was purified on SiO_2 (10% ethyl acetate in dichloromethane) to afford the title compound (150 mg, 11.3% yield).

Example 20: Synthesis of (4-Iodo-2,6-dimethoxypyridin-3-yl)carbamic acid *tert*-butyl ester



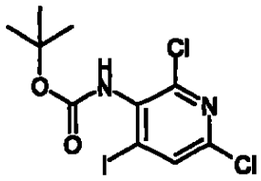
The title product was prepared from 2,6-dimethoxynicotinic acid in the same manner as in the preparation of (4-iodo-6-trifluoromethylpyridin-3-yl)carbamic acid *tert*-butyl ester.

Example 21: Synthesis of (6-Chloro-4-iodopyridin-3-yl)carbamic acid *tert*-butyl ester



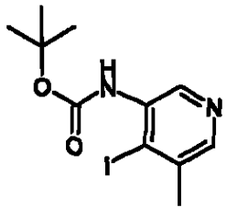
The title product was prepared from 6-chloronicotinic acid in the same manner as in the preparation of (4-iodo-6-trifluoromethylpyridin-3-yl)carbamic acid *tert*-butyl ester.

Example 22: Synthesis of (2,6-Dichloro-4-iodopyridin-3-yl)carbamic acid *tert*-butyl ester



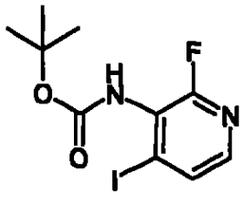
The title product was prepared from 2,6-dichloronicotinic acid in the same manner as in the preparation of (4-iodo-6-trifluoromethylpyridin-3-yl)carbamic acid *tert*-butyl ester.

Example 23: Synthesis of (4-Iodo-5-methylpyridin-3-yl)carbamic acid *tert*-butyl ester



The title product was prepared from 5-methylnicotinic acid in the same manner as in the preparation of (4-iodo-6-trifluoromethylpyridin-3-yl)carbamic acid *tert*-butyl ester.

Example 24: Synthesis of (2-Fluoro-4-iodopyridin-3-yl)carbamic acid *tert*-butyl ester



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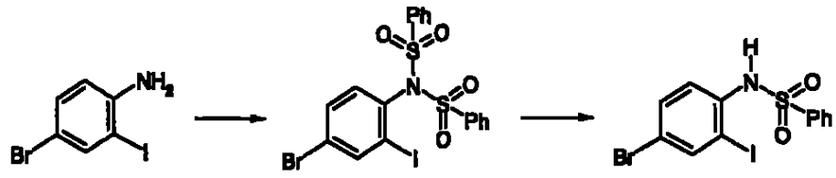
The title product was prepared from 2-fluoronicotinic acid in the same manner as in the preparation of (4-iodo-6-trifluoromethylpyridin-3-yl)carbamic acid *tert*-butyl ester.

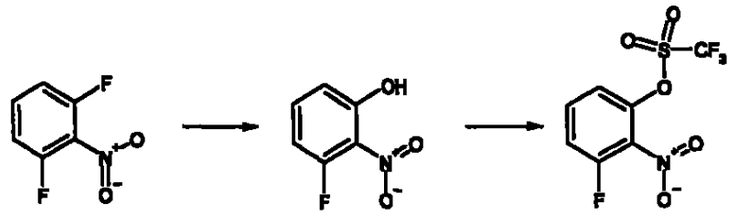
Example 25: Synthesis of *N*-(4-Bromo-2-iodophenyl)benzenesulfonamide



A solution of 4-bromo-2-iodoaniline (8.5 g, 28.5 mmol) in 200 mL of dichloromethane was sequentially treated with benzenesulfonyl chloride (15 mL, 117.5 mmol) and triethylamine (25 mL, 179.6 mmol). After 4 days, the mixture was diluted with 100 mL of saturated aqueous sodium bicarbonate solution and extracted with three 100 mL portions of ethyl acetate. The combined organic layers were washed with 50 mL of brine, three 60 mL portions of saturated aqueous ammonium chloride solution, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude product was triturated with diethyl ether to afford 5.74 g (35% yield) of *N,N*-bisbenzenesulfonyl-(4-bromo-2-iodoaniline).

A solution of tetrabutylammonium fluoride (1 M in THF, 11 mL) in 30 mL of THF was treated with *N,N*-bisbenzenesulfonyl-(4-bromo-2-iodoaniline) (5.78 g, 10 mmol) in several portions. After 18 hours, the mixture was diluted with of 40 mL of ethyl acetate and 40 mL of 1 N HCl. The phases were separated and the aqueous layer was extracted with two 40 mL portions of ethyl acetate. The combined organic layers were washed with two 20 mL portions of 1 N HCl, two 20 mL portions of saturated aqueous sodium bicarbonate solution, 20 mL of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo* to afford 3.95 g (90% yield) of the title compound as a solid, which was used without further purification.

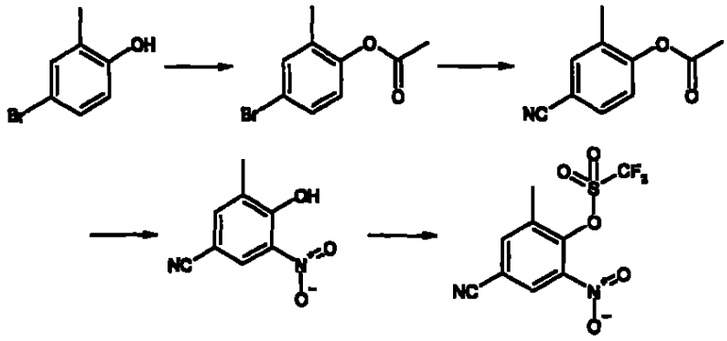
Example 26: Synthesis of Trifluoromethanesulfonic acid 3-fluoro-2-nitrophenyl ester



A solution of potassium *tert*-butoxide (1.23 g, 11 mmol) in 25 mL of anhydrous DMSO was stirred at room temperature for 30 minutes and treated with 1,3-difluoro-2-nitrobenzene (1.59 g, 10 mmol). After 18 hours, the mixture was diluted with 150 mL of 1 N aqueous sulfuric acid and extracted with three 50 mL portions of diethyl ether. The combined organic layers were washed with water, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The residue was dissolved in 50 mL of trifluoroacetic acid. After 30 minutes at room temperature, the mixture was concentrated *in vacuo*, treated with 50 mL of 1 N aqueous sodium hydroxide, and extracted with three 30 mL portions of diethyl ether. The aqueous layer was acidified with 1 N aqueous sulfuric acid and extracted with two 50 mL portions of dichloromethane. The combined dichloromethane layers were washed with water, dried over sodium sulfate, filtered, and concentrated *in vacuo* to give 1.3 g of 3-fluoro-2-nitrophenol as orange oil (61% yield).

An solution of 3-fluoro-2-nitrophenol (1.13 g, 7.2 mmol) and pyridine (0.65 mL, 8 mmol) in 15 mL of anhydrous dichloromethane was cooled in an ice bath and treated with a solution of triflic anhydride (1.33 mL, 7.9 mmol) in 3 mL of anhydrous dichloromethane. After 4 hours, the reaction mixture was diluted with 100 mL of dichloromethane, washed with two 30 mL portions of saturated aqueous sodium bicarbonate, two 30 mL portions of 1 N aqueous sulfuric acid, and two 30 mL portions of water, dried over sodium sulfate, filtered, and concentrated *in vacuo* to give 2 g of the title product as a light brown oil (96% yield).

Example 27: Synthesis of Trifluoromethanesulfonic acid 4-cyano-2-methyl-6-nitrophenyl ester



An ice-cold solution of 4-bromo-2-methylphenol (5.6 g, 30 mmol) and pyridine (6.1 mL, 75 mmol) in 50 mL of anhydrous dichloromethane was treated with a solution of acetyl chloride

(2.8 mL, 26 mmol) in 5 mL of anhydrous dichloromethane. After 2 hours, the reaction mixture was concentrated *in vacuo*. The resulting residue was treated with crushed ice, diluted with 150 mL of dichloromethane, washed with water, dried over sodium sulfate, filtered, and concentrated *in vacuo* to give 6.9 g of 4-bromo-2-methylphenyl acetate as a light brown oil (quantitative yield).

A solution of 4-bromo-2-methylphenyl acetate (6.9 g, 30 mol) in 75 mL of anhydrous dimethyl acetamide was treated with zinc cyanide (3 g, 25.6 mmol) and tetrakis(triphenylphosphine)palladium(0) (4.5 g, 3.9 mmol). The reaction mixture was heated at 100°C for 2 hours, cooled to room temperature, and treated with 300 mL of cold water. The resulting precipitate was filtered, washed with water, and air dried. Chromatography on SiO_2 (100% dichloromethane) afforded 5.2 g of 4-cyano-2-methylphenyl acetate as a colorless oil (99% yield), which solidified on standing.

A stirred solution of 4-cyano-2-methylphenyl acetate (5.2 g, 29.7 mmol) in 75 mL of methanol was treated with a solution of potassium carbonate (30 mmol, 4.15 g) in 25 mL of water at room temperature. After 30 minutes, the mixture was concentrated *in vacuo* and treated with 1 N sulfuric acid. The resulting precipitate was filtered, washed with water, and dried to give 3.1 g of 4-hydroxy-3-methylbenzonitrile as a white solid (78% yield).

A stirred solution of 4-hydroxy-3-methylbenzonitrile (3.1 g, 23.3 mmol) in 60 mL of anhydrous acetonitrile was cooled to -30°C and treated with nitronium tetrafluoroborate (3.4 g, 25.6 mmol) in portions. After 60 minutes, the reaction mixture was diluted with 100 mL of water. The resulting light yellow precipitate was filtered, washed with water, and dried to give 3.9 g of 4-hydroxy-3-methyl-5-nitrobenzonitrile (94% yield).

4-Hydroxy-3-methyl-5-nitrobenzonitrile was converted to the title product according to the procedure described for the preparation of trifluoromethanesulfonic acid 3-fluoro-2-nitrophenyl ester.

Example 28: Synthesis of 3-Fluoro-6-methyl-2-nitrophenol

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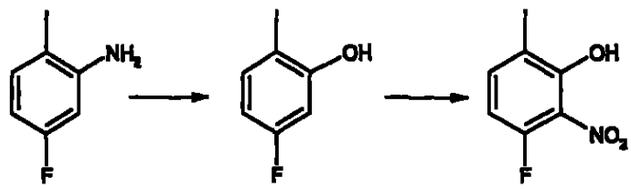
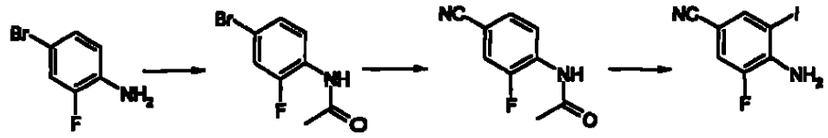


7 mL of a hot solution of concentrated sulfuric acid in 21 mL of water was added to 5-fluoro-2-methylphenylamine (5 g, 40 mmol). The mixture was cooled in an ice bath for 30 minutes and treated with a solution of sodium nitrite (3.38 g, 48 mmol) in 10 mL of water over a period of 10 minutes. After stirring at 0°C for 45 minutes, the reaction was diluted with 20 mL of cold water and treated with 0.3 g of urea. The resulting mixture was added to a stirred solution of 11 mL of concentrated sulfuric acid in 10 mL of water containing 15 g of anhydrous sodium sulfate at 130°C over 10 minutes. After an additional 5 minutes at 130°C, the reaction was allowed to cool to room temperature and was extracted with three 100 mL portions of dichloromethane. The combined organic layers were washed with two 50 mL portions of water and concentrated *in vacuo*. The reddish oil was dissolved in 250 mL of diethyl ether and washed with three 50 mL portions of 10% aqueous sodium hydroxide. The combined aqueous sodium hydroxide extracts were washed with two 50 mL portions of diethyl ether. The basic layer was acidified with 1 N aqueous HCl and extracted with three 100 mL portions of dichloromethane. The combined dichloromethane layers were washed with two 50 mL portions of brine, dried over sodium sulfate, filtered, and concentrated *in vacuo* to give a light reddish liquid. The crude was purified by chromatography on SiO_2 (10% ethyl acetate in hexanes) to give 5 g of 5-fluoro-2-methylphenol as a light brownish oil (99% yield).

A stirred solution of 5-fluoro-2-methylphenol (640 mg, 5 mmol) in 20 mL of anhydrous acetonitrile was cooled to -30°C to -40°C and treated with nitronium tetrafluoroborate (740 mg, 5.5 mmol). After 45 minutes, the reaction mixture was diluted with 100 mL of cold water and extracted with three 50 mL portions of dichloromethane. The combined organic layers were washed with three 25 mL portions of water, dried over sodium sulfate, and concentrated *in vacuo* to give a reddish crystalline solid. Chromatography over SiO_2 (5% ethyl acetate in hexanes) gave 0.58 g of the title product as bright yellow solid (68% yield).

The title compound was converted to the corresponding trifluoromethane sulfonate according to the procedure described in Example 26.

Example 29: Synthesis of 4-Amino-3-fluoro-5-iodobenzonitrile



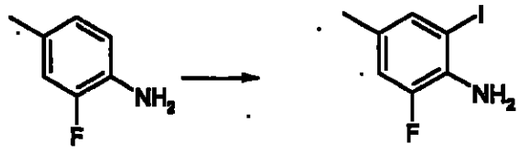
A solution of 4-bromo-2-fluorophenylamine (10.9 g, 57.4 mmol) and pyridine (9.4 mL, 115 mmol) in 50 mL of anhydrous dichloromethane was treated with acetyl chloride (3.33 mL, 63.1 mmol) at 0°C. After 10 minutes at 0°C and 10 minutes at room temperature, the mixture was concentrated *in vacuo* and the residue was treated with 300 mL of 1 N aqueous sulfuric acid. The organic layer was concentrated *in vacuo* to give 12.9 g of *N*-(4-bromo-2-fluorophenyl)acetamide as a light greyish solid (97% yield).

A solution of *N*-(4-bromo-2-fluorophenyl)acetamide (12.9 g, 55.4 mmol) in 125 mL of anhydrous dimethyl acetamide was heated in the presence of zinc cyanide (5.53 g, 47.1 mmol) and tetrakis(triphenylphosphine)palladium (0) (5.2 g, 4.5 mmol) at 100°C for 3 hours. The mixture was diluted with 300 mL of cold water, the resulting solid was filtered, washed with water, and dried. The filtrate was extracted with three 100 mL portions of ethyl acetate and the combined extracts were dried over sodium sulfate, filtered, and concentrated *in vacuo*. The resulting residue was combined with the solid from the filtration. This combined material was filtered through a silica gel column (100% dichloromethane followed by 100% ethyl acetate) to give 8.5 g of *N*-(4-cyano-2-fluorophenyl)acetamide as a light cream solid (86% yield).

A solution of sodium perborate (4.2 g, 27.3 mmols) and sodium tungstate (450 mg, 1.4 mmol) in a mixture of 20 mL of glacial acetic acid and 15 mL of acetic anhydride was treated with a solution of potassium iodide (2.3 g, 13.9 mmols) in 15 mL of water. The mixture was treated with 7.5 mL of concentrated sulfuric acid over 15 minutes. A suspension of *N*-(4-cyano-2-fluorophenyl)acetamide (1.79 g, 10 mmols) in 15 mL of glacial acetic acid was added to and the resulting mixture was heated at 50°C. After 1 hour, the mixture was poured into 300 mL of crushed ice and treated with 100 mL of a saturated solution of sodium thiosulfate followed by 100 mL of a sodium bisulfite solution. The mixture was extracted with three 100 mL portions

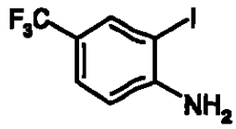
of dichloromethane and the combined organic layers were washed with three 50 mL portions of sodium bicarbonate solution, three 50 mL portions of water, dried over sodium sulfate, and concentrated *in vacuo* to give a light brownish solid. Chromatography on SiO_2 (50% ethyl acetate in hexanes) afforded 400 mg of the title product as a light brownish solid (15% yield).

Example 30: Synthesis of 2-Fluoro-6-iodo-4-methylphenylamine



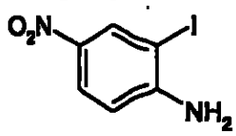
A solution of 2-fluoro-4-methylphenylamine (1.25 g, 10 mmol) in 5 mL of methanol was treated with a solution of iodine (1.27 g, 5 mmol) in a mixture of 25 mL of methanol and 3 mL of hydrogen peroxide over a period of 15 minutes at room temperature. After 18 hours, the reaction mixture was quenched with 30 mL of saturated aqueous sodium thiosulfate and extracted with three 50 mL portions of dichloromethane. The combined organic layers were washed with two 30 mL portions of saturated sodium bisulfite solution, three 50 mL portions of water, dried over sodium sulfate, and concentrated *in vacuo*. Chromatography on SiO_2 (10% ethyl acetate in hexanes) gave 1.1 g of the title product as a light brownish oil (44% yield).

Example 31: Synthesis of 2-Iodo-4-trifluoromethylphenylamine



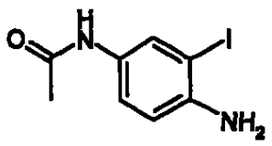
The title compound was prepared in the same manner as indicated for the synthesis of 2-fluoro-6-iodo-4-methylphenylamine.

Example 32: Synthesis of 2-Iodo-4-nitrophenylamine



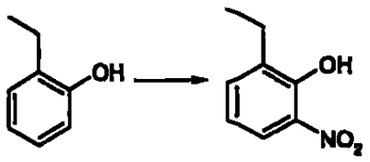
The title compound was prepared in the same manner as indicated for the synthesis of 2-fluoro-6-iodo-4-methylphenylamine.

Example 33: Synthesis of *N*-(4-Amino-3-Iodophenyl)acetamide



The title compound was prepared in the same manner as indicated for the synthesis of 2-fluoro-6-iodo-4-methylphenylamine.

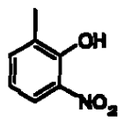
Example 34: Synthesis of 2-Ethyl-6-nitrophenol



A solution of 2-ethylphenol (2.44 g, 20 mmol) in 80 mL of anhydrous acetonitrile was treated with nitronium tetrafluoroborate (2.93 g, 22 mmols) in portions over a period of 5 minutes at -30°C to -40°C. After 20 minutes, the mixture was quenched with ice, treated with cold water and extracted with three 100 mL portions of dichloromethane. The combined organic layers were washed with two 30 mL portions of water, dried over sodium sulfate, filtered, and concentrated *in vacuo*. Chromatography on SiO_2 (20% ethyl acetate in hexanes) gave 2.0 g of 2-ethyl-6-nitrophenol as a yellow oil (60% yield).

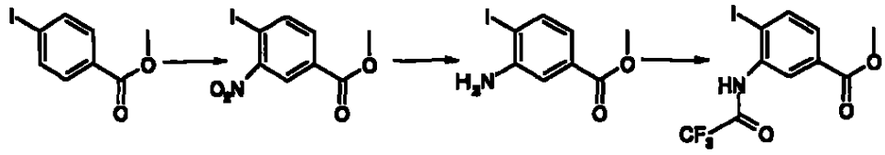
The title compound was converted to the corresponding trifluoromethane sulfonate according to the procedure described in Example 26.

Example 35: Synthesis of 2-Methyl-6-nitrophenol



The title compound was prepared in the same manner as indicated for the synthesis of 2-ethyl-6-nitrophenol and was converted to the corresponding trifluoromethane sulfonate according to the procedure described in Example 26.

Example 36: Synthesis of 4-Iodo-3-(2,2,2-trifluoroacetylamino)benzoic acid methyl ester



A solution of 4-iodobenzoic acid methyl ester (5.24 g, 20.0 mmol) in sulfuric acid was treated with 1.43 mL of concentrated nitric acid in a dropwise fashion at 0°C. After 5 hours at room temperature, the reaction mixture was heated to 40°C for 1 hour. The resulting orange solution was added to 100 g of ice, treated with 200 mL of ethyl acetate, shaken for 30 minutes, and filtered. The phases were separated and the aqueous layer was extracted with 200 mL of ethyl acetate. The combined organic layers were washed with saturated sodium bicarbonate solution and brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The residue was passed through a column of silica gel (100% ethyl acetate) to give 2.0 g of 4-iodo-3-nitrobenzoic acid methyl ester as a yellow solid (33% yield).

A solution of 4-iodo-3-nitrobenzoic acid methyl ester (2.0 g, 6.50 mmol) in 25 mL of absolute alcohol and 15 mL of glacial acetic acid was treated with iron powder (3.6 g, 65.0 mmol) and the mixture was heated at 80°C. After 1 hour, the reaction mixture was filtered through a pad of silica, washed with ethanol, and concentrated *in vacuo*. The residue was diluted with a solution of potassium carbonate and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo* to give 1.6 g of 3-amino-4-iodobenzoic acid methyl ester as a white solid (88% yield).

A solution of 3-amino-4-iodobenzoic acid methyl ester (1.59 g, 5.74 mmols) in 40 mL of dichloromethane was reacted with trifluoroacetic anhydride (3 mL, 21 mmol) at room temperature. After 30 minutes, the reaction mixture was concentrated *in vacuo* and the residue was taken up in cold water, filtered, and dried to give 2.1 g of the title product as an off-white solid (quantitative yield).

Example 37: Synthesis of 2-Methyl-5-phenyl-1*H*-pyrrolo[2,3-c]pyridine

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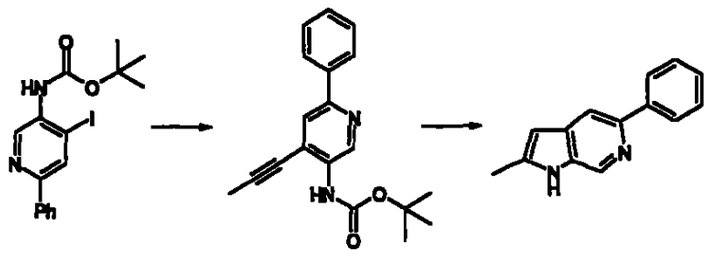
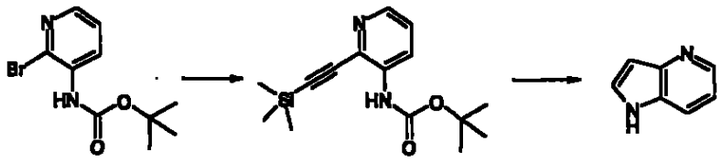


Propyne (0.60 mL, 11.4 mmol) was condensed in a pressure tube at -78°C. A solution of (4-iodo-6-phenylpyridin-3-yl)carbamic acid *tert*-butyl ester (900 mg, 2.27 mmol) in 2 mL of DMF, 6 mL of triethylamine, dichlorobis(triphenylphosphine)palladium (II) (80.2 mg, 0.114 mmol), and CuI (43.0 mg, 0.227 mmol) were added, the tube was sealed, and the mixture was stirred at room temperature overnight. The mixture was cooled to -78°C, the sealed tube was opened, and 20 mL of ethyl acetate and 10 mL of saturated aqueous ammonium chloride solution were added. The phases were separated and the aqueous layer was extracted with three 10 mL portions of ethyl acetate. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude product was purified on SiO_2 (0 to 40% ethyl acetate in hexanes, gradient) to give 670 mg of (6-phenyl-4-prop-1-ynylpyridin-3-yl)carbamic acid *tert*-butyl ester (96% yield).

A solution of (6-phenyl-4-prop-1-ynylpyridin-3-yl)carbamic acid *tert*-butyl ester (670 mg, 2.17 mmol) in a mixture of 33 mL of methanol and 11 mL of water was treated with DBU (2.0 mL, 13.4 mmol). The resulting mixture was heated at 60°C. After 24 hours, the mixture was concentrated *in vacuo*, 50 mL of water was added, the mixture was sonicated, and the resulting solid was filtered. The solid was dried over P_2O_5 in vacuum to give 450 mg of the title product as a yellow solid (99% yield), which was used without further purification.

Example 38: Synthesis of 1*H*-Pyrrolo[3,2-*b*]pyridine

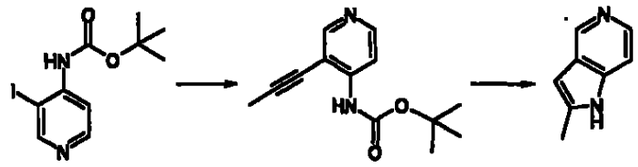


A mixture of (2-bromopyridin-3-yl)carbamic acid *tert*-butyl ester (1.09 mg, 4.00 mmol), (trimethylsilyl)acetylene (2.83 mL, 20.0 mmol), CuI (75.8 mg, 0.400 mmol), and

dichlorobis(triphenylphosphine)palladium (II) (141 mg, 0.200 mmol) in a mixture of 12 mL of triethylamine and 3.0 mL of anhydrous DMF were stirred at room temperature overnight. The reaction was diluted with 50 mL of diethyl ether and quenched with 50 mL of saturated aqueous ammonium chloride solution. The organic layer was washed with 20 mL of saturated aqueous ammonium chloride solution and the combined aqueous layers were extracted with three 20 mL portions of diethyl ether. The combined organic layers were then washed with 20 mL of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Chromatography on SiO_2 (20% to 30% ethyl acetate in hexanes, gradient) gave 500 mg of (2-trimethylsilanylethynylpyridin-3-yl)carbamic acid *tert*-butyl ester (43% yield).

A mixture of (2-trimethylsilanylethynylpyridin-3-yl)carbamic acid *tert*-butyl ester (500 mg, 1.72 mmol) in 5 mL of THF was treated with TBAF (1 M in THF, 10.3 mL) at room temperature. The mixture was heated at reflux for 8 hours, cooled to room temperature, diluted with 100 mL of diethyl ether, and quenched with 100 mL of water. The aqueous layer was extracted with three 50 mL portions of diethyl ether, and the combined organic layers were washed with 500 mL of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Chromatography on SiO_2 (100% CH_2Cl_2 to 10% MeOH in CH_2Cl_2, gradient) gave 160 mg of the title product as tan solid (79% yield).

Example 39: Synthesis of 2-Methyl-1*H*-pyrrolo[2,3-*c*]pyridine

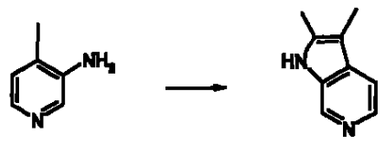


Propyne (6.3 mL, 124 mmol) was condensed in a pressure tube at -78°C. A solution of (3-iodopyridin-4-yl)carbamic acid *tert*-butyl ester (7.98 g, 24.9 mmol) in 15 mL of DMF, 60 mL of triethylamine, dichlorobis(triphenylphosphine)palladium (II) (877 mg, 1.25 mmol), and CuI (472 mg, 2.49 mmol) were added, and the tube was sealed and stirred at room temperature overnight. 200 mL of ethyl acetate and 100 mL of saturated aqueous ammonium chloride solution were added, the phases were separated and the aqueous layer was extracted with three 100 mL portions of ethyl acetate. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Chromatography on SiO_2 (25% to 40% ethyl

acetate in hexanes, gradient) afforded 5.65 g of (3-prop-1-ynylpyridin-4-yl)carbamic acid *tert*-butyl ester (98% yield).

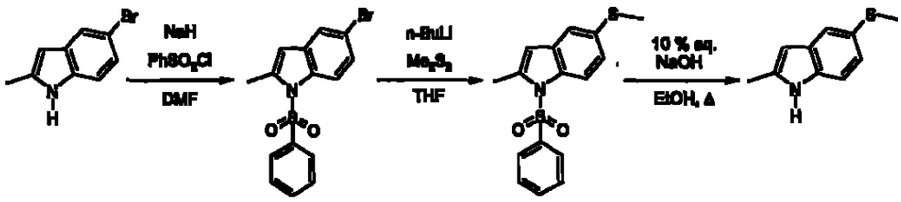
(3-Prop-1-ynylpyridin-4-yl)carbamic acid *tert*-butyl ester (5.65 g, 24.3 mmol) was treated with 30.4 mL of 4 M HCl in dioxane. The mixture was sonicated until the compound completely dissolved. After 15 hours, the mixture was concentrated *in vacuo*. The resulting brown solid (4.10 g) was dissolved in 65 mL of 1-methyl-2-pyrrolidinone (NMP) and treated with *tert*-BuOK (7.08 g, 63.2 mmol) at room temperature. After 18 hours, 300 mL of ethyl acetate and 300 mL of water were added. The phases were separated and the aqueous layer was extracted with five 100 mL portions of ethyl acetate. The combined organic layers were washed with two 20 mL portions of water, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Chromatography on SiO_2 (10% methanol in dichloromethane) yielded 2.85 g of the title product as yellow solid (89% yield).

Example 40: Synthesis of 2,3-Dimethyl-1*H*-pyrrolo[2,3-c]pyridine



In a pressure tube, a solution of iodopyridine (1.80 g, 8.18 mmol) in 20 mL of DMF was treated with 2-butyne (1.5 mL, 19.1 mmol), $Pd(dppf)_2Cl_2 \cdot CH_2Cl_2$ (357 mg, 0.438 mmol), lithium chloride (367 mg, 8.71 mmol), and sodium carbonate (1.82 g, 17.2 mmol). The tube was sealed and heated to 90°C. After 24 hours, the tube was cooled and opened. The resulting mixture was diluted with 20 mL of ethyl acetate and 20 mL of saturated aqueous ammonium chloride solution. The phases were separated and the aqueous layer was extracted with three 50 mL portions of ethyl acetate. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Flash chromatography (CH_2Cl_2 to 10% MeOH in CH_2Cl_2, gradient) afforded the title product as a brown solid (920 mg, 77% yield).

Example 41: Synthesis of 2-Methyl-5-methylsulfanyl-1*H*-indole



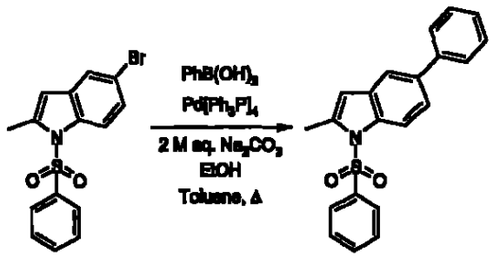
To a solution of 5-bromo-2-methyl-1*H*-indole (1.5 g, 7.14 mmol) in 10 mL of DMF was added 60% sodium hydride in mineral oil (189 mg, 7.9 mmol). Once hydrogen gas evolution ceased, the mixture stirred for 10 minutes and was then treated with 1 mL (7.83 mmol) of benzene sulfonyl chloride. The reaction was monitored by TLC (ethyl acetate-hexanes (5:95)) to afford a major new slightly less polar product than starting material. After 2 hours, the mixture was poured into 50 mL of saturated aqueous ammonium chloride solution and extracted with three 50 mL portions of ethyl acetate. The combined organic layers were washed with four 25 mL portions of brine, dried over magnesium sulfate, treated with activated carbon (NORIT A™), filtered through diatomaceous earth, and concentrated *in vacuo*. The residue was adsorbed onto silica gel and chromatographed on silica gel using ethyl acetate-hexanes (1:99, then 2:98, then 3:97) to afford 1.71 g (68.4% yield) of 1-benzenesulfonyl-5-bromo-2-methyl-1*H*-indole as a clear oil.

To a chilled solution of 1-benzenesulfonyl-5-bromo-2-methyl-1*H*-indole (350 mg, 0.99 mmol) in 4 mL of THF was added 440 µL (1.10 mmol) of *n*-BuLi (2.5 *M* solution in hexanes), followed by dimethyl disulfide (100 µL, 1.11 mmol). The mixture was stirred as it warmed to room temperature and was then quenched with ammonium chloride and extracted with three 15 mL portions of ethyl acetate. The combined organic layers were washed with three 15 mL portions of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude material was adsorbed onto silica gel and chromatographed on silica gel using ethyl acetate-hexanes (1:99, then 2:98) to afford 156 mg (44.3% yield) of 1-benzenesulfonyl-2-methyl-5-methylsulfanyl-1*H*-indole as a clear oil.

To a solution of 1-benzenesulfonyl-2-methyl-5-methylsulfanyl-1*H*-indole (156 mg, 0.49 mmol) in 10 mL of ethanol was added 10 mL of 10% aqueous sodium hydroxide solution. The mixture was warmed at reflux for 18 hours. The mixture was then diluted with 10 mL of brine and extracted with three 20 mL portions of ethyl acetate. The combined organic layers were

washed with two 10 mL portions of 10% aqueous sodium hydroxide solution, two 20 mL portions of saturated aqueous ammonium chloride, two 20 mL portions of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude product was adsorbed onto silica gel and chromatographed on silica gel using ethyl acetate-hexanes (1:99, then 2:98, then 3:97, then 5:96) to afford 62 mg (71.2% yield) of 2-methyl-5-methylsulfanyl-1*H*-indole.

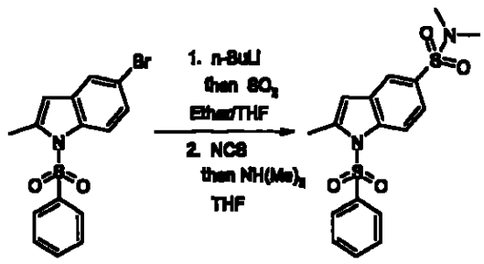
Example 42: Synthesis of 1-Benzenesulfonyl-2-methyl-5-phenyl-1*H*-indole



A mixture of 1-benzenesulfonyl-5-bromo-2-methyl-1*H*-indole (810 mg, 2.31 mmol), phenylboronic acid (850 mg, 6.97 mmol) and tetrakis(triphenylphosphine)palladium(0) (55 mg, 0.029 mmol) in 20 mL of toluene, 10 mL of ethanol, and 5 mL of 2 M sodium carbonate was warmed at reflux for 4 hours. The reaction was monitored by TLC (ethyl acetate-hexanes (5:95), 2x developed; and toluene-hexanes (1:1)) indicating a slightly more polar product. The mixture was cooled and diluted with 12% aqueous ammonium hydroxide solution and extracted with three 15 mL portions of ethyl acetate. The combined organic layers were washed with three 15 mL portions of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude mixture was adsorbed onto silica gel and chromatographed on silica gel using ethyl acetate-hexanes (1:99, then 2:98, then 3:97) to afford 731 mg (91% yield) of 1-benzenesulfonyl-2-methyl-5-phenyl-1*H*-indole.

Removal of the phenyl sulfonyl group as described in Example 41 gave 2-methyl-5-phenyl-1*H*-indole.

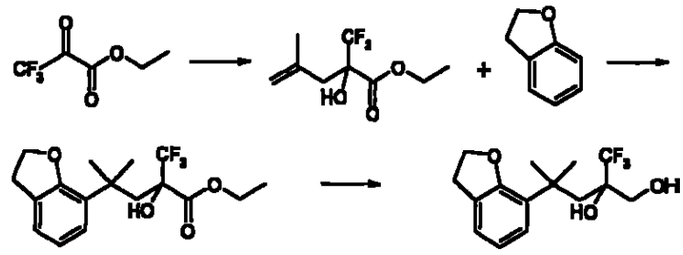
Example 43: Synthesis of 1-Benzenesulfonyl-2-methyl-1*H*-indole-5-sulfonic acid dimethylamide

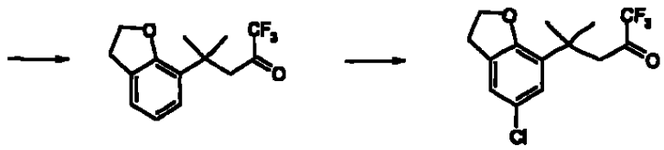


To a chilled (-78°C) solution of 1-benzenesulfonyl-5-bromo-2-methyl-1*H*-indole (505 mg, 1.44 mmol) in 5 mL of diethyl ether and 2 mL of THF was added 650 µL (1.63 mmol) of *n*-BuLi (2.5 M solution in hexanes). The mixture was stirred of 10 minutes and then sulfur dioxide (SO_2) gas was bubbled through the solution, resulting in a precipitate. The mixture was warmed to room temperature and filtered to afford 468 mg of the lithium sulfonate. This material was dissolved in 10 mL of THF and then *N*-chlorosuccinimide (200 mg, 1.49 mmol) was added. The mixture was stirred for 15 minutes and then 4 mL (8 mmol) of a 2 M solution of dimethylamine in THF was added. The mixture was then stirred for 1 hour and was diluted with saturated aqueous ammonium chloride solution and extracted with three 10 mL portions of ethyl acetate. The combined organics were washed with three 10 mL portions of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo* to afford 365 mg of 1-benzenesulfonyl-2-methyl-1*H*-indole-5-sulfonic acid dimethylamide.

Removal of the phenylsulfonyl group as described in Example 41 gave 2-methyl-1*H*-indole-5-sulfonic acid dimethylamide.

Example 44: Synthesis of 4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-one





A solution of ethyl trifluoropyruvate (124.84 g, 0.734 mol) in 2.0 L of THF was treated with methylallyl magnesium chloride (0.5 M in THF, 1.90 L, 0.954 mol) over 4 hours while the internal temperature was maintained below -60°C. The reaction mixture was allowed to reach room temperature overnight, concentrated *in vacuo* to remove THF, quenched with 1 L of saturated ammonium chloride solution, and extracted with three 1 L portions of diethyl ether. The combined organic phases were washed with 100 mL of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Vacuum distillation at 60 mmHg afforded 100.1 g of 2-hydroxy-4-methyl-2-trifluoromethylpent-4-enoic acid ethyl ester as a clear oil (b.p. 97°C-103°C, 60% yield).

A solution of 2-hydroxy-4-methyl-2-trifluoromethylpent-4-enoic acid ethyl ester (100 g, 442 mmol) and 2,3-dihydrobenzofuran (57.7 g, 480 mmol) in 500 mL of dichloroethane was treated with $AlCl_3$ (87.8 g, 660 mmol) while maintaining the internal temperature below 10°C. The reaction was allowed to warm to room temperature overnight and quenched with 1 L of cold 1 N HCl. The mixture was then extracted with three 1 L portions of ethyl acetate. The combined organic layers were washed with 1 L of saturated aqueous sodium bicarbonate solution, 1 L of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The residue was purified on SiO_2 (10% diethyl ether in hexanes). The resulting solid was recrystallized in hot hexanes to afford 39.5 g of 4-(2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentanoic acid ethyl ester as a white solid (26% yield).

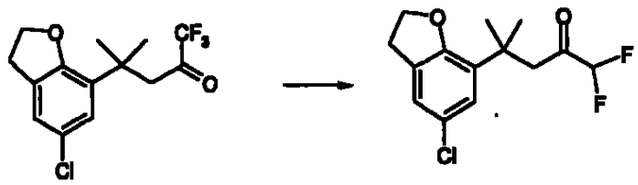
A suspension of LAH (4.52 g, 119 mmol) in 230 mL of THF was treated with a solution of 4-(2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentanoic acid ethyl ester (27.5 g, 79.4 mmol) in 40 mL of THF at 0°C over 30 minutes. After stirring overnight, the reaction was cooled to 0°C, quenched with 3 mL of water, and treated with 3 mL of 4 M sodium hydroxide solution. After 10 minutes, the mixture was treated with additional 18 mL portion of water and the resulting mixture was warmed to room temperature for 4 hours. The mixture was filtered and the filter cake was washed with five 100 mL portions of diethyl ether.

The filtrate was concentrated *in vacuo* to give 24.0 g of 4-(2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentane-1,2-diol as an oil (99% yield).

A solution of 4-(2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentane-1,2-diol (24.0 g, 78.9 mmol) and $NaIO_4$ (84.3 g, 394 mmol) in 360 mL of methanol was stirred at room temperature overnight. The resulting mixture was filtered through pad of CELITE® filter aid and the filter cake was washed with three 100 mL portions of methanol. The filtrate was concentrated *in vacuo*, taken up in hexanes, filtered again, and concentrated *in vacuo* to give 21.4 g of 4-(2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-one as colorless oil (quantitative yield), which was used without purification.

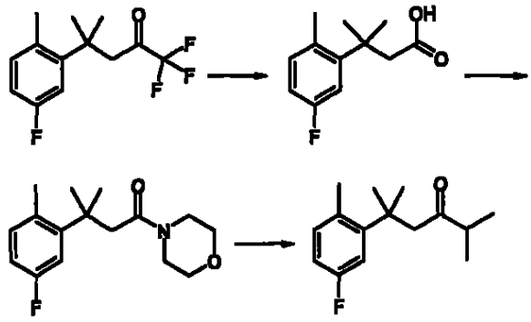
A solution of 4-(2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-one (20.8 g, 76.2 mmol) in 200 mL of acetic acid was treated with a solution of chlorine gas (Cl_2) in acetic acid (prepared by bubbling chlorine gas into acetic acid, ~1.19 M). The reaction was monitored by ^{1}H-NMR. The ratio of the starting material to product was determined based on the integration of CH_2 signal of the respective ketones (starting material: δ = 3.32 ppm; product: δ = 3.32 ppm). The concentration of the Cl_2 solution was recalculated based on the NMR ratios and an additional portion of Cl_2 solution was added (this process was repeated until NMR showed the complete consumption of the starting material). The mixture was quenched with 500 mL of water and solid sodium bicarbonate (~500 g) was added carefully during 1 hour. The mixture was poured onto 500 mL of ethyl acetate. The phases were separated and the aqueous layer was extracted with three 500 mL portions of ethyl acetate. The combined organic layers were washed with two 100 mL portions of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo* to afford 23.4 g of the title product (quantitative yield), which was used without purification.

Example 45: Synthesis of 4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methylpentan-2-one



A mixture of magnesium turnings (204 mg, 8.40 mmol) and trimethylsilyl chloride (2.13 mL, 16.8 mmol) in 10 mL of DMF was treated with 4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-one (1.23 g, 4.00 mmol) in 10 mL of DMF at 0°C. The resulting mixture was stirred at room temperature overnight. The mixture was filtered and concentrated *in vacuo*. The residue was suspended in 20 mL of THF and treated with TBAF (1 M in THF, 4.0 mL) at room temperature. After 15 minutes, the reaction was quenched with 25 mL of saturated aqueous ammonium chloride solution and diluted with 50 mL of diethyl ether. The phases were separated and the aqueous layer was extracted with three 50 mL portions of diethyl ether. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Chromatography on SiO_2 (100% hexanes to 10% diethyl ether in hexanes, gradient) afforded 550 mg of the title product (48% yield).

Example 46: Synthesis of 5-(5-Fluoro-2-methylphenyl)-2,5-dimethylhexan-3-one

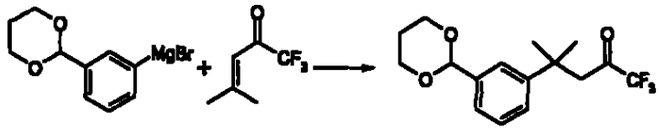


A solution of 1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-one (4.88 g, 18.6 mmol) was treated with sodium hydroxide solution (4 M in a mixture of 30% water in ethanol, 40 mL) at room temperature. The mixture was heated to 80°C for 1 hour. After cooling to room temperature, the mixture was diluted with 100 mL of water and extracted with three 100 mL portions of diethyl ether. The aqueous layer was treated with 150 mL of ethyl acetate and the resulting mixture was treated with 6 M HCl dropwise until the solution had a pH of 2. The phases were separated and the aqueous layer was extracted with three 100 mL portions of ethyl acetate. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated *in vacuo* to yield 3.92 g of 3-(5-fluoro-2-methylphenyl)-3-methylbutyric acid as an oil, which solidified upon standing and was used without further purification (quantitative yield).

A mixture of 3-(5-fluoro-2-methylphenyl)-3-methylbutyric acid (3.80 g, 18.0 mmol) in 15 mL of dichloromethane was treated with $SOCl_2$ (1.98 mL, 27.1 mmol) at 0°C. After 30 minutes, a mixture of morpholine (2.36 mL, 27.1 mmol) and pyridine (4.4 mL, 54.2 mmol) in 10 mL of dichloromethane was added to the reaction mixture at 0°C. After an additional 90 minutes, 60 mL of 2 M aqueous HCl solution was added, phases were separated and the aqueous layer was extracted with three 50 mL portions of dichloromethane. The combined organic phases were dried over magnesium sulfate, filtered, and concentrated *in vacuo* to give 5.03 g of 3-(5-fluoro-2-methylphenyl)-3-methyl-1-morpholin-4-ylbutan-1-one as an oil, which was used without further purification (quantitative yield).

A solution of 3-(5-fluoro-2-methylphenyl)-3-methyl-1-morpholin-4-ylbutan-1-one (200 mg, 0.716 mmol) in 2 mL of THF was treated with *i*-PrLi (0.7 M in pentane, 1.28 mL) at -78°C. The reaction mixture was stirred at -78°C for 1 hour, allowed to warm to room temperature, quenched with 1 mL of methanol and 5 mL of saturated aqueous ammonium chloride solution, and extracted with three 50 mL portions of ethyl acetate. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Chromatography on SiO_2 (100% hexanes to 25% ethyl acetate in hexanes, gradient) afforded 80.4 mg of the title product (48% yield).

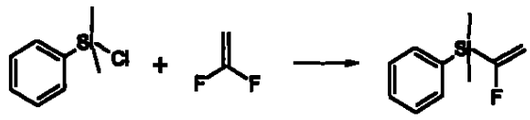
Example 47: Synthesis of 4-(3-[1,3]Dioxan-2-ylphenyl)-1,1,1-trifluoro-4-methylpentan-2-one



A solution of the Grignard reagent (generated from the reaction of 2-(3-bromophenyl)-[1,3]dioxane with magnesium turnings in THF, 0.25 M, 52.6 mL, 13.1 mmol) was treated with copper (I) iodide (2.5 g, 13.1 mmol) at 0°C. After 45 minutes, 1,1,1-trifluoro-4-methylpent-3-en-2-one (2 g, 13.1 mmol) was added, and the reaction mixture was slowly warmed to room temperature and stirred overnight. The mixture was quenched with aqueous saturated ammonium chloride solution and extracted with ethyl acetate. The combined organic layers were washed with aqueous saturated sodium chloride solution, dried with sodium sulfate, filtered, and concentrated *in vacuo*. The residue was triturated with hexanes and filtered. The

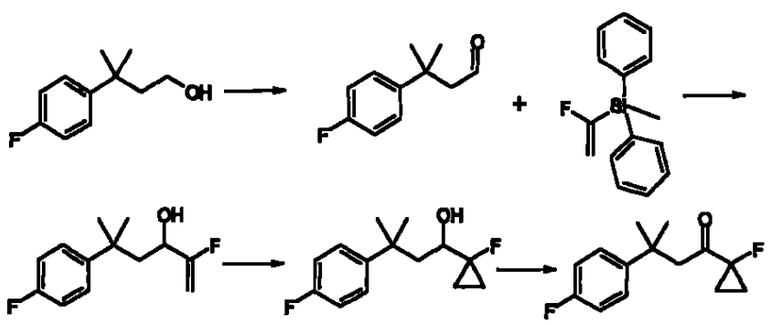
filtrate was concentrated *in vacuo* to give 1.78 g of the crude product, which was used without purification.

Example 48: Synthesis of (1-Fluorovinyl)dimethylphenylsilane



To a suspension of 4.4 g of lithium wire cut into small pieces in 200 mL of anhydrous THF stirred under argon and cooled on ice (internal temperature <10°C) was added dimethylphenylchlorosilane in 5 mL portions over 1 hour. The deep red color of the silyl lithium reagent appeared after approximately 0.75 hour. The mixture was stirred on ice for an additional 5 hours (internal temperature remained between 5°C and 10°C). The mixture was cooled on a dry ice/acetone bath and 1,1-difluoroethylene was introduced by filling a balloon connected to the reaction mixture and the reagent cylinder using a three-way valve. The balloon was filled with 1,1-difluoroethylene and emptied into the reaction mixture 10 times. The mixture was allowed to warm to room temperature (effervescence observed, probably from unreacted 1,1-difluoroethylene). The mixture was diluted with 200 mL of hexanes and filtered through a cotton wool plug. The filtrate was washed with water, dried, filtered, and concentrated *in vacuo*. Four fractional distillations under vacuum through a Vigreux column gave 4.6 g of product.

Example 49: Synthesis of 1-(1-Fluorocyclopropyl)-3-(4-fluorophenyl)-3-methylbutan-1-one



12 mL of a 2 M solution of oxalyl chloride in dichloromethane was diluted with 19 mL of dichloromethane and cooled on a dry ice/acetone bath. To this solution was added a dropwise a solution of 3.6 mL of DMSO in 16 mL of dichloromethane. After 10 minutes, a solution of 3-(4-fluorophenyl)-3-methylbutan-1-ol (3.6 g, 19.8 mmol) in 12 mL of dichloromethane was added and the mixture was stirred for 15 minutes. 14 mL of triethylamine was then added, the cooling bath was removed, and the reaction mixture was allowed to warm to room temperature and was quenched with water and diluted with hexanes. The organic layer was separated, washed with water, dried, filtered, and concentrated *in vacuo*. The residue was purified by chromatography over silica gel (eluent: hexanes to hexanes-dichloromethane (9:1), gradient) to give 1.2 g of 3-(4-fluorophenyl)-3-methylbutyraldehyde as an oil.

To a mixture of 3-(4-fluorophenyl)-3-methylbutyraldehyde (1.2 g, 6.6 mmol) and (1-fluorovinyl)methyldiphenylsilane in 5 mL of THF cooled on ice under nitrogen gas was added 1 mL of TBAF (1 M in THF). The mixture was allowed to warm to room temperature and left overnight. The solvent was evaporated and the residue was taken up in hexanes. The hexane soluble material was fractionated over silica gel (eluent: hexanes to hexanes-ethyl acetate (98:2)) to give a fraction (3.1 g) containing silylated product along with other silanes. This fraction was dissolved in 5 mL of THF and 10 mL of TBAF solution (1 M in THF) was added. The mixture was left at room temperature for 20 minutes, diluted with hexanes-ethyl acetate, and washed with water, dried, filtered, and concentrated *in vacuo*. Fractionation of the residue over silica gel (eluent: hexanes-ethyl acetate (99:1 to 9:1 gradient)) gave 1.73 g of the crude 2-fluoro-5-(4-fluorophenyl)-5-methylhex-1-en-3-ol as an oil which was used without additional purification.

To the above crude 2-fluoro-5-(4-fluorophenyl)-5-methylhex-1-en-3-ol (1.73 g, 7.65 mmol) stirred under nitrogen gas and cooled on ice, was added diethyl zinc (1.1 M in toluene, 8.0 mL). After 5 minutes, 1.0 mL of diiodomethane was added dropwise over 20 minutes and the mixture was stirred and allowed to come to room temperature and then stirred at room temperature for 4 days. 0.5 mL of water was then added to the reaction mixture, followed by ethyl acetate. The resulting mixture was then filtered through diatomaceous earth and the solvent was removed *in vacuo* and the residue was fractionated over silica gel (hexanes-

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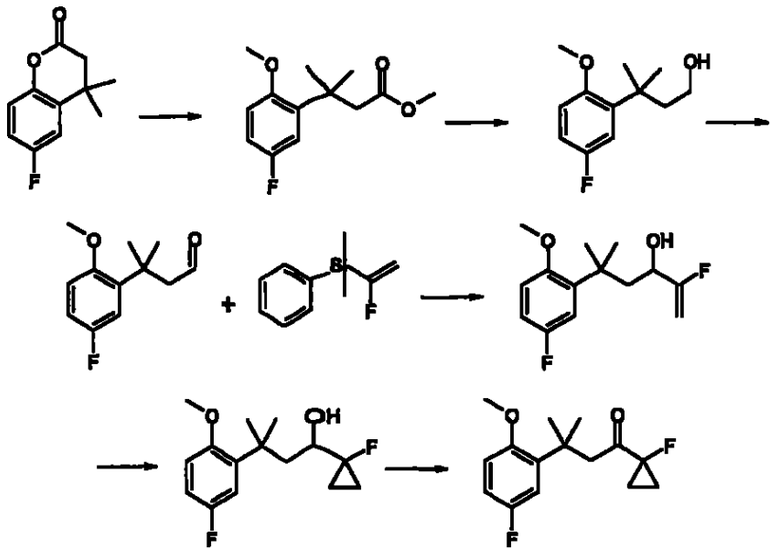
dichloromethane (1:1) to dichloromethane gradient) to give 1-(1-fluorocyclopropyl)-3-(4-fluorophenyl)-3-methylbutan-1-ol as an oil.

2.2 mL of a 2 M solution of oxalyl chloride in dichloromethane was diluted with 2.5 mL of dichloromethane and cooled on dry ice/acetone bath. To this solution was added a dropwise a solution of 0.7 mL of DMSO in 2.5 mL of dichloromethane. After 10 minutes, a solution of the above crude 1-(1-fluorocyclopropyl)-3-(4-fluorophenyl)-3-methylbutan-1-ol (0.72 g, 3.0 mmol) in 2 mL of dichloromethane was added and the mixture was stirred for 15 minutes. 4 mL of triethylamine was added, the cooling bath was removed, the mixture was allowed to warm to room temperature and was then quenched with water and diluted with hexanes. The organic layer was separated, washed with water, dried, filtered, and concentrated *in vacuo*. The residue was purified by chromatography over silica gel (eluent: hexanes to hexanes-dichloromethane (4:1) gradient) to give 0.37 g of the title product as an oil.

Example 50: Synthesis of 1-(1-Fluorocyclopropyl)-3-(5-fluoro-2-methoxyphenyl)-3-methylbutan-1-one



To a solution of 6-fluoro-4,4-dimethylchroman-2-one in 40 mL of DMSO was added a solution of 5.5 g of sodium hydroxide in 5 mL of water over 5 minutes (an exothermic reaction). After 20 minutes, methyl iodide (20 g) was added portionwise over 15 minutes and the mixture was

stirred at room temperature overnight. The mixture was diluted with hexanes, washed with water, dried, filtered, and concentrated *in vacuo* to give 12.4 g of the ester which was used without additional purification.

To a suspension of LAH (1.64 g) in 100 mL of THF stirred under argon was added dropwise over 30 minutes a solution of the above 3-(5-fluoro-2-methoxyphenyl)-3-methylbutyric acid methyl ester in 10 mL of THF (vigorous reaction). The mixture was stirred at room temperature overnight. The reaction was diluted with 200 mL of diethyl ether and quenched by the addition of 3 mL of water (added cautiously) and 3 mL of acetic acid. The mixture was filtered through diatomaceous earth and washed through with diethyl ether. Evaporation of the solvent gave 10.8 g of 3-(5-fluoro-2-methoxyphenyl)-3-methylbutan-1-ol, which was used without additional purification.

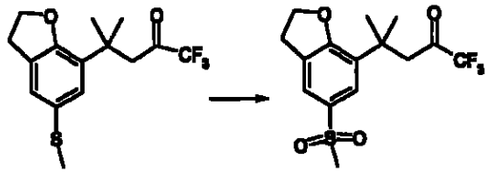
A solution of 3-(5-fluoro-2-methoxyphenyl)-3-methylbutan-1-ol (3.30 g, 15.5 mmol) in 40 mL of dichloromethane was treated with pyridinium chlorochromate (4.2 g, 19.5 mmol) portionwise over 5 minutes. The mixture was stirred for 3 hours, filtered through pad of CELITE® filter aid and the pad was wash with hexanes. The filtrate was concentrated *in vacuo*. Chromatography on SiO_2 (30% to 50% dichloromethane in hexanes, gradient) gave 2.5 g of 3-(5-Fluoro-2-methoxyphenyl)-3-methylbutyraldehyde as an oil (77% yield).

To a solution of 3-(5-fluoro-2-methoxyphenyl)-3-methylbutyraldehyde (1.1 g, 5.2 mmol) and the above (1-fluorovinyl)dimethylphenylsilane (2.2 g, 12.2 mmol) in 5 mL of THF was added 0.6 mL of tetrabutylammonium fluoride (1 M in THF) and the mixture was stirred at room temperature overnight. TLC showed partial conversion to product. Cesium fluoride (0.22 g) was added and the mixture was stirred at room temperature for 3 days. 2 mL of water and 2 mL of acetic acid were added and the mixture was warmed at 60°C for 2 hours to effect desilylation of any silylated product. The mixture was diluted with ethyl acetate, washed with water, dried, filtered and concentrated *in vacuo*. Fractionation of the residue over silica gel (eluent: hexanes-dichloromethane (3:1 to 1:3 gradient) gave 0.798 g (59.5% yield) of 2-fluoro-5-(5-fluoro-2-methoxyphenyl)-5-methylhex-1-en-3-ol as an oil which was used without additional purification.

To 2-fluoro-5-(5-fluoro-2-methoxyphenyl)-5-methylhex-1-en-3-ol, stirred under nitrogen gas and cooled on ice, was added 8.0 mL of diethyl zinc (1.1 M in toluene). After 5 minutes, 1.0 mL of diiodomethane was added dropwise over 20 minutes, and the mixture was stirred and allowed to come to room temperature and then stirred at room temperature for 2 days. Then 0.5 mL of water was added, followed by ethyl acetate, and the mixture was filtered through diatomaceous earth. The product was concentrated *in vacuo* and the residue was fractionated over silica gel (hexanes-dichloromethane (1:1) to dichloromethane, gradient) to give 0.8 g of 1-(1-fluorocyclopropyl)-3-(5-fluoro-2-methoxyphenyl)-3-methylbutan-1-ol as an oil which was used without additional purification.

6 mL of a 2 M solution of oxalyl chloride in dichloromethane was diluted with 5 mL of dichloromethane and cooled on dry ice/acetone bath. To this solution was added dropwise a solution of 1.5 mL of DMSO in 5 mL of dichloromethane. After 10 minutes, a solution of the crude 1-(1-fluorocyclopropyl)-3-(5-fluoro-2-methoxyphenyl)-3-methylbutan-1-ol (0.8 g, 3 mmol) in 4 mL of dichloromethane was added and the mixture was stirred for 15 minutes. 4 mL of triethylamine was added, the cooling bath was removed, and the reaction mixture was allowed to warm to room temperature, quenched with water, and diluted with hexanes. The organic layer was separated, washed with water, dried, filtered, and concentrated *in vacuo*. The residue was purified by chromatography over silica gel (eluent: hexanes to hexanes-ethyl acetate (10:1), gradient) to give 0.68 g of the title product as an oil which was used without additional purification.

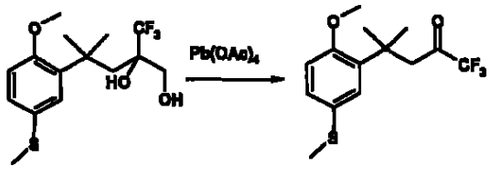
Example 51: Synthesis of 1,1,1-Trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-one



A stirred solution of 1,1,1-trifluoro-4-methyl-4-(5-methylsulfanyl-2,3-dihydrobenzofuran-7-yl)pentan-2-one (5.3 g, 16.7 mmol) in acetonitrile was slowly added a solution of $NaIO_4$ (10.7 g, 50 mmol) in 70 mL of water. After 10 minutes, $RuCl_3$ (50 mg, 0.24 mmol) was added and the stirring was continued at room temperature for 30 minutes. The mixture was concentrated

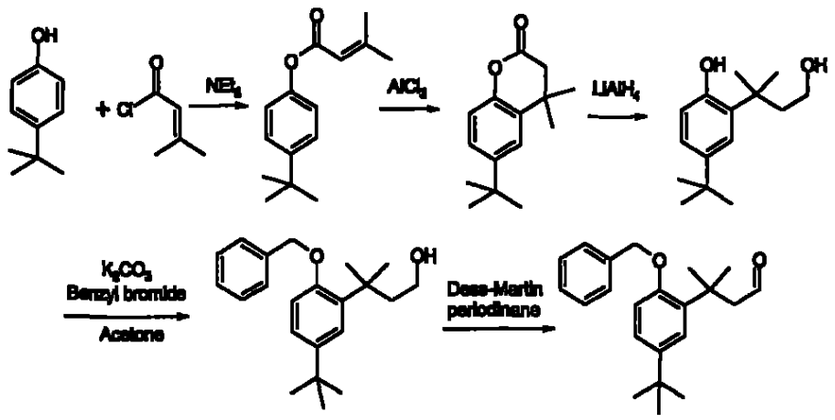
in vacuo, and the resulting greyish solid was filtered, washed with water, and dried to give 5.4 g of the title product, which was used without further purification (93% yield).

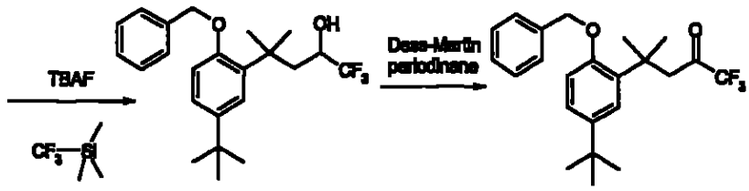
Example 52: Synthesis of 1,1,1-Trifluoro-4-(2-methoxy-5-methylsulfanylphenyl)-4-methylpentan-2-one



To a solution of 4-(2-methoxy-5-methylsulfanylphenyl)-4-methyl-2-trifluoromethylpentane-1,2-diol (1.5 g, 5.3 mmol) in 25 mL of methanol was added 2.4 g of lead (IV) acetate ($Pb(OAc)_4$) and the reaction mixture was stirred until TLC indicated the reaction was complete, after several hours. The reaction mixture was then filtered through a bed of diatomaceous earth and the filtrate was concentrated *in vacuo* to afford 1.12 g (83.8% yield) of 1,1,1-trifluoro-4-(2-methoxy-5-methylsulfanylphenyl)-4-methylpentan-2-one.

Example 53: Synthesis of 4-(2-Benzyloxy-5-*tert*-butylphenyl)-1,1,1-trifluoro-4-methylpentan-2-one





To a chilled solution of 4-*tert*-butylphenol (15 g, 100 mmol) and 11.12 mL of 3-methylbut-2-enoyl chloride in 200 mL of diethyl ether at 0°C was added 13.9 mL of triethylamine by addition funnel. The reaction mixture was warmed to room temperature and stirred until TLC indicated the reaction was complete. The reaction mixture was then filtered through diatomaceous earth, and the diethyl ether layer was washed two times with water, washed with brine, dried over magnesium sulfate, and concentrated *in vacuo* to leave 23 g of 3-methylbut-2-enoic acid 4-*tert*-butylphenyl ester as a brown oil that partially crystallized upon standing.

To a solution of 3-methylbut-2-enoic acid 4-*tert*-butylphenyl ester (23 g, 99 mmol) in 50 mL of carbon disulfide (CS_2) was added 19.8 g of aluminum chloride ($AlCl_3$) portionwise over the course of 1 hour, a very exothermic reaction. After stirring for several hours, TLC showed the reaction was complete. The reaction mixture was concentrated under a stream of nitrogen gas, and the residue poured over ice and extracted with ethyl acetate. The organics were combined, dried over magnesium sulfate, and concentrated *in vacuo*. The residue was purified on silica pad (0% to 5% ethyl acetate-hexanes) to give 8.1 g of 6-*tert*-butyl-4,4-dimethylchroman-2-one as an oil.

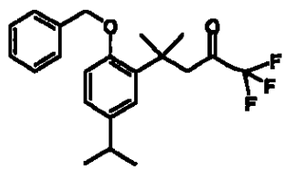
To a chilled suspension of 1.99 g of LAH in 60 mL of THF at 0°C was added a solution of 6-*tert*-butyl-4,4-dimethylchroman-2-one (8.1 g, 34.9 mmol) in 10 mL of THF by addition funnel. The reaction mixture was warmed to room temperature and stirred until TLC indicated the reaction was complete. After 1 hour, the reaction mixture was cooled in ice bath and carefully quenched with a minimum amount of water. The reaction mixture was then dried over magnesium sulfate and filtered through diatomaceous earth. The filtrate was concentrated *in vacuo*, the residue was taken up in hexanes, and the solids isolated by filtration to afford 5 g of 4-*tert*-butyl-2-(3-hydroxy-1,1-dimethylpropyl)phenol.

To a solution of 4-*tert*-butyl-2-(3-hydroxy-1,1-dimethylpropyl)phenol (2 g, 8.5 mmol) and 1.1 mL benzyl bromide in 10 mL of DMF was added 1.75 g of potassium carbonate (K_2CO_3) and the reaction mixture stirred at room temperature until TLC indicated that the reaction was complete. After stirring overnight, the reaction mixture was diluted with ice and extracted with diethyl ether. The organics were combined, washed four times with water, washed with brine, dried over magnesium sulfate, and concentrated *in vacuo*. The residue was purified on COMBIFLASH® apparatus (0% to 30% ethyl acetate-hexanes) to give 1.7 g of 3-(2-benzyloxy-5-*tert*-butylphenyl)-3-methylbutan-1-ol as an oil.

To a solution of 3-(2-benzyloxy-5-*tert*-butylphenyl)-3-methylbutan-1-ol (1.7 g, 5.2 mmol) in 20 mL of dichloromethane was added 3.27 g of Dess-Martin periodinane and reaction stirred until TLC indicated the reaction was complete. After 2 hours, the reaction mixture was passed through a pad of silica, eluting with 5% ethyl acetate-hexanes to afford 1.67 g of 3-(2-benzyloxy-5-*tert*-butylphenyl)-3-methylbutyraldehyde as an oil.

3-(2-Benzyloxy-5-*tert*-butylphenyl)-3-methylbutyraldehyde was converted to 4-(2-benzyloxy-5-*tert*-butylphenyl)-1,1,1-trifluoro-4-methylpentan-2-one using similar procedures as in Example 4 of U.S. Patent Application Pub. No. 2004/0023999.

Example 54: Synthesis of 4-(2-Benzyloxy-5-isopropylphenyl)-1,1,1-trifluoro-4-methylpentan-2-one



4-(2-Benzyloxy-5-isopropylphenyl)-1,1,1-trifluoro-4-methylpentan-2-one was prepared from 4-isopropylphenol in the same manner as described in the synthesis of 4-(2-benzyloxy-5-*tert*-butylphenyl)-1,1,1-trifluoro-4-methylpentan-2-one.

Example 55: Synthesis of 7-(4,4,4-Trifluoro-3-hydroxy-3-hydroxymethyl-1,1-dimethyl-butyl)-2,3-dihydrobenzofuran-5-sulfonic acid dimethylamide

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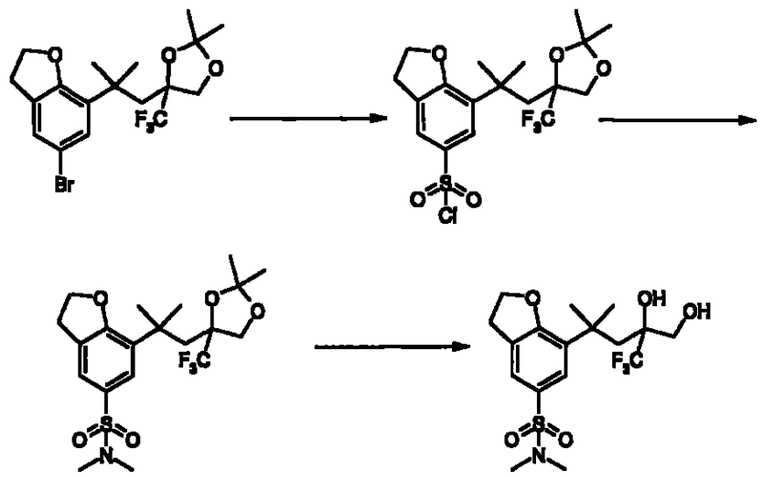


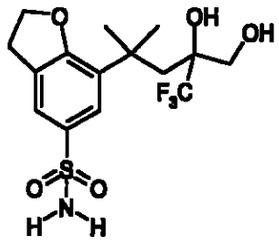
A solution of 5-bromo-7-[2-(2,2-dimethyl-4-trifluoromethyl-[1,3]dioxolan-4-yl)-1,1-dimethylethyl]-2,3-dihydrobenzofuran (4.0 g, 9.4 mmol) in 8 mL of THF was treated with *n*-BuLi (2.5 M in hexanes, 4.2 mL, 10.5 mmol) at -78°C. After 15 minutes, an excess of SO_2 gas was bubbled into the mixture and the reaction was monitored for the disappearance of the starting material. Next, the reaction mixture was concentrated under a stream of nitrogen gas, diluted with THF, and treated with *N*-chlorosuccinimide (1.48 g, 11.1 mmol). The mixture was stirred for 15 minutes and divided into three equal portions. A stock solution of sulfonyl chloride (1/3 of the mixture) in 8 mL of THF was treated with dimethylamine (2 M in THF, 10 mL, 20 mmol). After 30 minutes, the mixture was diluted with 20 mL of saturated aqueous ammonium chloride solution and extracted with three 10 mL portions of ethyl acetate. The combined organic layers were washed with three 10 mL portions of saturated aqueous ammonium chloride solution, two 10 mL portions of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude material was purified on silica gel (3% to 30% ethyl acetate in hexanes, gradient) to afford 1.18 g (83% yield) of 7-[2-(2,2-dimethyl-4-trifluoromethyl-[1,3]dioxolan-4-yl)-1,1-dimethyl-ethyl]-2,3-dihydrobenzofuran-5-sulfonic acid dimethylamide, which was used without further purification.

A mixture of 1.18 g (2.61 mmol) of 7-[2-(2,2-dimethyl-4-trifluoromethyl-[1,3]dioxolan-4-yl)-1,1-dimethyl-ethyl]-2,3-dihydrobenzofuran-5-sulfonic acid dimethylamide and 303 mg (1.59 mmol) of *p*-toluenesulfonic acid monohydrate in 20 mL of methanol was warmed at reflux for 3 days. The mixture was then cooled and diluted with 15 mL of saturated aqueous sodium

bicarbonate and extracted with three 15 mL portions of ethyl acetate. The combined organic layers were washed with two 15 mL portions of saturated aqueous sodium bicarbonate, two 15 mL portions of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The residue was triturated with ether to afford 845 mg (78% yield) of the title compound as a white solid.

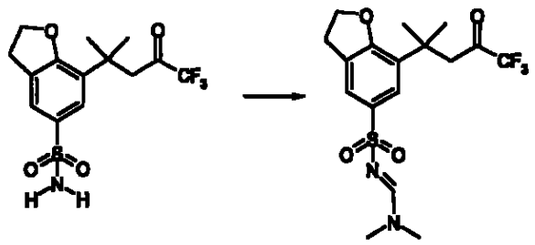
7-(4,4,4-Trifluoro-3-hydroxy-3-hydroxymethyl-1,1-dimethyl-butyl)-2,3-dihydrobenzofuran-5-sulfonic acid dimethylamide was converted to the corresponding trifluoromethyl ketone according to the method disclosed in U.S. Patent Application Pub. No. 2004/0029932, which is hereby incorporated by reference.

Example 56: Synthesis of 7-(4,4,4-Trifluoro-3-hydroxy-3-hydroxymethyl-1,1-dimethylbutyl)-2,3-dihydrobenzofuran-5-sulfonic acid amide



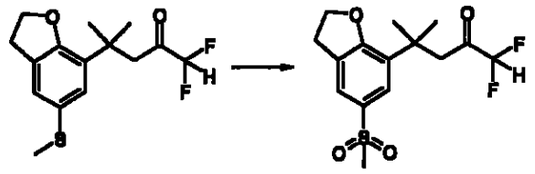
7-(4,4,4-Trifluoro-3-hydroxy-3-hydroxymethyl-1,1-dimethylbutyl)-2,3-dihydrobenzofuran-5-sulfonic acid amide was prepared from 5-bromo-7-[2-(2,2-dimethyl-4-trifluoromethyl-[1,3]dioxolan-4-yl)-1,1-dimethylethyl]-2,3-dihydrobenzofuran in the same manner as in the preparation of 7-(4,4,4-trifluoro-3-hydroxy-3-hydroxymethyl-1,1-dimethylbutyl)-2,3-dihydrobenzofuran-5-sulfonic acid dimethylamide.

Example 57: Synthesis of 7-(4,4,4-Trifluoro-1,1-dimethyl-3-oxobutyl)-2,3-dihydrobenzofuran-5-sulfonic acid 1-dimethylaminometh-(*E*)-ylideneamide



A solution of 7-(4,4,4-trifluoro-1,1-dimethyl-3-oxobutyl)-2,3-dihydrobenzofuran-5-sulfonic acid amide (870 mg, 2.47 mmol) in 30 mL of dichloromethane was reacted with *N,N*-dimethylforamide dimethyl acetal (580 mg, 4.86 mmol). After 30 minutes, the mixture was concentrated *in vacuo* to dryness. The resulting solid was triturated with diethyl ether and collected to afford 950 mg of the title compound (94% yield).

Example 58: Synthesis of 1,1-Difluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-one



To a solution of 1,1-difluoro-4-methyl-4-(5-methylsulfanyl-2,3-dihydrobenzofuran-7-yl)pentan-2-one (840 mg, 2.8 mmol) in 12 mL of MeCN and 4 mL of water was added sodium periodate (1.79 g, 8.4 mmol) followed by a crystal of ruthenium (III) chloride hydrate. The reaction was monitored by TLC until the thiol ether was no longer evident. After 1 hour, the reaction was concentrated *in vacuo*, diluted with water, and extracted with ethyl acetate. The combined organic layers were dried over magnesium sulfate, treated with carbon, filtered, and concentrated *in vacuo* to afford 910 mg (98% yield) of the title compound as a white solid.

Example 59: Synthesis of 4-Methoxy-3-methyl-3-phenylbutyraldehyde

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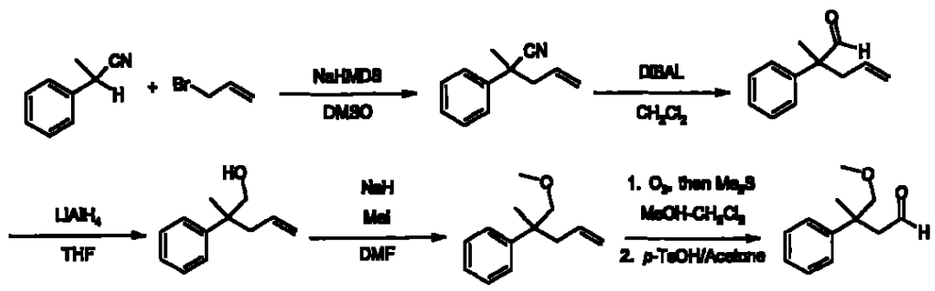

To a solution of 2-phenylpropionitrile (4.04 g, 30.79 mmol) in 40 mL of DMSO was added 34 mL (34 mmol) of a 1 M solution of sodium bis(trimethylsilyl)amide (NaHMDS) in THF over a 5 minute period. After 10 minutes, allyl bromide (6 mL, 69.33 mmol) was added dropwise (exothermic). The mixture was cooled with an ice-water bath. The mixture stirred for 20 minutes, becoming a solid mass. An additional 20 mL of DMSO was added. After 10 minutes, the mixture was diluted with 200 mL of ammonium chloride and extracted with three 100 mL portions of ethyl acetate. The combined organic layers were washed with six 75 mL portions of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo* to afford 5.25 g (99.5% yield) of 2-methyl-2-phenylpent-4-enenitrile as yellow oil which was used without further purification.

To a solution of 2-methyl-2-phenylpent-4-enenitrile (5.25 g, 30.65 mmol) in 150 mL of dichloromethane was added a 1 M solution of diisobutylaluminum hydride (DIBAL) (38 mL, 38 mmol) in dichloromethane over a 15 minute period. The reaction was monitored by TLC; after 1 hour, TLC (ethyl acetate-hexanes (1:9)) indicated a slightly less polar product. The reaction was poured into ice-cold 1 N aqueous HCl and the dichloromethane layer separated. The aqueous was extracted with two 50 mL portions of dichloromethane. The combined organic layers were washed with 50 mL of brine, two 50 mL portions of saturated aqueous sodium bicarbonate, 50 mL of brine, dried over magnesium sulfate, filtered through diatomaceous earth, and concentrated *in vacuo* to afford 4.6 g (86.1% yield) of 2-methyl-2-phenylpent-4-enal which was used without further purification.

To a solution of 2-methyl-2-phenylpent-4-enal (4.6 g, 26.4 mmol) in 100 mL of THF was added of lithium aluminum hydride (LAH) (2.6 g, 68.51 mmol) in several portions. The mixture stirred for 3 hours at room temperature and was then refluxed for 2 hours. The reaction

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was monitored by TLC with ethyl acetate-hexanes (1:9) indicating a new more polar product. The reaction was cooled and the excess LAH was cautiously quenched with water dropwise. The mixture was then diluted with 1 N aqueous HCl and extracted with 100 mL of hexanes and two 100 mL portions of ethyl acetate. The combined organic layers were washed with 50 mL of 1 N aqueous HCl, two 50 mL portions of brine, two 50 mL portions of saturated aqueous sodium bicarbonate, 50 mL of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude material was chromatographed on silica gel using hexanes to load the sample and then eluting with 1% to 15% ethyl acetate-hexanes to afford 3.2 g (68.8) of 2-methyl-2-phenylpent-4-en-1-ol.

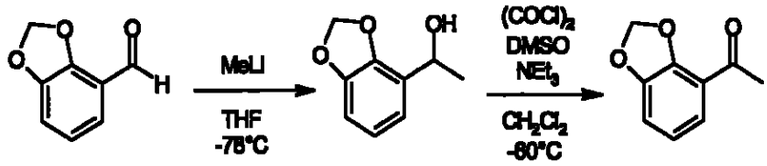
To a solution of 2-methyl-2-phenylpent-4-en-1-ol (3.2 g, 18.15 mmol) in 17 mL of DMF was added sodium hydride (1.25 g, 31.25 mmol, 60% in mineral oil). The mixture was stirred until foaming ceased and then methyl iodide (6 mL, 96 mmol) was added. After 2 hours, the mixture was quenched with 50 mL of saturated aqueous ammonium chloride solution and extracted with three 50 mL portions of ethyl acetate. The combined organic layers were washed with 30 mL of saturated aqueous ammonium chloride solution, five 25 mL portions of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo* to afford 3.4 g (98.4% yield) of (1-methoxymethyl-1-methylbut-3-enyl)benzene which was used without further purification.

To a chilled (-78°C) solution of (1-methoxymethyl-1-methylbut-3-enyl)benzene (1.67 g, 8.77 mmol) in methanol-dichloromethane was bubbled ozone gas until the solution turned blue. The excess ozone was then purged from the mixture with oxygen and then dimethyl sulfide (5 mL, 68 mmol) was added and the mixture was warmed to room temperature and stirred overnight. The mixture was then concentrated *in vacuo* to remove the excess dimethyl sulfide and diluted with 20 mL of ammonium chloride and extracted with three 15 mL portions of ethyl acetate. The combined organic layers were washed with three 15 mL portions of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo* to afford an oil which corresponded to the dimethyl acetal by ^{1}H-NMR. The crude product was diluted with 40 mL of acetone and *p*-TsOH (300 mg, 1.57 mmol) was added and the mixture was stirred at room temperature for 2 hours. The reaction was monitored by ^{1}H-NMR and indicated the presence of aldehyde and dimethyl acetal. The reaction was refluxed for 4 hours and monitored by TLC (ethyl acetate-hexanes (1:9)) and then cooled and diluted with saturated aqueous sodium

bicarbonate solution and extracted with three 15 mL portions of ethyl acetate. The combined organic layers were washed with two 10 mL portions of saturated aqueous sodium bicarbonate solution, two 10 mL portions of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo* to afford 1.45 g (85.9% yield) of 4-methoxy-3-methyl-3-phenylbutyraldehyde.

4-Methoxy-3-methyl-3-phenylbutyraldehyde was converted to 1,1,1-trifluoro-5-methoxy-4-methyl-4-phenylpentan-2-one as described previously in Example 26 of U.S. Patent Application Pub. No. 2004/0023999.

Example 60: Synthesis of 1-Benzo[1,3]dioxol-4-ylethanone



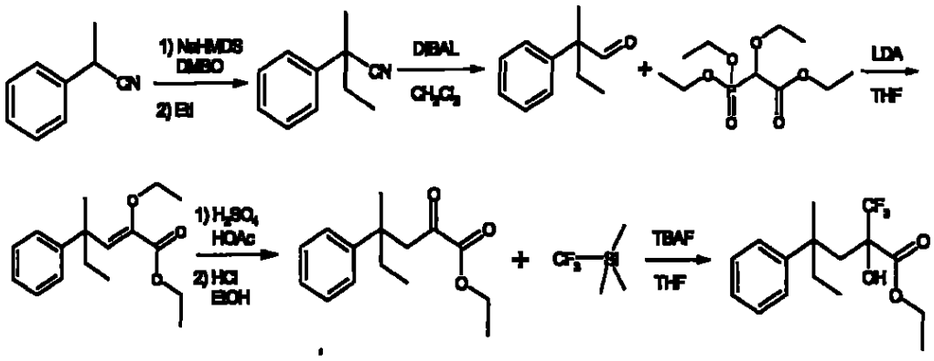
To a solution of benzo[1,3]dioxole-4-carbaldehyde (10 g, 66.7 mmol) in 200 mL THF at -78°C was added, via addition funnel, 43.7 mL of a 1.6 M MeLi solution in diethyl ether. The reaction was slowly warmed to room temperature and stirred overnight. A TLC of an aliquot showed reaction was complete. The reaction was then cooled to -78°C and quenched with saturated aqueous ammonium chloride and concentrated *in vacuo*. The residue was then extracted with ethyl acetate. The organics were combined, dried over magnesium sulfate, and concentrated *in vacuo* to give 11 g (99.4% yield) of 1-benzo[1,3]dioxol-4-ylethanol as a brown oil that crystallized upon standing.

To a solution of 1-benzo[1,3]dioxol-4-ylethanol (11 g, 66.3 mmol) in 100 mL of THF was added 17.26 g of manganese dioxide (MnO_2) in one portion and reaction was monitored by TLC. After several hours, TLC showed some product but significant alcohol left. More manganese dioxide was added and the solution stirred. TLC then showed mostly product but a significant amount of alcohol. The reaction mixture was then filtered through a bed of diatomaceous earth and the filtrate was concentrated *in vacuo* to give an oil that mostly crystallized on standing. To 9.24 mL of a solution of oxalyl chloride in 120 mL of dichloromethane at -60°C was added a solution of 15 mL of DMSO in 20 mL of dichloromethane. After 10 minutes, a solution of above alcohol/ketone mixture (53 mmol) in

20 mL of dichloromethane was added, followed 15 minutes later by 44.3 mL of triethylamine. The reaction was allowed to slowly warm to room temperature overnight. The reaction mixture was then poured onto ice and the organic layer was washed with five 100 mL portions of water, then brine, and then dried over magnesium sulfate. The organics were concentrated *in vacuo* to leave tan solids and the solids were triturated with hexanes, collected by filtration, and dried to give 9.33 g (85.8% yield) of 1-benzo[1,3]dioxol-4-ylethanone.

1-Benzo[1,3]dioxol-4-ylethanone was converted to 4-benzo[1,3]dioxol-4-yl-1,1,1-trifluoro-4-methylpentan-2-one according to Example 26 of U.S. Patent Application Pub. No. 2004/0023999.

Example 61: Synthesis of 2-Hydroxy-4-methyl-4-phenyl-2-trifluoromethylhexanoic acid ethyl esters



To a solution of 2-phenylpropionitrile (5 g, 38 mmol) in 50 mL of DMSO was added 42 mL of 1 M THF solution of sodium bis(trimethylsilyl)amide (NaHMDS). After 15 minutes, the reaction was cooled to 0°C and 4.6 mL of ethyl iodide was added. The reaction was then stirred for 30 minutes. As TLC showed the reaction was complete, the reaction mixture was poured into water and extracted with diethyl ether. The organics were combined, washed four times with water, washed with brine, dried over magnesium sulfate, and concentrated *in vacuo* to give 6.1 g of 2-methyl-2-phenylbutyronitrile as an oil.

To a solution of 2-methyl-2-phenylbutyronitrile (6.1 g, 38.3 mmol) in 50 mL of dichloromethane at room temperature was added 57 mL of 1 M DIBAL in dichloromethane via syringe. The reaction was stirred for 30 minutes, at which time TLC of aliquot showed the

reaction was complete. The reaction mixture was carefully poured into 100 mL of 1 N HCl and the layers were separated. The organics were concentrated *in vacuo* and taken up in diethyl ether, combined with the aqueous layer, and extracted with diethyl ether. The organics were then combined, dried over magnesium sulfate, and concentrated *in vacuo*. The residue was purified on silica gel column (0% to 2% ethyl acetate in hexanes) to give 4.2 g of 2-methyl-2-phenylbutyraldehyde as colorless oil.

To a solution of (diethoxyphosphoryl)ethoxyacetic acid ethyl ester (7.4 g, 27.6 mmol) in 30 mL of THF, at 0°C, was added 16 mL of 1.8 M LDA in heptane/THF/ethylbenzene. The reaction mixture was stirred for 30 minutes and then a solution of 2-methyl-2-phenylbutyraldehyde (4.2 g, 25.9 mmol) in 30 mL of THF was added dropwise by syringe. The reaction mixture was then warmed to room temperature, quenched with saturated aqueous ammonium chloride solution, and extracted with diethyl ether. The organics were combined, dried over magnesium sulfate and concentrated *in vacuo* to give 8.3 g of a 2:1 mixture of *E* and *Z* isomers of 2-ethoxy-4-methyl-4-phenylhex-2-enoic acid ethyl ester as orange oil.

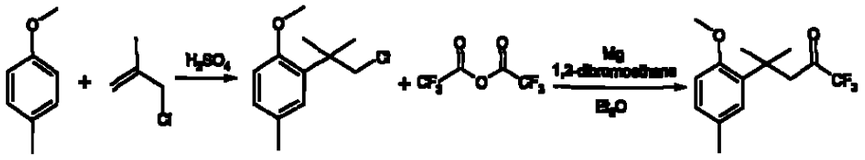
To a solution of 2-ethoxy-4-methyl-4-phenylhex-2-enoic acid ethyl ester (8.3 g, 30 mmol) in 25 mL of HOAc was added 116.5 mL of aqueous 1 M sulfuric acid solution. The reaction mixture was stirred at room temperature for several hours. As TLC showed no reaction, the reaction mixture was placed in a 100°C oil bath and stirred overnight. As TLC was then inconclusive, 2 mL more aqueous 1 M sulfuric acid and 20 mL of HOAc were added. After 1 hour, TLC of an aliquot showed major olefin isomer (more polar spot) consumed and minor isomer spot remaining (product may co-spot with minor isomer). The reaction mixture was then cooled to room temperature and extracted with diethyl ether. Organics were combined, washed with four portions of water, washed with brine, dried over magnesium sulfate, and concentrated *in vacuo* to afford 2.5 g of an orange oil. ^{1}H-NMR showed 1:1 mixture of minor isomer and aldehyde. The aqueous layer was extracted with ethyl acetate and the ethyl acetate extracts were combined, dried over magnesium sulfate, and concentrated *in vacuo* to leave a brown liquid. ^{1}H-NMR showed significant ethyl acetate and HOAc and desired product as the ketoacid. The ketoacid solution was taken up in 200 mL of ethanol, treated with 1 mL of concentrated HCl, and heated to reflux overnight. TLC then showed a new, less polar spot. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. The residue was then diluted with

water and extracted with diethyl ether. The organics were combined, dried over magnesium sulfate, and concentrated *in vacuo* to leave 4.3 g of 4-methyl-2-oxo-4-phenylhexanoic acid ethyl ester as an orange oil.

To a solution of 4-methyl-2-oxo-4-phenylhexanoic acid ethyl ester (4.3 g, 17.3 mmol) and 3.6 mL of trifluoromethyltrimethylsilane in 50 mL of THF was added 1.5 mL (0.1 equiv) of 1 M TBAF solution and reaction stirred at room temperature until the ketoester was shown to be consumed by TLC, about 30 minutes. The remainder of the TBAF (17.5 mL) was then added and the reaction mixture stirred for 1 hour. TLC then showed the reaction was complete. The reaction mixture was concentrated *in vacuo*, the residue diluted with 1 N HCl and extracted with diethyl ether. The organics were combined, dried over magnesium sulfate, and concentrated *in vacuo* to leave a brown oil. The oil was taken up in hexanes (cloudy appearance), activated charcoal was added, and the resulting solution filtered through diatomaceous earth and concentrated *in vacuo* to leave 3.8 g (83% yield) of a diastereomeric mixture of 2-hydroxy-4-methyl-4-phenyl-2-trifluoromethylhexanoic acid ethyl esters as a light green oil.

The diastereomeric mixture of esters was converted to the corresponding trifluoromethyl ketone according to Example 1 of U.S. Patent Application Pub. No. 2004/0023999.

Example 62: Synthesis of 1,1,1-Trifluoro-4-(2-methoxy-5-methylphenyl)-4-methylpentan-2-one

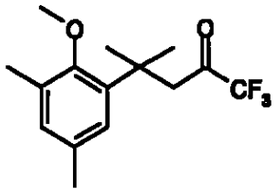


To a yellow solution of 4-methylanisole (20 g, 183.5 mmol) and 1.7 mL of concentrated sulfuric acid was added 19.17 mL of 3-chloro-2-methylpropene by addition funnel. The reaction became warm and turned dark purple. After 20 minutes, solids began to precipitate. TLC of an aliquot showed some starting anisole left and a new, slightly less polar spot forming. The reaction mixture was stirred overnight and TLC then showed that the reaction was complete. The reaction mixture was poured onto ice and extracted with diethyl ether. The

organics were combined, dried over magnesium sulfate, and concentrated *in vacuo* to leave an oil. The residue was taken up in hexanes, cooled to -78°C, and the solids collected by filtration to give 14 g of 2-(2-chloro-1,1-dimethylethyl)-1-methoxy-4-methylbenzene as an oil upon warming. The filtrate was concentrated *in vacuo* to give 15.5 g of a 4:1 mixture of product and starting anisole.

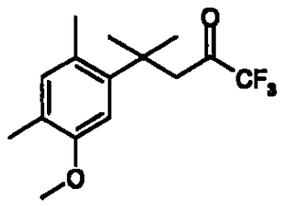
To a suspension of magnesium turnings (1.87 g) in 30 mL of anhydrous diethyl ether under argon in a water bath was added 1.62 mL of dibromoethane slowly by syringe such that the internal reaction temperature did not go above 27°C. A solution of 2-(2-chloro-1,1-dimethylethyl)-1-methoxy-4-methylbenzene (4 g, 18.9 mmol) and additional dibromoethane (1.62 mL) in 20 mL of diethyl ether was added by addition funnel at a rate that kept the internal temperature below 25°C. The reaction mixture became green and a fine precipitate formed. After 1 hour, the reaction mixture was cooled to -78°C; solids clumped on the bottom of the reaction mixture and stirring was stopped. A solution of 3.98 mL of trifluoroacetic anhydride in 4 mL of diethyl ether was added to the reaction mixture by addition funnel while swirling the reaction mixture by hand. The reaction mixture was then warmed to room temperature, stirring resumed above -40°C. TLC of an aliquot showed a new slightly more polar spot and starting material. The reaction mixture was then poured onto cold 1 N HCl and extracted with diethyl ether. The organics were combined, dried over magnesium sulfate, and concentrated *in vacuo*. The residue was purified on silica gel column (0% to 5% ethyl acetate-hexanes) to give 1.7 g (41% yield) of 1,1,1-trifluoro-4-(2-methoxy-5-methylphenyl)-4-methylpentan-2-one as a clear oil.

Example 63: Synthesis of 1,1,1-Trifluoro-4-(2-methoxy-3,5-dimethylphenyl)-4-methylpentan-2-one



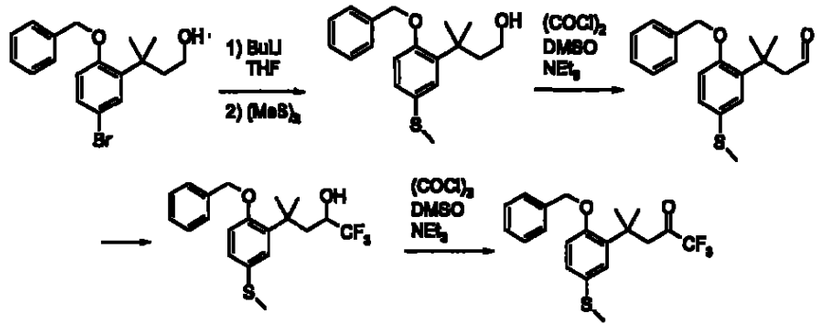
The title product was prepared from 1-methoxy-2,4-dimethylbenzene according to the same procedure described in the synthesis of 1,1,1-trifluoro-4-(2-methoxy-5-methylphenyl)-4-methylpentan-2-one.

Example 64: Synthesis of 1,1,1-Trifluoro-4-(5-methoxy-2,4-dimethylphenyl)-4-methylpentan-2-one



The title product was prepared from 1-methoxy-2,4-dimethylbenzene according to the same procedure described in the synthesis of 1,1,1-trifluoro-4-(2-methoxy-5-methylphenyl)-4-methylpentan-2-one.

Example 65: 4-(2-benzyloxy-5-methylsulfanylphenyl)-1,1,1-trifluoro-4-methylpentan-2-one



To a solution of 3-(2-benzyloxy-5-bromophenyl)-3-methylbutan-1-ol (3 g, 8.6 mmol) in 50 mL of THF at -78°C was added 7.56 mL of *n*-BuLi (2.5 M solution in hexanes) and the reaction mixture was stirred for 10 minutes. Then 1.55 mL of dimethyldisulfide was added and the reaction mixture was warmed to room temperature. After 20 minutes, TLC showed a new, slightly more polar spot (major) with very little else. The reaction mixture was then quenched with saturated aqueous ammonium chloride solution and extracted with diethyl ether. The

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organics were combined, dried over magnesium sulfate, and concentrated *in vacuo* to 2.84 g of 3-(2-benzyloxy-5-methylsulfanylphenyl)-3-methylbutan-1-ol as an oil.

To a solution of 1.57 mL of oxalyl chloride in 15 mL of dichloromethane at -60°C was added a solution of 2.55 mL of DMSO in 5 mL of dichloromethane. After 10 minutes, a solution of 3-(2-benzyloxy-5-methylsulfanylphenyl)-3-methylbutan-1-ol (2.84 g, 8.9 mmol) in 5 mL of dichloromethane was added (solids quickly precipitated), followed 15 minutes later by 7.5 mL triethylamine and the reaction mixture became very thick with solids. The reaction mixture was then warmed to room temperature and monitored by TLC. After 1 hour, TLC of an aliquot showed reaction was complete, so water was added to the reaction mixture and the resulting layers were separated. The aqueous layer was washed with dichloromethane and the organics were combined, washed four times with water, washed with brine, dried over magnesium sulfate, and concentrated *in vacuo* to afford a yellow oil. The residue was purified on SiO_2 (0% to 10% ethyl acetate-hexanes) to give 2.2 g (78.7% yield) of 3-(2-benzyloxy-5-methylsulfanylphenyl)-3-methylbutyraldehyde as a colorless oil that slowly crystallized upon standing.

3-(2-Benzyloxy-5-methylsulfanylphenyl)-3-methylbutyraldehyde was converted to 4-(2-benzyloxy-5-methylsulfanylphenyl)-1,1,1-trifluoro-4-methylpentan-2-ol as in Example 26 of U.S. Patent Application Pub. No. 2004/0023999.

4-(2-Benzyloxy-5-methylsulfanylphenyl)-1,1,1-trifluoro-4-methylpentan-2-ol was oxidized to 4-(2-benzyloxy-5-methylsulfanylphenyl)-1,1,1-trifluoro-4-methylpentan-2-one using Swern conditions as above.

Example 66: Synthesis of 1,1,1-Trifluoro-4-methyl-4-(5-pyrimidin-5-yl-2,3-dihydrobenzofuran-7-yl)pentan-2-one

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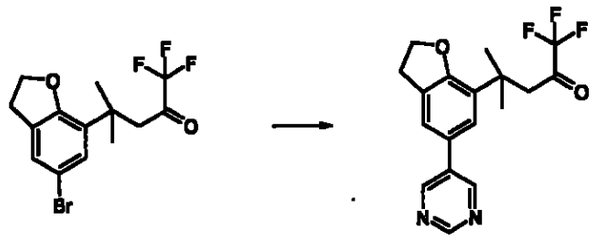
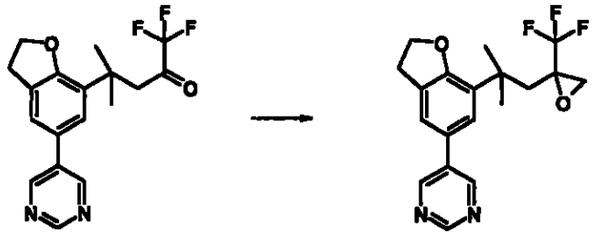


To a mixture of 4-(5-bromo-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-one (1.00 g, 2.8 mmol), pyrimidine-5-boronic acid (529 mg, 4.3 mmol) and potassium carbonate (787 mg) in a sealed tube was added 20 mL of MeOH-DME-DMF (3:2:1). After stirring at room temperature for 10 minutes, tetrakis(triphenylphosphine)palladium(0) (329 mg) was added and the reaction mixture was heated at 120°C for 40 minutes. After cooling to room temperature, the crude mixture was filtered through a cotton plug with the aid of ethyl acetate. The filtrate was concentrated *in vacuo* to remove most of the methanol, redissolved in 160 mL of ethyl acetate, and washed with 80 mL of aqueous 1 N sodium hydroxide solution, 80 mL of water, and 80 mL of brine respectively. The organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. Purification by column chromatography with 20% to 30% ethyl acetate-hexanes afforded 620 mg (62% yield) of the title compound.

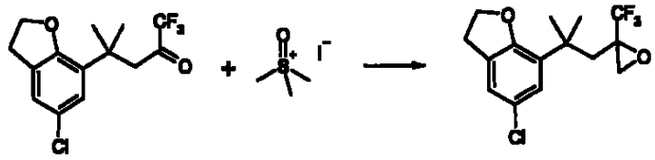
Example 67: Synthesis of 5-{7-[1,1-Dimethyl-2-(2-trifluoromethyloxiranyl)ethyl]-2,3-dihydrobenzofuran-5-yl}pyrimidine



To a solution of 1,1,1-trifluoro-4-methyl-4-(5-pyrimidin-5-yl-2,3-dihydrobenzofuran-7-yl)pentan-2-one (620 mg, 1.8 mmol) in 5 mL of anhydrous DMSO-THF (1:1) was added 2.64 mL of a trimethylsulfoxonium ylide solution (stock solution prepared by reaction of NaH (242 mg, 60% dispersion in mineral oil) with trimethylsulfoxonium iodide (1.33 g, 6.0 mmol) in 7.50 mL of anhydrous DMSO for 30 minutes) dropwise over 5 minutes. After stirring for 2 hour at room temperature, the reaction mixture was poured into 40 mL of water and extracted with diethyl ether (200 mL total volume). The combined organic phases were washed with

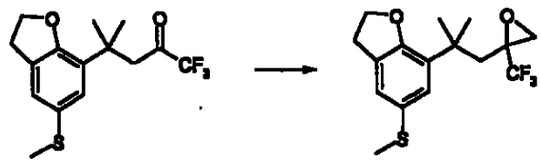
water, brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo* to afford 651 mg (99% yield) of the title compound as a pale yellow oil which was used without further purification.

Example 68: Synthesis of 5-Chloro-7-[1,1-dimethyl-2-(2-trifluoromethyloxiranyl)ethyl]-2,3-dihydrobenzofuran



To a solution of trimethylsulfoxonium iodide (343 mg, 1.56 mmol) in 3 mL of anhydrous DMSO was treated with NaH (60% in mineral oil, 66.0 mg, 1.65 mmol) in portions and the mixture was stirred at room temperature for 30 minutes. The mixture was transferred to a solution of 4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-one (400 mg, 1.30 mmol) in 1 mL of anhydrous DMSO over 5 minutes and the resulting mixture was stirred overnight. The mixture was quenched with water and extracted with three 20 mL portions of ethyl acetate. The combined organic layers were washed with two 5 mL portions of water, dried over magnesium sulfate, filtered, and concentrated *in vacuo* to afford 380 mg (91% yield) of the title product as a yellow oil. The crude product was sufficiently pure and used without further purification.

Example 69: Synthesis of 7-[1,1-Dimethyl-2-(2-trifluoromethyloxiranyl)ethyl]-5-methylsulfanyl-2,3-dihydrobenzofuran



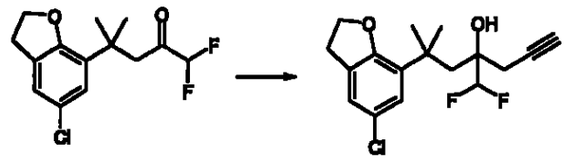
To a suspension of trimethylsulfoxonium iodide (1.36 g, 6.1 mmol) in 7.7 mL of anhydrous DMSO was added sodium hydride (60% dispersion in mineral oil, 246 mg). The resulting solution was stirred at room temperature for 30 minutes and was then added dropwise to a solution of 1,1,1-trifluoro-4-methyl-4-(5-methylsulfanyl-2,3-dihydrobenzofuran-7-yl)pentan-2-one (1.63 g, 6.2 mmol) in 6.5 mL of anhydrous DMSO. After 2 hours, 100 mL of water was

added and the resulting mixture was extracted with three 100 mL portions of diethyl ether. The combined organic phases were washed twice with water, aqueous saturated sodium chloride solution, dried over magnesium sulfate, filtered, and concentrated *in vacuo* to afford the title compound, 1.64 g (95% yield) which was used without further purification.

Example 70: Synthesis of 7-[1,1-Dimethyl-2-(2-trifluoromethyloxiranyl)ethyl]-5-methanesulfonyl-2,3-dihydrobenzofuran

To a solution of 7-[1,1-dimethyl-2-(2-trifluoromethyloxiranyl)ethyl]-5-methylsulfanyl-2,3-dihydrobenzofuran (535 mg, 1.9 mmol) in 30 mL of acetonitrile and 10 mL of water was added sodium periodate (1.03 g, 4.8 mmol) followed by ruthenium (III) chloride (1 mg). After 2 hours, the reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic phases were dried over magnesium sulfate, filtered, and concentrated *in vacuo* to afford the title compound as a tan solid, 568 mg (95% yield) which was used without further purification.

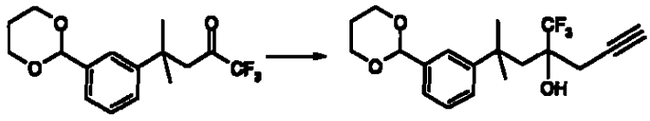
Example 71: Synthesis of 6-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-4-difluoromethyl-6-methylhept-1-yn-4-ol



Aluminum foil (108 mg, 4.00 mmol) and mercuric chloride (*ca.* 1 mg, 0.01 mmol) in 3.5 mL of anhydrous THF were vigorously stirred for 20 minutes. Propargyl bromide (80% in toluene, 0.45 mL, 4.00 mmol) was added slowly (the reaction mixture became warm) and the resulting mixture was stirred at 40°C for 1 hour. The dark gray propargyl aluminum sesquibromide solution was added to a solution of 4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methylpentan-2-one (380 mg, 1.32 mmol) in 10 mL of anhydrous THF at 0°C and the reaction was allowed to slowly warmed to room temperature and stirred overnight. The mixture was

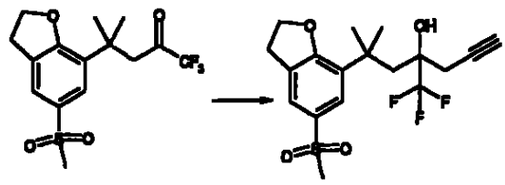
concentrated *in vacuo*, quenched with ice and water, and the aqueous layer was extracted with ethyl acetate. The combined organic extracts were dried over magnesium sulfate and concentrated *in vacuo* to give 420 mg of the title product as an oil (97% yield), which was used without further purification.

Example 72: Synthesis of 6-(3-[1,3]Dioxan-2-ylphenyl)-6-methyl-4-trifluoromethylhept-1-yn-4-ol



Aluminum amalgam was prepared from aluminum foil (1.16 g, 14.4 mmol) and mercuric chloride (12 mg, catalytic amount) in 20 mL of anhydrous THF by vigorously stirring the mixture at room temperature for 1 hour under an argon atmosphere. A solution of propargyl bromide (4.80 mL, 80 wt.% in toluene, 43.1 mmol) in 25 mL of anhydrous THF was slowly added to a stirred suspension maintaining a temperature of 30°C-40°C, and after addition, stirring at 40°C was continued until a dark gray solution was obtained (*ca.* 1 hour). The propargyl aluminum sesquibromide solution was added to a solution of 4-(3-[1,3]dioxan-2-ylphenyl)-1,1,1-trifluoro-4-methylpentan-2-one (5.6 g, 14.2 mmol) in 100 mL of anhydrous diethyl ether at -78°C. The reaction mixture was stirred at this temperature for 3 hours, and then was allowed to warm to room temperature, at which time it was stirred for 12 hours. The reaction mixture was then poured into 20 mL of ice-water and extracted with four 30 mL portions of diethyl ether. The combined extracts were washed with 20 mL of brine, dried over magnesium sulfate, and concentrated *in vacuo*. Chromatography on silica gel (100% hexanes to 40% ethyl acetate in hexanes, gradient) afforded 2.5 g of the title compound as an oil (50% yield).

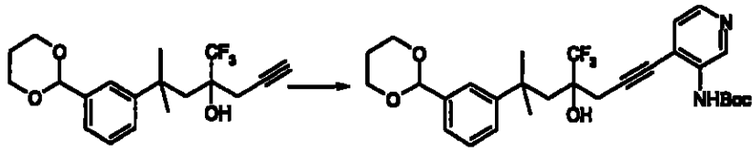
Example 73: Synthesis of 6-(5-Methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-6-methyl-4-trifluoromethylhept-1-yn-4-ol



40 mL of anhydrous THF was added to a mixture of aluminum foil (1.25 g, 4.6 mmol) and mercuric chloride (100 mg, 0.37 mmol). The resulting mixture was vigorously stirred for 1 hour, cooled in an ice bath, and treated with propargyl bromide (80% by wt. solution in toluene, 62.9 mmol, 7 mL). The reaction mixture was stirred at 0°C for 1 hour and at room temperature for 30 minutes.

A solution of 1,1,1-trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-one (5.4 g, 15.4 mmol) in a mixture of 10 mL of anhydrous diethyl ether and 10 mL of anhydrous THF was treated with the organoaluminum reagent at -78°C. After 1 hour at -78°C and 1 hour at room temperature, the reaction mixture was quenched with saturated ammonium chloride solution and diluted with water. The aqueous layer was extracted with three 100 mL portions of ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, filtered, and concentrated *in vacuo* to give 6.3 g of the title product as a solid, which was used without further purification (quantitative yield).

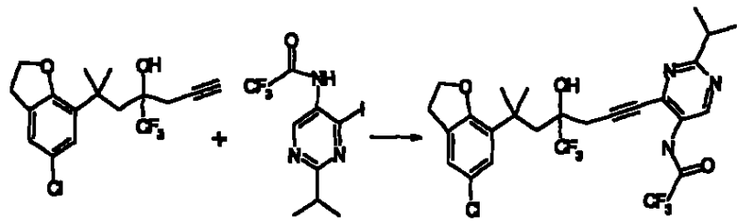
Example 74: Synthesis of {4-[6-(3-[1,3]Dioxan-2-ylphenyl)-4-hydroxy-6-methyl-4-trifluoromethylhept-1-ynyl]pyridin-3-yl}carbamic acid *tert*-butyl ester



A mixture of 6-(3-[1,3]dioxan-2-ylphenyl)-6-methyl-4-trifluoromethylhept-1-yn-4-ol (300 mg, 0.84 mmol), (4-iodopyridin-3-yl)carbamic acid *tert*-butyl ester (270 mg, 0.84 mmol), bis(triphenylphosphine)palladium(II) chloride catalyst (29.6 mg, 0.04 mmol) and copper (I) iodide (16 mg, 0.08 mmol) in 4 mL of anhydrous triethylamine and 1 mL of anhydrous DMF was stirred at room temperature for 12 hours. The reaction mixture was then diluted with 30 mL of diethyl ether and washed with 20 mL of aqueous saturated ammonium chloride solution and 20 mL of brine. The organic layer was dried over magnesium sulfate and concentrated *in vacuo*. Column chromatography over silica gel with hexanes-ethyl acetate (5:1 to 1:1) provided 250 mg of the title compound as a foam (54% yield).

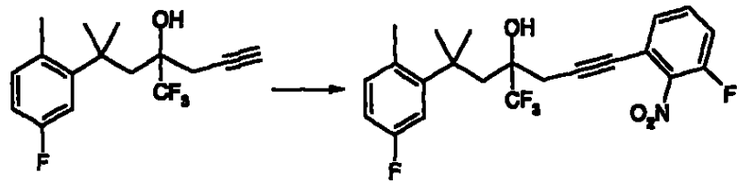
269
287

Example 75: Synthesis of *N*-[4-[6-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-4-hydroxy-6-methyl-4-trifluoromethylhept-1-ynyl]-2-isopropylpyrimidin-5-yl]-2,2,2-trifluoroacetamide



A mixture of chlorodihydrobenzofuran alkyne (185 mg, 0.533 mmol), iodopyrimidine (144 mg, 0.4 mmol), copper (I) iodide (9.5 mg, 0.05 mmol), and dichlorobis(triphenylphosphine)palladium (II) (17.5 mg, 0.025 mmol) in 0.8 mL of anhydrous acetonitrile and 0.25 mL of anhydrous triethylamine was stirred at room temperature. After 1 hour, LC-MS indicated no starting alkyne but showed a major peak at M+H = 578 corresponding to the desired compound and a minor peak for the dimer at M+H = 691. The crude reaction mixture was purified by silica gel column chromatography eluting with a gradient of 0%-25% ethyl acetate in hexanes to give the title compound as a brownish oil, (120 mg, 52% yield), M+H = 577.

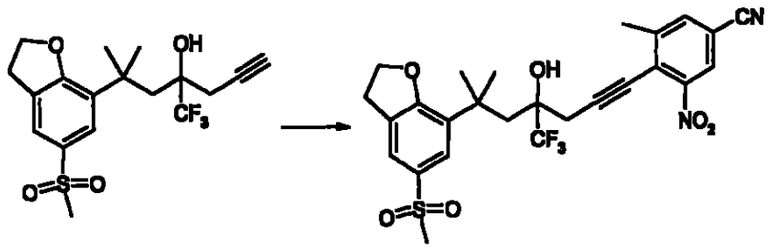
Example 76: Synthesis of 6-(5-Fluoro-2-methylphenyl)-1-(3-fluoro-2-nitrophenyl)-6-methyl-4-trifluoromethylhept-1-yn-4-ol



A mixture of trifluoromethanesulfonic acid 3-fluoro-2-nitrophenyl ester (149 mg, 0.52 mmol), dichlorobis(triphenylphosphine)palladium (II) (20 mg, 0.028 mmol), copper (I) iodide (14 mg, 0.074 mmol), tetrabutyl ammonium iodide (200 mg, 0.54 mmol), 0.25 mL of anhydrous triethylamine, 0.5 mL of anhydrous acetonitrile, and 0.5 mL of anhydrous tetrahydrofuran was stirred at room temperature for 30 minutes. The resulting mixture was treated with 6-(5-fluoro-2-methylphenyl)-6-methyl-4-trifluoromethylhept-1-yn-4-ol (145 mg, 0.48 mmol) and stirred at room temperature for 18 hours. The crude product was purified by chromatography on SiO_2

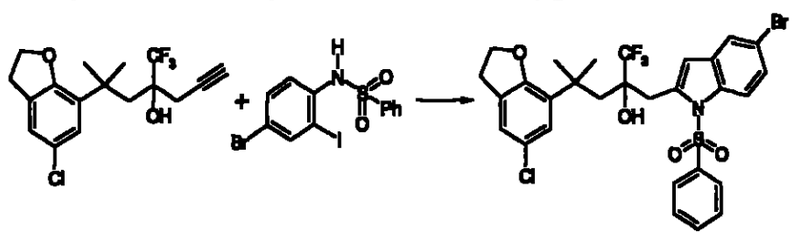
(50% hexanes in dichloromethane) to give 96 mg of the title product as light yellow oil, (45% yield).

Example 77: Synthesis of 4-[4-Hydroxy-6-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-6-methyl-4-trifluoromethylhept-1-ynyl]-3-methyl-5-nitrobenzonitrile



A mixture of trifluoromethanesulfonic acid 4-cyano-2-methyl-6-nitrophenyl ester (217 mg, 0.7 mmol), dichlorobis(triphenylphosphine)palladium (II) (24.6 mg, 0.035 mmol), copper (I) iodide (13.3 mg, 0.7 mmol), and 6-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-6-methyl-4-trifluoromethylhept-1-yn-4-ol (273 mg, 0.7 mmol) in a mixture of 0.8 mL of anhydrous toluene and 0.3 mL of anhydrous triethylamine was heated in a microwave at 60°C for 10 minutes. The reaction mixture was applied to a column of SiO_2 (50% ethyl acetate in hexanes) to give 165 mg of the title product as a light yellow oil (43% yield).

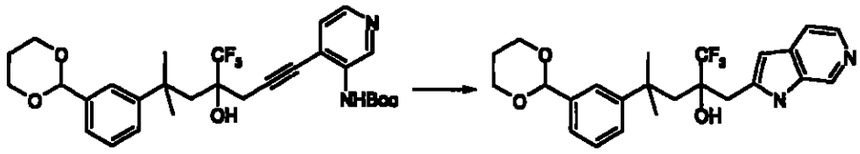
Example 78: Synthesis of 2-(1-Benzenesulfonyl-5-bromo-1*H*-indol-2-ylmethyl)-4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-ol



A mixture of 6-(5-chloro-2,3-dihydrobenzofuran-7-yl)-6-methyl-4-trifluoromethylhept-1-yn-4-ol (170 mg, 0.49 mmol), *N*-(4-bromo-2-iodophenyl)benzenesulfonamide (220 mg, 0.50 mmol), dichlorobis(triphenylphosphine)palladium (II) (20 mg, 0.03 mmol), and copper (I) iodide (10 mg, 0.05 mmol) in 1 mL of DMF and 0.7 mL of triethylamine was warmed at 70°C. After 45 minutes, the mixture was cooled and diluted with 7 mL of saturated aqueous ammonium chloride solution and extracted with three 7 mL portions of ethyl acetate. The combined

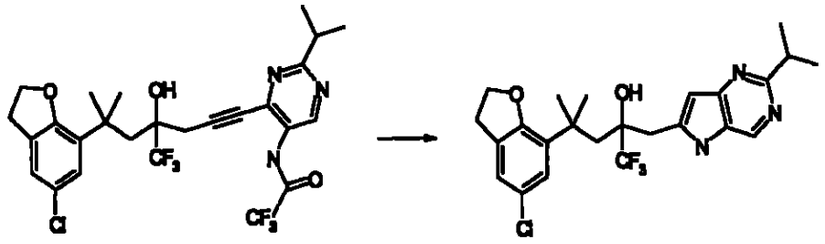
organic layers were washed with two 7 mL portions of saturated aqueous ammonium chloride solution, four 7 mL portions of brine, dried over magnesium sulfate, filtered and concentrated *in vacuo*. The crude residue was purified on silica gel eluting with ethyl acetate-hexanes (0-30% gradient) to afford 126 mg (39% yield) of the title compound.

Example 79: Synthesis of 4-(3-[1,3]dioxan-2-ylphenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol



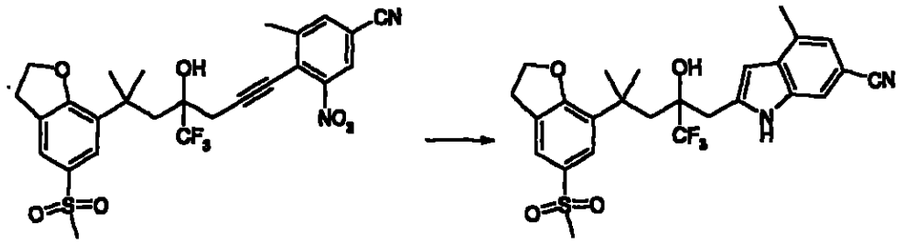
To a solution of {4-[6-(3-[1,3]dioxan-2-ylphenyl)-4-hydroxy-6-methyl-4-trifluoromethylhept-1-ynyl]pyridin-3-yl}carbamic acid *tert*-butyl ester (250 mg, 0.46 mmol) in 5 mL of methanol-water (4:1) was added DBU (0.7 mL, 4.6 mmol) and the reaction mixture heated to 65°C for 2 hour. The solution was concentrated *in vacuo* and the product precipitated from water. The precipitation was filtered and dried to give 176 mg of the title compound as a white solid (86% yield).

Example 80: Synthesis of 4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(2-isopropyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)-4-methylpentan-2-ol



To a solution of *N*-{4-[6-(5-chloro-2,3-dihydrobenzofuran-7-yl)-4-hydroxy-6-methyl-4-trifluoromethylhept-1-ynyl]-2-isopropylpyrimidin-5-yl}-2,2,2-trifluoroacetamide (58 mg, 0.1 mmol) in 1 mL of anhydrous dioxane was added tetramethylguanidine (0.05 mL, 0.4 mmol) and the reaction mixture stirred and heated in oil bath maintained at 100°C for 1 hour. Purification by preparative TLC over silica gel eluting with 5% methanol in dichloromethane provided the title compound as a light cream colored solid, (25 mg, 52% yield) M+H = 482.

Example 81: Synthesis of 2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile



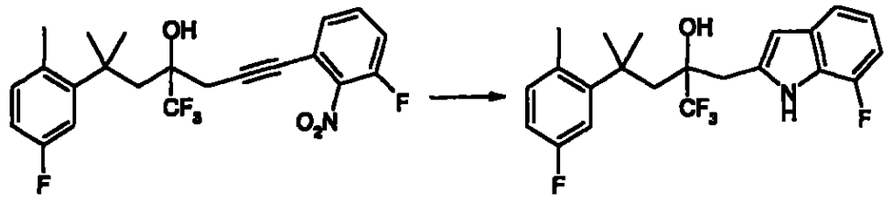
A stirred solution of 4-[4-hydroxy-6-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-6-methyl-4-trifluoromethylhept-1-ynyl]-3-methyl-5-nitrobenzonitrile. (165 mg, 0.3 mmol) in 6 mL of absolute ethanol was treated with 4 mL of glacial acetic acid and iron powder (335 mg, 6 mmol). The resulting mixture was heated at 90°C for 30 minutes, cooled to room temperature, diluted with 200 mL of dichloromethane, and filtered through a pad of CELITE® filter aid. The filtrate was washed with three 50 mL portions of saturated aqueous sodium carbonate solution and two 25 mL portions of brine, dried over sodium sulfate, filtered, and concentrated *in vacuo* to give 140 mg of 3-amino-4-[4-hydroxy-6-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-6-methyl-4-trifluoromethylhept-1-ynyl]-5-methylbenzonitrile as a light brownish oil (90% yield).

A stirred solution of 3-amino-4-[4-hydroxy-6-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-6-methyl-4-trifluoromethylhept-1-ynyl]-5-methylbenzonitrile (140 mg, 0.27 mmol) in 5 mL of anhydrous dichloromethane was cooled in an ice bath and treated with trifluoroacetic anhydride (0.075 mL, 0.54 mmol). After 5 minutes, the mixture was concentrated *in vacuo*. Chromatography on SiO_2 (100% dichloromethane) gave 155 mg of *N*-{5-cyano-2-[4-hydroxy-6-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-6-methyl-4-trifluoromethylhept-1-ynyl]-3-methylphenyl}-2,2,2-trifluoroacetamide as a light brownish oil (93% yield).

A solution of *N*-{5-cyano-2-[4-hydroxy-6-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-6-methyl-4-trifluoromethylhept-1-ynyl]-3-methylphenyl}-2,2,2-trifluoroacetamide (154 mg, 0.25 mmol) in 0.6 mL of anhydrous DMSO was heated in the presence of 1,1,3,3-tetramethylguanidine (0.094 mL, 0.75 mmol) in a microwave at 140°C for 10 minutes. The

reaction was quenched with a mixture of 1 N sulfuric acid and 10 mL of crushed ice. The resulting precipitate was filtered, washed with water, and dried. Preparative TLC chromatography (50% ethyl acetate in hexanes, followed by 15% ethyl acetate in dichloromethane) gave 23 mg of the title product as an off-white solid (18% yield).

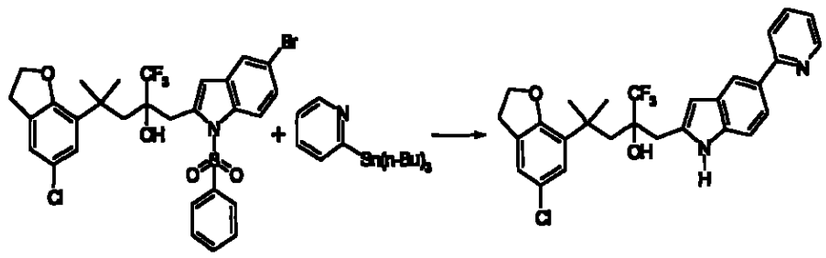
Example 82: Synthesis of 1,1,1-Trifluoro-2-(7-fluoro-1*H*-indol-2-ylmethyl)-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol



A stirred solution of 6-(5-fluoro-2-methylphenyl)-1-(3-fluoro-2-nitrophenyl)-6-methyl-4-trifluoromethylhept-1-yn-4-ol (1.05 g, 2.4 mmol) in 6 mL of absolute ethanol and 2 mL of glacial acetic acid was treated with iron powder (800 mg, 14.3 mmol). The resulting mixture was heated at 80°C for 2 hours, cooled to room temperature, diluted with diethyl ether, filtered through a pad of CELITE® filter aid, and concentrated *in vacuo*. The residue was dissolved in diethyl ether, treated with anhydrous potassium carbonate, filtered, and concentrated *in vacuo* to give 900 mg of 1-(2-amino-3-fluorophenyl)-6-(5-fluoro-2-methylphenyl)-6-methyl-4-trifluoromethylhept-1-yn-4-ol as a light browniah oil (92% yield), which was used without purification.

A solution of 1-(2-amino-3-fluorophenyl)-6-(5-fluoro-2-methylphenyl)-6-methyl-4-trifluoromethylhept-1-yn-4-ol (900 mg, 2.2 mmol) in 10 mL of anhydrous dioxane was treated with dichlorobis(triphenylphosphine)palladium (II) (250 mg, 0.36 mmol) and the mixture was heated at 100°C for 60 hours. The crude reaction mixture was purified on SiO_2 (20% dichloromethane in hexanes) to afford 700 mg of the title product as a yellow oil (78% yield).

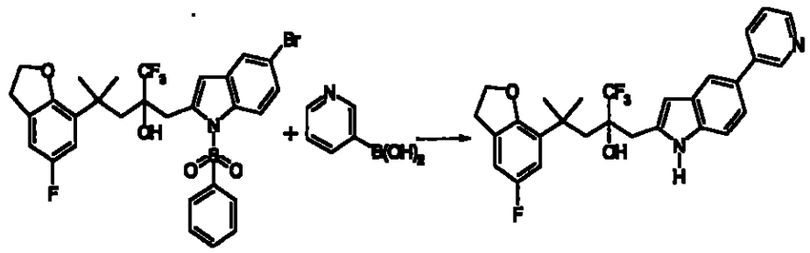
Example 83: Synthesis of 4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-pyridin-2-yl-1*H*-indol-2-ylmethyl)pentan-2-ol



A mixture of 2-(1-benzenesulfonyl-5-bromo-1*H*-indol-2-ylmethyl)-4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-ol (30 mg, 0.046 mmol), 2-tributylstannanylpyridine (72 mg, 0.196 mmol) and dichlorobis(triphenylphosphine)palladium (II) (10 mg) was warmed at reflux for 2 hours. The mixture was then cooled and diluted with diethyl ether, a few drops of DBU were added, and the mixture was diluted with water and extracted with ethyl acetate. The crude material was partially purified on silica gel by preparative TLC eluting with ethyl acetate-hexanes (35:65) to afford partially purified product contaminated with tin byproducts.

A mixture of the above 2-(1-benzenesulfonyl-5-pyridin-2-yl-1*H*-indol-2-ylmethyl)-4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-ol (30.1 mg, 0.046 mmol, theoretical maximum from above) in 5 mL of methanol and 5 mL of 10% aqueous sodium hydroxide solution was warmed at reflux. After 4 hours, the mixture was diluted with 7 mL of brine and extracted with three 5 mL portions of ethyl acetate. The combined organic layers were washed with three 5 mL portions of saturated aqueous sodium bicarbonate solution, 5 mL of brine, two 5 mL portions of saturated aqueous ammonium chloride solution, 5 mL of brine, dried over magnesium sulfate, filtered and concentrated *in vacuo*. The crude material was purified by silica gel preparative TLC using ethyl acetate-hexanes (1:1). The material from the preparative TLC plate when concentrated *in vacuo* from diethyl ether-hexanes afforded 10 mg (42% yield) of the title compound.

Example 84: Synthesis of 1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-pyridin-3-yl-1*H*-indol-2-ylmethyl)pentan-2-ol

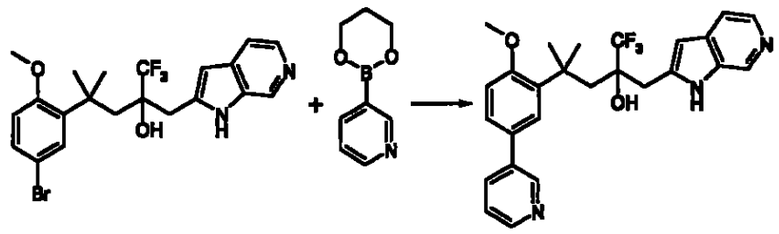


A mixture of 2-(1-benzenesulfonyl-5-bromo-1*H*-indol-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol (100 mg, 0.156 mmol), pyridine-3-boronic acid (80 mg, 0.65 mmol), and tetrakis(triphenylphosphine)palladium (0) (25 mg, 0.022 mmol) in 6 mL of toluene, 3 mL of ethanol, and 1.5 mL of 2 M aqueous sodium carbonate solution was heated at reflux. The reaction was monitored by TLC (ethyl acetate-hexanes (6:4)). The mixture was then diluted with saturated aqueous ammonium chloride solution and extracted with three 10 mL portions of ethyl acetate. The combined organic layers were washed with three 10 mL portions of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude material was purified on silica gel using ethyl acetate-hexanes (gradient 10-60%) to afford 88 mg (88% yield) of material. Recrystallization from diethyl ether-hexanes afforded 76 mg (76% yield) of 2-(1-benzenesulfonyl-5-pyridin-3-yl-1*H*-indol-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol.

To a solution of the above 2-(1-benzenesulfonyl-5-pyridin-3-yl-1*H*-indol-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol (71 mg, 0.11 mmol) in 5 mL of THF was added a 1 M solution of tetrabutylammonium fluoride (0.5 mL, 0.5 mmol) in THF and the mixture was warmed at 80°C. After 18 hours, the mixture was concentrated *in vacuo* and diluted with 1 N aqueous sodium hydroxide solution and extracted with three 5 mL portions of ethyl acetate. The combined organic layers were washed with two 5 mL portions of 1 N aqueous sodium hydroxide solution, 5 mL of brine, three 5 mL portions of saturated aqueous ammonium chloride solution, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The residue was purified on silica gel eluting with methanol-dichloromethane (0:100, then 0.5:99.5, then 1:99) to afford 46 mg (83% yield) of the title compound.

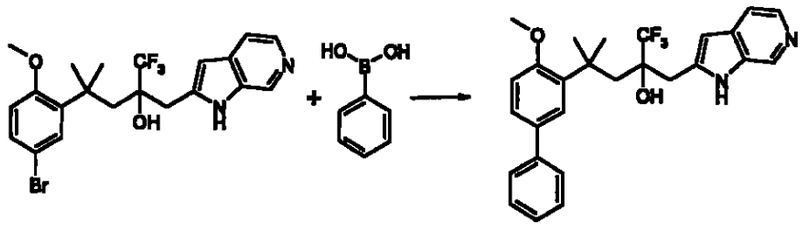
Example 85: Synthesis of 1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol

~~276~~ 294



A mixture of 4-(5-bromo-2-methoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol (188 mg, 0.4 mmol), pyridine 3-boronic acid 1,3-propanediol cyclic ester (89 mg, 0.6 mmol), potassium carbonate (K_2CO_3; 166 mg, 1.2 mmol), and $Pd(PPh_3)_4$ (46.2 mg, 0.04 mmol) in 3.0 mL of DME-MeOH-DMF (1:1.5:0.5) was microwaved for 20 minutes at 120°C, cooled to room temperature, diluted with 20 mL of ethyl acetate and filtered through diatomaceous earth. The filtrate was washed with 5 mL of 1.0 M aqueous sodium hydroxide solution, water, and brine, dried over magnesium sulfate, and concentrated *in vacuo*. The residue was purified by silica gel chromatography to yield 90 mg (48% yield) of the title compound as a white foam.

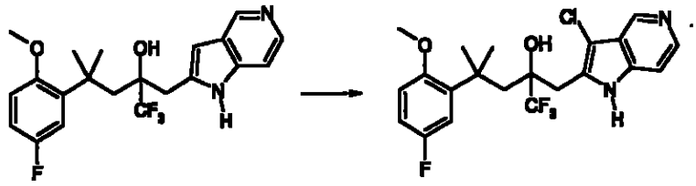
Example 86: Synthesis of 1,1,1-Trifluoro-4-(4-methoxybiphenyl-3-yl)-4-methyl-2-(1*H*-pyrrolo[2,3-c]pyridin-2-ylmethyl)pentan-2-ol



A mixture of 4-(5-bromo-2-methoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol (188 mg, 0.4 mmol), $Pd(OAc)_2$ (9 mg, 0.04 mmol), DCyBPP ((2-dicyclohexylphosphino)biphenyl, 28 mg, 0.08 mmol), and KF (93 mg, 1.6 mmol) in 3 mL of THF at room temperature was treated with phenylboronic acid (74 mg, 0.6 mmol). The reaction mixture was microwaved for 20 minutes at 120°C, cooled to room temperature, diluted with 20 mL of ethyl acetate and filtered through diatomaceous earth. The filtrate was washed with 5 mL of 1.0 M aqueous sodium hydroxide solution, water, and 5 mL of brine. The organic phase was dried over magnesium sulfate, filtered, and the solvent evaporated *in vacuo*. The

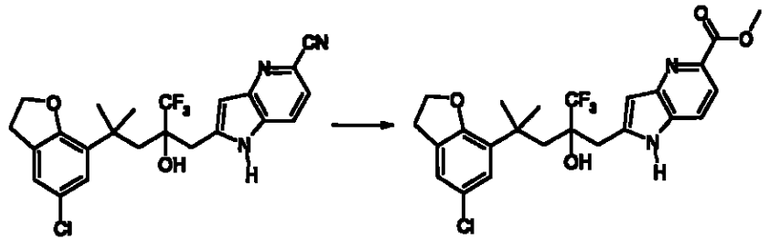
residue was purified silica gel chromatography to provide 75 mg (40% yield) of the title compound as a white solid.

Example 87: Synthesis of 2-(3-Chloro-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol



A solution of trichloroacetyl chloride (0.045 mL, 0.403 mmol) in 0.5 mL of DMF was treated with a solution of 1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol (33.0 mg, 0.081 mmol) in 0.5 mL of DMF at room temperature. After 2 days, the reaction was quenched with 2 mL of ice-water and 2 mL of cold 1 N sodium hydroxide solution. The resulting mixture was extracted with three 5 mL portions of ethyl acetate. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. Chromatography on SiO_2 (100% dichloromethane to 10% methanol in dichloromethane, gradient) gave 20.0 mg of the title product (56% yield).

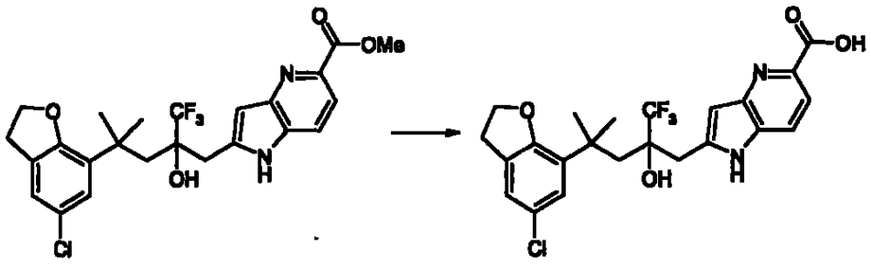
Example 88: Synthesis of 2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carboxylic acid methyl ester



2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile (300 mg, 0.65 mmol) was dissolved in 10 mL of methanol at room temperature. HCl gas was introduced for 2 minutes. The mixture was heated to reflux overnight. The solvent was removed *in vacuo*. The residue was diluted with 50 mL of ethyl acetate and neutralized with 30 mL of a saturated sodium carbonate solution. The organic layer was separated. The aqueous layer was extracted with three 50 mL portions of ethyl acetate.

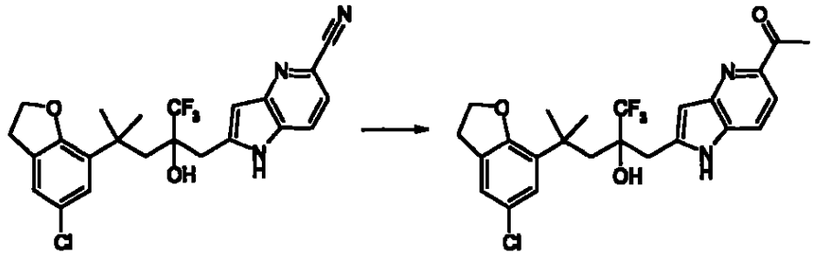
The organic layers were combined, washed with brine, dried over sodium sulfate, and the solvent was removed *in vacuo*. The residue was purified by flash chromatography (deactivated SiO_2 with 2% triethylamine, eluting with CH_2Cl_2 to CH_2Cl_2-MeOH (95:5)) to give the title compound (263 mg, 82% yield).

Example 89: Synthesis of 2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carboxylic acid



2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carboxylic acid *methyl* ester (100 mg, 0.2 *mmol*) was dissolved in 2 mL of THF-MeOH-water (3:1:1). Lithium hydroxide monohydrate (25 mg, 0.6 mmol) was added. The reaction was stirred at room temperature for 4 hours. The mixture was diluted with 5 mL of water and 6 N HCl solution was used to adjust the pH to about 2. The organic was extracted with three 50 mL portions of ethyl acetate, washed with brine, and dried over anhydrous sodium sulfate. The solvent was removed *in vacuo* to give the title compound (13.5 mg, 14% yield).

Example 90: Synthesis of 1-{2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}ethanone



2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile (100 mg, 0.22 *mmol*) was dissolved in 6 mL of THF. The

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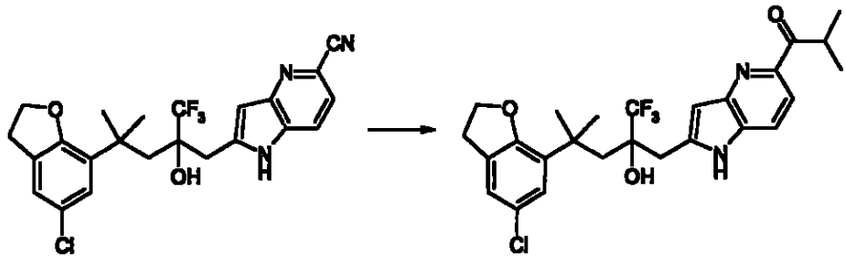
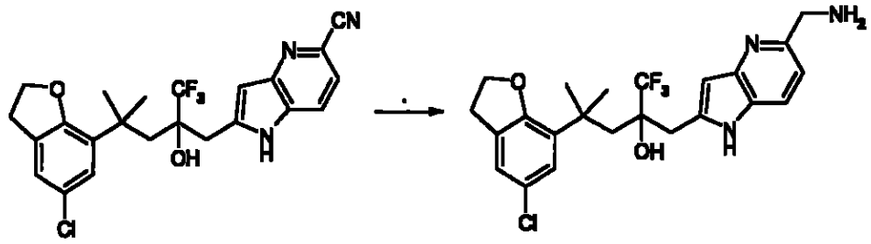
solution was cooled to -78°C. Methyl magnesium iodide (3 M in diethyl ether, 1.2 mL, 3.6 mmol) was added. The reaction was stirred overnight and the temperature was allowed to come to room temperature. The reaction was quenched with 10 mL of saturated aqueous ammonium chloride solution and extracted with three 50 mL portions of ethyl acetate. The organic layers were combined and dried over magnesium sulfate. The solvent was removed *in vacuo*. The residue was purified by flash chromatography (eluting with CH_2Cl_2 to 95:5 CH_2Cl_2-MeOH) to give the title compound (36 mg, 35% yield).

Example 91: Synthesis of 1-{2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}-2-methylpropan-1-one



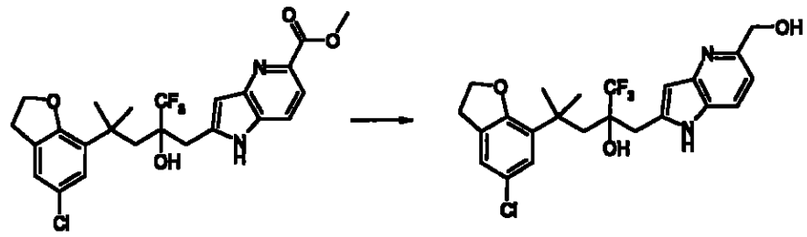
2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile (50 mg, 0.11 mmol) was dissolved in 3 mL of THF. Isopropyl magnesium chloride (2 M in THF, 0.15 mL, 0.3 mmol) was added, followed by CuBr (7 mg, 0.05 mmol). The reaction was stirred at reflux (75°C) for 30 minutes. The mixture was cooled to room temperature. The reaction was quenched with 1 mL of water, followed by 3 drops of concentrated HCl. The mixture was stirred for 10 minutes, and neutralized with saturated sodium carbonate solution until the pH was 8. The reaction mixture was extracted with ethyl acetate and washed with brine. The solvent was removed *in vacuo*. The residue was purified by preparative HPLC (medium polar condition) to give the title compound (39 mg, 70% yield).

Example 92: Synthesis of 2-(5-Aminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-ol



2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile (100 mg, 0.22 mmol) was dissolved in 3 mL of THF and borane-methyl sulfide (10 M, 0.065 mL, 0.648 mmol) was added. The reaction was heated at reflux for 1 hour and then cooled to room temperature. 1 mL of a 6 N HCl solution was then added. The reaction was heated at reflux overnight. The reaction was cooled to room temperature, diluted with 50 mL of ethyl acetate, and then quenched with saturated sodium carbonate solution until the pH was 12. The organic layer was separated and aqueous layer was extracted with three 50 mL portions of ethyl acetate. The combined organic fractions were dried over sodium sulfate and the solvent was removed *in vacuo*. The residue was purified by preparative HPLC (polar condition) to give the title compound (49 mg, 49% yield).

Example 93: Synthesis of 4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(5-hydroxymethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-methylpentan-2-ol



To a solution of the starting ester (0.995 g, 2.00 mmol) in 35.0 mL of THF was added lithium aluminum hydride (2.40 mL, 2.40 mmol) dropwise at 0°C. The reaction was allowed to come to room temperature then stirred for 2 hours. TLC analysis (5% MeOH-CH_2Cl_2, 0.5% NH_4OH) showed the appearance of one product spot and consumption of all starting material. The solution was diluted with 50 mL of THF and quenched with a water-THF solution (3.0 mL of water and 50 mL of THF). To this magnesium sulfate was added and the resulting slurry was stirred for 30 minutes. The suspension was filtered through diatomaceous earth and the THF was evaporated to give the title compound as a yellow foam (0.882 g, 94.0% yield).

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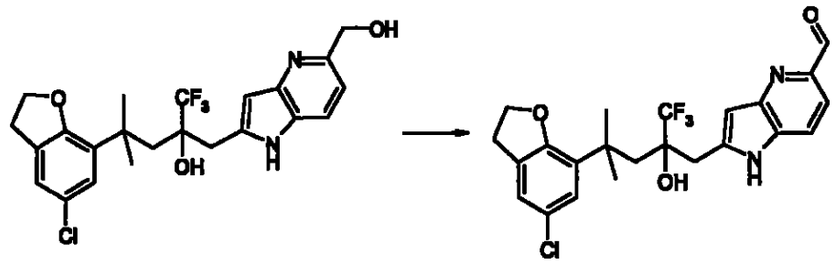
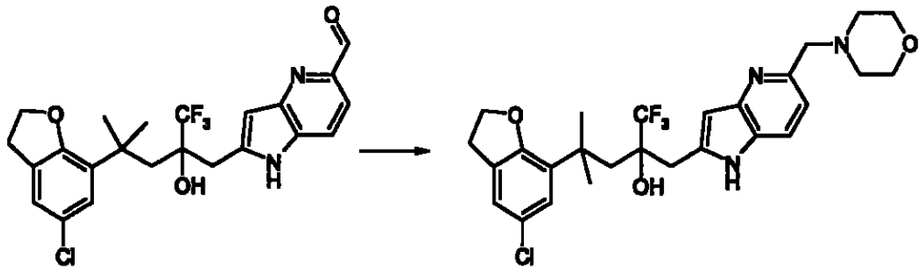
Example 94: Synthesis of 2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbaldehyde



To a solution of alcohol of Example 93 (0.882 g, 1.88 mmol) in 25 mL of acetone was added manganese (IV) oxide (3.99 g, 9.41 mmol). The black suspension was stirred at room temperature for 1 hour. The solution was filtered through diatomaceous earth and the acetone was evaporated *in vacuo* to give the title compound (0.625 g, 74.0% yield) as a yellow foam.

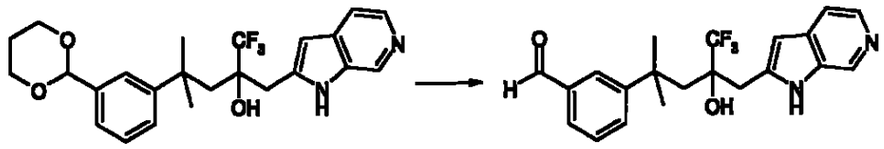
Example 95: Synthesis of 4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)pentan-2-ol



To a solution of the aldehyde of Example 94 (0.050 g, 0.107 mmol) and 0.078 mL of acetic acid in 3.0 mL of dichloroethane was added morpholine (0.233 mL, 2.68 mmol) at 0°C. The reaction was allowed to stir at room temperature for 30 minutes. To this yellow solution was added triacetoxy sodium borohydride (0.057 mg, 0.268 mmol), then continued stirring at room temperature for 14 hours. The reaction mixture was diluted with 10 mL of ethyl acetate and 2 mL of 3% ammonium hydroxide solution. The biphasic system was separated and the aqueous phase was extracted with ethyl acetate. The combined organic layers were washed with three 20 mL portions of water, brine, dried over sodium sulfate, filtered and the solvent was evaporated *in vacuo* to give yellow oil. This crude material was applied onto a flash column

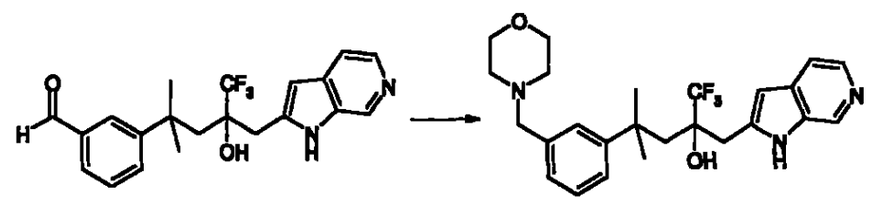
and eluted with 5% MeOH-CH_2Cl_2, 0.5% NH_4OH, to give the title compound (0.018 g, 32.0% yield) as a white foam.

Example 96: Synthesis of 3-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]benzaldehyde



A mixture of 4-(3-[1,3]dioxan-2-ylphenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol (160 mg, 0.36 mmol), 2 mL of ethanol, 1 mL of water, and pyridinium *p*-toluenesulfonic acid (200 mg, 0.8 mmol) was stirred at room temperature for 14 hours and then concentrated *in vacuo* to remove ethanol. The residue was diluted with ethyl acetate and water. The aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with aqueous saturated sodium bicarbonate solution and brine, and dried over sodium sulfate. Removal of the solvent *in vacuo* afforded 134 mg (95% yield) of the title compound.

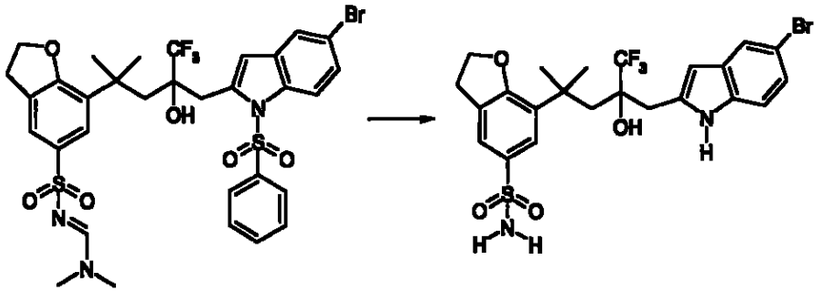
Example 97: Synthesis of 1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylmethylphenyl)-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol



To a solution of 3-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]benzaldehyde (50 mg, 0.13 mmol), 3 mL of dichloroethane, and acetic acid (0.1 mL, 1.6 mmol) in an ice bath was added morpholine (0.28 mL, 3.20 mmol) in one batch. The solution was warmed to room temperature and stirred for 0.5 hours. Triacetoxy sodium borohyride (68 g, 0.32 mmol) was added in a single portion and the reaction stirred at room temperature for 3.0 hours. The solution was diluted with ethyl acetate and 3 mL of 3% ammonium hydroxide solution was added. The biphasic system was transferred to a separatory funnel and the aqueous layer was removed and back-extracted with ethyl acetate. The

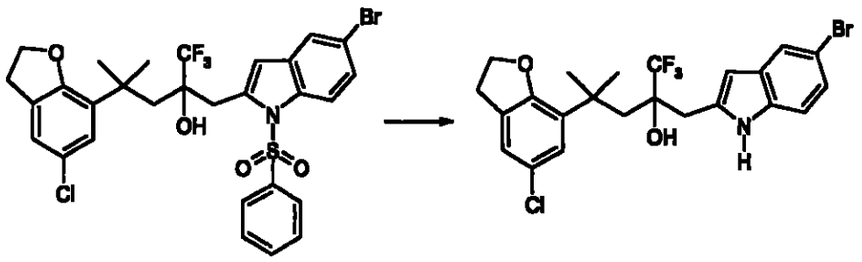
combined organic layers were washed with brine, dried over magnesium sulfate, filtered, and the solvent was evaporated *in vacuo*. The product was eluted from a flash chromatography column with dichloromethane-methanol, and evaporation of the solvent *in vacuo* yielded the title compound (27 mg, 45% yield).

Example 98: Synthesis of 7-[3-(5-Bromo-1*H*-indol-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-2,3-dihydrobenzofuran-5-sulfonic acid amide



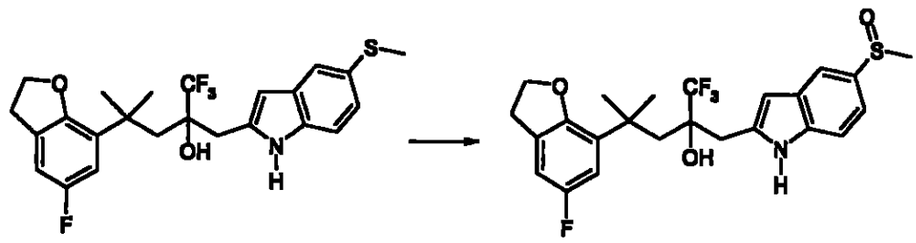
A mixture of 7-[3-(1-benzenesulfonyl-5-bromo-1*H*-indol-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-2,3-dihydrobenzofuran-5-sulfonic acid 1-dimethylaminometh(*E*)-ylideneamide (167 mg, 0.22 mmol) in 10 mL of methanol and 3 mL of 10% aqueous sodium hydroxide solution was warmed at reflux. After 24 hours, the mixture was diluted with 10 mL of brine and extracted with three 10 mL portions of ethyl acetate. The combined organic layers were washed with two 5 mL portions of saturated aqueous sodium bicarbonate solution, 5 mL of brine, three 5 mL portions of saturated aqueous ammonium chloride solution, 5 mL of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude material was chromatographed on silica gel using ethyl acetate-hexanes (0-50% gradient) and then triturated with diethyl ether-hexanes to afford 79 mg (64% yield) of the title compound.

Example 99: Synthesis of 2-(5-Bromo-1*H*-indol-2-ylmethyl)-4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-ol



A mixture of 2-(1-benzenesulfonyl-5-bromo-1*H*-indol-2-ylmethyl)-4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-ol (30 mg, 0.046 mmol) in 5 mL of methanol and 5 mL of 10% aqueous sodium hydroxide solution was warmed at reflux. After 18 hours, the mixture was diluted with brine and extracted with three 7 mL portions of ethyl acetate. The combined organic layers were washed with three 5 mL portions of brine, three 5 mL portions of saturated aqueous ammonium chloride solution, 5 mL of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude material was purified by preparative TLC (1 mm, silica gel, ethyl acetate-hexanes (3:7)) to afford 15 mg (63% yield) of the title compound.

Example 100: Synthesis of 1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-2-(5-methanesulfinyl-1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol



To a solution of 1,1,1-trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-methylsulfanyl-1*H*-indol-2-ylmethyl)pentan-2-ol (25 mg, 0.053 mmol) in 10 mL of methanol was added sodium periodate (150 mg, 0.70 mmol). After 1 hour, the mixture was diluted with brine and extracted with three 10 mL portions of ethyl acetate. The combined organic layers were washed with three 7 mL portions of brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The crude residue was purified by preparative TLC on silica gel eluting with ethyl acetate to afford 19.8 mg (77% yield) of the title compound.

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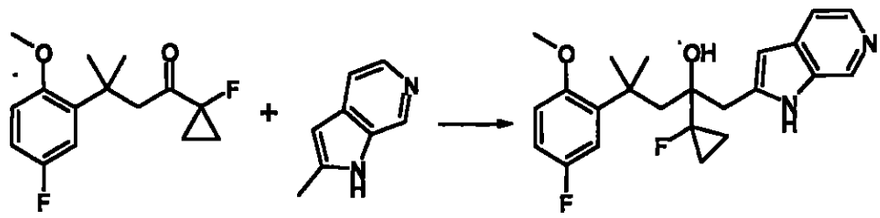
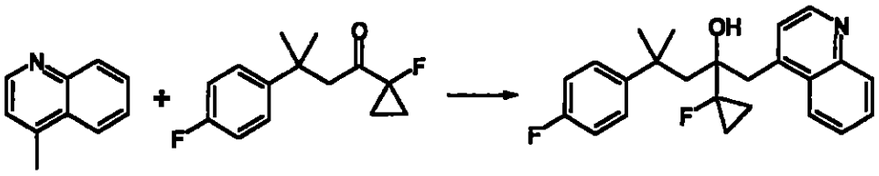
Example 101: Synthesis of 2-(1-Fluorocyclopropyl)-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol



To a solution of 2-methyl-1*H*-pyrrolo[2,3-*c*]pyridine (80.0 mg, 0.605 mmol) in 2 mL of THF cooled to -78°C was added 0.70 mL of *n*-BuLi (1.6 M in hexanes). After 5 minutes, *tert*-BuOK (1 M in THF, 0.75 mL) was added and the mixture was warmed to room temperature for 1 hour. The mixture was cooled to -78°C and the above 1-(1-fluorocyclopropyl)-3-(5-fluoro-2-methoxyphenyl)-3-methylbutan-1-one (150 mg, 0.600 mmol) was added as a solution in 0.5 mL of THF. The mixture was stirred for 30 minutes at -78°C and warmed to room temperature. 5 mL of ethyl acetate was added and the organic phase was washed with water, dried, filtered, and evaporated. Preparative layer chromatography (developer: dichloromethane-ethanol (95:5)) gave 100 mg of the title compound as an oil that solidified on standing (45% yield).

Example 102: Synthesis of 2-(1-Fluorocyclopropyl)-4-(4-fluorophenyl)-4-methyl-1-quinolin-4-ylpentan-2-ol



To a solution of 4-methylquinoline (69 mg, 0.482 mmol) in THF cooled on dry ice/acetone was added 0.4 mL of lithium diisopropylamide (1.5 M in hexanes). The mixture was placed in a cold bath at -20°C to -30°C for 15 minutes and then cooled to -78°C. 1-(1-Fluorocyclopropyl)-3-(4-fluorophenyl)-3-methylbutan-1-one (49 mg, 0.206 mmol) was added dropwise as a solution in 0.5 mL of THF. The cold bath was then removed and the mixture stirred for 1 hour. The reaction was quenched by addition of 0.5 mL of water and diluted with ethyl acetate. The organic phase was separated, washed with water, dried, filtered, and the solvent evaporated *in vacuo*. Fractionation of the residue by preparative layer chromatography

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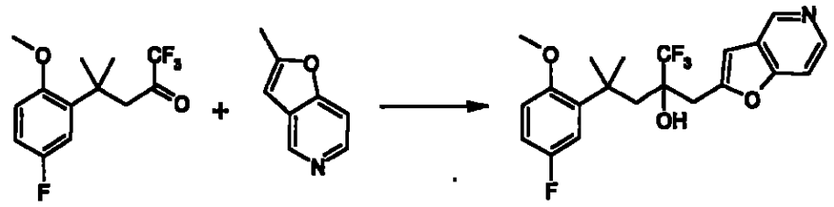
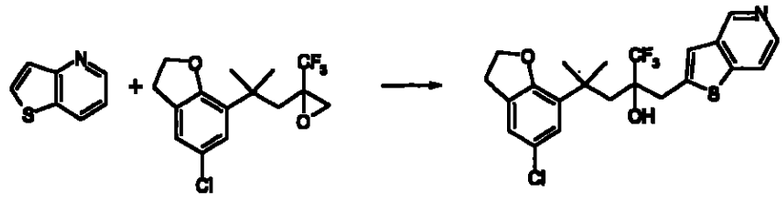
(developer: ethyl acetate-hexanes (2:1)) gave the title compound (0.019 g, 24% yield) (slightly less polar than lepidine) as an oil that crystallized on standing in hexanes, m.p. 152°C-155°C.

Example 103: Synthesis of 1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-furo[3,2-c]pyridin-2-ylmethyl-4-methylpentan-2-ol



A solution of 2-methylfuro[3,2-*c*]pyridine (prepared according to the procedure by T. Kitamura, K. Tsuda, and Y. Fujiwara, Tetrahedron Lett. 1998, 39, pp. 5375-5376) (26.0 mg, 0.195 mmol) in 2 mL of THF was treated with lithium diisopropylamide (LDA; 1.5 M in cyclohexane, 195 µL) dropwise at -78°C. The mixture was stirred for 30 minutes (the color changed from yellow to orange-red) and was slowly treated with a solution of 1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-one (81.5 mg, 0.293 mmol) in 1 mL of THF. The reaction was stirred at -78°C for 4.5 hours, quenched with 5 mL of saturated ammonium chloride solution, and diluted with 20 mL of ethyl acetate. The phases were separated and the aqueous layer was extracted with three 10 mL portions of ethyl acetate. The combined organic layers were washed with brine, dried over magnesium sulfate, and concentrated *in vacuo*. Flash chromatography (ethyl acetate-hexanes, 5% to 50% gradient) gave 36.0 mg (45% yield) of the title product as a clear oil.

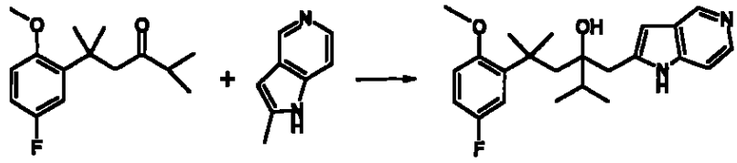
Example 104: Synthesis of 4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-thieno[3,2-c]pyridin-2-ylmethylpentan-2-ol



A solution of thieno[3,2-*c*]pyridine (prepared according to the procedure by J.H. Wikel, M.L. Denney, and R.T.J. Vasileff, Heterocyclic Chem. 1993, 30, pp. 289-290) (152 mg, 1.12 mmol)

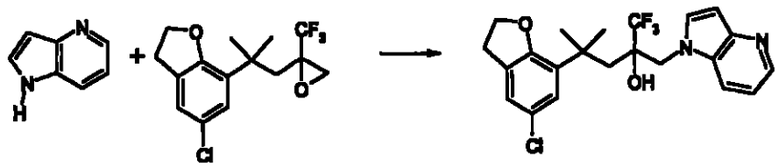
in 2 mL of THF was treated with 450 μL of *n*-BuLi (2.5 M in hexanes) in a dropwise manner at -78°C. The resulting dark reaction mixture was stirred for 30 minutes and treated with a solution of 5-chloro-7-[1,1-dimethyl-2-(2-trifluoromethyloxiranyl)ethyl]-2,3-dihydrobenzofuran (180 mg, 0.561 mmol) in 0.5 mL of THF. The reaction was allowed to warm to room temperature overnight and quenched with a mixture of 5 mL of saturated ammonium chloride solution and 10 mL of ethyl acetate. The phases were separated and the aqueous layer was extracted with three 10 mL portions of ethyl acetate. The combined organic layers were washed with brine, dried over magnesium sulfate, and concentrated *in vacuo*. Flash chromatography (ethyl acetate-hexanes, 20%-30% gradient) gave 33.5 mg (13% yield) of the title product as yellow foam.

Example 105: Synthesis of 5-(5-Fluoro-2-methoxyphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol



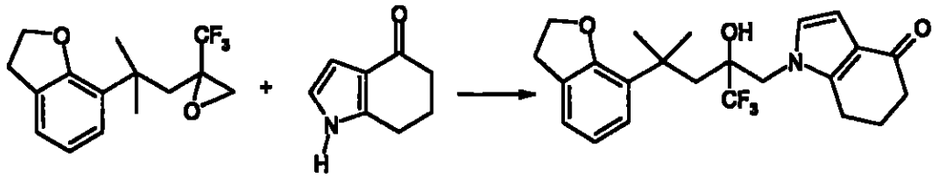
A solution of 2-methyl-1*H*-pyrrolo[3,2-*c*]pyridine (69 mg, 0.52 mmol) in 4 mL of THF was treated with 610 μL of *n*-BuLi (2.5 M in hexanes) at -78°C. After 5 minutes, *tert*-BuOK (1 M in THF, 1.0 mL) was added and the mixture was warmed to room temperature for 1.5 hours. The orange reaction mixture was cooled to -78°C and 5-(5-fluoro-2-methoxyphenyl)-2,5-dimethylhexan-3-one (110 mg, 0.436 mmol) in 2 mL of THF was added dropwise. The mixture was stirred at -78°C for 30 minutes, warmed to room temperature, quenched with 10 mL of saturated ammonium chloride solution, and diluted with 20 mL of ethyl acetate. The phases were separated and the aqueous layer was extracted with two 10 mL portions of ethyl acetate. The combined organic layers were dried over magnesium sulfate and concentrated *in vacuo*. Chromatography on SiO_2 (MeOH in CH_2Cl_2, gradient, 0% to 10%) afforded 71.4 mg (43% yield) of the product as a white solid.

Example 106: Synthesis of 4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol



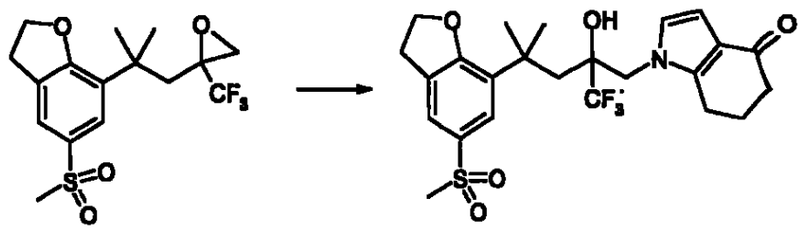
A solution of 1*H*-pyrrolo[3,2-*b*]pyridine (33.0 mg, 0.279 mmol) in 4 mL of DMF was treated with NaH (60% in mineral oil, 16.8 mg, 0.419 mmol) at room temperature. After 30 minutes, 5-chloro-7-[1,1-dimethyl-2-(2-trifluoromethyloxiranyl)ethyl]-2,3-dihydrobenzofuran (188 mg, 0.558 mmol) was added and the resulting mixture was stirred overnight. The reaction was then diluted with 5 mL of ethyl acetate and quenched with 5 mL of saturated ammonium chloride solution. The aqueous layer was extracted with 5 mL of ethyl acetate. The combined organic layers were dried over magnesium sulfate, filtered, and concentrated *in vacuo*. The residue was triturated with diethyl ether to afford 55.0 mg (45% yield) of the title product as white solid.

Example 107: Synthesis of 1-[4-(2,3-Dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one



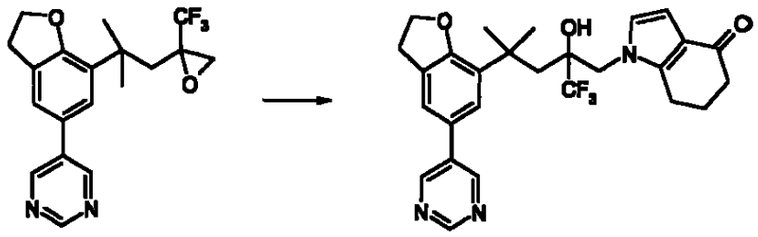
To a suspension of 7-[1,1-dimethyl-2-(2-trifluoromethyloxiranyl)ethyl]-2,3-dihydrobenzofuran (59.2 mg, 0.21 mmol) and 1,5,6,7-tetrahydroindol-4-one (56.0 mg, 0.41 mmol) in 0.4 mL of anhydrous ethanol was added 0.077 mL of sodium ethoxide solution (21 wt% in ethanol). The reaction mixture was then heated at 85°C for 16 hours. The resulting mixture was poured into half-saturated sodium bicarbonate and extracted with ethyl acetate. The combined organic phases were dried over sodium sulfate, filtered, and concentrated *in vacuo*. The residue was purified by silica gel chromatography (eluted with 35% ethyl acetate-hexanes) to give 58.4 mg (66% yield) of the title compound as a white solid, m.p. 145°C-146°C.

Example 108: Synthesis of 1-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one



To a suspension of 7-[1,1-dimethyl-2-(2-trifluoromethyloxiranyl)ethyl]-5-methanesulfonyl-2,3-dihydrobenzofuran (101 mg, 0.33 mmol) and 1,5,6,7-tetrahydroindol-4-one (74.9 mg, 0.56 mmol) in 0.75 mL of anhydrous ethanol was added sodium ethoxide (21 wt.% solution in ethanol, 103 μL). After heating at 85°C for 16 hours, the reaction mixture was diluted with ethyl acetate, dried over sodium sulfate, filtered, and concentrated *in vacuo*. The residue was purified by column chromatography with silica gel (eluted with 50% to 60% ethyl acetate-hexanes) to give 80.0 mg (58% yield) of the title compound as a white solid, m.p. 207°C-208°C.

Example 109: Synthesis of 1-[2-Hydroxy-4-methyl-4-(5-pyrimidin-5-yl-2,3-dihydrobenzofuran-7-yl)-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one



To a suspension of 5-{7-[1,1-dimethyl-2-(2-trifluoromethyloxiranyl)ethyl]-2,3-dihydrobenzofuran-5-yl}pyrimidine (56.0 mg, 0.15 mmol) and 1,5,6,7-tetrahydroindol-4-one (41.6 mg, 0.31 mmol) in 1.0 mL of anhydrous ethanol was added sodium ethoxide solution (0.057 mL, 21 wt.% in ethanol). The reaction mixture was heated at 85°C for 15 hours. After cooling to room temperature, the reaction mixture was concentrated onto silica gel (for dry loading) and purified by silica gel chromatography (eluted with 40% to 70% ethyl acetate-hexanes) to give 42.0 mg (55% yield) of the title compound as a white solid, m.p. 213°C-214°C.

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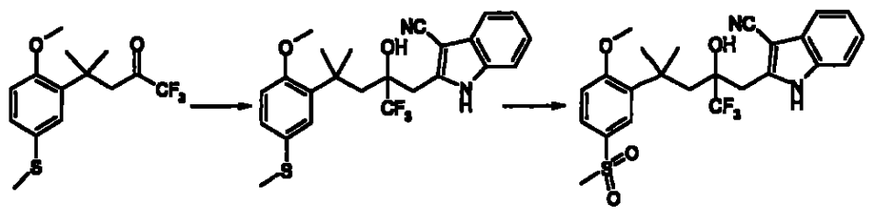
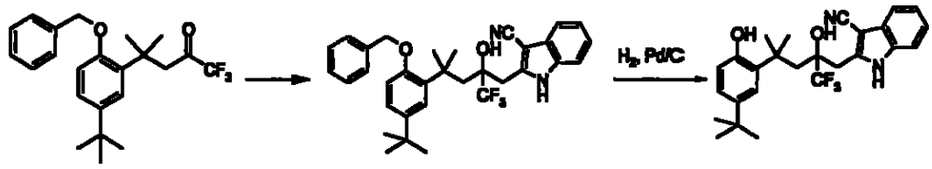
Example 110: 2-[2-Hydroxy-4-(5-methanesulfonyl-2-methoxyphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile



1,1,1-Trifluoro-4-(2-methoxy-5-methylsulfanylphenyl)-4-methylpentan-2-one was converted to 2-[2-Hydroxy-4-(2-methoxy-5-methylsulfanylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile in a similar manner to Example 4 of U.S. Patent Application Pub. No. 2004/0023999.

2-[2-Hydroxy-4-(2-methoxy-5-methylsulfanylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile was oxidized to 2-[2-hydroxy-4-(5-methanesulfonyl-2-methoxyphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile according to Example 4 of U.S. Patent Application Pub. No. 2004/0023999.

Example 111: Synthesis of 2-[4-(5-*tert*-butyl-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile



4-(2-Benzyloxy-5-*tert*-butylphenyl)-1,1,1-trifluoro-4-methylpentan-2-one was converted to 2-[4-(5-*tert*-butyl-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile using similar procedures as in Example 4 of U.S. Patent Application Pub. No. 2004/0023999.

Example 112: Synthesis of 2-[2-Hydroxy-4-(2-hydroxy-5-isopropylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile

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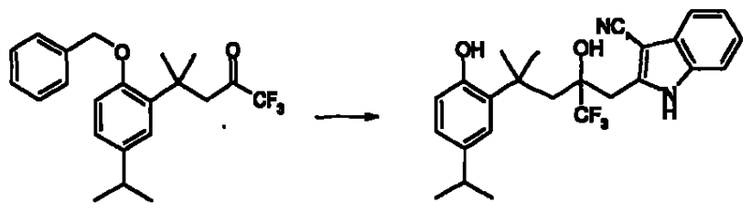
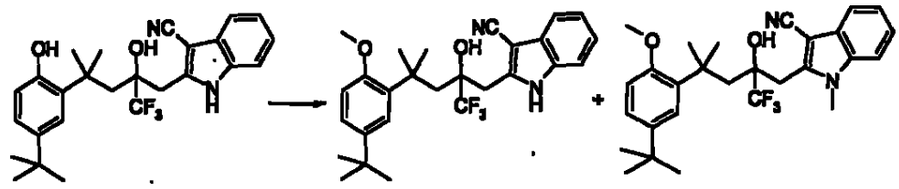


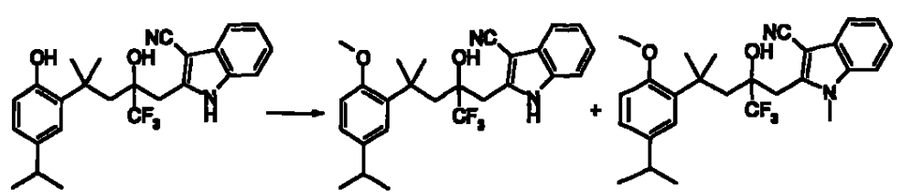
4-(2-Benzyloxy-5-isopropylphenyl)-1,1,1-trifluoro-4-methylpentan-2-one was converted to 2-[2-hydroxy-4-(2-hydroxy-5-isopropylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile using a similar procedure as described in the synthesis of 2-[4-(5-*tert*-butyl-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile.

Example 113: Synthesis of 2-[4-(5-*tert*-Butyl-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile and 2-[4-(5-*tert*-Butyl-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1-methyl-1*H*-indole-3-carbonitrile



2-[4-(5-*tert*-Butyl-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile was alkylated to give 2-[4-(5-*tert*-butyl-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile and 2-[4-(5-*tert*-butyl-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1-methyl-1*H*-indole-3-carbonitrile in a similar manner described for the alkylation of 3-(2-benzyloxy-5-*tert*-butylphenyl)-3-methylbutan-1-ol in Example 53.

Example 114: Synthesis of 2-[2-Hydroxy-4-(5-isopropyl-2-methoxyphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile and 2-[2-Hydroxy-4-(5-isopropyl-2-methoxyphenyl)-4-methyl-2-trifluoromethylpentyl]-1-methyl-1*H*-indole-3-carbonitrile



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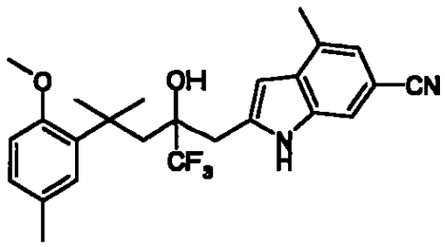
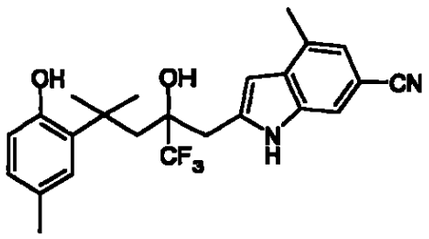
2-[2-Hydroxy-4-(2-hydroxy-5-isopropylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile was alkylated to give 2-[2-hydroxy-4-(5-isopropyl-2-methoxyphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile and 2-[2-Hydroxy-4-(5-isopropyl-2-methoxyphenyl)-4-methyl-2-trifluoromethylpentyl]-1-methyl-1*H*-indole-3-carbonitrile in a similar manner described for the alkylation of 3-(2-benzyloxy-5-*tert*-butylphenyl)-3-methylbutan-1-ol in Example 53.

Example 115: Synthesis of 2-[2-Hydroxy-4-(2-methoxy-5-methylphenyl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile



1,1,1-Trifluoro-4-(2-methoxy-5-methylphenyl)-4-methylpentan-2-one was converted to 2-[2-hydroxy-4-(2-methoxy-5-methylphenyl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile as in Example 8 of U.S. Patent Application Pub. No. 2004/0023999.

Example 116: Synthesis of 2-[2-Hydroxy-4-(2-hydroxy-5-methylphenyl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile



2-[2-Hydroxy-4-(2-methoxy-5-methylphenyl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile was converted to 2-[2-hydroxy-4-(2-hydroxy-5-methylphenyl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile as in Example 8 of U.S. Patent Application Pub. No. 2004/0023999.

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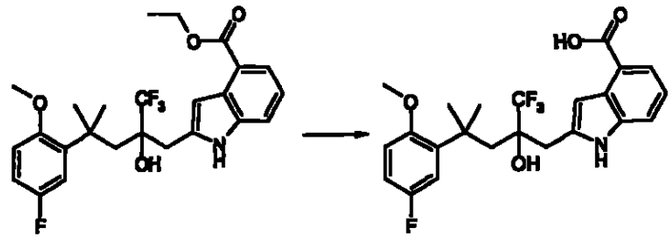
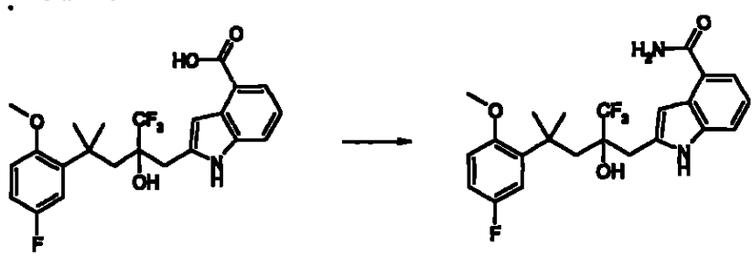
Example 117: Synthesis of 2-[4-(5-fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carboxylic acid



A solution of 2-[4-(5-fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carboxylic acid ethyl ester (220 mg, 0.470 mmol) in 10 mL of methanol was treated with a solution of potassium hydroxide (85 mg, 1.5 mmol) in 3 mL of water. The resulting mixture was stirred at room temperature for 4 hours, refluxed for 6 hours, cooled to room temperature, and concentrated *in vacuo*. The residue was treated with cold 1 N sulfuric acid and extracted with three 30 mL portions of dichloromethane. The combined organic layers were washed with water, dried over sodium sulfate, filtered, and concentrated *in vacuo* to give 190 mg of the title product as a light cream solid (89% yield).

Example 118: Synthesis of 2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carboxylic acid amide



A solution 2-[4-(5-fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carboxylic acid (170 mg, 0.375 mmol) in 2 mL of acetonitrile was treated with 105 mL of triethylamine and TBTU (133 mg, 0.413 mmol). After 15 minutes, 53.6 mL of ammonium hydroxide solution was added. The resulting reaction mixture was diluted with water and extracted with dichloromethane. The organic layer was dried over sodium sulfate, filtered, and concentrated *in vacuo*. Chromatography on SiO_2 (50% ethyl acetate in hexanes) gave 170 mg of the title product as an off-white solid (quantitative yield).

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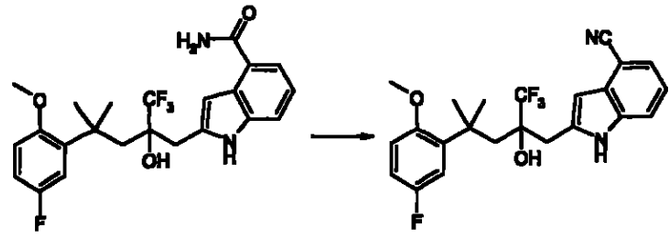
Example 119: Synthesis of 2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carbonitrile



A solution 2-[4-(5-fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carboxylic acid amide (95 mg, 0.21 mmol) in 1 mL of DMF was reacted with cyanuric chloride (46 mg, 0.25 mmol). After 3 hours, the mixture was treated with sodium bicarbonate, extracted with dichloromethane. The organic layer was dried over sodium sulfate, filtered, and concentrated *in vacuo* to give 33 mg of the title product as off-white solid (36% yield).

Resolution to the (+)- and (-)-enantiomers was accomplished by chiral HPLC on a CHIRALCEL™ OD column, eluting with 15% to 25% isopropanol-hexanes.

Assessment of Biological Properties

Compounds of the invention were evaluated for binding to the steroid receptor by a fluorescence polarization competitive binding assay. Detailed descriptions for preparation of recombinant glucocorticoid receptor (GR) complex used in the assay is described in U.S. Patent Application Pub. No. 2003/0017503, which is incorporated herein by reference in its entirety. Preparation of the tetramethyl rhodamine (TAMRA)-labeled dexamethasone probe was accomplished using a standard literature procedure (M. Pons *et al.*, J. Steroid Biochem., 1985, 22, pp. 267-273).

A. Glucocorticoid Receptor Competitive Binding Assay

Step 1. Characterization of the Fluorescent Probe

The wavelengths for maximum excitation and emission of the fluorescent probe should first be measured. An example of such a probe is rhodamine (TAMRA)-labeled dexamethasone.

The affinity of the probe for the steroid receptor was then determined in a titration experiment. The fluorescence polarization value of the probe in assay buffer was measured on an SLM-

8100 fluorometer using the excitation and emission maximum values described above. Aliquots of expression vector lysate were added and fluorescence polarization was measured after each addition until no further change in polarization value was observed. Non-linear least squares regression analysis was used to calculate the dissociation constant of the probe from the polarization values obtained for lysate binding to the probe.

Step 2. Screening for Inhibitors of Probe Binding

This assay uses fluorescence polarization (FP) to quantitate the ability of test compounds to compete with tetramethyl rhodamine (TAMRA)-labeled dexamethasone for binding to a human glucocorticoid receptor (GR) complex prepared from an insect expression system. The assay buffer was: 10 mM TES, 50 mM KCl, 20 mM $Na_2MoO_4 \cdot 2H_2O$, 1.5 mM EDTA, 0.04% w/v CHAPS, 10% v/v glycerol, 1 mM dithiothreitol, pH 7.4. Test compounds were dissolved to 1 mM in neat DMSO and then further diluted to 10x assay concentration in assay buffer supplemented with 10% v/v DMSO. Test compounds were serially diluted at 10x assay concentrations in 10% DMSO-containing buffer in 96-well polypropylene plates. Binding reaction mixtures were prepared in 96-well black Dynex microtiter plates by sequential addition of the following assay components to each well: 15 µL of 10x test compound solution, 85 µL of GR-containing baculovirus lysate diluted 1:170 in assay buffer, and 50 µL of 15 nM TAMRA-labeled dexamethasone. Positive controls were reaction mixtures containing no test compound; negative controls (blanks) were reaction mixtures containing 0.7 µM to 2 µM dexamethasone. The binding reactions were incubated for 1 hour at room temperature and then read for fluorescence polarization in the LJL Analyst set to 550 nm excitation and 580 nm emission, with the Rhodamine 561 dichroic mirror installed. IC_{50} values were determined by iterative non-linear curve fitting of the FP signal data to a 4-parameter logistic equation.

Compounds found to bind to the glucocorticoid receptor may be evaluated for binding to the progesterone receptor (PR), estrogen receptor (ER), and mineralocorticoid receptors (MR) to evaluate the compound's selectivity for GR. The protocols for PR and MR are identical to the above GR method, with the following exceptions: PR insect cell lysate is diluted 1:7.1 and MR lysate diluted 1:9.4. PR probe is TAMRA-labeled mifepristone, used at a final concentration of 5 nM in the assay, and the negative controls (blanks) were reactions containing mifepristone at 0.7 µM to 2 µM.

The ER protocol is similar to the above protocols, but uses PanVera kit receptor, fluorescein-labeled probe. The assay components are made in the same volumes as above, to produce final assay concentrations for ER of 15 nM and ES2 probe of 1 nM. In addition, the component order of addition is modified from the above assays: probe is added to the plate first, followed by receptor and test compound. The plates are read in the LJL Analyst set to 485 nm excitation and 530 nm emission, with the Fluorescein 505 dichroic mirror installed.

Compounds found to bind to the glucocorticoid receptor may be evaluated for dissociation of transactivation and transrepression by assays cited in the Background of the Invention (C.M. Bamberger and H.M. Schulte, Eur. J. Clin. Invest., 2000, 30 (suppl. 3) pp. 6-9) or by the assays described below.

B. Glucocorticoid Receptor Cell Assays

1. Induction of Aromatase in Fibroblasts (Cell Assay for Transactivation).

Dexamethasone, a synthetic ligand to the glucocorticoid receptor (GR), induces expression of aromatase in human foreskin fibroblast cells. The activity of aromatase is measured by the conversion of testosterone to estradiol in culture media. Compounds that exhibit binding to GR are evaluated for their ability to induce aromatase activity in human foreskin fibroblasts.

Human foreskin fibroblast cells (ATCC Cat. No. CRL-2429, designation CCD112SK) are plated on 96 well plates at 50,000 cells per well 5 days before use, in Iscove's Modified Dulbecco's Media (GibcoBRL Life Technologies Cat No. 12440-053) supplemented with 10% charcoal filtered FBS (Clonetech Cat No. SH30068) and Gentamycin (GibcoBRL Life Technologies Cat. No. 15710-064). On the day of the experiment, the media in the wells is replaced with fresh media. Cells are treated with test compounds to final concentrations of 10^{-5} M to 10^{-8} M, and testosterone to a final concentration of 300 ng/mL. Each well has a total volume of 100 µL. Samples are made in duplicates. Control wells include: (a) wells that receive testosterone only, and (b) wells that receive testosterone plus 2 µM of dexamethasone to provide maximum induction of aromatase. Plates are incubated at 37°C overnight (15 to 18 hours), and supernatants are harvested at the end of incubation. Estradiol in the supernatant is measured using ELISA kits for estradiol (made by ALPCO, obtained from American

Laboratory Products Cat. No. 020-DR-2693) according to the manufacture's instruction. The amount of estradiol is inversely proportional to the ELISA signals in each well. The extent of aromatase induction by test compounds is expressed as a relative percentage to dexamethasone. EC_{50} values of test compounds are derived by non-linear curve fitting.

2. Inhibition of IL-6 Production in Fibroblasts (Cell Assay for Transrepression)

Human foreskin fibroblast cells produce IL-6 in response to stimulation by proinflammatory cytokine IL-1. This inflammatory response, as measured by the production of IL-6, can be effectively inhibited by dexamethasone, a synthetic ligand to the glucocorticoid receptor (GR). Compounds that exhibit binding to GR are evaluated for their ability to inhibit IL-6 production in human foreskin fibroblasts.

Human foreskin fibroblast cells (ATCC Cat. No. CRL-2429) are plated on 96 well plates at 5,000 cells per well the day before use, in Iscove's Modified Dulbecco's Media (GibcoBRL Life Technologies Cat. No. 12440-053) supplemented with 10% charcoal filtered FBS (Clonetech Cat. No. SH30068) and Gentamycin (GibcoBRL Life Technologies Cat. No. 15710-064). On the next day, media in the wells is replaced with fresh media. Cells are treated with IL-1 (rhIL-1α, R&D Systems Cat. No. 200-LA) to a final concentration of 1 ng/mL, and with test compounds to final concentrations of 10^{-5} M to 10^{-8} M, in a total volume of 200 μL per well. Samples are done in duplicates. Background control wells do not receive test compounds or IL-1. Positive control wells receive IL-1 only and represent maximum (or 100%) amount of IL-6 production. Plates are incubated at 37°C overnight (15 to 18 hours), and supernatants are harvested at the end of incubation. IL-6 levels in the supernatants are determined by the ELISA kits for IL-6 (MedSystems Diagnostics GmbH, Vienna, Austria, Cat. No. BMS213TEN) according to manufacture's instructions. The extent of inhibition of IL-6 by test compounds is expressed in percentage relative to positive controls. IC_{50} values of test compounds are derived by non-linear curve fitting.

Evaluation of agonist or antagonist activity of compounds binding to the glucocorticoid receptor may be determined by any of the assays.

3. Modulation of Tyrosine Aminotransferase (TAT) Induction in Rat Hepatoma Cells

Testing of compounds for agonist or antagonist activity in induction of tyrosine aminotransferase (TAT) in rat hepatoma cells.

H4-II-E-C3 cells were incubated overnight in 96 well plates (20,000 cells/100 µL/well) in MEM medium containing 10% heat inactivated FBS and 1% nonessential amino acids. On the next day, cells were stimulated with the indicated concentrations of dexamethasone or test compound (dissolved in DMSO, final DMSO concentration 0.2%) for 18 hours. Control cells were treated with 0.2% DMSO. After 18 hours, the cells were lysed in a buffer containing 0.1% Triton X-100 and the TAT activity was measured in a photometric assay using tyrosine and alpha-ketoglutarate as substrates.

For measuring antagonist activity, the hepatoma cells were pre-stimulated by addition of dexamethasone (concentration ranges from 3×10^{-9} M to 3×10^{-8} M) shortly before the test compound was applied to the cells. The steroidal non-selective GR/PR antagonist mifepristone was used as control.

4. Modulation of MMTV-Luc Induction in HeLa Cells

Testing of compounds for agonist or antagonist activity in stimulation of MMTV-(mouse mammary tumor virus) promoter in HeLa cells.

HeLa cells were stably co-transfected with the pHHLuc-plasmid containing a fragment of the MMTV-LTR (-200 to +100 relative to the transcription start site) cloned in front of the luciferase gene (Nordeen, 1988) and the pcDNA3.1 plasmid (Invitrogen) constitutively expressing the resistance for the selective antibiotic GENETICIN®. Clones with best induction of the MMTV-promoter were selected and used for further experiments.

Cells were cultured overnight in DMEM medium without phenol red, supplemented with 3% CCS (charcoal treated calf serum) and then transferred to 96 well plates (15,000 cells/100 µL/well). On the next day, activation of the MMTV-promoter was stimulated by addition of test compound or dexamethasone dissolved in DMSO (final concentration 0.2%). Control cells were treated with DMSO only. After 18 hours, the cells were lysed with cell lysis reagent

(Promega, Cat. No. E1531), luciferase assay reagent (Promega, Cat. No. E1501) was added and the glow luminescence was measured using a luminometer (BMG, Offenburg).

For measuring antagonist activity, the MMTV-promoter was pre-stimulated by adding dexamethasone (3×10^{-9} M to 3×10^{-8} M) shortly before the test compound was applied to the cells. The steroidal non-selective GR/PR antagonist mifepristone was used as control.

5. Modulation of IL-8 Production in U937 Cells

Testing of compounds for agonist or antagonist activity in GR-mediated inhibition of LPS-induced IL-8 secretion in U-937 cells.

U-937 cells were incubated for 2 to 4 days in RPMI1640 medium containing 10% CCS (charcoal treated calf serum). The cells were transferred to 96 well plates (40,000 cells/100 µL/well) and stimulated with 1 µg/mL LPS (dissolved in PBS) in the presence or absence of dexamethasone or test compound (dissolved in DMSO, final concentration 0.2%). Control cells were treated with 0.2% DMSO. After 18 hours, the IL-8 concentration in the cell supernatant was measured by ELISA, using the "OptEIA human IL-8 set" (Pharmingen, Cat. No. 2654KI).

For measuring antagonist activity, the LPS-induced IL-8 secretion was inhibited by adding dexamethasone (3×10^{-9} M to 3×10^{-8} M) shortly before the test compound was applied to the cells. The steroidal non-selective GR/PR antagonist mifepristone was used as control.

6. Modulation of ICAM-Luc Expression in HeLa Cells

Testing of compounds for agonist or antagonist activity in inhibition of TNF-alpha-induced activation of the ICAM-promoter in HeLa cells.

HeLa cells were stably co-transfected with a plasmid containing a 1.3 kb fragment of the human ICAM-promoter (-1353 to -9 relative to the transcription start site, Ledebur and Parks, 1995) cloned in front of the luciferase gene and the pcDNA3.1 plasmid (Invitrogen) which constitutively expresses the resistance for the antibiotic GENETICIN®. Clones with best induction of the ICAM-promoter were selected and used for further experiments. Cells were

transferred to 96 well plates (15,000 cells/100 µL/well) in DMEM medium supplemented with 3% CCS. On the following day the activation of the ICAM-promoter was induced by addition of 10 ng/mL recombinant TNF-alpha (R&D System, Cat. No. 210-TA). Simultaneously the cells were treated with the test compound or dexamethasone (dissolved in DMSO, final concentration 0.2%). Control cells were treated with DMSO only. After 18 hours, the cells were lysed with cell lysis reagent (Promega, Cat. No. E1531), luciferase assay reagent (Promega, Cat. No. E1501) was added and glow luminescence was measured using a luminometer (BMG, Offenburg).

For measuring antagonist activity, the TNF-alpha-induced activation of the ICAM-promoter was inhibited by adding dexamethasone (3×10^{-9} M to 3×10^{-8} M) shortly before the test compound was applied to the cells. The steroidal non-selective GR/PR antagonist mifepristone was used as control.

In general, the preferred potency range in the above assays is between 0.1 nM and 10 µM, the more preferred potency range is 0.1 nM to 1 µM, and the most preferred potency range is 0.1 nM to 100 nM.

Representative compounds of the invention have been tested and have shown activity as modulators of the glucocorticoid receptor function in one or more of the above assays. For example, the following compounds of the invention of Formula (IA) have demonstrated potent activity in the GR binding assay:

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(4,6-Dimethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-pyrrolo[3,2-*c*]pyridine-6-carbonitrile;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridine-5-carbonitrile;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*c*]pyridine-4-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-thieno[2,3-*d*]pyridazin-2-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(2-methyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*d*]pyridazin-2-ylmethyl)pentan-2-ol;

2-(4,6-Dimethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(4,6-dimethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile;

2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(7-fluoro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5,7-Dichloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5-trifluoromethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(5-methoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-methoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(5-methoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(7-fluoro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-trifluoromethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(5-chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(5-methyl-2,3-dihydrobenzofuran-7-yl)-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-pyrrolo[2,3-*b*]pyridin-1-ylmethylpentan-2-ol;

2-Benzo[*b*]thiophen-2-ylmethyl-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-thieno[2,3-*c*]pyridin-2-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-[4-((*Z*)propenyl)-3-vinylpyrazol-1-ylmethyl]pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,4-dimethyl-1-thieno[2,3-*c*]pyridin-2-ylpentan-2-ol;

4-(5-Fluoro-2-methylphenyl)-2,4-dimethyl-1-thieno[2,3-*c*]pyridin-2-ylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(5-methyl-2,3-dihydrobenzofuran-7-yl)-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(3-Dimethylaminomethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-pyrrolo[3,2-*c*]pyridin-1-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-furo[3,2-*c*]pyridin-2-ylmethyl-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

1,1-Difluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

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1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-thieno[3,2-c]pyridin-2-ylmethylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-thieno[3,2-*c*]pyridin-2-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-thieno[3,2-c]pyridin-2-ylmethylpentan-2-ol;

2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carboxylic acid dimethylamide;

{2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-6-yl}morpholin-4-ylmethanone;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carboxylic acid dimethylamide;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carboxylic acid dimethylamide;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-6-yl}morpholin-4-ylmethanone;

2-[4-(2,3-Dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

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2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carboxylic acid amide;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carboxylic acid amide;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-nitro-1*H*-indol-2-ylmethyl)butyl]phenol;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carbonitrile;

2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carbonitrile;

N-{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}acetamide;

1,1,1-Trifluoro-4-(4-fluoro-2-methoxyphenyl)-2-(7-fluoro-4-methyl-1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-(7-fluoro-4-methyl-1*H*-indol-2-ylmethyl)-3-hydroxy-1,1-dimethylbutyl]phenol;

2-[4-(3-[1,3]Dioxolan-2-ylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid-2-trimethylsilanylethyl ester;

2-[4-(4-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}piperidin-1-ylmethanone;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid methylamide;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}pyrrolidin-1-ylmethanone;

1-{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}piperidin-4-one;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid (2-hydroxyethyl)amide;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}(4-hydroxypiperidin-1-yl)methanone;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}(3-hydroxypyrrolidin-1-yl)methanone;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid cyanomethylamide;

({2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}amino)acetic acid methyl ester;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid carbamoylmethylamide;

4-({2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}amino)butyric acid methyl ester;

({2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}amino)acetic acid;

4-({2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}amino)butyric acid;

2-[4-(3-Dimethylaminomethylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-trifluoromethyl-1*H*-indol-2-ylmethyl)butyl]phenol;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid amide;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid dimethylamide;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid cyanomethylamide;

{2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}pyrrolidin-1-ylmethanone;

{2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}morpholin-4-ylmethanone;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid amide;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}morpholin-4-ylmethanone;

2-(4-Benzo[1,3]dioxol-4-yl-2-hydroxy-4-methyl-2-trifluoromethylpentyl)-4-methyl-1*H*-indole-6-carbonitrile;

1,1,1-Trifluoro-4-methyl-4-phenyl-2-quinolin-4-ylmethylhexan-2-ol;

2-[2-Hydroxy-4-methyl-4-(5-methylsulfanyl-2,3-dihydrobenzofuran-7-yl)-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

7-(4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-quinolin-4-ylmethylbutyl)-2,3-dihydrobenzofuran-5-carbonitrile;

2-[2-Hydroxy-4-(2-hydroxy-5-methylphenyl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-methylsulfanyl-1*H*-indol-2-ylmethyl)pentan-2-ol;

2-[2-Hydroxy-4-(5-methanesulfonyl-2-methoxyphenyl)-4-methyl-2-trifluoromethyl-pentyl]-1*H*-indole-3-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-phenyl-1*H*-indol-2-ylmethyl)pentan-2-ol;

2-[4-(5-*tert*-Butyl-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethyl-pentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(2-hydroxy-5-isopropylphenyl)-4-methyl-2-trifluoromethyl-pentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(2-hydroxy-3,5-dimethylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(5-hydroxy-2,4-dimethylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

2-[4-(5-*tert*-Butyl-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(5-isopropyl-2-methoxyphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(2-methoxy-5-methylphenyl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*o*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*m*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-(2-fluorophenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(2-fluorophenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorophenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

3-(4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-quinolin-4-ylmethylbutyl)phenol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-(2-trifluoromethylphenyl)pentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-(4-trifluoromethylphenyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-(4-trifluoromethylphenyl)pentan-2-ol;

4-(3-Chlorophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

4-(3-Chlorophenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(4-Dimethylaminophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

4-Biphenyl-3-yl-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(3-Bromophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

4-(2-Difluoromethoxy-5-fluorophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

4-Biphenyl-3-yl-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

4-(4-Dimethylaminophenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,6-dihydropyrrolo[2,3-*c*]pyridin-5-one;

2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-6-methyl-1,6-dihydropyrrolo[2,3-*c*]pyridin-5-one;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-methoxy-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

2-[4-(3-Dimethylaminomethylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-pyridin-2-ylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-pyridin-4-yl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*o*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*m*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-pyridin-4-ylmethylpentan-2-ol;

4-Fluoro-2-[4,4,4-trifluoro-3-(2-fluoropyridin-4-ylmethyl)-3-hydroxy-1,1-dimethylbutyl]phenol;

2-[3-(2-Bromopyridin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

2-(6,8-Dimethylquinolin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

4-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]pyridine-2-carbonitrile;

2,6-Dichloro-4-[4-(5-fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]nicotinonitrile;

2,6-Dichloro-4-[4-(5-fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]nicotinonitrile;

2-(2,6-Dichloroquinolin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-[3-(2-Chloro-8-methylquinolin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

2-[3-(2,6-Dichloroquinolin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

4-(2,3-Dihydrobenzofuran-7-yl)-2-(2,6-dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(3-fluorophenyl)-4-methylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(4-fluorophenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-methyl-4-*m*-tolylpentan-2-ol;

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1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(2-methylquinolin-4-ylmethyl)pentan-2-ol;

4-Fluoro-2-(4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-quinolin-4-ylmethylbutyl)phenol;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(2-methylquinolin-4-ylmethyl)butyl]phenol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(7-methylquinolin-4-ylmethyl)pentan-2-ol;

2-[3-(2,6-Dimethylpyridin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-5-fluorophenol;

1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-(2-methylquinolin-4-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(3-methyl-1*H*-indol-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-(2-trifluoromethylphenyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(7-fluoro-4-methylquinolin-8-yl)-4-methylpentan-2-ol;

4-(2,6-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

2-(3-Bromo-1*H*-indol-2-ylmethyl)-1,1,1-trifluoro-4-(3-fluorophenyl)-4-methylpentan-2-ol;

4-(3,4-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluoro-4-methylphenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-3-methylphenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluoro-4-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-2-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(3,4-Dimethylphenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(2,5-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-(2-methoxy-5-methylphenyl)-4-methylpentan-2-ol;

4-Methyl-2-[4,4,4-trifluoro-3-hydroxy-3-(1*H*-indol-2-ylmethyl)-1,1-dimethylbutyl]phenol;

4-(2,5-Dimethylphenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(2,5-Dimethoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-c]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-(2-trifluoromethylphenyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-4-methylpentan-2-ol;

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2-(2,4-Dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-(2-Amino-4-chloro-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol; and

2-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol,

or a tautomer, prodrug, solvate, or salt thereof.

In addition, the following compounds of the invention of Formula (IA) have been tested and have shown activity as potent agonists of the glucocorticoid receptor function in one or more of the above assays:

4-Pyrimidin-5-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(4,6-Dimethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-pyrrolo[3,2-*c*]pyridine-6-carbonitrile;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridine-5-carbonitrile;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*c*]pyridine-4-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-thieno[2,3-*d*]pyridazin-2-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*d*]pyridazin-2-ylmethyl)pentan-2-ol;

2-(4,6-Dimethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(4,6-dimethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile;

2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(7-fluoro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5,7-Dichloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5-trifluoromethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(5-methoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-methoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(5-methoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(7-fluoro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-trifluoromethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(5-chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(5-methyl-2,3-dihydrobenzofuran-7-yl)-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-thieno[2,3-*c*]pyridin-2-ylmethylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,4-dimethyl-1-thieno[2,3-*c*]pyridin-2-ylpentan-2-ol;

4-(5-Fluoro-2-methylphenyl)-2,4-dimethyl-1-thieno[2,3-*c*]pyridin-2-ylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(5-methyl-2,3-dihydrobenzofuran-7-yl)-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(3-Dimethylaminomethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

1,1-Difluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-thieno[3,2-*c*]pyridin-2-ylmethylpentan-2-ol;

2-[4-(2,3-Dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-nitro-1*H*-indol-2-ylmethyl)butyl]phenol;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carbonitrile;

2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carbonitrile;

N-{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl} acetamide;

1,1,1-Trifluoro-4-(4-fluoro-2-methoxyphenyl)-2-(7-fluoro-4-methyl-1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-(7-fluoro-4-methyl-1*H*-indol-2-ylmethyl)-3-hydroxy-1,1-dimethylbutyl]phenol;

2-[4-(3-[1,3]Dioxolan-2-ylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile;

2-[4-(4-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid methylamide;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}pyrrolidin-1-ylmethanone;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}(3-hydroxypyrrolidin-1-yl)methanone;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid cyanomethylamide;

({2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}amino)acetic acid methyl ester;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid carbamoylmethylamide;

4-({2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}amino)butyric acid methyl ester;

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4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-trifluoromethyl-1*H*-indol-2-ylmethyl)butyl]phenol;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid amide;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid dimethylamide;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid cyanomethylamide;

{2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}pyrrolidin-1-ylmethanone;

{2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}morpholin-4-ylmethanone;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid amide;

{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}morpholin-4-ylmethanone;

2-(4-Benzo[1,3]dioxol-4-yl-2-hydroxy-4-methyl-2-trifluoromethylpentyl)-

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4-methyl-1*H*-indole-6-carbonitrile;

1,1,1-Trifluoro-4-methyl-4-phenyl-2-quinolin-4-ylmethylhexan-2-ol;

2-[2-Hydroxy-4-methyl-4-(5-methylsulfanyl-2,3-dihydrobenzofuran-7-yl)-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

7-(4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-quinolin-4-ylmethylbutyl)-2,3-dihydrobenzofuran-5-carbonitrile;

2-[2-Hydroxy-4-(2-hydroxy-5-methylphenyl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-methylsulfanyl-1*H*-indol-2-ylmethyl)pentan-2-ol;

2-[2-Hydroxy-4-(5-methanesulfonyl-2-methoxyphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

2-[4-(5-*tert*-Butyl-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(2-hydroxy-5-isopropylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(2-hydroxy-3,5-dimethylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(5-hydroxy-2,4-dimethylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

2-[4-(5-*tert*-Butyl-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-

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1*H*-indole-3-carbonitrile;

2-[2-Hydroxy-4-(5-isopropyl-2-methoxyphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*o*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*m*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-(2-fluorophenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(2-fluorophenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorophenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

3-(4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-quinolin-4-ylmethylbutyl)phenol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-(2-trifluoromethylphenyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-(4-trifluoromethylphenyl)pentan-2-ol;

4-(3-Chlorophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

4-(3-Chlorophenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-Biphenyl-3-yl-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

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4-(3-Bromophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

4-(2-Difluoromethoxy-5-fluorophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

4-(4-Dimethylaminophenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-methoxy-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

2-[4-(3-Dimethylaminomethylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-pyridin-2-ylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*o*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*m*-tolylpentan-2-ol;

4-Fluoro-2-[4,4,4-trifluoro-3-(2-fluoropyridin-4-ylmethyl)-3-hydroxy-1,1-dimethylbutyl]phenol;

2-[3-(2-Bromopyridin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

2-(6,8-Dimethylquinolin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

4-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]pyridine-2-carbonitrile;

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2,6-Dichloro-4-[4-(5-fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]nicotinonitrile;

2,6-Dichloro-4-[4-(5-fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]nicotinonitrile;

2-[3-(2,6-Dichloroquinolin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

4-(2,3-Dihydrobenzofuran-7-yl)-2-(2,6-dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(3-fluorophenyl)-4-methylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(4-fluorophenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-methyl-4-*m*-tolylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(2-methylquinolin-4-ylmethyl)pentan-2-ol;

4-Fluoro-2-(4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-quinolin-4-ylmethylbutyl)phenol;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(2-methylquinolin-4-ylmethyl)butyl]phenol;

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2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(7-methylquinolin-4-ylmethyl)pentan-2-ol;

2-[3-(2,6-Dimethylpyridin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-5-fluorophenol;

1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-(2-methylquinolin-4-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(3-methyl-1*H*-indol-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-(2-trifluoromethylphenyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(7-fluoro-4-methylquinolin-8-yl)-4-methylpentan-2-ol;

4-(2,6-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

2-(3-Bromo-1*H*-indol-2-ylmethyl)-1,1,1-trifluoro-4-(3-fluorophenyl)-4-methylpentan-2-ol;

4-(3,4-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluoro-4-methylphenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-3-methylphenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluoro-4-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-2-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(3,4-Dimethylphenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(2,5-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-(2-methoxy-5-methylphenyl)-4-methylpentan-2-ol;

4-Methyl-2-[4,4,4-trifluoro-3-hydroxy-3-(1*H*-indol-2-ylmethyl)-1,1-dimethylbutyl]phenol;

4-(2,5-Dimethylphenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol;

4-(2,5-Dimethoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-(2-trifluoromethylphenyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-4-methylpentan-2-ol;

2-(2,4-Dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-(2-Amino-4-chloro-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

4-(5-Bromo-2-methoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Bromo-2-methoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

2-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-[5-(ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-methylpentan-2-ol;

2-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-phenylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-pyrrolidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4'-Methoxy-3'-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-2-carbonitrile;

2-(5-Diethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-[5-(isopropylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-4-methylpentan-2-ol;

4-(3-Bromophenyl)-1,1,1-trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(3-pyrimidin-5-ylphenyl)pentan-2-ol;

3'-{3-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl}-4'-hydroxybiphenyl-2-carbonitrile;

4'-Hydroxy-3'-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-2-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)pentan-2-ol;

4-Chloro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)butyl]phenol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-pyrrolo[3,2-*c*]pyridine-6-carbonitrile;

2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridine-5-carbonitrile;

1-{2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}ethanone;

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2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carboxylic acid amide;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(5-hydroxymethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

2-(5-Aminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)butyl]phenol;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)butyl]phenol;

1,1,1-Trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(3-phenyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(3-phenyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1-{2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}propan-1-one;

1-{2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}-2-methylpropan-1-one;

1,1,1-Trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-thiophen-3-ylphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(4-methoxybiphenyl-3-yl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]phenol;

4-Thiophen-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]phenol;

3-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]biphenyl-4-ol;

1,1,1-Trifluoro-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(5-pyrimidin-5-yl-2,3-dihydrobenzofuran-7-yl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(5-phenoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-phenyl-2-(3-phenyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(3-phenyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-ylmethyl)pentan-2-ol;

4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-phenoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol;

1,1,1-Trifluoro-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-4-(5-pyrimidin-5-yl-2,3-dihydrobenzofuran-7-yl)pentan-2-ol;

4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]phenol;

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5-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)butyl]phenol;

1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylmethylphenyl)-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-2-[5-(4-fluorophenyl)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-4-methylpentan-2-ol;

2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-[3-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

2-[3-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-5-fluorophenol;

5-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol;

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4-(5-Bromo-2-methoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-Bromo-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyrimidin-5-yiphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(3-[1,3]Dioxan-2-ylphenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(4-methoxybiphenyl-3-yl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-thiophen-3-ylphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylmethylphenyl)-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

3-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-4-ol;

4-Thiophen-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol;

4-Thiophen-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol;

4-Thiophen-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol;

4'-Methoxy-3'-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-2-carbonitrile;

4'-Methoxy-3'-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-3-carbonitrile;

1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(3-Chlorophenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]phenol;

1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylmethylphenyl)-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(3-pyridin-3-ylphenyl)-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(3-pyrimidin-5-ylphenyl)-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-pyridin-2-yl-1*H*-indol-2-ylmethyl)pentan-2-ol;

2-(5-Bromo-1*H*-indol-2-ylmethyl)-4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-2-(5-methanesulfinyl-1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol;

3-{2-[4-(5-Fluoro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}benzonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-pyridin-4-yl-1*H*-indol-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-pyridin-3-yl-1*H*-indol-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-pyrimidin-5-yl-1*H*-indol-2-ylmethyl)pentan-2-ol;

2-[5-(4-Dimethylaminophenyl)-1*H*-indol-2-ylmethyl]-1,1,1-trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol;

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1,1,1-Trifluoro-2-(7-fluoro-4-methyl-1*H*-indol-2-ylmethyl)-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol;

2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile;

2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carbonitrile;

1,1,1-Trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(4-methyl-1*H*-indol-2-ylmethyl)pentan-2-ol;

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carbonitrile;

2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carbonitrile;

2-(4-Ethyl-1*H*-indol-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(2-isopropyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(2-isopropyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)butyl]phenol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)butyl]phenol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(2-chloro-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-phenyl-2-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-methylphenyl)-4-methyl-2-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-methylphenyl)-4-methyl-2-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

2-(5-Ethoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Bromo-2-methoxyphenyl)-2-(5-dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

4-(5-Bromo-2-methoxyphenyl)-1,1,1-trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-trifluoromethylphenyl)-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(4-methoxybiphenyl-3-yl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(2-methoxy-5-thiophen-3-ylphenyl)-4-methylpentan-2-ol;

2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methyl-4-phenylpentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(4-methoxybiphenyl-3-yl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methylpentan-2-ol;

4-Bromo-2-[3-(5-chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-*dimethylbutyl]phenol;*

2-[3-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

2-[2-Hydroxy-4-(4-hydroxybiphenyl-3-yl)-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridin-5-ol;

1,1,1-Trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methyl-4-(5-phenyl-2,3-dihydrobenzofuran-7-yl)pentan-2-ol;

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2-[2-Hydroxy-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridin-5-ol;

Trifluoromethanesulfonic acid 2-[4-(5-fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridin-5-yl ester;

1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-phenyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorophenyl)-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methyl-4-phenylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylmethylphenyl)-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(5-methoxy-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-methoxy-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(5-chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(4-methoxy-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

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2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,4-dihydropyrrolo[3,2-*b*]pyridin-5-one;

2-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(2-methoxy-5-thiophen-3-ylphenyl)-4-methylpentan-2-ol;

2-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methyl-4-(5-methylsulfanyl-2,3-dihydrobenzofuran-7-yl)pentan-2-ol;

4-(5-Bromo-2-methoxyphenyl)-2-(5-chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-naphthalen-1-ylphenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(2'-Chloro-4-methoxybiphenyl-3-yl)-1,1,1-trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methylpentan-2-ol;

4'-Methoxy-3'-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-2-carbonitrile;

4-(2'-Chloro-4-methoxybiphenyl-3-yl)-1,1,1-trifluoro-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

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2-[3-(3-Dimethylaminomethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

1,1,1-Trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-(3-Chloro-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-methyl-4-(5-methylsulfanyl-2,3-dihydrobenzofuran-7-yl)-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol; and

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol,

or a tautomer, prodrug, solvate, or salt thereof.

The following compounds of the invention of Formula (IB) have been tested and have shown activity as agonists of the glucocorticoid receptor function in one or more of the above assays:

2-Cyclopropyl-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[3,2-*c*]pyridin-2-yl)pentan-2-ol;

2-Cyclopropyl-4-(5-fluoro-2-methylphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

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4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-cyclopropyl-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

2-Cyclopropyl-4-(5-fluoro-2-methylphenyl)-4-methyl-1-(1*H*-pyrrolo[3,2-*c*]pyridin-2-yl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-cyclopropyl-4-methyl-1-(1*H*-pyrrolo[3,2-*c*]pyridin-2-yl)pentan-2-ol;

5-(5-Fluoro-2-methoxyphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methoxyphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

2-(5-Fluoro-2-methoxyphenyl)-2,5,5-trimethyl-4-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)heptan-4-ol;

1,1-Difluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

5-(5-Fluoro-2-methylphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

1,1-Difluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

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5-(5-Fluoro-2-methoxyphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methoxyphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

2-(1-Fluorocyclopropyl)-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol;

2-[4,4-Difluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]-4-fluorophenol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

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5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

5-(5-Fluoro-2-methylphenyl)-2,5-dimethyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol; and

2-[2-Difluoromethyl-2-hydroxy-4-(5-methanesulfinyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentyl]-4-methyl-1*H*-indole-6-carbonitrile,

or a tautomer, prodrug, solvate, or salt thereof.

The following compounds of the invention of Formula (IC) have been tested and have shown activity as agonists of the glucocorticoid receptor function in one or more of the above assays:

1-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl1,5,6,7-tetrahydroindol-4-one;

1-[4-(2,3-Dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

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1-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[2-Hydroxy-4-methyl-4-(5-pyrimidin-5-yl-2,3-dihydrobenzofuran-7-yl)-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[2-Hydroxy-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[2-Hydroxy-4-(2-hydroxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one;

1-[2-Hydroxy-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one; and

1-[2-Hydroxy-4-(2-hydroxy-5-pyridin-3-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one,

or a tautomer, prodrug, solvate, or salt thereof.

The following compound of the invention of Formula (ID) have been tested and have shown activity as agonists of the glucocorticoid receptor function in one or more of the above assays:

5,5,5-Trifluoro-2-methyl-2-phenyl-4-quinolin-4-ylmethylpentane-1,4-diol, or a tautomer, prodrug, solvate, or salt thereof.

The invention also provides methods of modulating the glucocorticoid receptor function in a patient comprising administering to the patient a compound according to the invention. If the purpose of modulating the glucocorticoid receptor function in a patient is to treat a disease-state or condition, the administration preferably comprises a therapeutically or pharmaceutically effective amount of a pharmaceutically acceptable compound according to the invention. If the purpose of modulating the glucocorticoid receptor function in a patient is for a diagnostic or

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other purpose (e.g., to determine the patient's suitability for therapy or sensitivity to various sub-therapeutic doses of the compounds according to the invention), the administration preferably comprises an effective amount of a compound according to the invention, that is, the amount necessary to obtain the desired effect or degree of modulation.

7. Inhibition of Osteocalcin Production from Osteoblast Cell Line MG-63

Human osteosarcoma MG-63 cells (ATCC, Cat. No. CRL-1427) are plated on 96 well plates at 20,000 cells per well the day before use in 200 µL media of 99% D-MEM/F-12 (Gibco-Invitrogen, Cat. No. 11039-021), supplemented with 1% penicillin and streptomycin (Gibco-Invitrogen, Cat. No. 15140-122), 10 µg/mL Vitamin C (Sigma, Cat. No. A-4544), and 1% charcoal filtered Fetal Bovine Serum (HyClone, Cat. No. SH30068.02). The next day, wells are replaced with fresh media. Cells are treated with Vitamin D (Sigma, Cat. No. D1530) to a final concentration of 10 nM, and with the test compounds in concentrations of 10^{-6} M to 10^{-9} M, in a total volume of 200 µL per well. Samples are done in duplicates. Background control wells do not receive Vitamin D or compounds. Positive control wells receive Vitamin D only, without compounds, and represent maximum (100%) amount of osteocalcin production. Plates are incubated at 37°C incubator for 48 hours and supernatants are harvested at the end of incubation. Amounts of osteocalcin in the supernatants are determined by the Glype osteocalcin ELISA kit (Zymed, Cat. No. 99-0054) according to manufacture's protocol. Inhibition of osteocalcin by test compounds is expressed in percentage relative to positive controls. IC_{50} values of the test compounds are derived by non-lineal curve fitting.

The following compounds of Formula (IA) inhibit the vitamin D stimulated production of osteocalcin:

2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-pyrrolo[3,2-*c*]pyridine-6-carbonitrile;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*d*]pyridazin-2-ylmethyl)pentan-2-ol;

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4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(4,6-dimethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(5-methoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid amide;

2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid cyanomethylamide;

{2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}pyrrolidin-1-ylmethanone;

1,1,1-Trifluoro-4,4-dimethyl-5-phenyl-2-quinolin-4-ylmethylpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-[5-(ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-methylpentan-2-ol;

4-(3-Bromophenyl)-1,1,1-trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(5-pyrimidin-5-yl-2,3-dihydrobenzofuran-7-yl)pentan-2-ol;

2-[3-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol;

4-(3-Chlorophenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-pyridin-3-yl-1*H*-indol-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol;

2-[2-Hydroxy-4-(4-hydroxybiphenyl-3-yl)-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridin-5-ol;

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4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol; and

1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol,

or a tautomer, prodrug, solvate, or salt thereof.

Methods of Therapeutic Use

As pointed out above, the compounds of the invention are useful in modulating the glucocorticoid receptor function. In doing so, these compounds have therapeutic use in treating disease-states and conditions mediated by the glucocorticoid receptor function or that would benefit from modulation of the glucocorticoid receptor function.

As the compounds of the invention modulate the glucocorticoid receptor function, they have very useful anti-inflammatory and antiallergic, immune-suppressive, and anti-proliferative activity and they can be used in patients as drugs, particularly in the form of pharmaceutical compositions as set forth below, for the treatment of disease-states and conditions.

The agonist compounds according to the invention can be used in patients as drugs for the treatment of the following disease-states or indications that are accompanied by inflammatory, allergic, and/or proliferative processes:

(i) Lung diseases: chronic, obstructive lung diseases of any genesis, particularly bronchial asthma and chronic obstructive pulmonary disease (COPD); adult respiratory distress syndrome (ARDS); bronchiectasis; bronchitis of various genesis; all forms of restrictive lung diseases, particularly allergic alveolitis; all forms of lung edema, particularly toxic lung edema; all forms of interstitial lung diseases of any genesis, e.g., radiation pneumonitis; and sarcoidosis and granulomatoses, particularly Boeck disease.

(ii) Rheumatic diseases or autoimmune diseases or joint diseases: all forms of rheumatic diseases, especially rheumatoid arthritis, acute rheumatic fever, and polymyalgia rheumatica; reactive arthritis; rheumatic soft tissue diseases; inflammatory soft tissue

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diseases of other genesis; arthritic symptoms in degenerative joint diseases (arthroses); traumatic arthritis; collagenoses of any genesis, e.g., systemic lupus erythematosus, scleroderma, polymyositis, dermatomyositis, Sjögren syndrome, Still disease, and Felty syndrome;

(iii) Allergic diseases: all forms of allergic reactions, e.g., angioneurotic edema, hay fever, insect bites, allergic reactions to drugs, blood derivatives, contrast agents, etc., anaphylactic shock (anaphylaxis), urticaria, angioneurotic edema, and contact dermatitis;

(iv) Vasculitis diseases: panarteritis nodosa, polyarteritis nodosa, arteritis temporalis, Wegner granulomatosis, giant cell arthritis, and erythema nodosum;

(v) Dermatological diseases: atopic dermatitis, particularly in children; psoriasis; pityriasis rubra pilaris; erythematous diseases triggered by various noxa, e.g., rays, chemicals, burns, etc.; bullous dermatoses; diseases of the lichenoid complex; pruritus (e.g., of allergic genesis); seborrheic dermatitis; rosacea; pemphigus vulgaris; erythema multiforme exudativum; balanitis; vulvitis; hair loss, such as occurs in alopecia areata; and cutaneous T cell lymphomas;

(vi) Renal diseases: nephrotic syndrome; and all types of nephritis, e.g., glomerulonephritis;

(vii) Hepatic diseases: acute liver cell disintegration; acute hepatitis of various genesis, e.g., viral, toxic, drug-induced; and chronically aggressive and/or chronically intermittent hepatitis;

(viii) Gastrointestinal diseases: inflammatory bowel diseases, e.g., regional enteritis (Crohn disease), colitis ulcerosa; gastritis; peptic esophagitis (refluxoesophagitis); and gastroenteritis of other genesis, e.g., nontropical sprue;

(ix) Proctological diseases: anal eczema; fissures; hemorrhoids; and idiopathic proctitis;

(x) Eye diseases: allergic keratitis, uveitis, or iritis; conjunctivitis; blepharitis; neuritis nervi optici; choroiditis; and sympathetic ophthalmia;

(xi) Diseases of the ear, nose, and throat (ENT) area: allergic rhinitis or hay fever; otitis externa, e.g., caused by contact eczema, infection, etc.; and otitis media;

(xii) Neurological diseases: brain edema, particularly tumor-related brain edema; multiple sclerosis; acute encephalomyelitis; meningitis; acute spinal cord injury; stroke; and various forms of seizures, e.g., nodding spasms;

(xiii) Blood diseases: acquired hemolytic anemia; and idiopathic thrombocytopenia;

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(xiv) Tumor diseases: acute lymphatic leukemia; malignant lymphoma; lymphogranulomatoses; lymphosarcoma; extensive metastases, particularly in mammary, bronchial, and prostatic carcinoma;

(xv) Endocrine diseases: endocrine ophthalmopathy; endocrine orbitopathia; thyrotoxic crisis; Thyroiditis de Quervain; Hashimoto thyroiditis; Morbus Basedow; granulomatous thyroiditis; struma lymphomatosa; and Grave disease;

(xvi) Organ and tissue transplantations and graft-versus-host diseases;

(xvii) Severe states of shock, e.g., septic shock, anaphylactic shock, and systemic inflammatory response syndrome (SIRS);

(xviii) Substitution therapy in: congenital primary adrenal insufficiency, e.g., adrenogenital syndrome; acquired primary adrenal insufficiency, e.g., Addison disease, autoimmune adrenalitis, post-infection, tumors, metastases, etc.; congenital secondary adrenal insufficiency, e.g., congenital hypopituitarism; and acquired secondary adrenal insufficiency, e.g., post-infection, tumors, metastases, etc.;

(xix) Pain of inflammatory genesis, e.g., lumbago; and

(xx) various other disease-states or conditions including type I diabetes (insulin-dependent diabetes), osteoarthritis, Guillain-Barre syndrome, restenosis following percutaneous transluminal coronary angioplasty, Alzheimer disease, acute and chronic pain, atherosclerosis, reperfusion injury, bone resorption diseases, congestive heart failure, myocardial infarction, thermal injury, multiple organ injury secondary to trauma, acute purulent meningitis, necrotizing enterocolitis and syndromes associated with hemodialysis, leukopheresis, and granulocyte transfusion.

In addition, the compounds according to the invention can be used for the treatment of any other disease-states or conditions not mentioned above which have been treated, are treated, or will be treated with synthetic glucocorticoids (see, e.g., H.J. Hatz, Glucocorticoide: Immunologische Grundlagen, Pharmakologie und Therapierichtlinien [Glucocorticoids: Immunological Fundamentals, Pharmacology, and Therapeutic Guidelines], Stuttgart: Verlagsgesellschaft mbH, 1998, which is hereby incorporated by reference in its entirety). Most or all of the indications (i) through (xx) mentioned above are described in detail in H.J. Hatz, Glucocorticoide: Immunologische Grundlagen, Pharmakologie und Therapierichtlinien. Furthermore, the compounds of the invention can also be used to treat disorders other than

those listed above or mentioned or discussed herein, including in the Background of the Invention.

The antagonist compounds according to the invention, whether full antagonists or partial antagonists, can be used in patients as drugs for the treatment of the following disease-states or indications, without limitation: type II diabetes (non-insulin-dependent diabetes); obesity; cardiovascular diseases; hypertension; arteriosclerosis; neurological diseases, such as psychosis and depression; adrenal and pituitary tumors; glaucoma; and Cushing syndrome based on an ACTH secreting tumor like pituitary adenoma. In particular, the compounds of the invention are useful for treating obesity and all disease-states and indications related to a deregulated fatty acids metabolism such as hypertension, atherosclerosis, and other cardiovascular diseases. Using the compounds of the invention that are GR antagonists, it should be possible to antagonize both the carbohydrate metabolism and fatty acids metabolism. Thus, the antagonist compounds of the invention are useful in treating all disease-states and conditions that involve increased carbohydrate, protein, and lipid metabolism and would include disease-states and conditions leading to catabolism like muscle frailty (as an example of protein metabolism).

Methods of Diagnostic Use

The compounds of the invention may also be used in diagnostic applications and for commercial and other purposes as standards in competitive binding assays. In such uses, the compounds of the invention may be used in the form of the compounds themselves or they may be modified by attaching a radioisotope, luminescence, fluorescent label or the like in order to obtain a radioisotope, luminescence, or fluorescent probe, as would be known by one of skill in the art and as outlined in Handbook of Fluorescent Probes and Research Chemicals, 6th Edition, R.P. Haugland (ed.), Eugene: Molecular Probes, 1996; Fluorescence and Luminescence Probes for Biological Activity, W.T. Mason (ed.), San Diego: Academic Press, 1993; Receptor-Ligand Interaction. A Practical Approach, R.C. Hulme (ed.), Oxford: IRL Press, 1992, each of which is hereby incorporated by reference in their entireties.

General Administration and Pharmaceutical Compositions

When used as pharmaceuticals, the compounds of the invention are typically administered in the form of a pharmaceutical composition. Such compositions can be prepared using

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procedures well-known in the pharmaceutical art and comprise at least one compound of the invention. The compounds of the invention may also be administered alone or in combination with adjuvants that enhance stability of the compounds of the invention, facilitate administration of pharmaceutical compositions containing them in certain embodiments, provide increased dissolution or dispersion, increased inhibitory activity, provide adjunct therapy, and the like. The compounds according to the invention may be used on their own or in conjunction with other active substances according to the invention, optionally also in conjunction with other pharmacologically active substances. In general, the compounds of this invention are administered in a therapeutically or pharmaceutically effective amount, but may be administered in lower amounts for diagnostic or other purposes.

In particular, the compounds of the invention are useful in combination with glucocorticoids or corticosteroids. As pointed out above, standard therapy for a variety of immune and inflammatory disorders includes administration of corticosteroids, which have the ability to suppress immunologic and inflammatory responses (A.P. Truhan *et al.*, Annals of Allergy, 1989, 62, pp. 375-391; J.D. Baxter, Hospital Practice, 1992, 27, pp. 111-134; R.P. Kimberly, Curr. Opin. Rheumatol., 1992, 4, pp. 325-331; M.H. Weisman, Curr. Opin. Rheumatol., 1995, 7, pp. 183-190; W. Sterry, Arch. Dermatol. Res., 1992, 284 (Suppl.), pp. S27-S29). While therapeutically beneficial, however, the use of corticosteroids is associated with a number of side effects, ranging from mild to possibly life threatening, especially with prolonged and/or high dose steroid usage. Accordingly, methods and compositions that enable the use of a lower effective dosage of corticosteroids (referred to as the "steroid sparing effect") would be highly desirable to avoid unwanted side effects. The compounds of the invention provide such a steroid sparing effect by achieving the desired therapeutic effect while allowing the use of lower doses and less frequent administration of glucocorticoids or corticosteroids.

Administration of the compounds of the invention, in pure form or in an appropriate pharmaceutical composition, can be carried out using any of the accepted modes of administration of pharmaceutical compositions. Thus, administration can be, for example, orally, buccally (e.g., sublingually), nasally, parenterally, topically, transdermally, vaginally, or rectally, in the form of solid, semi-solid, lyophilized powder, or liquid dosage forms, such as, for example, tablets, suppositories, pills, soft elastic and hard gelatin capsules, powders,

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solutions, suspensions, or aerosols, or the like, preferably in unit dosage forms suitable for simple administration of precise dosages. The pharmaceutical compositions will generally include a conventional pharmaceutical carrier or excipient and a compound of the invention as the/an active agent, and, in addition, may include other medicinal agents, pharmaceutical agents, carriers, adjuvants, diluents, vehicles, or combinations thereof. Such pharmaceutically acceptable excipients, carriers, or additives as well as methods of making pharmaceutical compositions for various modes or administration are well-known to those of skill in the art. The state of the art is evidenced, e.g., by Remington: The Science and Practice of Pharmacy, 20th Edition, A. Gennaro (ed.), Lippincott Williams & Wilkins, 2000; Handbook of Pharmaceutical Additives, Michael & Irene Ash (eds.), Gower, 1995; Handbook of Pharmaceutical Excipients, A.H. Kibbe (ed.), American Pharmaceutical Ass'n, 2000; H.C. Ansel and N.G. Popovish, Pharmaceutical Dosage Forms and Drug Delivery Systems, 5th ed., Lea and Febiger, 1990; each of which is incorporated herein by reference in their entireties to better describe the state of the art.

As one of skill in the art would expect, the forms of the compounds of the invention utilized in a particular pharmaceutical formulation will be selected (e.g., salts) that possess suitable physical characteristics (e.g., water solubility) that is required for the formulation to be efficacious.

Pharmaceutical compositions suitable for buccal (sub-lingual) administration include lozenges comprising a compound of the present invention in a flavored base, usually sucrose, and acacia or tragacanth, and pastilles comprising the compound in an inert base such as gelatin and glycerin or sucrose and acacia.

Pharmaceutical compositions suitable for parenteral administration comprise sterile aqueous preparations of a compound of the present invention. These preparations are preferably administered intravenously, although administration can also be effected by means of subcutaneous, intramuscular, or intradermal injection. Injectable pharmaceutical formulations are commonly based upon injectable sterile saline, phosphate-buffered saline, oleaginous suspensions, or other injectable carriers known in the art and are generally rendered sterile and isotonic with the blood. The injectable pharmaceutical formulations may therefore be provided

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as a sterile injectable solution or suspension in a nontoxic parenterally acceptable diluent or solvent, including 1,3-butanediol, water, Ringer's solution, isotonic sodium chloride solution, fixed oils such as synthetic mono- or diglycerides, fatty acids such as oleic acid, and the like. Such injectable pharmaceutical formulations are formulated according to the known art using suitable dispersing or setting agents and suspending agents. Injectable compositions will generally contain from 0.1 to 5% w/w of a compound of the invention.

Solid dosage forms for oral administration of the compounds include capsules, tablets, pills, powders, and granules. For such oral administration, a pharmaceutically acceptable composition containing a compound(s) of the invention is formed by the incorporation of any of the normally employed excipients, such as, for example, pharmaceutical grades of mannitol, lactose, starch, pregelatinized starch, magnesium stearate, sodium saccharine, talcum, cellulose ether derivatives, glucose, gelatin, sucrose, citrate, propyl gallate, and the like. Such solid pharmaceutical formulations may include formulations, as are well-known in the art, to provide prolonged or sustained delivery of the drug to the gastrointestinal tract by any number of mechanisms, which include, but are not limited to, pH sensitive release from the dosage form based on the changing pH of the small intestine, slow erosion of a tablet or capsule, retention in the stomach based on the physical properties of the formulation, bioadhesion of the dosage form to the mucosal lining of the intestinal tract, or enzymatic release of the active drug from the dosage form.

Liquid dosage forms for oral administration of the compounds include emulsions, microemulsions, solutions, suspensions, syrups, and elixirs, optionally containing pharmaceutical adjuvants in a carrier, such as, for example, water, saline, aqueous dextrose, glycerol, ethanol and the like. These compositions can also contain additional adjuvants such as wetting, emulsifying, suspending, sweetening, flavoring, and perfuming agents.

Topical dosage forms of the compounds include ointments, pastes, creams, lotions, gels, powders, solutions, sprays, inhalants, eye ointments, eye or ear drops, impregnated dressings and aerosols, and may contain appropriate conventional additives such as preservatives, solvents to assist drug penetration and emollients in ointments and creams. Topical application may be once or more than once per day depending upon the usual medical considerations.

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Furthermore, preferred compounds for the present invention can be administered in intranasal form via topical use of suitable intranasal vehicles. The formulations may also contain compatible conventional carriers, such as cream or ointment bases and ethanol or oleyl alcohol for lotions. Such carriers may be present as from about 1% up to about 98% of the formulation, more usually they will form up to about 80% of the formulation.

Transdermal administration is also possible. Pharmaceutical compositions suitable for transdermal administration can be presented as discrete patches adapted to remain in intimate contact with the epidermis of the recipient for a prolonged period of time. To be administered in the form of a transdermal delivery system, the dosage administration will, of course, be continuous rather than intermittent throughout the dosage regimen. Such patches suitably contain a compound of the invention in an optionally buffered, aqueous solution, dissolved and/or dispersed in an adhesive, or dispersed in a polymer. A suitable concentration of the active compound is about 1% to 35%, preferably about 3% to 15%.

For administration by inhalation, the compounds of the invention are conveniently delivered in the form of an aerosol spray from a pump spray device not requiring a propellant gas or from a pressurized pack or a nebulizer with the use of a suitable propellant, e.g., dichlorodifluoromethane, trichlorofluoromethane, dichlorotetrafluoroethane, tetrafluoroethane, heptafluoropropane, carbon dioxide, or other suitable gas. In any case, the aerosol spray dosage unit may be determined by providing a valve to deliver a metered amount so that the resulting metered dose inhaler (MDI) is used to administer the compounds of the invention in a reproducible and controlled way. Such inhaler, nebulizer, or atomizer devices are known in the prior art, for example, in PCT International Publication Nos. WO 97/12687 (particularly Figure 6 thereof, which is the basis for the commercial RESPIMAT® nebulizer); WO 94/07607; WO 97/12683; and WO 97/20590, to which reference is hereby made and each of which is incorporated herein by reference in their entireties.

Rectal administration can be effected utilizing unit dose suppositories in which the compound is admixed with low-melting water-soluble or insoluble solids such as fats, cocoa butter, glycerinated gelatin, hydrogenated vegetable oils, mixtures of polyethylene glycols of various molecular weights, or fatty acid esters of polyethylene glycols, or the like. The active

compound is usually a minor component, often from about 0.05 to 10% by weight, with the remainder being the base component.

In all of the above pharmaceutical compositions, the compounds of the invention are formulated with an acceptable carrier or excipient. The carriers or excipients used must, of course, be acceptable in the sense of being compatible with the other ingredients of the composition and must not be deleterious to the patient. The carrier or excipient can be a solid or a liquid, or both, and is preferably formulated with the compound of the invention as a unit-dose composition, for example, a tablet, which can contain from 0.05% to 95% by weight of the active compound. Such carriers or excipients include inert fillers or diluents, binders, lubricants, disintegrating agents, solution retardants, resorption accelerators, absorption agents, and coloring agents. Suitable binders include starch, gelatin, natural sugars such as glucose or β-lactose, corn sweeteners, natural and synthetic gums such as acacia, tragacanth or sodium alginate, carboxymethylcellulose, polyethylene glycol, waxes, and the like. Lubricants include sodium oleate, sodium stearate, magnesium stearate, sodium benzoate, sodium acetate, sodium chloride, and the like. Disintegrators include starch, methyl cellulose, agar, bentonite, xanthan gum, and the like.

Generally, a therapeutically effective daily dose is from about 0.001 mg to about 15 mg/kg of body weight per day of a compound of the invention; preferably, from about 0.1 mg to about 10 mg/kg of body weight per day; and most preferably, from about 0.1 mg to about 1.5 mg/kg of body weight per day. For example, for administration to a 70 kg person, the dosage range would be from about 0.07 mg to about 1050 mg per day of a compound of the invention, preferably from about 7.0 mg to about 700 mg per day, and most preferably from about 7.0 mg to about 105 mg per day. Some degree of routine dose optimization may be required to determine an optimal dosing level and pattern.

Pharmaceutically acceptable carriers and excipients encompass all the foregoing additives and the like.

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Examples of Pharmaceutical Formulations

A. TABLETS	
Component	Amount per tablet (mg)
active substance	100
lactose	140
corn starch	240
polyvinylpyrrolidone	15
magnesium stearate	5
TOTAL	500

The finely ground active substance, lactose, and some of the corn starch are mixed together. The mixture is screened, then moistened with a solution of polyvinylpyrrolidone in water, kneaded, wet-granulated and dried. The granules, the remaining corn starch and the magnesium stearate are screened and mixed together. The mixture is compressed to produce tablets of suitable shape and size.

B. TABLETS	
Component	Amount per tablet (mg)
active substance	80
lactose	55
corn starch	190
polyvinylpyrrolidone	15
magnesium stearate	2
microcrystalline cellulose	35
sodium-carboxymethyl starch	23
TOTAL	400

The finely ground active substance, some of the corn starch, lactose, microcrystalline cellulose, and polyvinylpyrrolidone are mixed together, the mixture is screened and worked with the remaining corn starch and water to form a granulate which is dried and screened. The sodium-

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carboxymethyl starch and the magnesium stearate are added and mixed in and the mixture is compressed to form tablets of a suitable size.

C. COATED TABLETS	
Component	Amount per tablet (mg)
active substance	5
lactose	30
corn starch	41.5
polyvinylpyrrolidone	3
magnesium stearate	0.5
TOTAL	90

The active substance, corn starch, lactose, and polyvinylpyrrolidone are thoroughly mixed and moistened with water. The moist mass is pushed through a screen with a 1 mm mesh size, dried at about 45°C and the granules are then passed through the same screen. After the magnesium stearate has been mixed in, convex tablet cores with a diameter of 6 mm are compressed in a tablet-making machine. The tablet cores thus produced are coated in known manner with a covering consisting essentially of sugar and talc. The finished coated tablets are polished with wax.

D. CAPSULES	
Component	Amount per capsule (mg)
active substance	50
corn starch	268.5
magnesium stearate	1.5
TOTAL	320

The substance and corn starch are mixed and moistened with water. The moist mass is screened and dried. The dry granules are screened and mixed with magnesium stearate. The finished mixture is packed into size 1 hard gelatine capsules.

E. AMPOULE SOLUTION	
Component	Amount per ampoule
active substance	50 mg
sodium chloride	50 mg
water for inj.	5 mL

The active substance is dissolved in water at its own pH or optionally at pH 5.5 to 6.5 and sodium chloride is added to make it isotonic. The solution obtained is filtered free from pyrogens and the filtrate is transferred under aseptic conditions into ampoules which are then sterilized and sealed by fusion. The ampoules contain 5 mg, 25 mg, and 50 mg of active substance.

F. SUPPOSITORIES	
Component	Amount per suppository (mg)
active substance	50
solid fat	1650
TOTAL	1700

The hard fat is melted. At 40°C, the ground active substance is homogeneously dispersed therein. The mixture is cooled to 38°C and poured into slightly chilled suppository molds.

G. METERING AEROSOL	
Component	Amount
active substance	0.005
sorbitan trioleate	0.1
monofluorotrichloromethane and difluorodichloromethane (2:3)	to 100

The suspension is transferred into a conventional aerosol container with a metering valve. Preferably, 50 μL of suspension are delivered per spray. The active substance may also be metered in higher doses if desired (e.g., 0.02% by weight).

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H. POWDER FOR INHALATION	
Component	Amount
active substance	1.0 mg
lactose monohydrate	to 25 mg

I. POWDER FOR INHALATION	
Component	Amount
active substance	2.0 mg
lactose monohydrate	to 25 mg

J. POWDER FOR INHALATION	
Component	Amount
active substance	1.0 mg
lactose monohydrate	to 5 mg

K. POWDER FOR INHALATION	
Component	Amount
active substance	2.0 mg
lactose monohydrate	to 5 mg

In Examples H, I, J, and K, the powder for inhalation is produced in the usual way by mixing the individual ingredients together.

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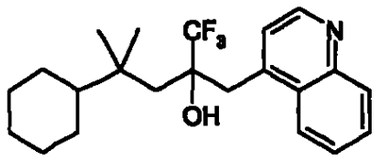
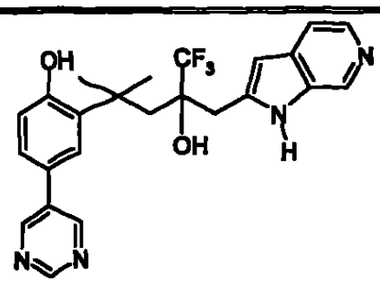
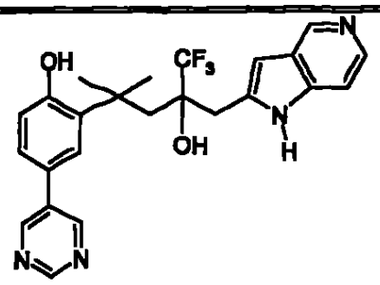
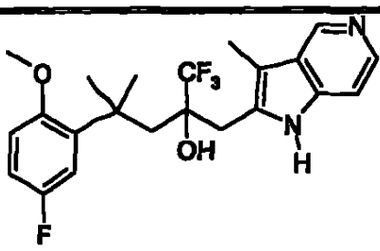
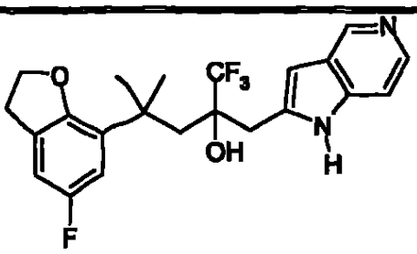
IA	
A	B
4-Cyclohexyl-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol	
4-Pyrimidin-5-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	
4-Pyrimidin-5-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]phenol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	

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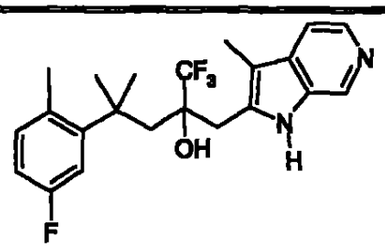
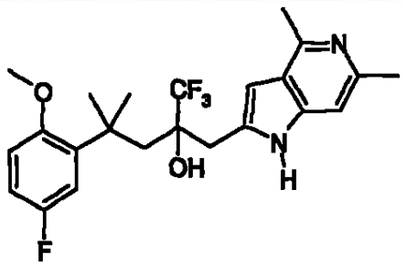
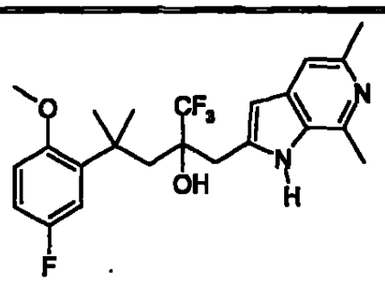
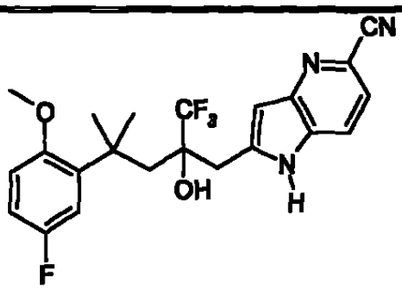
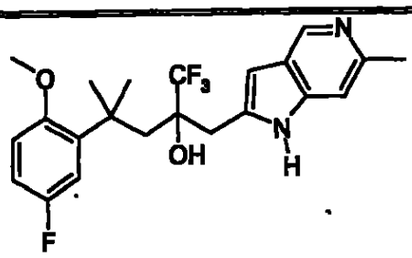
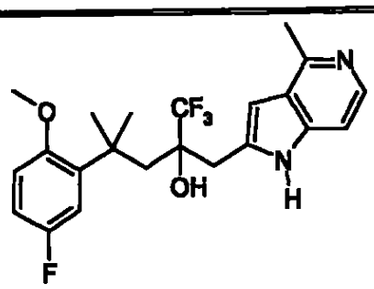
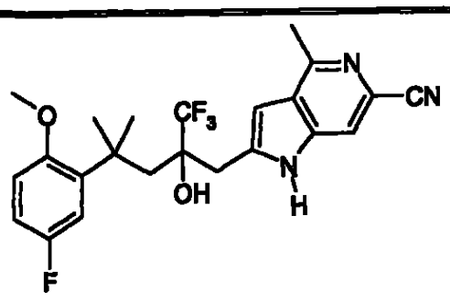
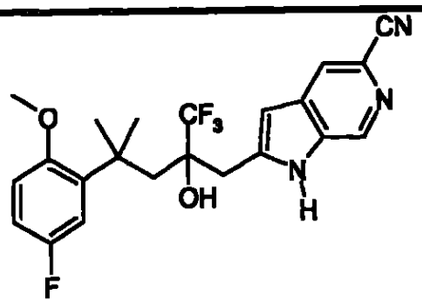
IA	
A	B
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
2-(4,6-Dimethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	
2-(5,7-Dimethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile	

IA	
A	B
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-pyrrolo[3,2-*c*]pyridine-6-carbonitrile	
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridine-5-carbonitrile	

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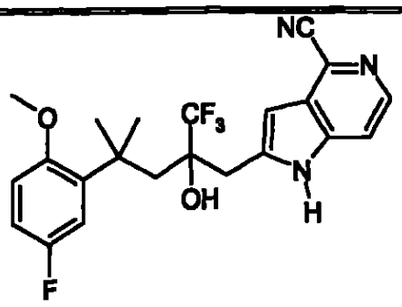
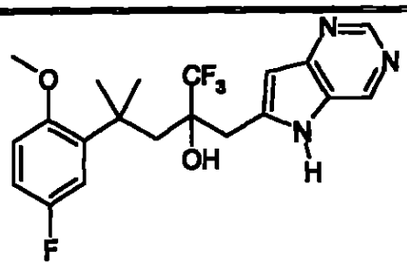
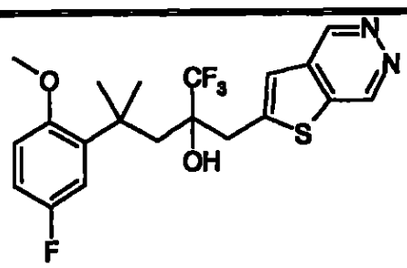
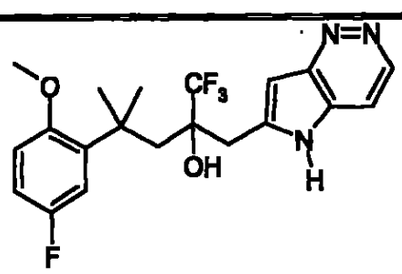
IA	
A	B
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*c*]pyridine-4-carbonitrile	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-thieno[2,3-*d*]pyridazin-2-ylmethylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)pentan-2-ol	

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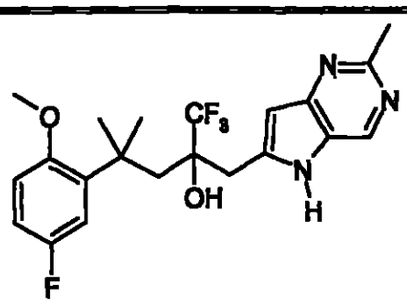
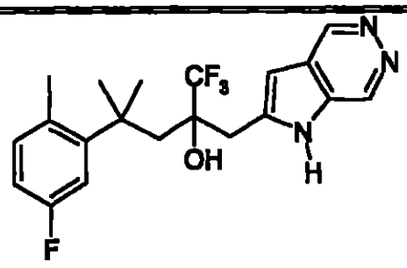
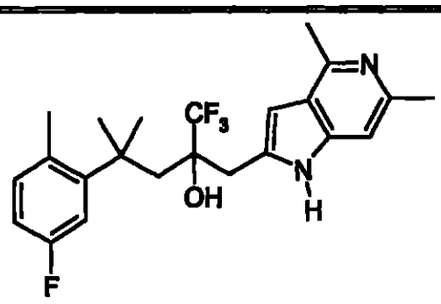
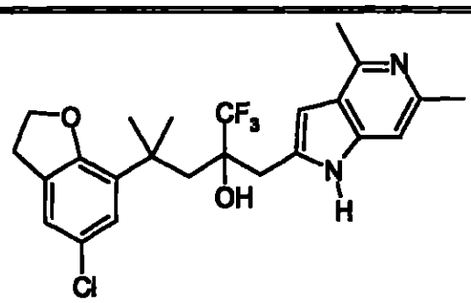
IA	
A	B
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(2-methyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*d*]pyridazin-2-ylmethyl)pentan-2-ol	
2-(4,6-Dimethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(4,6-dimethyl-1*H*-pyrrolo[3,2-c]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol	

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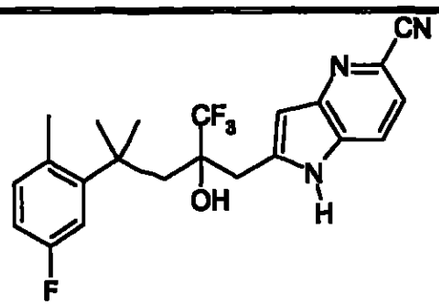
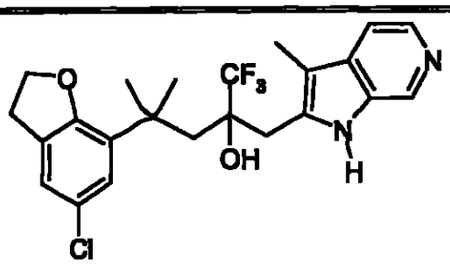
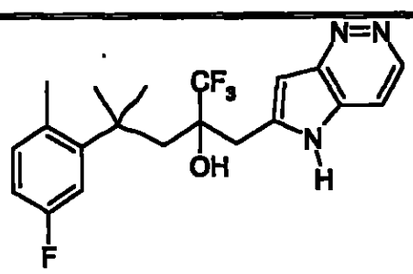
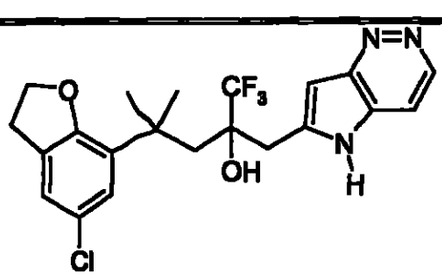
IA	
A	B
2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)pentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)pentan-2-ol	

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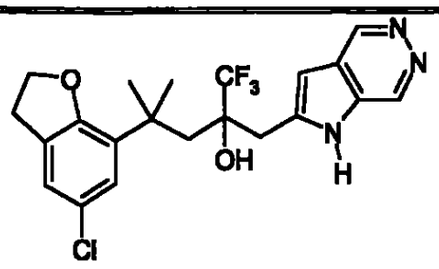
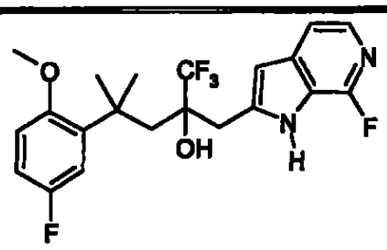
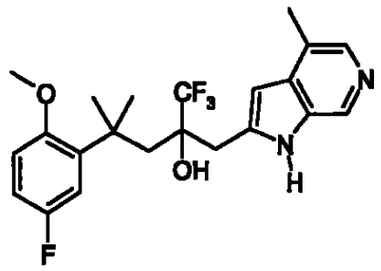
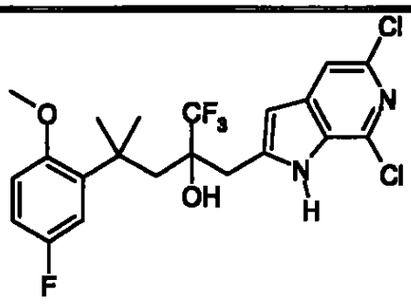
IA	
A	B
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*d*]pyridazin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(7-fluoro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
2-(5,7-Dichloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	

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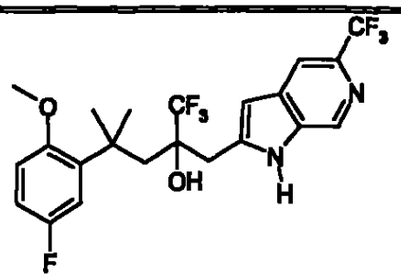
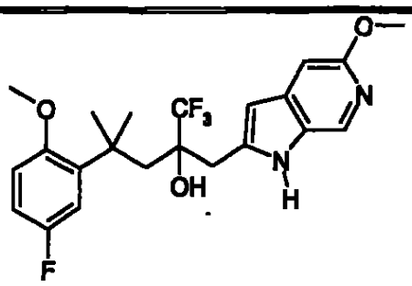
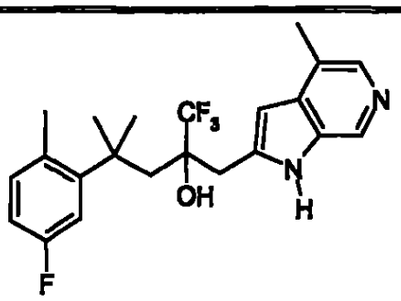
IA	
A	**B**
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5-trifluoromethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(5-methoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

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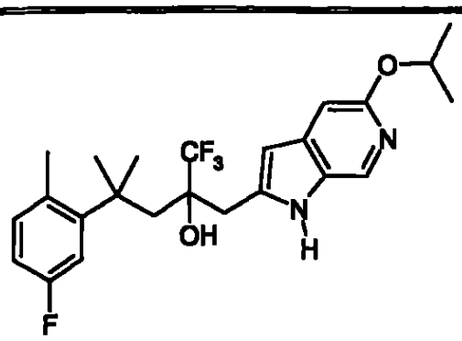
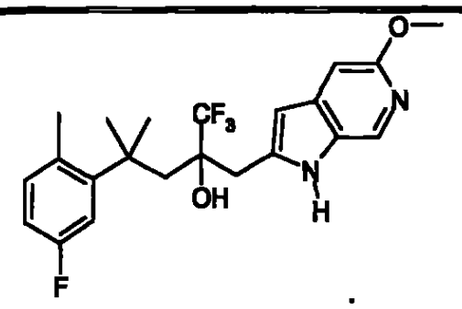
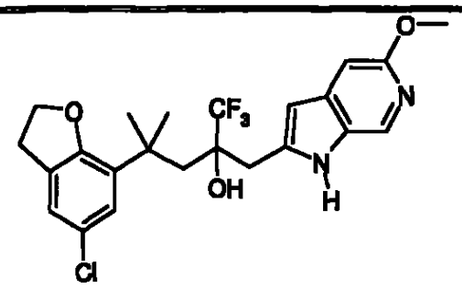
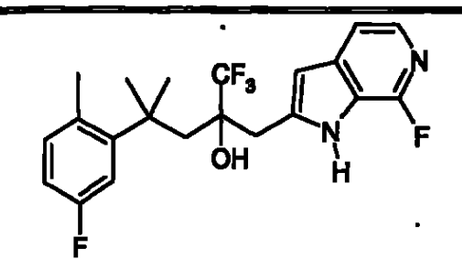
IA	
A	B
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-methoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(5-methoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(7-fluoro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	

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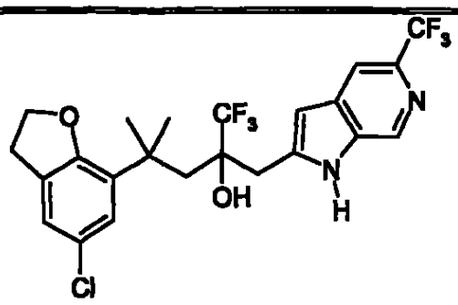
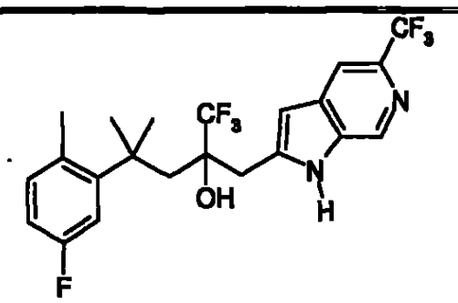
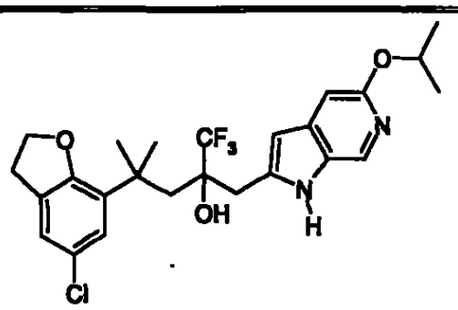
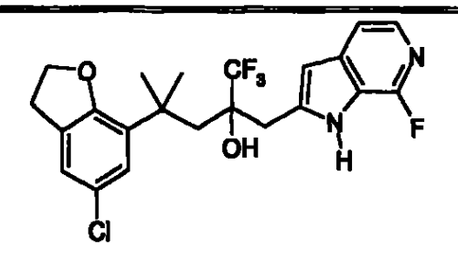
IA	
A	B
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-trifluoromethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-trifluoromethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(7-fluoro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	

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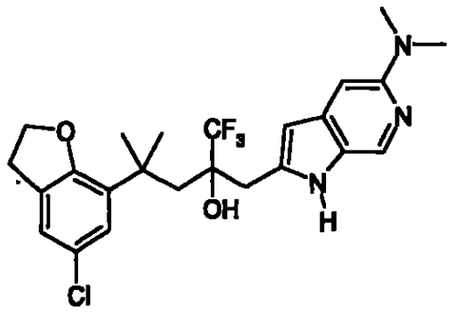
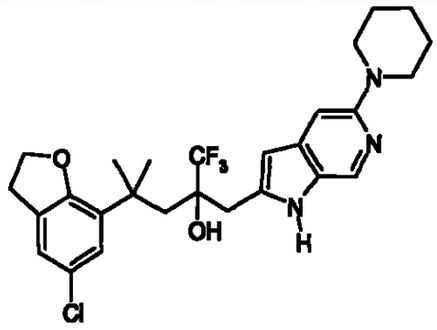
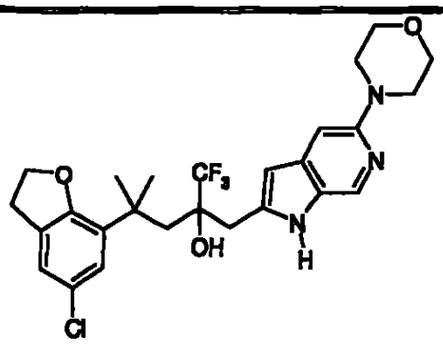
IA	
A	B
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(5-dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

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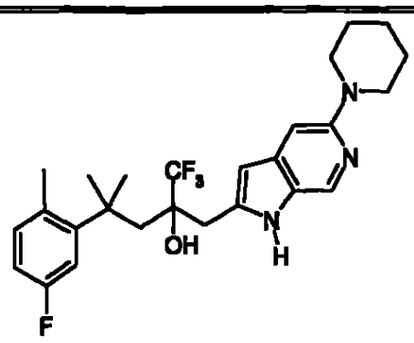
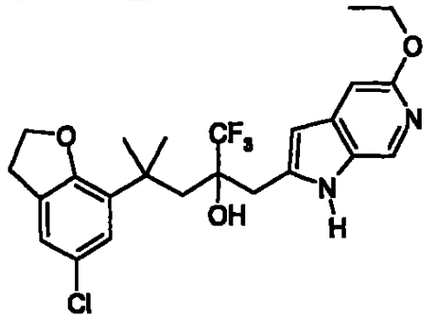
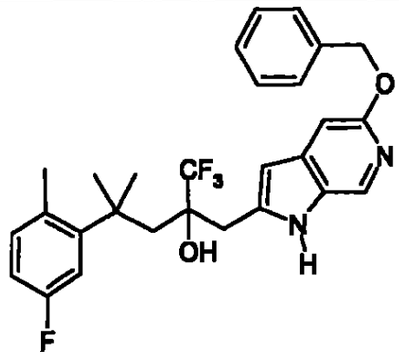
397

IA	
A	B
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(5-ethoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol	
2-(5-Benzyloxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol	

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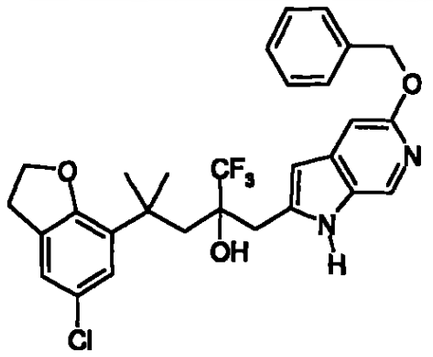
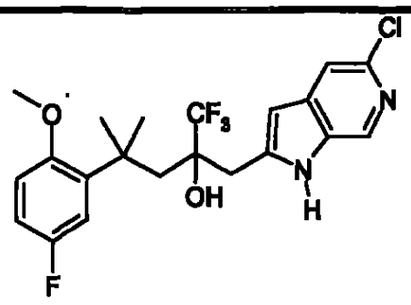
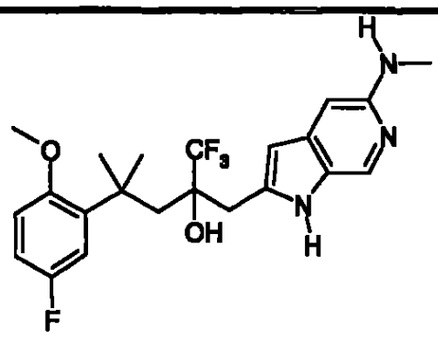
IA	
A	B
2-(5-Benzyloxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(5-chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-[5-(methylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]pentan-2-ol	

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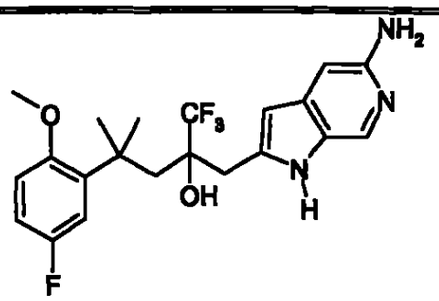
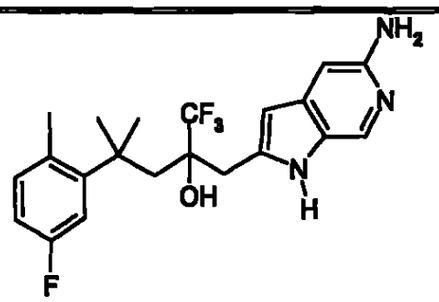
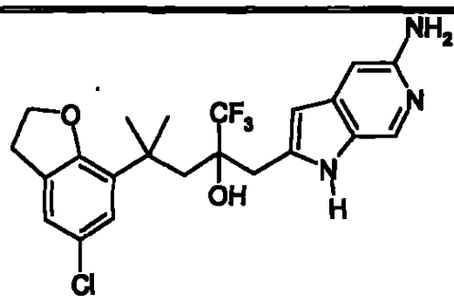
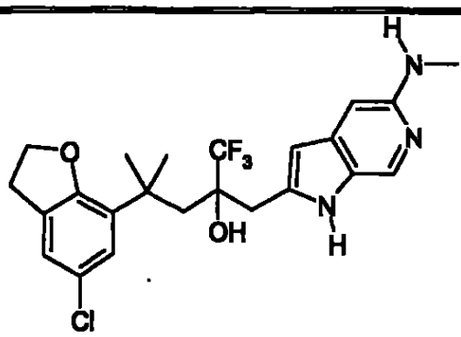
IA	
A	B
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5-amino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(6-amino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(5-amino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-methylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

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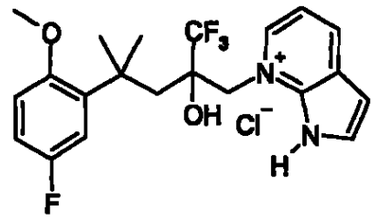
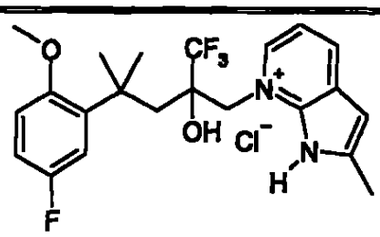
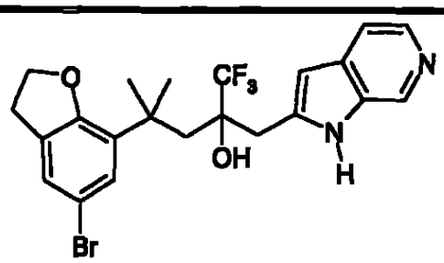
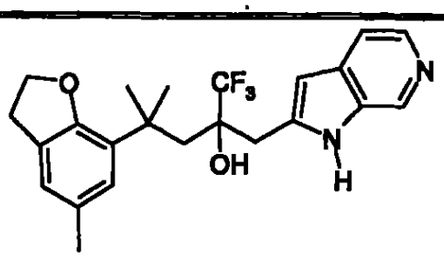
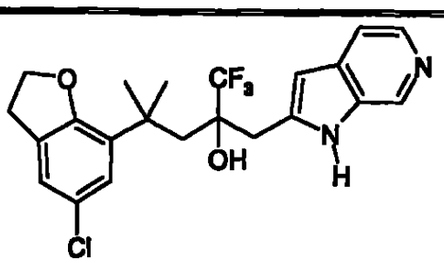
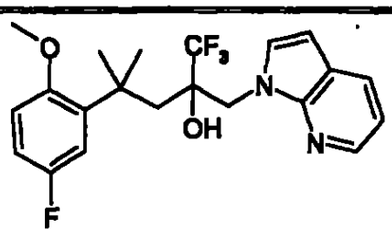
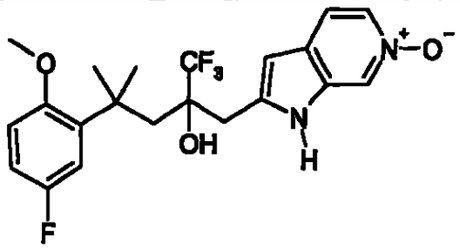
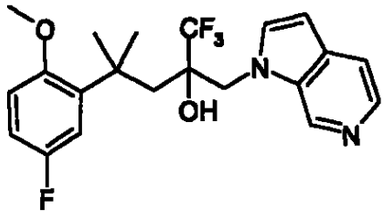
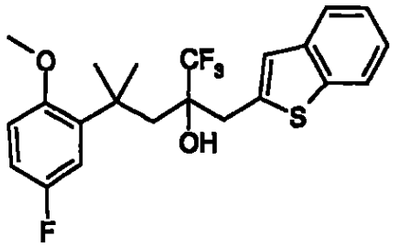
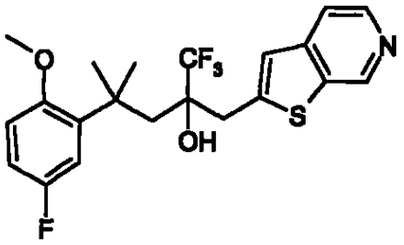
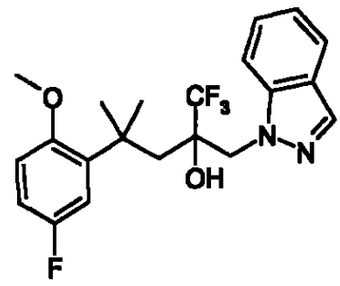
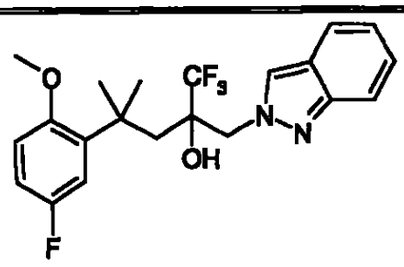
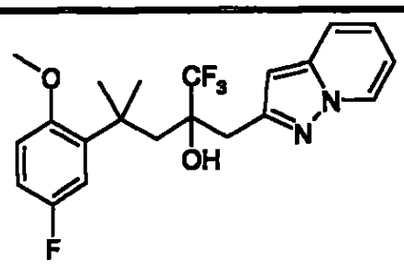
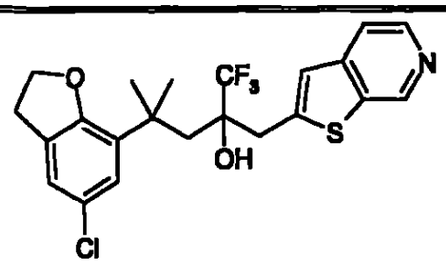
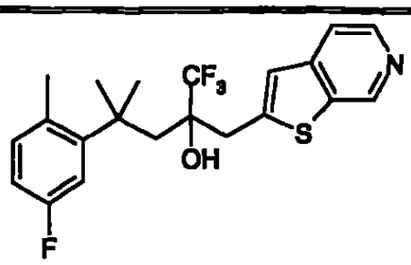
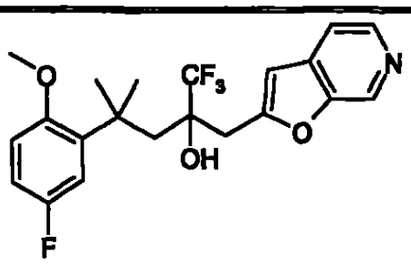
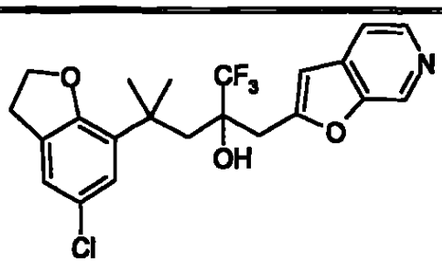
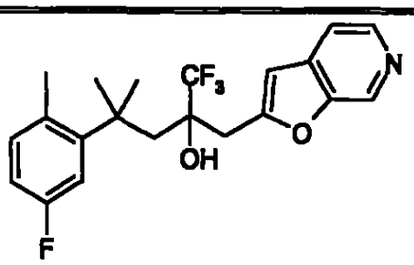
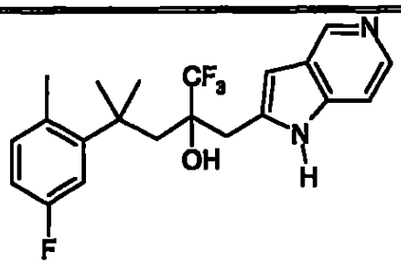
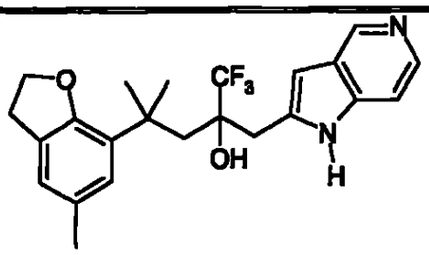
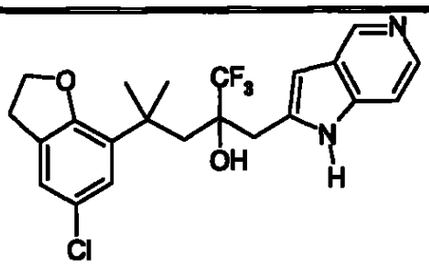
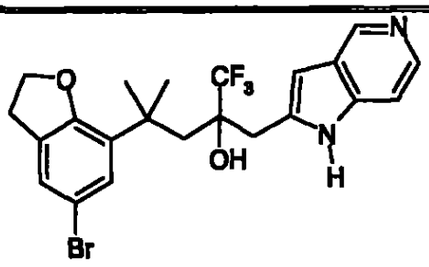
IA	
A	B
7-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*b*]pyridin-7-ium chloride	
6-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-2-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-6-ium chloride	
4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(5-methyl-2,3-dihydrobenzofuran-7-yl)-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

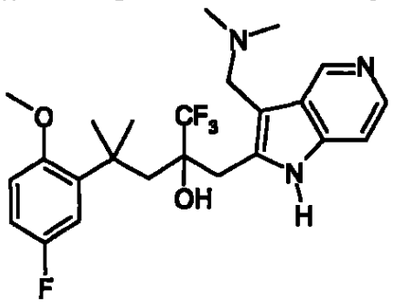
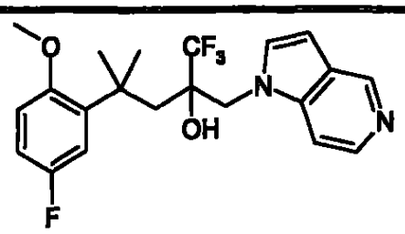
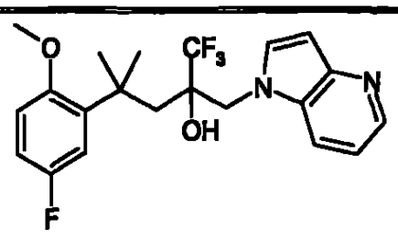
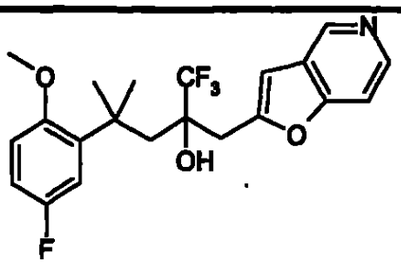
IA	
A	B
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-pyrrolo[2,3-*b*]pyridin-1-ylmethylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(6-oxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-pyrrolo[2,3-*c*]pyridin-1-ylmethylpentan-2-ol	
2-Benzo[*b*]thiophen-2-ylmethyl-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-thieno[2,3-*c*]pyridin-2-ylmethylpentan-2-ol	

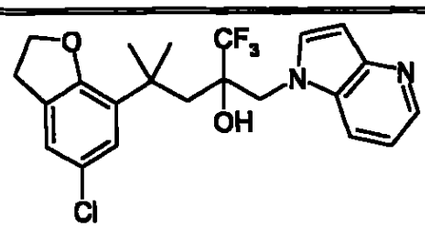
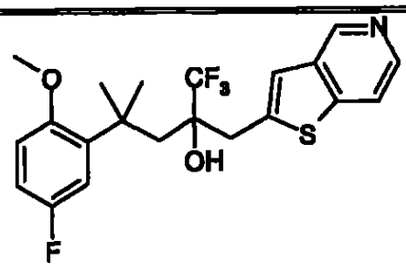
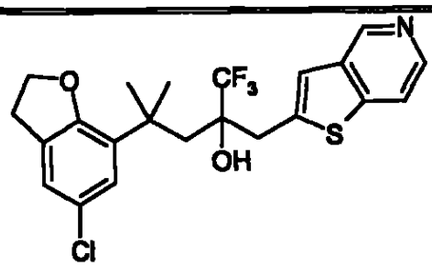
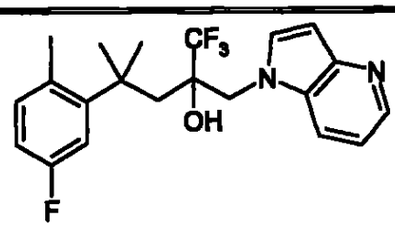
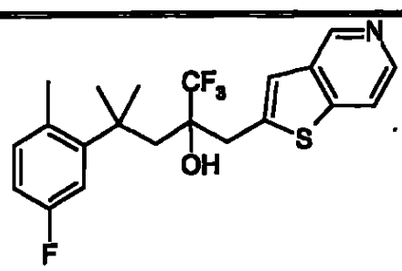
IA	
A	B
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-indazol-1-ylmethyl-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-[4-((Z)propenyl)-3-vinylpyrazol-1-ylmethyl]pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-pyrazolo[1,5-*a*]pyridin-2-ylmethylpentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,4-dimethyl-1-thieno[2,3-*c*]pyridin-2-ylpentan-2-ol	

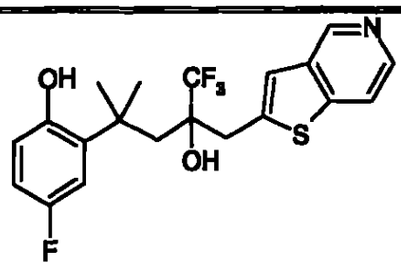
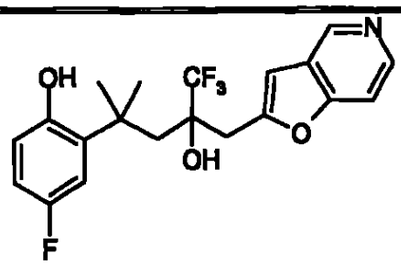
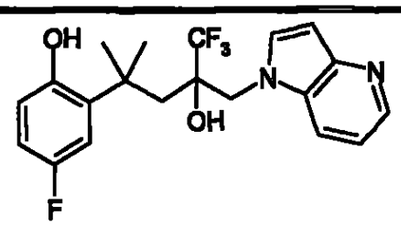
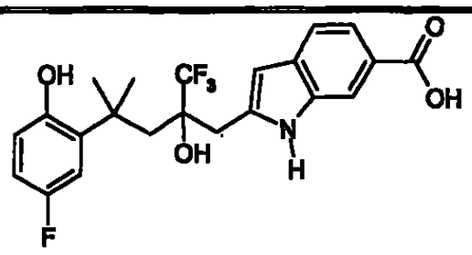
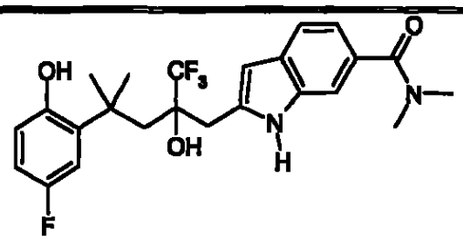
IA	
A	B
4-(5-Fluoro-2-methylphenyl)-2,4-dimethyl-1-thieno[2,3-*c*]pyridin-2-ylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-furo[2,3-*c*]pyridin-2-ylmethyl-4-methylpentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1-furo[2,3-*c*]pyridin-2-yl-2,4-dimethylpentan-2-ol	
4-(5-Fluoro-2-methylphenyl)-1-furo[2,3-*c*]pyridin-2-yl-2,4-dimethylpentan-2-ol	

IA	
A	**B**
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(5-methyl-2,3-dihydrobenzofuran-7-yl)-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	

387.
405

IA	
A	**B**
2-(3-Dimethylaminomethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-pyrrolo[3,2-*c*]pyridin-1-ylmethylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-furo[3,2-*c*]pyridin-2-ylmethyl-4-methylpentan-2-ol	

IA	
A	B
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-thieno[3,2-*c*]pyridin-2-ylmethylpentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-thieno[3,2-*c*]pyridin-2-ylmethylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-thieno[3,2-*c*]pyridin-2-ylmethylpentan-2-ol	

IA	
A	B
4-Fluoro-2-(4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-thieno[3,2-*c*]pyridin-2-ylmethylbutyl)phenol	
4-Fluoro-2-(4,4,4-trifluoro-3-furo[3,2-*c*]pyridin-2-ylmethyl-3-hydroxy-1,1-dimethylbutyl)phenol	
4-Fluoro-2-(4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-pyrrolo[3,2-*b*]pyridin-1-ylmethylbutyl)phenol	
2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carboxylic acid	
2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carboxylic acid dimethylamide	

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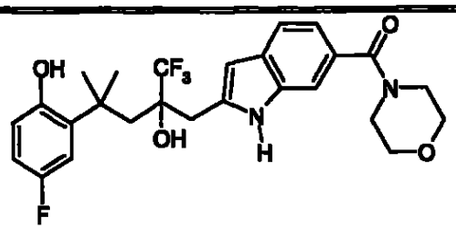
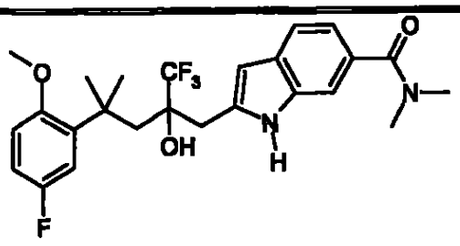
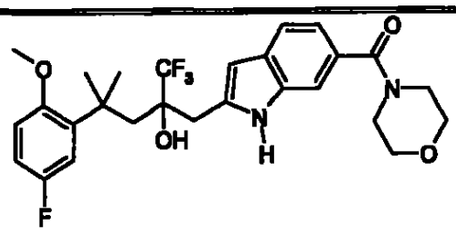
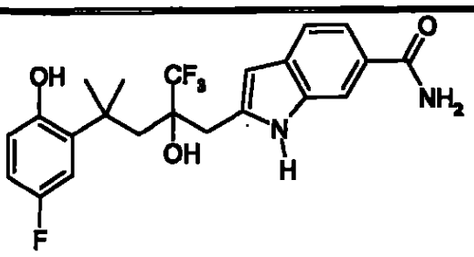
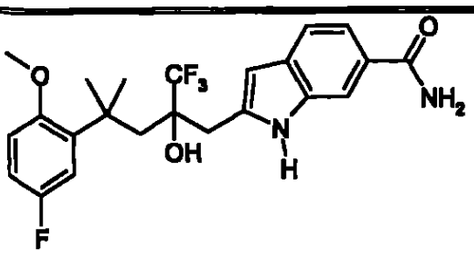
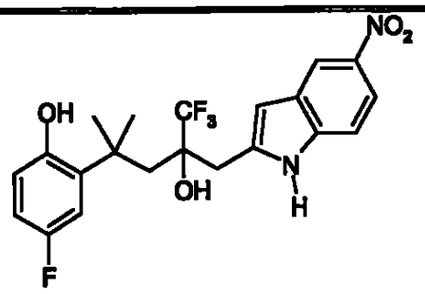
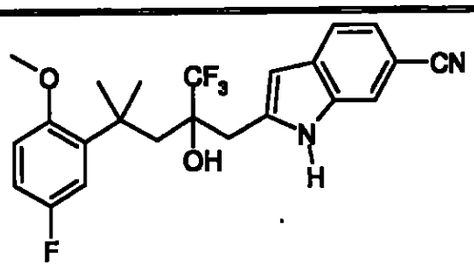
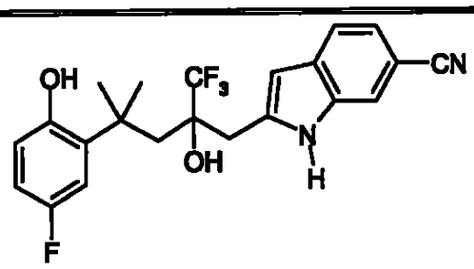
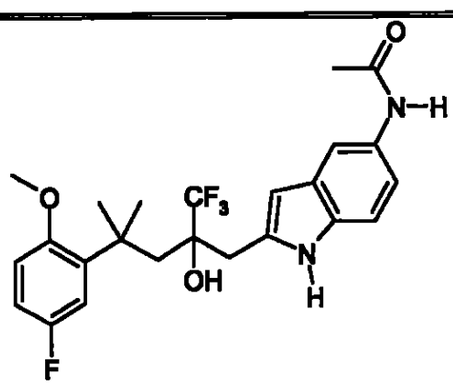
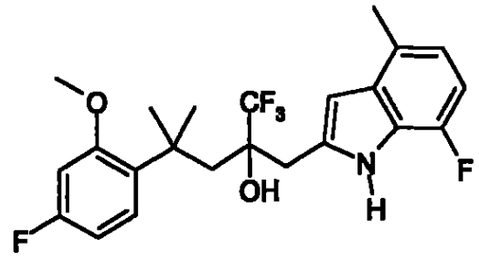
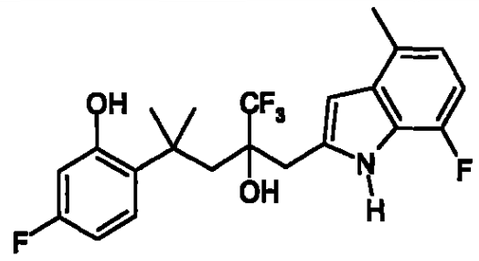
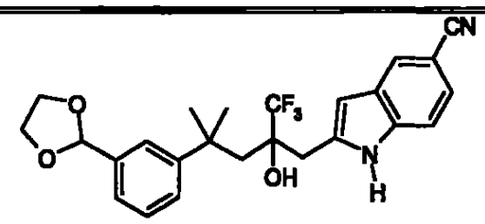
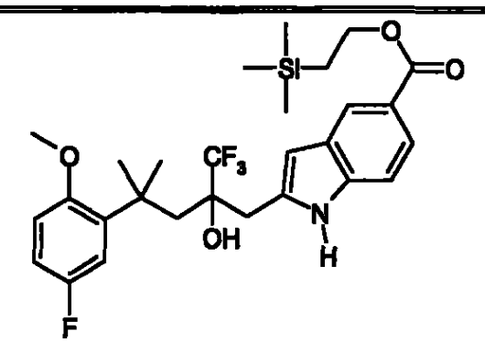
408

IA	
A	B
{2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-6-yl}morpholin-4-ylmethanone	
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carboxylic acid dimethylamide	
{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-6-yl}morpholin-4-ylmethanone	
2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carboxylic acid amide	
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carboxylic acid amide	

IA	
A	B
4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-nitro-1*H*-indol-2-ylmethyl)butyl]phenol	
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carbonitrile	
2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carbonitrile	
N-{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}acetamide	

IA	
A	**B**
1,1,1-Trifluoro-4-(4-fluoro-2-methoxyphenyl)-2-(7-fluoro-4-methyl-1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol	
5-Fluoro-2-[4,4,4-trifluoro-3-(7-fluoro-4-methyl-1*H*-indol-2-ylmethyl)-3-hydroxy-1,1-dimethylbutyl]phenol	
2-[4-(3-[1,3]Dioxolan-2-ylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile	
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid-2-trimethylsilanylethyl ester	

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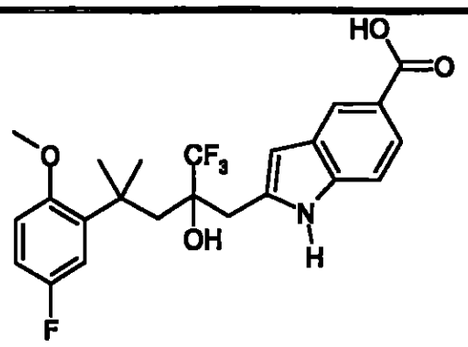
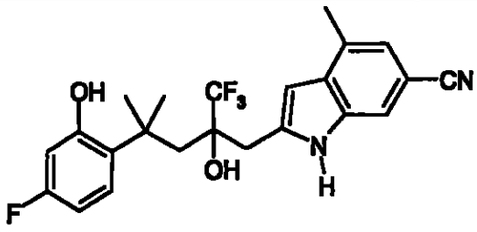
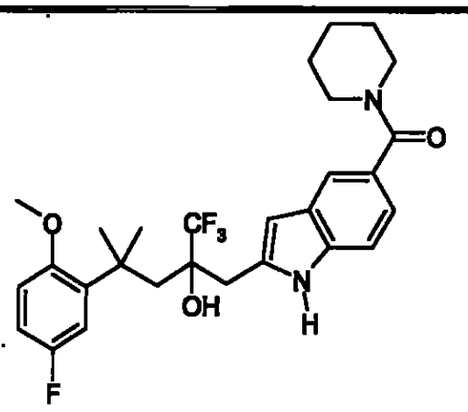
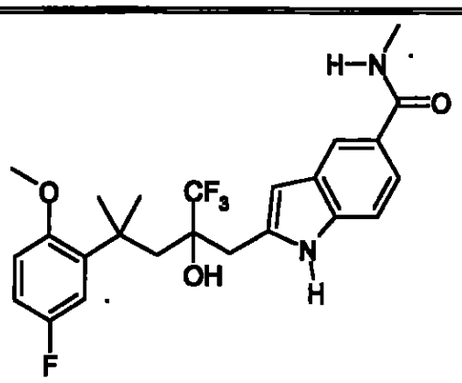
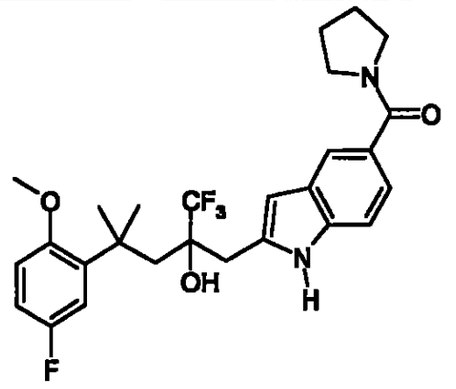
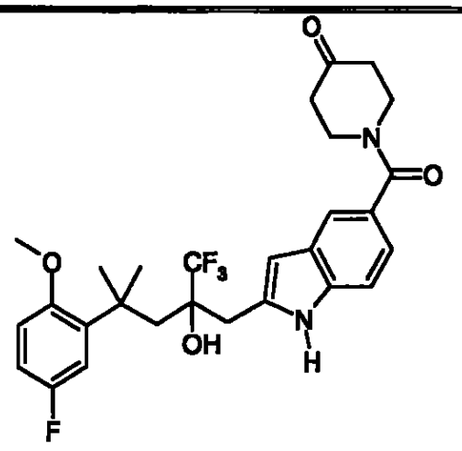
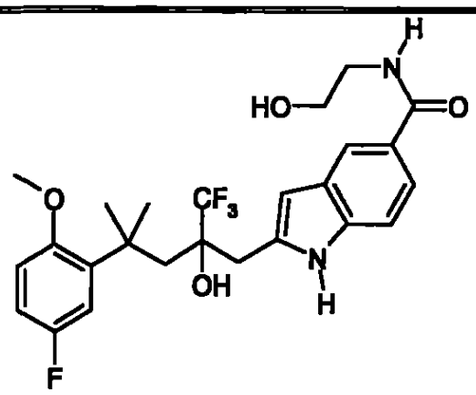
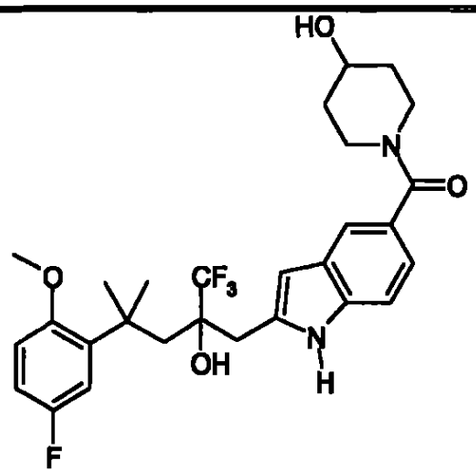
411

IA	
A	B
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid	
2-[4-(4-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile	
{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}piperidin-1-ylmethanone	

393
412

IA	
A	B
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid methylamide	
{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}pyrrolidin-1-ylmethanone	
1-{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}piperidin-4-one	

IA	
A	B
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid (2-hydroxyethyl)amide	
{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}(4-hydroxypiperidin-1-yl)methanone	

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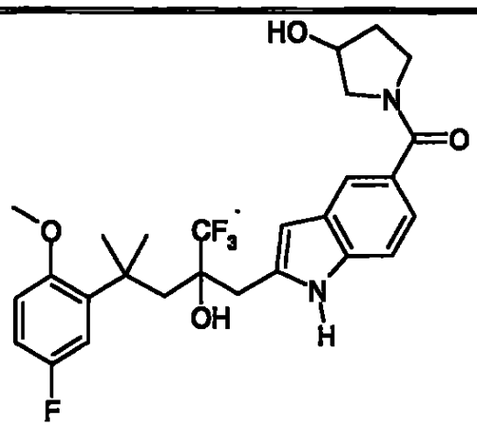
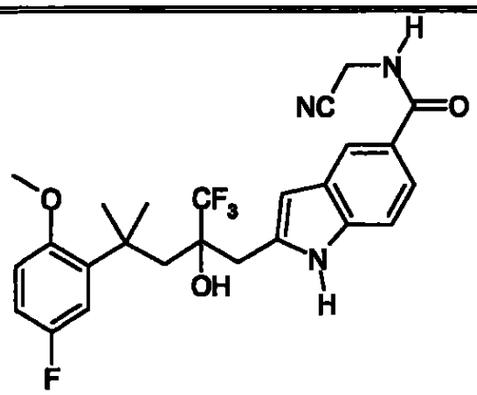
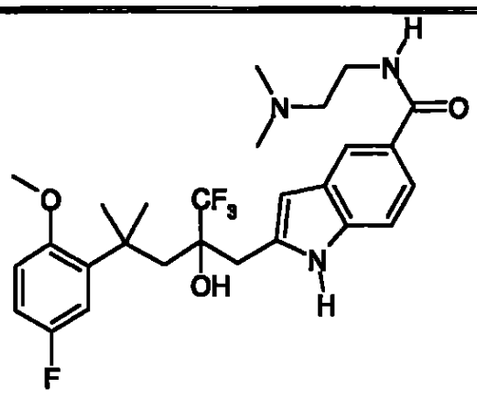
414

IA	
A	B
{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}(3-hydroxypyrrolidin-1-yl)methanone	
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid cyanomethylamide	
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid (2-dimethylaminoethyl)amide	

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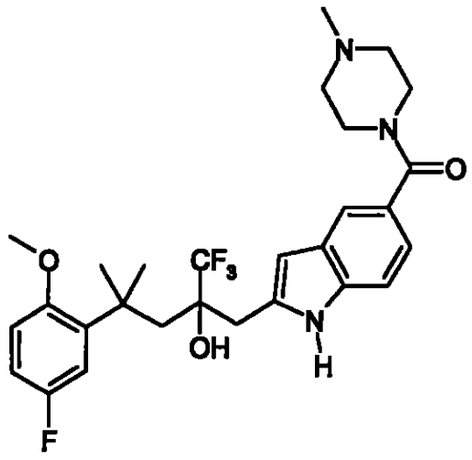
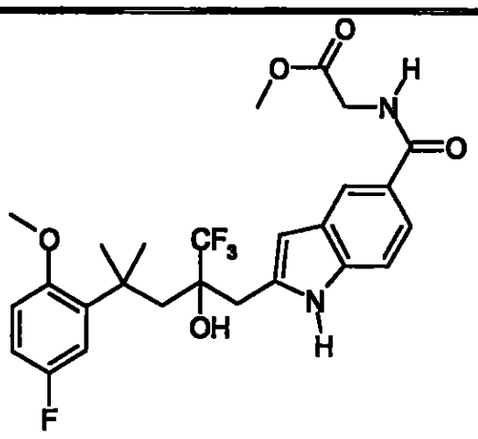
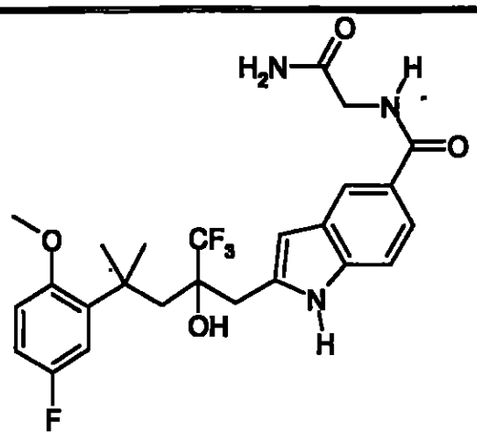
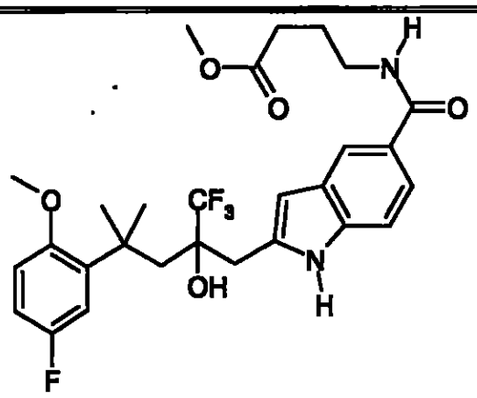
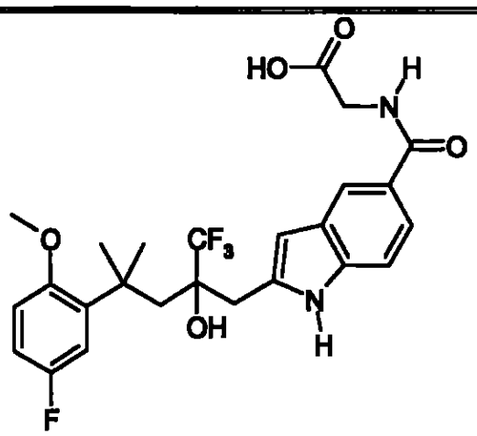
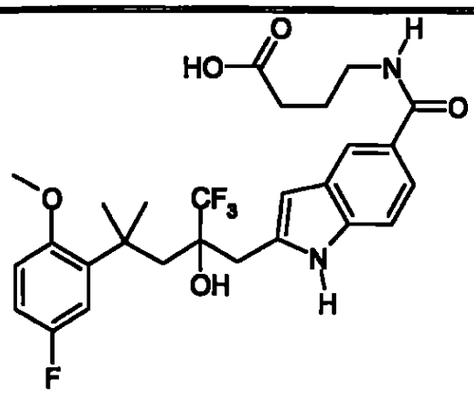
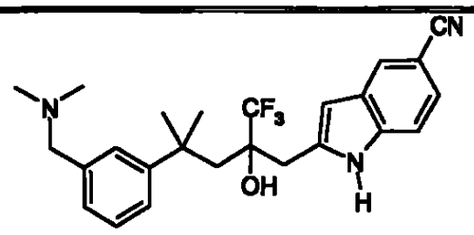
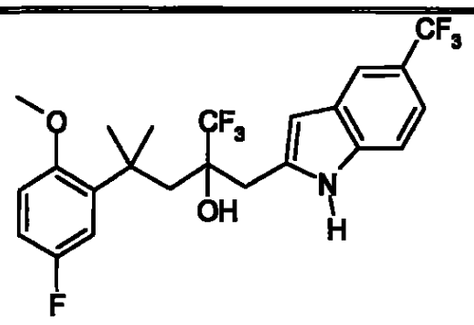
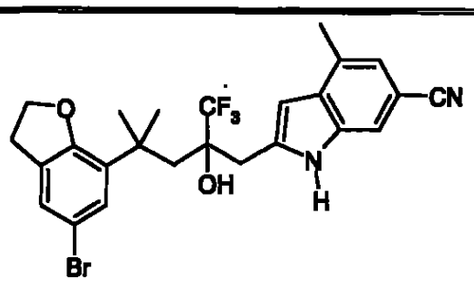
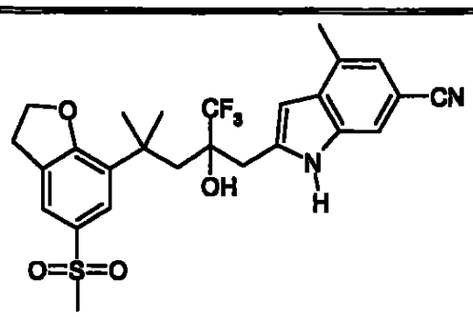
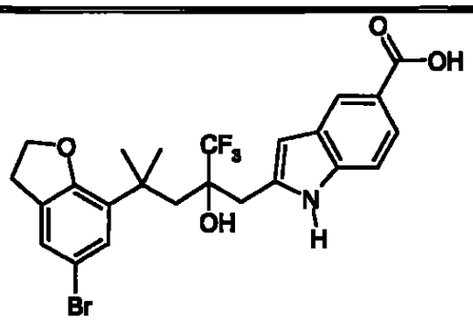
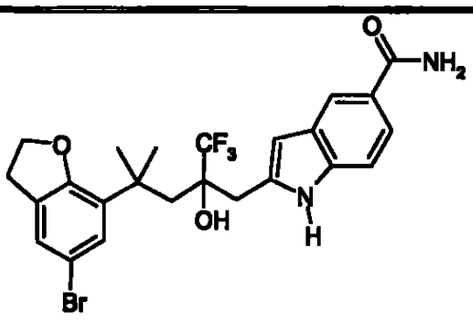
415

IA	
A	B
{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}(4-methylpiperazin-1-yl)methanone	
({2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}amino)acetic acid methyl ester	

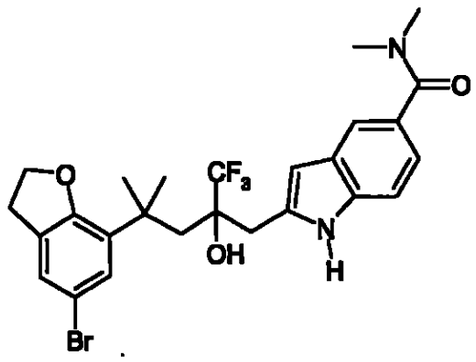
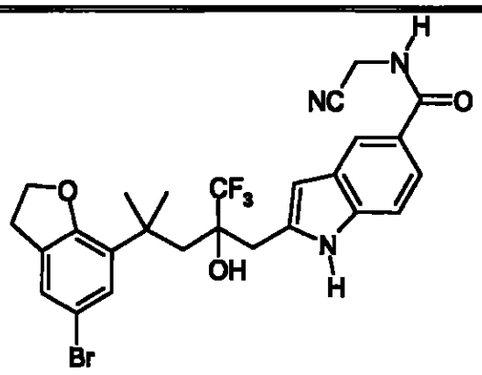
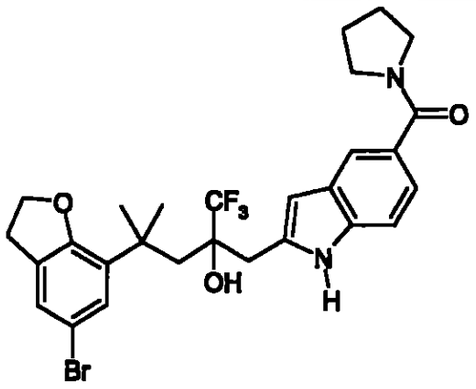
IA	
A	**B**
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid carbamoylmethylamide	
4-({2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}amino)butyric acid methyl ester	
({2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}amino)acetic acid	

IA	
A	B
4-({2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonyl}amino)butyric acid	
2-[4-(3-Dimethylaminomethylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile	
4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-trifluoromethyl-1*H*-indol-2-ylmethyl)butyl]phenol	
2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile	

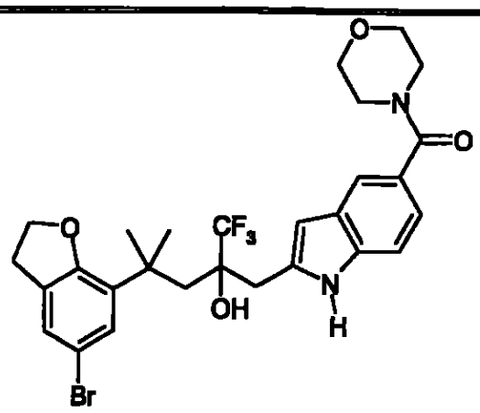
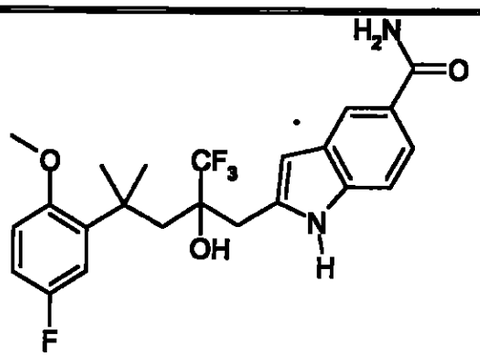
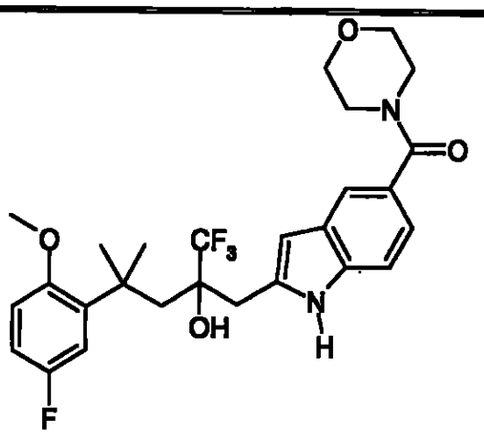
399
418

IA	
A	**B**
2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile	
2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid	
2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid amide	

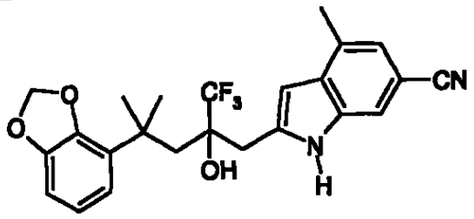
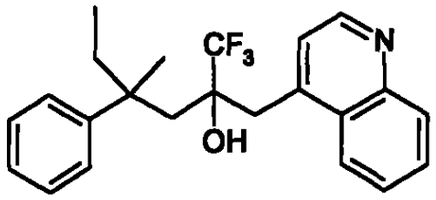
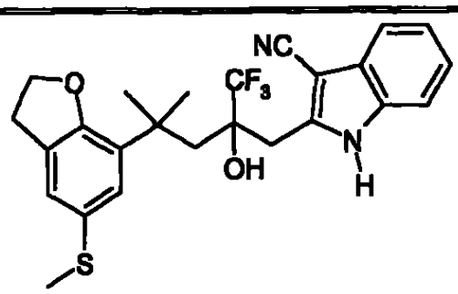
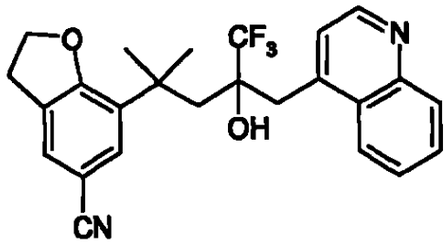
400
419

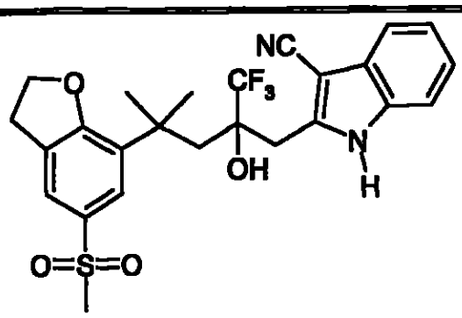
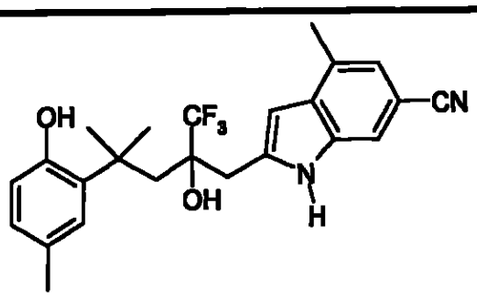
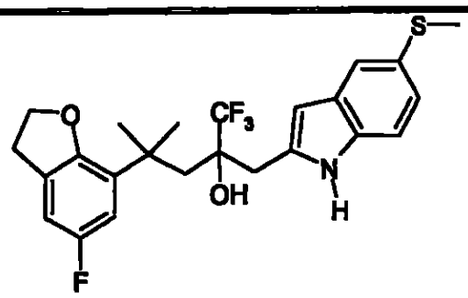
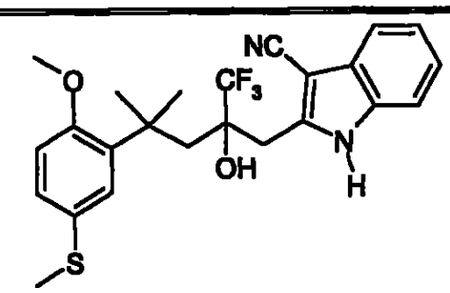
IA	
A	B
2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid dimethylamide	
2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid cyanomethylamide	
{2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}pyrrolidin-1-ylmethanone	

401
420

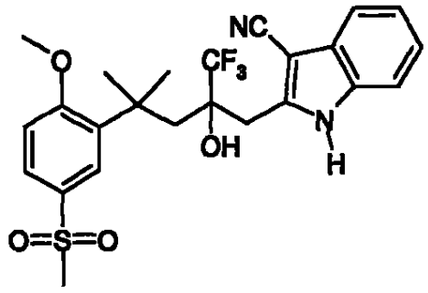
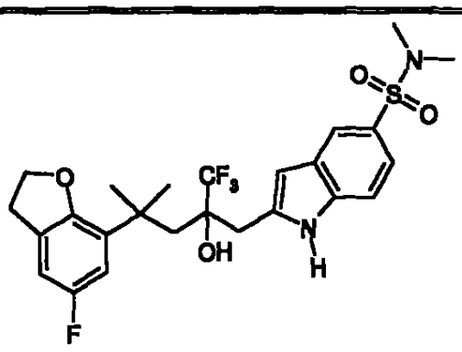
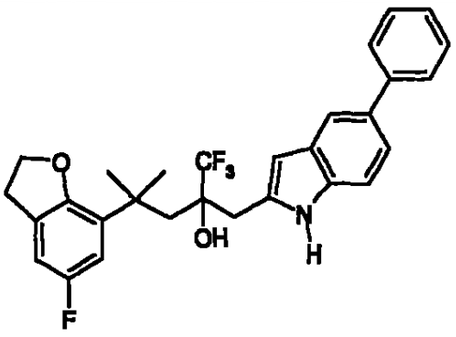
IA	
A	B
{2-[4-(5-Bromo-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}morpholin-4-ylmethanone	
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carboxylic acid amide	
{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}morpholin-4-ylmethanone	

402
421

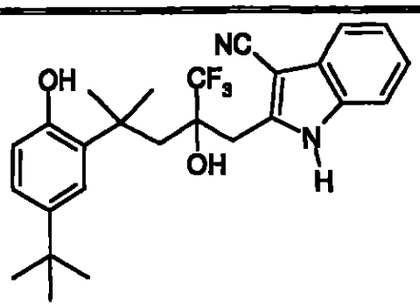
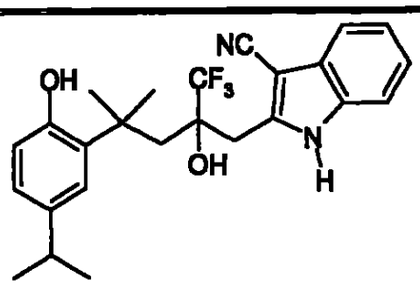
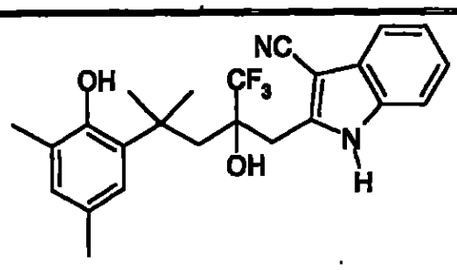
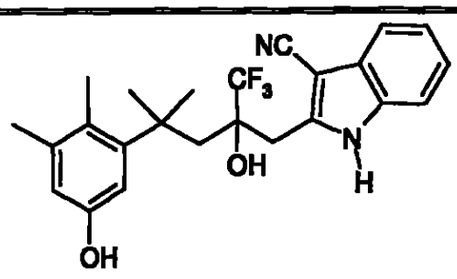
IA	
A	B
2-(4-Benzo[1,3]dioxol-4-yl-2-hydroxy-4-methyl-2-trifluoromethylpentyl)-4-methyl-1*H*-indole-6-carbonitrile	
1,1,1-Trifluoro-4-methyl-4-phenyl-2-quinolin-4-ylmethylhexan-2-ol	
2-[2-Hydroxy-4-methyl-4-(5-methylsulfanyl-2,3-dihydrobenzofuran-7-yl)-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile	
7-(4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-quinolin-4-ylmethylbutyl)-2,3-dihydrobenzofuran-5-carbonitrile	

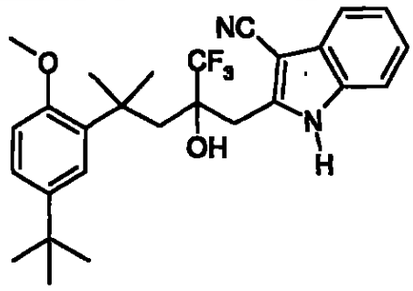
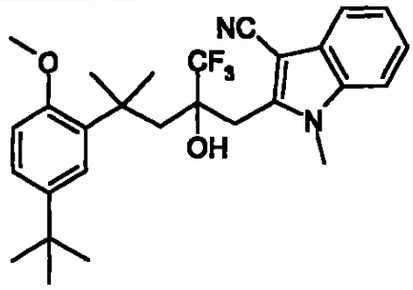
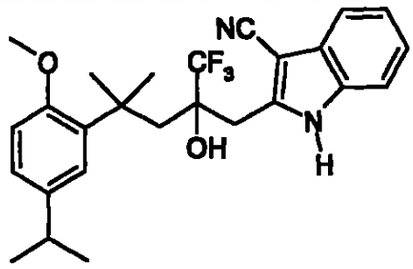
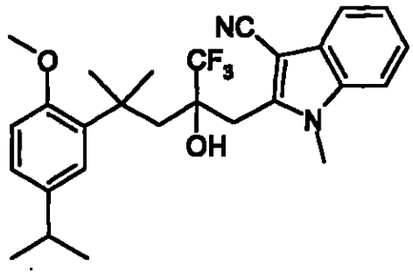
IA	
A	**B**
2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile	
2-[2-Hydroxy-4-(2-hydroxy-5-methylphenyl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile	
1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-methylsulfanyl-1*H*-indol-2-ylmethyl)pentan-2-ol	
2-[2-Hydroxy-4-(2-methoxy-5-methylsulfanylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile	

404
423

IA	
A	B
2-[2-Hydroxy-4-(5-methanesulfonyl-2-methoxyphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile	
2-[4-(5-Fluoro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-sulfonic acid dimethylamide	
1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-phenyl-1*H*-indol-2-ylmethyl)pentan-2-ol	

405
424

IA	
A	B
2-[4-(5-*tert*-Butyl-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile	
2-[2-Hydroxy-4-(2-hydroxy-5-isopropylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile	
2-[2-Hydroxy-4-(2-hydroxy-3,5-dimethylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile	
2-[2-Hydroxy-4-(5-hydroxy-2,4-dimethylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile	

IA	
A	B
2-[4-(5-*tert*-Butyl-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile	
2-[4-(5-*tert*-Butyl-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1-methyl-1*H*-indole-3-carbonitrile	
2-[2-Hydroxy-4-(5-isopropyl-2-methoxyphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile	
2-[2-Hydroxy-4-(5-isopropyl-2-methoxyphenyl)-4-methyl-2-trifluoromethylpentyl]-1-methyl-1*H*-indole-3-carbonitrile	

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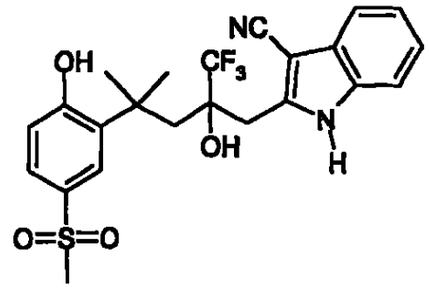
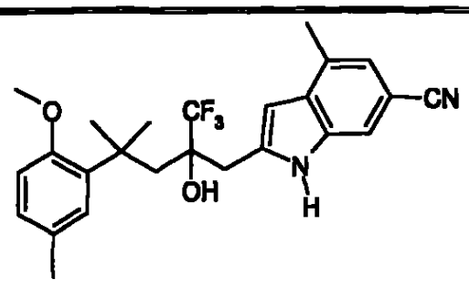
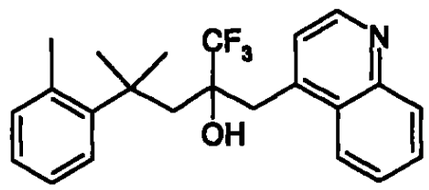
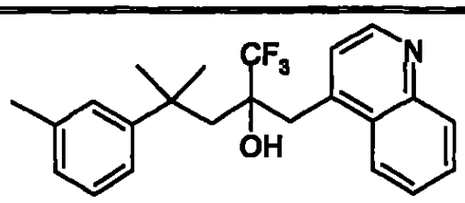
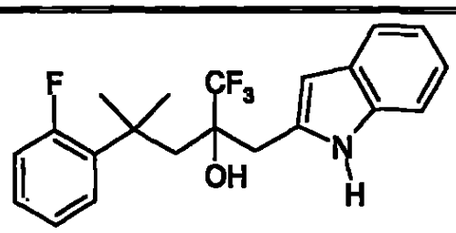
426

IA	
A	**B**
2-[2-Hydroxy-4-(2-hydroxy-5-methanesulfonylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-3-carbonitrile	
2-[2-Hydroxy-4-(2-methoxy-5-methylphenyl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-indole-6-carbonitrile	
1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*o*-tolylpentan-2-ol	
1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-*m*-tolylpentan-2-ol	
1,1,1-Trifluoro-4-(2-fluorophenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol	

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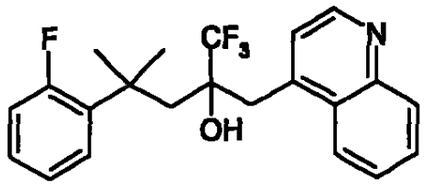
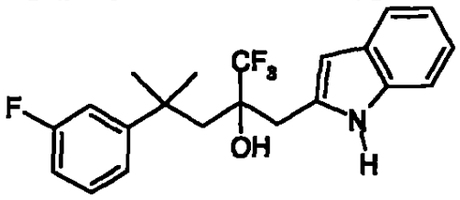
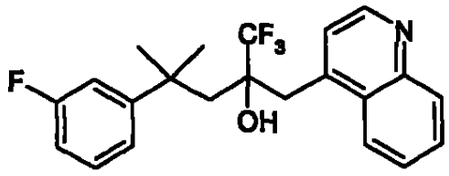
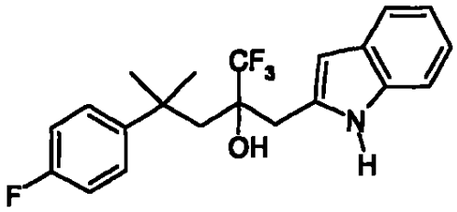
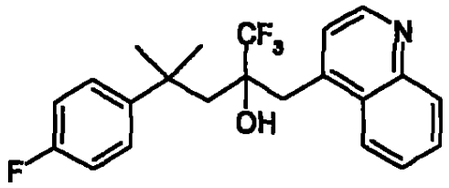
IA	
A	B
1,1,1-Trifluoro-4-(2-fluorophenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol	
1,1,1-Trifluoro-4-(3-fluorophenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol	
1,1,1-Trifluoro-4-(4-fluorophenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol	

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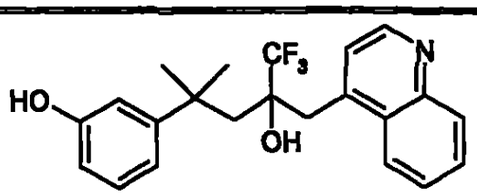
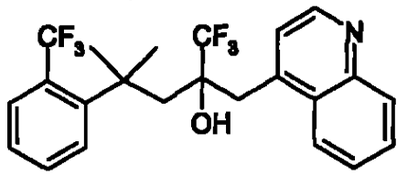
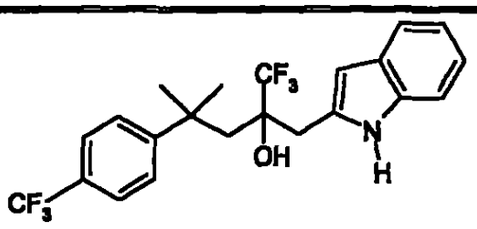
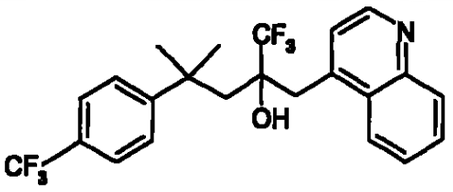
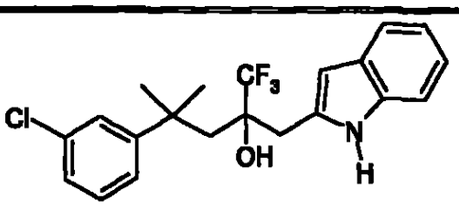
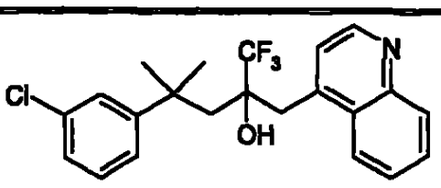
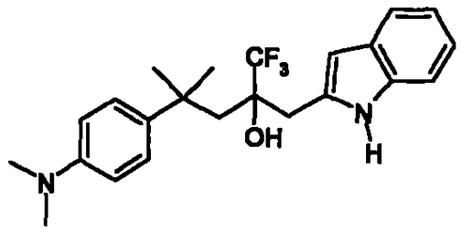
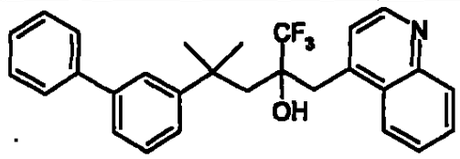
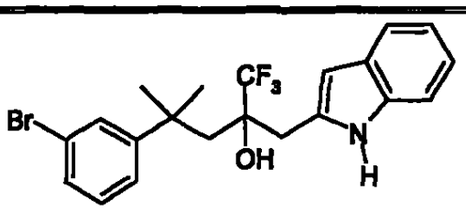
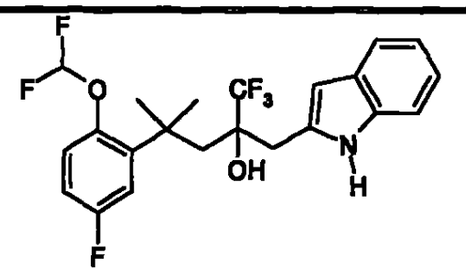
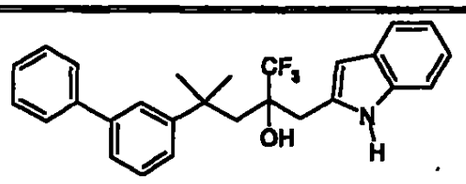
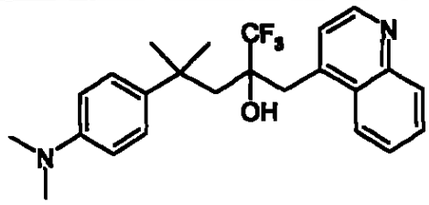
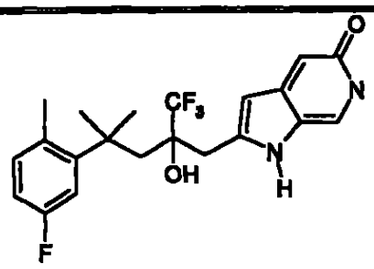
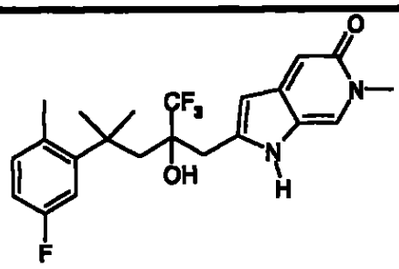
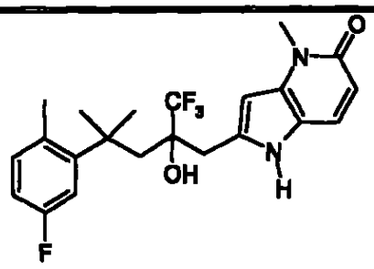
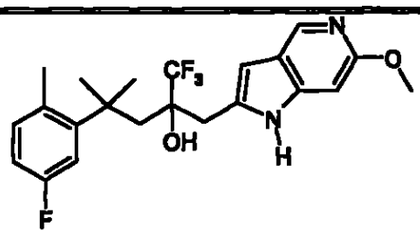
IA	
A	B
3-(4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-quinolin-4-ylmethylbutyl)phenol	
1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-(2-trifluoromethylphenyl)pentan-2-ol	
1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-(4-trifluoromethylphenyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-2-quinolin-4-ylmethyl-4-(4-trifluoromethylphenyl)pentan-2-ol	
4-(3-Chlorophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol	
4-(3-Chlorophenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol	

IA	
A	**B**
4-(4-Dimethylaminophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol	
4-Biphenyl-3-yl-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol	
4-(3-Bromophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol	
4-(2-Difluoromethoxy-5-fluorophenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol	
4-Biphenyl-3-yl-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol	

IA	
A	**B**
4-(4-Dimethylaminophenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol	
2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,6-dihydropyrrolo[2,3-*c*]pyridin-5-one	
2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-6-methyl-1,6-dihydropyrrolo[2,3-*c*]pyridin-5-one	
2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1,4-dihydropyrrolo[3,2-*b*]pyridin-5-one	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(6-methoxy-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	

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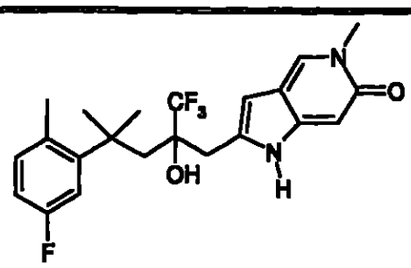
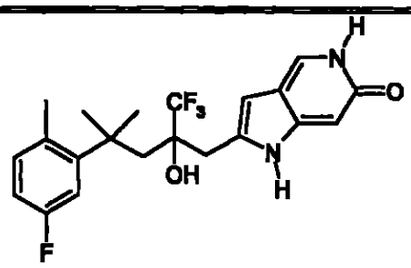
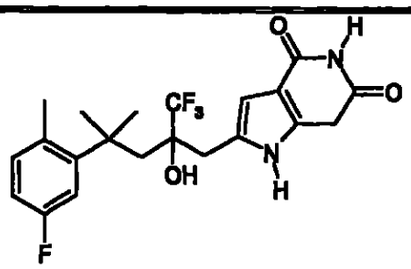
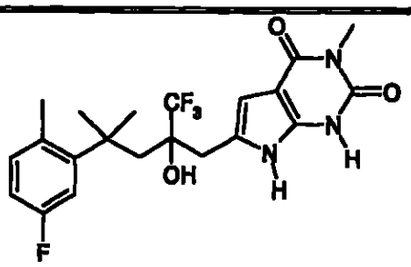
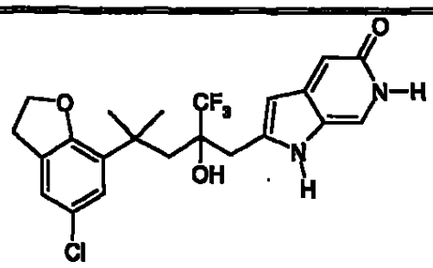
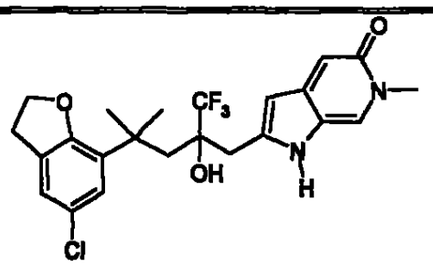
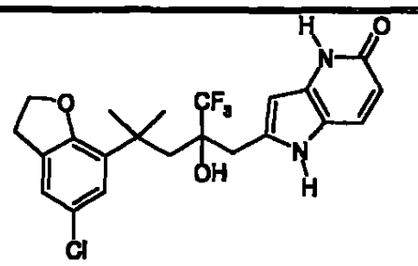
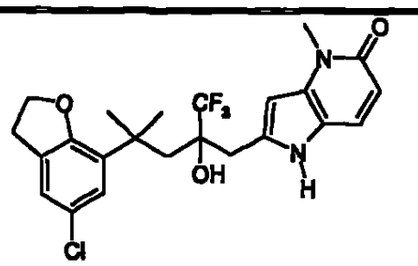
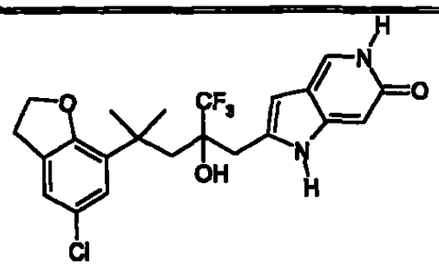
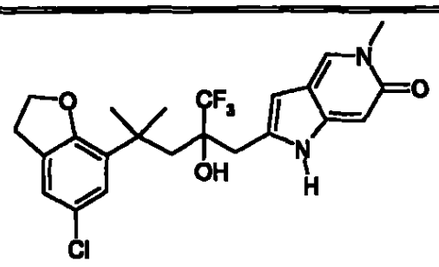
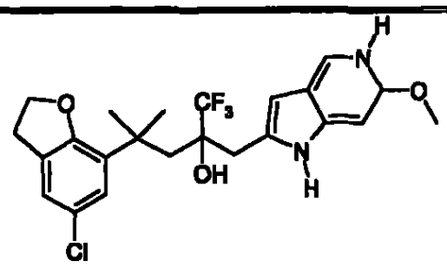
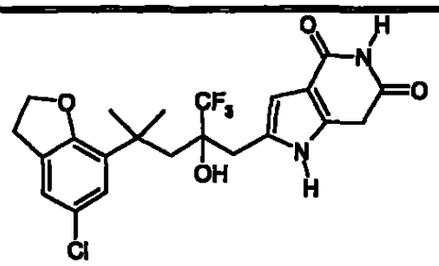
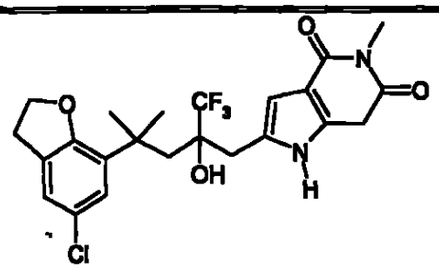
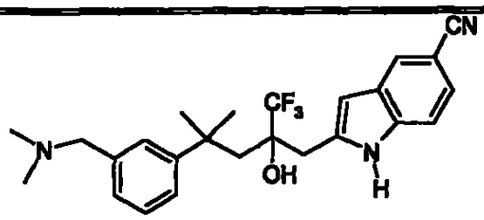
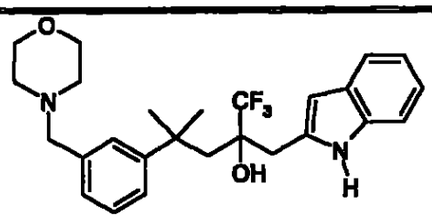
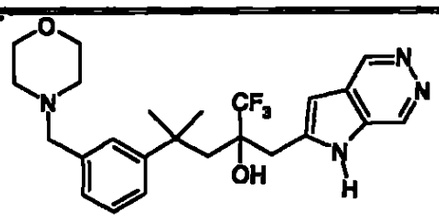
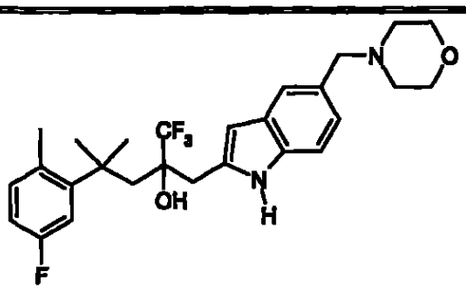
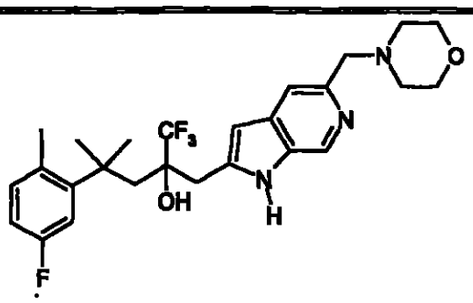
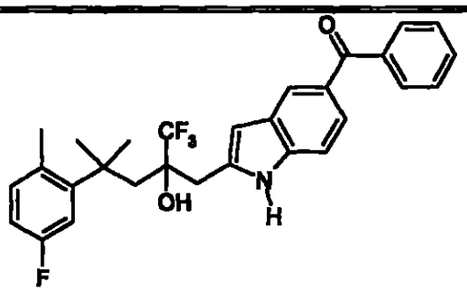
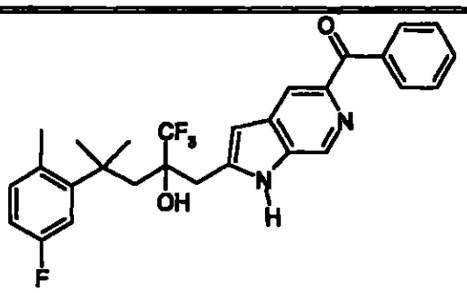
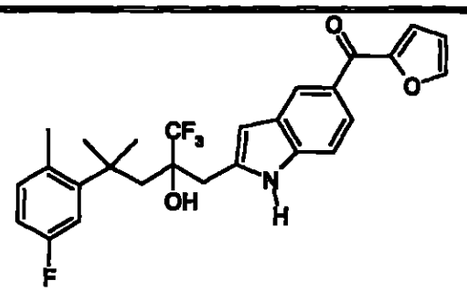
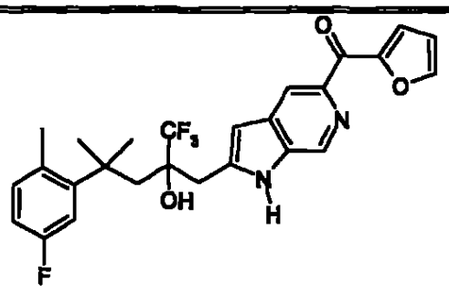
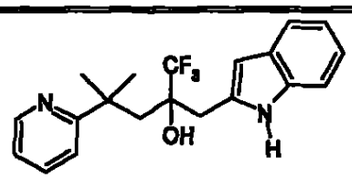
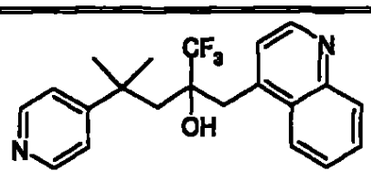
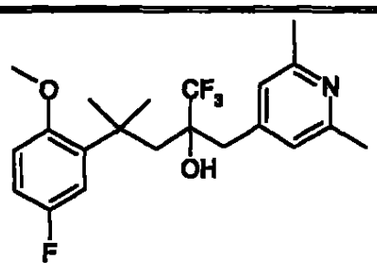
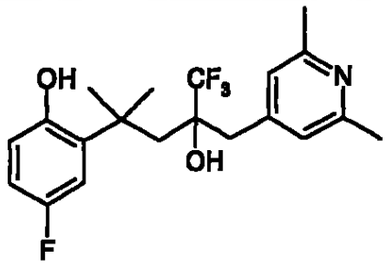
IA	
A	B
2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-5-methyl-1,5-dihydropyrrolo[3,2-*c*]pyridin-6-one	
2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,3a-dihydropyrrolo[3,2-*c*]pyridin-6-one	
2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,7-dihydropyrrolo[3,2-*c*]pyridine-4,6-dione	
6-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-3-methyl-1,7-dihydropyrrolo[2,3-*d*]pyrimidine-2,4-dione	

IA	
A	B
2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,6-dihydropyrrolo[2,3-*c*]pyridin-5-one	
2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-6-methyl-1,6-dihydropyrrolo[2,3-*c*]pyridin-5-one	
2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,4-dihydropyrrolo[3,2-*b*]pyridin-5-one	
2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-4-methyl-1,4-dihydropyrrolo[3,2-*b*]pyridin-5-one	

IA	
A	**B**
2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,5-dihydropyrrolo[3,2-*c*]pyridin-6-one	
2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-5-methyl-1,5-dihydropyrrolo[3,2-*c*]pyridin-6-one	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(6-methoxy-5,6-dihydro-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	
2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,7-dihydropyrrolo[3,2-*c*]pyridine-4,6-dione	

IA	
A	**B**
6-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-3-methyl-1,7-dihydropyrrolo[2,3-*d*]pyrimidine-2,4-dione	
2-[4-(3-Dimethylaminomethylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile	
1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-(3-morpholin-4-ylmethylphenyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylmethylphenyl)-2-(1*H*-pyrrolo[2,3-*d*]pyridazin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-morpholin-4-ylmethyl-1*H*-indol-2-ylmethyl)pentan-2-ol	

IA	
A	**B**
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
{2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}phenylmethanone	
{2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridin-5-yl}phenylmethanone	
{2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}furan-2-ylmethanone	

IA	
A	B
{2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridin-5-yl}furan-2-ylmethanone	
1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-pyridin-2-ylpentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-pyridin-4-yl-2-quinolin-4-ylmethylpentan-2-ol	
2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	
2-[3-(2,6-Dimethylpyridin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol	

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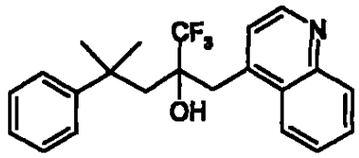
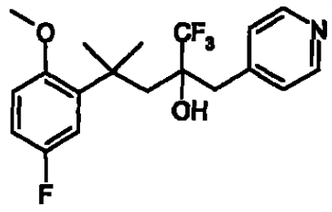
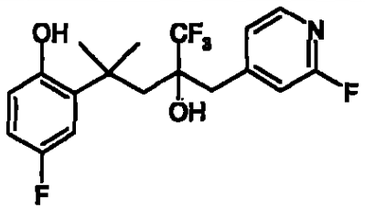
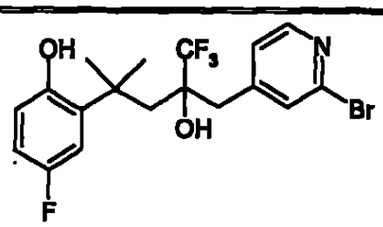
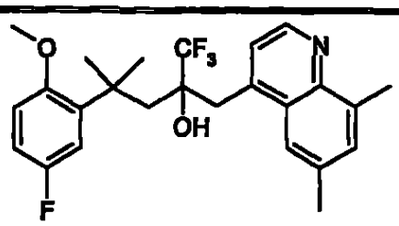
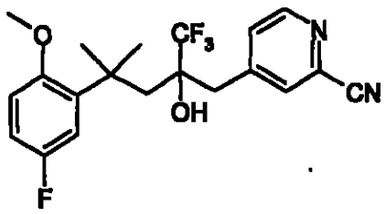
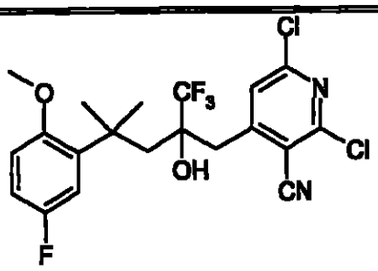
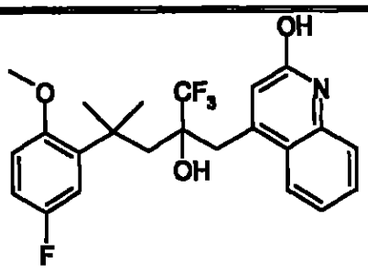
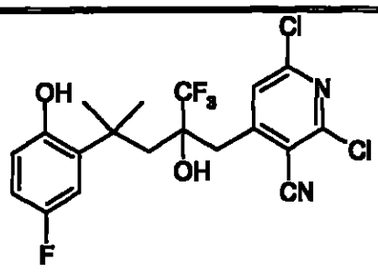
IA	
A	B
1,1,1-Trifluoro-4,4-dimethyl-5-phenyl-2-quinolin-4-ylmethylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-pyridin-4-ylmethylpentan-2-ol	
4-Fluoro-2-[4,4,4-trifluoro-3-(2-fluoropyridin-4-ylmethyl)-3-hydroxy-1,1-dimethylbutyl]phenol	
2-[3-(2-Bromopyridin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol	
2-(6,8-Dimethylquinolin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	

IA	
A	B
4-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]pyridine-2-carbonitrile	
2,6-Dichloro-4-[4-(5-fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]nicotinonitrile	
4-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]quinolin-2-ol	
2,6-Dichloro-4-[4-(5-fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]nicotinonitrile	

420

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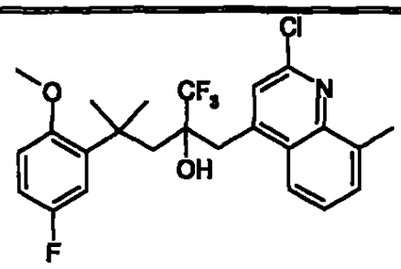
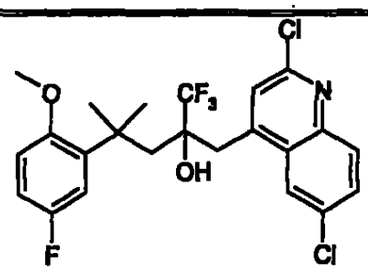
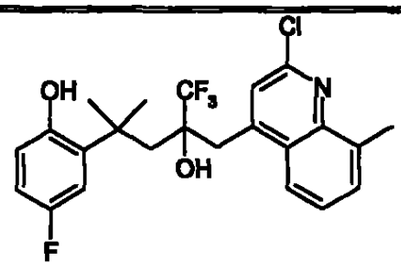
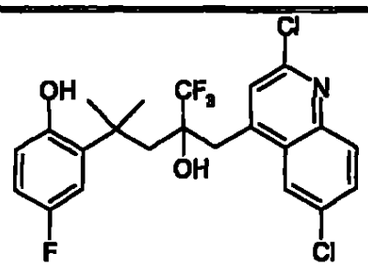
IA	
A	**B**
2-(2-Chloro-8-methylquinolin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	
2-(2,6-Dichloroquinolin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	
2-[3-(2-Chloro-8-methylquinolin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol	
2-[3-(2,6-Dichloroquinolin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol	

427

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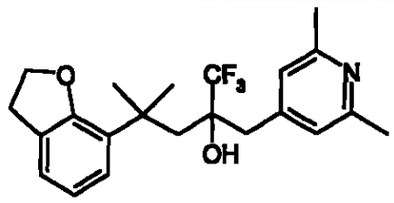
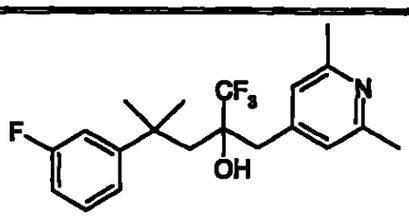
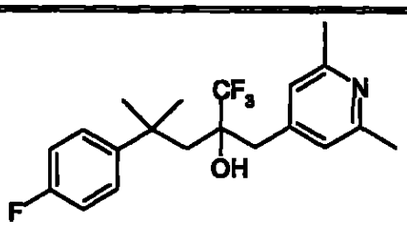
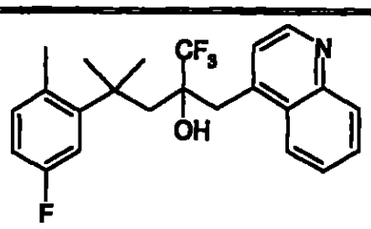
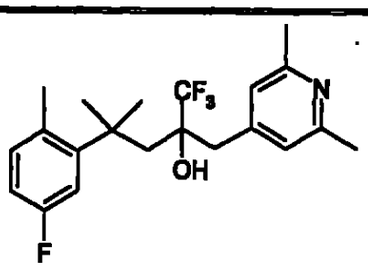
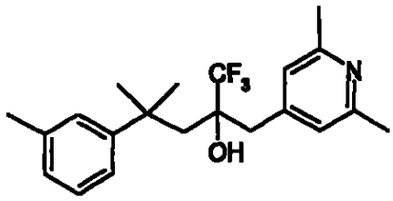
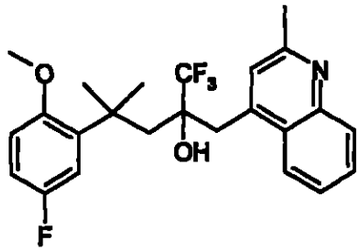
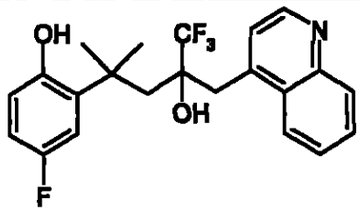
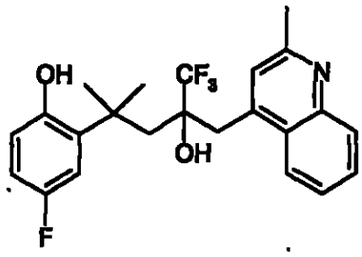
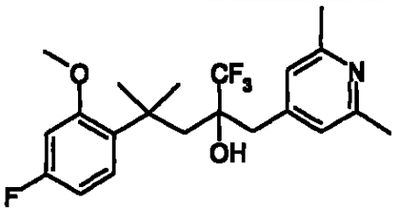
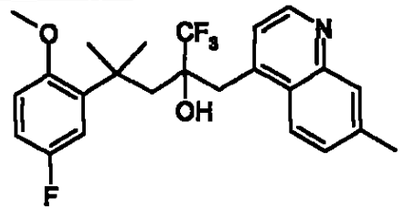
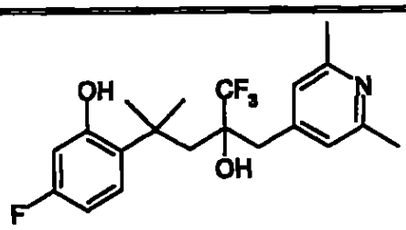
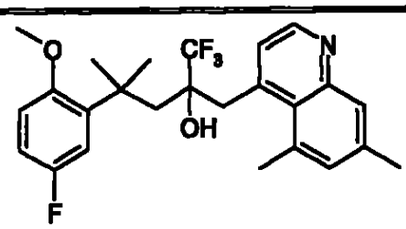
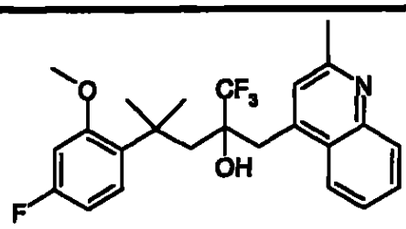
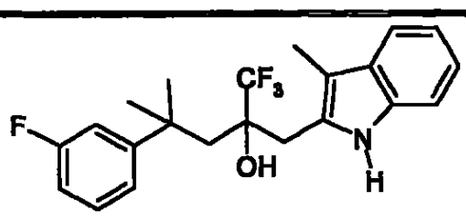
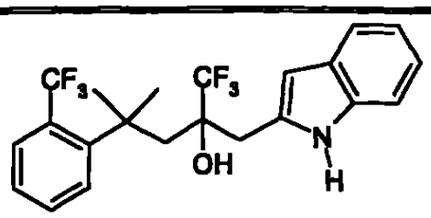
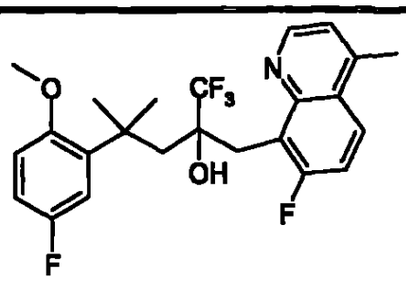
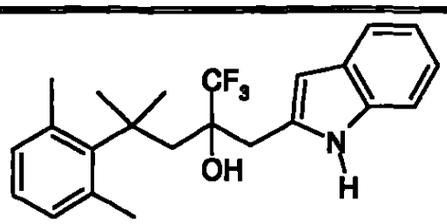
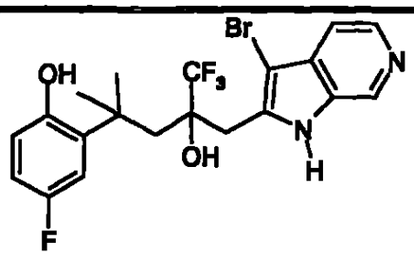
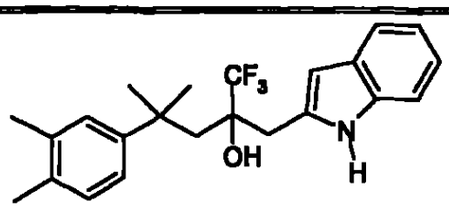
IA	
A	B
4-(2,3-Dihydrobenzofuran-7-yl)-2-(2,6-dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol	
2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(3-fluorophenyl)-4-methylpentan-2-ol	
2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(4-fluorophenyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol	
2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol	

422

441

IA	
A	**B**
2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-methyl-4-*m*-tolylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(2-methylquinolin-4-ylmethyl)pentan-2-ol	
4-Fluoro-2-(4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-quinolin-4-ylmethylbutyl)phenol	
4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(2-methylquinolin-4-ylmethyl)butyl]phenol	
2-(2,6-Dimethylpyridin-4-ylmethyl)-1,1,1-trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	

IA	
A	B
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(7-methylquinolin-4-ylmethyl)pentan-2-ol	
2-[3-(2,6-Dimethylpyridin-4-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-5-fluorophenol	
2-(5,7-Dimethylquinolin-4-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-(2-methylquinolin-4-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(3-methyl-1*H*-indol-2-ylmethyl)pentan-2-ol	

IA	
A	**B**
1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methyl-4-(2-trifluoromethylphenyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(7-fluoro-4-methylquinolin-8-yl)-4-methylpentan-2-ol	
4-(2,6-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol	
2-(3-Bromo-1*H*-indol-2-ylmethyl)-1,1,1-trifluoro-4-(3-fluorophenyl)-4-methylpentan-2-ol	
4-(3,4-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol	

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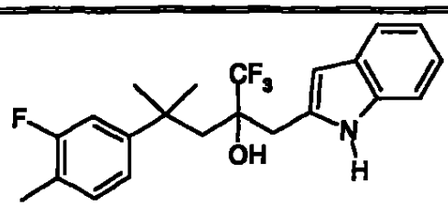
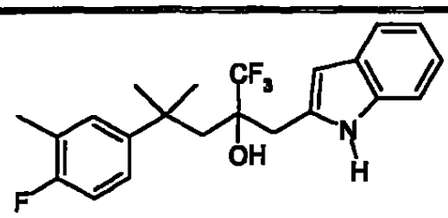
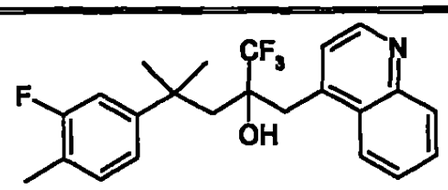
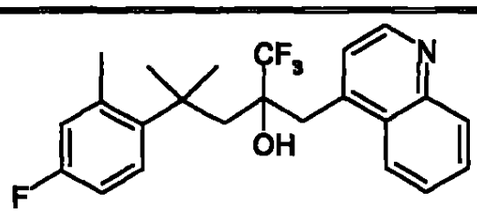
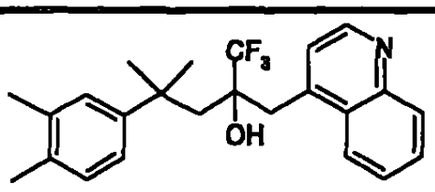
444

IA	
A	B
1,1,1-Trifluoro-4-(3-fluoro-4-methylphenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(4-fluoro-3-methylphenyl)-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(3-fluoro-4-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol	
1,1,1-Trifluoro-4-(4-fluoro-2-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol	
4-(3,4-Dimethylphenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol	

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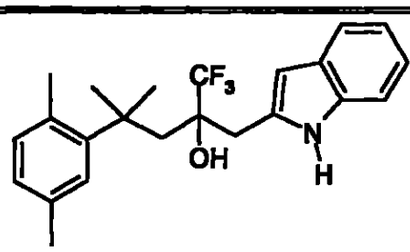
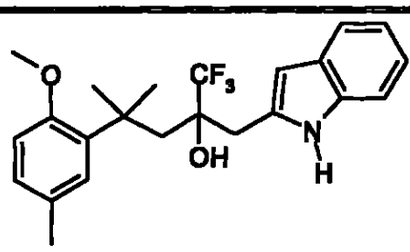
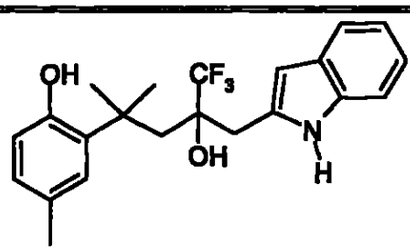
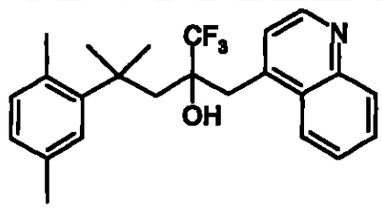
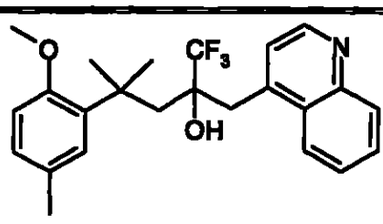
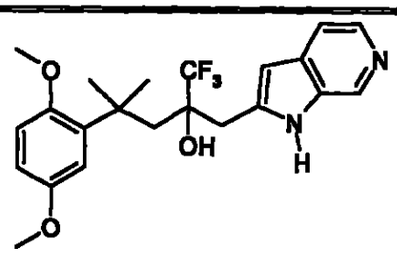
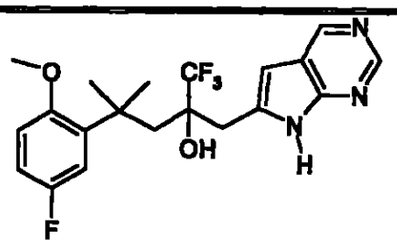
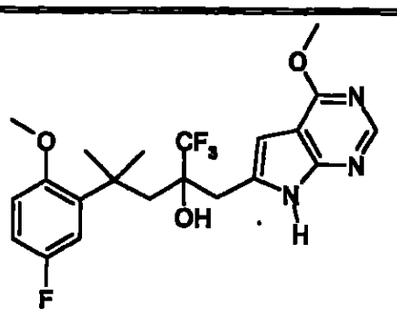
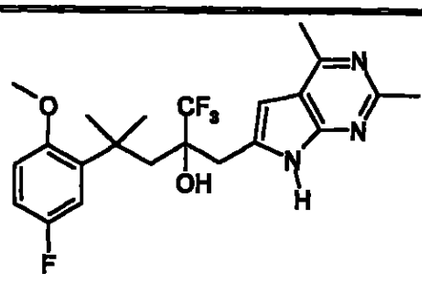
IA	
A	**B**
4-(2,5-Dimethylphenyl)-1,1,1-trifluoro-2-(1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-2-(1*H*-indol-2-ylmethyl)-4-(2-methoxy-5-methylphenyl)-4-methylpentan-2-ol	
4-Methyl-2-[4,4,4-trifluoro-3-hydroxy-3-(1*H*-indol-2-ylmethyl)-1,1-dimethylbutyl]phenol	
4-(2,5-Dimethylphenyl)-1,1,1-trifluoro-4-methyl-2-quinolin-4-ylmethylpentan-2-ol	
1,1,1-Trifluoro-4-(2-methoxy-5-methylphenyl)-4-methyl-2-quinolin-4-ylmethylpentan-2-ol	

IA	
A	**B**
4-(2,5-Dimethoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(4-methoxy-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-4-methylpentan-2-ol	
2-(2,4-Dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	

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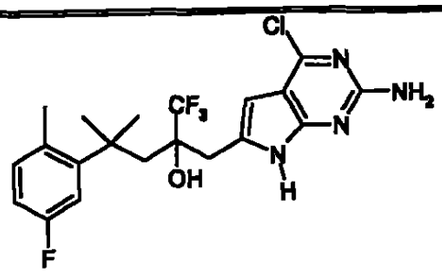
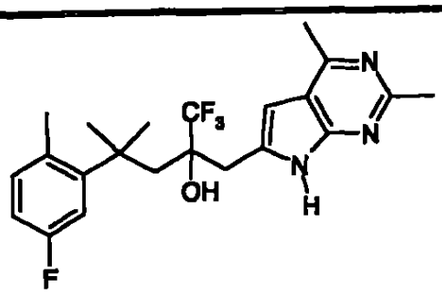
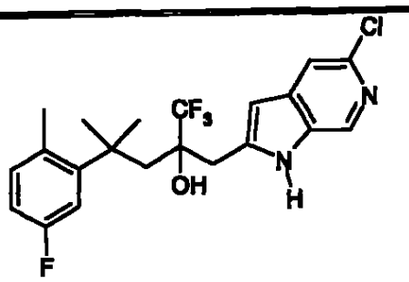
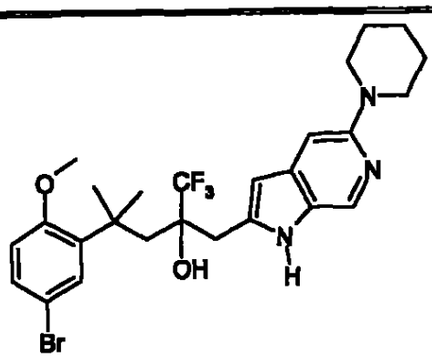
IA	
A	B
2-(2-Amino-4-chloro-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	
2-(2,4-Dimethyl-7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol	
2-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol	
4-(5-Bromo-2-methoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-c]pyridin-2-ylmethyl)pentan-2-ol	

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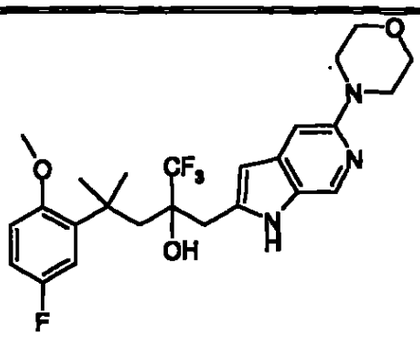
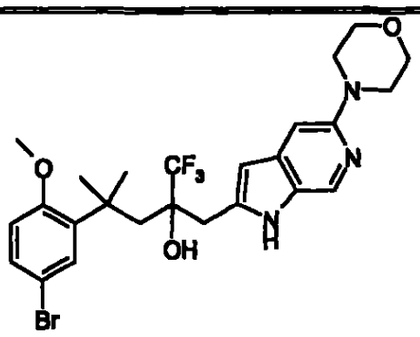
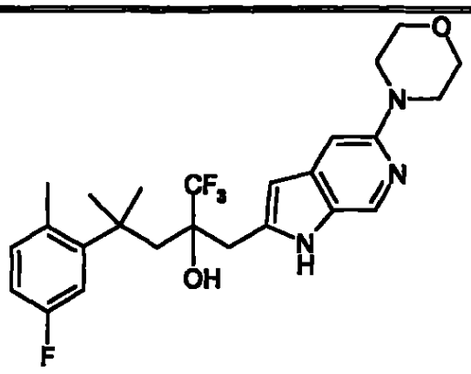
IA	
A	**B**
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-(5-Bromo-2-methoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

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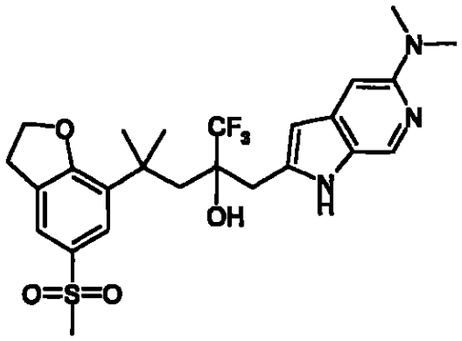
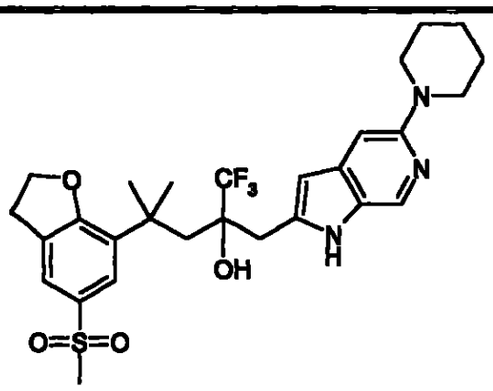
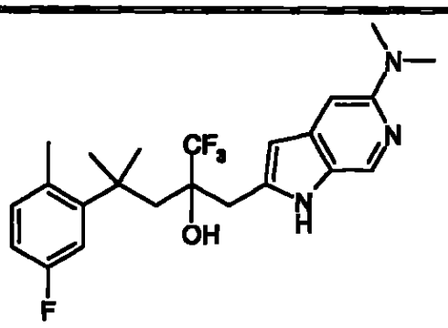
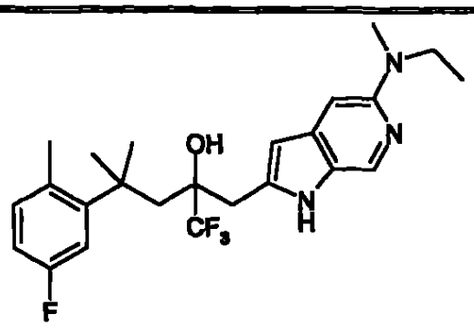
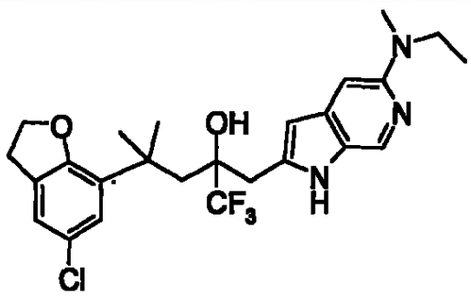
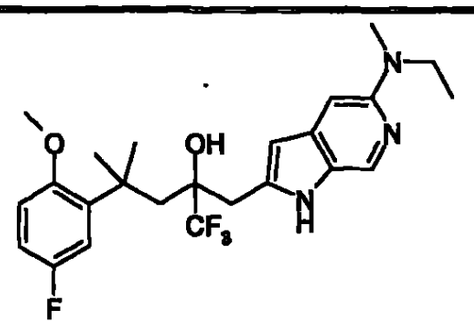
IA	
A	B
2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol	

IA	
A	B
2-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-[5-(ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-methylpentan-2-ol	
2-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	

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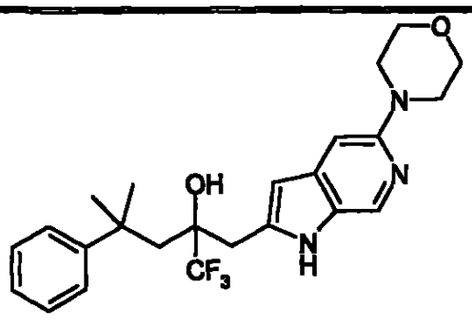
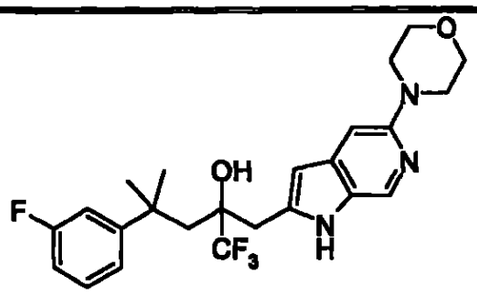
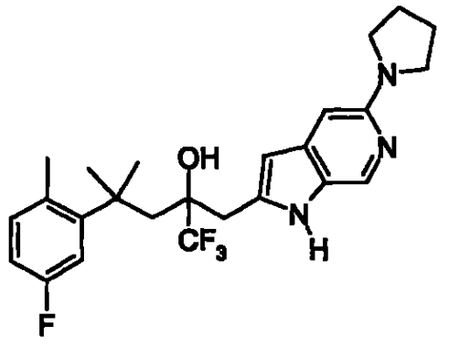
IA	
A	**B**
1,1,1-Trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-phenylpentan-2-ol	
1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-pyrrolidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

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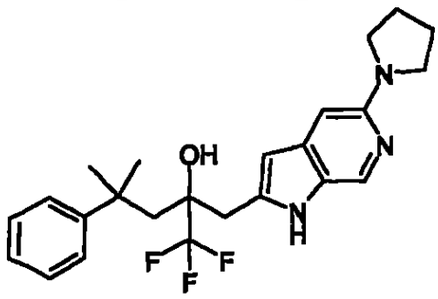
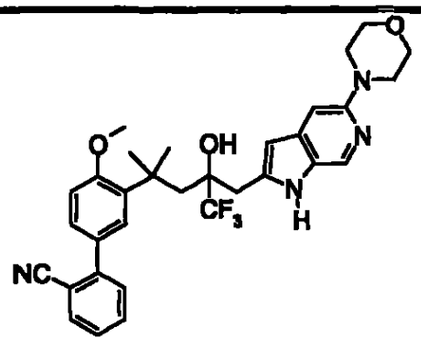
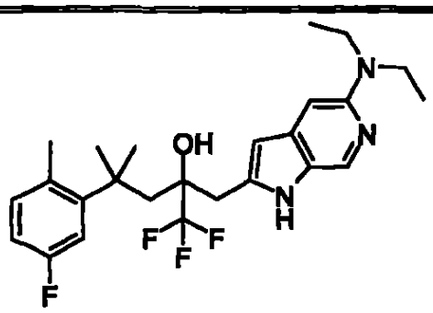
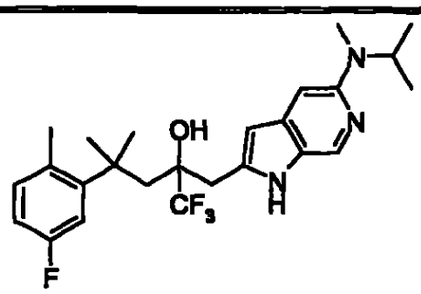
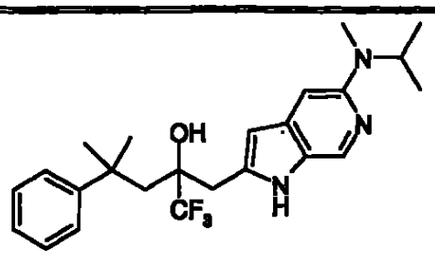
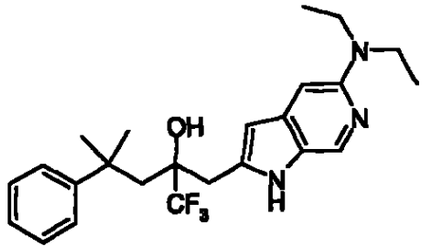
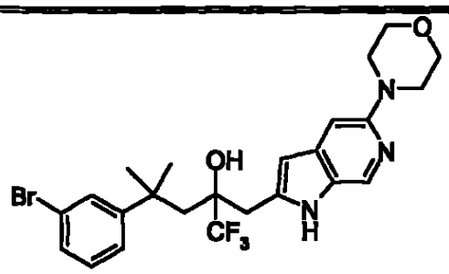
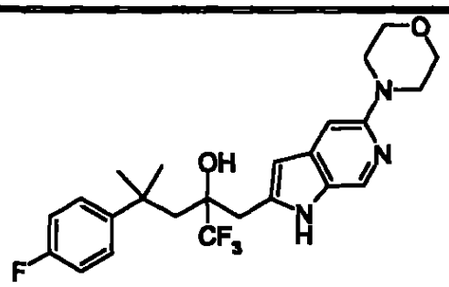
IA	
A	B
1,1,1-Trifluoro-4-methyl-4-phenyl-2-(5-pyrrolidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4'-Methoxy-3'-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-2-carbonitrile	
2-(5-Diethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-[5-(isopropylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-4-methylpentan-2-ol	

IA	
A	B
1,1,1-Trifluoro-2-[5-(isopropylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-4-methyl-4-phenylpentan-2-ol	
2-(5-Diethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methyl-4-phenylpentan-2-ol	
4-(3-Bromophenyl)-1,1,1-trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

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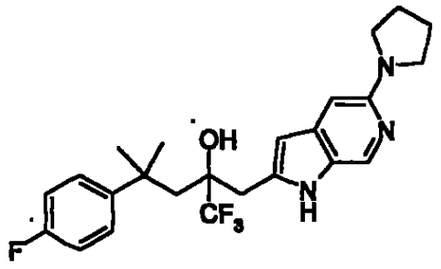
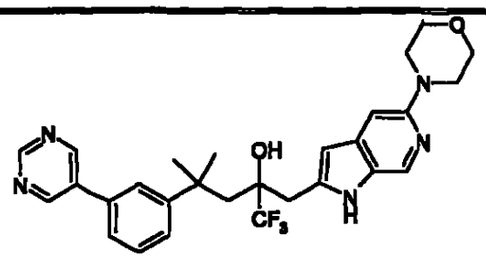
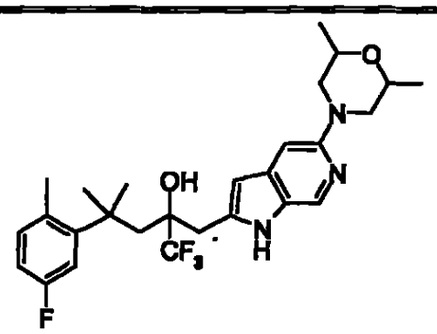
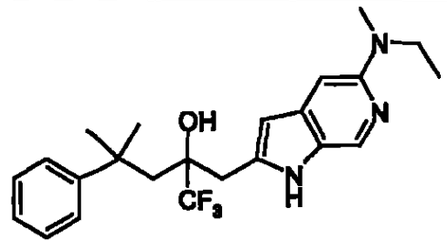
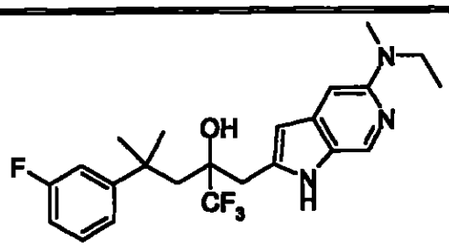
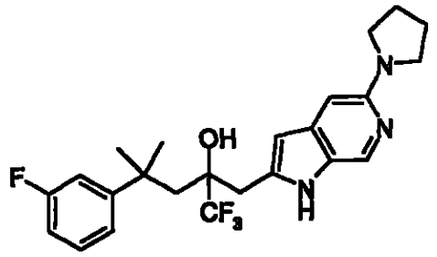
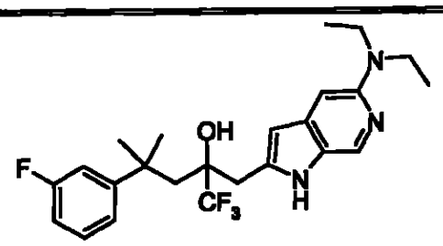
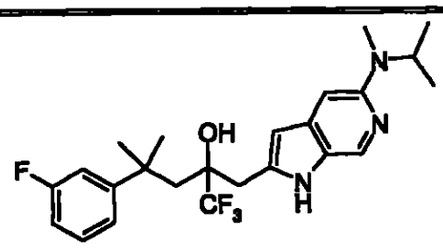
IA	
A	B
1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-(5-pyrrolidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(3-pyrimidin-5-ylphenyl)pentan-2-ol	
2-[5-(2,6-Dimethylmorpholin-4-yl)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol	
2-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-methyl-4-phenylpentan-2-ol	

IA	
A	B
2-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-(3-fluorophenyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(5-pyrrolidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
2-(5-Diethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(3-fluorophenyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(3-fluorophenyl)-2-[5-(isopropylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-4-methylpentan-2-ol	

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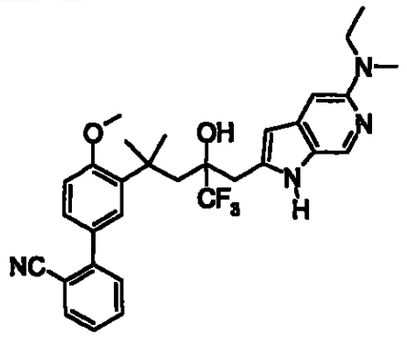
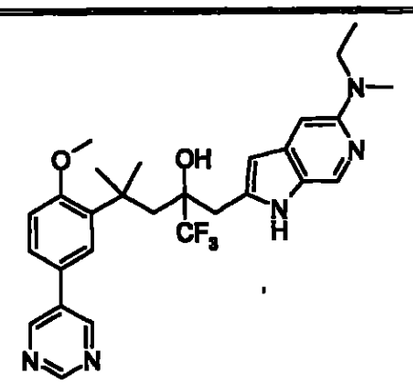
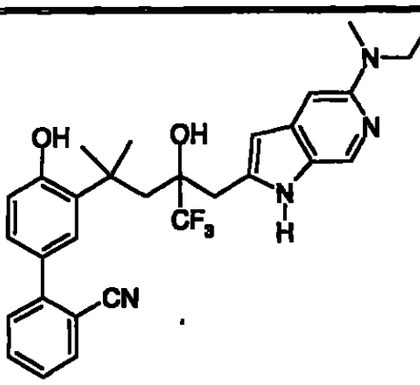
IA	
A	**B**
3'-{3-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl}-4'-methoxybiphenyl-2-carbonitrile	
2-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methylpentan-2-ol	
3'-{3-[5-(Ethylmethylamino)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl}-4'-hydroxybiphenyl-2-carbonitrile	

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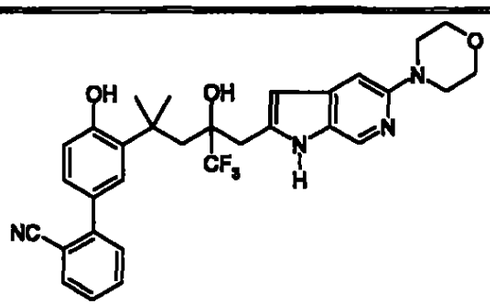
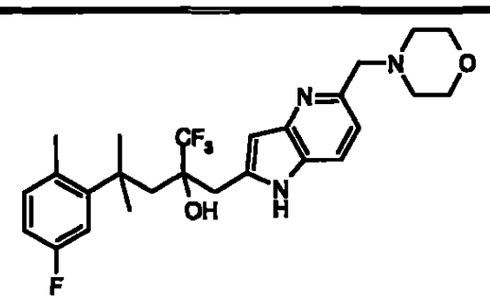
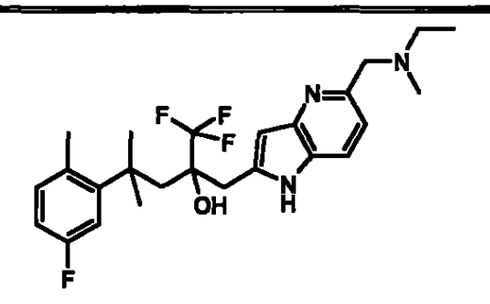
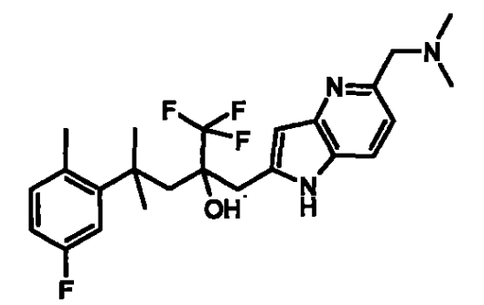
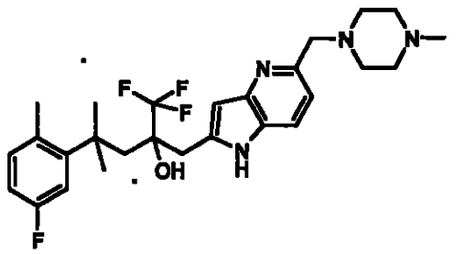
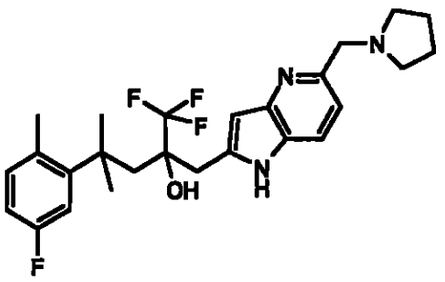
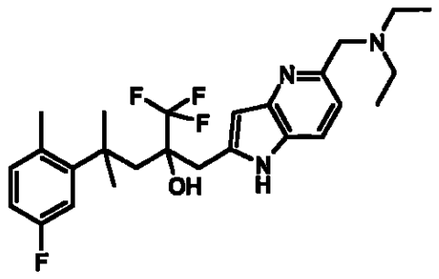
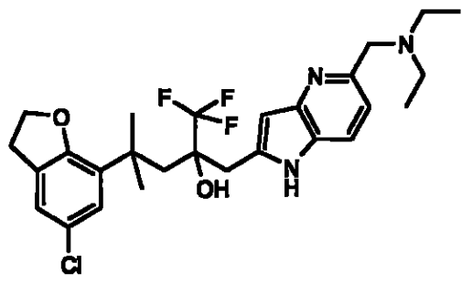
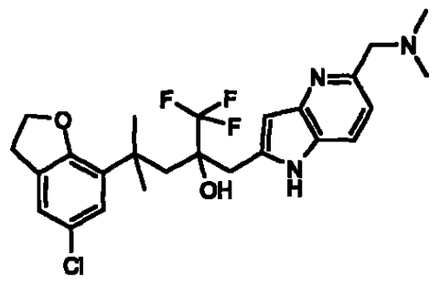
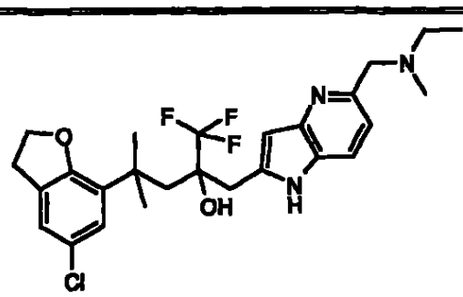
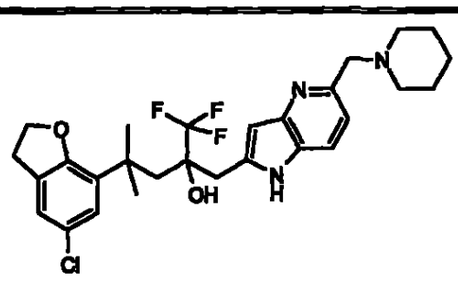
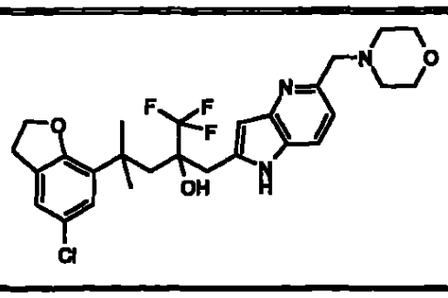
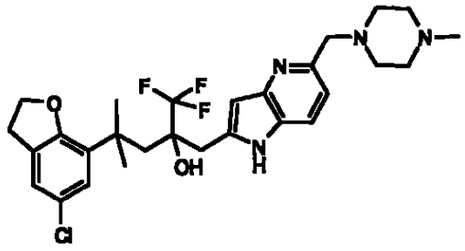
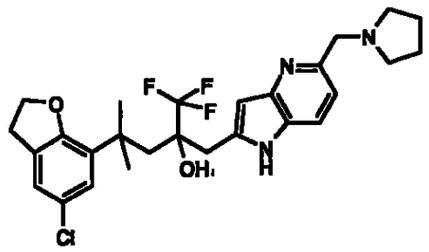
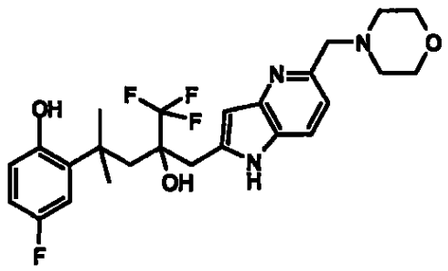
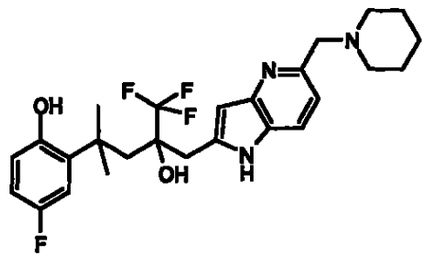
IA	
A	B
4'-Hydroxy-3'-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-2-carbonitrile	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)pentan-2-ol	
2-{5-[(Ethylmethylamino)methyl]-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl}-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol	
2-(5-Dimethylaminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol	

IA	
A	**B**
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-[5-(4-methylpiperazin-1-ylmethyl)-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl]pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-pyrrolidin-1-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)pentan-2-ol	
2-(5-Diethylaminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(5-diethylaminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol	

IA	
A	B
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(5-dimethylaminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-{5-[(ethylmethylamino)methyl]-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl}-1,1,1-trifluoro-4-methylpentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-piperidin-1-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)pentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)pentan-2-ol	

IA	
A	**B**
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-[5-(4-methylpiperazin-1-ylmethyl)-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl]pentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-pyrrolidin-1-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)pentan-2-ol	
4-Chloro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)butyl]phenol	
4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)butyl]phenol	

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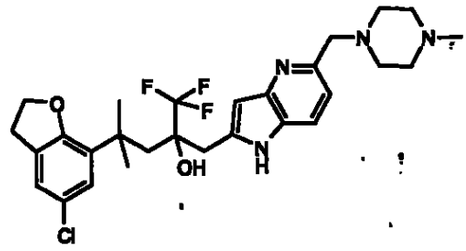
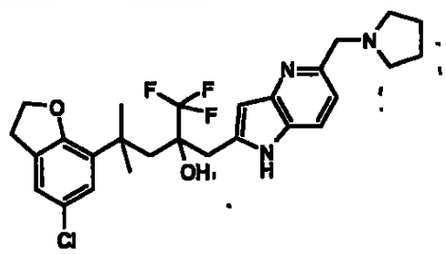
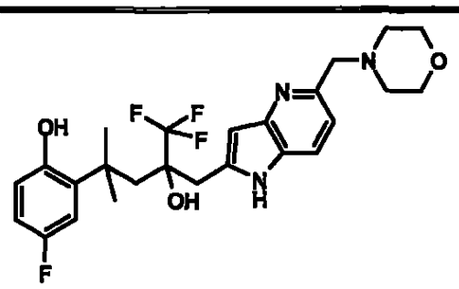
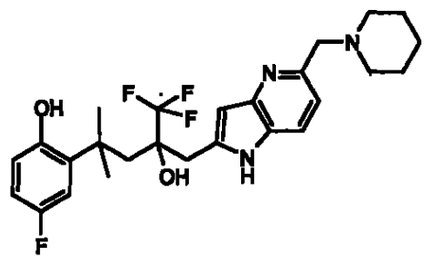
IA	
A	**B**
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-[5-(4-methylpiperazin-1-ylmethyl)-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl]pentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-pyrrolidin-1-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)pentan-2-ol	
4-Chloro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)butyl]phenol	
4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)butyl]phenol	

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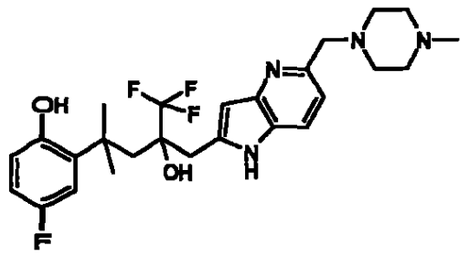
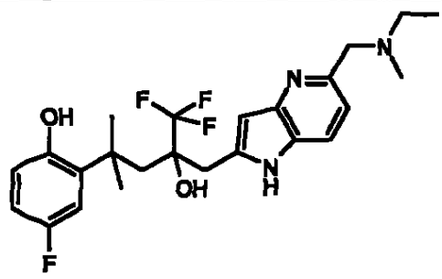
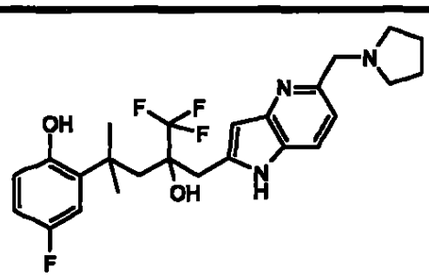
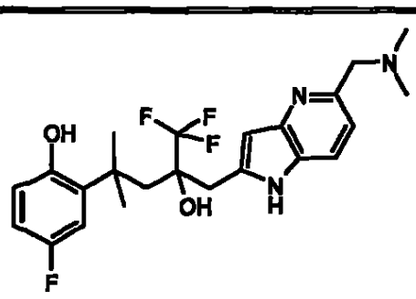
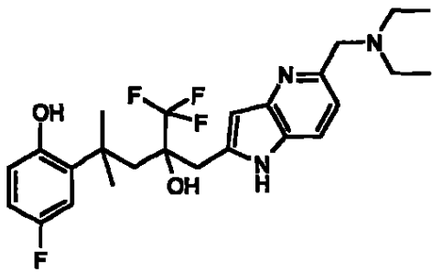
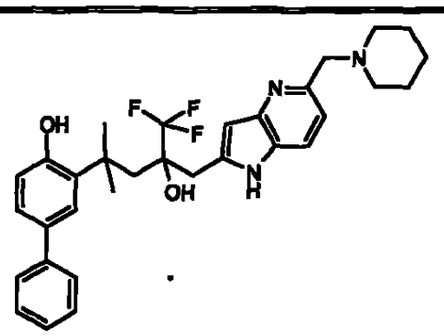
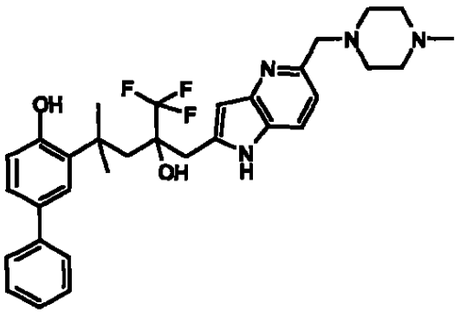
IA	
A	**B**
4-Fluoro-2-{4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-[5-(4-methylpiperazin-1-ylmethyl)-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl]butyl}phenol	
2-(3-{5-[(Ethylmethylamino)methyl]-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl}-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl)-4-fluorophenol	
4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-pyrrolidin-1-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)butyl]phenol	
2-[3-(5-Dimethylaminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol	

IA	
A	**B**
2-[3-(5-Diethylaminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol	
3-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)butyl]biphenyl-4-ol	
3-{4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-[5-(4-methylpiperazin-1-ylmethyl)-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl]butyl}biphenyl-4-ol	

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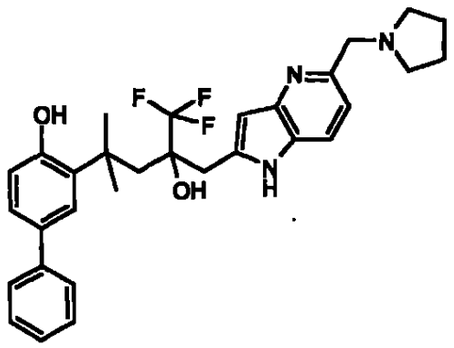
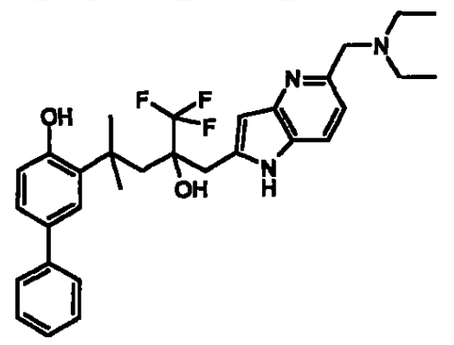
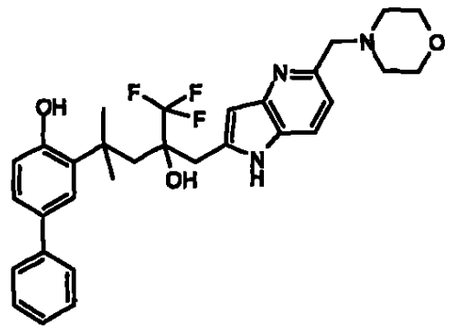
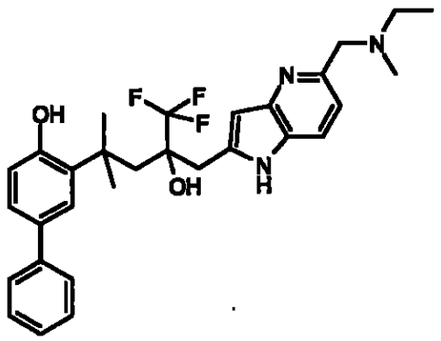
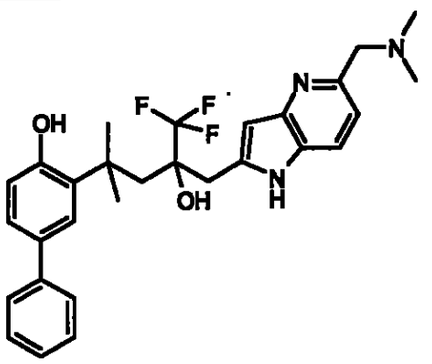
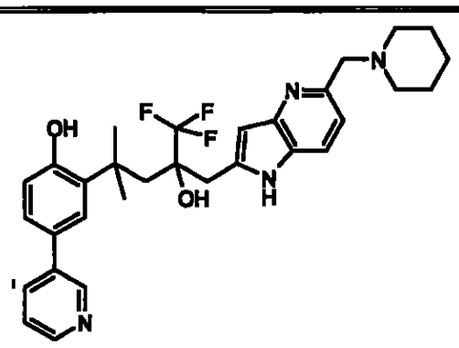
IA	
A	**B**
3-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(5-pyrrolidin-1-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)butyl]biphenyl-4-ol	
3-[3-(5-Diethylaminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]biphenyl-4-ol	
3-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)butyl]biphenyl-4-ol	

IA	
A	B
3-(3-{5-[(Ethylmethylamino)methyl]-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl}-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl)biphenyl-4-ol	
3-[3-(5-Dimethylaminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]biphenyl-4-ol	
4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)butyl]phenol	

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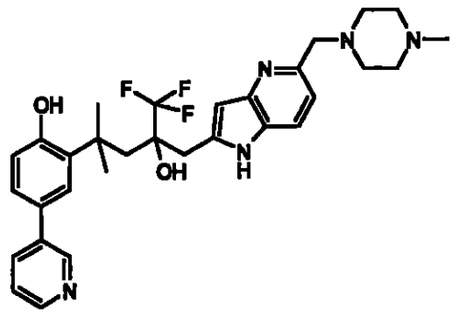
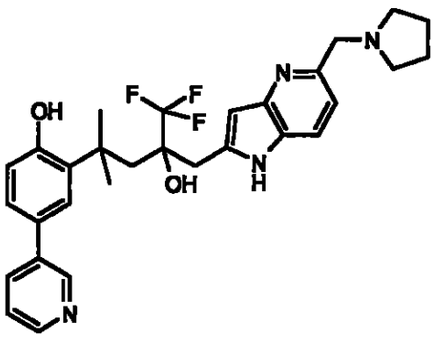
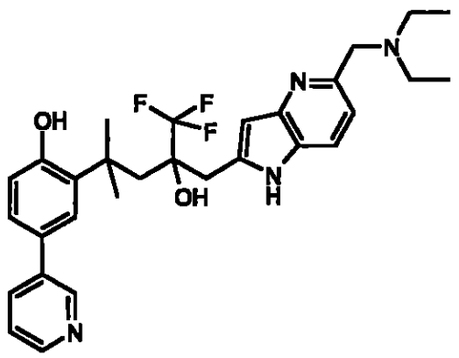
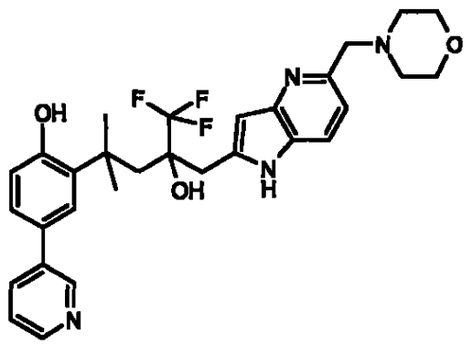
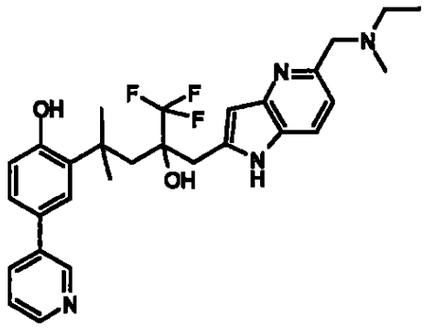
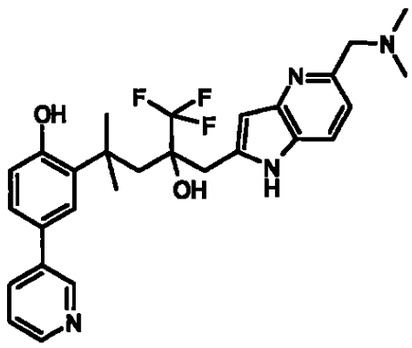
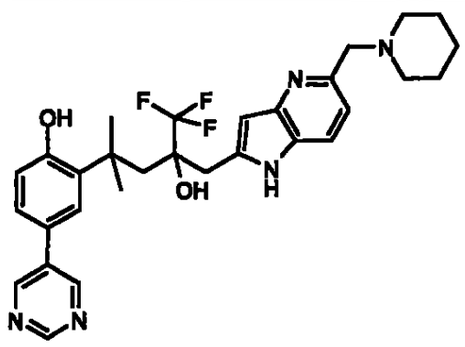
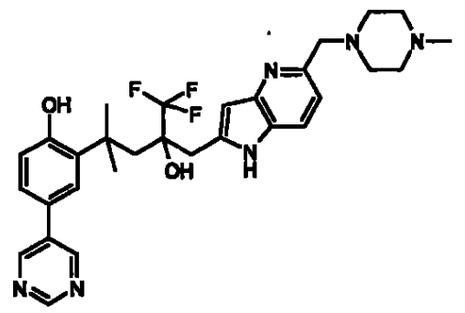
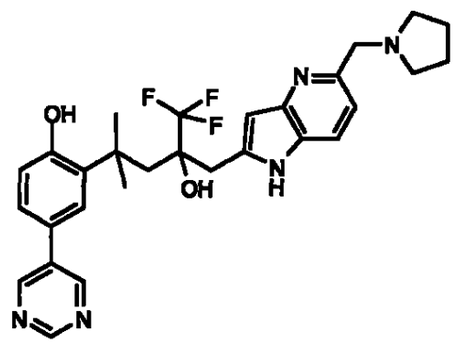
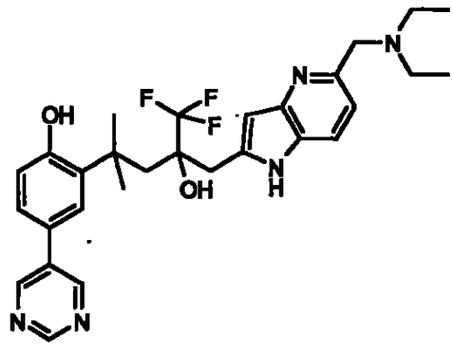
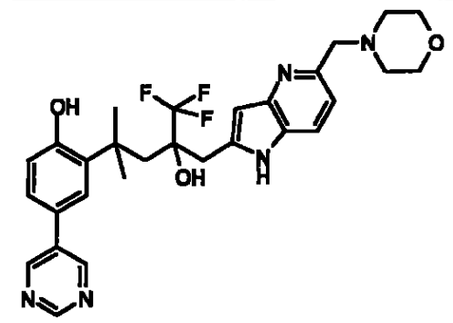
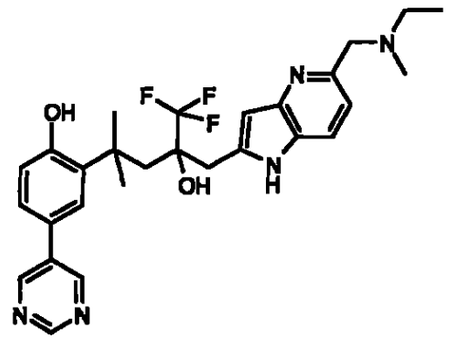
466

IA	
A	**B**
4-Pyridin-3-yl-2-{4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-[5-(4-methylpiperazin-1-ylmethyl)-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl]butyl}phenol	
4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-pyrrolidin-1-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)butyl]phenol	
2-[3-(5-Diethylaminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-pyridin-3-ylphenol	

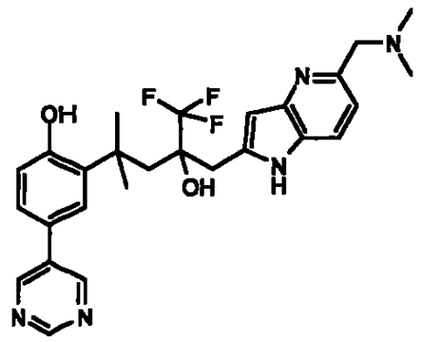
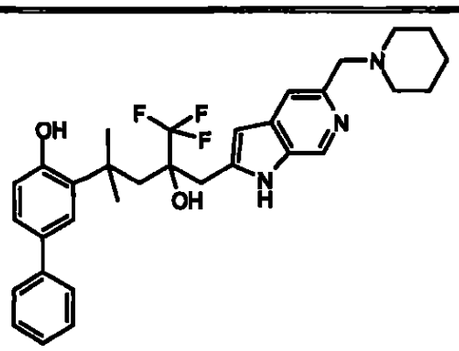
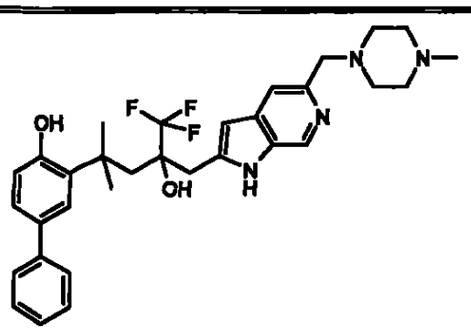
AA8
467

IA	
A	B
4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)butyl]phenol	
2-(3-{5-[(Ethylmethylamino)methyl]-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl}-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl)-4-pyridin-3-ylphenol	
2-[3-(5-Dimethylaminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-pyridin-3-ylphenol	

IA	
A	B
4-Pyrimidin-5-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)butyl]phenol	
4-Pyrimidin-5-yl-2-{4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-[5-(4-methylpiperazin-1-ylmethyl)-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl]butyl}phenol	
4-Pyrimidin-5-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-pyrrolidin-1-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)butyl]phenol	

IA	
A	B
2-[3-(5-Diethylaminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-pyrimidin-5-ylphenol	
4-Pyrimidin-5-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)butyl]phenol	
2-(3-{5-[(Ethylmethylamino)methyl]-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl}-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl)-4-pyrimidin-5-ylphenol	

457
470

IA	
A	B
2-[3-(5-Dimethylaminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-pyrimidin-5-ylphenol	
3-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-ylmethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-4-ol	
3-{4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-[5-(4-methylpiperazin-1-ylmethyl)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]butyl}biphenyl-4-ol	

452

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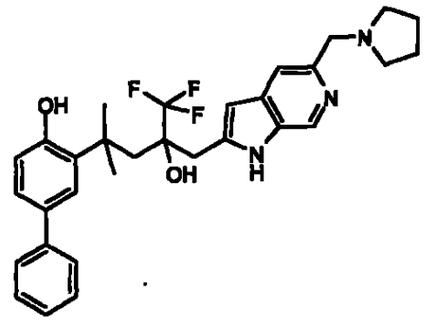
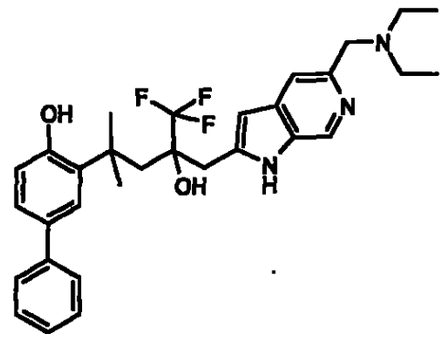
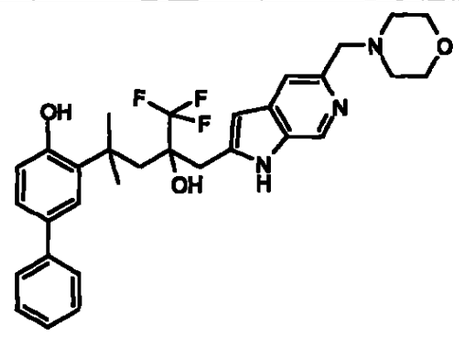
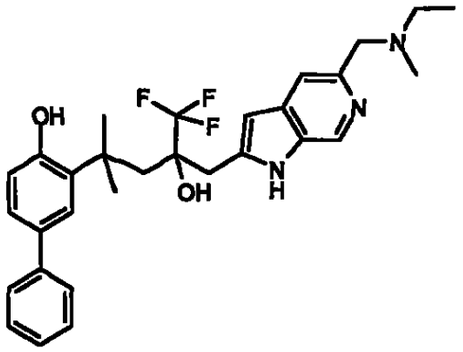
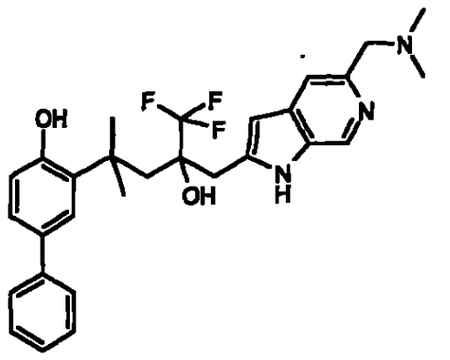
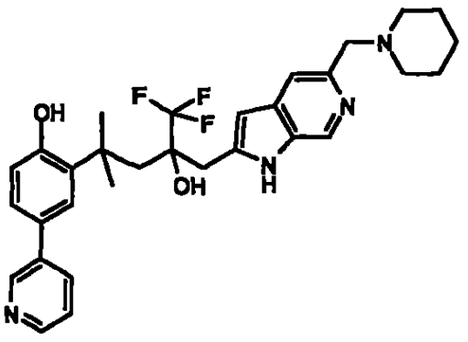
IA	
A	B
3-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(5-pyrrolidin-1-ylmethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-4-ol	
3-[3-(5-Diethylaminomethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]biphenyl-4-ol	
3-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-4-ol	

455
472

IA	
A	B
3-(3-{5-[(Ethylmethylamino)methyl]-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl}-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl)biphenyl-4-ol	
3-[3-(5-Dimethylaminomethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]biphenyl-4-ol	
4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-ylmethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	

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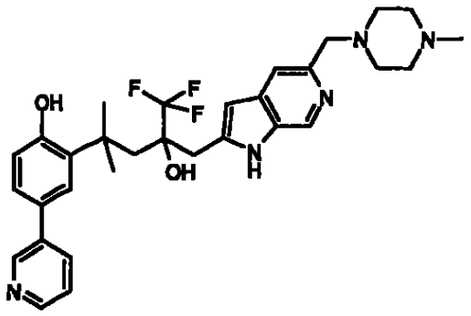
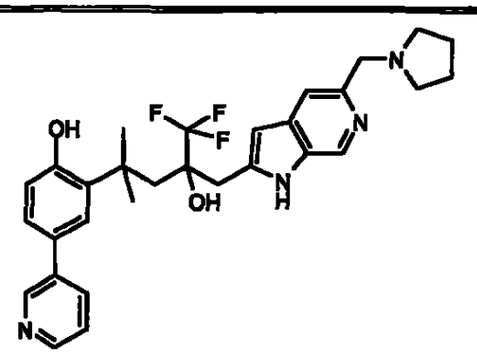
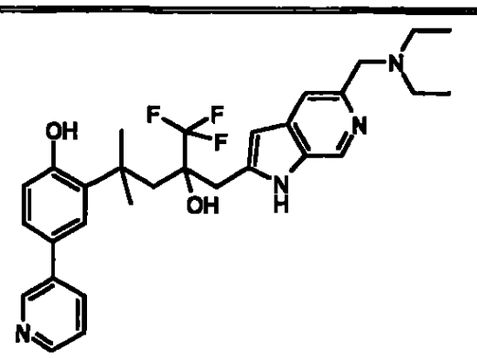
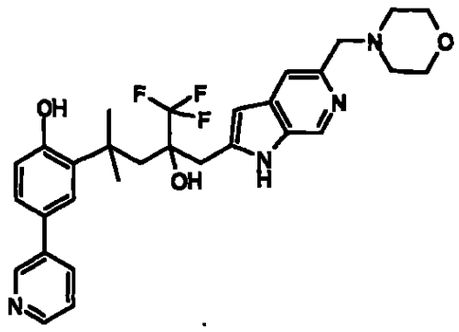
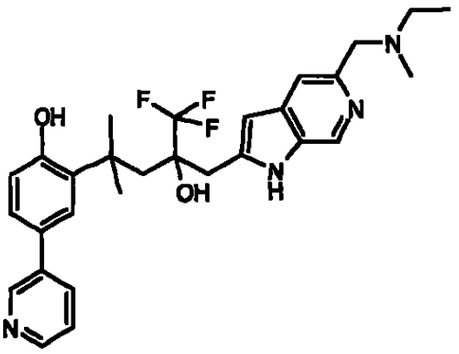
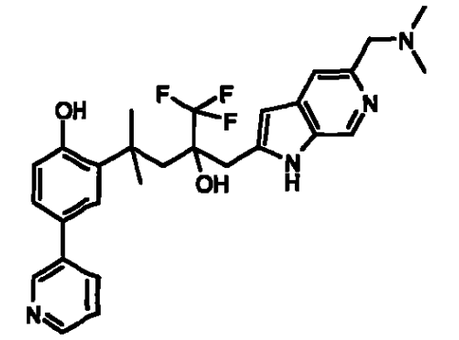
473

IA	
A	B
4-Pyridin-3-yl-2-{4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-[5-(4-methylpiperazin-1-ylmethyl)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]butyl}phenol	
4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-pyrrolidin-1-ylmethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	
2-[3-(5-Diethylaminomethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-pyridin-3-ylphenol	

IA	
A	**B**
4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	
2-(3-{5-[(Ethylmethylamino)methyl]-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl}-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl)-4-pyridin-3-ylphenol	
2-[3-(5-Dimethylaminomethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-pyridin-3-ylphenol	

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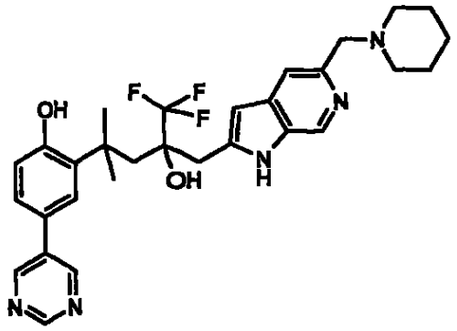
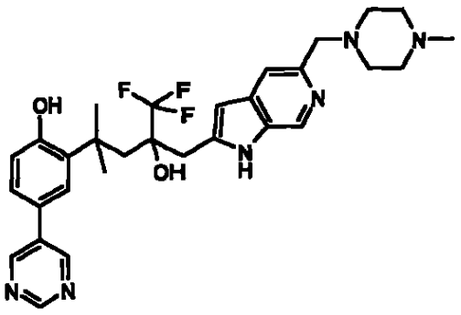
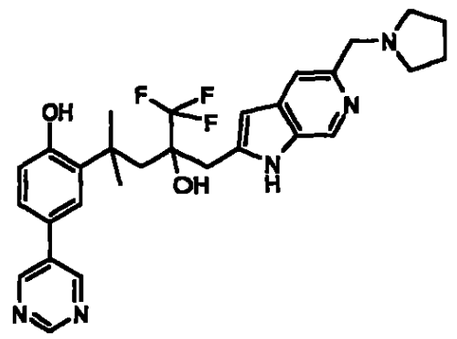
IA	
A	B
4-Pyrimidin-5-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-ylmethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	
4-Pyrimidin-5-yl-2-{4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-[5-(4-methylpiperazin-1-ylmethyl)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]butyl}phenol	
4-Pyrimidin-5-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-pyrrolidin-1-ylmethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	

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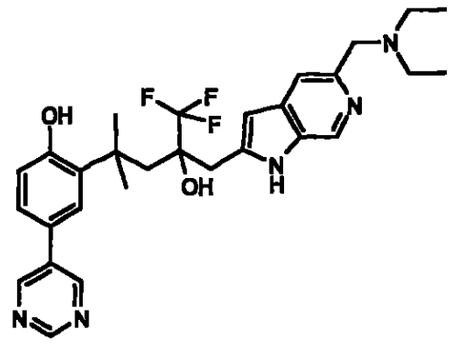
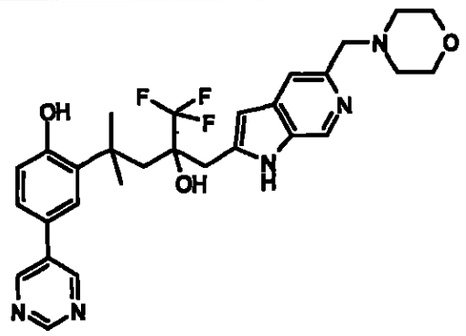
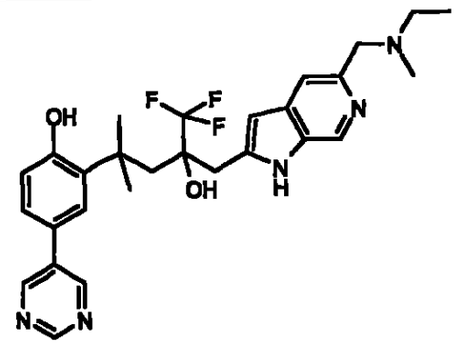
IA	
A	B
2-[3-(5-Diethylaminomethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-pyrimidin-5-ylphenol	
4-Pyrimidin-5-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-ylmethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	
2-(3-{5-[(Ethylmethylamino)methyl]-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl}-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl)-4-pyrimidin-5-ylphenol	

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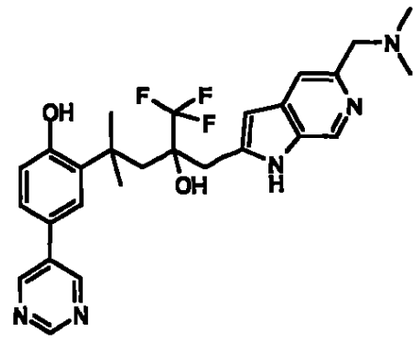
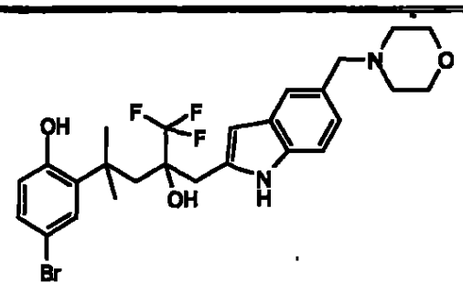
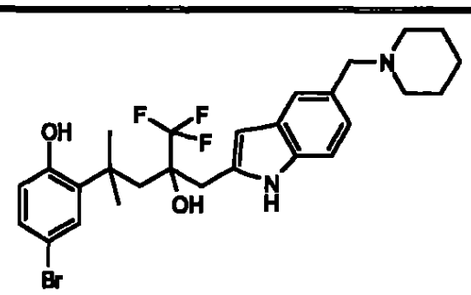
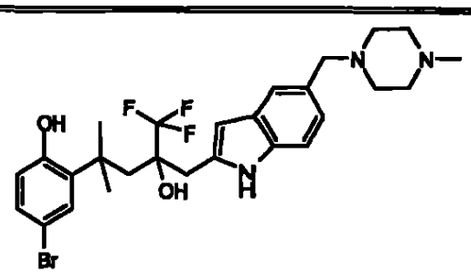
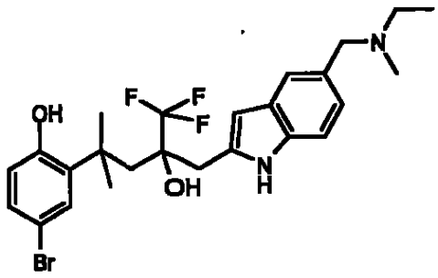
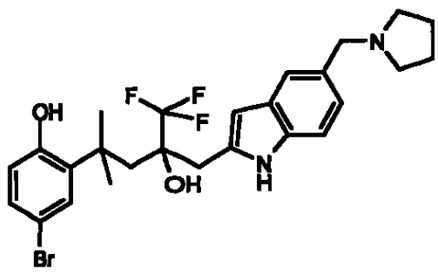
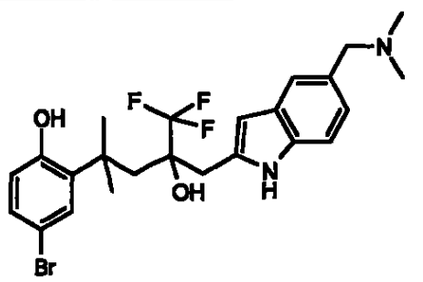
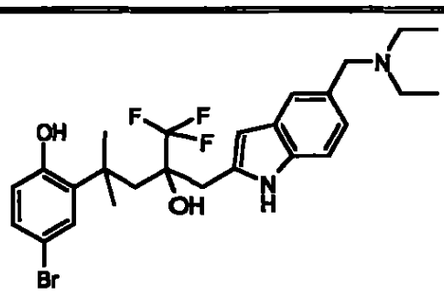
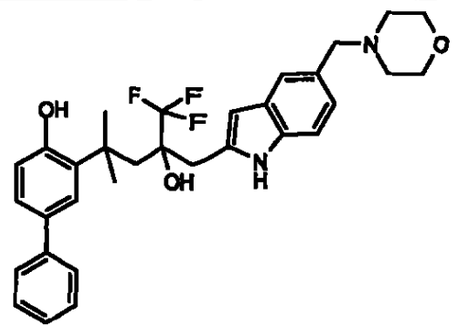
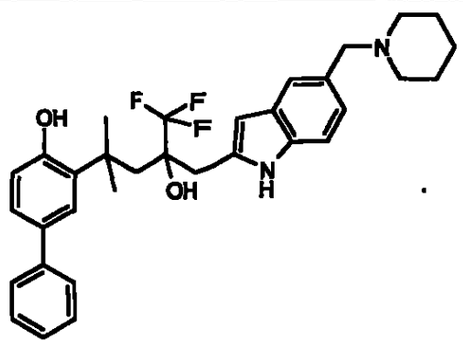
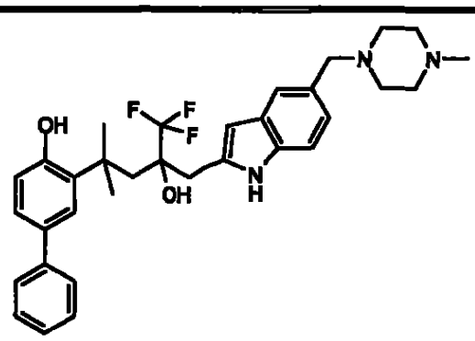
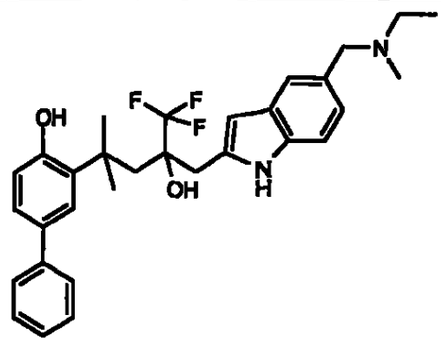
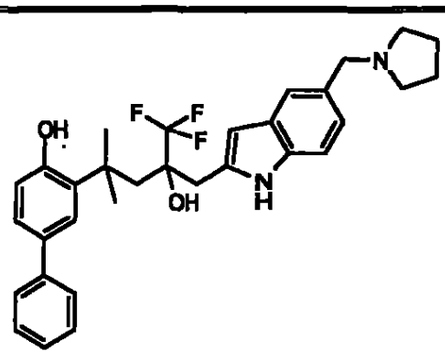
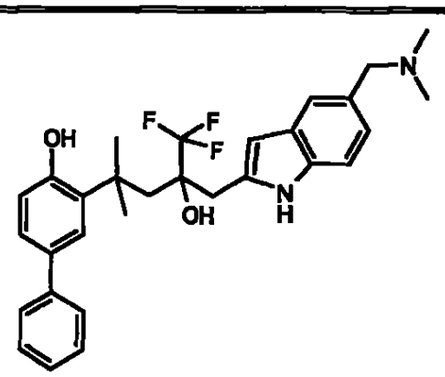
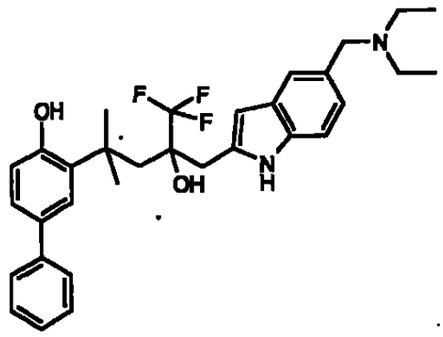
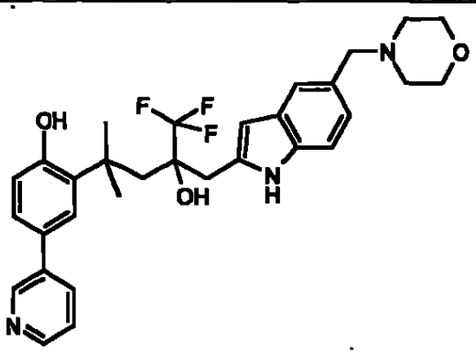
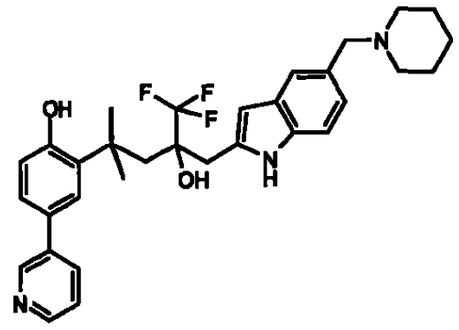
IA	
A	**B**
2-[3-(5-Dimethylaminomethyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-pyrimidin-5-ylphenol	
4-Bromo-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-ylmethyl-1*H*-indol-2-ylmethyl)butyl]phenol	
4-Bromo-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-ylmethyl-1*H*-indol-2-ylmethyl)butyl]phenol	
4-Bromo-2-{4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-[5-(4-methylpiperazin-1-ylmethyl)-1*H*-indol-2-ylmethyl]butyl}phenol	

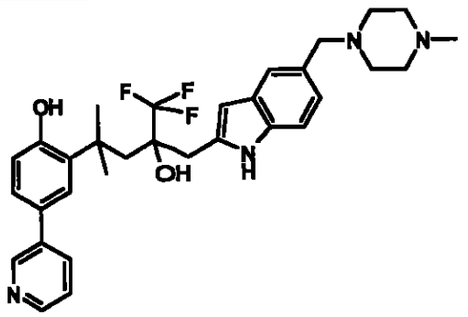
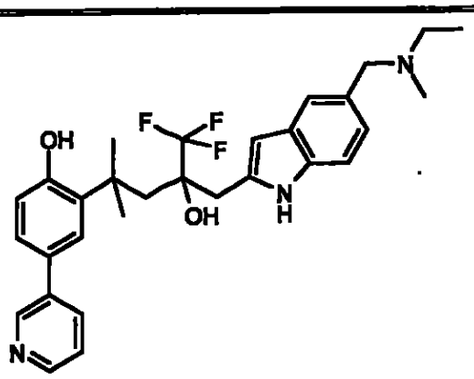
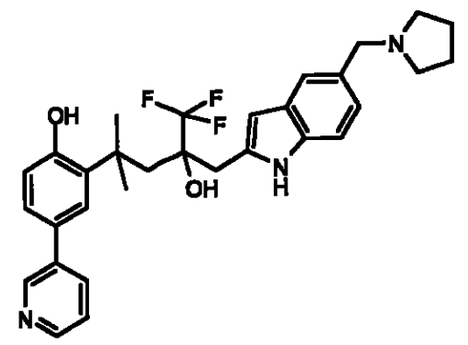
IA	
A	B
4-Bromo-2-(3-{5-[(ethylmethylamino)methyl]-1*H*-indol-2-ylmethyl}-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl)phenol	
4-Bromo-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-pyrrolidin-1-ylmethyl-1*H*-indol-2-ylmethyl)butyl]phenol	
4-Bromo-2-[3-(5-dimethylaminomethyl-1*H*-indol-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]phenol	
4-Bromo-2-[3-(5-diethylaminomethyl-1*H*-indol-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]phenol	

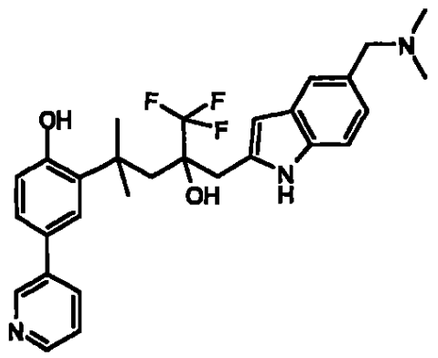
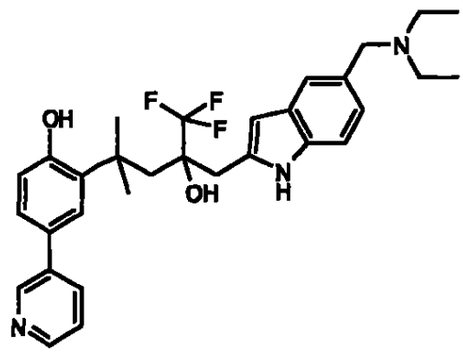
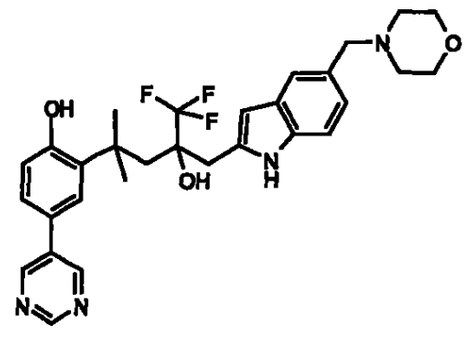
IA	
A	**B**
3-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-ylmethyl-1*H*-indol-2-ylmethyl)butyl]biphenyl-4-ol	
3-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-ylmethyl-1*H*-indol-2-ylmethyl)butyl]biphenyl-4-ol	
3-{4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-[5-(4-methylpiperazin-1-ylmethyl)-1*H*-indol-2-ylmethyl]butyl}biphenyl-4-ol	

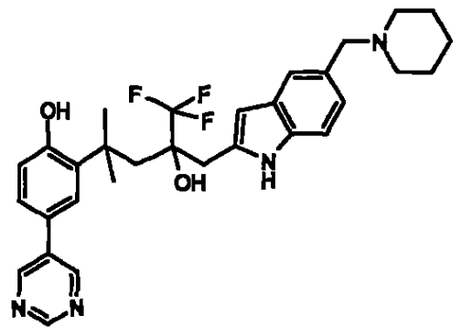
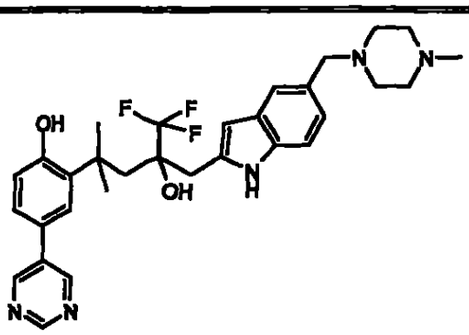
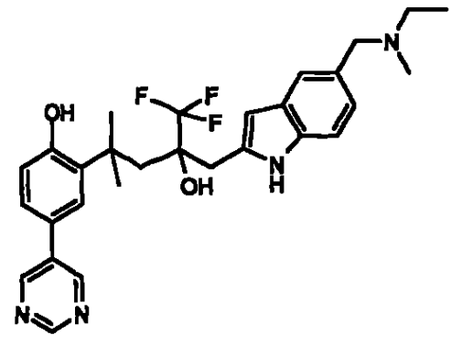
467
480

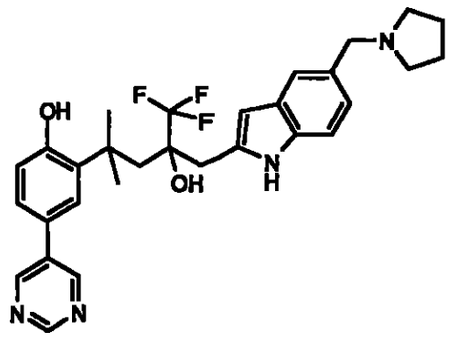
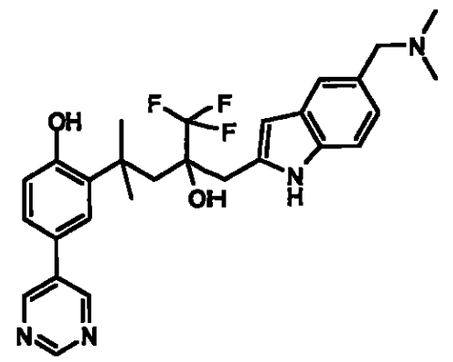
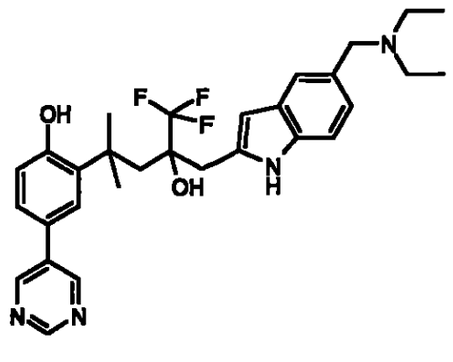
IA	
A	B
3-(3-{5-[(Ethylmethylamino)methyl]-1*H*-indol-2-ylmethyl}-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl)biphenyl-4-ol	
3-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(5-pyrrolidin-1-ylmethyl-1*H*-indol-2-ylmethyl)butyl]biphenyl-4-ol	
3-[3-(5-Dimethylaminomethyl-1*H*-indol-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]biphenyl-4-ol	

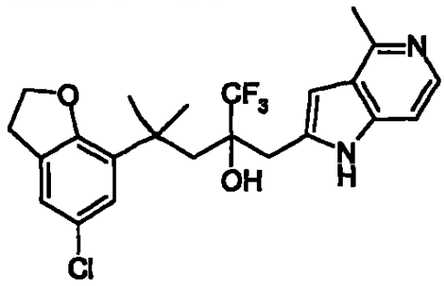
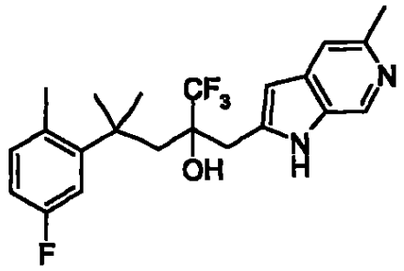
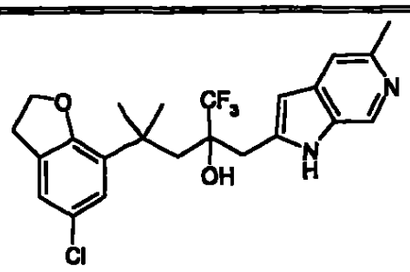
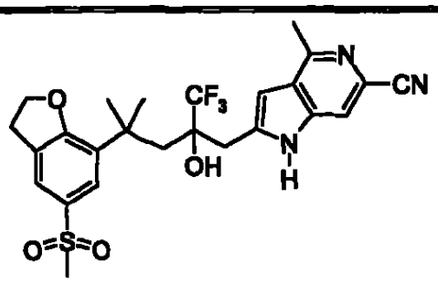
IA	
A	B
3-[3-(5-Diethylaminomethyl-1*H*-indol-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]biphenyl-4-ol	
4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-ylmethyl-1*H*-indol-2-ylmethyl)butyl]phenol	
4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-ylmethyl-1*H*-indol-2-ylmethyl)butyl]phenol	

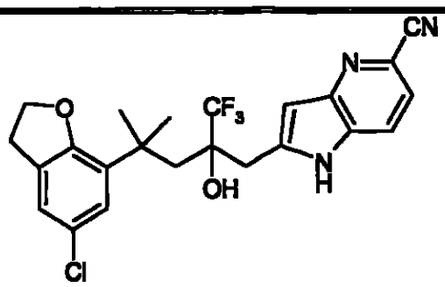
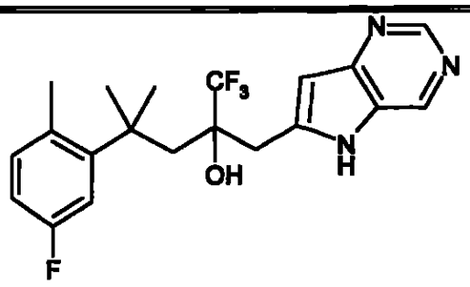
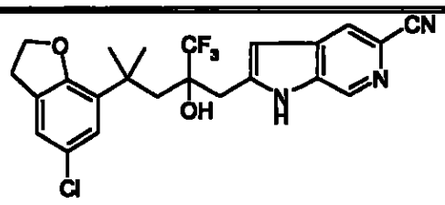
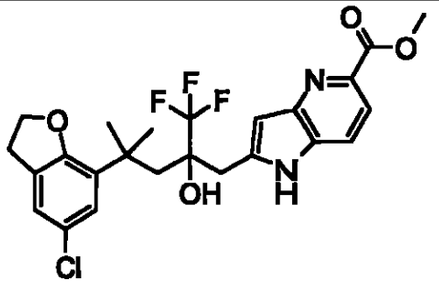
IA	
A	B
4-Pyridin-3-yl-2-{4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-[5-(4-methylpiperazin-1-ylmethyl)-1*H*-indol-2-ylmethyl]butyl}phenol	
2-(3-{5-[(Ethylmethylamino)methyl]-1*H*-indol-2-ylmethyl}-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl)-4-pyridin-3-ylphenol	
4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-pyrrolidin-1-ylmethyl-1*H*-indol-2-ylmethyl)butyl]phenol	

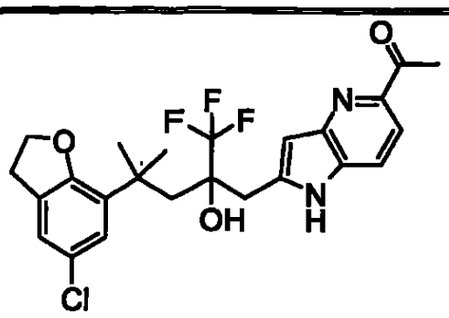
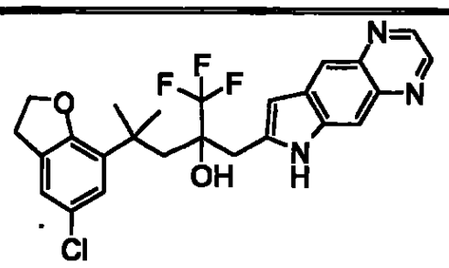
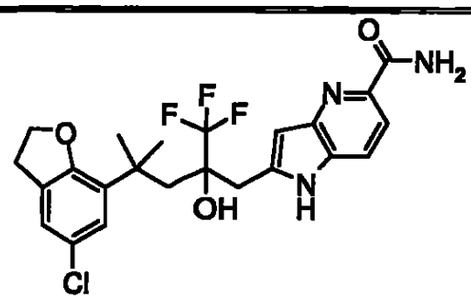
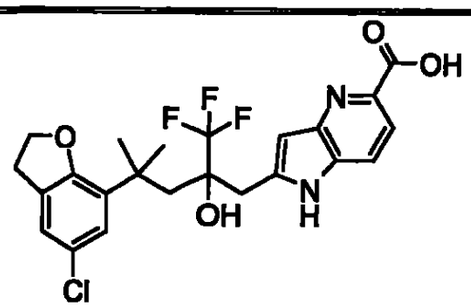
IA	
A	**B**
2-[3-(5-Dimethylaminomethyl-1*H*-indol-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-pyridin-3-ylphenol	
2-[3-(5-Diethylaminomethyl-1*H*-indol-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-pyridin-3-ylphenol	
4-Pyrimidin-5-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-ylmethyl-1*H*-indol-2-ylmethyl)butyl]phenol	

IA	
A	B
4-Pyrimidin-5-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-ylmethyl-1*H*-indol-2-ylmethyl)butyl]phenol	
4-Pyrimidin-5-yl-2-{4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-[5-(4-methylpiperazin-1-ylmethyl)-1*H*-indol-2-ylmethyl]butyl}phenol	
2-(3-{5-[(Ethylmethylamino)methyl]-1*H*-indol-2-ylmethyl}-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl)-4-pyrimidin-5-ylphenol	

IA	
A	**B**
4-Pyrimidin-5-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-pyrrolidin-1-ylmethyl-1*H*-indol-2-ylmethyl)butyl]phenol	
2-[3-(5-Dimethylaminomethyl-1*H*-indol-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-pyrimidin-5-ylphenol	
2-[3-(5-Diethylaminomethyl-1*H*-indol-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-pyrimidin-5-ylphenol	

IA	
A	**B**
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-4-methyl-1*H*-pyrrolo[3,2-*c*]pyridine-6-carbonitrile	

IA	
A	**B**
2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	
2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridine-5-carbonitrile	
2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carboxylic acid methyl ester	

IA	
A	B
1-{2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}ethanone	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(6*H*-pyrrolo[2,3-g]quinoxalin-7-ylmethyl)pentan-2-ol	
2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carboxylic acid amide	
2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carboxylic acid	

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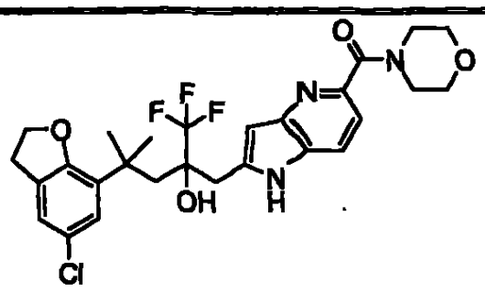
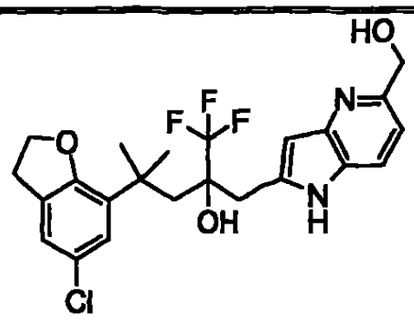
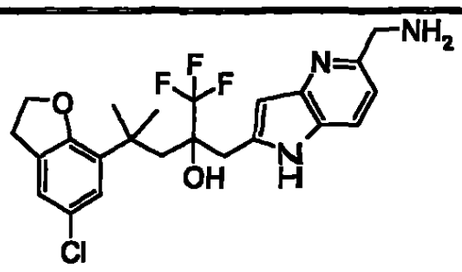
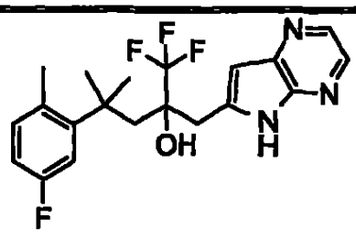
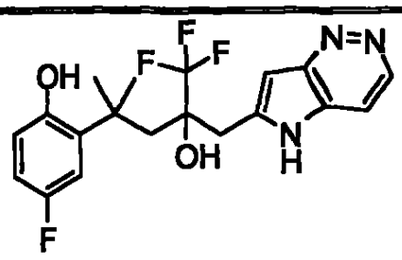
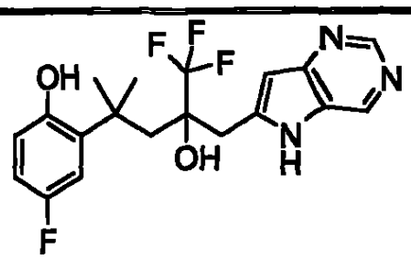
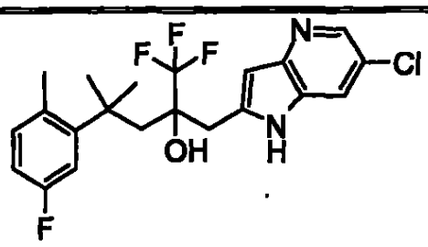
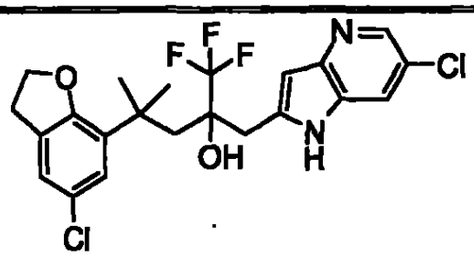
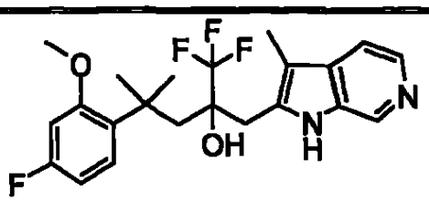
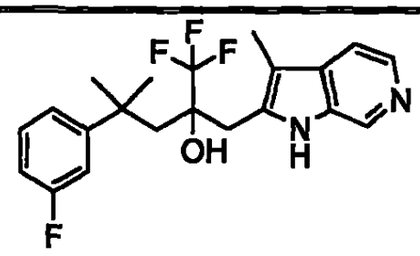
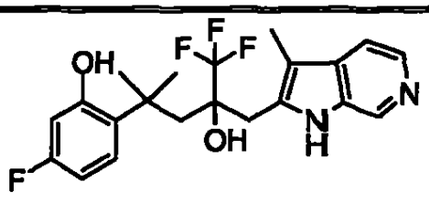
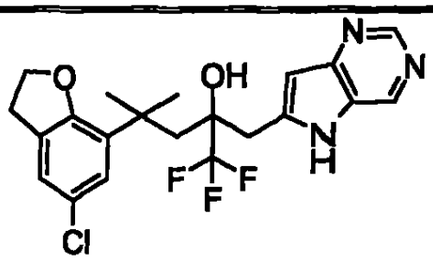
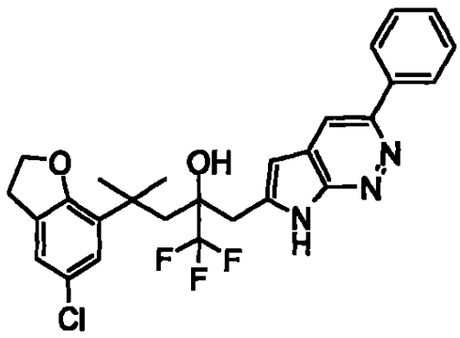
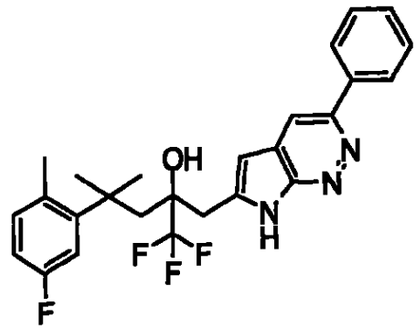
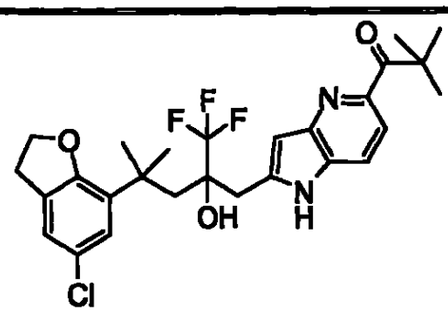
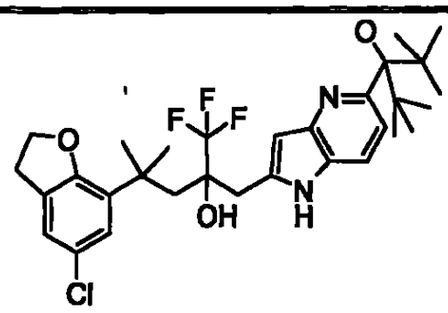
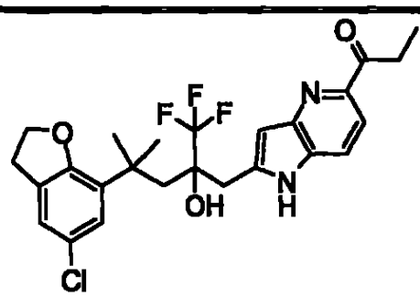
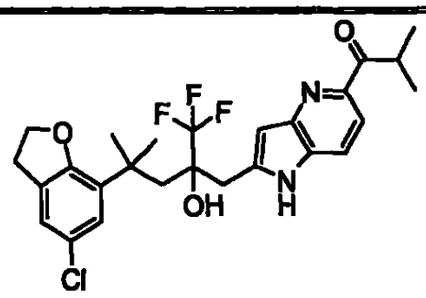
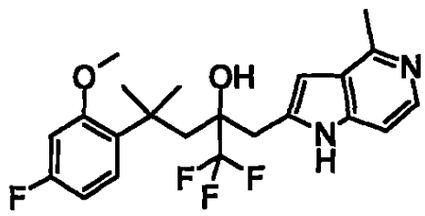
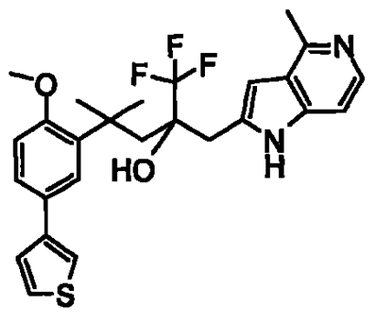
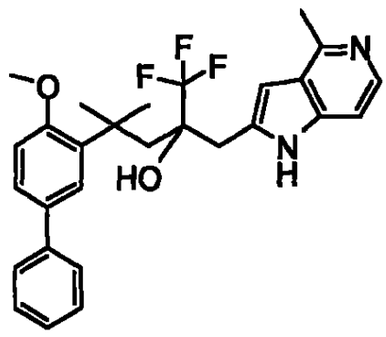
IA	
A	B
{2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}morpholin-4-ylmethanone	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(5-hydroxymethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	
2-(5-Aminomethyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)pentan-2-ol	

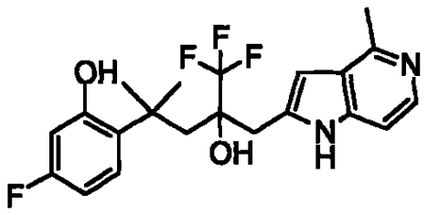
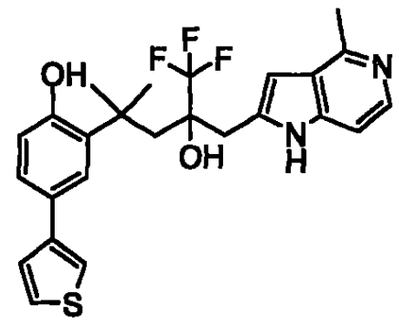
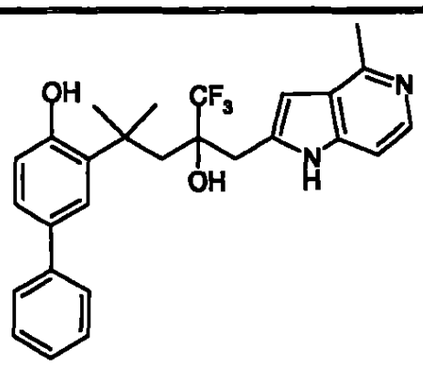
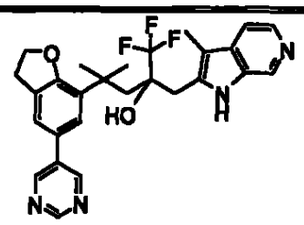
IA	
A	**B**
4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5*H*-pyrrolo[3,2-*c*]pyridazin-6-ylmethyl)butyl]phenol	
4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)butyl]phenol	
2-(6-Chloro-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(6-chloro-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

491

IA	
A	**B**
1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
5-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(3-phenyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-ylmethyl)pentan-2-ol	

IA	
A	B
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(3-phenyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-ylmethyl)pentan-2-ol	
1-{2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}-2,2-dimethylpropan-1-one	
2-[5-(1-*tert*-Butyl-1-hydroxy-2,2-dimethylpropyl)-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl]-4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-ol	
1-{2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}propan-1-one	

IA	
A	B
1-{2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}-2-methylpropan-1-one	
1,1,1-Trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(2-methoxy-5-thiophen-3-ylphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(4-methoxybiphenyl-3-yl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	

IA	
A	**B**
5-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]phenol	
4-Thiophen-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]phenol	
3-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]biphenyl-4-ol	
1,1,1-Trifluoro-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(5-pyrimidin-5-yl-2,3-dihydrobenzofuran-7-yl)pentan-2-ol	

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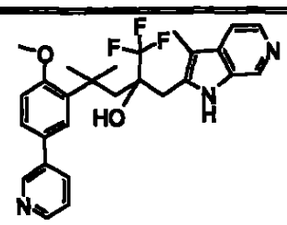
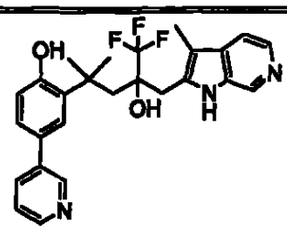
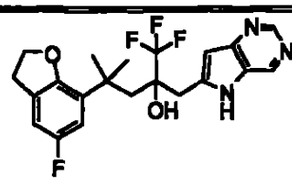
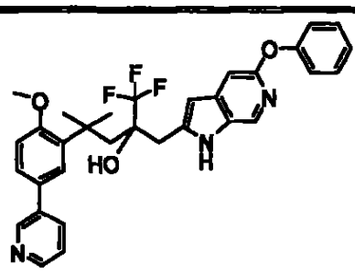
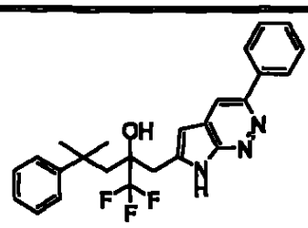
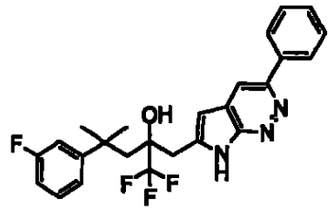
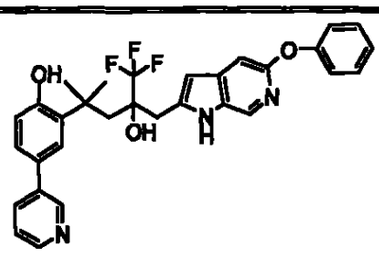
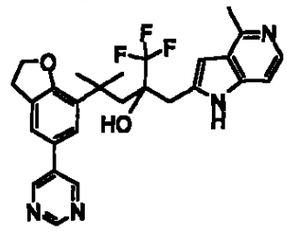
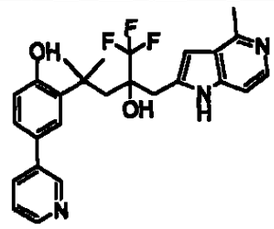
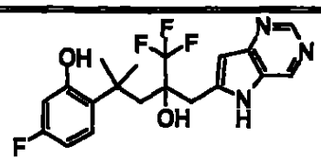
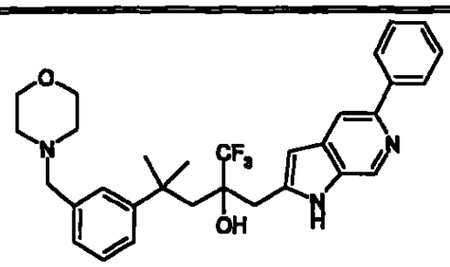
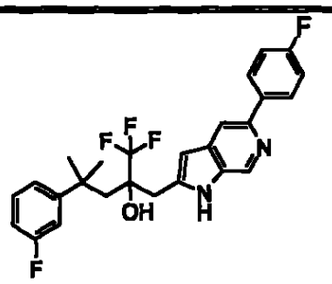
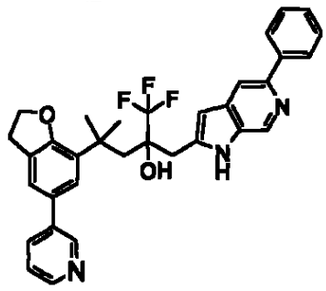
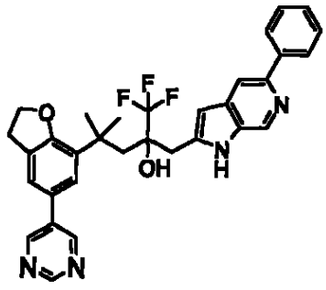
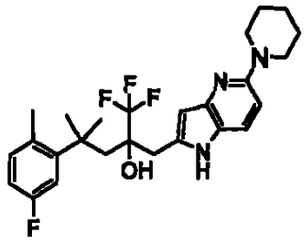
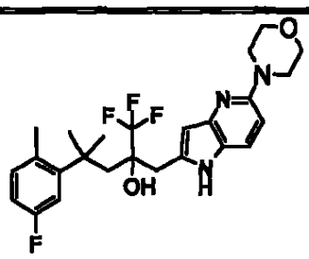
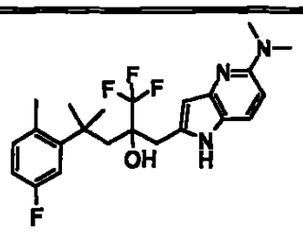
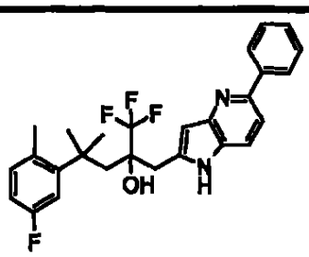
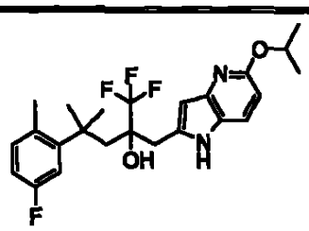
IA	
A	**B**
1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	
1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(5-phenoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-phenyl-2-(3-phenyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-ylmethyl)pentan-2-ol	

IA	
A	**B**
1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(3-phenyl-7*H*-pyrrolo[2,3-*c*]pyridazin-6-ylmethyl)pentan-2-ol	
4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-phenoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	
1,1,1-Trifluoro-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-4-(5-pyrimidin-5-yl-2,3-dihydrobenzofuran-7-yl)pentan-2-ol	
4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]phenol	
5-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)butyl]phenol	

IA	
A	B
1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylmethylphenyl)-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(3-fluorophenyl)-2-[5-(4-fluorophenyl)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-methyl-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(5-pyridin-3-yl-2,3-dihydrobenzofuran-7-yl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(5-pyrimidin-5-yl-2,3-dihydrobenzofuran-7-yl)pentan-2-ol	

IA	
A	B
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)pentan-2-ol	
2-(5-Dimethylamino-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-phenyl-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-isopropoxy-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	

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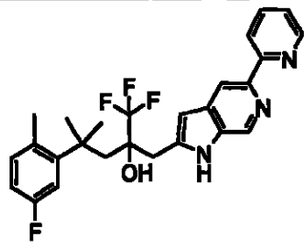
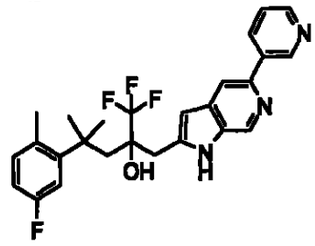
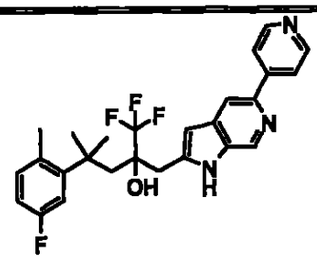
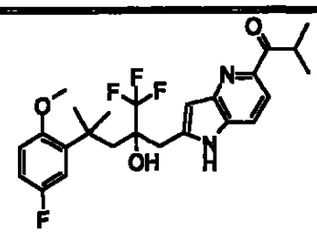
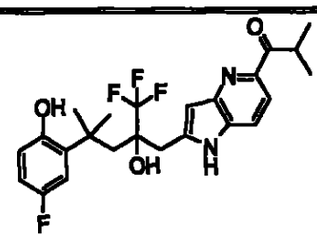
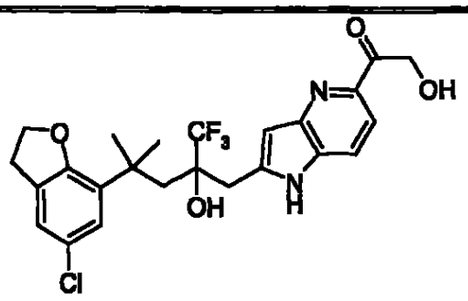
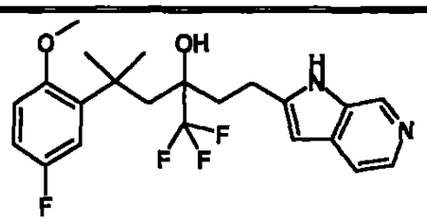
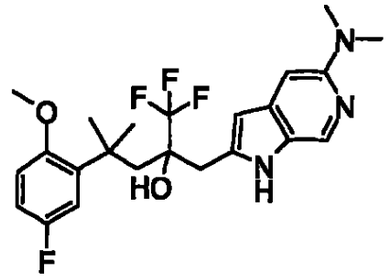
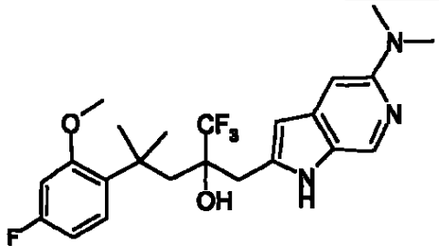
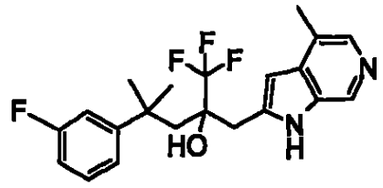
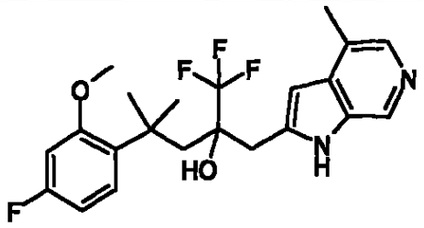
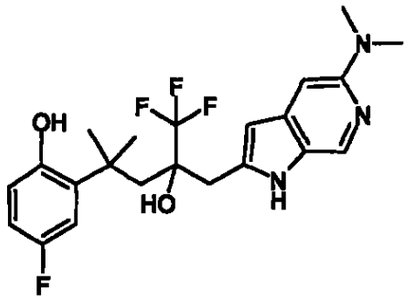
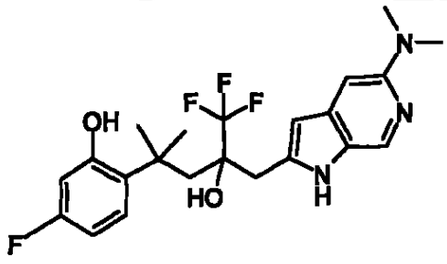
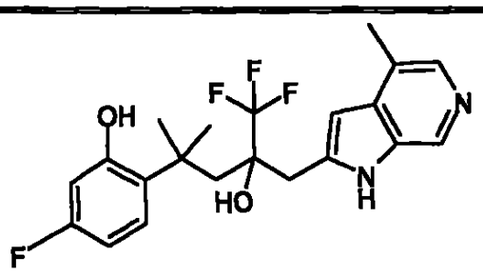
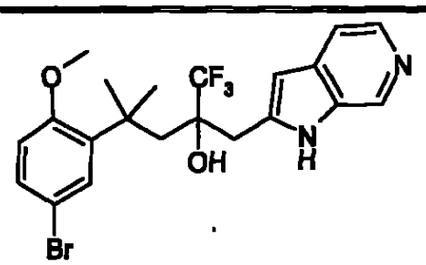
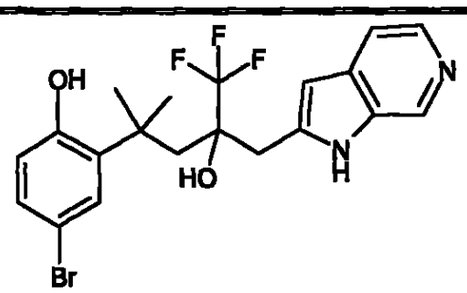
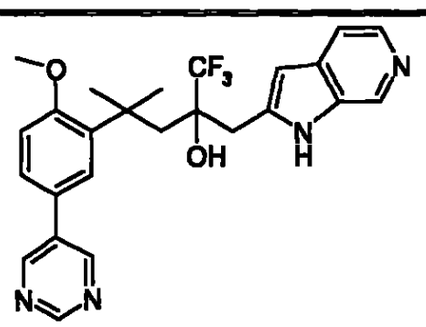
IA	
A	**B**
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-pyridin-2-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-pyridin-3-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-pyridin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1-{2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}-2-methylpropan-1-one	
1-{2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}-2-methylpropan-1-one	

IA	
A	B
1-{2-[4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridin-5-yl}-2-hydroxyethanone	
5-(5-Fluoro-2-methoxyphenyl)-5-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)-3-trifluoromethylhexan-3-ol	
2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	
2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	

IA	
A	**B**
1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
2-[3-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol	
2-[3-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-5-fluorophenol	

IA	
A	**B**
5-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	
4-(5-Bromo-2-methoxyphenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-Bromo-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	
1,1,1-Trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

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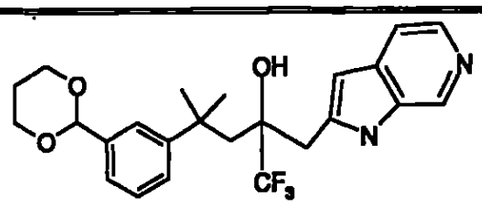
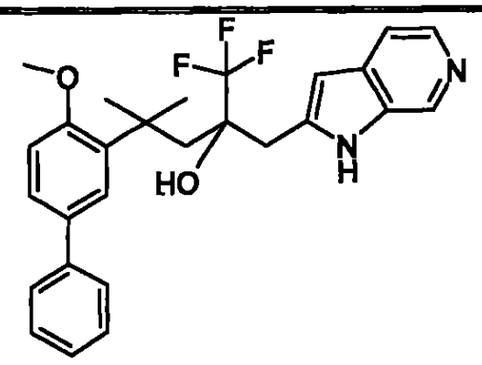
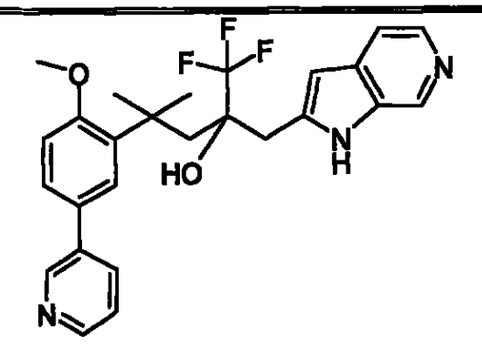
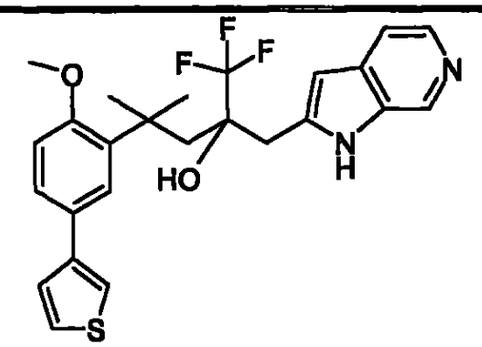
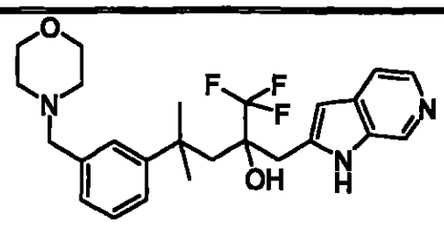
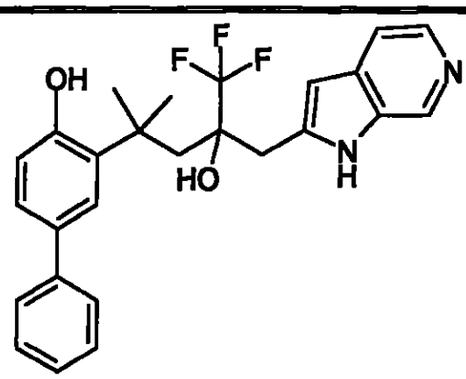
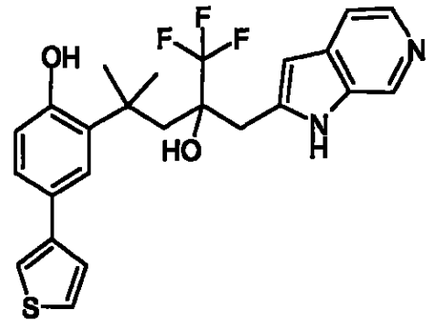
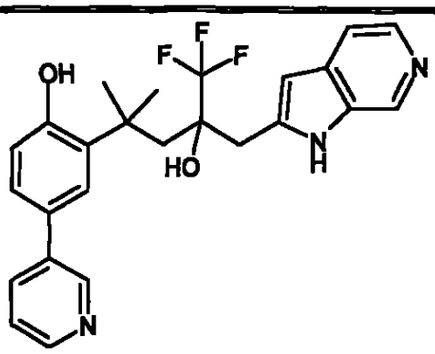
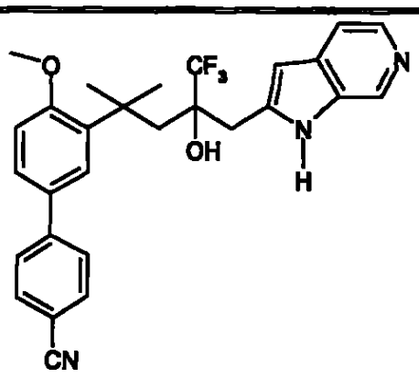
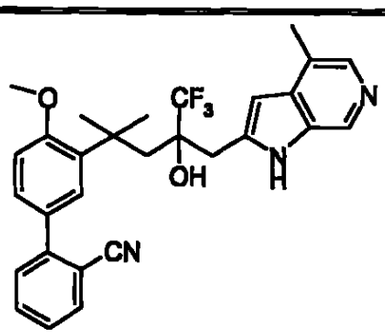
IA	
A	B
4-(3-[1,3]Dioxan-2-ylphenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(4-methoxybiphenyl-3-yl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(2-methoxy-5-thiophen-3-ylphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

IA	
A	**B**
1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylmethylphenyl)-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
3-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-4-ol	
4-Thiophen-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	

IA	
A	B
4-Thiophen-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	
4-Thiophen-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	
4'-Methoxy-3'-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-2-carbonitrile	

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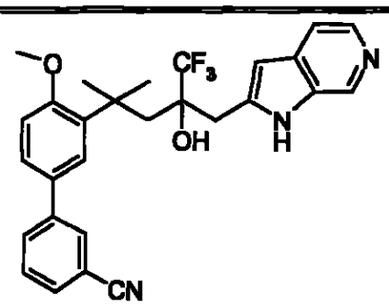
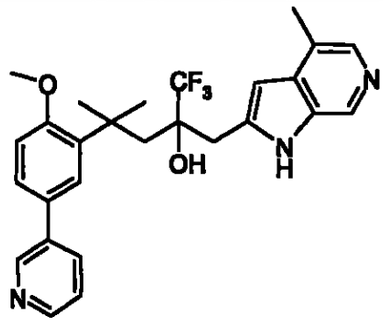
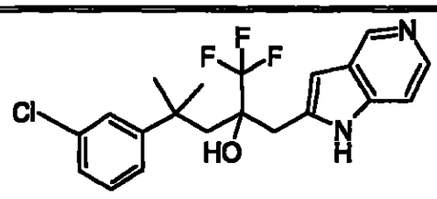
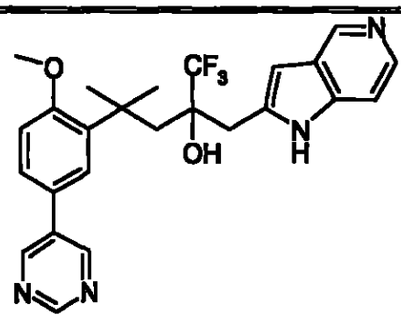
IA	
A	B
4'-Methoxy-3'-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-3-carbonitrile	
1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-(3-Chlorophenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	

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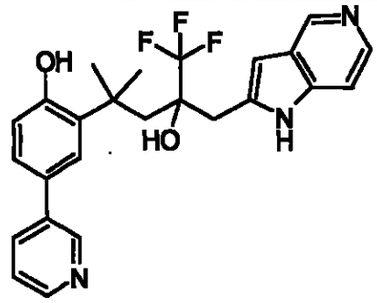
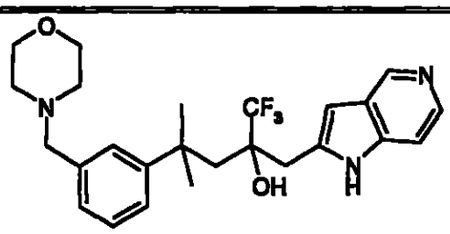
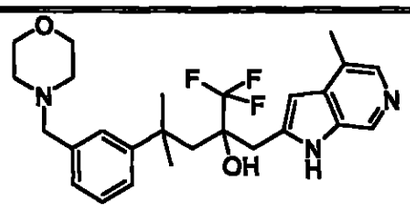
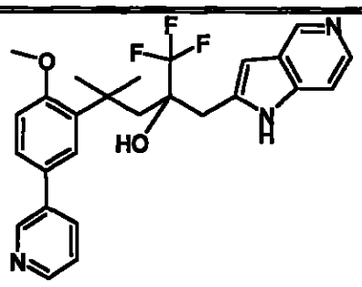
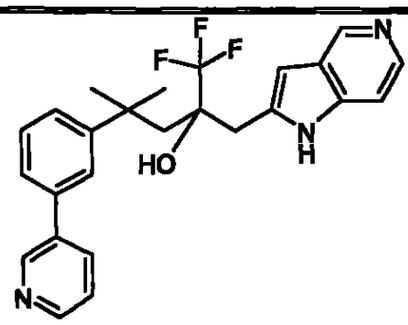
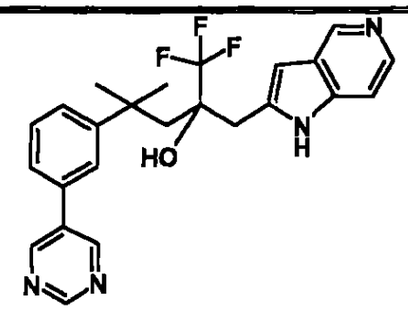
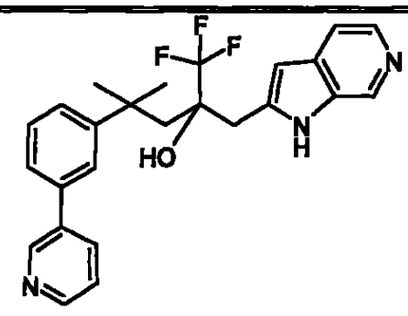
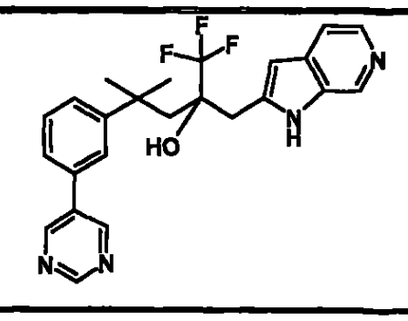
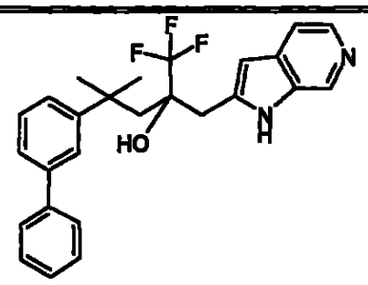
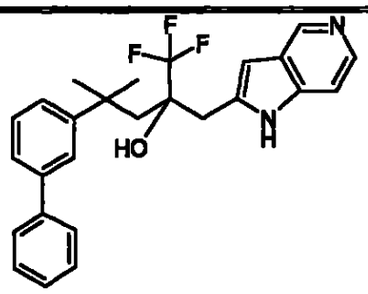
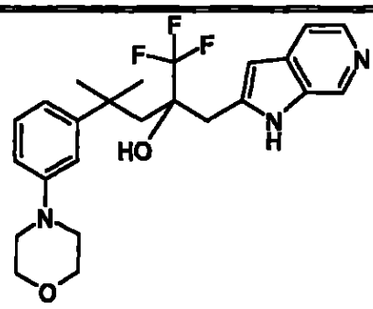
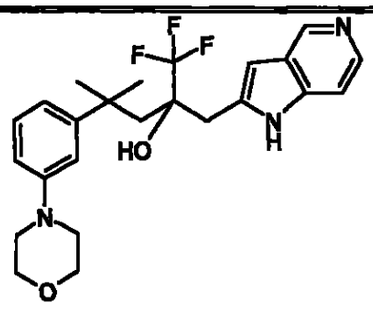
507

IA	
A	B
4-Pyridin-3-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]phenol	
1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylmethylphenyl)-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(3-morpholin-4-ylmethylphenyl)pentan-2-ol	
1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	

IA	
A	B
1,1,1-Trifluoro-4-methyl-4-(3-pyridin-3-ylphenyl)-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(3-pyrimidin-5-ylphenyl)-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(3-pyridin-3-ylphenyl)-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(3-pyrimidin-5-ylphenyl)-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

IA	
A	B
4-Biphenyl-3-yl-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-Biphenyl-3-yl-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylphenyl)-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylphenyl)-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	

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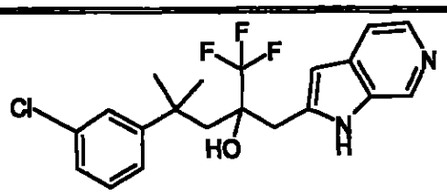
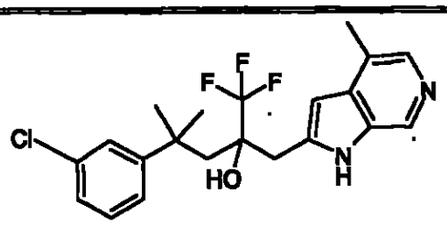
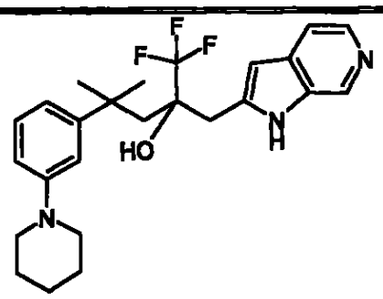
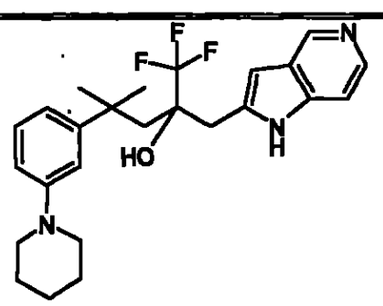
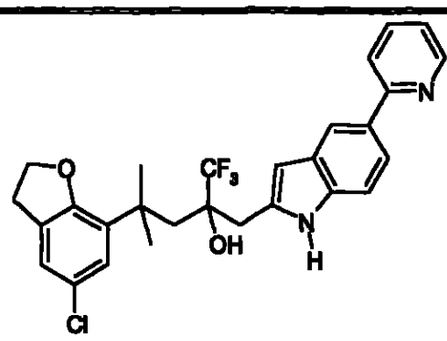
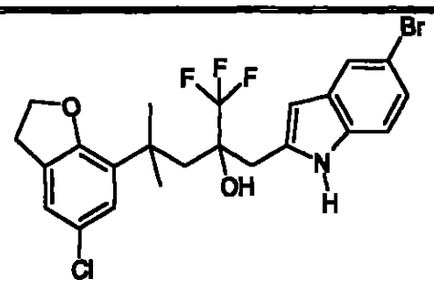
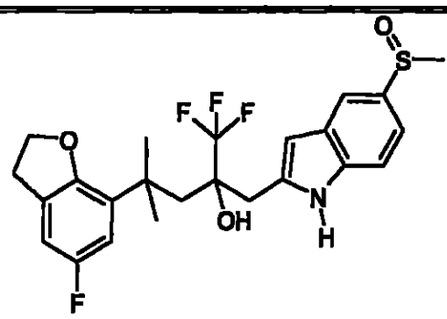
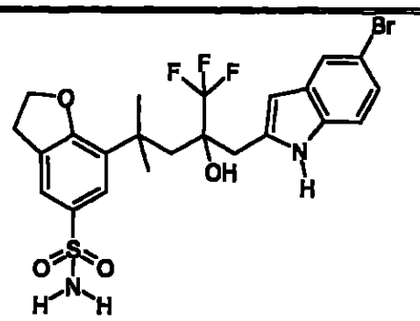
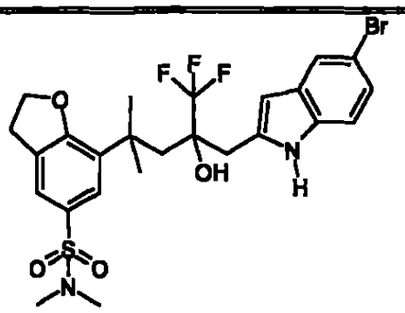
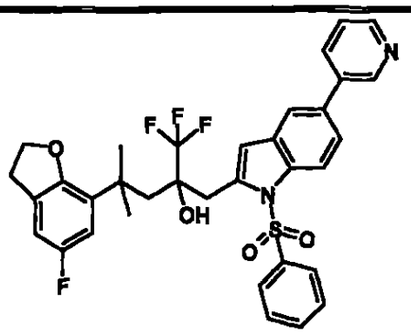
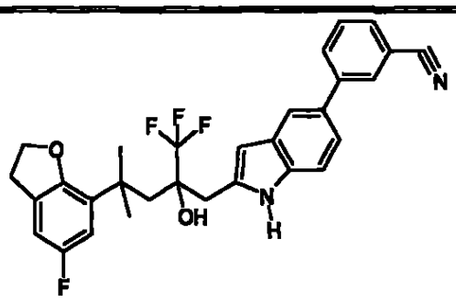
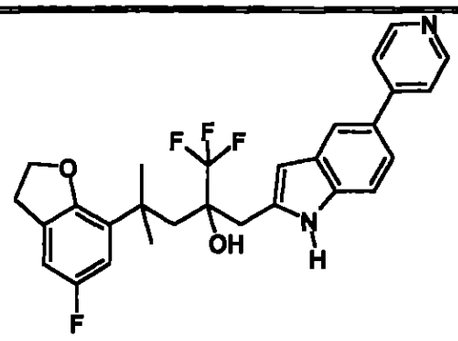
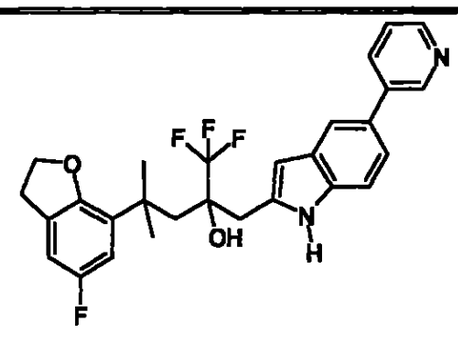
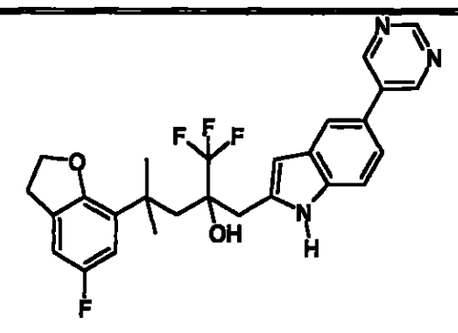
510

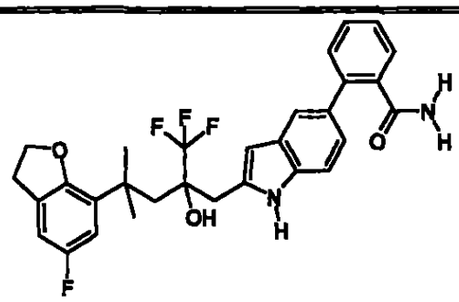
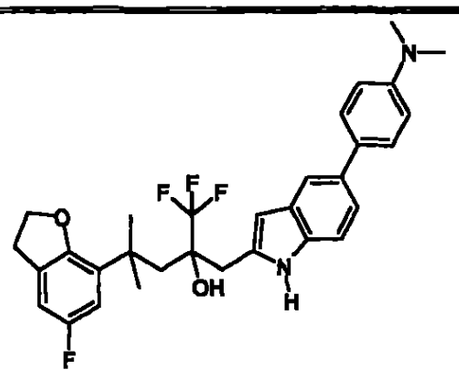
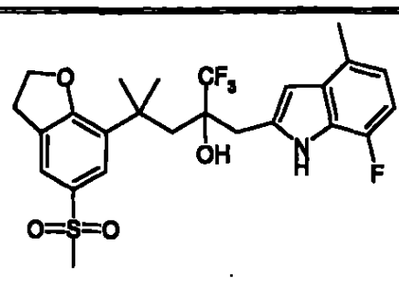
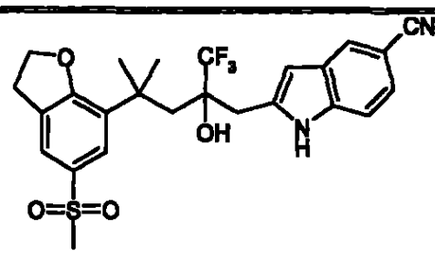
IA	
A	B
4-(3-Chlorophenyl)-1,1,1-trifluoro-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-(3-Chlorophenyl)-1,1,1-trifluoro-4-methyl-2-(4-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(3-piperidin-1-ylphenyl)-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(3-piperidin-1-ylphenyl)-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	

492
511

IA	
A	**B**
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-pyridin-2-yl-1*H*-indol-2-ylmethyl)pentan-2-ol	
2-(5-Bromo-1*H*-indol-2-ylmethyl)-4-(5-chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-2-(5-methanesulfinyl-1*H*-indol-2-ylmethyl)-4-methylpentan-2-ol	
7-[3-(5-Bromo-1*H*-indol-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-2,3-dihydrobenzofuran-5-sulfonic acid amide	

IA	
A	**B**
7-[3-(5-Bromo-1*H*-indol-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-2,3-dihydrobenzofuran-5-sulfonic acid dimethylamide	
2-(1-Benzenesulfonyl-5-pyridin-3-yl-1*H*-indol-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol	
3-{2-[4-(5-Fluoro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}benzonitrile	

IA	
A	**B**
1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-pyridin-4-yl-1*H*-indol-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-pyridin-3-yl-1*H*-indol-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(5-pyrimidin-5-yl-1*H*-indol-2-ylmethyl)pentan-2-ol	

IA	
A	B
2-{2-[4-(5-Fluoro-2,3-dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indol-5-yl}benzamide	
2-[5-(4-Dimethylaminophenyl)-1*H*-indol-2-ylmethyl]-1,1,1-trifluoro-4-(5-fluoro-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-2-(7-fluoro-4-methyl-1*H*-indol-2-ylmethyl)-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol	
2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile	

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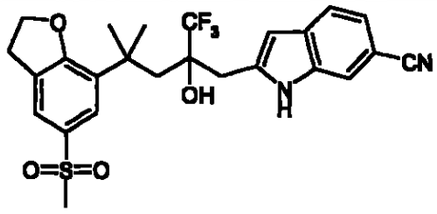
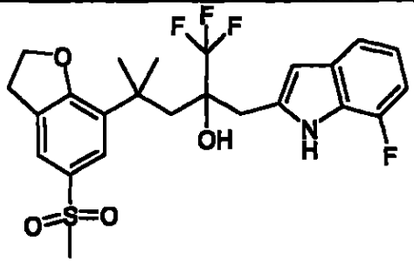
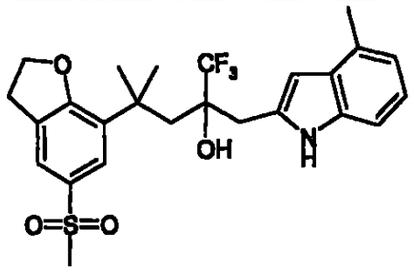
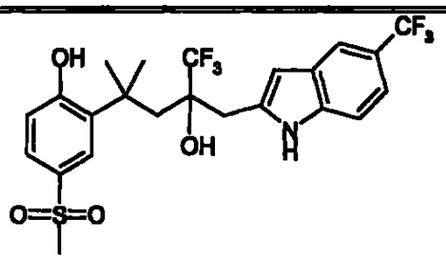
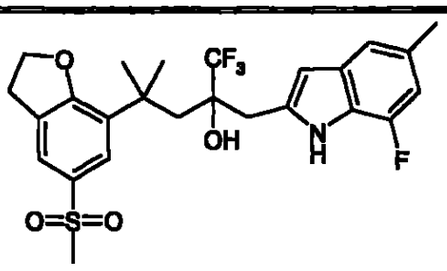
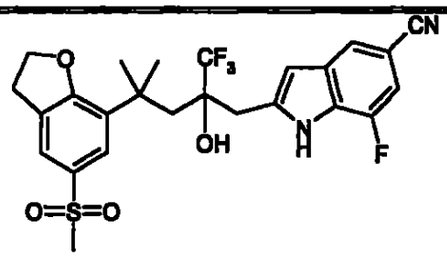
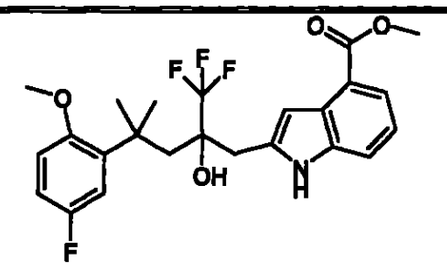
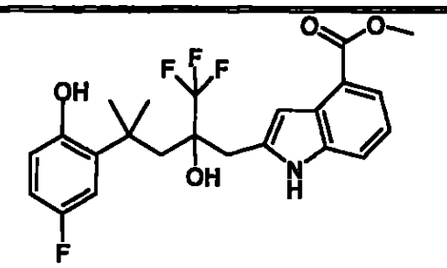
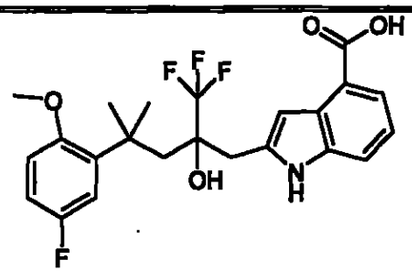
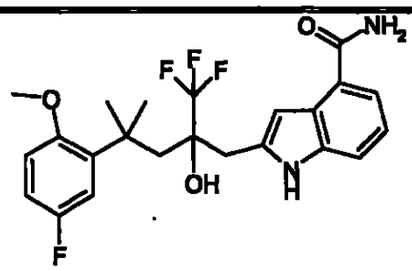
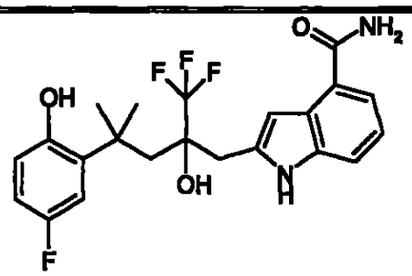
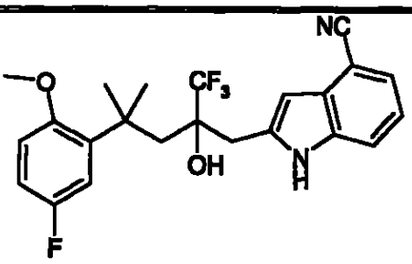
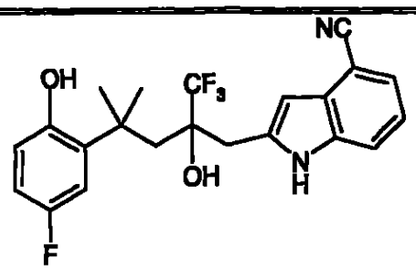
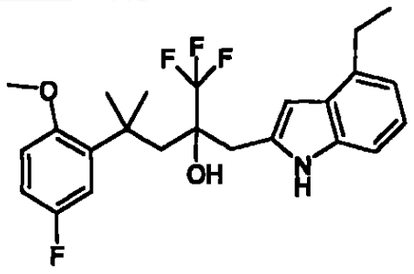
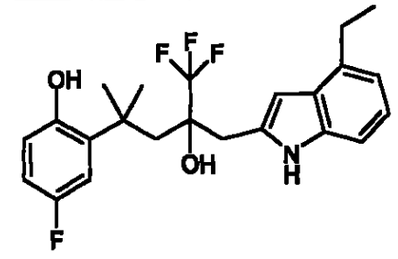
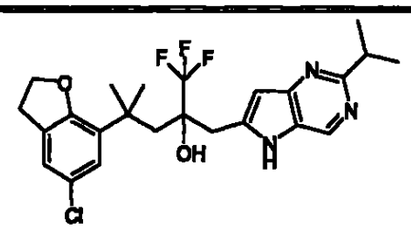
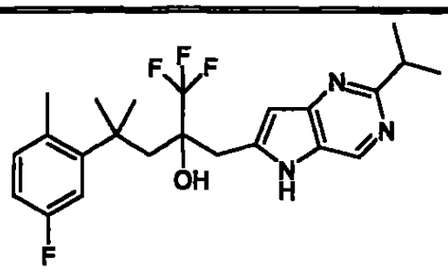
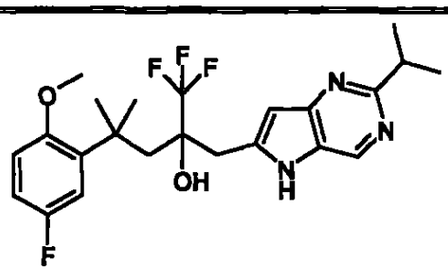
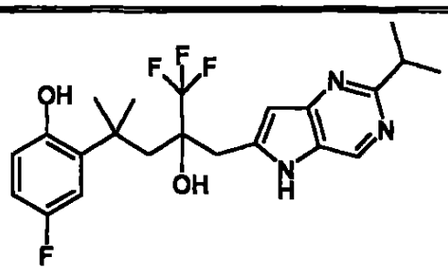
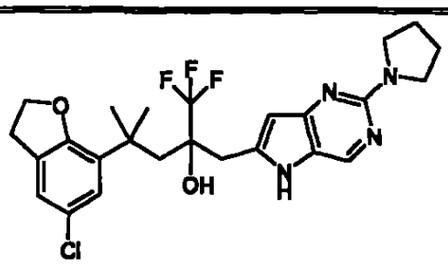
IA	
A	B
2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-6-carbonitrile	
1,1,1-Trifluoro-2-(7-fluoro-1*H*-indol-2-ylmethyl)-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(4-methyl-1*H*-indol-2-ylmethyl)pentan-2-ol	
4-Methanesulfonyl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-trifluoromethyl-1*H*-indol-2-ylmethyl)butyl]phenol	

S16

IA	
A	**B**
1,1,1-Trifluoro-2-(7-fluoro-5-methyl-1*H*-indol-2-ylmethyl)-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol	
7-Fluoro-2-[2-hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-5-carbonitrile	
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carboxylic acid methyl ester	
2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carboxylic acid methyl ester	

IA	
A	**B**
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carboxylic acid	
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carboxylic acid amide	
2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carboxylic acid amide	
2-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carbonitrile	

IA	
A	B
2-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-indole-4-carbonitrile	
2-(4-Ethyl-1*H*-indol-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	
2-[3-(4-Ethyl-1*H*-indol-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(2-isopropyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)-4-methylpentan-2-ol	

IA	
A	**B**
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(2-isopropyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-2-(2-isopropyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)-4-methylpentan-2-ol	
4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-3-(2-isopropyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)-1,1-dimethylbutyl]phenol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	

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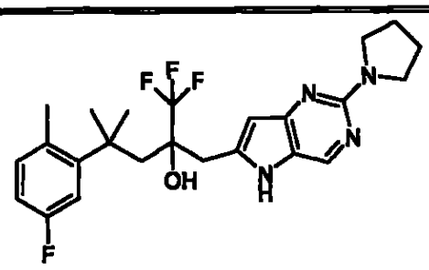
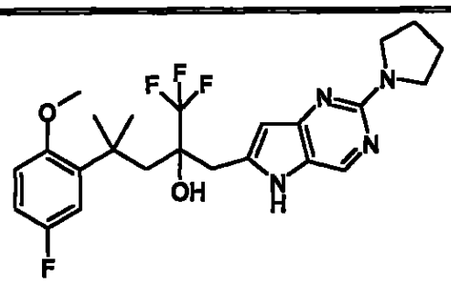
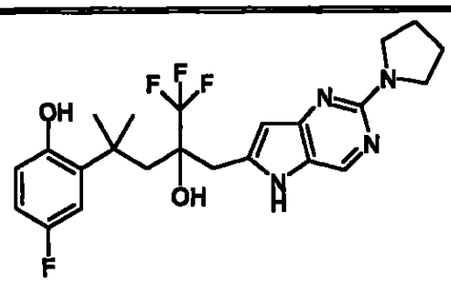
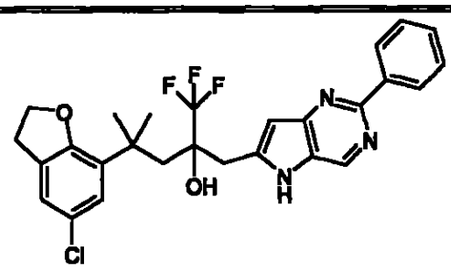
IA	
A	**B**
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4--methyl-2-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	
4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)butyl]phenol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	

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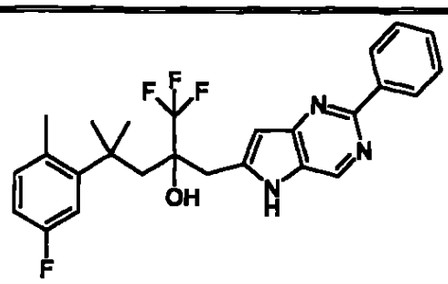
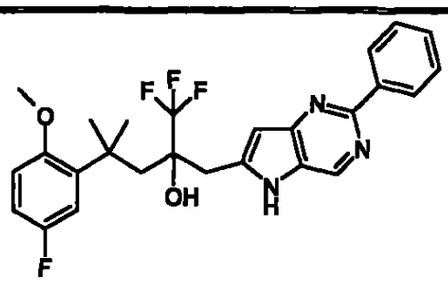
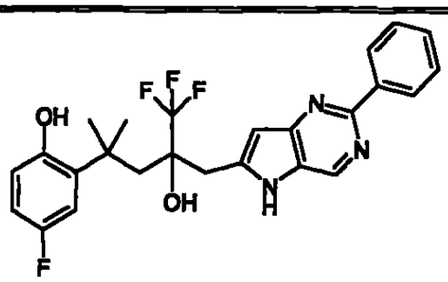
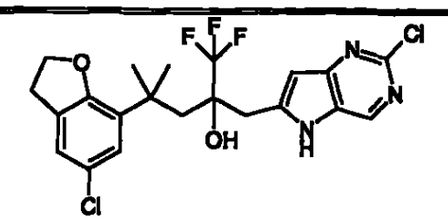
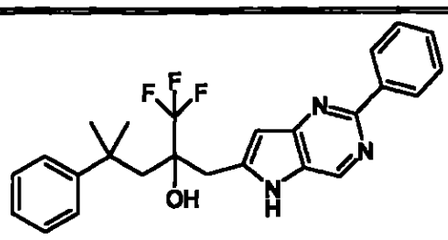
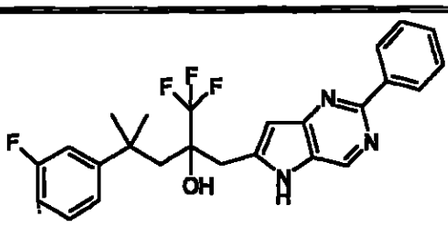
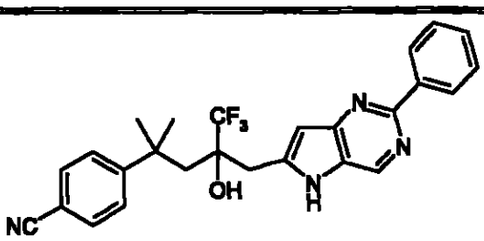
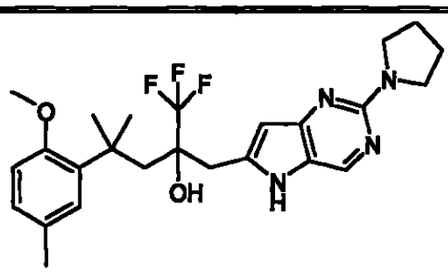
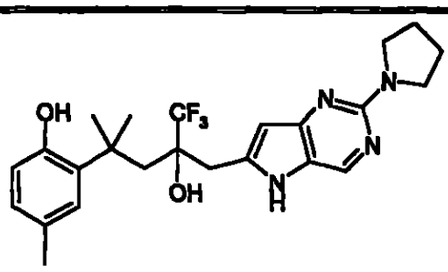
IA	
A	**B**
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	
4-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)butyl]phenol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(2-chloro-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol	

IA	
A	**B**
1,1,1-Trifluoro-4-methyl-4-phenyl-2-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	
4-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(2-phenyl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)butyl]benzonitrile	
1,1,1-Trifluoro-4-(2-methoxy-5-methylphenyl)-4-methyl-2-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(2-methoxy-5-methylphenyl)-4-methyl-2-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	

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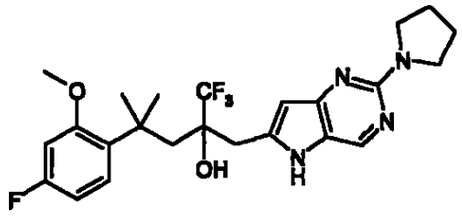
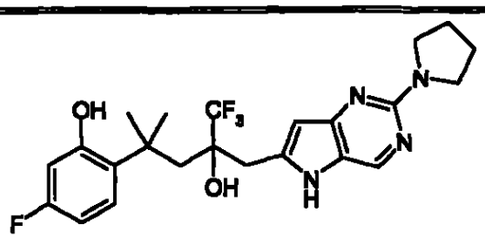
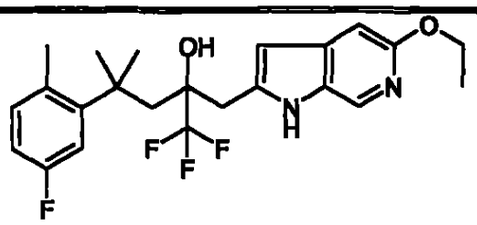
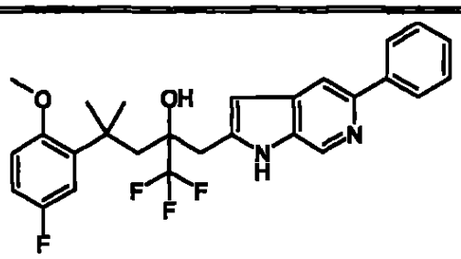
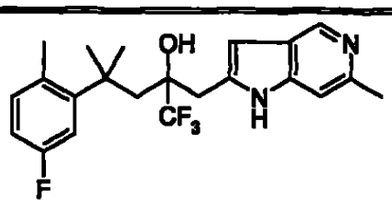
IA	
A	**B**
1,1,1-Trifluoro-4-(4-fluoro-2-methoxyphenyl)-4-methyl-2-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	
5-Fluoro-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(2-pyrrolidin-1-yl-5*H*-pyrrolo[3,2-*d*]pyrimidin-6-ylmethyl)butyl]phenol	
2-(5-Ethoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	

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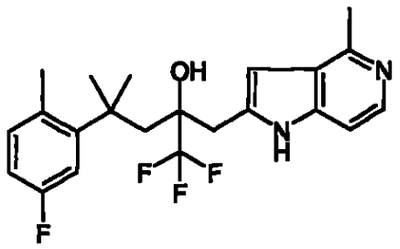
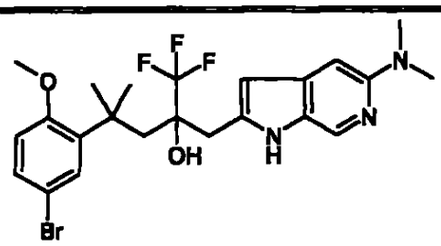
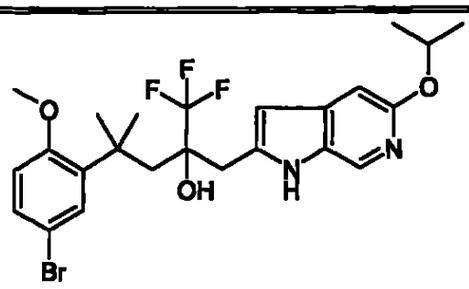
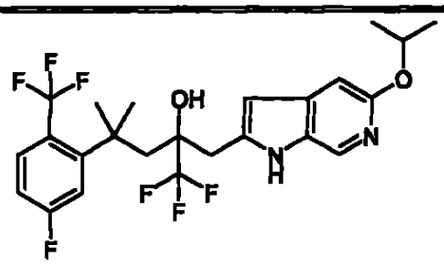
IA	
A	B
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(4-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-(5-Bromo-2-methoxyphenyl)-2-(5-dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol	
4-(5-Bromo-2-methoxyphenyl)-1,1,1-trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-trifluoromethylphenyl)-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	

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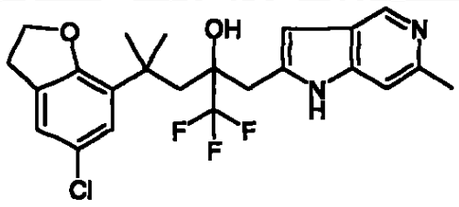
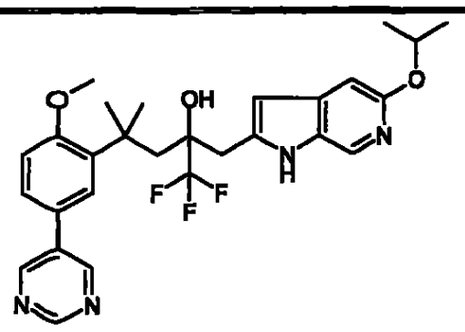
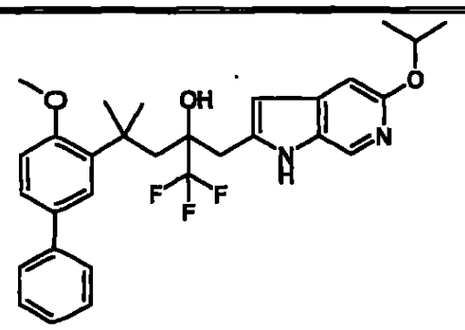
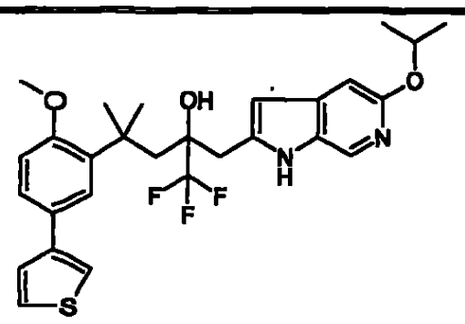
IA	
A	B
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(4-methoxybiphenyl-3-yl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(2-methoxy-5-thiophen-3-ylphenyl)-4-methylpentan-2-ol	

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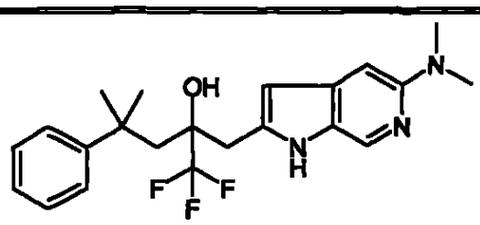
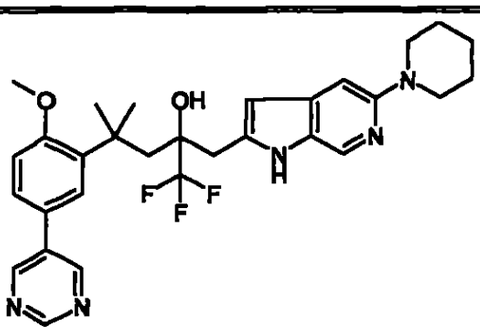
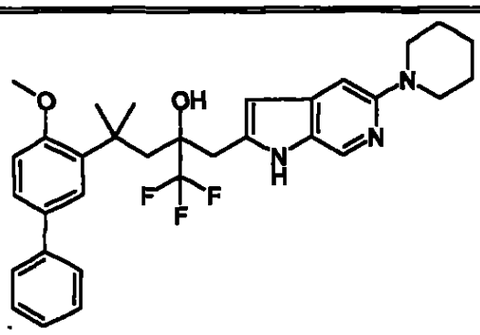
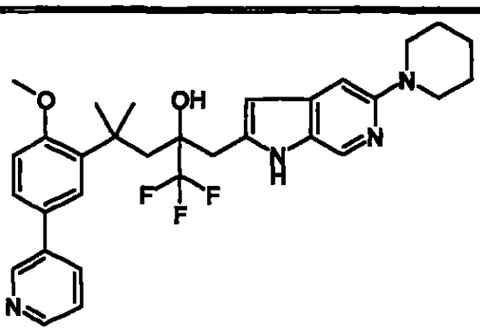
IA	
A	**B**
2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methyl-4-phenylpentan-2-ol	
1,1,1-Trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(4-methoxybiphenyl-3-yl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

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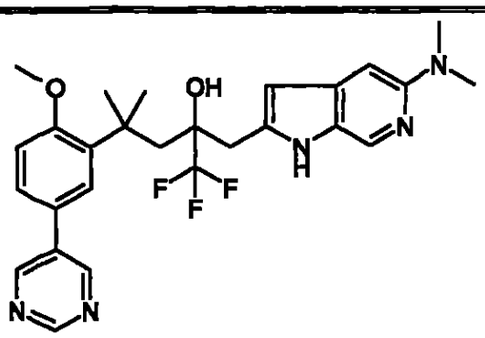
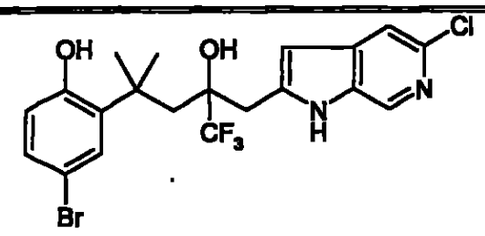
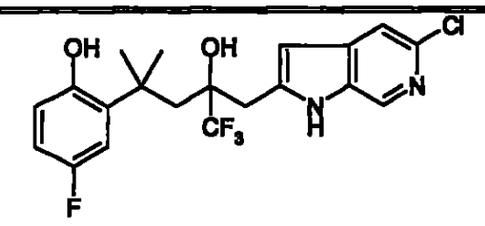
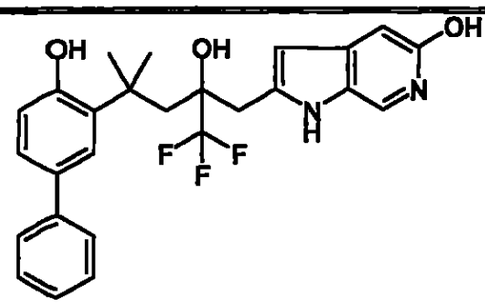
527

IA	
A	**B**
2-(5-Dimethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methylpentan-2-ol	
4-Bromo-2-[3-(5-chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]phenol	
2-[3-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol	
2-[2-Hydroxy-4-(4-hydroxybiphenyl-3-yl)-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridin-5-ol	

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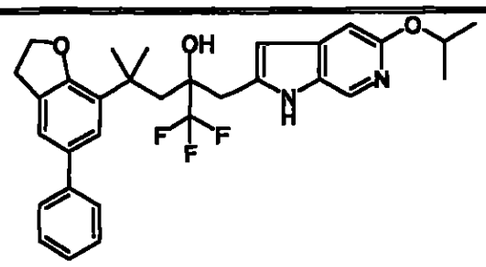
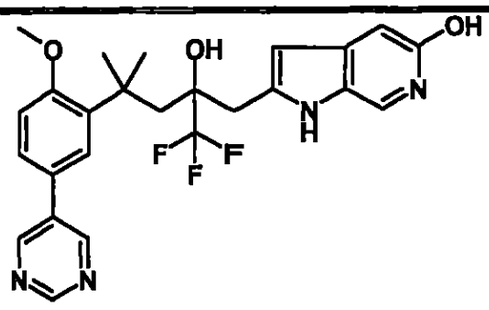
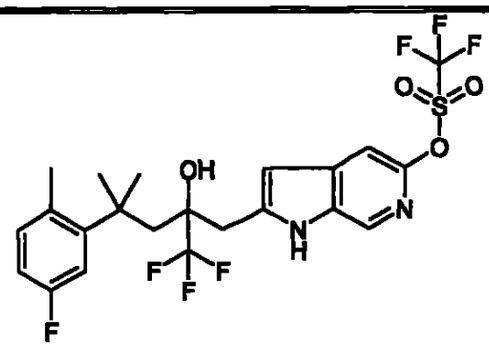
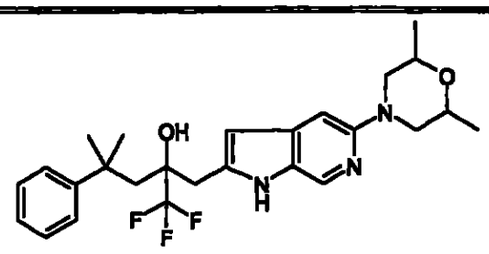
IA	
A	**B**
1,1,1-Trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methyl-4-(5-phenyl-2,3-dihydrobenzofuran-7-yl)pentan-2-ol	
2-[2-Hydroxy-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridin-5-ol	
Trifluoromethanesulfonic acid 2-[4-(5-fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[2,3-*c*]pyridin-5-yl ester	
2-[5-(2,6-Dimethylmorpholin-4-yl)-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl]-1,1,1-trifluoro-4-methyl-4-phenylpentan-2-ol	

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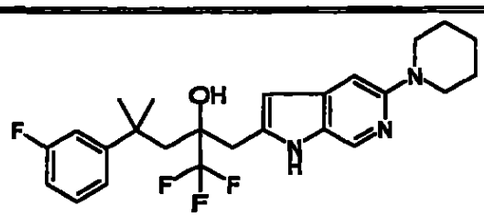
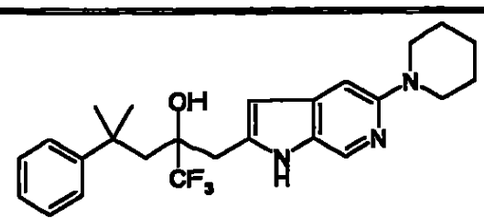
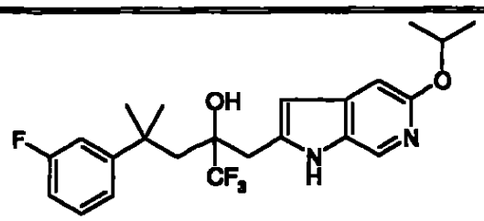
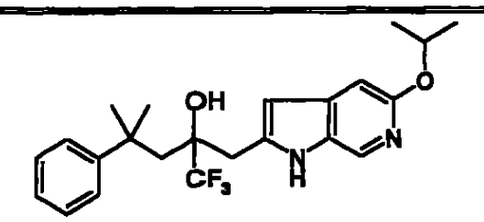
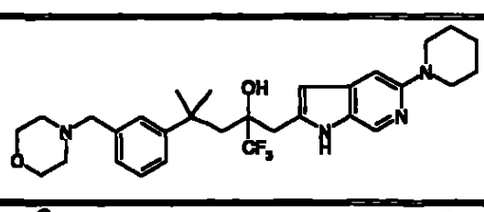
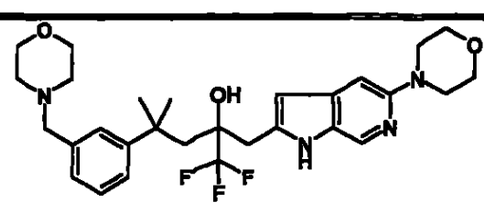
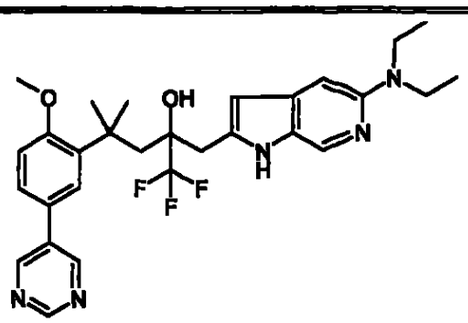
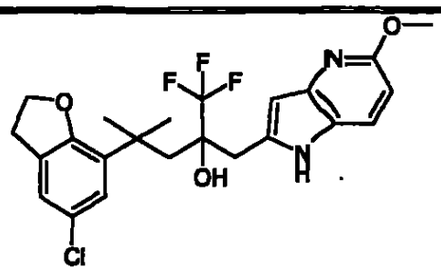
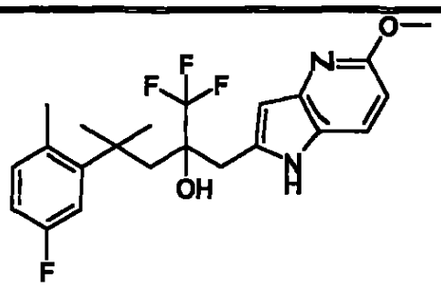
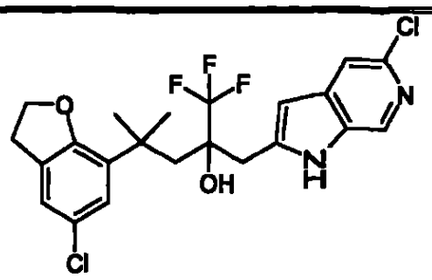
IA	
A	B
1,1,1-Trifluoro-4-(3-fluorophenyl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-phenyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(3-fluorophenyl)-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-2-(5-isopropoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-methyl-4-phenylpentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylmethylphenyl)-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylmethylphenyl)-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

IA	
A	B
2-(5-Diethylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methylpentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-2-(5-methoxy-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(5-methoxy-1*H*-pyrrolo[3,2-*b*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-(5-chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol	

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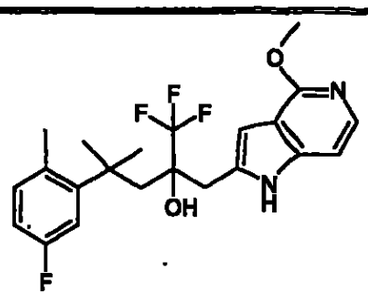
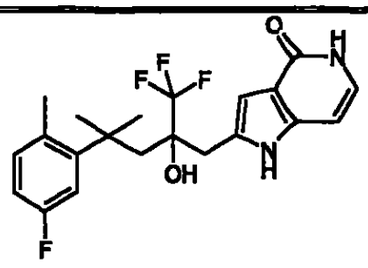
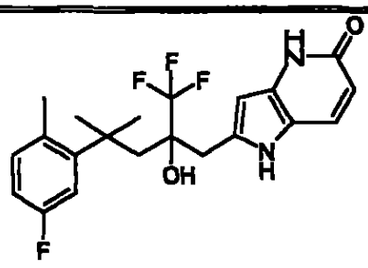
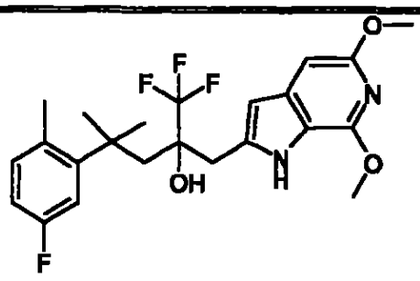
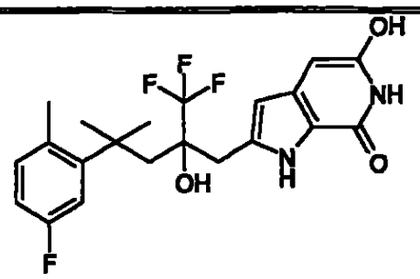
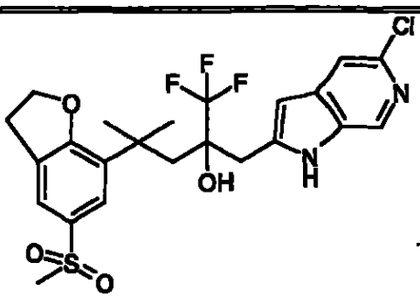
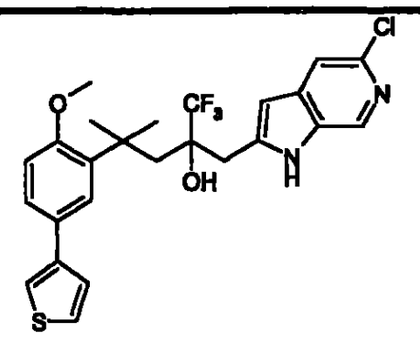
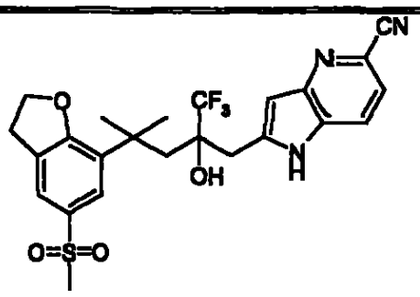
IA	
A	**B**
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-2-(4-methoxy-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-4-methylpentan-2-ol	
2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,5-dihydropyrrolo[3,2-*c*]pyridin-4-one	
2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,4-dihydropyrrolo[3,2-*b*]pyridin-5-one	
2-(5,7-Dimethoxy-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methylphenyl)-4-methylpentan-2-ol	

IA	
A	**B**
2-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-5-hydroxy-1,6-dihydropyrrolo[2,3-*c*]pyridin-7-one	
2-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol	
2-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(2-methoxy-5-thiophen-3-ylphenyl)-4-methylpentan-2-ol	
2-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-1*H*-pyrrolo[3,2-*b*]pyridine-5-carbonitrile	

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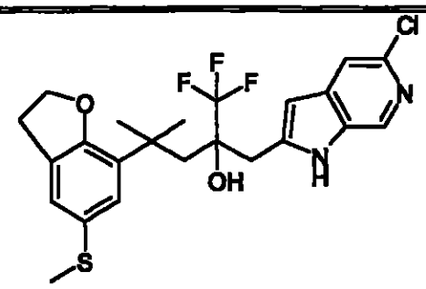
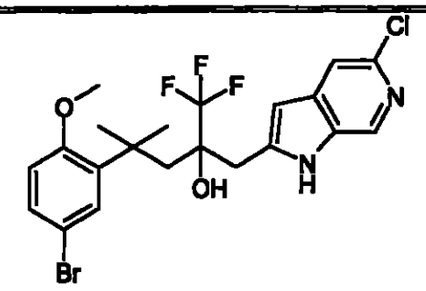
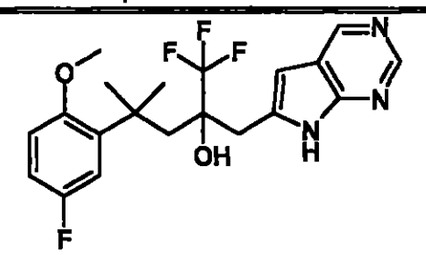
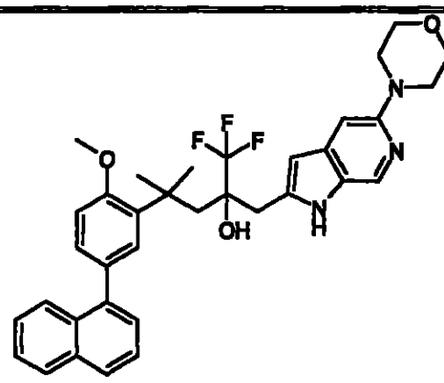
IA	
A	**B**
2-(5-Chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methyl-4-(5-methylsulfanyl-2,3-dihydrobenzofuran-7-yl)pentan-2-ol	
4-(5-Bromo-2-methoxyphenyl)-2-(5-chloro-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(7*H*-pyrrolo[2,3-*d*]pyrimidin-6-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(2-methoxy-5-naphthalen-1-ylphenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

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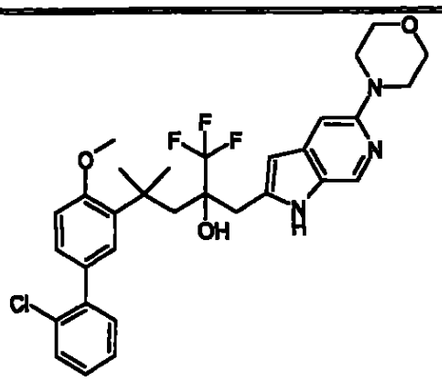
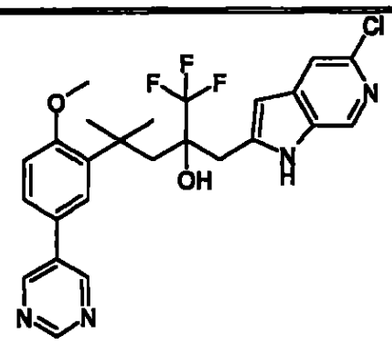
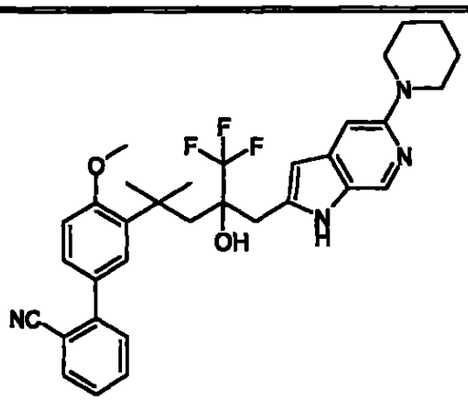
IA	
A	B
4-(2'-Chloro-4-methoxybiphenyl-3-yl)-1,1,1-trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-c]pyridin-2-ylmethyl)pentan-2-ol	
2-(5-Chloro-1*H*-pyrrolo[2,3-c]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methylpentan-2-ol	
4'-Methoxy-3'-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-c]pyridin-2-ylmethyl)butyl]biphenyl-2-carbonitrile	

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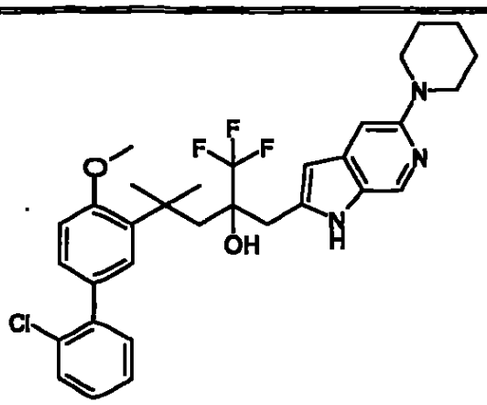
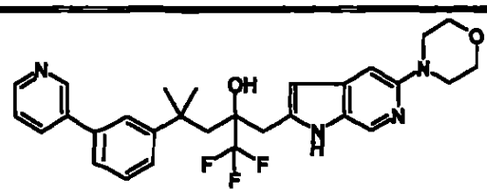
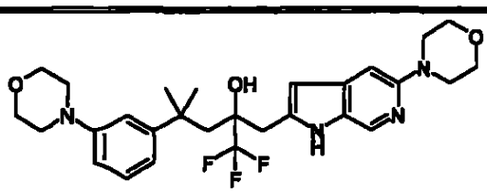
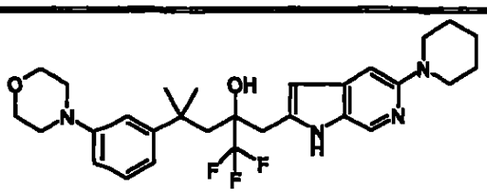
IA	
A	B
4-(2'-Chloro-4-methoxybiphenyl-3-yl)-1,1,1-trifluoro-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(3-pyridin-3-ylphenyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylphenyl)-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(3-morpholin-4-ylphenyl)-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

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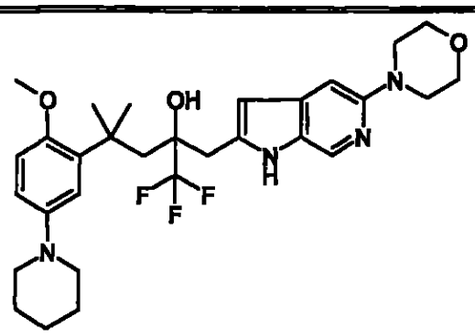
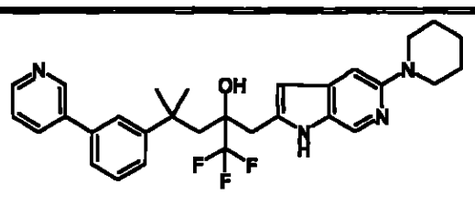
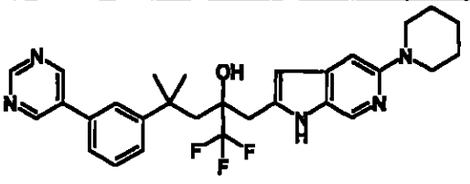
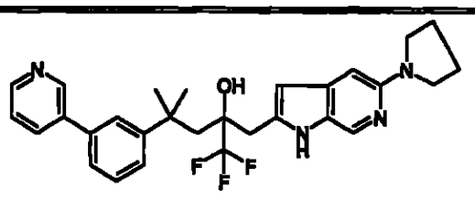
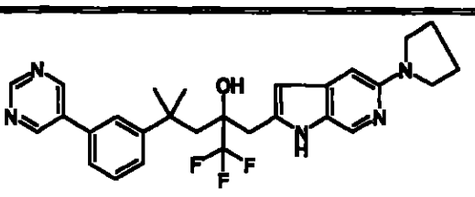
IA	
A	B
1,1,1-Trifluoro-4-(2-methoxy-5-piperidin-1-ylphenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(3-pyridin-3-ylphenyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)-4-(3-pyrimidin-5-ylphenyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(3-pyridin-3-ylphenyl)-2-(5-pyrrolidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(3-pyrimidin-5-ylphenyl)-2-(5-pyrrolidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

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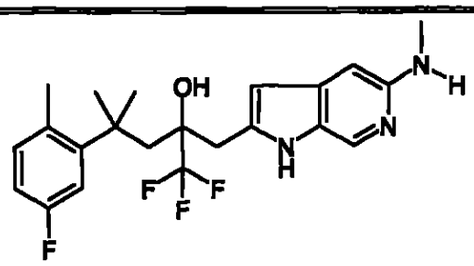
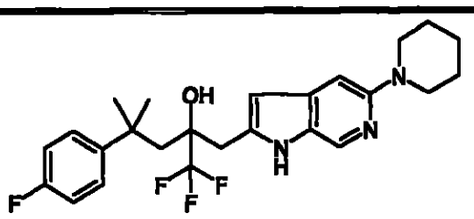
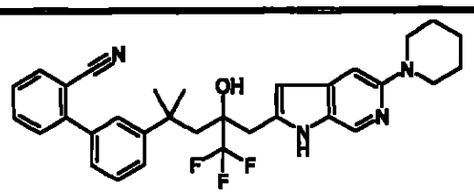
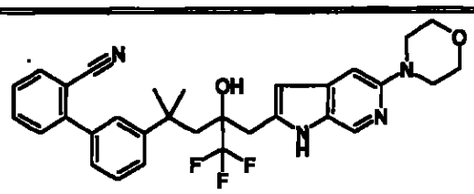
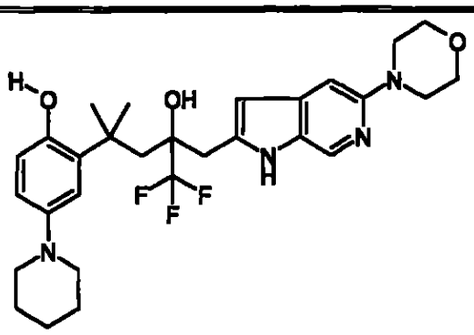
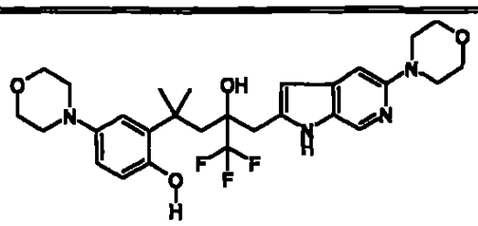
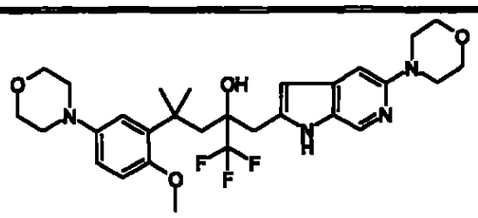
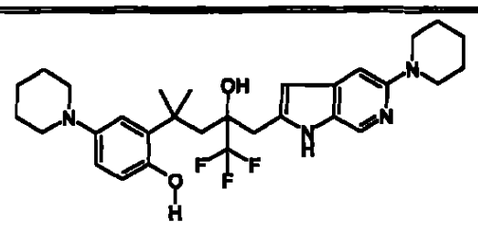
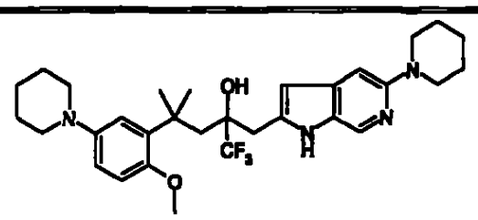
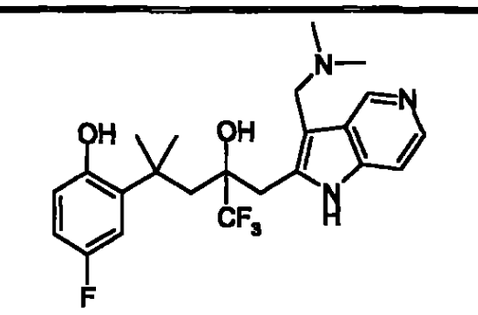
IA	
A	B
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-methylamino-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(4-fluorophenyl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
3'-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-2-carbonitrile	
3'-[4,4,4-Trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]biphenyl-2-carbonitrile	
4-Piperidin-1-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	

IA	
A	**B**
4-Morpholin-4-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	
1,1,1-Trifluoro-4-(2-methoxy-5-morpholin-4-ylphenyl)-4-methyl-2-(5-morpholin-4-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-Piperidin-1-yl-2-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)butyl]phenol	
1,1,1-Trifluoro-4-(2-methoxy-5-piperidin-1-ylphenyl)-4-methyl-2-(5-piperidin-1-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
2-[3-(3-Dimethylaminomethyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-4,4,4-trifluoro-3-hydroxy-1,1-dimethylbutyl]-4-fluorophenol	

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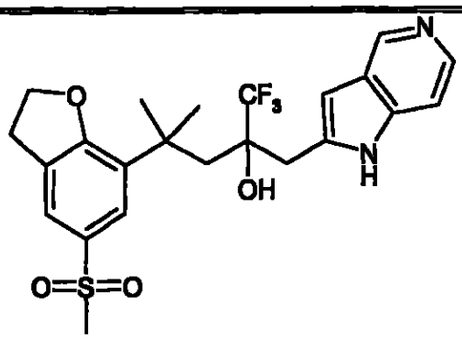
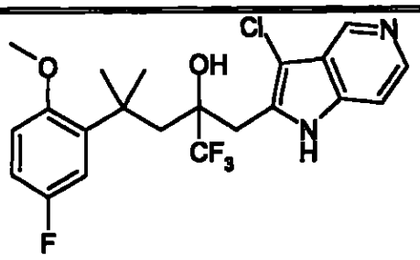
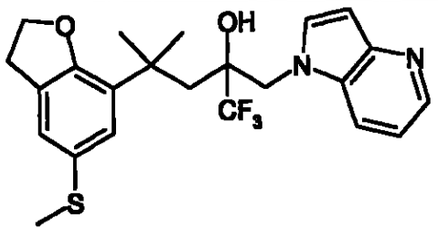
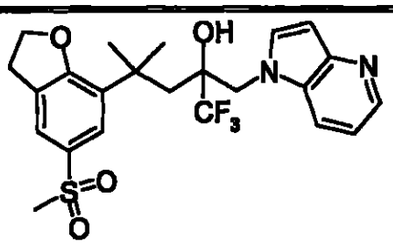
IA	
A	B
1,1,1-Trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
2-(3-Chloro-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)-1,1,1-trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methylpentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(5-methylsulfanyl-2,3-dihydrobenzofuran-7-yl)-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol	
1,1,1-Trifluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol	

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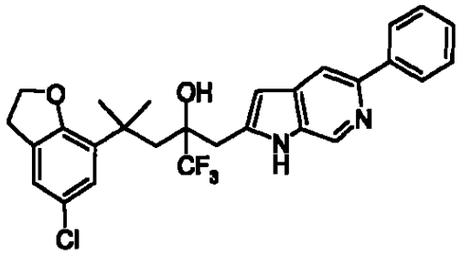
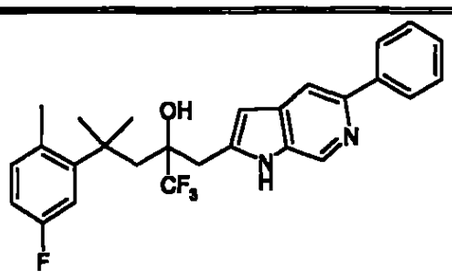
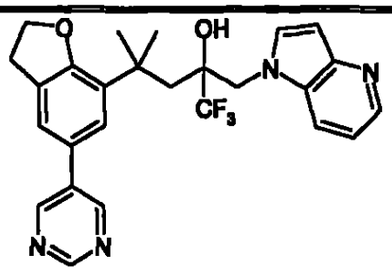
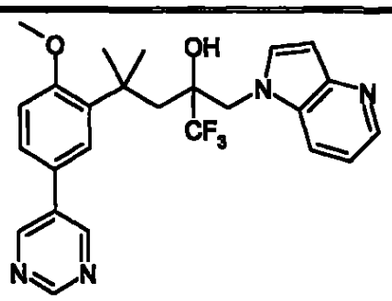
IA	
A	B
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1,1-trifluoro-4-methyl-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-(5-fluoro-2-methylphenyl)-4-methyl-2-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
1,1,1-Trifluoro-4-methyl-4-(5-pyrimidin-5-yl-2,3-dihydrobenzofuran-7-yl)-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol	
1,1,1-Trifluoro-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol	

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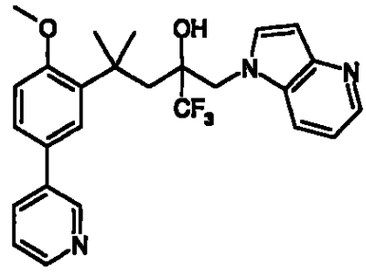
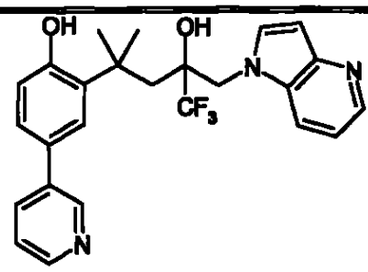
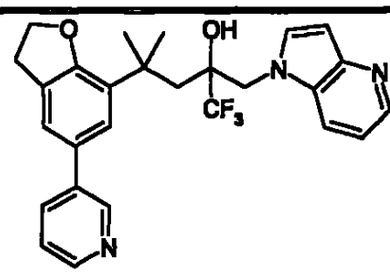
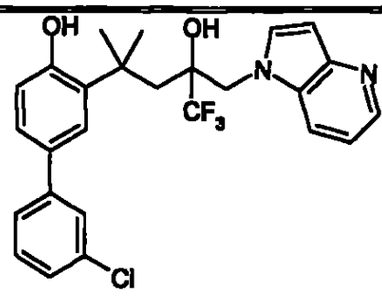
IA	
A	B
1,1,1-Trifluoro-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol	
4-Pyridin-3-yl-2-(4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-pyrrolo[3,2-*b*]pyridin-1-ylmethylbutyl)phenol	
1,1,1-Trifluoro-4-methyl-4-(5-pyridin-3-yl-2,3-dihydrobenzofuran-7-yl)-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol	
3'-Chloro-3-(4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-pyrrolo[3,2-*b*]pyridin-1-ylmethylbutyl)biphenyl-4-ol	

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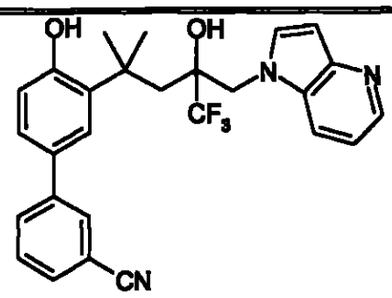
IA	
A	B
4'-Hydroxy-3'-(4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-pyrrolo[3,2-*b*]pyridin-1-ylmethylbutyl)biphenyl-3-carbonitrile	
or a tautomer, prodrug, solvate, or salt thereof.	

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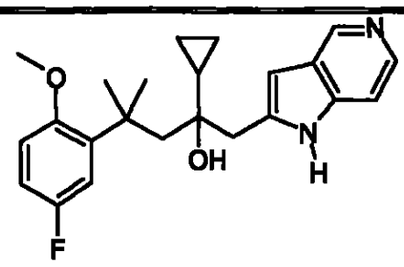
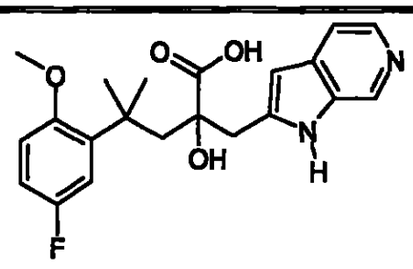
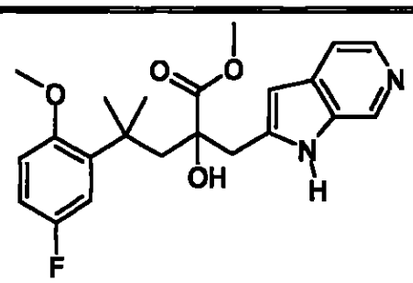
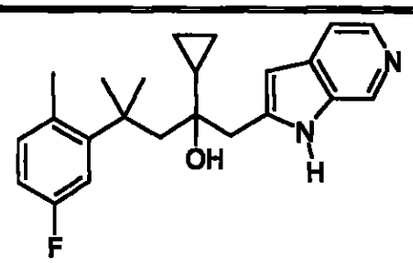
IB	
A	B
2-Cyclopropyl-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[3,2-*c*]pyridin-2-yl)pentan-2-ol	
4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentanoic acid	
4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentanoic acid methyl ester	
2-Cyclopropyl-4-(5-fluoro-2-methylphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol	

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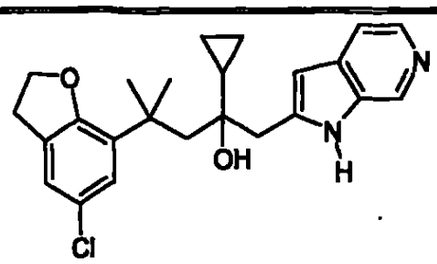
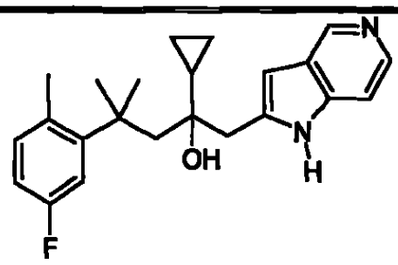
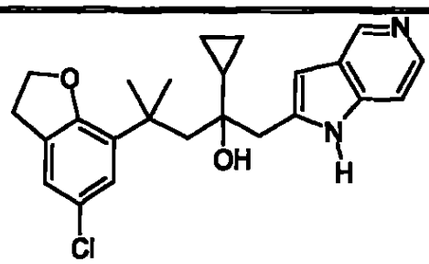
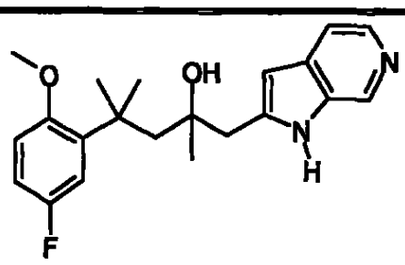
IB	
A	B
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-cyclopropyl-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol	
2-Cyclopropyl-4-(5-fluoro-2-methylphenyl)-4-methyl-1-(1*H*-pyrrolo[3,2-*c*]pyridin-2-yl)pentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2-cyclopropyl-4-methyl-1-(1*H*-pyrrolo[3,2-*c*]pyridin-2-yl)pentan-2-ol	
4-(5-Fluoro-2-methoxyphenyl)-2,4-dimethyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol	

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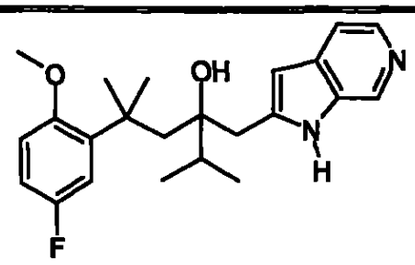
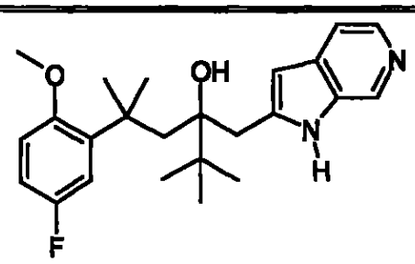
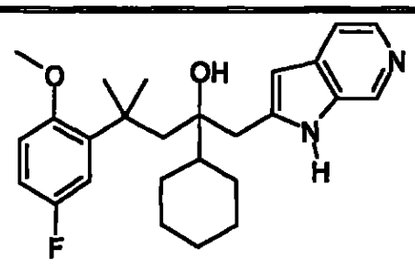
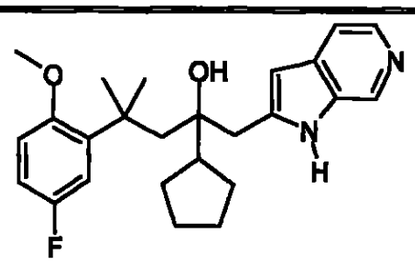
IB	
A	B
5-(5-Fluoro-2-methoxyphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	
5-(5-Fluoro-2-methoxyphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	
2-Cyclohexyl-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol	
2-Cyclopentyl-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol	

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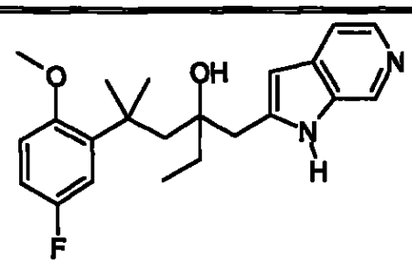
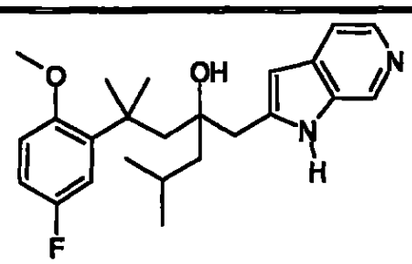
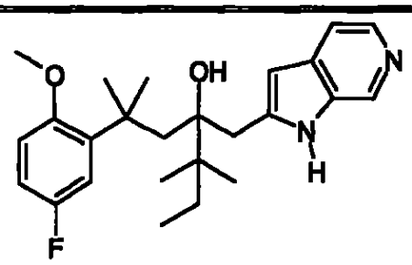
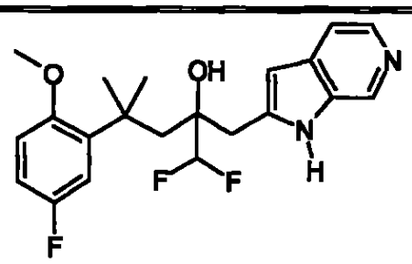
IB	
A	B
5-(5-Fluoro-2-methoxyphenyl)-5-methyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	
2-(5-Fluoro-2-methoxyphenyl)-2,6-dimethyl-4-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)heptan-4-ol	
2-(5-Fluoro-2-methoxyphenyl)-2,5,5-trimethyl-4-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)heptan-4-ol	
1,1-Difluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	

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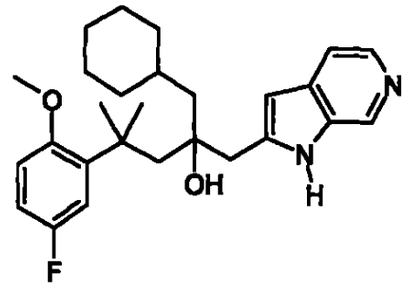
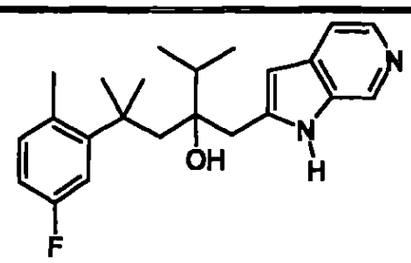
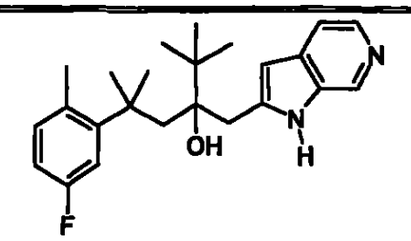
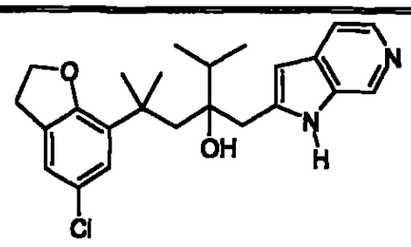
IB	
A	B
1-Cyclohexyl-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
5-(5-Fluoro-2-methylphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	
5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	
5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	

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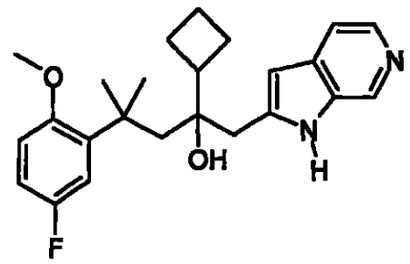
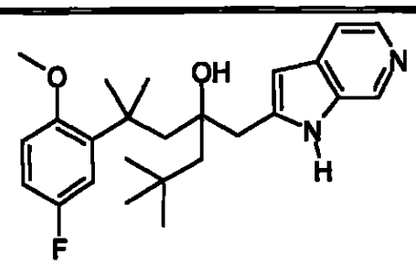
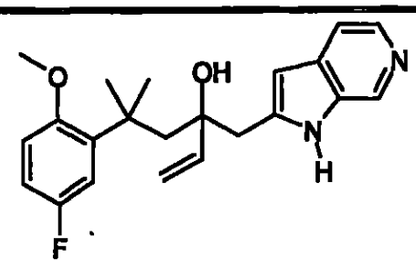
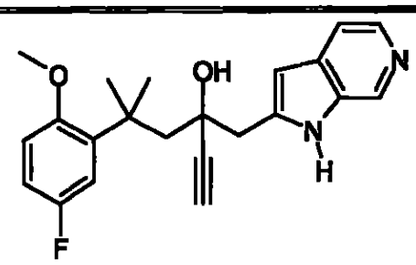
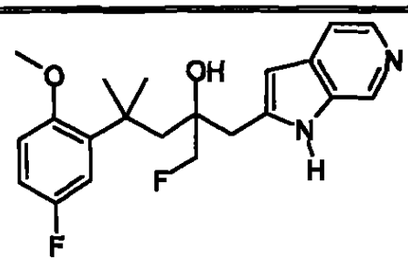
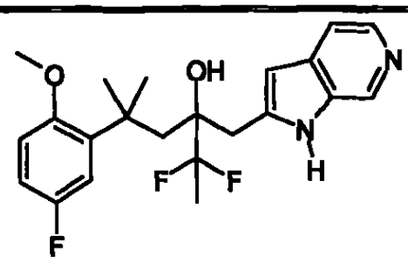
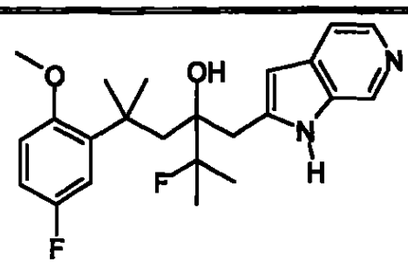
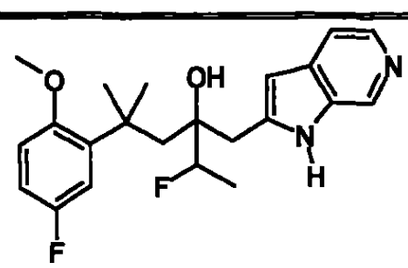
IB	
A	B
2-Cyclobutyl-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol	
2-(5-Fluoro-2-methoxyphenyl)-2,6,6-trimethyl-4-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)heptan-4-ol	
5-(5-Fluoro-2-methoxyphenyl)-5-methyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hex-1-en-3-ol	
5-(5-Fluoro-2-methoxyphenyl)-5-methyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hex-1-yn-3-ol	

S30

S49

IB	
A	B
1-Fluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
2,2-Difluoro-5-(5-fluoro-2-methoxyphenyl)-5-methyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	
2-Fluoro-5-(5-fluoro-2-methoxyphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	
2-Fluoro-5-(5-fluoro-2-methoxyphenyl)-5-methyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	

534

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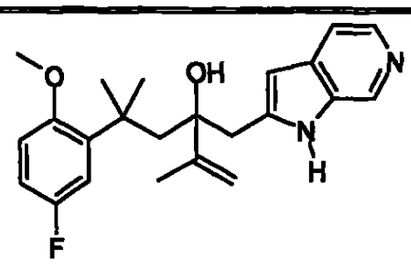
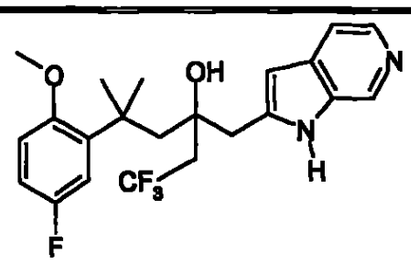
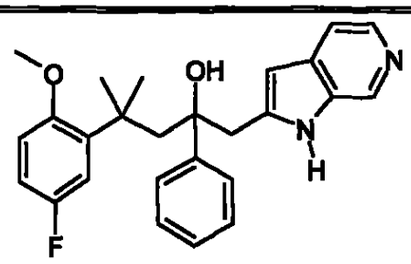
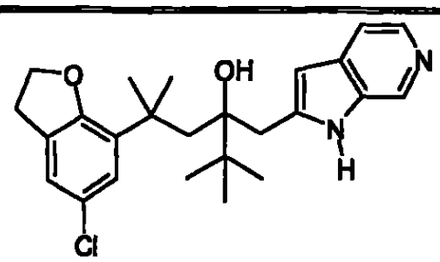
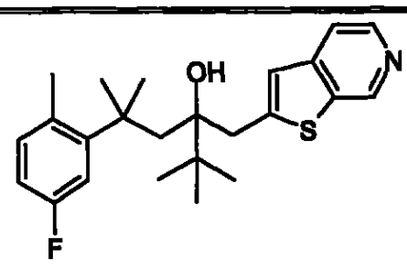
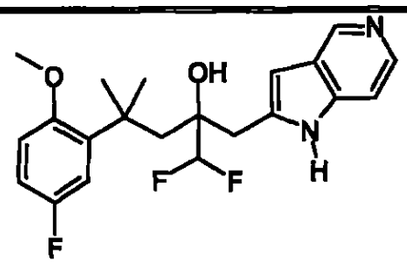
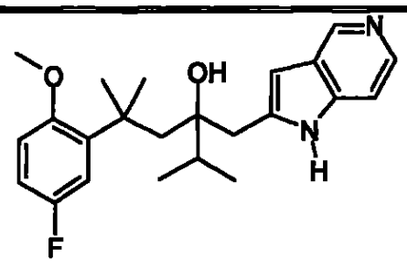
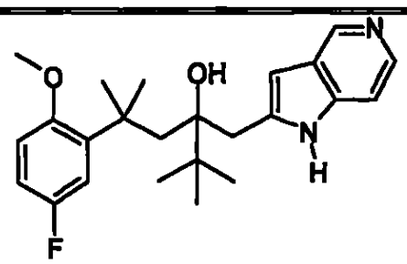
IB	
A	B
5-(5-Fluoro-2-methoxyphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hex-1-en-3-ol	
1,1,1-Trifluoro-5-(5-fluoro-2-methoxyphenyl)-5-methyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	
4-(5-Fluoro-2-methoxyphenyl)-4-methyl-2-phenyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol	
5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	

532
551

IB	
A	B
5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-thieno[2,3-*c*]pyridin-2-ylmethylhexan-3-ol	
1,1-Difluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
5-(5-Fluoro-2-methoxyphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol	
5-(5-Fluoro-2-methoxyphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol	

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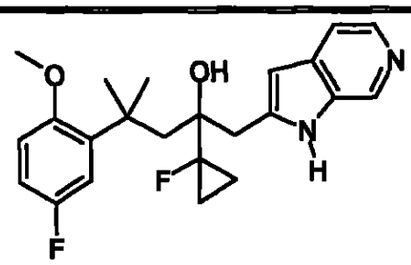
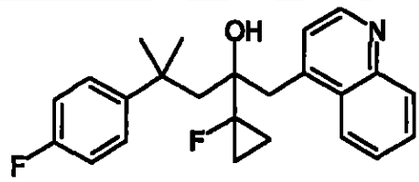
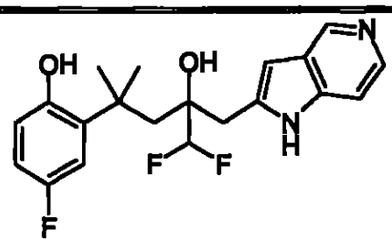
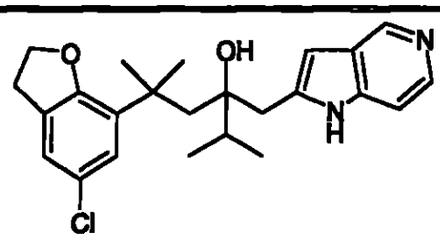
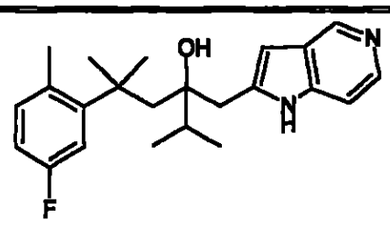
552

IB	
A	B
2-(1-Fluorocyclopropyl)-4-(5-fluoro-2-methoxyphenyl)-4-methyl-1-(1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol	
2-(1-Fluorocyclopropyl)-4-(4-fluorophenyl)-4-methyl-1-quinolin-4-ylpentan-2-ol	
2-[4,4-Difluoro-3-hydroxy-1,1-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)butyl]-4-fluorophenol	
5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol	
5-(5-Fluoro-2-methylphenyl)-2,5-dimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol	

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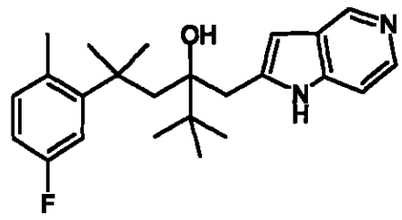
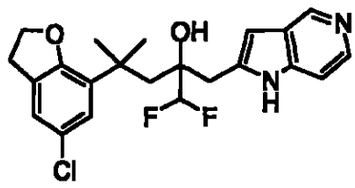
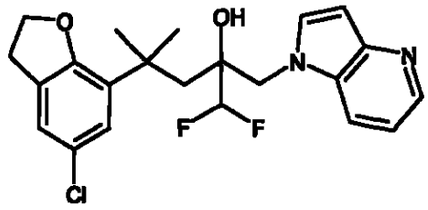
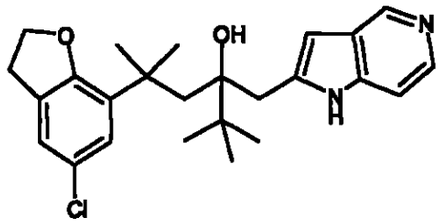
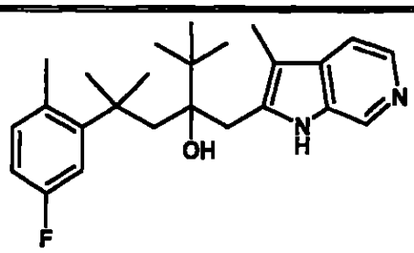
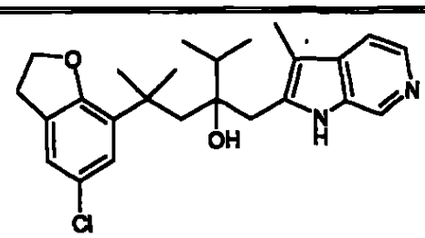
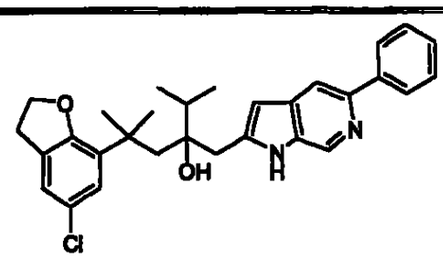
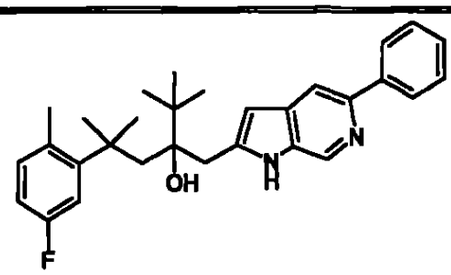
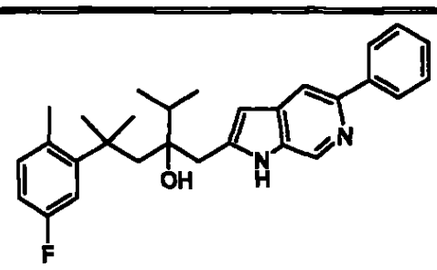
553

IB	
A	B
5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methyl-2-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methyl-2-pyrrolo[3,2-*b*]pyridin-1-ylmethylpentan-2-ol	
5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,2,5-trimethyl-3-(1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)hexan-3-ol	
5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	

IB	
A	**B**
5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(3-methyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	
5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	
5-(5-Fluoro-2-methylphenyl)-2,2,5-trimethyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	
5-(5-Fluoro-2-methylphenyl)-2,5-dimethyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	

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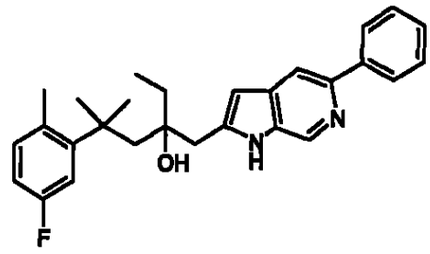
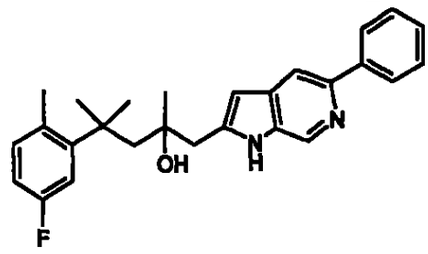
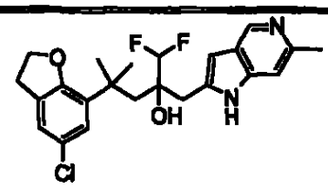
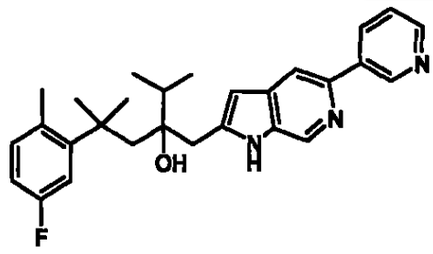
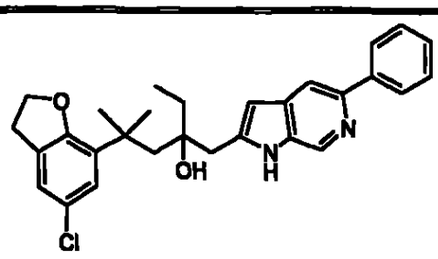
555

IB	
A	B
5-(5-Fluoro-2-methylphenyl)-5-methyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	
4-(5-Fluoro-2-methylphenyl)-2,4-dimethyl-1-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol	
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-1,1-difluoro-4-methyl-2-(6-methyl-1*H*-pyrrolo[3,2-*c*]pyridin-2-ylmethyl)pentan-2-ol	
5-(5-Fluoro-2-methylphenyl)-2,5-dimethyl-3-(5-pyridin-3-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	
5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-5-methyl-3-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	

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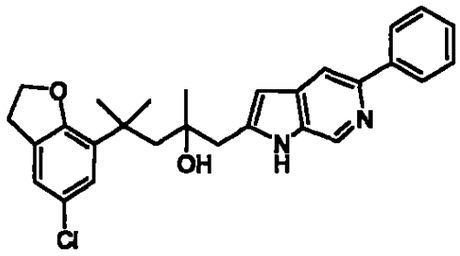
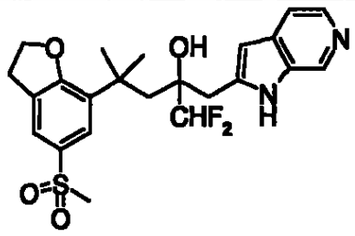
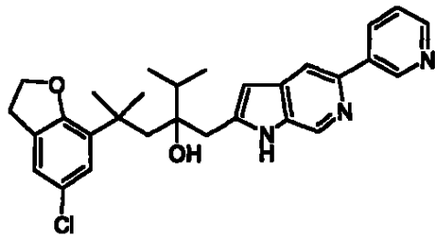
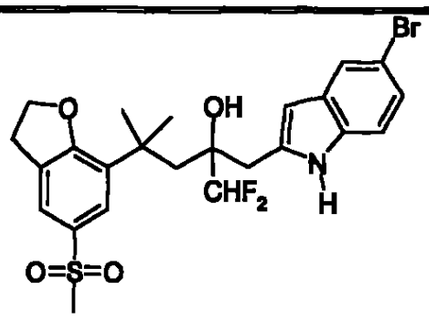
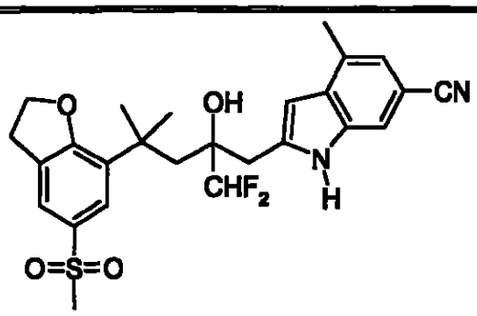
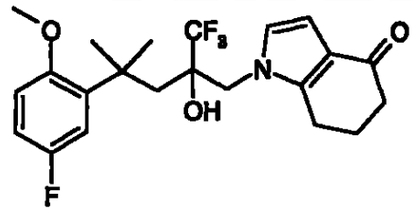
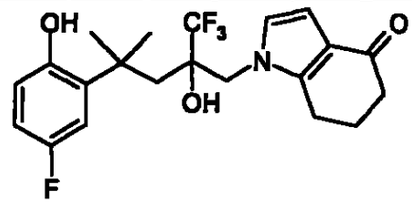
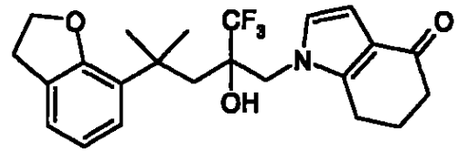
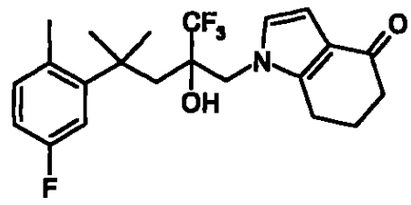
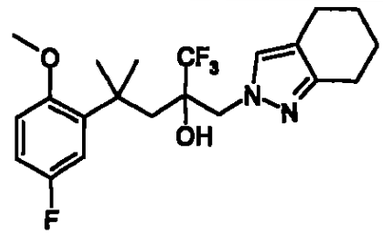
IB	
A	B
4-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,4-dimethyl-1-(5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridin-2-yl)pentan-2-ol	
1,1-Difluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-(1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)pentan-2-ol	
5-(5-Chloro-2,3-dihydrobenzofuran-7-yl)-2,5-dimethyl-3-(5-pyridin-3-yl-1*H*-pyrrolo[2,3-*c*]pyridin-2-ylmethyl)hexan-3-ol	
2-(5-Bromo-1*H*-indol-2-ylmethyl)-1,1-difluoro-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentan-2-ol	

IB	
A	B
2-[2-Difluoromethyl-2-hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methylpentyl]-4-methyl-1*H*-indole-6-carbonitrile	
or a tautomer, prodrug, solvate, or salt thereof.	

IC	
A	B
1-[4-(5-Fluoro-2-methoxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one	
1-[4-(5-Fluoro-2-hydroxyphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl-1,5,6,7-tetrahydroindol-4-one	
1-[4-(2,3-Dihydrobenzofuran-7-yl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one	
1-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one	
1,1,1-Trifluoro-4-(5-fluoro-2-methoxyphenyl)-4-methyl-2-(4,5,6,7-tetrahydroindazol-2-ylmethyl)pentan-2-ol	

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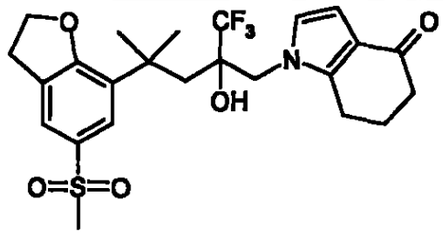
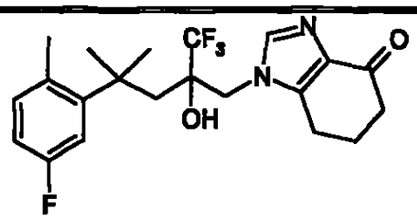
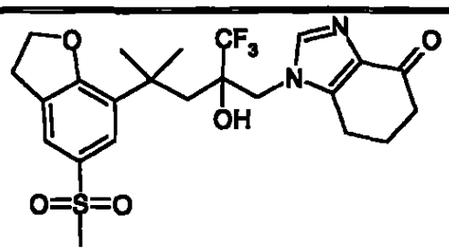
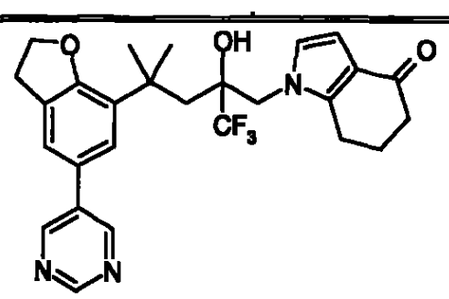
IC	
A	B
1-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one	
1-[4-(5-Fluoro-2-methylphenyl)-2-hydroxy-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydrobenzoimidazol-4-one	
1-[2-Hydroxy-4-(5-methanesulfonyl-2,3-dihydrobenzofuran-7-yl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydrobenzoimidazol-4-one	
1-[2-Hydroxy-4-methyl-4-(5-pyrimidin-5-yl-2,3-dihydrobenzofuran-7-yl)-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one	

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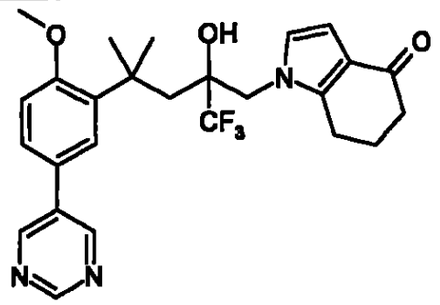
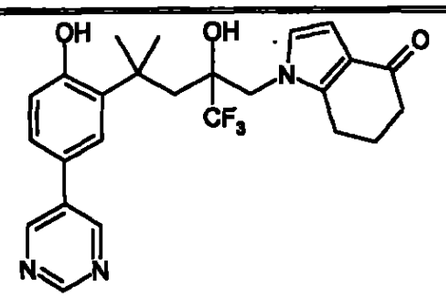
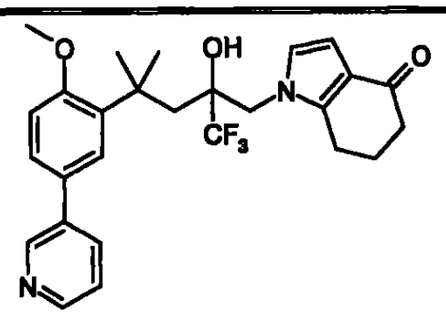
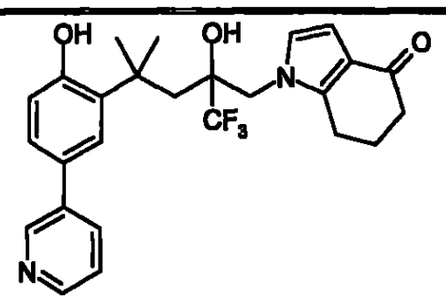
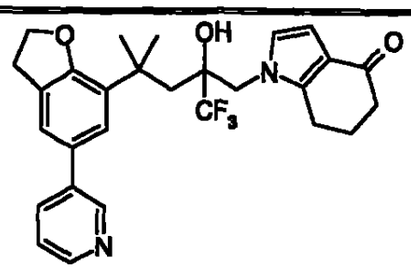
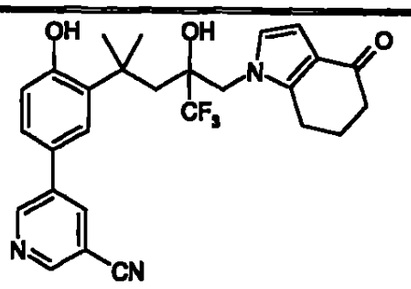
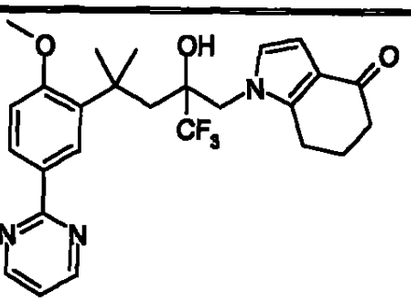
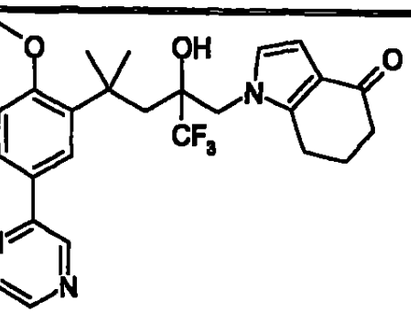
IC	
A	B
1-[2-Hydroxy-4-(2-methoxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one	
1-[2-Hydroxy-4-(2-hydroxy-5-pyrimidin-5-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one	
1-[2-Hydroxy-4-(2-methoxy-5-pyridin-3-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one	
1-[2-Hydroxy-4-(2-hydroxy-5-pyridin-3-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one	

IC	
A	B
1-[2-Hydroxy-4-methyl-4-(5-pyridin-3-yl-2,3-dihydrobenzofuran-7-yl)-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one	
5-{4-Hydroxy-3-[4,4,4-trifluoro-3-hydroxy-1,1-dimethyl-3-(4-oxo-4,5,6,7-tetrahydroindol-1-ylmethyl)butyl]phenyl}nicotinonitrile	
1-[2-Hydroxy-4-(2-methoxy-5-pyrimidin-2-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one	
1-[2-Hydroxy-4-(2-methoxy-5-pyrazin-2-ylphenyl)-4-methyl-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one	

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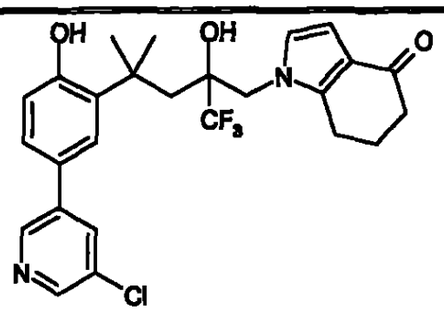
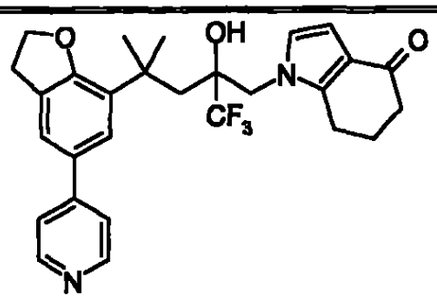
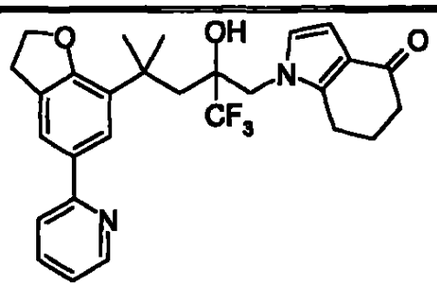
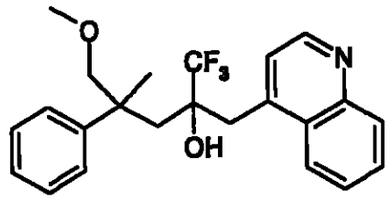
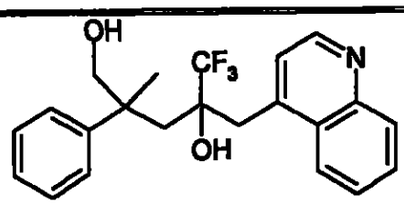
IC	
A	B
1-{4-[5-(5-Chloropyridin-3-yl)-2-hydroxyphenyl]-2-hydroxy-4-methyl-2-trifluoromethylpentyl}-1,5,6,7-tetrahydroindol-4-one	
1-[2-Hydroxy-4-methyl-4-(5-pyridin-4-yl-2,3-dihydrobenzofuran-7-yl)-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one	
1-[2-Hydroxy-4-methyl-4-(5-pyridin-2-yl-2,3-dihydrobenzofuran-7-yl)-2-trifluoromethylpentyl]-1,5,6,7-tetrahydroindol-4-one	
or a tautomer, prodrug, solvate, or salt thereof.	

ID	
A	B
1,1,1-Trifluoro-5-methoxy-4-methyl-4-phenyl-2-quinolin-4-ylmethylpentan-2-ol	
5,5,5-Trifluoro-2-methyl-2-phenyl-4-quinolin-4-ylmethylpentane-1,4-diol	
or a tautomer, prodrug, solvate, or salt thereof.	

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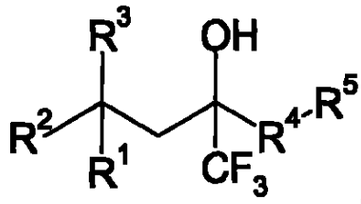
We Claim:

1. A compound of Formula (IA)



(IA)

wherein:

R^1 is an aryl or heteroaryl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_5 alkoxy, C_2-C_5 alkenyloxy, C_2-C_5 alkynyloxy, aryloxy, acyl, C_1-C_5 alkoxycarbonyl, C_1-C_5 alkanoyloxy, C_1-C_5 alkanoyl, aroyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, aminocarbonyloxy, C_1-C_5 alkylaminocarbonyloxy, C_1-C_5 dialkylaminocarbonyloxy, C_1-C_5 alkanoylamino, C_1-C_5 alkoxycarbonylamino, C_1-C_5 alkylsulfonylamino, aminosulfonyl, C_1-C_5 alkylaminosulfonyl, C_1-C_5 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, trifluoromethoxy, nitro, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl; or C_1-C_5 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with one to three substituent groups selected from methyl, methoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl;

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R^2 and R^3 are each independently hydrogen or C_1-C_3 alkyl, or R^2 and R^3 together with the carbon atom they are commonly attached to form a C_3-C_8 spiro cycloalkyl ring;

R^4 is C_1-C_3 alkyl, C_2-C_3 alkenyl, or C_2-C_3 alkynyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^4 is independently C_1-C_3 alkyl, hydroxy, halogen, amino, or oxo; and

R^5 is a heteroaryl group optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_2-C_3 alkynyloxy, aryloxy, acyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, heterocyclylcarbonyl, aroyl aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, aminocarbonyloxy, C_1-C_3 alkylaminocarbonyloxy, C_1-C_3 dialkylaminocarbonyloxy, C_1-C_3 alkanoylamino, C_1-C_3 alkoxycarbonylamino, C_1-C_3 alkylsulfonylamino, aminosulfonyl, C_1-C_3 alkylaminosulfonyl, C_1-C_3 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, nitro, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_3 alkyl; or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^5 is optionally independently substituted with one to three substituent groups selected from C_1-C_3 alkyl, C_1-C_3 alkoxy, acyl, C_1-C_3 silanyloxy, C_1-C_3 alkoxycarbonyl, carboxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_3 alkyl, or trifluoromethyl,

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or a tautomer, prodrug, solvate, or salt thereof.

2. The compound of Formula (IA) according to claim 1, wherein:

R^1 is phenyl, naphthyl, dihydrobenzofuranyl, benzofuranyl, chromanyl, dihydroindolyl, indolyl, dihydrobenzothienyl, benzothienyl, benzodioxolanyl, dihydrobenzoxazolyl, benzoxazolyl, benzisoxazolyl, benzpyrazolyl, benzimidazolyl, thienyl, quinolinyl, pyridinyl, pyrimidinyl, or pyrazinyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_1-C_3 alkanoyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, halogen, hydroxy, carboxy, cyano, trifluoromethyl, trifluoromethoxy, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with a substituent group selected from methyl, methoxy, halogen, hydroxy, oxo, cyano, or amino;

R^2 and R^3 are each independently hydrogen or C_1-C_3 alkyl, or R^2 and R^3 together with the carbon atom they are commonly attached to form a C_3-C_6 spiro cycloalkyl ring;

R^4 is CH_2; and

R^5 is an imidazolyl, pyridyl, indolyl, azaindolyl, diazaindolyl, benzofuranyl, furanopyridinyl, furanopyrimidinyl, imidazolopyrimidinyl, imidazolopyridazinyl, imidazolopyrazinyl, benzothienyl, thienopyridinyl, thienopyrimidinyl, thienopyridazinyl, benzoxazolyl, oxazolopyridinyl, benzothiazolyl, thiazolopyridinyl, benzimidazolyl, imidazolopyridinyl, quinolinyl, or isoquinolinyl group, each optionally independently substituted with one to three substituent groups,

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wherein each substituent group of R^5 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, phenyl, hydroxy, C_1-C_3 alkoxy, methoxycarbonyl, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, heterocyclylcarbonyl, fluoro, chloro, bromo, oxo, cyano, trifluoromethyl, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^5 is optionally independently substituted with a substituent group selected from methyl, methoxy, fluoro, chloro, bromo, trifluoromethyl, hydroxy, cyano, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl

or a tautomer, prodrug, solvate, or salt thereof.

3. The compound of Formula (IA) according to claim 1, wherein:

R^1 is phenyl, naphthyl, pyridyl, chromanyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one or two substituent groups,

wherein each substituent group of R^1 is independently methyl, ethyl, methoxy, ethoxy, fluoro, chloro, bromo, hydroxy, trifluoromethyl, trifluoromethoxy, cyano, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

R^2 and R^3 are each independently methyl, or R^2 and R^3 together with the carbon atom they are commonly attached to form a spiro cyclopropyl ring;

R^4 is CH_2; and

R^5 is a pyridyl, indolyl, azaindolyl, diazaindolyl, benzofuranyl, furanopyridinyl, thienopyridinyl, benzoxazolyl, benzimidazolyl, quinolinyl, or isoquinolinyl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently methyl, phenyl, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, morpholinylcarbonyl, fluoro, chloro, bromo, cyano, or trifluoromethyl, hydroxyl, cyano, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl

or a tautomer, prodrug, solvate, or salt thereof.

4. The compound of Formula (IA) according to claim 1, wherein R^2 and R^3 together with the carbon atom they are commonly attached to form a C_3-C_8 spiro cycloalkyl ring.

5. The compound of Formula (IA) according to claim 1, wherein R^2 and R^3 are each independently hydrogen or C_1-C_5 alkyl.

6. The compound of Formula (IA) according to claim 1, wherein:

R^1 is phenyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_1-C_3 alkanoyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone; and

R^2 and R^3 are each independently hydrogen or C_1-C_3 alkyl,

or a tautomer, prodrug, solvate, or salt thereof.

7. The compound of Formula (IA) according to claim 1, wherein:

R^3 is a pyridyl, indolyl, azaindolyl, diazaindolyl, benzofuranyl, furanopyridinyl, thienopyridinyl, benzoxazolyl, benzimidazolyl, quinolinyl, or isoquinolinyl group, each optionally independently substituted with one to three substituent groups,

or a tautomer, prodrug, solvate, or salt thereof.

8. The compound of Formula (IA) according to claim 1, wherein:

R^1 is thienyl, phenyl, naphthyl, dihydrobenzofuranyl, benzofuranyl, chromanyl, dihydroindolyl, indolyl, dihydrobenzothienyl, benzothienyl, benzodioxolyl, dihydrobenzoxazolyl, benzoxazolyl, benzisoxazolyl, benzpyrazolyl, benzimidazolyl, thienyl, quinolinyl, pyridinyl, pyrimidinyl, or pyrazinyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_1-C_3 alkanoyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, aryl, heteroaryl, halogen, hydroxy, carboxy, cyano, heterocyclyl, trifluoromethyl, trifluoromethoxy, nitro, aminosulfonyl, dialkylaminosulfonyl, amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with one or two substituent groups selected from methyl, methoxy, halogen, hydroxy, oxo, cyano, morpholinyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl;

R^2 and R^3 are each independently hydrogen or C_1-C_3 alkyl, or R^2 and R^3 together with the carbon atom they are commonly attached to form a C_3-C_6 spiro cycloalkyl ring;

R^4 is CH_3; and

R^3 is an imidazolyl, pyridyl, indolyl, indazolyl, azaindolyl, diazaindolyl, benzofuranyl, furanopyridinyl, furanopyrimidinyl, imidazolopyrimidinyl, imidazolopyridazinyl, imidazolopyrazinyl, benzothienyl, thienopyridinyl, thienopyrimidinyl, thienopyridazinyl, benzoxazolyl, oxazolopyridinyl, benzothiazolyl, thiazolopyridinyl, benzimidazolyl, imidazolopyridinyl, quinolinyl, or isoquinolinyl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^3 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, phenyl, heteroaryl, heterocyclyl, acyl, dialkylaminosulfonyl, C_1-C_3 alkoxy, methoxycarbonyl, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, heterocyclylcarbonyl, hydroxy, oxo, fluoro, chloro, bromo, cyano, trifluoromethyl, amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl; or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^3 is optionally independently substituted with one or two substituent groups selected from methyl, methoxy, fluoro, chloro, bromo, oxo, trifluoromethyl, hydroxy, cyano, morpholinyl, pyrrolidinyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl,

or a tautomer, prodrug, solvate, or salt thereof.

9. The compound of Formula (IA) according to claim 1, wherein:

R^1 is thienyl, phenyl, naphthyl, pyridyl, chromanyl, benzodioxolyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one or two substituent groups,

wherein each substituent group of R^1 is independently methyl, ethyl, methoxy, ethoxy, fluoro, chloro, bromo, hydroxy, trifluoromethyl, trifluoromethoxy, morpholinylmethyl, dimethylaminomethyl, aminosulfonyl, dimethylaminosulfonyl, phenyl, pyrimidinyl, pyridinyl, thienyl, naphthalenyl, morpholinyl, piperidinyl, cyano, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with one or two groups selected from cyano, chloro, bromo, or fluoro;

R^2 and R^3 are each independently methyl or ethyl, or R^2 and R^3 together with the carbon atom they are commonly attached to form a spiro cyclopropyl ring;

R^4 is CH_2; and

R^5 is a pyridyl, indolyl, azaindolyl, diazaindolyl, benzofuranyl, thienopyridazinyl, furanopyridinyl, thienopyridinyl, benzoxazolyl, benzimidazolyl, quinolinyl, or isoquinolinyl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently methyl, phenyl, methoxy, ethoxy, isopropoxy, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, morpholinylcarbonyl, morpholinyl, piperidinyl, phenoxy, pyrrolidinyl, acetyl, pivaloyl, ethylcarbonyl, isopropylcarbonyl, pyridinyl, pyrimidinyl, trifluoromethyl, fluoro, chloro, bromo, hydroxy, cyano, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl or trifluoromethyl,

wherein each substituent group of R^5 is optionally independently substituted with one or two substituent groups selected from cyano, halogen, methyl, dimethylamino, morpholinyl, pyrrolidinyl, or piperidinyl,

or a tautomer, prodrug, solvate, or salt thereof.

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10. The compound of Formula (IA) according to claim 1, wherein:

R^1 is phenyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_1-C_3 alkanoyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, aryl, heteroaryl, heterocyclyl, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone; and

R^2 and R^3 are each independently hydrogen or C_1-C_3 alkyl,

or a tautomer, prodrug, solvate, or salt thereof.

11. The compound of Formula (IA) according to claim 1, wherein:

R^5 is a pyridyl, indolyl, azaindolyl, diazaindolyl, benzofuranyl, thienopyridazinyl furanopyridinyl, thienopyridinyl, benzoxazolyl, benzimidazolyl, quinolinyl, or isoquinolinyl group, each optionally independently substituted with one to three substituent groups,

or a tautomer, prodrug, solvate, or salt thereof.

12. A pharmaceutical composition comprising an effective amount of a compound according to one of claims 1 to 11, or a tautomer, prodrug, solvate, or salt thereof, and a pharmaceutically acceptable excipient or carrier.

13. A compound of Formula (IB)

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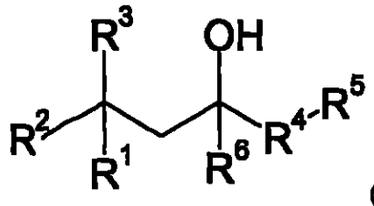

(IB)

wherein:

R^1 is an aryl or heteroaryl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_5 alkoxy, C_2-C_5 alkenyloxy, C_2-C_5 alkynyloxy, aryloxy, acyl, C_1-C_5 alkoxycarbonyl, C_1-C_5 alkanoyloxy, C_1-C_5 alkanoyl, aroyl, aminocarbonyl, C_1-C_5 alkylaminocarbonyl, C_1-C_5 dialkylaminocarbonyl, aminocarbonyloxy, C_1-C_5 alkylaminocarbonyloxy, C_1-C_5 dialkylaminocarbonyloxy, C_1-C_5 alkanoylamino, C_1-C_5 alkoxycarbonylamino, C_1-C_5 alkylsulfonylamino, aminosulfonyl, C_1-C_5 alkylaminosulfonyl, C_1-C_5 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, trifluoromethoxy, nitro, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl; or C_1-C_5 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with one to three substituent groups selected from methyl, methoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl;

R^2 and R^3 are each independently C_1-C_5 alkyl;

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R^4 is C_1-C_5 alkyl, C_2-C_5 alkenyl, or C_2-C_5 alkynyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^4 is independently C_1-C_3 alkyl, hydroxy, halogen, amino, or oxo;

R^5 is a heteroaryl group optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_5 alkoxy, C_2-C_5 alkenyloxy, C_2-C_5 alkynyloxy, aryloxy, acyl, C_1-C_5 alkoxycarbonyl, C_1-C_5 alkanoyloxy, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, aminocarbonyloxy, C_1-C_5 alkylaminocarbonyloxy, C_1-C_5 dialkylaminocarbonyloxy, C_1-C_5 alkanoylamino, C_1-C_5 alkoxycarbonylamino, C_1-C_5 alkylsulfonylamino, aminosulfonyl, C_1-C_5 alkylaminosulfonyl, C_1-C_5 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, nitro, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl; or C_1-C_5 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^5 is optionally independently substituted with one to three substituent groups selected from C_1-C_5 alkyl, C_1-C_5 alkoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl, or trifluoromethyl,

R^6 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, carbocycle, heterocyclyl, aryl, heteroaryl, carbocycle-C_1-C_8 alkyl, aryl-C_1-C_8 alkyl, aryl-C_1-C_8 haloalkyl, heterocyclyl-C_1-C_8 alkyl, carboxy, alkoxycarbonyl heteroaryl-C_1-C_8 alkyl, carbocycle-C_2-C_8 alkenyl,

aryl-C_2-C_8 alkenyl, heterocyclyl-C_2-C_8 alkenyl, or heteroaryl-C_2-C_8 alkenyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, C_3-C_8 cycloalkyl, phenyl, C_1-C_5 alkoxy, phenoxy, C_1-C_5 alkanoyl, aroyl, C_1-C_5 alkoxycarbonyl, C_1-C_5 alkanoyloxy, aminocarbonyloxy, C_1-C_5 alkylaminocarbonyloxy, C_1-C_5 dialkylaminocarbonyloxy, aminocarbonyl, C_1-C_5 alkylaminocarbonyl, C_1-C_5 dialkylaminocarbonyl, C_1-C_5 alkanoylamino, C_1-C_5 alkoxycarbonylamino, C_1-C_5 alkylsulfonylamino, C_1-C_5 alkylaminosulfonyl, C_1-C_5 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, oxo, trifluoromethyl, nitro, amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl; or C_1-C_5 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein R^6 cannot be trifluoromethyl,

or a tautomer, prodrug, solvate, or salt thereof.

14. The compound of Formula (IB) according to claim 13, wherein:

R^1 is thienyl, phenyl, dihydrobenzofuranyl, benzofuranyl, dihydroindolyl, indolyl, dihydrobenzothienyl, benzothienyl, benzodioxolanyl, benzoxazolyl, benzisoxazolyl, benzpyrazolyl, benzimidazolyl, quinolinyl, pyridinyl, pyrimidinyl, or pyrazinyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_1-C_3 alkanoyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with a substituent group selected from methyl, methoxy, halogen, hydroxy, oxo, cyano,

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heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl;

R^2 and R^3 are each independently C_1-C_3 alkyl;

R^4 is CH_2;

R^5 is a pyridyl, indolyl, azaindolyl, benzofuranyl, furanylpyridinyl, imidazolopyridinyl, imidazolopyrimidinyl, imidazolopyridazinyl, imidazolopyrazinyl, benzothienyl, thienopyridinyl, benzoxazolyl, benzothiazolyl, benzimidazolyl, quinolinyl, or isoquinolinyl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, phenyl, hydroxyl, oxo, C_1-C_3 alkoxy, methoxycarbonyl, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, heterocyclylcarbonyl, fluoro, chloro, bromo, cyano, trifluoromethyl, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^5 is optionally independently substituted with a substituent group selected from methyl, methoxy, fluoro, chloro, bromo, cyano, trifluoromethyl; heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl and

R^6 is C_1-C_3 alkyl, C_2-C_3 alkenyl, C_3-C_6 cycloalkyl, phenyl, C_3-C_6 cycloalkyl-C_1-C_3 alkyl, phenyl-C_1-C_3 alkyl, phenyl-C_1-C_3 haloalkyl, C_3-C_6 cycloalkyl-C_2-C_3 alkenyl, phenyl-C_2-C_3 alkenyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3

dialkylaminocarbonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

or a tautomer, prodrug, solvate, or salt thereof.

15. The compound of Formula (IB) according to claim 13, wherein:

R^1 is thienyl, phenyl, pyridyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one or two substituent groups,

wherein each substituent group of R^1 is independently methyl, ethyl, methoxy, ethoxy, fluoro, chloro, bromo, hydroxy, trifluoromethyl, cyano; or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone;

R^2 and R^3 are each methyl;

R^4 is CH_2;

R^5 is a pyridyl, indolyl, azaindolyl, diazaindolyl, benzofuranyl, benzoxazolyl, benzimidazolyl, quinolinyl, or isoquinolinyl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently methyl, phenyl, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminocarbonyl, morpholinylcarbonyl, hydroxy, oxo, fluoro, chloro, cyano, or trifluoromethyl; and

R^6 is C_1-C_3 alkyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkylmethyl-, or benzyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently methyl, methoxy, fluoro, chloro, bromo, cyano, trifluoromethyl, or hydroxy,

or a tautomer, prodrug, solvate, or salt thereof.

16. The compound of Formula (IB) according to claim 13, wherein:

R^1 is thienyl, phenyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_1-C_3 alkanoyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone; and

R^2 and R^3 are each independently C_1-C_3 alkyl,

or a tautomer, prodrug, solvate, or salt thereof.

17. The compound of Formula (IB) according to claim 13, wherein:

R^1 is thienyl, phenyl, naphthyl, pyridyl, chromanyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one or two substituent groups,

wherein each substituent group of R^1 is independently methyl, ethyl, methoxy, ethoxy, fluoro, chloro, bromo, hydroxy, trifluoromethyl, cyano, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone;

R^2 and R^3 are each methyl;

R^4 is CH_3;

R^5 is a pyridyl, indolyl, azaindolyl, diazaindolyl, benzofuranyl, furanopyridinyl, thienopyridinyl, benzoxazolyl, benzimidazolyl, quinolinyl, or isoquinolinyl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently methyl, phenyl, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminoaminocarbonyl, morpholinylcarbonyl, pyridinyl, hydroxy, fluoro, chloro, bromo, cyano, or trifluoromethyl; and

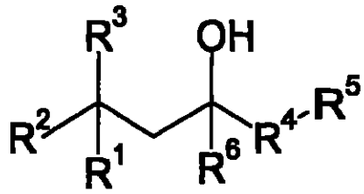
R^6 is C_1-C_5 alkyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkylmethyl-, or benzyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently methyl, methoxy, fluoro, chloro, bromo, cyano, trifluoromethyl, or hydroxy,

or a tautomer, prodrug, solvate, or salt thereof.

18. A pharmaceutical composition comprising an effective amount of a compound according to one of claims 13 to 17, or a tautomer, prodrug, solvate, or salt thereof, and a pharmaceutically acceptable excipient or carrier.

19. A compound of Formula (IC)



(IC)

wherein:

R^1 is an aryl or heteroaryl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_5 alkoxy, C_2-C_5 alkenyloxy, C_2-C_5 alkynyloxy, aryloxy, acyl, C_1-C_5 alkoxycarbonyl, C_1-C_5 alkanoyloxy, C_1-C_5 alkanoyl, aroyl, aminocarbonyl, C_1-C_5 alkylaminocarbonyl, C_1-C_5

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dialkylaminocarbonyl, aminocarbonyloxy, C_1-C_3 alkylaminocarbonyloxy, C_1-C_3 dialkylaminocarbonyloxy, C_1-C_3 alkanoylamino, C_1-C_3 alkoxycarbonylamino, C_1-C_3 alkylsulfonylamino, aminosulfonyl, C_1-C_3 alkylaminosulfonyl, C_1-C_3 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, trifluoromethoxy, nitro, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_3 alkyl; or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with one to three substituent groups selected from methyl, methoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_3 alkyl,

R^2 and R^3 are each independently C_1-C_3 alkyl;

R^4 is C_1-C_3 alkyl, C_2-C_3 alkenyl, or C_2-C_3 alkynyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^4 is independently C_1-C_3 alkyl, hydroxy, halogen, or oxo;

R^5 is a heteroaryl group fused with a saturated or partially saturated carbocyclic ring optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_2-C_3 alkynyloxy, aryloxy, acyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, aminocarbonyloxy, C_1-C_3 alkylaminocarbonyloxy, C_1-C_3 dialkylaminocarbonyloxy, C_1-C_3 alkanoylamino, C_1-C_3

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alkoxycarbonylamino, C_1-C_3 alkylsulfonylamino, C_1-C_3 alkylaminosulfonyl, C_1-C_3 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, nitro, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_3 alkyl; or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^5 is optionally independently substituted with one to three substituent groups selected from C_1-C_3 alkyl, C_1-C_3 alkoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_3 alkyl, or trifluoromethyl; and

R^6 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, carbocycle, heterocyclyl, aryl, heteroaryl, carbocycle-C_1-C_8 alkyl, carboxy, trifluoromethyl, alkoxycarbonyl, aryl-C_1-C_8 alkyl, aryl-C_1-C_8 haloalkyl, heterocyclyl-C_1-C_8 alkyl, heteroaryl-C_1-C_8 alkyl, carbocycle-C_2-C_8 alkenyl, aryl-C_2-C_8 alkenyl, heterocyclyl-C_2-C_8 alkenyl, or heteroaryl-C_2-C_8 alkenyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_3-C_8 cycloalkyl, phenyl, C_1-C_3 alkoxy, phenoxy, C_1-C_3 alkanoyl, aroyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, aminocarbonyloxy, C_1-C_3 alkylaminocarbonyloxy, C_1-C_3 dialkylaminocarbonyloxy, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, C_1-C_3 alkanoylamino, C_1-C_3 alkoxycarbonylamino, C_1-C_3 alkylsulfonylamino, C_1-C_3 alkylaminosulfonyl, C_1-C_3 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, oxo, trifluoromethyl, nitro, amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_3 alkyl; or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

or a tautomer, prodrug, solvate, or salt thereof.

20. The compound of Formula (IC) according to claim 19, wherein:

R^1 is thienyl, phenyl, naphthyl, dihydrobenzofuranyl, benzofuranyl, chromanyl, dihydroindolyl, indolyl, dihydrobenzothienyl, benzothienyl, benzodioxolanyl, benzoxazolyl, benzisoxazolyl, benzpyrazolyl, benzimidazolyl, thienyl, quinolinyl, pyridinyl, pyrimidinyl, or pyrazinyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_1-C_3 alkanoyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with a substituent group selected from methyl, methoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl;

R^2 and R^3 are each independently C_1-C_3 alkyl;

R^4 is CH_2;

R^5 is a N-linked heteroaryl with a fused 5-7 membered saturated carbocyclic ring optionally and independently substituted with one to three substituent groups

wherein each substituent group of R^5 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, phenyl, C_1-C_3 alkoxy, methoxycarbonyl, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, heterocyclylcarbonyl, fluoro, chloro, bromo, cyano, trifluoromethyl, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^5 is optionally independently substituted with a substituent group selected from methyl, methoxy, fluoro, chloro, bromo, trifluoromethyl, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl; and

R^6 is C_1-C_3 alkyl, C_2-C_3 alkenyl, C_3-C_6 cycloalkyl, trifluoromethyl, phenyl, C_3-C_6 cycloalkyl-C_1-C_3 alkyl, phenyl-C_1-C_3 alkyl, phenyl-C_1-C_3 haloalkyl, C_3-C_6 cycloalkyl-C_2-C_3 alkenyl, phenyl-C_2-C_3 alkenyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

or a tautomer, prodrug, solvate, or salt thereof.

21. The compound of Formula (IC) according to claim 19, wherein:

R^1 is thienyl, phenyl, naphthyl, pyridyl, chromanyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one or two substituent groups,

wherein each substituent group of R^1 is independently methyl, ethyl, methoxy, ethoxy, fluoro, chloro, bromo, hydroxy, trifluoromethyl, cyano, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone;

R^2 and R^3 are each methyl;

R^4 is CH_3;

R^5 is a N-linked pyrrole, pyrazole, or imidazole fused to a 5-7 membered saturated carbocyclic ring optionally and independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently methyl, phenyl, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminoaminocarbonyl, morpholinylcarbonyl, fluoro, chloro, bromo, cyano, hydroxy, oxo, or trifluoromethyl; and

R^6 is C_1-C_3 alkyl, C_3-C_6 cycloalkyl, trifluoromethyl, C_3-C_6 cycloalkylmethyl-, or benzyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently methyl, methoxy, fluoro, chloro, bromo, cyano, trifluoromethyl, or hydroxy,

or a tautomer, prodrug, solvate, or salt thereof.

22. The compound of Formula (IC) according to claim 19, wherein:

R^1 is thienyl, phenyl, naphthyl, dihydrobenzofuranyl, benzofuranyl, chromanyl, dihydroindolyl, indolyl, dihydrobenzothienyl, benzothienyl, benzodioxolanyl, benzoxazolyl, benziscoxazolyl, benzpyrazolyl, benzimidazolyl, thienyl, quinolinyl, pyridinyl, pyrimidinyl, or pyrazinyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_1-C_3 alkanoyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, aryl, heteroaryl, heterocyclyl, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with a substituent group selected from methyl, methoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl;

R^2 and R^3 are each independently C_1-C_3 alkyl;

R^4 is CH_2;

R^5 is a N-linked heteroaryl with a fused 5-7 membered saturated carbocyclic ring optionally and independently substituted with one to three substituent groups

wherein each substituent group of R^5 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, phenyl, C_1-C_3 alkoxy, methoxycarbonyl, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, heterocyclylcarbonyl, fluoro, chloro, bromo, cyano, trifluoromethyl, hydroxyl, oxo, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^5 is optionally independently substituted with a substituent group selected from methyl, methoxy, fluoro, chloro, bromo, trifluoromethyl, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl; and

R^6 is C_1-C_3 alkyl, C_2-C_3 alkenyl, C_3-C_6 cycloalkyl, trifluoromethyl, phenyl, C_3-C_6 cycloalkyl-C_1-C_3 alkyl, phenyl-C_1-C_3 alkyl, phenyl-C_1-C_3 haloalkyl, C_3-C_6 cycloalkyl-C_2-C_3 alkenyl, phenyl-C_2-C_3 alkenyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

or a tautomer, prodrug, solvate, or salt thereof.

23. The compound of Formula (IC) according to claim 19, wherein:

R^1 is thienyl, phenyl, naphthyl, pyridyl, chromanyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one or two substituent groups,

wherein each substituent group of R^1 is independently methyl, ethyl, methoxy, ethoxy, fluoro, chloro, bromo, hydroxy, trifluoromethyl, pyridinyl, pyrimidinyl, pyrazinyl, cyano, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone;

wherein each substituent group of R^1 is optionally independently substituted with a substituent group selected from cyano or halogen

R^2 and R^3 are each methyl;

R^4 is CH_2;

R^5 is a N-linked pyrrole, pyrazole, or imidazole fused to a 5-7 membered saturated carbocyclic ring optionally and independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently methyl, phenyl, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminoaminocarbonyl, morpholinylcarbonyl, fluoro, chloro, bromo, cyano, hydroxy, oxo, or trifluoromethyl; and

R^6 is C_1-C_3 alkyl, C_3-C_6 cycloalkyl, trifluoromethyl, C_3-C_6 cycloalkylmethyl-, or benzyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently methyl, methoxy, fluoro, chloro, bromo, cyano, trifluoromethyl, or hydroxy,

or a tautomer, prodrug, solvate, or salt thereof.

24. The compound of Formula (IC) according to claim 19, wherein:

R^1 is thienyl, phenyl, naphthyl, pyridyl, chromanyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one or two substituent groups,

wherein each substituent group of R^1 is independently methyl, ethyl, methoxy, ethoxy, fluoro, chloro, bromo, hydroxy, trifluoromethyl, furanyl, thienyl, pyrrolyl, pyrrolidinyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, pyrazolidinyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, thiadiazolyl, pyridinyl, piperidinyl, morpholinyl, thiomorpholinyl, pyridazinyl, pyrimidinyl, pyrazinyl, piperazinyl, indolyl, benzofuranyl, benzothienyl, indazolyl, benzimidazolyl, cyano, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone;

wherein each substituent group of R^1 is optionally independently substituted with a substituent group selected from C_1-C_3 alkyl, C_1-C_3 alkoxy, C_1-C_3 alkoxycarbonyl, acyl, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, C_1-C_3 alkanoylamino, hydroxyl, cyano, halogen or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl,

R^2 and R^3 are each methyl;

R^4 is CH_2;

R^5 is a N-linked pyrrole, pyrazole, or imidazole fused to a 5-7 membered saturated carbocyclic ring optionally and independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently methyl, phenyl, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminoaminocarbonyl, morpholinylcarbonyl, fluoro, chloro, bromo, cyano, hydroxy, oxo, or trifluoromethyl; and

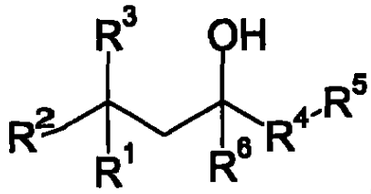
R^6 is C_1-C_3 alkyl, C_3-C_6 cycloalkyl, trifluoromethyl, C_3-C_6 cycloalkylmethyl-, or benzyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently methyl, methoxy, fluoro, chloro, bromo, cyano, trifluoromethyl, or hydroxy,

or a tautomer, prodrug, solvate, or salt thereof.

25. A pharmaceutical composition comprising an effective amount of a compound according to one of claims 19 to 24, or a tautomer, prodrug, solvate, or salt thereof, and a pharmaceutically acceptable excipient or carrier.

26. A compound of Formula (ID)



(ID)

wherein:

R^1 is an aryl or heteroaryl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_5 alkoxy, C_2-C_5 alkenyloxy, C_2-C_5 alkynyloxy, aryloxy, acyl, C_1-C_5 alkoxycarbonyl, C_1-C_5 alkanoyloxy, C_1-C_5 alkanoyl, aroyl, aminocarbonyl, C_1-C_5 alkylaminocarbonyl, C_1-C_5

570
589

dialkylaminocarbonyl, aminocarbonyloxy, C_1-C_3 alkylaminocarbonyloxy, C_1-C_3 dialkylaminocarbonyloxy, C_1-C_3 alkanoylamino, C_1-C_3 alkoxycarbonylamino, C_1-C_3 alkylsulfonylamino, aminosulfonyl, C_1-C_3 alkylaminosulfonyl, C_1-C_3 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, trifluoromethoxy, nitro, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_3 alkyl; or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with one to three substituent groups selected from methyl, methoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_3 alkyl;

R^2 and R^3 are each independently C_1-C_3 alkyl, wherein one or both are independently substituted with hydroxy, C_1-C_3 alkoxy, C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone, amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl;

R^4 is C_1-C_3 alkyl, C_2-C_3 alkenyl, or C_2-C_3 alkynyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^4 is independently C_1-C_3 alkyl, hydroxy, halogen, or oxo;

R^5 is a heteroaryl group optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl, heteroaryl, C_1-C_3 alkoxy, C_2-C_3

alkenyloxy, C_2-C_5 alkynyloxy, aryloxy, acyl, C_1-C_5 alkoxycarbonyl, C_1-C_5 alkanoyloxy, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, aminocarbonyloxy, C_1-C_5 alkylaminocarbonyloxy, C_1-C_5 dialkylaminocarbonyloxy, C_1-C_5 alkanoylamino, C_1-C_5 alkoxycarbonylamino, C_1-C_5 alkylsulfonylamino, C_1-C_5 alkylaminosulfonyl, C_1-C_5 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, trifluoromethoxy, trifluoromethylthio, nitro, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl; or C_1-C_5 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^5 is optionally independently substituted with one to three substituent groups selected from C_1-C_3 alkyl, C_1-C_3 alkoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl or aryl; or ureido wherein either nitrogen atom is optionally independently substituted with C_1-C_5 alkyl or trifluoromethyl; and

R^6 is hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, carbocycle, heterocyclyl, aryl, heteroaryl, trifluoromethyl, carbocycle-C_1-C_8 alkyl, carboxy, alkoxycarbonyl, aryl-C_1-C_8 alkyl, aryl-C_1-C_8 haloalkyl, heterocyclyl-C_1-C_8 alkyl, heteroaryl-C_1-C_8 alkyl, carbocycle-C_2-C_8 alkenyl, aryl-C_2-C_8 alkenyl, heterocyclyl-C_2-C_8 alkenyl, or heteroaryl-C_2-C_8 alkenyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, C_3-C_8 cycloalkyl, phenyl, C_1-C_5 alkoxy, phenoxy, C_1-C_5 alkanoyl, aroyl, C_1-C_5 alkoxycarbonyl, C_1-C_5 alkanoyloxy, aminocarbonyloxy, C_1-C_5 alkylaminocarbonyloxy, C_1-C_5 dialkylaminocarbonyloxy, aminocarbonyl, C_1-C_5 alkylaminocarbonyl, C_1-C_5 dialkylaminocarbonyl, C_1-C_5 alkanoylamino, C_1-C_5 alkoxycarbonylamino, C_1-C_5 alkylsulfonylamino, C_1-C_5 alkylaminosulfonyl, C_1-C_5 dialkylaminosulfonyl, halogen, hydroxy, carboxy, cyano, oxo, trifluoromethyl, nitro, amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_5 alkyl; or ureido wherein

either nitrogen atom is optionally independently substituted with C_1-C_3 alkyl; or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

or a tautomer, prodrug, solvate, or salt thereof.

27. The compound of Formula (ID) according to claim 26, wherein:

R^1 is thienyl, phenyl, naphthyl, dihydrobenzofuranyl, benzofuranyl, chromanyl, dihydroindolyl, indolyl, dihydrobenzothienyl, benzothienyl, benzodioxolanyl, benzoxazolyl, benzisoxazolyl, benzpyrazolyl, benzimidazolyl, thienyl, quinolinyl, pyridinyl, pyrimidinyl, or pyrazinyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_1-C_3 alkanoyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^1 is optionally independently substituted with a substituent group selected from methyl, methoxy, halogen, hydroxy, oxo, cyano, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl;

R^2 and R^3 are each independently C_1-C_3 alkyl wherein one or both are independently substituted with hydroxy, C_1-C_3 alkoxy,

R^4 is CH_2;

R^5 is an imidazolyl, pyridyl, indolyl, azaindolyl, diazaindolyl, benzofuranyl, furanopyridinyl, furanopyrimidinyl, benzothienyl, thienopyridinyl, thienopyrimidinyl, benzoxazolyl, oxazolopyridinyl, benzothiazolyl, thiazolopyridinyl, benzimidazolyl,

imidazolopyridinyl, quinolinyl, or isoquinolinyl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, phenyl, C_1-C_3 alkoxy, methoxycarbonyl, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, heterocyclylcarbonyl, fluoro, chloro, bromo, cyano, trifluoromethyl, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

wherein each substituent group of R^5 is optionally independently substituted with a substituent group selected from methyl, methoxy, fluoro, chloro, bromo, trifluoromethyl, heteroaryl, heterocyclyl, or amino wherein the nitrogen atom is optionally independently mono- or di-substituted by C_1-C_3 alkyl or aryl and

R^6 is C_1-C_3 alkyl, C_2-C_3 alkenyl, C_3-C_6 cycloalkyl, trifluoromethyl, phenyl, C_3-C_6 cycloalkyl-C_1-C_3 alkyl, phenyl-C_1-C_3 alkyl, phenyl-C_1-C_3 haloalkyl, C_3-C_6 cycloalkyl-C_2-C_3 alkenyl, phenyl-C_2-C_3 alkenyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, aminocarbonyl, C_1-C_3 alkylaminocarbonyl, C_1-C_3 dialkylaminocarbonyl, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone,

or a tautomer, prodrug, solvate, or salt thereof.

28. The compound of Formula (ID) according to claim 26, wherein:

R^1 is thienyl, phenyl, naphthyl, pyridyl, chromanyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one or two substituent groups,

wherein each substituent group of R^1 is independently methyl, ethyl, methoxy, ethoxy, fluoro, chloro, bromo, hydroxy, trifluoromethyl, cyano, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone;

R^2 and R^3 are each methyl wherein one or both are independently substituted with hydroxy, methoxy;

R^4 is CH_3;

R^5 is a pyridyl, indolyl, azaindolyl, benzofuranyl, furanopyridinyl, thienopyridinyl, benzoxazolyl, benzimidazolyl, quinolinyl, or isoquinolinyl group, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^5 is independently methyl, phenyl, methoxycarbonyl, aminocarbonyl, methylaminocarbonyl, dimethylaminoaminocarbonyl, morpholinylcarbonyl, fluoro, chloro, bromo, cyano, or trifluoromethyl; and

R^6 is C_1-C_3 alkyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkylmethyl-, trifluoromethyl, or benzyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^6 is independently methyl, methoxy, fluoro, chloro, bromo, cyano, trifluoromethyl, or hydroxy,

or a tautomer, prodrug, solvate, or salt thereof.

29. The compound of Formula (ID) according to claim 26, wherein:

R^1 is phenyl, dihydrobenzofuranyl, or benzofuranyl, each optionally independently substituted with one to three substituent groups,

wherein each substituent group of R^1 is independently C_1-C_3 alkyl, C_2-C_3 alkenyl, C_2-C_3 alkynyl, C_1-C_3 alkoxy, C_2-C_3 alkenyloxy, C_1-C_3 alkanoyl, C_1-C_3 alkoxycarbonyl, C_1-C_3 alkanoyloxy, halogen, hydroxy, carboxy, cyano, trifluoromethyl, nitro, or C_1-C_3 alkylthio wherein the sulfur atom is optionally oxidized to a sulfoxide or sulfone; and

R^2 and R^3 are each independently C_1-C_3 alkyl each optionally independently substituted with hydroxy, C_1-C_3 alkoxy,

or a tautomer, prodrug, solvate, or salt thereof.

30. A pharmaceutical composition comprising an effective amount of a compound according to one of claims 26 to 29, or a tautomer, prodrug, solvate, or salt thereof, and a pharmaceutically acceptable excipient or carrier.

31. A method of modulating the glucocorticoid receptor function in a patient, the method comprising administering to the patient an effective amount of a pharmaceutically acceptable compound according to one of claims 1 to 11, 13 to 17, 19 to 24, or 26 to 29, or a tautomer, prodrug, solvate, or salt thereof.

32. A method of treating a disease-state or condition mediated by the glucocorticoid receptor function in a patient in need of such treatment, the method comprising administering to the patient an effective amount of a pharmaceutically acceptable compound according to one of claims 1 to 11, 13 to 17, 19 to 24, or 26 to 29, or a tautomer, prodrug, solvate, or salt thereof.

33. A method of treating a disease-state or condition selected from: type II diabetes, obesity, cardiovascular diseases, hypertension, arteriosclerosis, neurological diseases, adrenal and pituitary tumors, and glaucoma, in a patient in need of such treatment, the method comprising administering to the patient an effective amount of a pharmaceutically acceptable compound according to one of claims 1 to 11, 13 to 17, 19 to 24, or 26 to 29, or a tautomer, prodrug, solvate, or salt thereof.

34. A method of treating a disease characterized by inflammatory, allergic, or proliferative processes, in a patient in need of such treatment, the method comprising administering to the patient an effective amount of a pharmaceutically acceptable compound according to one of claims 1 to 11, 13 to 17, 19 to 24, or 26 to 29, or a tautomer, prodrug, solvate, or salt thereof.

35. The method according to claim 34, wherein the disease is selected from: (i) lung diseases; (ii) rheumatic diseases/autoimmune diseases/joint diseases; (iii) allergic diseases; (iv) vasculitis diseases; (v) dermatological diseases; (vi) renal diseases; (vii) hepatic diseases; (viii) gastrointestinal diseases; (ix) proctological diseases; (x) eye diseases; (xi) diseases of the ear, nose, and throat (ENT) area; (xii) neurological diseases; (xiii) blood diseases; (xiv) tumor diseases; (xv) endocrine diseases; (xvi) organ and tissue transplantations and graft-versus-host diseases; (xvii) severe states of shock; (xviii) substitution therapy; and (xix) pain of inflammatory genesis.

36. The method according to claim 35, wherein the disease is selected from: type I diabetes, osteoarthritis, Guillain-Barre syndrome, restenosis following percutaneous transluminal coronary angioplasty, Alzheimer disease, acute and chronic pain, atherosclerosis, reperfusion injury, bone resorption diseases, congestive heart failure, myocardial infarction, thermal injury, multiple organ injury secondary to trauma, acute purulent meningitis, necrotizing enterocolitis, and syndromes associated with hemodialysis, leukopheresis, and granulocyte transfusion.

37. A method of treating a disease-state or condition mediated by the glucocorticoid receptor function in a patient in need of such treatment, the method comprising sequentially or simultaneously administering to the patient: (a) an effective amount of a pharmaceutically acceptable compound according to one of claims 1 to 11, 13 to 17, 19 to 24, or 26 to 29, or a tautomer, prodrug, solvate, or salt thereof; and (b) a pharmaceutically acceptable glucocorticoid.

38. A kit for the *in vitro* diagnostic determination of the glucocorticoid receptor function in a sample, comprising:

(a) a diagnostically effective amount of a compound according to one of claims 1, 13, 19, or 26, or a tautomer, prodrug, solvate, or salt thereof; and

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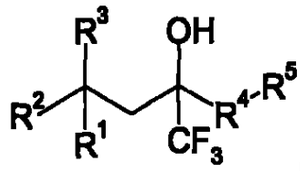
(b) instructions for use of the diagnostic kit.

39. A method of making a compound of Formula (IA)



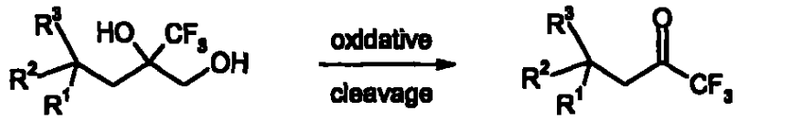
(IA)

where R^1, R^2, R^3, R^4, and R^5 are as defined in claim 1, the method comprising:

(a) reacting an ester of Formula (II) with a suitable reducing agent in a suitable solvent to form a diol of Formula (III)

II III ;

(b) reacting the diol of Formula (III) under suitable oxidative cleavage conditions to form a ketone of Formula (IV)



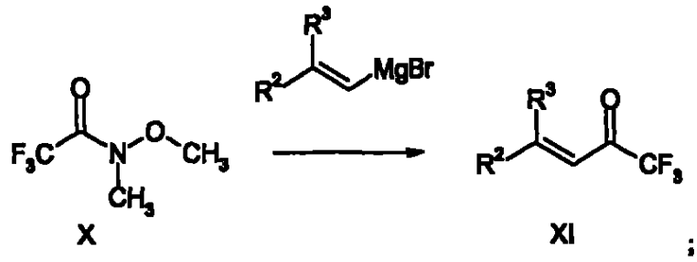
III IV ; and

(c) reacting the ketone of Formula (IV) with a suitable organometallic reagent R^5R^4M where M is Li or MgX and X is Cl, Br, or I, in a suitable solvent to form the compound of Formula (IA)

IV IA ; or

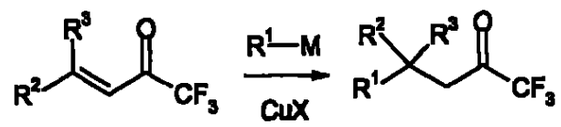
(a') reacting the trifluoroacetamide of Formula (X) with a vinyl magnesium bromide compound bearing R^2 and R^3 in a suitable solvent to provide the trifluoromethylenone of Formula (XI)

578
597



X XI ;

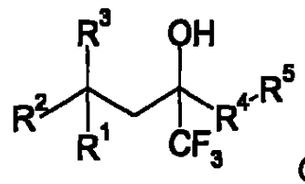
(b') reacting the trifluoromethylenone of Formula (XI) with a suitable organocopper reagent generated from an organometallic reagent R^1M where M is Li or MgX and a copper salt CuX, where X is Cl, Br, or I, in a suitable solvent to form the ketone of Formula (IV)



XI IV ; and

performing step (c) as set forth above.

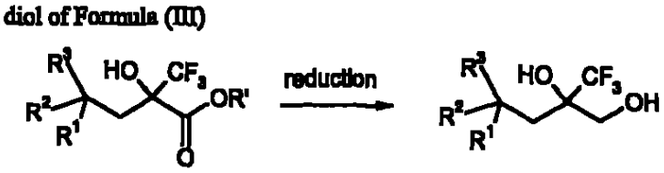
40. A method of making a compound of Formula (IA)



(IA)

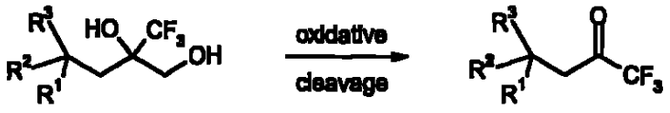
where R^1, R^2, R^3, R^4, and R^5 are as defined claim 1, the method comprising:

(a'') reacting an ester of Formula (II) with a suitable reducing agent in a suitable solvent to form a diol of Formula (III)



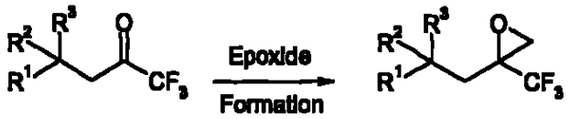
II III ;

(b''') reacting the diol of Formula (III) under suitable oxidative cleavage conditions to form a ketone of Formula (IV)



III IV ;

(c") reacting the ketone of Formula (IV) with a suitable epoxidizing reagent, such as a suitable sulfur ylide, in a suitable solvent to form the epoxide of Formula (V)

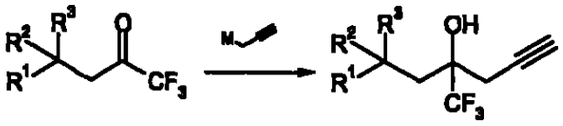


IV V ;

(d1") reacting the epoxide of Formula (V) with a suitable metal acetylide reagent, where M is a suitable metal and PG is an appropriate protecting group, in a suitable solvent to afford a protected alkyne intermediate, followed by removing the protecting group to form an alkyne of Formula (XXXI)

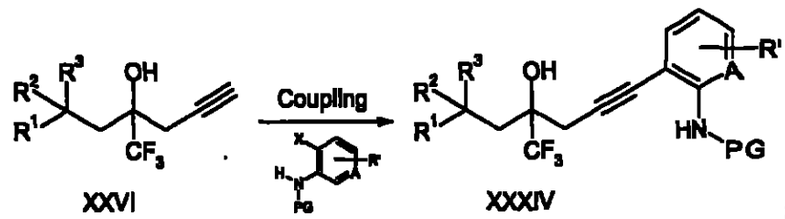
V XXXI , or

(d2") reacting the ketone of Formula (IV) with a suitable propargylating reagent in a suitable solvent to form alkyne of Formula (XXXI)



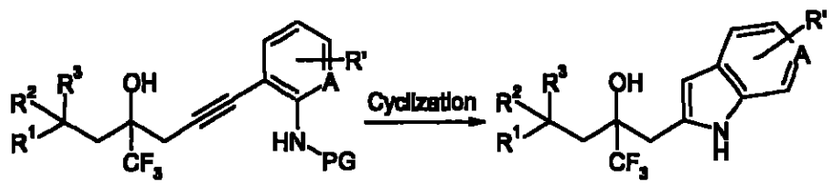
IV XXXI ;

(e") reacting the alkyne of Formula (XXXI) with a suitable coupling partner, such as optionally substituted and protected anilines or amino pyridines, wherein R^a is a R^5 substituent as defined in claim 1, A is a C or N, X is I or Br, and PG is H or a suitable protecting group, in the presence of suitable catalysts, base and solvent to form alkyne of Formula (XXXIV)



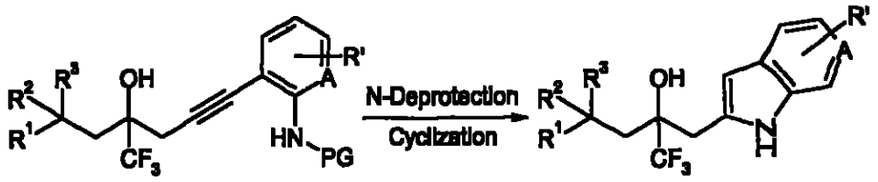
XXVI XXXIV ; and

(f1") cyclizing the alkyne of Formula (XXXIV) in the presence of a suitable base and in a suitable solvent to form the compound of Formula (IA)



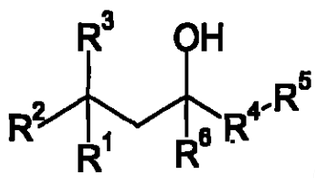
XXXIV (IA) , or

(f2") N-deprotecting of the compound of Formula (XXXIV) by reaction with a suitable acid in a suitable solvent to form an amine salt, followed by cyclizing of the amine salt in the presence of a suitable base and in a suitable solvent to form the compound of Formula (IA)



XXXIV (IA)

41. A method of making a compound of Formula (IB)

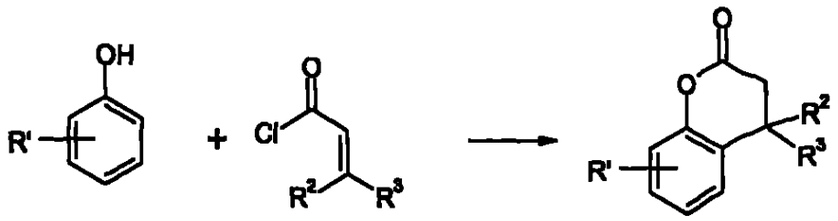


(IB)

where R^1, R^2, R^3, R^4, R^5, and R^6 are as defined in claim 13, the method comprising:

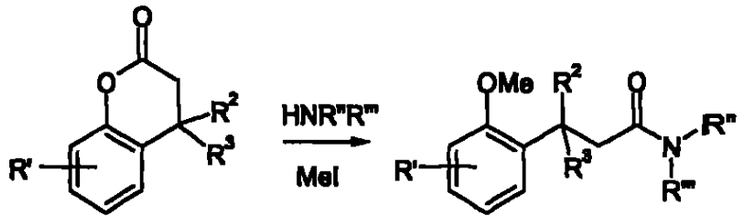
(a) reacting an optionally substituted phenol of Formula (XV) with an acryloyl chloride of Formula (XVI) in the presence of a suitable base, followed by cyclization of the

intermediate ester by treatment with a suitable Lewis acid to form a lactone of Formula (XVII)



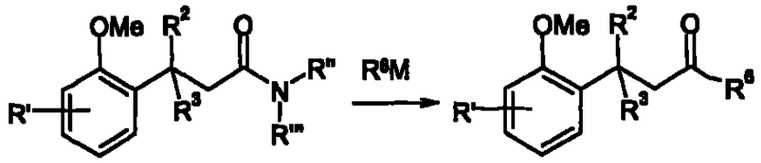
XV XVI XVII ;

(b) reacting the lactone of Formula (XVII) with a suitable amine HNR'R'', followed by treatment of the intermediate phenol with methyl iodide in the presence of a suitable base to form an amide of Formula (XVIII)



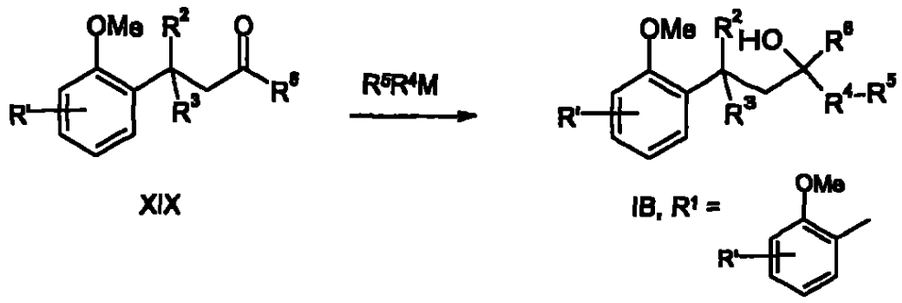
XVII XVIII ;

(c) reacting the amide of Formula (XVIII) with a suitable organometallic reagent R^6M, where M is Li or MgX and X is Cl, Br, or I, in a suitable solvent to form a ketone of Formula (XIX)



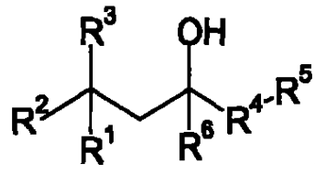
XVIII XIX ;

(d) reacting the ketone of Formula (XIX) with a suitable organometallic reagent R^5R^4M where M is Li or MgX and X is Cl, Br, or I, in a suitable solvent to form the compound of Formula (IB)



XIX IB, R^1 =

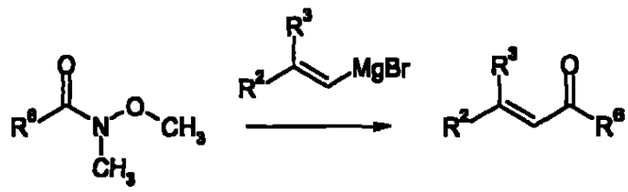
42. A method of making a compound of Formula (IB)



(IB)

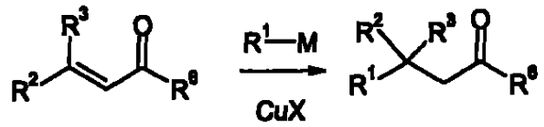
where R^1, R^2, R^3, R^4, R^5, and R^6 are as defined in claim 13, the method comprising:

(a') reacting an amide of Formula (XXXVI) with a vinyl magnesium bromide compound bearing R^2 and R^3 in a suitable solvent to provide an enone of Formula (XXXVII)



XXXVI XXXVII ;

(b') reacting the enone of Formula (XXXVII) with a suitable organocopper reagent generated from an organometallic reagent R^1M, where M is Li or MgX, and a copper salt CuX, where X is Cl, Br, or I, in a suitable solvent to form a ketone of Formula (XX)



XXXVII XX ; and

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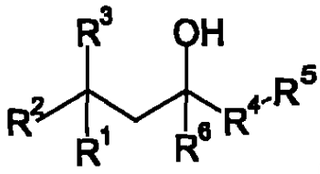
602

(c') reacting the ketone of Formula (XX) with a suitable organometallic reagent R^5R^4M, where M is Li or MgX, and X is Cl, Br, or I, in a suitable solvent to form the compound of Formula (IB)

XX IB

43. A method of making a compound of Formula (IB)



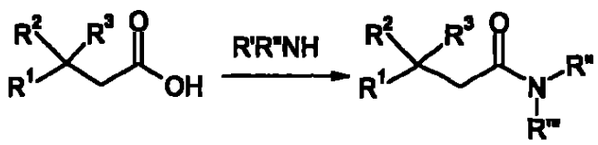
(IB)

where R^1, R^2, R^3, R^4, R^5, and R^6 are as defined in claim 13, the method comprising:

(a") reacting a ketone of Formula (IV) with a suitable base and in a suitable solvent mixture to provide an acid of Formula (XXIX)

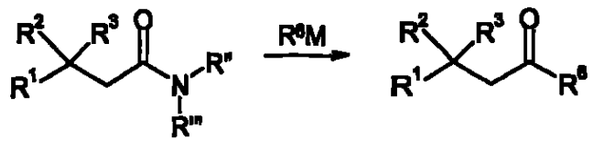
IV XXIX ;

(b") reacting the acid of Formula (XXIX) with a suitable amine HNR"R"', such that -NR"R"' will function as a leaving group in the subsequent reaction, under suitable coupling conditions to form the amide of Formula (XXX)



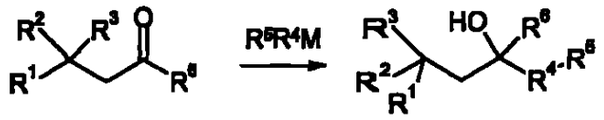
XXIX XXX ;

(c") reacting the amide of Formula (XXX) with a suitable organometallic reagent, such as a Grignard reagent, where M is MgBr or MgCl, or an organolithium reagent, where M is Li, in a suitable solvent to provide a ketone of Formula (XX)



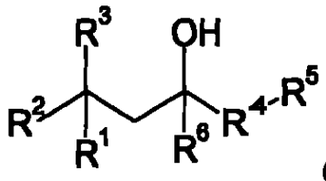
XXX XX ; and

(d") reacting the ketone of Formula (XX) with a suitable organometallic reagent R^5R^4M, where M is Li or MgX, and X is Cl, Br, or I, in a suitable solvent to form the compound of Formula (IB)



XX IB

44. A method of making a compound of Formula (IC)



(IC)

where R^1, R^2, R^3, R^4, R^5, and R^6 are as defined in claim 19, the method comprising:

(a) reacting an ester of Formula (II) with a suitable reducing agent in a suitable solvent to form a diol of Formula (III)

II III

(b) reacting the diol of Formula (III) with a suitable alkyl or aryl sulfonyl chloride reagent, such that $R'SO_2O$ functions as a leaving group in the next step, followed by reacting the resulting intermediate with a suitable base to provide an epoxide of Formula (V)

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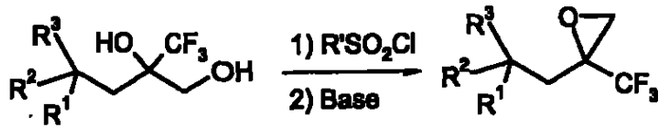
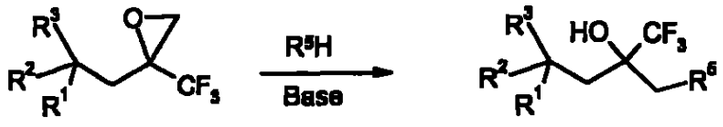


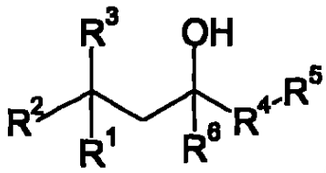
III V ;

(c) reacting the epoxide of Formula (V) with an appropriate nucleophile R^5H, in the presence of a suitable base, to provide the compound of Formula (IC)



V IC .

45. A method of making a compound of Formula (IC)



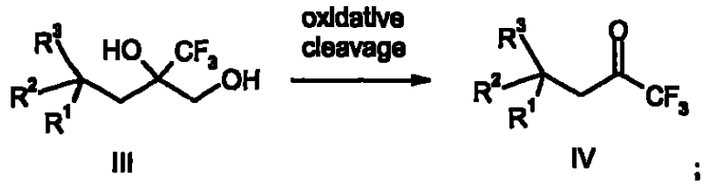
(IC)

where R^1, R^2, R^3, R^4, R^5, and R^6 are as defined in claim 19, the method comprising:

(a') reacting an ester of Formula (II) with a suitable reducing agent in a suitable solvent to form a diol of Formula (III)

II III ;

(b') reacting the diol of Formula (III) under suitable oxidative cleavage conditions to form a ketone of Formula (IV)

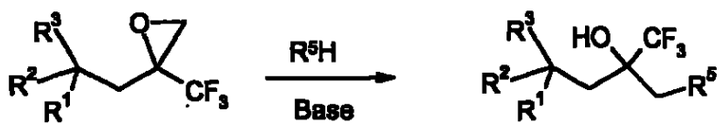


III IV ;

(c') reacting the ketone of Formula (IV) with a suitable epoxidizing reagent, such as a suitable sulfur ylide, in a suitable solvent to provide an epoxide of Formula (V)

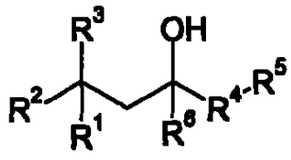
; and

(d') reacting the epoxide of Formula (V) with an appropriate nucleophile R^5H, in the presence of a suitable base, to provide the compound of Formula (IC)



V IC

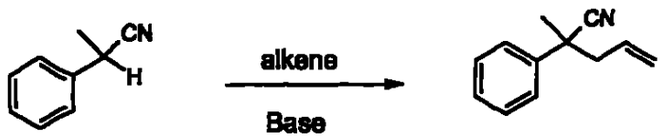
46. A method of making a compound of Formula (ID)



(ID)

where R^1, R^2, R^3, R^4, R^5, and R^6 are as defined in claim 26, the method comprising:

(a) reacting a cyano compound of Formula (XXXVIII) with a suitable alkene in the presence of a suitable base to provide an alkene of Formula (XXXIX)



XXXVIII XXXIX ;

(b) reacting the alkene of Formula (XXXIX) with a suitable reducing agent to provide an aldehyde of Formula (XXXX)

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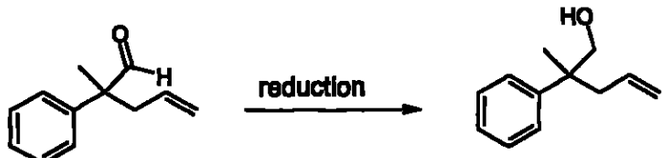
606

XXXIX XXXX ;

(c) reacting the aldehyde of Formula (XXXX) with a suitable reducing agent to provide an alcohol of Formula (XXXXI)

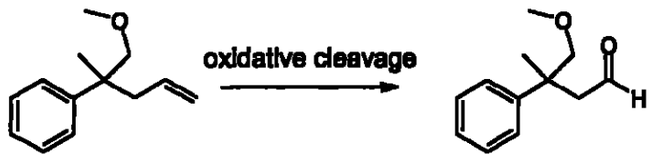


XXXX XXXXI ;

(d) reacting the alcohol of Formula (XXXXI) with a suitable alkylating agent in the presence of a suitable base to provide an ether of Formula (XXXXII)

XXXXI XXXXII ;

(e) reacting the ether of Formula (XXXXII) under suitable oxidative cleavage conditions to provide an aldehyde of Formula (XXXXIII)



XXXXII XXXXIII ;

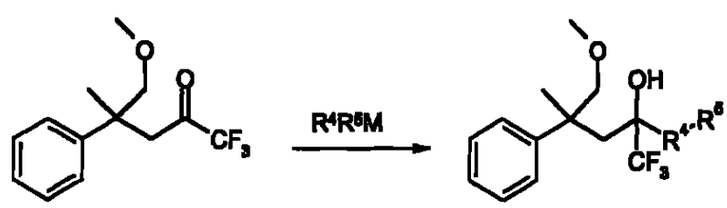
(f) reacting the aldehyde of Formula (XXXXIII) with a suitable nucleophilic trifluoromethylating reagent to provide the trifluoromethyl alcohol of Formula (XXXXIV)

XXXXIII XXXXIV ;

(g) reacting the trifluoromethyl alcohol of Formula (XXXXIV) with a suitable oxidizing reagent to provide the trifluoromethylketone of Formula (XXXXV)

XXXXIV XXXXV ; and

(h) reacting the ketone of Formula (XXXXV) with a suitable organometallic reagent R^5R^6M, where M is Li or MgX, and X is Cl, Br, or I,in a suitable solvent to form the compound of Formula (ID)



XXXXV ID

MIMÉTICOS DE GLUCOC RTICOIDES, MÉTODOS DE PREPARACIÓN, COMPOSICIONES FARMACÉUTICAS Y USOS DE LOS MISMOS

Campo de la Invención

La presente invención se refiere a miméticos o ligandos de glucocorticoides, métodos de preparación de tales compuestos, su uso en composiciones farmacéuticas, y su uso para modular la función del receptor de glucorticoides, tratar estados o cuadros de enfermedad mediados por la función del receptor de glucocorticoides en un paciente con necesidad de tal tratamiento, y otros usos.

Antecedentes de la Invención

Los glucocorticoides, una clase de corticosteroides, son hormonas endógenas con un fuerte efecto sobre el sistema inmune y múltiples sistemas orgánicos. Ellos suprimen una cantidad de funciones inmunes e inflamatorias mediante la inhibición de citoquinas inflamatorias, tales como, IL-1, IL-2, IL-6, y TNF, la inhibición de metabolitos del ácido araquidónico incluyendo prostaglandinas y leucotrienos, la supresión de linfocitos T y la reducción de la expresión de moléculas de adhesión en células endoteliales (P.J. Barnes, Clin. Sci., 1998, 94, pp. 557-572; P.J. Barnes *et al.*, Trends Pharmacol. Sci., 1993, 14, pp. 436-441). Adicionalmente a estos efectos, los glucocorticoides estimulan la producción de glucosa en el hígado y el catabolismo de las proteínas, influyen en el balance electrolítico y del agua, reducen la absorción de calcio e inhiben la función de los osteoblastos.

Las actividades anti-inflamatorias e inmunosupresoras de los glucocorticoides endógenos estimularon el desarrollo de derivados de glucocorticoides sintéticos incluyendo dexametasona, prednisona y prednisolona (L. Parente, Glucocorticoids, N.J. Goulding y R.J. Flowers (eds.), Boston: Birkhauser, 2001, pp. 35-54). Estos han sido de amplia aplicación en el tratamiento de trastornos inflamatorios, inmunes y alérgicos, incluyendo enfermedades reumáticas, tales como artritis reumatoidea, artritis juvenil y espondilitis anquilosante, enfermedades dermatológicas incluyendo psoriasis y pénfigo, trastornos alérgicos incluyendo rinitis alérgica, dermatitis atópica y dermatitis de contacto, enfermedades pulmonares incluyendo asma y la enfermedad de obstrucción pulmonar crónica (COPD) y otras enfermedades inmunes e inflamatorias incluyendo la enfermedad de Crohn, colitis ulcerativa, lupus eritematoso sistémico, hepatitis activa crónica autoinmune, osteoartritis, tendinitis y bursitis (J. Toogood, Glucocorticoids, N.J. Goulding y R.J. Flowers (eds.), Boston: Birkhauser, 2001, pp. 161-174). Se han utilizado asimismo para ayudar a prevenir el rechazo en el transplante de órganos.

Desafortunadamente, además de los efectos terapéuticos deseados de los glucocorticoides, su uso está asociado a una cantidad de efectos colaterales adversos,

de los cuales algunos pueden ser graves y poner en peligro la vida. Estos incluyen alteraciones en el balance de fluidos y electrolítico, edemas, aumento de peso, hipertensión, flojedad muscular, desarrollo o agravamiento de la diabetes mellitus y osteoporosis. Por lo tanto, sería particularmente deseable un compuesto que presentara un perfil con efectos colaterales reducidos, mientras que el mantenimiento de los poderosos efectos antiinflamatorios sería particularmente deseable, en especial al tratar una enfermedad crónica.

Los efectos de los glucocorticoides son mediados a nivel celular por el receptor de glucocorticoides (R.H. Oakley y J. Cidlowski, Glucocorticoids, N.J. Goulding y R.J. Flowers (eds.), Boston: Birkhauser, 2001, pp. 55-80). El receptor de glucocorticoides forma parte de una clase de receptores intracelulares relacionados estructuralmente que al acoplarse con un ligando pueden funcionar como un factor de transcripción que afecta la expresión génica (R.M. Evans, Science, 1988, 240, pp. 889-895). Otros miembros de la familia de los receptores esteroides incluyen los receptores de mineralocorticoides, de progesterona, de estrógenos y de andrógenos. Además de los efectos previamente mencionados para los glucocorticoides, las hormonas que actúan sobre la familia de este receptor ejercen una profunda influencia sobre la homeostasis del cuerpo, el metabolismo de los minerales, la respuesta al estrés y el desarrollo de las características sexuales. Glucocorticoids, N.J. Goulding y R.J. Flowers (eds.), Boston: Birkhauser, 2001, se incorpora aquí en su totalidad a título de referencia para describir mejor el estado dla técnica.

Se propuso un mecanismo molecular que da cuenta de los efectos antiinflamatorios beneficiosos y los efectos colaterales no deseados (p.ej., S. Heck *et al.*, EMBO J, 1994, 17, pp. 4087-4095; H.M. Reichardt *et al.*, Cell, 1998, 93, pp. 531-541; F. Tronche *et al.*, Curr. Opin. en Genetics y Dev., 1998, 8, pp. 532-538). Se cree que muchos de los efectos colaterales metabólicos y cardiovasculares son el resultado de un proceso llamado transactivación. En la transactivación, la traslocación del receptor de glucocorticoides unido a un ligando al núcleo es seguida por la unión de elementos de respuesta a glucocorticoides (GREs) en la región promotora de genes asociados a efectos colaterales, por ejemplo la fosfoenolpiruvato carboxi quinasa (PEPCK), en el caso de producción aumentada de glucosa. El resultado es un índice aumentado de transcripción de estos genes que, se cree, da lugar finalmente a los efectos colaterales observados. Se cree que los efectos antiinflamatorios se deben a un proceso llamado transrepresión. En general, la transrepresión es un proceso independiente de la unión al ADN que resulta de la inhibición de vías mediadas por NF-kB y AP-1, llevando a regular

por disminución muchos de los mediadores inflamatorios e inmunes. Además, se cree que una cantidad de los efectos colaterales observados puede deberse a la reactividad cruzada de los glucocorticoides actualmente disponibles con otros receptores esteroides, particularmente los receptores de mineralcorticoides y de progesterona.

Así, puede ser posible descubrir ligandos para los receptores de glucocorticoides que sean altamente selectivos y, al unirse, puedan disociar las vías de transactivación y transrepresión, brindando agentes terapéuticos con un perfil de efectos colaterales reducido. Se han descripto sistemas de ensayo para determinar los efectos sobre la transactivación y la transrepresión (p.ej., C.M. Bamberger y H.M. Schulte, Eur. J. Clin. Invest., 2000, 30 (suppl. 3), pp. 6-9). Puede determinarse la selectividad para el receptor de glucocorticoides comparando la afinidad de unión por este receptor con la de otros receptores de familias de esteroides, incluyendo los mencinados anteriormente.

Los glucocorticoides también estimulan la producción de glucosa en el hígado mediante un proceso llamado gicuconeogénesis y se cree que este proceso es mediado por eventos de transactivación. La mayor producción de glucosa puede estimular la diabetes tipo II, por esa razón un compuesto que inhiba selectivamente la producción de glucosa mediada por glucocorticoides puede ser de utilidad terapéutica en esta indicación (J.E. Freidman *et al.*, J. Biol. Chem., 1997, 272, pp. 31475-31481).

Se han descripto nuevos ligandos para el receptor de glucocorticoides en la bibliografía científica y de patentes. Por ejemplo, la Publicación Internacional PCT Nº WO 99/33786 revela compuestos de trifenilpropanamida con potencial aplicación en el tratamiento de enfermedades inflamatorias. La Publicación Internacional PCT Nº WO 00/66522 describe compuestos no esteroidales como moduladores selectivos del receptor de glucocorticoides potencialmente útiles para el tratamiento de enfermedades metabólicas e inflamatorias. La Publicación Internacional PCT Nº WO 99/41256 describe moduladores tetracíclicos del recptor glucocorticoide con potencial utilidad para el tratamiento de enfermedades inflamatorias, autoinmunes e inmunes. La Patente Norteamericana U.S. Nº 5,688,810 describe diferentes compuestos no esteroidales como moduladores de receptores de glucocorticoides y otros esteroides. La Publicación Internacional PCT Nº WO 99/63976 describe un antagonista de glucocorticoides no esteroide selectivo del hígado potencialmente útil para el tratamiento de la diabetes. La Publicación Internacional PCT Nº WO 00/32584 revela compuestos no esteroides que presentan actividad anti-inflamatoria con disociación entre los efectos anti-inflamatorios y metabólicos. La Publicación Internacional PCT Nº WO 98/54159 describe acilanilidas ciclicamente sustituidas no esteroides con actividad mixta de gestágenos y andrógenos.

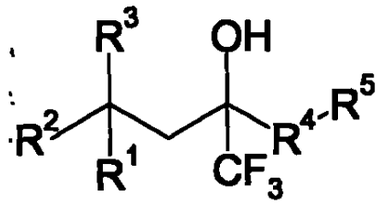
La Patente Norteamerica U.S. Nº 4,880,839 describe acilanilidas que presentan actividad progestacional y la EP 253503 revela acilanilidas con propiedades antiandrogénicas. La Publicación Internacional PCT Nº WO 97/27852 describe amidas que son inhibidoras de la farnesil-proteína transferasa.

Un compuesto que interactúa con el receptor de glucocorticoides en un ensayo de unión puede ser un agonista o un antagonista. Las propiedades agonistas del compuesto pueden ser evaluadas en los ensayos de transactivación o transrepresión previamente descriptos. Dada la eficacia demostrada por los medicamentos glucocorticoides disponibles para enfermedades inflamatorias e inmunes y sus efectos colaterales adversos, se mantiene la necesidad de contar con nuevos agonistas de receptores de glucocorticoides con selectividad sobre otros miembros de la familia de receptores de esteroides y una disociación de las actividades de transactivación y transrepresión. Alternativamente, se puede encontrar que el compuesto presenta actividad antagonista. Como se mencionó previamente, los glucocorticoides estimulan la producción de glucosa en el hígado. La mayor producción de glucosa inducida por el exceso de glucocorticoides puede exacerbar la diabetes existente o desencadenar una diabetes latente. Así, un ligando para el receptor de glucocorticoides que se descubrió como antagonista, puede ser útil, por lo tanto, para el tratamiento o la prevención de la diabetes.

Las solicitudes previas Acta U.S. Nº 60/367.798, presentada el 26 de marzo de 2002, Acta U.S. Nº 60/431.817, presentada el 12 de diciembre de 2002, Acta U.S. Nº 60/442.404 presentada el 24 de enero de 2003, y la solicitud de patente Norteamericana U.S. Pub. Nº 2004/0023999, se incorporan, cada una en su totalidad, a título de referencia.

Breve Descripción de la Invención

La presente invención está dirigida a compuestos de Fórmula (IA)



(IA)

donde:

R^1 es un grupo arilo o heteroarilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, cicloalquilo C_3-C_8, heterocicilo, arilo, heteroarilo,

alcoxi C_1-C_8, alqueniloxi C_2-C_8, alquiniloxi C_2-C_8, ariloxi, acilo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_8, alcanoilo C_1-C_8, aroilo, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilaminocarboniloxi C_1-C_8, dialquilaminocarboniloxi C_1-C_8, alcanoilamino C_1-C_8, alcoxicarbonilamino C_1-C_8, alquilsulfonilamino C_1-C_8, aminosulfonilo, alquilaminosulfonilo C_1-C_8, dialquilaminosulfonilo C_1-C_8, halógeno, hidroxi, carboxi, ciano, trifluorometilo, trifluorometoxi, nitro, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_8; o alquiltio C_1-C_8 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^1 está en forma opcional independientemente sustituido con uno a tres grupos sustituyentes seleccionados de metilo, metoxi, halógeno, hidroxi, oxo, ciano, heteroarilo, heterociclilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_8;

R^2 y R^3 son cada uno independientemente hidrógeno o alquilo C_1-C_8, o R^2 y R^3 junto con el átomo de carbono al que están unidos usualmente forman un anillo espiro cicloalquilo C_3-C_8;

R^4 es alquilo C_1-C_8, alquenilo C_2-C_8, o alquinilo C_2-C_8, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^4 es independientemente alquilo C_1-C_3, hidroxi, halógeno, amino, u oxo; y

R^5 es un grupo heteroarilo independientemente sustituido en forma opcional con uno a tres grupos sustituyentes ,

donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, cicloalquilo C_3-C_8, heterociclilo, arilo, heteroarilo, alcoxi C_1-C_8, alqueniloxi C_2-C_8, alquiniloxi C_2-C_8, ariloxi, acilo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_8, heterociclilcarbonilo, aroilo, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilaminocarboniloxi C_1-C_8, dialquilaminocarboniloxi C_1-C_8, alcanoilamino C_1-C_8, alcoxicarbonilamino C_1-C_8, alquilsulfonilamino C_1-C_8, aminosulfonilo, alquilaminosulfonilo C_1-C_8, dialquilaminosulfonilo C_1-C_8, halógeno, hidroxi, carboxi,

ciano, trifluorometilo, trifluorometoxi, trifluorometiltio, nitro o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_3; o alquiltio C_1-C_6 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^5 está independientemente sustituido en forma opcional con uno a tres grupos sustituyentes seleccionados de alquilo C_1-C_3, alcoxi C_1-C_3, acilo, silaniloxi C_1-C_3, alcoxicarbonilo C_1-C_5, carboxi, halógeno, hidroxi, oxo, ciano, arilo, heteroarilo, heterociclilo o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_3, o trifluorometilo,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto de la invención incluye compuestos de Fórmula (IA), donde:

R^1 es tienilo, fenilo, naftilo, dihidrobenzofuranilo, benzofuranilo, cromanilo, dihidroindolilo, indolilo, dihidrobenzotienilo, benzotienilo, benzodioxolanilo, dihidrobenzoxazolilo, benzoxazolilo, benzoisoxazolilo, benzopirazolilo, benzoimidazolilo, tienilo, quinolinilo, piridinilo, pirimidinilo o pirazinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, heterociclilo, trifluorometilo, trifluorometoxi, nitro, amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_6, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^1 está en forma opcional independientemente sustituido con un grupo sustituyente seleccionado de metilo, metoxi, halógeno, hidroxi, oxo, ciano o amino;

R^2 y R^3 son cada uno independientemente hidrógeno o alquilo C_1-C_3, o R^2 y R^3 junto con el átomo de carbono al que están unidos usualmente forman un anillo espiro cicloalquilo C_3-C_6;

R^4 es CH_2; y

R^5 es un grupo imidazolilo, piridilo, indolilo, indazolilo, azaindolilo, diazaindolilo, benzofuranilo, furanopiridinilo, furanopirimidinilo, imidazolopirimidinilo, imidazolopiridazinilo, imidazolopirazinilo, benzotienilo, tienopiridinilo, tienopirimidinilo, tienopiridazinilo, benzoxazolilo, oxazolopiridinilo, benzotiazolilo, tiazolopiridinilo, benzoimidazolilo, imidazolopiridinilo, quinolinilo o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, fenilo, alcoxi C_1-C_3, metoxicarbonilo, aminocarbonilo, alquilaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, heterociclilcarbonilo, hidroxi, oxo, fluoro, cloro, bromo, ciano, trifluorometilo, amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_6, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^5 está en forma opcional independientemente sustituido con un grupo sustituyente seleccionado de metilo, metoxi, fluoro, cloro, bromo, oxo, o trifluorometilo, hidroxi, ciano, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_5 o arilo,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto más de la invención incluye compuestos de Fórmula (IA), donde:

R^1 es tienilo, fenilo, naftilo, piridilo, cromanilo, dihidrobenzofuranilo o benzofuranilo, cada uno en forma opcional independientemente sustituido con uno o dos grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente metilo, etilo, metoxi, etoxi, fluoro, cloro, bromo, hidroxi, trifluorometilo, trifluorometoxi, ciano o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona;

R^2 y R^3 son cada uno independientemente metilo o etilo, o R^2 y R^3 junto con el átomo de carbono al que están unidos usualmente forman un anillo espiro ciclopropilo;

R^4 es CH_2; y

R^5 es un grupo piridilo, indolilo, azaindolilo, diazaindolilo, benzofuranilo, furanopiridinilo, tienopiridinilo, benzoxazolilo, benzoimidazolilo, quinolinilo, o isoquinolinilo, cada uno

sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^6 es independientemente metilo, fenilo, metoxi, etoxi, isopropoxi, metoxicarbonilo, aminocarbonilo, metilaminocarbonilo, dimetilaminocarbonilo, morfolinilcarbonilo, morfolinilo, piperidinilo, trifluorometilo, fluoro, cloro, bromo, hidroxi, ciano o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_5 o arilo o trifluorometilo,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto más de la invención incluye compuestos de Fórmula (IA), donde:

R^1 es fenilo, dihidrobenzofuranilo, o benzofuranilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona; y

R^2 y R^3 son cada uno independientemente hidrógeno o alquilo C_1-C_3,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto más de la invención incluye compuestos de Fórmula (IA), donde:

R^6 es un grupo piridilo, indolilo, azaindolilo, diazaindolilo, benzofuranilo, furanopiridinilo, tienopiridinilo, benzoxazolilo, benzoimidazolilo, quinolinilo, o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto de la invención incluye compuestos de Fórmula (IA), donde:

R^1 es tienilo, fenilo, naftilo, dihidrobenzofuranilo, benzofuranilo, cromanilo, dihidroindolilo, indolilo, dihidrobenzotienilo, benzotienilo, benzodioxolilo, dihidrobenzoxazolilo, benzoxazolilo, bencisoxazolilo, benzopirazolilo, benzoimidazolilo, tienilo, quinolinilo, piridinilo, pirimidinilo o pirazinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente C_1-C_3 alquilo, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, arilo, heteroarilo, halógeno, hidroxi,

carboxi, ciano, heterocicilio, trifluorometilo, trifluorometoxi, nitro, aminosulfonilo, dialquilaminosulfonilo, amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_5 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_5, o alquiltio C_1-C_2 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^1 está en forma opcional independientemente sustituido con uno o dos grupos sustituyentes seleccionados de metilo, metoxi, halógeno, hidroxi, oxo, ciano, morfolinilo o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_5;

R^2 y R^3 son cada uno independientemente hidrógeno o alquilo C_1-C_3, o R^2 y R^3 junto con el átomo de carbono al que están unidos usualmente forman un anillo espiro cicloalquilo C_3-C_6;

R^4 es CH_2; y

R^5 es un grupo imidazolilo, piridilo, indolilo, indazolilo, azaindolilo, diazaindolilo, benzofuranilo, furanopiridinilo, furanopirimidinilo, imidazolopirimidinilo, imidazolopiridazinilo, imidazolopirazinilo, benzotienilo, tienopiridinilo, tienopirimidinilo, tienopiridazinilo, benzoxazolilo, oxazolopiridinilo, benzotiazolilo, tiazolopiridinilo, benzoimidazolilo, imidazolopiridinilo, quinolinilo o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, fenilo, heteroarilo, heterocicilio, acilo, dialquilaminosulfonilo, alcoxi C_1-C_3, metoxicarbonilo, aminocarbonilo, alquilaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, heterocicilcarbonilo, hidroxi, oxo, fluoro, cloro, bromo, ciano, trifluorometilo, amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_5 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_5; o alquiltio C_1-C_2 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^5 está en forma opcional independientemente sustituido con uno o dos grupos sustituyentes seleccionados de metilo, metoxi, fluoro, cloro, bromo, oxo, trifluorometilo, hidroxi, ciano, morfolinilo, pirrolidinilo o amino donde el átomo de nitrógeno en

forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto más de la invención incluye compuestos de Fórmula (IA), donde:

R^1 es tienilo, fenilo, naftilo, piridilo, cromanilo, benzodioxolilo, dihidrobenzofuranilo, o benzofuranilo, cada uno en forma opcional independientemente sustituido con uno o dos grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente metilo, etilo, metoxi, etoxi, fluoro, cloro, bromo, hidroxi, trifluorometilo, trifluorometoxi, morfolinilmetilo, dimetilaminometilo, aminosulfonilo, dimetilaminosulfonilo, fenilo, pirimidinilo, piridinilo, tienilo, naftalenilo, morfolinilo, piperidinilo, ciano, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^1 está en forma opcional independientemente sustituido con uno o dos grupos seleccionados de ciano, cloro, bromo o fluoro;

R^2 y R^3 son cada uno independientemente metilo o etilo, o R^2 y R^3 junto con el átomo de carbono al que están unidos usualmente forman un anillo espiro ciclopropilo;

R^4 es CH_2; y

R^5 es un grupo piridilo, indolilo, azaindolilo, diazaindolilo, benzofuranilo, tienopiridazinilo, furanopiridinilo, tienopiridinilo, benzoxazolilo, benzoimidazolilo, quinolinilo o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente metilo, fenilo, metoxi, etoxi, isopropoxi, metoxicarbonilo, aminocarbonilo, metilaminocarbonilo, dimetilaminocarbonilo, morfolinilcarbonilo, morfolinilo, piperidinilo, fenoxi, pirrolidinilo, acetilo, pivaloilo, etilcarbonilo, isopropilcarbonilo, piridinilo, pirimidinilo, trifluorometilo, fluoro, cloro, bromo, hidroxi, ciano o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con C_1-C_6 alquilo o arilo o trifluorometilo,

donde cada grupo sustituyente de R^5 está en forma opcional independientemente sustituido con uno o dos grupos sustituyentes seleccionados de ciano, halógeno, metilo, dimetilamino, morfolinilo, pirrolidinilo, o piperidinilo,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto más de la invención incluye compuestos de Fórmula (IA), donde:

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R^1 es fenilo, dihidrobenzofuranilo o benzofuranilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona; y

R^2 y R^3 son cada uno independientemente hidrógeno o alquilo C_1-C_3,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto más de la invención incluye compuestos de Fórmula (IA), donde:

R^5 es un grupo piridilo, indolilo, azaindolilo, diazaindolilo, benzofuranilo, tienopiridazinilo furanopiridinilo, tienopiridinilo, benzoxazolilo, benzoimidazolilo, quinolinilo o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Los compuestos representativos de Fórmula (IA) de acuerdo con la invención se agregan aquí como Tabla IA, donde la columna A es la denominación del compuesto de acuerdo a la nomenclatura estándar y la columna B es la correspondiente estructura química.

Los compuestos preferidos de Fórmula (IA) incluyen los siguientes:

4-ciclohexil-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

4-pirimidin-5-il-2[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(1H-pirrolo[2,3-c]piridin-2-ilmetil)butil]fenol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(3-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(3-metil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

2-(4,6-Dimetil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

2-(5,7-Dimetil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-pirrolo[3,2-*c*]piridina-6-carbonitrilo;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-*c*]piridina-5-carbonitrilo;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*c*]piridina-4-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-tieno[2,3-*d*]piridazin-2-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(2-metil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(1*H*-pirrolo[2,3-*d*]piridazin-2-ilmetil)pentan-2-ol;

2-(4,6-Dimetil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(4,6-dimetil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*d*]piridazin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(7-fluoro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(5,7-Dicloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5-trifluorometil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(5-metoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(5-metoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(5-metoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(7-fluoro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-trifluorometil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5-trifluorometil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(7-fluoro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(5-dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

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1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(5-etoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

2-(5-Benciloxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

2-(5-Benciloxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(5-cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-[5-(metilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5-amino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(6-amino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(5-amino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-metilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

Cloruro de 7-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-*b*]piridin-7-io;

Cloruro de 6-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-2-metil-1*H*-pirrolo[2,3-*c*]piridin-6-io;

4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(5-metil-2,3-dihidrobenzofuran-7-il)-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-pirrolo[2,3-*b*]piridin-1-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(6-oxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-pirrolo[2,3-*c*]piridin-1-ilmetilpentan-2-ol;

2-Benzo[*b*]tiofen-2-ilmetil-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-tieno[2,3c]piridin-2-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-indazol-1-ilmetil-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-[4-((Z)propenil)-3-vinilpirazol-1-ilmetil]pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-pirazolo[1,5-*a*]piridin-2-ilmetilpentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,4-dimetil-1-tieno[2,3-*c*]piridin-2-ilpentan-2-ol;
4-(5-Fluoro-2-metilfenil)-2,4-dimetil-1-tieno[2,3-*c*]piridin-2-ilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-furo[2,3-*c*]piridin-2-ilmetil-4-metilpentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1-furo[2,3-*c*]piridin-2-il-2,4-dimetilpentan-2-ol;
4-(5-Fluoro-2-metilfenil)-1-furo[2,3-*c*]piridin-2-il-2,4-dimetilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-metil-4-(5-metil-2,3-dihidrobenzofuran-7-il)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
2-(3-Dimetilaminometil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-pirrolo[3,2-*c*]piridin-1-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-furo[3,2-*c*]piridin-2-ilmetil-4-metilpentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;
1,1-Difluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-tieno[3,2-c]piridin-2-ilmetilpentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-tieno[3,2-*c*]piridin-2-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-tieno[3,2-*c*]piridin-2-ilmetilpentan-2-ol;
4-Fluoro-2-(4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-tieno[3,2-*c*]piridin-2-ilmetilbutil)fenol;
4-Fluoro-2-(4,4,4-trifluoro-3-furo[3,2-*c*]piridin-2-ilmetil-3-hidroxi-1,1-dimetilbutil)fenol;

4-Fluoro-2-(4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-pirrolo[3,2-*b*]piridin-1-ilmetilbutil)fenol;

Ácido 2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carboxílico;

Dimetilamida del ácido 2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carboxílico;

{2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-il}morfolin-4-ilmetanona;

Dimetilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carboxílico;

Dimetilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-il}morfolin-4-ilmetanona;

2-[4-(2,3-Dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

Amida del ácido 2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carboxílico;

Amida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carboxílico;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-nitro-1*H*-indol-2-ilmetil)butil]fenol;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carbonitrilo;

2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carbonitrilo;

N-[2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}acetamida;

1,1,1-Trifluoro-4-(4-fluoro-2-metoxifenil)-2-(7-fluoro-4-metil-1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-(7-fluoro-4-metil-1*H*-indol-2-ilmetil)-3-hidroxi-1,1-dimetilbutil]fenol;

2-[4-(3-[1,3]Dioxolan-2-ilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonitrilo;

2-Trimetilsililetil éster del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

2-[4-(4-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}piperidin-1-ilmetanona;

Metilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}pirrolidin-1-ilmetanona;

1-{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}piperidin-4-ona;

(2-hidroxietil)amida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}(4-hidroxipiperidin-1-il)metanona;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}(3-hidroxipirrolidin-1-il)metanona;

Cianometilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

(2-Dimetilaminoetil)amida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}(4-metilpiperazin-1-il)metanona;

Metil éster del ácido ({2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}amino)acético;

Carbamoilmetilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Metil éster del ácido 4-({2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}amino)butírico;

Ácido ({2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}amino)acético;

Ácido 4-({2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}amino)butírico;

2-[4-(3-Dimetilaminometilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonitrilo;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-trifluorometil-1*H*-indol-2-ilmetil)butil]fenol;

2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

Ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Amida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Dimetilamida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Clanometilamida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}pirrolidin-1-ilmetanona;

{2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}morfolin-4-ilmetanona;

Amida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}morfolin-4-ilmetanona;

2-(4-Benzo[1,3]dioxol-4-il-2-hidroxi-4-metil-2-trifluorometilpentil)-4-metil-1*H*-indol-6-carbonitrilo;

1,1,1-Trifluoro-4-metil-4-fenil-2-quinolin-4-ilmetilhexan-2-ol;

2-[2-Hidroxi-4-metil-4-(5-metilsulfanil-2,3-dihidrobenzofuran-7-il)-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

7-(4,4,4-Trifluoro-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)-2,3-dihidrobenzofuran-5-carbonitrilo;

2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(2-hidroxi-5-metilfenil)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-metilsulfanil-1*H*-indol-2-ilmetil)pentan-2-ol;

2-[2-Hidroxi-4-(2-metoxi-5-metilsulfanilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(5-metansulfonil-2-metoxifenil)-4-metil-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo;

Dimetilamida del ácido 2-[4-(5-Fluoro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-sulfónico;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-fenil-1*H*-indol-2-ilmetil)pentan-2-ol;

2-[4-(5-*ter*-Butil-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(2-hidroxi-5-isopropilfenil)-4-metil-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(2-hidroxi-3,5-dimetilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(5-hidroxi-2,4-dimetilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[4-(5-*ter*-Butil-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[4-(5-*ter*-Butil-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1-metil-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(5-isopropil-2-metoxifenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(5-isopropil-2-metoxifenil)-4-metil-2-trifluorometilpentil]-1-metil-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(2-hidroxi-5-metansulfonilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(2-metoxi-5-metilfenil)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*o*-tolilpentan-2-ol;

1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*m*-tolilpentan-2-ol;

1,1,1-Trifluoro-4-(2-fluorofenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(2-fluorofenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorofenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorofenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
3-(4,4,4-Trifluoro-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)fenol;
1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-(2-trifluorometilfenil)pentan-2-ol;
1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-(4-trifluorometilfenil)pentan-2-ol;
1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-(4-trifluorometilfenil)pentan-2-ol;
4-(3-Clorofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
4-(3-Clorofenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(4-Dimetilaminofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
4-Bifenil-3-il-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(3-Bromofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
4-(2-Difluorometoxi-5-fluorofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
4-Bifenil-3-il-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
4-(4-Dimetilaminofenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,6-dihidropirrolo[2,3-*c*]piridin-5-ona;
2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-6-metil-1,6-dihidropirrolo[2,3-*c*]piridin-5-ona;
2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1,4-dihidropirrolo[3,2-*b*]piridin-5-ona;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(6-metoxi-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;
2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-5-metil-1,5-dihidropirrolo[3,2-*c*]piridin-6-ona;
2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,3a-dihidropirrolo[3,2-*c*]piridin-6-ona;
2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,7-dihidropirrolo[3,2-*c*]piridina-4,6-diona;
6-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-3-metil-1,7-dihidropirrolo[2,3-*d*]pirimidina-2,4-diona;
2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,6-dihidropirrolo[2,3-*c*]piridin-5-ona;
2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-6-metil-1,6-dihidropirrolo[2,3-*c*]piridin-5-ona;
2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,4-dihidropirrolo[3,2-*b*]piridin-5-ona;

2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1,4-dihidropirrolo[3,2-*b*]piridin-5-ona;

2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,5-dihidropirrolo[3,2-*c*]piridin-6-ona;

2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-5-metil-1,5-dihidropirrolo[3,2-*c*]piridin-6-ona;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(6-metoxi-5,6-dihidro-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,7-dihidropirrolo[3,2-*c*]piridina-4,6-diona;

6-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-3-metil-1,7-dihidropirrolo[2,3-*d*]pirimidina-2,4-diona;

2-[4-(3-Dimetilaminometilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonitrilo;

1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-(3-morfolin-4-ilmetilfenil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(1*H*-pirrolo[2,3-*d*]piridazin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5-morfolin-4-ilmetil-1*H*-indol-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5-morfolin-4-ilmetil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

{2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}fenilmetanona;

{2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-*c*]piridin-5-il}fenilmetanona;

{2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}furan-2-ilmetanona;

{2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-*c*]piridin-5-il}furan-2-ilmetanona;

1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-piridin-2-ilpentan-2-ol;

4-(3-Cloro-2-fluoro-5-trifluorometilbencil)-5,5,5-trifluoro-4-hidroxi-2-metil-2-fenilpentannitrilo;

1,1,1-Trifluoro-4-metil-4-piridin-4-il-2-quinolin-4-ilmetilpentan-2-ol;

2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

2-[3-(2,6-Dimetilpiridin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;

1,1,1-Trifluoro-4,4-dimetil-5-fenil-2-quinolin-4-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-piridin-4-ilmetilpentan-2-ol;
4-Fluoro-2-[4,4,4-trifluoro-3-(2-fluoropiridin-4-ilmetil)-3-hidroxi-1,1-dimetilbutil]fenol;
2-[3-(2-Bromopiridin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;
2-(6,8-Dimetilquinolin-4-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
4-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]piridina-2-carbonitrilo;
2,6-Dicloro-4-[4-(5-fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil] nicotinonitrilo;
4-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]quinolin-2-ol;
2,6-Dicloro-4-[4-(5-fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil] nicotinonitrilo;
2-(2-Cloro-8-metilquinolin-4-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
2-(2,6-Dicloroquinolin-4-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
2-[3-(2-Cloro-8-metilquinolin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;
2-[3-(2,6-Dicloroquinolin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;
4-(2,3-Dihidrobenzofuran-7-il)-2-(2,6-dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(3-fluorofenil)-4-metilpentan-2-ol;
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(4-fluorofenil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-metil-4-*m*-tolilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(2-metilquinolin-4-ilmetil)pentan-2-ol;
4-Fluoro-2-(4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)fenol;
4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(2-metilquinolin-4-ilmetil)butil]fenol;
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(4-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(7-metilquinolin-4-ilmetil)pentan-2-ol;
2-[3-(2,6-Dimetilpiridin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-5-fluorofenol;
2-(5,7-Dimetilquinolin-4-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(4-fluorofenil)-4-metil-2-(2-metilquinolin-4-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(3-metil-1*H*-indol-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-(2-trifluorometilfenil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(7-fluoro-4-metilquinolin-8-il)-4-metilpentan-2-ol;

4-(2,6-Dimetilfenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
2-(3-Bromo-1*H*-indol-2-ilmetil)-1,1,1-trifluoro-4-(3-fluorofenil)-4-metilpentan-2-ol;
4-(3,4-Dimetilfenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(3-fluoro-4-metilfenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(4-fluoro-3-metilfenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(3-fluoro-4-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(4-fluoro-2-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(3,4-Dimetilfenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(2,5-Dimetilfenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-(2-metoxi-5-metilfenil)-4-metilpentan-2-ol;
4-Metil-2-[4,4,4-trifluoro-3-hidroxi-3-(1*H*-indol-2-ilmetil)-1,1-dimetilbutil]fenol;
4-(2,5-Dimetilfenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(2-metoxi-5-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(2,5-Dimetoxifenil)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(4-metoxi-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-4-metilpentan-2-ol;
2-(2,4-Dimetil-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
2-(2-Amino-4-cloro-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
2-(2,4-Dimetil-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;
2-(5-Cloro-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;
4-(5-Bromo-2-metoxifenil)-1,1,1-trifluoro-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
4-(5-Bromo-2-metoxifenil)-1,1,1-trifluoro-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

2-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-[5-(etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluoro-4-metilpentan-2-ol;

2-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-fenilpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5-pirrolidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-fenil-2-(5-pirrolidin-1-il-1*H*-pirrolo [2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4'-Metoxi-3'-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]bifenil-2-carbonitrilo;

2-(5-Dietilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-[5-(isopropilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-4-metilpentan-2-ol;

1,1,1-Trifluoro-2-[5-(isopropilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-4-metil-4-fenilpentan-2-ol;

2-(5-Dietilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metil-4-fenilpentan-2-ol;

4-(3-Bromofenil)-1,1,1-trifluoro-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorofenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorofenil)-4-metil-2-(5-pirrolidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-(3-pirimidin-5-ilfenil)pentan-2-ol;

2-[5-(2,6-Dimetilmorfolin-4-il)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

2-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluoro-4-metil-4-fenilpentan-2-ol;

2-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluoro-4-(3-fluorofenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(5-pirrolidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(5-Dietilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(3-fluorofenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-2-[5-(isopropilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-4-metilpentan-2-ol;

3'-[3-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4'-metoxibifenil-2-carbonitrilo;

2-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluoro-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metilpentan-2-ol;

3'-[3-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4'-hidroxibifenil-2-carbonitrilo;

4'-Hidroxi-3'-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]bifenil-2-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5-morfolin-4-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)pentan-2-ol;

2-(5-Dimetilaminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-[5-(4-metilpiperazin-1-ilmetil)-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil]pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(5-dimetilaminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-morfolin-4-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)pentan-2-ol;

4-Cloro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)butil]fenol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-pirrolo[3,2-*c*]piridina-6-carbonitrilo;

2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-*c*]piridina-5-carbonitrilo;

Metil éster del ácido 2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carboxílico;

1-{2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il}etanona;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(6*H*-pirrolo[2,3-g]quinoxalin-7-ilmetil)pentan-2-ol;

Amida del ácido 2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carboxílico;

Ácido 2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carboxílico;

{2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il}morfolin-4-ilmetanona;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(5-hidroximetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-metilpentan-2-ol;

2-(5-Aminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)pentan-2-ol;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)-butil]fenol;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)butil]-fenol;

2-(6-Cloro-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(6-cloro-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-2-metoxifenil)-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-butil]fenol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(3-fenil-7*H*-pirrolo[2,3-*c*]-piridazin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(3-fenil-7*H*-pirrolo[2,3-*c*]piridazin-6-ilmetil)pentan-2-ol;

1-{2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il}-2,2-dimetilpropan-1-ona;

2-[5-(1-*ter*-Butil-1-hidroxi-2,2-dimetilpropil)-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil]-4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ol;

1-{2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il}propan-1-ona;

1-{2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il}-2-metilpropan-1-ona;

1,1,1-Trifluoro-4-(4-fluoro-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-tiofen-3-ilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(4-metoxibifenil-3-il)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]fenol;

4-Tiofen-3-il-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]fenol;

3-[4,4,4-Trifluoro-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]bifenil-4-ol;

1,1,1-Trifluoro-4-metil-2-(3-metil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-(5-pirimidin-5-il-2,3-dihidrobenzofuran-7-il)pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(3-metil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

4-Piridin-3-il-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(3-metil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]fenol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(5-fenoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-fenil-2-(3-fenil-7*H*-pirrolo[2,3-c]piridazin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(3-fenil-7*H*-pirrolo[2,3-c]piridazin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(5-fenoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-fenil-2-(3-fenil-7*H*-pirrolo[2,3-c]piridazin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(3-fenil-7*H*-pirrolo[2,3-c]piridazin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(5-fenil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-2-[5-(4-fluorofenil)-1*H*-pirrolo[2,3-c]piridin-2-ilmetil]-4-metilpentan-2-ol;

2-(5-Dimetilamino-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

2-(5-Dimetilamino-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluoro-4-(4-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-[3-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;

2-[3-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-5-fluorofenol;

5-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]fenol;

4-(5-Bromo-2-metoxifenil)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-Bromo-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]-fenol;

1,1,1-Trifluoro-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-pentan-2-ol;

4-(3-[1,3]Dioxan-2-ilfenil)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(4-metoxibifenil-3-il)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-tiofen-3-ilfenil)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-pentan-2-ol;

3-[4,4,4-Trifluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]bifenil-4-ol;

4-Tiofen-3-il-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-butil]fenol;

4-Tiofen-3-il-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]-fenol;

4-Tiofen-3-il-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]-fenol;

4'-Metoxi-3'-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]bifenil-2-carbonitrilo;

4'-Metoxi-3'-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]-bifenil-3-carbonitrilo;

1,1,1-Trifluoro-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(3-Clorofenil)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

4-Piridin-3-il-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]-fenol;

1,1,1-Trifluoro-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(3-piridin-3-ilfenil)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(3-pirimidin-5-ilfenil)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(3-piridin-3-ilfenil)-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(3-pirimidin-5-ilfenil)-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-piridin-2-il-1*H*-indol-2-ilmetil)pentan-2-ol;

2-(5-Bromo-1*H*-indol-2-ilmetil)-4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-2-(5-metansulfinil-1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

Amida del ácido 7-[3-(5-Bromo-1*H*-indol-2-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-2,3-dihidrobenzofuran-5-sulfónico;

Dimetilamida del ácido 7-[3-(5-Bromo-1*H*-indol-2-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-2,3-dihidrobenzofuran-5-sulfónico;

2-(1-Bencensulfonil-5-piridin-3-il-1*H*-indol-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol;

3-{2-[4-(5-Fluoro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}benzonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-piridin-4-il-1*H*-indol-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-piridin-3-il-1*H*-indol-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-pirimidin-5-il-1*H*-indol-2-ilmetil)pentan-2-ol;

2-{2-[4-(5-Fluoro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}benzamida;

2-[5-(4-Dimetilaminofenil)-1*H*-indol-2-ilmetil]-1,1,1-trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol;

1,1,1-Trifluoro-2-(7-fluoro-4-metil-1*H*-indol-2-ilmetil)-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol;

2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonitrilo;

2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carbonitrilo;

1,1,1-Trifluoro-2-(7-fluoro-1*H*-indol-2-ilmetil)-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-(4-metil-1*H*-indol-2-ilmetil)pentan-2-ol;

4-Metansulfonil-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-trifluorometil-1*H*-indol-2-ilmetil)butil]fenol;

1,1,1-Trifluoro-2-(7-fluoro-5-metil-1*H*-indol-2-ilmetil)-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol;

7-Fluoro-2-[2-hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonitrilo;

Metil éster del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-4-carboxílico;

Metil éster del ácido 2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-4-carboxílico;

Ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-4-carboxílico;

Amida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-4-carboxílico;

Amida del ácido 2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-4-carboxílico;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-4-carbonitrilo;

2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-4-carbonitrilo;

2-(4-Etil-1*H*-indol-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

2-[3-(4-Etil-1*H*-indol-2-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(2-isopropil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(2-isopropil-5*H*-pirrolo[3, 2-*d*]pirimidin-6-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(2-isopropil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)-4-metilpentan-2-ol;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-3-(2-isopropil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)-1,1-dimetilbutil]fenol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)butil]fenol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(2-fenil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(2-fenil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(2-fenil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(2-fenil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)butil]fenol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(2-cloro-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-metil-4-fenil-2-(2-fenil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(2-fenil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

4-[4,4,4-Trifluoro-3-hidroxi-1,1-dimetil-3-(2-fenil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)butil] benzonitrilo;

1,1,1-Trifluoro-4-(2-metoxi-5-metilfenil)-4-metil-2-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-*d*] pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-metilfenil)-4-metil-2-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-*d*] pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-2-metoxifenil)-4-metil-2-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-*d*] pirimidin-6-ilmetil)pentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)butil]fenol;

2-(5-Etoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Bromo-2-metoxifenil)-2-(5-dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

4-(5-Bromo-2-metoxifenil)-1,1,1-trifluoro-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-trifluorometilfenil)-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-(4-metoxibifenil-3-il)-4-metilpentan-2-ol;

1,1,1-Trifluoro-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-(2-metoxi-5-tiofen-3-ilfenil)-4-metilpentan-2-ol;

2-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metil-4-fenilpentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(4-metoxibifenil-3-il)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metilpentan-2-ol;

4-Bromo-2-[3-(5-cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]fenol;

2-[3-(5-Cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;

2-[2-Hidroxi-4-(4-hidroxibifenil-3-il)-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-*c*]piridin-5-ol;

1,1,1-Trifluoro-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metil-4-(5-fenil-2,3-dihidrobenzofuran-7-il)pentan-2-ol;

2-[2-Hidroxi-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-*c*]piridin-5-ol;

2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-*c*]piridin-5-il éster del ácido trifluorometansulfónico;

2-[5-(2,6-Dimetilmorfolin-4-il)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluoro-4-metil-4-fenilpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-fenil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metil-4-fenilpentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(5-Dietilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(5-metoxi-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(5-metoxi-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(5-cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(4-metoxi-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,5-dihidropirrolo[3,2-*c*]piridin-4-ona;

2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,4-dihidropirrolo[3,2-*b*]piridin-5-ona;

2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-5-hidroxi-1,6-dihidropirrolo[2,3-*c*]piridin-7-ona;

2-(5-Cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol;

2-(5-Cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(2-metoxi-5-tiofen-3-ilfenil)-4-metilpentan-2-ol;

2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;

2-(5-Cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metil-4-(5-metilsulfanil-2,3-dihidrobenzofuran-7-il)pentan-2-ol;

4-(5-Bromo-2-metoxifenil)-2-(5-cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-naftalen-1-ilfenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(2'-Cloro-4-metoxibifenil-3-il)-1,1,1-trifluoro-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]-piridin-2-ilmetil)pentan-2-ol;

2-(5-Cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metilpentan-2-ol;

4'-Metoxi-3'-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]bifenil-2-carbonitrilo;

4-(2'-Cloro-4-metoxibifenil-3-il)-1,1,1-trifluoro-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]-piridin-2-ilmetil)pentan-2-ol;

2-[3-(3-Dimetilaminometil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;

1,1,1-Trifluoro-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-(1*H*-pirrolo[3,2-*c*]-piridin-2-ilmetil)pentan-2-ol;

2-(3-Cloro-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(5-metilsulfanil-2,3-dihidrobenzofuran-7-il)-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-fenil-1*H*-pirrolo[2,3-*c*]-piridin-2-ilmetil)pentan-2-ol; y

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-pentan-2-ol,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Compuestos más preferidos de Fórmula (IA) incluyen:

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(3-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(4,6-Dimetil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-pirrolo[3,2-*c*]piridina-6-carbonitrilo;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-*c*]piridina-5-carbonitrilo;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*c*]piridina-4-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-tieno[2,3-*d*]piridazin-2-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(2-metil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(1*H*-pirrolo[2,3-*d*]piridazin-2-ilmetil)pentan-2-ol;

2-(4,6-Dimetil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(4,6-dimetil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;

2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(7-fluoro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(5,7-Dicloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5-trifluorometil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(5-metoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(5-metoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(5-metoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(7-fluoro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-trifluorometil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(5-cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(5-metil-2,3-dihidrobenzofuran-7-il)-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-pirrolo[2,3-*b*]piridin-1-ilmetilpentan-2-ol;

2-Benzo[*b*]tiofen-2-ilmetil-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-tieno[2,3c]piridin-2-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-[4-((*Z*)propenil)-3-vinilpirazol-1-ilmetil]pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,4-dimetil-1-tieno[2,3-*c*]piridin-2-ilpentan-2-ol;
4-(5-Fluoro-2-metilfenil)-2,4-dimetil-1-tieno[2,3-*c*]piridin-2-ilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-metil-4-(5-metil-2,3-dihidrobenzofuran-7-il)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
2-(3-Dimetilaminometil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-pirrolo[3,2-*c*]piridin-1-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-furo[3,2-*c*]piridin-2-ilmetil-4-metilpentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;
1,1-Difluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-tieno[3,2-*c*]piridin-2-ilmetilpentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-tieno[3,2-*c*]piridin-2-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-tieno[3,2-*c*]piridin-2-ilmetilpentan-2-ol;
dimetilamida del ácido 2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carboxílico;
{2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-il}morfolin-4-ilmetanona;
Dimetilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometil-pentil]-1*H*-indol-6-carboxílico;
Dimetilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometil-pentil]-1*H*-indol-6-carboxílico;
{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-il}morfolin-4-ilmetanona;

2-[4-(2,3-Dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

Amida del ácido 2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carboxílico;

Amida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carboxílico;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-nitro-1*H*-indol-2-ilmetil)butil]fenol;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carbonitrilo;

2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carbonitrilo;

N-{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}acetamida;

1,1,1-Trifluoro-4-(4-fluoro-2-metoxifenil)-2-(7-fluoro-4-metil-1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-(7-fluoro-4-metil-1*H*-indol-2-ilmetil)-3-hidroxi-1,1-dimetilbutil]fenol;

2-[4-(3-[1,3]Dioxolan-2-ilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonitrilo;

2-Trimetilsilaniletil éster del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

2-[4-(4-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}piperidin-1-ilmetanona;

Metilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}pirrolidin-1-ilmetanona;

1-{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}piperidin-4-ona;

(2-Hidroxietil)amida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}(4-hidroxipiperidin-1-il)metanona;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}(3-hidroxipirrolidin-1-il)metanona;

Clanometilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Metil éster del ácido ({2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}amino)acético;

Carbamoilmetilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Metil éster del ácido 4-({2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}amino)butírico;

Ácido ({2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}amino)acético ;

Ácido 4-({2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}amino)butírico;

2-[4-(3-Dimetilaminometilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonitrilo;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-trifluorometil-1*H*-indol-2-ilmetil)butil]fenol;

2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

Ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Amida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Dimetilamida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Clanometilamida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}pirrolidin-1-ilmetanona;

{2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}morfolin-4-ilmetanona;

Amida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}morfolin-4-ilmetanona;

2-(4-Benzo[1,3]dioxol-4-il-2-hidroxi-4-metil-2-trifluorometilpentil)-4-metil-1*H*-indol-6-carbonitrilo;

1,1,1-Trifluoro-4-metil-4-fenil-2-quinolin-4-ilmetilhexan-2-ol;

2-[2-Hidroxi-4-metil-4-(5-metilsulfanil-2,3-dihidrobenzofuran-7-il)-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

7-(4,4,4-Trifluoro-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)-2,3-dihidrobenzofuran-5-carbonitrilo;

2-[2-Hidroxi-4-(2-hidroxi-5-metilfenil)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-metilsulfanil-1*H*-indol-2-ilmetil)pentan-2-ol;

2-[2-Hidroxi-4-(5-metansulfonil-2-metoxifenil)-4-metil-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-fenil-1*H*-indol-2-ilmetil)pentan-2-ol;

2-[4-(5-*ter*-Butil-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(2-hidroxi-5-isopropilfenil)-4-metil-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(2-hidroxi-3,5-dimetilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(5-hidroxi-2,4-dimetilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[4-(5-*ter*-Butil-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(5-isopropil-2-metoxifenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(2-metoxi-5-metilfenil)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*o*-tolilpentan-2-ol;

1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*m*-tolilpentan-2-ol;

1,1,1-Trifluoro-4-(2-fluorofenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(2-fluorofenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(4-fluorofenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(4-fluorofenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
3-(4,4,4-Trifluoro-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)fenol;
1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-(2-trifluorometilfenil)pentan-2-ol;
1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-(4-trifluorometilfenil)pentan-2-ol;
1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-(4-trifluorometilfenil)pentan-2-ol;
4-(3-Clorofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
4-(3-Clorofenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(4-Dimetilaminofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
4-Bifenil-3-il-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(3-Bromofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
4-(2-Difluorometoxi-5-fluorofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
4-Bifenil-3-il-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
4-(4-Dimetilaminofenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,6-dihidropirrolo[2,3-*c*]piridin-5-ona;
2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-6-metil-1,6-dihidropirrolo[2,3-*c*]piridin-5-ona;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(5-metoxi-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-metilpentan-2-ol;
2-[4-(3-Dimetilaminometilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonitrilo;
1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-piridin-2-ilpentan-2-ol;
1,1,1-Trifluoro-4-metil-4-piridin-4-il-2-quinolin-4-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*o*-tolilpentan-2-ol;
1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*m*-tolilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-piridin-4-ilmetilpentan-2-ol;
4-Fluoro-2-[4,4,4-trifluoro-3-(2-fluoropiridin-4-ilmetil)-3-hidroxi-1,1-dimetilbutil]fenol;
2-[3-(2-Bromopiridin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;
2-(6,8-Dimetilquinolin-4-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
4-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]piridina-2-carbonitrilo;
2,6-Dicloro-4-[4-(5-fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil] nicotinonitrilo;

2,6-Dicloro-4-[4-(5-fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil] nicotinonitrilo;

2-(2,6-Dicloroquinolin-4-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

2-[3-(2-Cloro-8-metilquinolin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;

2-[3-(2,6-Dicloroquinolin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;

4-(2,3-Dihidrobenzofuran-7-il)-2-(2,6-dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(3-fluorofenil)-4-metilpentan-2-ol;

2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(4-fluorofenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-metil-4-*m*-tolilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(2-metilquinolin-4-ilmetil)pentan-2-ol;

4-Fluoro-2-(4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)fenol;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(2-metilquinolin-4-ilmetil)butil]fenol;

2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(4-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(7-metilquinolin-4-ilmetil)pentan-2-ol;

2-[3-(2,6-Dimetilpiridin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-5-fluorofenol;

1,1,1-Trifluoro-4-(4-fluorofenil)-4-metil-2-(2-metilquinolin-4-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(3-metil-1*H*-indol-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-(2-trifluorometilfenil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(7-fluoro-4-metilquinolin-8-il)-4-metilpentan-2-ol;

4-(2,6-Dimetilfenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

2-(3-Bromo-1*H*-indol-2-ilmetil)-1,1,1-trifluoro-4-(3-fluorofenil)-4-metilpentan-2-ol;

4-(3,4-Dimetilfenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluoro-4-metilfenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-3-metilfenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluoro-4-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-2-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

4-(3,4-Dimetilfenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

4-(2,5-Dimetilfenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-(2-metoxi-5-metilfenil)-4-metilpentan-2-ol;

4-Metil-2-[4,4,4-trifluoro-3-hidroxi-3-(1*H*-indol-2-ilmetil)-1,1-dimetilbutil]fenol;

4-(2,5-Dimetilfenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(2,5-Dimetoxifenil)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-(2-trifluorometilfenil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(4-metoxi-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-4-metilpentan-2-ol;
2-(2,4-Dimetil-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
2-(2-Amino-4-cloro-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol; y
2-(5-Cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol,
o un tautómero, un profármaco, un solvato o sal de los mismos.

Los compuestos más preferidos de Fórmula (IA) incluyen:
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(3-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
2-(4,6-Dimetil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-pirrolo[3,2-*c*]piridina-6-carbonitrilo;
2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-*c*]piridina-5-carbonitrilo;
2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*c*]piridina-4-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-tieno[2,3-*d*]piridazin-2-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(1*H*-pirrolo[2,3-*d*]piridazin-2-ilmetil)pentan-2-ol;

2-(4,6-Dimetil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(4,6-dimetil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;

2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(7-fluoro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(5,7-Dicloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5-trifluorometil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(5-metoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(5-metoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(5-metoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(7-fluoro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-trifluorometil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
2-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(5-cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;
4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-metil-4-(5-metil-2,3-dihidrobenzofuran-7-il)-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-tieno[2,3-*c*]piridin-2-ilmetilpentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,4-dimetil-1-tieno[2,3-*c*]piridin-2-ilpentan-2-ol;
4-(5-Fluoro-2-metilfenil)-2,4-dimetil-1-tieno[2,3-*c*]piridin-2-ilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-metil-4-(5-metil-2,3-dihidrobenzofuran-7-il)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(3-Dimetilaminometil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-furo[3,2-*c*]piridin-2-ilmetil-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;

1,1-Difluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-tieno[3,2-*c*]piridin-2-ilmetilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-tieno[3,2-*c*]piridin-2-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-tieno[3,2-*c*]piridin-2-ilmetilpentan-2-ol;

2-[4-(2,3-Dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-nitro-1*H*-indol-2-ilmetil)butil]fenol;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carbonitrilo;

2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carbonitrilo;

N-{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}acetamida;

1,1,1-Trifluoro-4-(4-fluoro-2-metoxifenil)-2-(7-fluoro-4-metil-1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-(7-fluoro-4-metil-1*H*-indol-2-ilmetil)-3-hidroxi-1,1-dimetilbutil]fenol;

2-[4-(3-[1,3]Dioxolan-2-ilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonitrilo;

2-[4-(4-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}piperidin-1-ilmetanona;

metilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}pirrolidin-1-ilmetanona;

(2-hidroxietil)amida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}(3-hidroxipirrolidin-1-il)metanona;

cianometilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Metil éster del ácido ({2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}amino)acético;

Carbamoilmetilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Metil éster del ácido 4-({2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometil-pentil]-1*H*-indol-5-carbonil}amino)butírico;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-trifluorometil-1*H*-indol-2-ilmetil)butil]fenol;

2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

Amida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Dimetilamida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Cianometilamida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}pirrolidin-1-ilmetanona;

{2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}morfolin-4-ilmetanona;

Amida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}morfolin-4-ilmetanona;

2-(4-Benzo[1,3]dioxol-4-il-2-hidroxi-4-metil-2-trifluorometilpentil)-4-metil-1*H*-indol-6-carbonitrilo;

1,1,1-Trifluoro-4-metil-4-fenil-2-quinolin-4-ilmetilhexan-2-ol;

2-[2-Hidroxi-4-metil-4-(5-metilsulfanil-2,3-dihidrobenzofuran-7-il)-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo;

7-(4,4,4-Trifluoro-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)-2,3-dihidrobenzofuran-5-carbonitrilo;

2-[2-Hidroxi-4-(2-hidroxi-5-metilfenil)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-metilsulfanil-1*H*-indol-2-ilmetil)pentan-2-ol;

2-[2-Hidroxi-4-(5-metansulfonil-2-metoxifenil)-4-metil-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo;

2-[4-(5-*ter*-Butil-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(2-hidroxi-5-isopropilfenil)-4-metil-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(2-hidroxi-3,5-dimetilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(5-hidroxi-2,4-dimetilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[4-(5-*ter*-Butil-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(5-isopropil-2-metoxifenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*o*-tolilpentan-2-ol;

1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*m*-tolilpentan-2-ol;

1,1,1-Trifluoro-4-(2-fluorofenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(2-fluorofenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorofenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorofenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

3-(4,4,4-Trifluoro-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)fenol;

1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-(2-trifluorometilfenil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-(4-trifluorometilfenil)pentan-2-ol;

4-(3-Clorofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

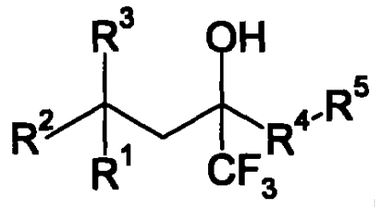
4-(3-Clorofenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

4-Bifenil-3-il-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(3-Bromofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
4-(2-Difluorometoxi-5-fluorofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
4-(4-Dimetilaminofenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-6-metil-1,6-dihidropirrolo[2,3-*c*]piridin-5-ona;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(5-metoxi-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-metilpentan-2-ol;
2-[4-(3-Dimetilaminometilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonitrilo;
1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-piridin-2-ilpentan-2-ol;
1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*o*-tolilpentan-2-ol;
1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*m*-tolilpentan-2-ol;
4-Fluoro-2-[4,4,4-trifluoro-3-(2-fluoropiridin-4-ilmetil)-3-hidroxi-1,1-dimetilbutil]fenol;
2-[3-(2-Bromopiridin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;
2-(6,8-Dimetilquinolin-4-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
4-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]piridina-2-carbonitrilo;
2,6-Dicloro-4-[4-(5-fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil] nicotinonitrilo;
2,6-Dicloro-4-[4-(5-fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil] nicotinonitrilo;
2-[3-(2,6-Dicloroquinolin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;
4-(2,3-Dihidrobenzofuran-7-il)-2-(2,6-dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(3-fluorofenil)-4-metilpentan-2-ol;
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(4-fluorofenil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-metil-4-*m*-tolilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(2-metilquinolin-4-ilmetil)pentan-2-ol;
4-Fluoro-2-(4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)fenol;
4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(2-metilquinolin-4-ilmetil)butil]fenol;
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(4-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(7-metilquinolin-4-ilmetil)pentan-2-ol;
2-[3-(2,6-Dimetilpiridin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-5-fluorofenol;

1,1,1-Trifluoro-4-(4-fluorofenil)-4-metil-2-(2-metilquinolin-4-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(3-metil-1*H*-indol-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-(2-trifluorometilfenil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(7-fluoro-4-metilquinolin-8-il)-4-metilpentan-2-ol;
4-(2,6-Dimetilfenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
2-(3-Bromo-1*H*-indol-2-ilmetil)-1,1,1-trifluoro-4-(3-fluorofenil)-4-metilpentan-2-ol;
4-(3,4-Dimetilfenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(3-fluoro-4-metilfenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(4-fluoro-3-metilfenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(3-fluoro-4-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(4-fluoro-2-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(3,4-Dimetilfenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(2,5-Dimetilfenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-(2-metoxi-5-metilfenil)-4-metilpentan-2-ol;
4-Metil-2-[4,4,4-trifluoro-3-hidroxi-3-(1*H*-indol-2-ilmetil)-1,1-dimetilbutil]fenol;
4-(2,5-Dimetilfenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(2-metoxi-5-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(2,5-Dimetoxifenil)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-(2-trifluorometilfenil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(4-metoxi-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-4-metilpentan-2-ol;
2-(2,4-Dimetil-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
2-(2-Amino-4-cloro-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol; y
2-(5-Cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol,

o un tautómero, un profármaco, un solvato o sal de los mismos.

La invención también provee un método de preparación de un compuesto de Fórmula (IA)



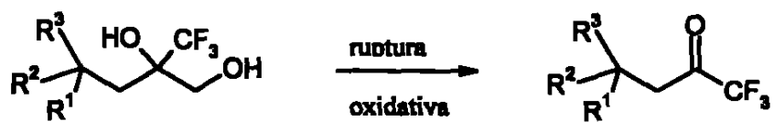
(IA)

donde R^1, R^2, R^3, R^4 y R^5 son como se definieron previamente, comprendiendo el método:

(a) hacer reaccionar un éster de Fórmula (II) con un agente reductor adecuado en un solvente adecuado para formar un diol de Fórmula (III)

II III ;

(b) hacer reaccionar el diol de Fórmula (III) en condiciones adecuadas de ruptura oxidativa para formar una cetona de Fórmula (IV)



III IV ; y

(c) hacer reaccionar la cetona de Fórmula (IV) con un reactivo organometálico adecuado R^5R^4M donde M es Li o MgX y X es Cl, Br o I, en un solvente adecuado para formar el compuesto de Fórmula (IA)

IV IA ; o

(a') hacer reaccionar la trifluoroacetamida de Fórmula (X) con un bromuro de vinil magnesio portador de R^2 y R^3 en un solvente adecuado para obtener la trifluorometilenona de Fórmula (XI)

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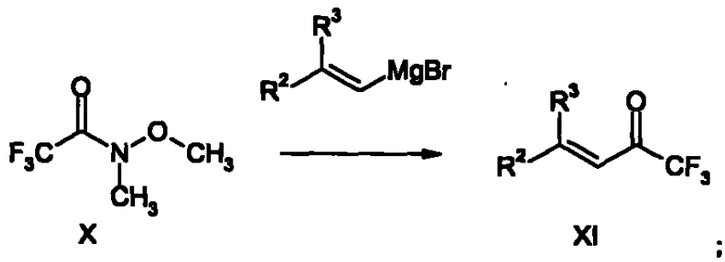
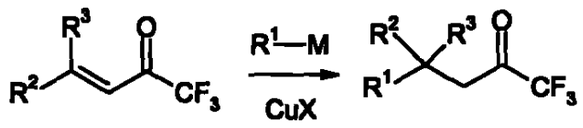


X XI ;

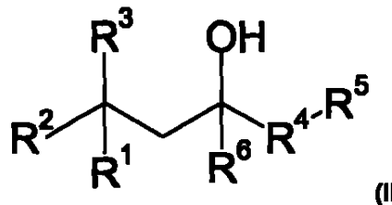
(b') hacer reaccionar la trifluorometilenona de Fórmula (XI) con un reactivo adecuado organocuproso producido a partir de un reactivo organometálico R^6R^4M, donde M es Li o MgX y una sal de cobre CuX, donde X es Cl, Br o I, en un solvente adecuado para formar la cetona de Fórmula (IV)



XI IV ; y

llevar a cabo el paso (c) como se indicó anteriormente.

La presente invención también está dirigida a compuestos de Fórmula (IB)



(IB)

donde:

R^1 es un grupo arilo o heteroarilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, cicloalquilo C_3-C_8, heterocicilo, arilo, heteroarilo, alcoxi C_1-C_8, alqueniloxi C_2-C_8, alquiniloxi C_2-C_8, ariloxi, acilo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_8, alcanoilo C_1-C_8, aroilo, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilaminocarboniloxi C_1-C_8, dialquilaminocarboniloxi C_1-C_8, alcanoilamino C_1-C_8, alcoxicarbonilamino C_1-C_8, alquilsulfonilamino C_1-C_8, aminosulfonilo, alquilaminosulfonilo C_1-C_8, dialquilaminosulfonilo C_1-C_8, halógeno, hidroxi, carboxi, ciano, trifluorometilo, trifluorometoxi, nitro, o amino donde el átomo de nitrógeno

en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_6; o alquiltio C_1-C_6 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^1 está sustituido independientemente en forma opcional con uno a tres grupos sustituyentes seleccionados de metilo, metoxi, halógeno, hidroxi, oxo, ciano, heteroarilo, heterocicilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_6;

R^2 y R^3 son cada uno independientemente alquilo C_1-C_6;

R^4 es alquilo C_1-C_6, alquenilo C_2-C_6, o alquinilo C_2-C_6, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^4 es independientemente alquilo C_1-C_3, hidroxi, halógeno, amino u oxo;

R^5 es un grupo heteroarilo sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_6, alquenilo C_2-C_6, alquinilo C_2-C_6, cicloalquilo C_3-C_8, heterocicilo, arilo, heteroarilo, alcoxi C_1-C_6, alqueniloxi C_2-C_6, alquiniloxi C_2-C_6, ariloxi, acilo, alcoxicarbonilo C_1-C_6, alcanoiloxi C_1-C_6, heterocicilcarbonilo, aroílo, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilaminocarboniloxi C_1-C_6, dialquilaminocarboniloxi C_1-C_6, alcanoilamino C_1-C_6, alcoxicarbonilamino C_1-C_6, alquilsulfonilamino C_1-C_6, aminosulfonilo, alquilaminosulfonilo C_1-C_6, dialquilaminosulfonilo C_1-C_6, halógeno, hidroxi, carboxi, ciano, trifluorometilo, trifluorometoxi, trifluorometiltio, nitro, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_6; o alquiltio C_1-C_6 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^5 está sustituido independientemente en forma opcional con uno a tres grupos sustituyentes seleccionados de alquilo C_1-C_3, alcoxi C_1-C_3, halógeno, hidroxi, oxo, ciano, arilo, heteroarilo, heterocicilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; o ureido

donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_6, o trifluorometilo,

R^8 es hidrógeno, alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, carbocicilo, heterocicilo, arilo, heteroarilo, carbocicilo-alquilo C_1-C_8, carboxi, alcoxicarbonilo, aril-alquilo C_1-C_8, aril-haloalquilo C_1-C_8, heterocicil-alquilo C_1-C_8, heteroaril-alquilo C_1-C_8, carbocicilo-alquenilo C_2-C_8, aril-alquenilo C_2-C_8, heterocicil-alquenilo C_2-C_8, o heteroaril-alquenilo C_2-C_8, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^8 es independientemente alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, cicloalquilo C_3-C_8, fenilo, alcoxi C_1-C_8, fenoxi, alcanoilo C_1-C_8, aroilo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_8, aminocarboniloxi, alquilaminocarboniloxi C_1-C_8, dialquilaminocarboniloxi C_1-C_8, aminocarbonilo, alquilaminocarbonilo C_1-C_8, dialquilaminocarbonilo C_1-C_8, alcanoilamino C_1-C_8, alcoxicarbonilamino C_1-C_8, alquilsulfonilamino C_1-C_8, alquilaminosulfonilo C_1-C_8, dialquilaminosulfonilo C_1-C_8, halógeno, hidroxi, carboxi, ciano, oxo, trifluorometilo, nitro, amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_8; o alquiltio C_1-C_8 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde R^8 no puede ser trifluorometilo,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto de la invención incluye compuestos de Fórmula (IB), donde:

R^1 es tienilo, fenilo, naftilo, dihidrobenzofuranilo, benzofuranilo, cromanilo, dihidroindolilo, indolilo, dihidrobenzotienilo, benzotienilo, benzodioxolanilo, benzoxazolilo, benzoisoxazolilo, benzopirazolilo, benzoimidazolilo, tienilo, quinolinilo, piridinilo, pirimidinilo o pirazinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

donde cada grupo sustituyente de R^1 está sustituido independientemente en forma opcional con un grupo sustituyente seleccionado de metilo, metoxi,

halógeno, hidroxi, oxo, ciano, heteroarilo, heterociclilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo;

R^2 y R^3 son cada uno independientemente C_1-C_3 alquilo;

R^4 es CH_2;

R^5 es un grupo imidazolilo, piridilo, indolilo, azaindolilo, diazaindolilo, benzofuranilo, furanopiridinilo, furanopirimidinilo, benzotienilo, tienopiridinilo, tienopirimidinilo, benzoxazolilo, oxazolopiridinilo, benzotiazolilo, tiazolopiridinilo, benzoimidazolilo, imidazolopiridinilo, imidazolopirimidinilo, imidazolopiridazinilo, imidazolopirazinilo, quinolinilo o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, fenilo, alcoxi C_1-C_3, metoxicarbonilo, aminocarbonilo, alquilaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, heterociclilcarbonilo, hidroxi, fluoro, cloro, bromo, ciano, trifluorometilo, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

donde cada grupo sustituyente de R^5 está sustituido independientemente en forma opcional con un grupo sustituyente seleccionado de metilo, metoxi, fluoro, cloro, bromo, trifluorometilo, heteroarilo, heterociclilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; y

R^6 es alquilo C_1-C_8, alquenilo C_2-C_8, cicloalquilo C_3-C_8, fenilo, cicloalquil-C_3-C_8-alquilo C_1-C_3, fenilo alquilo C_1-C_3, fenil-haloalquilo C_1-C_3, cicloalquil-C_3-C_8-alquenilo C_2-C_3, fenil-alquenilo C_2-C_3, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^6 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, aminocarbonilo, C_1-C_3, alquilaminocarbonilo C_1-C_3 dialquilaminocarbonilo, halógeno, hidroxi, oxo, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto más de la invención incluye compuestos de Fórmula (IB), donde:

R^1 es tienilo, fenilo, naftilo, piridilo, cromanilo, dihidrobenzofuranilo, o benzofuranilo, cada uno en forma opcional independientemente sustituido con uno o dos grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente metilo, etilo, metoxi, etoxi, fluoro, cloro, bromo, hidroxi, trifluorometilo, ciano o alquiltio C_1-C_6 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona;

R^2 y R^3 son cada uno metilo;

R^4 es CH_2;

R^5 es un grupo piridilo, indolilo, azaindolilo, diazaindolilo, benzofuranilo, furanopiridinilo, tienopiridinilo, benzoxazolilo, benzoimidazolilo, quinolinilo, o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente metilo, fenilo, metoxicarbonilo, aminocarbonilo, metilaminocarbonilo, dimetilaminoaminocarbonilo, morfolinilcarbonilo, hidroxi, fluoro, cloro, bromo, ciano o trifluorometilo; y

R^6 es alquilo C_1-C_3, cicloalquilo C_3-C_6, cicloalquilmetilo C_3-C_6 o bencilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^6 es independientemente metilo, metoxi, fluoro, cloro, bromo, ciano, trifluorometilo o hidroxi,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto más de la invención incluye compuestos de Fórmula (IB), donde:

R^1 es fenilo, dihidrobenzofuranilo o benzofuranilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona; y

R^2 y R^3 son cada uno independientemente alquilo C_1-C_3,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto más de la invención incluye compuestos de Fórmula (IB), donde:

R^1 es tienilo, fenilo, naftilo, piridilo, cromanilo, dihidrobenzofuranilo o benzofuranilo, cada uno en forma opcional independientemente sustituido con uno o dos grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente metilo, etilo, metoxi, etoxi, fluoro, cloro, bromo, hidroxi, trifluorometilo, ciano o alquiltio C_1-C_6 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona;

R^2 y R^3 son cada uno metilo;

R^4 es CH_2;

R^5 es un grupo piridilo, indolilo, azaindolilo, diazaindolilo, benzofuranilo, furanopiridinilo, tienopiridinilo, benzoxazolilo, benzoimidazolilo, quinolinilo, o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente metilo, fenilo, metoxicarbonilo, aminocarbonilo, metilaminocarbonilo, dimetilaminoaminocarbonilo, morfolinilcarbonilo, piridinilo, hidroxi, fluoro, cloro, bromo, ciano o trifluorometilo; y

R^6 es alquilo C_1-C_6, cicloalquilo C_3-C_6, cicloalquilmetilo C_3-C_6 o bencilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^6 es independientemente metilo, metoxi, fluoro, cloro, bromo, ciano, trifluorometilo o hidroxi,

o un tautómero, un profármaco, un solvato o sal de los mismos.

En los aspectos anteriores de la invención de los compuestos de Fórmula (IB), se prefiere que R^6 no sea hidrógeno.

Los compuestos representativos de Fórmula (IB) de acuerdo con la invención se agregan aquí como Tabla IB, donde la columna A es la denominación del compuesto de acuerdo a la nomenclatura estándar y la columna B es la correspondiente estructura química.

Los compuestos preferidos de Fórmula (IB) incluyen los siguientes:

2-Ciclopropil-4-(5-fluoro-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[3,2-*c*]piridin-2-il)pentan-2-ol;

2-Ciclopropil-4-(5-fluoro-2-metilfenil)-4-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-ciclopropil-4-metil-1-(1*H*-pirrolo[2,3-c]piridin-2-il)pentan-2-ol;

2-Ciclopropil-4-(5-fluoro-2-metilfenil)-4-metil-1-(1*H*-pirrolo[3,2-*c*]piridin-2-il)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-ciclopropil-4-metil-1-(1*H*-pirrolo[3,2-c]piridin-2-il)pentan-2-ol;

4-(5-Fluoro-2-metoxifenil)-2,4-dimetil-1-(1*H*-pirrolo[2,3-c]piridin-2-il)pentan-2-ol;

5-(5-Fluoro-2-metoxifenil)-2,5-dimetil-3-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metoxifenil)-2,2,5-trimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;
2-Ciclohexil-4-(5-fluoro-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol;
2-Ciclopentil-4-(5-fluoro-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol;
5-(5-Fluoro-2-metoxifenil)-5-metil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;
2-(5-Fluoro-2-metoxifenil)-2,6-dimetil-4-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)heptan-4-ol;
2-(5-Fluoro-2-metoxifenil)-2,5,5-trimetil-4-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)heptan-4-ol;
1,1-Difluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
1-Ciclohexil-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
5-(5-Fluoro-2-metilfenil)-2,5-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;
5-(5-Fluoro-2-metilfenil)-2,2,5-trimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;
2-Ciclobutil-4-(5-fluoro-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol;
2-(5-Fluoro-2-metoxifenil)-2,6,6-trimetil-4-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)heptan-4-ol;
5-(5-Fluoro-2-metoxifenil)-5-metil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hex-1-en-3-ol;
5-(5-Fluoro-2-metoxifenil)-5-metil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hex-1-in-3-ol;
1-Fluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
2,2-Difluoro-5-(5-fluoro-2-metoxifenil)-5-metil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;
2-Fluoro-5-(5-fluoro-2-metoxifenil)-2,5-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;
2-Fluoro-5-(5-fluoro-2-metoxifenil)-5-metil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;
5-(5-Fluoro-2-metoxifenil)-2,5-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hex-1-en-3-ol;
1,1,1-Trifluoro-5-(5-fluoro-2-metoxifenil)-5-metil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;
4-(5-Fluoro-2-metoxifenil)-4-metil-2-fenil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol;
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,2,5-trimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil) hexan-3-ol;
5-(5-Fluoro-2-metilfenil)-2,2,5-trimetil-3-tieno[2,3-*c*]piridin-2-ilmetilhexan-3-ol;
1,1-Difluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
5-(5-Fluoro-2-metoxifenil)-2,5-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;
5-(5-Fluoro-2-metoxifenil)-2,2,5-trimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;

2-(1-Fluorociclopropil)-4-(5-fluoro-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol;

2-(1-Fluorociclopropil)-4-(4-fluorofenil)-4-metil-1-quinolin-4-ilpentan-2-ol;

2-[4,4-Difluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]-4-fluorofenol;

5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metilfenil)-2,5-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metilfenil)-2,2,5-trimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluoro-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluoro-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;

5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,2,5-trimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metilfenil)-2,2,5-trimetil-3-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metilfenil)-2,2,5-trimetil-3-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metilfenil)-2,5-dimetil-3-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluoro-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1-Difluoro-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(5-Bromo-1*H*-indol-2-ilmetil)-1,1-difluoro-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol; y

2-[2-Difluorometil-2-hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentil]-4-metil-1*H*-indol-6-carbonitrilo,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Compuestos más preferidos de Fórmula (IB) incluyen:

2-Ciclopropil-4-(5-fluoro-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[3,2-*c*]piridin-2-il)pentan-2-ol;

2-Ciclopropil-4-(5-fluoro-2-metilfenil)-4-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-ciclopropil-4-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol;

2-Ciclopropil-4-(5-fluoro-2-metilfenil)-4-metil-1-(1*H*-pirrolo[3,2-*c*]piridin-2-il)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-ciclopropil-4-metil-1-(1*H*-pirrolo[3,2-*c*]piridin-2-il)pentan-2-ol;

4-(5-Fluoro-2-metoxifenil)-2,4-dimetil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol;

5-(5-Fluoro-2-metoxifenil)-2,5-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metoxifenil)-2,2,5-trimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

2-Ciclopentil-4-(5-fluoro -2-metoxifenil)-4-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol;

5-(5-Fluoro-2-metoxifenil)-5-metil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

2-(5-Fluoro-2-metoxifenil)-2,6-dimetil-4-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)heptan-4-ol;

2-(5-Fluoro-2-metoxifenil)-2,5,5-trimetil-4-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)heptan-4-ol;

1,1-Difluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1-Ciclohexil-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

5-(5-Fluoro-2-metilfenil)-2,5-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metilfenil)-2,2,5-trimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

1,1-Difluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

5-(5-Fluoro-2-metoxifenil)-2,5-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metoxifenil)-2,2,5-trimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;

2-(1-Fluorociclopropil)-4-(5-fluoro-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol;

2-(1-Fluorociclopropil)-4-(4-fluorofenil)-4-metil-1-quinolin-4-ilpentan-2-ol;

2-[4,4-Difluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]-4-fluorofenol;

5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metilfenil)-2,5-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metilfenil)-2,2,5-trimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluoro-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

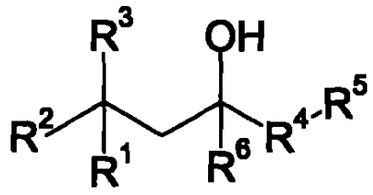
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluoro-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,2,5-trimetil-3-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)hexan-3-ol;
5-(5-Fluoro-2-metilfenil)-2,2,5-trimetil-3-(3-metil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol;
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(3-metil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol;
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(5-fenil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol;
5-(5-Fluoro-2-metilfenil)-2,2,5-trimetil-3-(5-fenil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol;
5-(5-Fluoro-2-metilfenil)-2,5-dimetil-3-(5-fenil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluoro-4-metil-2-(6-metil-1*H*-pirrolo[3,2-c]-piridin-2-ilmetil)pentan-2-ol;
1,1-Difluoro-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-(1*H*-pirrolo[2,3-c]-piridin-2-ilmetil)pentan-2-ol;
2-(5-Bromo-1*H*-indol-2-ilmetil)-1,1-difluoro-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol; y
2-[2-Difluorometil-2-hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentil]-4-metil-1*H*-indol-6-carbonitrilo,
o un tautómero, un profármaco, un solvato o sal de los mismos.

Los compuestos más preferidos de Fórmula (IB) incluyen:
2-Ciclopropil-4-(5-fluoro-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[3,2-c]piridin-2-il)pentan-2-ol;
2-Ciclopropil-4-(5-fluoro-2-metilfenil)-4-metil-1-(1*H*-pirrolo[2,3-c]piridin-2-il)pentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-ciclopropil-4-metil-1-(1*H*-pirrolo[2,3-c]piridin-2-il)pentan-2-ol;
2-Ciclopropil-4-(5-fluoro-2-metilfenil)-4-metil-1-(1*H*-pirrolo[3,2-c]piridin-2-il)pentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-ciclopropil-4-metil-1-(1*H*-pirrolo[3,2-c]piridin-2-il)pentan-2-ol;
5-(5-Fluoro-2-metoxifenil)-2,5-dimetil-3-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol;
5-(5-Fluoro-2-metoxifenil)-2,2,5-trimetil-3-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol;
2-Ciclopentil-4-(5-fluoro-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[2,3-c]piridin-2-il)pentan-2-ol;
2-(5-Fluoro-2-metoxifenil)-2,5,5-trimetil-4-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)heptan-4-ol;
1,1-Difluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

5-(5-Fluoro-2-metilfenil)-2,5-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;
5-(5-Fluoro-2-metilfenil)-2,2,5-trimetil-3-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol;
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol;
1,1-Difluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol;
5-(5-Fluoro-2-metoxifenil)-2,5-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;
5-(5-Fluoro-2-metoxifenil)-2,2,5-trimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;
2-(1-Fluorociclopropil)-4-(5-fluoro-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[2,3-c]piridin-2-il)pentan-2-ol;
2-(1-Fluorociclopropil)-4-(4-fluorofenil)-4-metil-1-quinolin-4-ilpentan-2-ol;
2-[4,4-Difluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]-4-fluorofenol;
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)hexan-3-ol;
5-(5-Fluoro-2-metilfenil)-2,5-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;
5-(5-Fluoro-2-metilfenil)-2,2,5-trimetil-3-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)hexan-3-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluoro-4-metil-2-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluoro-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,2,5-trimetil-3-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)hexan-3-ol;
5-(5-Fluoro-2-metilfenil)-2,2,5-trimetil-3-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(3-metil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol;
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(5-fenil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluoro-4-metil-2-(6-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol;
2-(5-Bromo-1*H*-indol-2-ilmetil)-1,1-difluoro-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol; y
2-[2-Difluorometil-2-hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentil]-4-metil-1*H*-indol-6-carbonitrilo,

o un tautómero, un profármaco, un solvato o sal de los mismos.

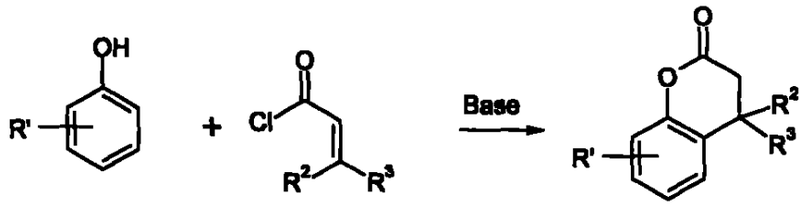
La invención ofrece además métodos para preparar un compuesto de Fórmula (IB). Un método para preparar un compuesto de Fórmula (IB)



(IB)

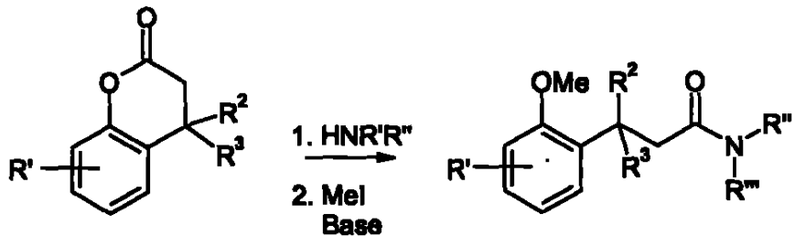
donde R^1 es un grupo 2-metoxifenilo opcionalmente sustituido y R^2, R^3, R^4, R^5 y R^6 son como se definieron previamente, comprendiendo el método:

(a) hacer reaccionar un fenol opcionalmente sustituido de Fórmula (XXII) con un cloruro de acriloilo de Fórmula (XIII) en presencia de una base adecuada, seguido de ciclación del éster intermediario por tratamiento con un ácido de Lewes adecuado para formar una lactona de Fórmula (XIV)



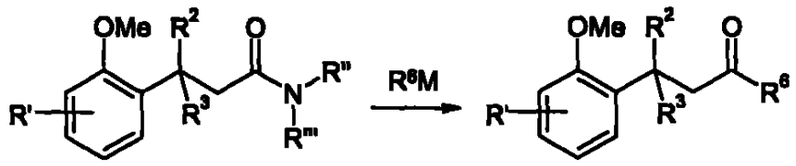
XII XIII XIV ;

(b) hacer reaccionar la lactona de Fórmula (XIV) con una amina adecuada HNR'R", seguido de tratamiento del fenol intermediario con yoduro de metilo en presencia de una base adecuada para formar una amida de Fórmula (XV)



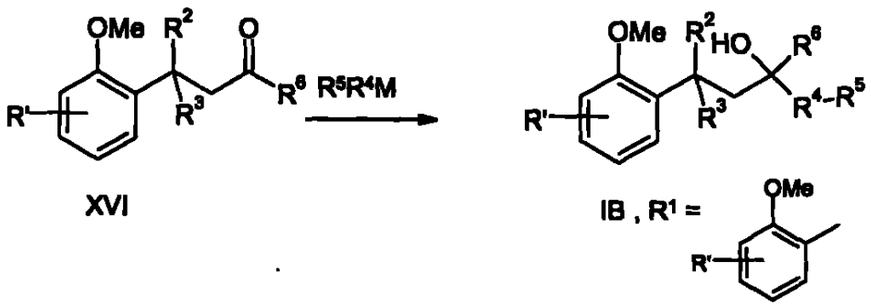
XIV XV ;

(c) hacer reaccionar la amida de Fórmula (XV) con un reactivo organometálico R^6M adecuado, donde M es Li o MgX y X es Cl, Br o I, en un solvente adecuado para formar una cetona de Fórmula (XVI)



XV XVI ;

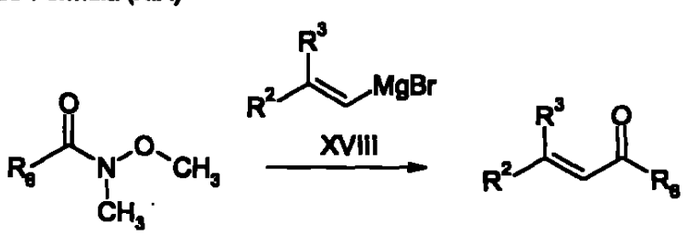
(d) hacer reaccionar la cetona de Fórmula (XVI) con un reactivo organometálico R^5R^4M adecuado, donde M es Li o MgX y X es Cl, Br o I, en un solvente adecuado para formar el compuesto de Fórmula (IB)



XVI IB , R^1 =

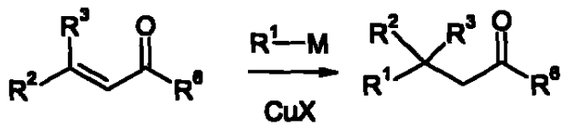
Un segundo método para preparar un compuesto de Fórmula (IB) comprende:

(a') hacer reaccionar una amida de Fórmula (XVII) con un bromuro de vinil magnesio portador de R^2 y R^3 de Fórmula (XVIII) en un solvente adecuado para dar una enona de Fórmula (XIX)



XVII XVIII XIX ;

(b') hacer reaccionar la enona de Fórmula (XIX) con un reactivo organocuproso generado a partir de un reactivo organometálico R^1M, donde M es Li o MgX, y una sal de cobre CuX, donde X es Cl, Br o I, en un solvente adecuado para formar una cetona de Fórmula (XX)

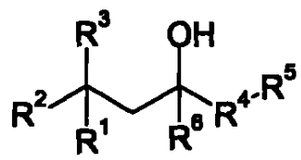


XIX XX ; y

(c') hacer reaccionar la cetona de Fórmula (XX) con un reactivo organometálico R^5R^4M adecuado, donde M es Li o MgX, y X es Cl, Br o I, en un solvente adecuado para formar el compuesto de Fórmula (IB)

XX IB

La presente invención está dirigida a compuestos de Fórmula (IC)



(IC)

donde:

R^1 es un grupo arilo o heteroarilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, cicloalquilo C_3-C_8, heterociclilo, arilo, heteroarilo, alcoxi C_1-C_8, alqueniloxi C_2-C_8, alquiniloxi C_2-C_8, ariloxi, acilo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_8, alcanoilo C_1-C_8, aroilo, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilaminocarboniloxi C_1-C_8, dialquilaminocarboniloxi C_1-C_8, alcanoilamino C_1-C_8, alcoxicarbonilamino C_1-C_8, alquilsulfonilamino C_1-C_8, aminosulfonilo, alquilaminosulfonilo C_1-C_8, dialquilaminosulfonilo C_1-C_8, halógeno, hidroxi, carboxi, ciano, trifluorometilo, trifluorometoxi, nitro o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_8; o alquiltio C_1-C_8 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

donde cada grupo sustituyente de R^1 está sustituido independientemente en forma opcional con uno a tres grupos sustituyentes seleccionados de metilo, metoxi, halógeno, hidroxi, oxo, ciano, heteroarilo, heterociclilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_6;

R^2 y R^3 son cada uno independientemente alquilo C_1-C_6;

R^4 es alquilo C_1-C_6, alquenilo C_2-C_6, o alquinilo C_2-C_6, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^4 es independientemente C_1-C_3 alquilo, hidroxi, halógeno u oxo;

R^5 es un grupo heteroarilo fusionado con un anillo carbocíclico saturado o parcialmente saturado en forma opcional independientemente sustituido con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_6, alquenilo C_2-C_6, alquinilo C_2-C_6, cicloalquilo C_3-C_8, heterociclilo, arilo, heteroarilo, alcoxi C_1-C_6, alqueniloxi C_2-C_6, alquiniloxi C_2-C_6, ariloxi, acilo, alcoxicarbonilo C_1-C_6, alcanoiloxi C_1-C_6, heterociclilcarbonilo, aroilo, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilaminocarboniloxi C_1-C_6, dialquilaminocarboniloxi C_1-C_3, alcanoilamino C_1-C_5, alcoxicarbonilamino C_1-C_6, alquilsulfonilamino C_1-C_3, aminosulfonilo, alquilaminosulfonilo C_1-C_6, dialquilaminosulfonilo C_1-C_6, halógeno, hidroxi, carboxi, ciano, trifluorometilo, trifluorometoxi, trifluorometiltio, nitro o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_6; o alquiltio C_1-C_6 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

donde cada grupo sustituyente de R^5 está sustituido independientemente en forma opcional con uno a tres grupos sustituyentes seleccionados de alquilo C_1-C_3, alcoxi C_1-C_3, acilo, silaniloxi C_1-C_3, alcoxicarbonilo C_1-C_6, carboxi, halógeno, hidroxi, oxo, ciano, arilo, heteroarilo, heterociclilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_3, o trifluorometilo,

R^6 es hidrógeno, alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, carbociclo, heterociclilo, arilo, heteroarilo, carbociclo-alquilo C_1-C_8, carboxi, alcoxicarbonilo, aril-alquilo C_1-C_8, aril-haloalquilo C_1-C_8, heterociclil-alquilo C_1-C_8, heteroaril-alquilo C_1-C_8, carbociclo-alquenilo C_2-C_8, aril-alquenilo C_2-C_8, heterociclil-alquenilo C_2-C_8, o heteroaril-alquenilo C_2-C_8, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^6 es independientemente alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, cicloalquilo C_3-C_8, fenilo, alcoxi C_1-C_8, fenoxi, alcanoilo C_1-C_8, aroilo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_8, aminocarboniloxi, alquilaminocarboniloxi C_1-C_8, dialquilaminocarboniloxi C_1-C_8, aminocarbonilo, alquilaminocarbonilo C_1-C_8, dialquilaminocarbonilo C_1-C_8, alcanoilamino C_1-C_8, alcoxicarbonilamino C_1-C_8, alquilsulfonilamino C_1-C_8, alquilaminosulfonilo C_1-C_8, dialquilaminosulfonilo C_1-C_8, halógeno, hidroxi, carboxi, ciano, oxo, trifluorometilo, nitro, amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_8; o alquiltio C_1-C_8 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto de la invención incluye compuestos de Fórmula (IC), donde:

R^1 es tienilo, fenilo, naftilo, dihidrobenzofuranilo, benzofuranilo, cromanilo, dihidroindolilo, indolilo, dihidrobenzotienilo, benzotienilo, benzodioxolanilo, benzoxazolilo, benzoisoxazolilo, benzopirazolilo, benzoimidazolilo, tienilo, quinolinilo, piridinilo, pirimidinilo, o pirazinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

donde cada grupo sustituyente de R^1 está sustituido independientemente en forma opcional con un grupo sustituyente seleccionado de metilo, metoxi, halógeno, hidroxi, oxo, ciano, heteroarilo, heterociclilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo;

R^2 y R^3 son cada uno independientemente alquilo C_1-C_3;

R^4 es CH_2;

R^5 es un heteroarilo N-enlazado con un anillo carbocíclico saturado de 5-7 miembros fusionado en forma opcional e independientemente sustituido con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, fenilo, alcoxi C_1-C_3, metoxicarbonilo, aminocarbonilo, alquilaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, heterociclilcarbonilo, fluoro, cloro, bromo, ciano, trifluorometilo, hidroxilo, oxo, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

donde cada grupo sustituyente de R^5 está sustituido independientemente en forma opcional con un grupo sustituyente seleccionado de metilo, metoxi, fluoro, cloro, bromo, trifluorometilo, heteroarilo, heterociclilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; y

R^6 es alquilo C_1-C_6, alquenilo C_2-C_6, cicloalquilo C_3-C_6, trifluorometilo, fenilo, cicloalquil-C_3-C_6-alquilo C_1-C_3, fenil-alquilo C_1-C_3, fenil-haloalquilo C_1-C_3, cicloalquil-C_3-C_6 alquenilo C_2-C_3, fenil-alquenilo C_2-C_3, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^6 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, aminocarbonilo, alquilcaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3, donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto más de la invención incluye compuestos de Fórmula (IC), donde:

R^1 es tienilo, fenilo, naftilo, piridilo, cromanilo, dihidrobenzofuranilo, o benzofuranilo, cada uno en forma opcional independientemente sustituido con uno o dos grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente metilo, etilo, metoxi, etoxi, fluoro, cloro, bromo, hidroxi, trifluorometilo, ciano, o alquiltio C_1-C_6 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona;

R^2 y R^3 son cada uno metilo;

R^4 es CH_2;

R^5 es un pirrol, pirazol o imidazol unido por el N, fusionado a un anillo carbocíclico saturado de 5-7 miembros, en forma opcional e independientemente sustituido con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente metilo, fenilo, metoxicarbonilo, aminocarbonilo, metilaminocarbonilo, dimetilamino-aminocarbonilo, morfolinilcarbonilo, fluoro, cloro, bromo, ciano, hidroxi, oxo o trifluorometilo; y

R^6 es alquilo C_1-C_8, cicloalquilo C_3-C_8, trifluorometilo, fenilo, cicloalquilmetilo C_3-C_8 o bencilo cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes

donde cada grupo sustituyente de R^6 es independientemente metilo, metoxi, fluoro, cloro, bromo, ciano, trifluorometilo o hidroxi,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto de la invención incluye compuestos de Fórmula (IC), donde:

R^1 es tienilo, fenilo, naftilo, dihidrobenzofuranilo, benzofuranilo, cromanilo, dihidroindolilo, indolilo, dihidrobenzotienilo, benzotienilo, benzodioxolanilo, benzoxazolilo, benzoisoxazolilo, benzopirazolilo, benzoimidazolilo, tienilo, quinolinilo, piridinilo, pirimidinilo o pirazinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, arilo, heteroarilo, heterocicilo, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

donde cada grupo sustituyente de R^1 está sustituido independientemente en forma opcional con un grupo sustituyente seleccionado de metilo, metoxi, halógeno, hidroxi, oxo, ciano, heteroarilo, heterocicilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo;

R^2 y R^3 son cada uno independientemente alquilo C_1-C_3;

R^4 es CH_2;

R^5 es un heteroarilo unido por el N con un anillo carbocíclico saturado de 5-7 miembros fusionado en forma opcional e independientemente sustituido con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^6 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, fenilo, alcoxi C_1-C_3, metoxicarbonilo, aminocarbonilo, alquilaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, heterociclilcarbonilo, fluoro, cloro, bromo, ciano, trifluorometilo, hidroxilo, oxo, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

donde cada grupo sustituyente de R^6 está sustituido independientemente en forma opcional con un grupo sustituyente seleccionado de metilo, metoxi, fluoro, cloro, bromo, trifluorometilo, heteroarilo, heterocicilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; y

R^8 es alquilo C_1-C_6, alquenilo C_2-C_6, cicloalquilo C_3-C_8, trifluorometilo, fenilo, cicloalquil-C_3-C_6-alquilo C_1-C_3, fenil-alquilo C_1-C_3, fenil-haloalquilo C_1-C_3, cicloalquil-C_3-C_6 alquenilo C_2-C_3, fenil-alquenilo C_2-C_3, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^8 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, aminocarbonilo, alquilaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3, donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto más de la invención incluye compuestos de Fórmula (IC), donde:

R^1 es tienilo, fenilo, naftilo, piridilo, cromanilo, dihidrobenzofuranilo, o benzofuranilo, cada uno en forma opcional independientemente sustituido con uno o dos grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente metilo, etilo, metoxi, etoxi, fluoro, cloro, bromo, hidroxi, trifluorometilo, piridinilo, pirimidinilo, pirazinilo, ciano, o alquiltio C_1-C_6 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona;

donde cada grupo sustituyente de R^1 está sustituido independientemente en forma opcional con un grupo sustituyente seleccionado de ciano o halógeno

R^2 y R^3 son cada uno metilo;

R^4 es CH_2;

R^5 es pirrol, pirazol o imidazol unido por el N, fusionado con un anillo carbocíclico saturado de 5-7 miembros en forma opcional e independientemente sustituido con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^8 es independientemente metilo, fenilo, metoxicarbonilo, aminocarbonilo, metilaminocarbonilo, dimetilaminoaminocarbonilo, morfolinilcarbonilo, fluoro, cloro, bromo, ciano, hidroxi, oxo o trifluorometilo; y

R^9 es alquilo C_1-C_3, cicloalquilo C_3-C_8, trifluorometilo, cicloalquilmetilo C_3-C_8, o bencilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^9 es independientemente metilo, metoxi, fluoro, cloro, bromo, ciano, trifluorometilo o hidroxi,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Los compuestos representativos de Fórmula (IC) de acuerdo con la invención se agregan aquí como Tabla IC, donde la columna A es la denominación del compuesto de acuerdo a la nomenclatura estándar y la columna B es la correspondiente estructura química.

Los compuestos preferidos de Fórmula (IC) incluyen los siguientes:

1-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil-1,5,6,7-tetrahidroindol-4-ona;

1-[4-(2,3-Dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[2-Hidroxi-4-metil-4-(5-pirimidin-5-il-2,3-dihidrobenzofuran-7-il)-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[2-Hidroxi-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[2-Hidroxi-4-(2-hidroxi-5-pirimidin-5-ilfenil)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[2-Hidroxi-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[2-Hidroxi-4-(2-hidroxi-5-piridin-3-ilfenil)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona; y

1-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Compuestos más preferidos de Fórmula (IC) incluyen los siguientes:

1-[2-Hidroxi-4-metil-4-(5-pirimidin-5-il-2,3-dihidrobenzofuran-7-il)-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[2-Hidroxi-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[2-Hidroxi-4-(2-hidroxi-5-pirimidin-5-ilfenil)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[2-Hidroxi-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona; y

1-[2-Hidroxi-4-(2-hidroxi-5-piridin-3-ilfenil)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Los compuestos más preferidos de Fórmula (IC) incluyen los siguientes:

1-[2-Hidroxi-4-metil-4-(5-pirimidin-5-il-2,3-dihidrobenzofuran-7-il)-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[2-Hidroxi-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

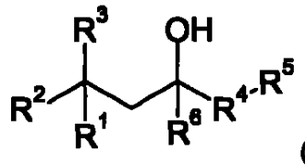
1-[2-Hidroxi-4-(2-hidroxi-5-pirimidin-5-ilfenil)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[2-Hidroxi-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona; y

1-[2-Hidroxi-4-(2-hidroxi-5-piridin-3-ilfenil)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona,

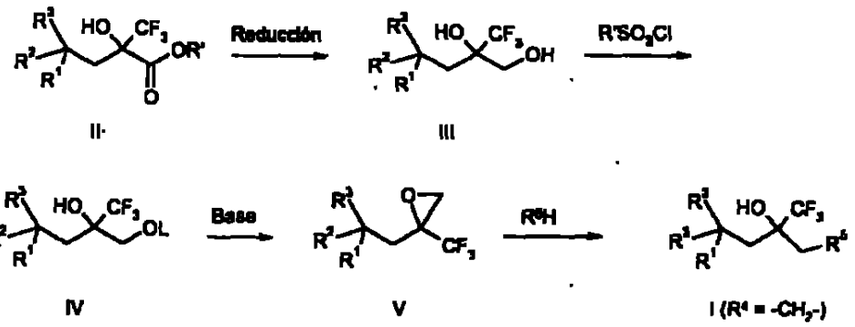
o un tautómero, un profármaco, un solvato o sal de los mismos.

La invención además ofrece métodos para preparar un compuesto de Fórmula (IC)

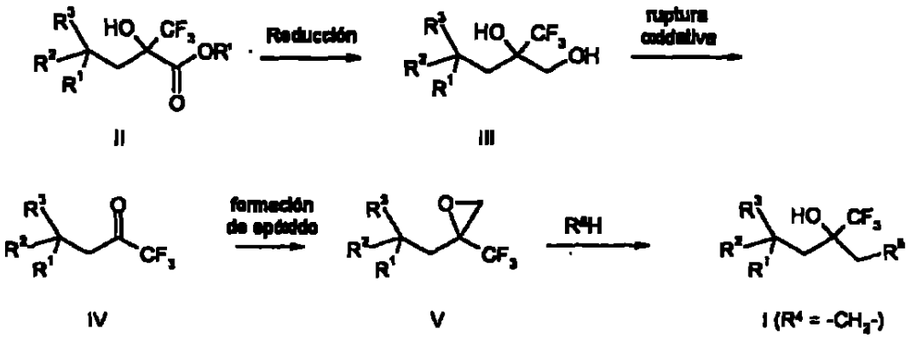


(IC).

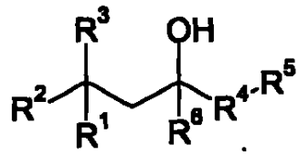
A continuación se muestra una secuencia de síntesis para preparar un compuesto de Fórmula (IC).



A continuación se muestra un segundo método de preparación de un compuesto de Fórmula (IC)



La presente invención también está dirigida a compuestos de Fórmula (ID)



(ID)

donde:

R^1 es un grupo arilo o heteroarilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, cicloalquilo C_3-C_8, heterociclilo, arilo, heteroarilo, alcoxi C_1-C_8, alqueniloxi C_2-C_8, alquiniloxi C_2-C_8, ariloxi, acilo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_8, alcanoilo C_1-C_8, aroilo, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilaminocarboniloxi C_1-C_8, dialquilaminocarboniloxi C_1-C_8, alcanoilamino C_1-C_8, alcoxicarbonilamino C_1-C_8, alquilsulfonilamino C_1-C_8, aminosulfonilo,

alquilaminosulfonilo C_1-C_6, dialquilaminosulfonilo C_1-C_6, halógeno, hidroxi, carboxi, ciano, trifluorometilo, trifluorometoxi, nitro, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente austituido con alquilo C_1-C_6; o alquiltio C_1-C_6 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

donde cada grupo sustituyente de R^1 está sustituido independientemente en forma opcional con uno a tres grupos sustituyentes seleccionados de metilo, metoxi, halógeno, hidroxi, oxo, ciano, heteroarilo, heterociclilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_6;

R^2 y R^3 son cada uno independientemente alquilo C_1-C_6, donde uno o ambos están independientemente sustituidos con hidroxi, alcoxi C_1-C_6, alquiltio C_1-C_6 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona, amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo;

R^4 es alquilo C_1-C_6, alquenilo C_2-C_6, o alquinilo C_2-C_6, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^4 es independientemente alquilo C_1-C_3, hidroxi, halógeno u oxo;

R^5 es un grupo heteroarilo independientemente sustituido en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_6, alquenilo C_2-C_6, alquinilo C_2-C_6, cicloalquilo C_3-C_6, heterociclilo, arilo, heteroarilo, alcoxi C_1-C_6, alqueniloxi C_2-C_6, alquiniloxi C_2-C_6, ariloxi, acilo, alcoxicarbonilo C_1-C_6, alcaniloxi C_1-C_6, heterociclilcarbonilo, aroilo, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilaminocarboniloxi C_1-C_6, dialquilaminocarboniloxi C_1-C_6, alcanoilamino C_1-C_6, alcoxicarbonilamino C_1-C_6, alquilsulfonilamino C_1-C_6, aminosulfonilo, alquilaminosulfonilo C_1-C_6, dialquilaminosulfonilo C_1-C_6, halógeno, hidroxi, carboxi, ciano, trifluorometilo, trifluorometoxi, trifluorometiltio, nitro, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6; o ureido donde el átomo de nitrógeno en forma opcional está

independientemente sustituido con alquilo C_1-C_8; o alquiltio C_1-C_8 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

donde cada grupo sustituyente de R^5 está sustituido independientemente en forma opcional con uno a tres grupos sustituyentes seleccionados de alquilo C_1-C_3, alcoxi C_1-C_3, acilo, silanilioxi C_1-C_3, alcoxicarbonilo C_1-C_3, carboxi, halógeno, hidroxi, oxo, ciano, arilo, heteroarilo, heterocicilio, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_5, o trifluorometilo,

R^6 es hidrógeno, alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, carbocicilo, heterocicilio, arilo, heteroarilo, carbocicilo-alquilo C_1-C_8, carboxi, alcoxicarbonilo, aril-alquilo C_1-C_8, aril-haloalquilo C_1-C_8, heterocicil-alquilo C_1-C_8, heteroaril-alquilo C_1-C_8, carbocicilo-alquenilo C_2-C_8, aril-alquenilo C_2-C_8, heterocicil-alquenilo C_2-C_8, o heteroaril-alquenilo C_2-C_8, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^6 es independientemente alquilo C_1-C_5, alquenilo C_2-C_5, alquinilo C_2-C_5, cicloalquilo C_3-C_8, fenilo, alcoxi C_1-C_5, fenoxi, alcanoilo C_1-C_5, aroilo, alcoxicarbonilo C_1-C_5, alcanoiloxi C_1-C_5, aminocarboniloxi, alquilaminocarboniloxi C_1-C_5, dialquilaminocarboniloxi C_1-C_5, aminocarbonilo, alquilaminocarbonilo C_1-C_5, dialquilaminocarbonilo C_1-C_5, alcanoilamino C_1-C_5, alcoxicarbonilamino C_1-C_5, alquilsulfonilamino C_1-C_5, alquilaminosulfonilo C_1-C_5, dialquilaminosulfonilo C_1-C_5, halógeno, hidroxi, carboxi, ciano, oxo, trifluorometilo, nitro, amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_5; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_5; o alquiltio C_1-C_5 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto de la invención incluye compuestos de Fórmula (ID), donde:

R^1 es tienilo, fenilo, naftilo, dihidrobenzofuranilo, benzofuranilo, cromanilo, dihidroindolilo, indolilo, dihidrobenzotienilo, benzotienilo, benzodioxolanilo, benzoxazolilo, benzoisoxazolilo, benzopirazolilo, benzoimidazolilo, tienilo, quinolinilo, piridinilo, pirimidinilo o pirazinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes.

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

donde cada grupo sustituyente de R^1 está sustituido independientemente en forma opcional con un grupo sustituyente seleccionado de metilo, metoxi, halógeno, hidroxi, oxo, ciano, heteroarilo, heterociclilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo;

R^2 y R^3 son cada uno independientemente alquilo C_1-C_3, donde uno o ambos están independientemente sustituidos con hidroxi, alcoxi C_1-C_6;

R^4 es CH_2;

R^5 es un grupo imidazolilo, piridilo, indolilo, azaindolilo, diazaindolilo, benzofuranilo, furanopiridinilo, furanopirimidinilo, benzotienilo, tienopiridinilo, tienopirimidinilo, benzoxazolilo, oxazolopiridinilo, benzotiazolilo, tiazolopiridinilo, benzoimidazolilo, imidazolopiridinilo, imidazolopirimidinilo, imidazolopiridazinilo, imidazolopirazinilo, quinolinilo o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, fenilo, alcoxi C_1-C_3, metoxicarbonilo, aminocarbonilo, alquilaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, heterociclilcarbonilo, fluoro, cloro, bromo, ciano, trifluorometilo, hidroxilo, oxo, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

donde cada grupo sustituyente de R^5 está sustituido independientemente en forma opcional con un grupo sustituyente seleccionado de metilo, metoxi, fluoro, cloro, bromo, trifluorometilo, heteroarilo, heterociclilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; y

R^6 es alquilo C_1-C_8, alquenilo C_2-C_8, cicloalquilo C_3-C_8, trifluorometilo, fenilo, cicloalquil-C_3-C_8-alquilo C_1-C_3, fenil-alquilo C_1-C_3, fenil-haloalquilo C_1-C_3, cicloalquil-C_3-C_8 alquenilo C_2-C_3, fenil-alquenilo C_2-C_3, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^6 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, aminocarbonilo,

alquiloaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3, donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto más de la invención incluye compuestos de Fórmula (ID), donde:

R^1 es tienilo, fenilo, naftilo, piridilo, cromanilo, dihidrobenzofuranilo, o benzofuranilo, cada uno en forma opcional independientemente sustituido con uno o dos grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente metilo, etilo, metoxi, etoxi, fluoro, cloro, bromo, hidroxi, trifluorometilo, ciano, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona;

R^2 y R^3 son cada uno metilo, donde uno o ambos están independientemente sustituidos con hidroxi o metoxi;

R^4 es CH_2;

R^5 es un grupo piridilo, indolilo, azaindolilo, benzofuranilo, furanopiridinilo, tienopiridinilo, benzoxazolilo, benzoimidazolilo, quinolinilo o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente metilo, fenilo, metoxicarbonilo, aminocarbonilo, metilaminocarbonilo, dimetilaminoaminocarbonilo, morfolinilcarbonilo, fluoro, cloro, bromo, ciano o trifluorometilo; y

R^6 es alquilo C_1-C_3, cicloalquilo C_3-C_6, cicloalquilmetilo C_3-C_6, trifluorometilo o bencilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^6 es independientemente metilo, metoxi, fluoro, cloro, bromo, ciano, trifluorometilo o hidroxi,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Otro aspecto más de la invención incluye compuestos de Fórmula (ID), donde:

R^1 es fenilo, dihidrobenzofuranilo o benzofuranilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o a sulfona, y

R^2 y R^3 son cada uno independientemente alquilo C_1-C_3 cada uno en forma opcional independientemente sustituido con hidroxi, alcoxi C_1-C_3,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Los compuestos representativos de Fórmula (ID) de acuerdo con la invención se agregan aquí como Tabla ID, donde la columna A es la denominación del compuesto de acuerdo a la nomenclatura estándar y la columna B es la correspondiente estructura química.

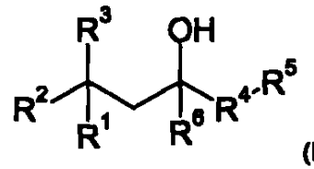
Los compuestos preferidos de Fórmula (ID) incluyen los siguientes:

1,1,1-Trifluoro-5-metoxi-4-metil-4-fenil-2-quinolin-4-ilmetilpentan-2-ol; y

5,5,5-Trifluoro-2-metil-2-fenil-4-quinolin-4-ilmetilpentan-1,4-diol,

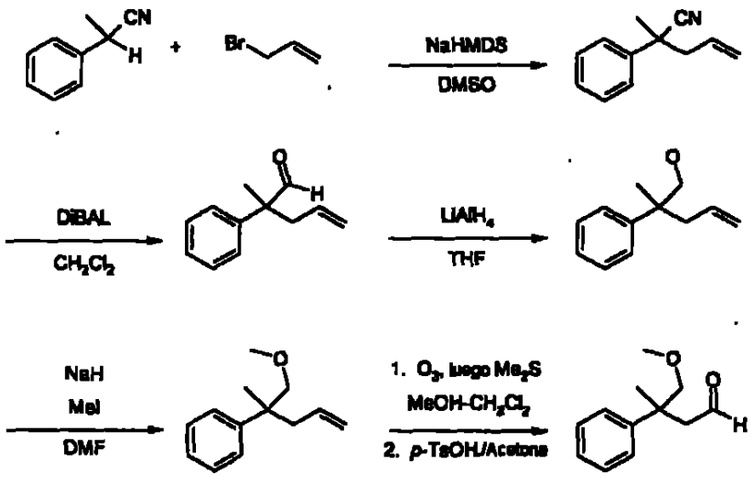
o un tautómero, un profármaco, un solvato o sal de los mismos.

La invención ofrece además métodos para preparar un compuesto de Fórmula (ID).



(ID)

Un método de preparación de los compuestos de Fórmula (ID) es vía el aldehído



intermediario que se muestra a continuación.

En otro aspecto de la invención, los compuestos de acuerdo con la invención se formulan para dar composiciones farmacéuticas que comprenden una cantidad efectiva,

de preferencia una cantidad farmacéuticamente efectiva de un compuesto de acuerdo con la invención o un tautómero, un profármaco, un solvato o sal de los mismos y un excipiente o vehículo aceptables para uso farmacéutico.

La invención asimismo ofrece un método para modular la función del receptor de glucocorticoides en un paciente, comprendiendo el método administrar a un paciente una cantidad efectiva de un compuesto de acuerdo con la invención o un tautómero, un profármaco, un solvato o una sal de los mismos.

La invención ofrece además un método para tratar un estado o un cuadro patológico mediado por la función del receptor de glucocorticoides en un paciente con necesidad de tal tratamiento, comprendiendo el método administrar a un paciente una cantidad efectiva de un compuesto de acuerdo con la invención o un tautómero, un profármaco, un solvato o una sal de los mismos.

Además la invención también ofrece un método para tratar un estado o un cuadro patológico seleccionado de: diabetes tipo II, obesidad, enfermedades cardiovasculares, hipertensión, arterioesclerosis, enfermedades neurológicas, tumores adrenales o pituitarios y glaucoma, en un paciente con necesidad de tal tratamiento, comprendiendo el método administrar a un paciente una cantidad efectiva de un compuesto de acuerdo con la invención o un tautómero, un profármaco, un solvato o una sal de los mismos.

La invención también ofrece un método para tratar una enfermedad caracterizada por procesos inflamatorios, alérgicos o proliferativos, en un paciente con necesidad de tal tratamiento, comprendiendo el método administrar a un paciente una cantidad efectiva de un compuesto aceptable para uso farmacéutico de acuerdo con la invención o un tautómero, un profármaco, un solvato o una sal del mismo. En una forma de realización preferida de la invención, las enfermedades caracterizadas por procesos inflamatorios, alérgicos o proliferativos se seleccionan de: (i) enfermedades pulmonares; (ii) enfermedades reumáticas o enfermedades autoinmunes o enfermedades combinadas; (iii) enfermedades alérgicas; (iv) enfermedades vasculares; (v) enfermedades dermatológicas; (vi) enfermedades renales; (vii) enfermedades hepáticas; (viii) enfermedades gastrointestinales; (ix) enfermedades proctológicas; (x) enfermedades oculares; (xi) enfermedades del área de la garganta, nariz y oídos (GNO); (xii) enfermedades neurológicas; (xiii) enfermedades de la sangre; (xiv) enfermedades tumorales; (xv) enfermedades endócrinas; (xvi) transplantes de órganos y tejidos y reacciones de injerto contra huésped; (xvii) estados severos de shock; (xviii) terapia de sustitución; y (xix) dolor de génesis inflamatoria. En otra realización preferida de la invención, la enfermedad caracterizada por procesos inflamatorios, alérgicos o

proliferativos se selecciona de: diabetes tipo I, osteoartritis, síndrome de Guillain-Barre, restenosis posterior a angioplastia coronaria transluminal percutánea, enfermedad de Alzheimer, dolores graves y crónicos, ateroesclerosis, lesión de reperfusión, enfermedades de resorción ósea, falla cardiaca congestiva, infarto de miocardio, lesión térmica, lesión orgánica múltiple como consecuencia de trauma, meningitis aguda purulenta, enterocolitis necrotizante y síndromes asociados con hemodiálisis, leucoferesis y transfusión de granulocitos.

La invención además ofrece métodos para tratar los estados o cuadros patológicos previamente mencionados en un paciente con necesidad de tal tratamiento, comprendiendo los métodos administrar en forma secuencial o simultánea a un paciente: (a) una cantidad efectiva de un compuesto aceptable para uso farmacéutico de acuerdo con la invención o un tautómero, un profármaco, solvato o una sal del mismo; y (b) un glucocorticoide aceptable para uso farmacéutico.

La invención además ofrece un método para ensayar la función del receptor de glucocorticoides en una muestra, que comprende: (a) poner en contacto la muestra con una cantidad seleccionada de un compuesto de acuerdo con la invención o un tautómero, profármaco, solvato o una sal del mismo; y (b) detectar la cantidad del compuesto de acuerdo con la invención o un tautómero, profármaco, solvato o sal del mismo unida a los receptores de glucocorticoides en la muestra. En una forma de realización preferida de la invención, el compuesto de acuerdo con la invención o un tautómero, profármaco, solvato o sal del mismo se marca con un marcador detectable seleccionado de: un radiomarcador, un marcador fluorescente, un marcador quimioluminiscente, un cromóforo y un marcador de spin.

La invención asimismo ofrece un método para visualizar la distribución del receptor de glucocorticoides en una muestra o en un paciente, comprendiendo el método: (a) poner en contacto la muestra o administrar a un paciente un compuesto de acuerdo con la invención o un tautómero, profármaco, solvato o sal del mismos que presenta un marcador detectable; (b) detectar la distribución espacial y cantidad del compuesto de acuerdo con la invención o un tautómero, profármaco, solvato o sal del mismo que presenta un marcador detectable ligado a receptores de glucocorticoides en la muestra o en un paciente utilizando un medio de visualización para obtener una imagen; y (c) mostrar una imagen de la distribución espacial y la cantidad del compuesto de acuerdo con la invención o un tautómero, profármaco, solvato o sal del mismo que presenta un marcador detectable ligado a receptores de glucocorticoides en la muestra. En una forma de realización preferida de la invención, el medio de visualización se selecciona de:

radiocentellografía, imagen de resonancia magnética nuclear (MRI), tomografía computada (CT scan), o tomografía de emisión de positrones (PET).

La invención asimismo ofrece un kit para la determinación diagnóstica *in vitro* de la función del receptor de glucocorticoides en una muestra, que comprende: (a) una cantidad efectiva con fines diagnósticos de un compuesto de acuerdo con la invención o un tautómero, profármaco, solvato o sal del mismo; y (b) instrucciones para el uso del kit de diagnóstico.

Se prefiere que los compuestos de Fórmula (IA), (IB), (IC), y (ID) excluyan los compuestos revelados en la Solicitud de Patente Norteamericana publicada U.S. Nº 2004/0023999.

Breve Descripción de las Tablas

En la Tabla IA se enumeran compuestos representativos de la Fórmula (IA).

En la Tabla IB se enumeran compuestos representativos de la Fórmula (IB).

En la Tabla IC se enumeran compuestos representativos de la Fórmula (IC).

En la Tabla ID se enumeran compuestos representativos de la Fórmula (ID).

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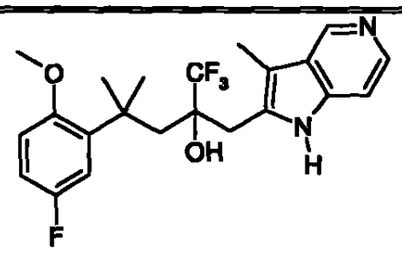
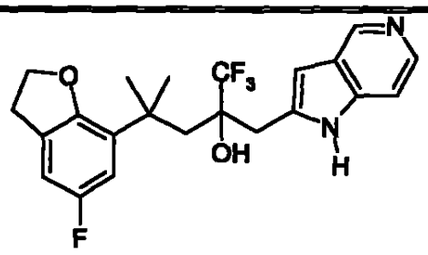
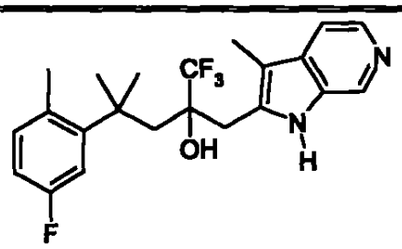
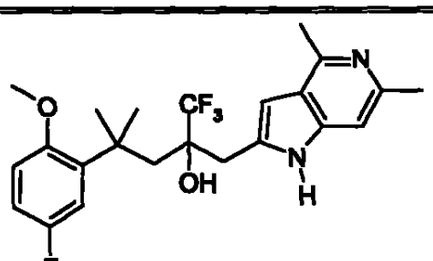
IA	
A	B
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(3-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2,3-dihidrobenzofuran-7-il)-4-metil-2-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(3-metil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
2-(4,6-Dimetil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metoxifenil)-4-metilpentan-2-ol	

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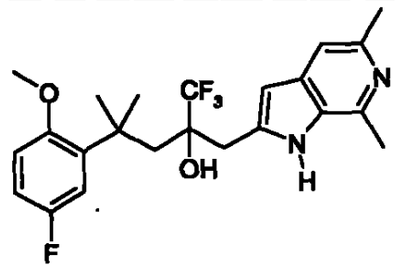
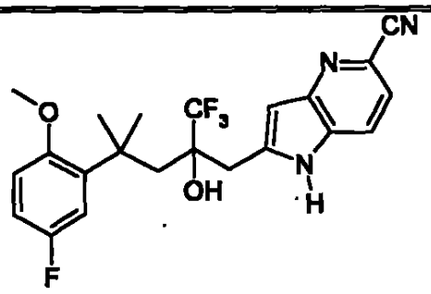
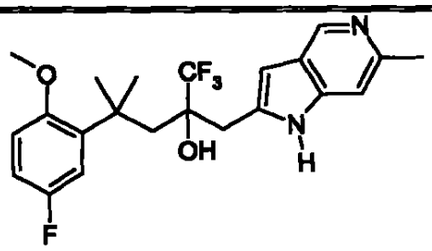
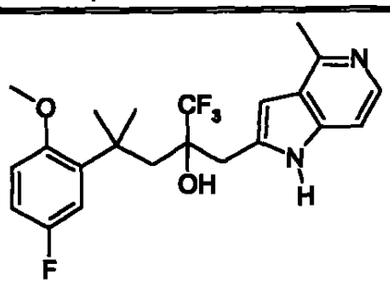
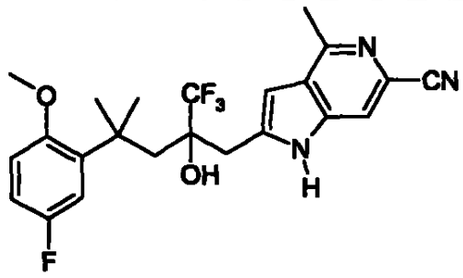
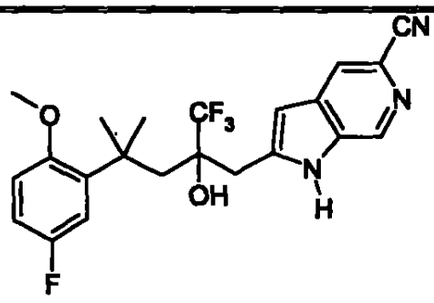
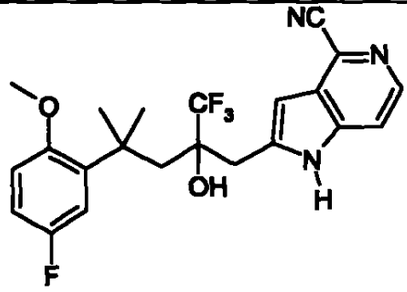
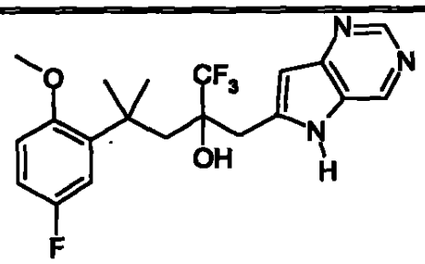
IA	
A	B
2-(5,7-Dimetil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metoxifenil)-4-metilpentan-2-ol	
2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-carbonitrilo	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol	

IA	
A	**B**
2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-4-metil-1*H*-pirrolo[3,2-c]piridin-6-carbonitrilo	
2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[2,3-c]piridin-5-carbonitrilo	
2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[3,2-c]piridin-4-carbonitrilo	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol	

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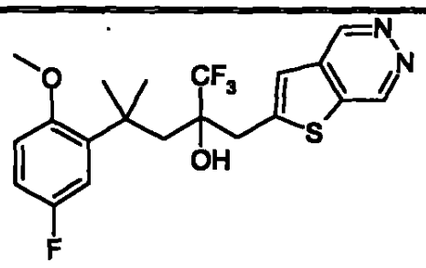
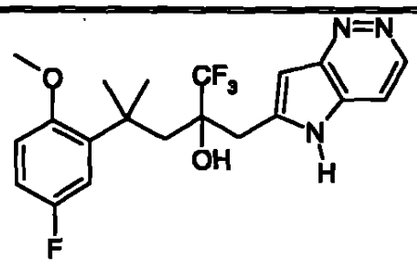
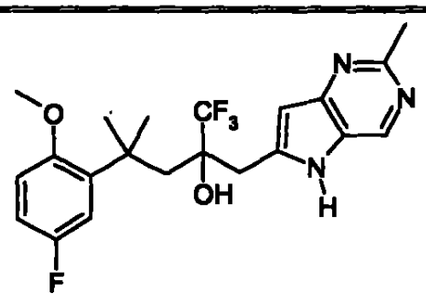
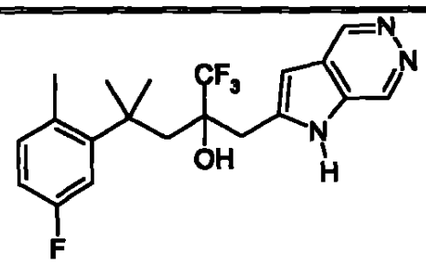
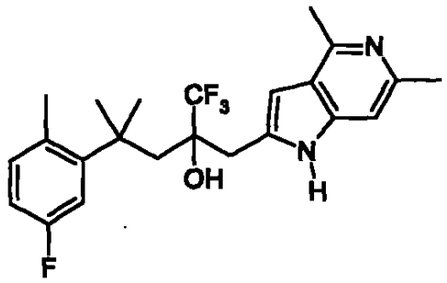
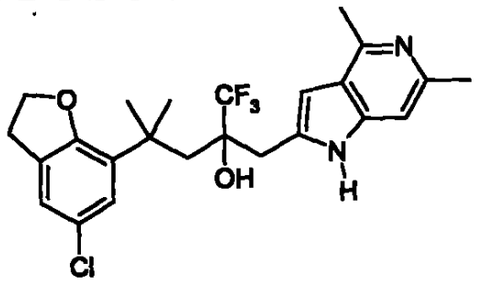
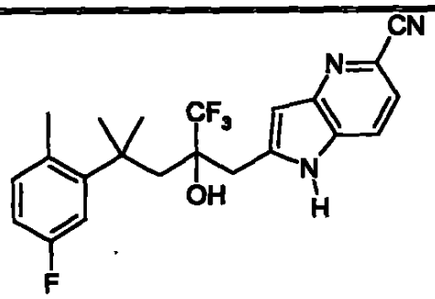
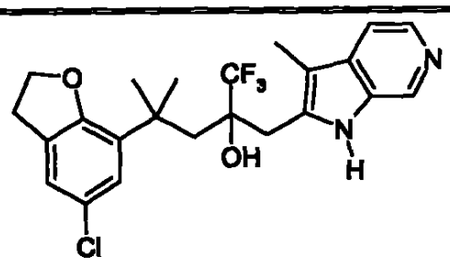
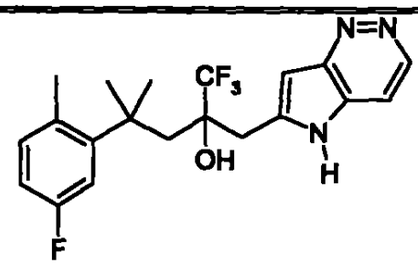
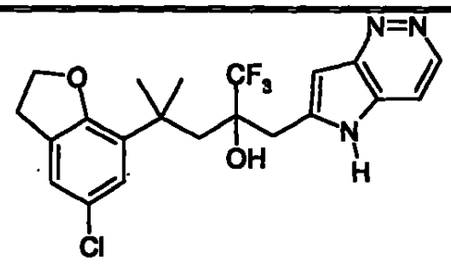
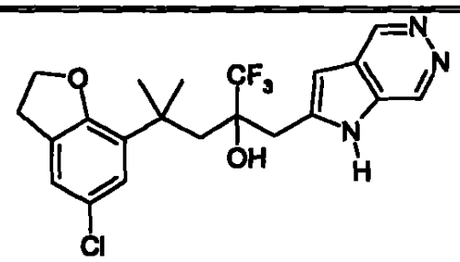
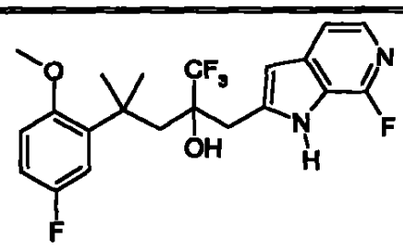
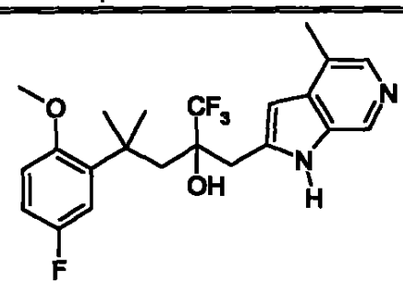
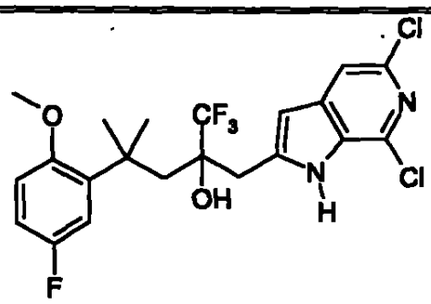
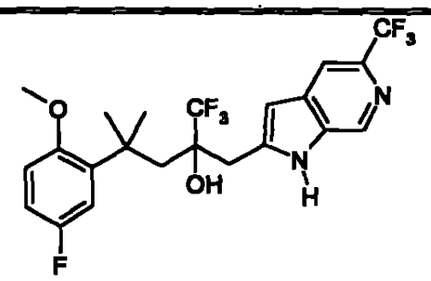
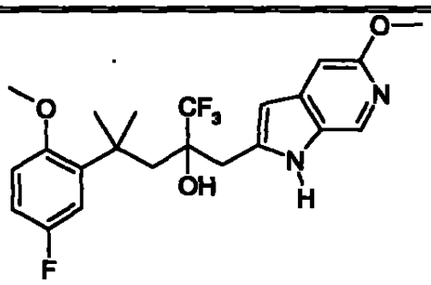
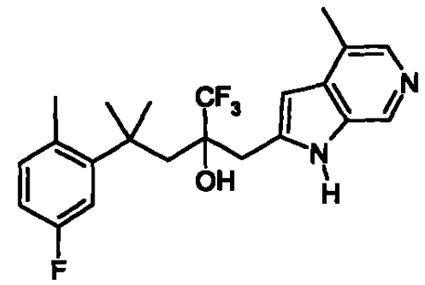
IA	
A	B
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-tieno[2,3-*d*]piridazin-2-ilmetilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(2-metil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(1*H*-pirrolo[2,3-*d*]piridazin-2-ilmetil)pentan-2-ol	

IA	
A	B
2-(4,6-Dimetil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metilfenil)-4-metilpentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(4,6-dimetil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluor-4-metilpentan-2-ol	
2-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-carbonitrilo	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	

IA	
A	B
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(1*H*-pirrolo[2,3-*d*]piridazin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-2-(7-fluor-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	

IA	
A	B
2-(5,7-Dicloro-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metoxifenil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(5-trifluormetil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-2-(5-metoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	

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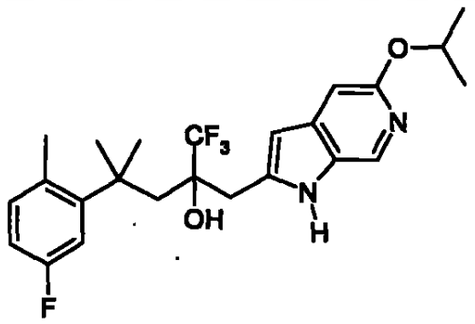
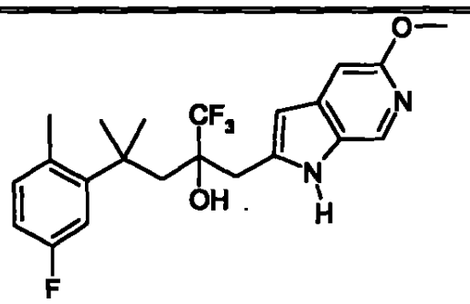
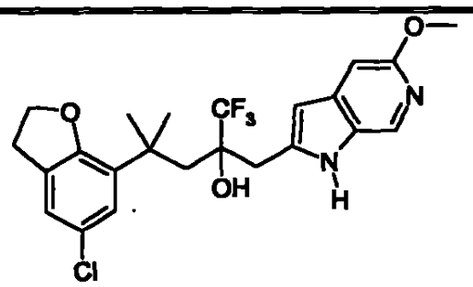
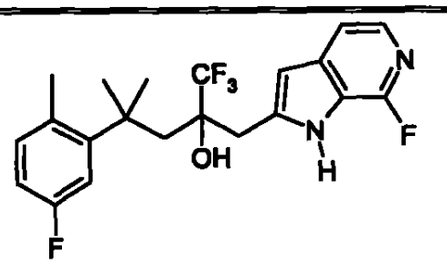
IA	
A	**B**
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-2-(5-metoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-2-(5-metoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-2-(7-fluor-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol	

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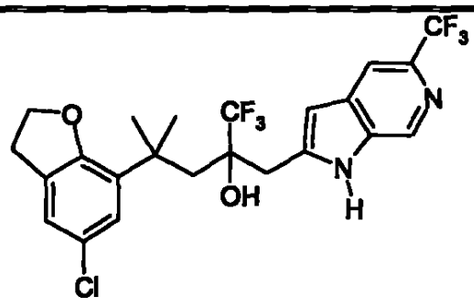
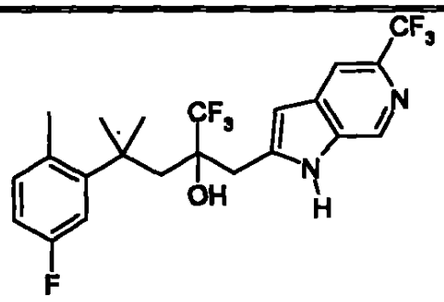
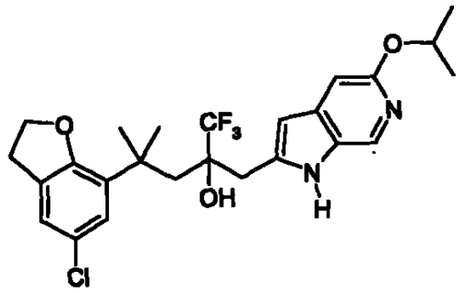
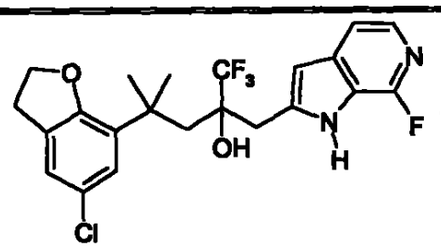
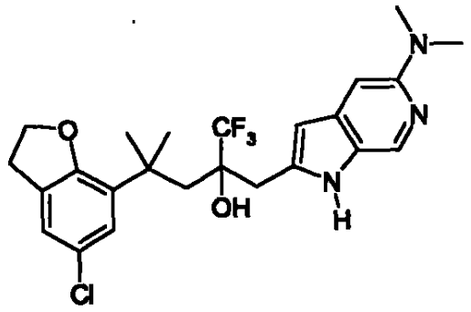
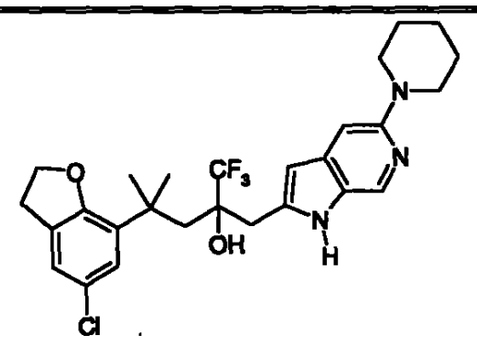
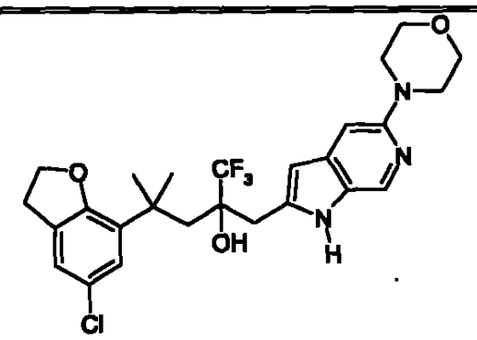
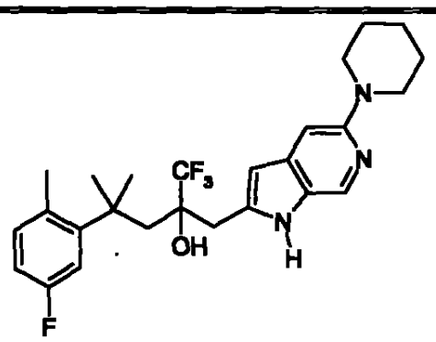
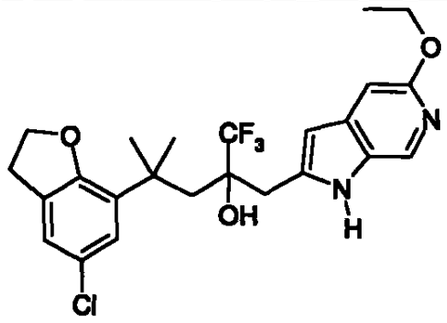
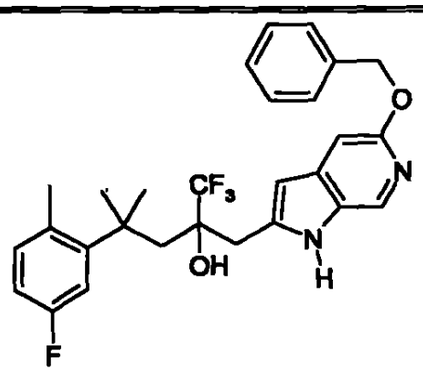
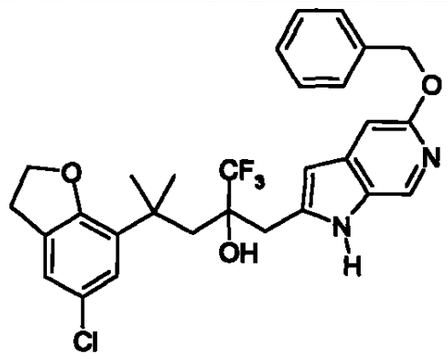
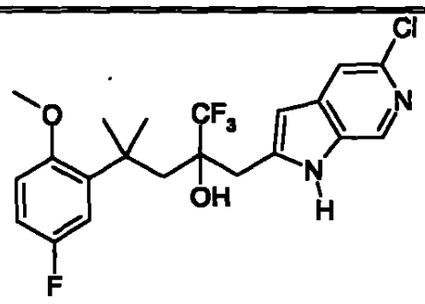
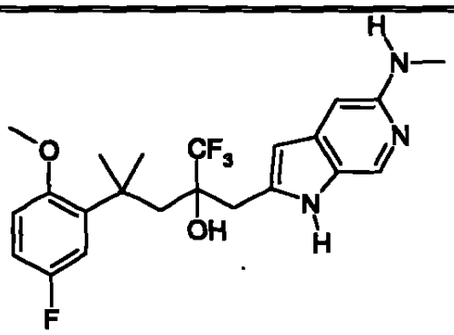
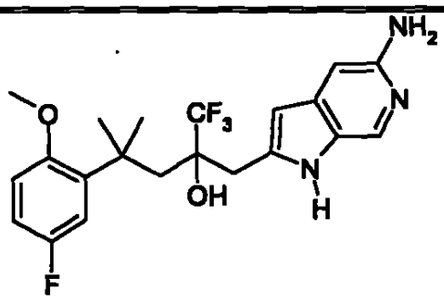
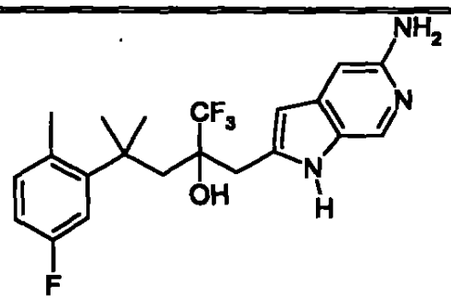
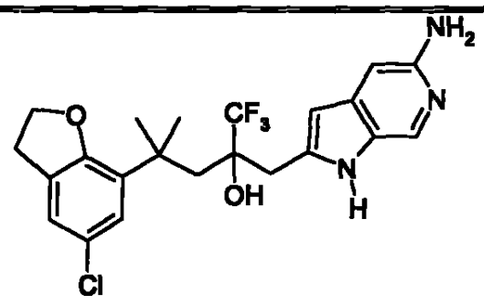
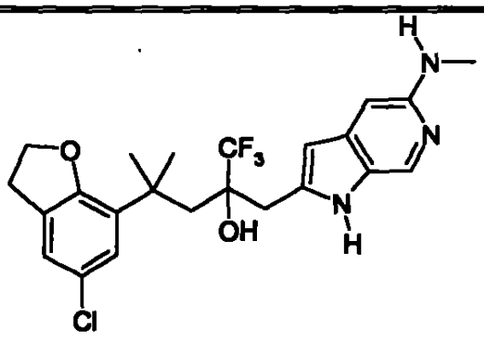
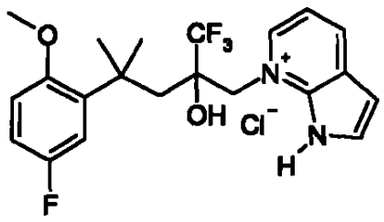
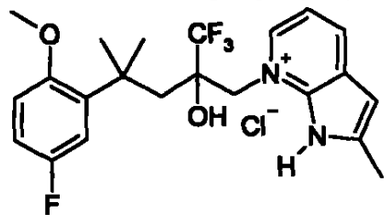
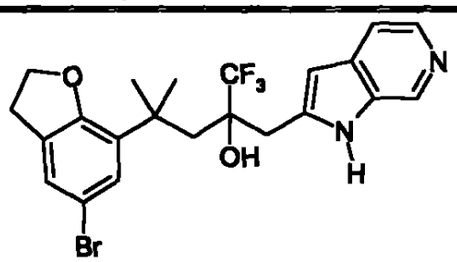
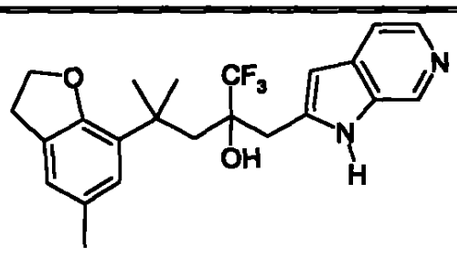
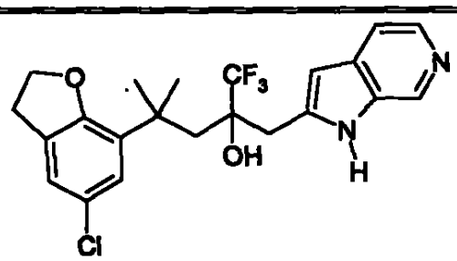
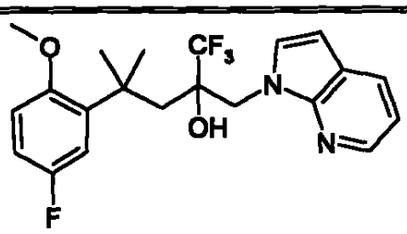
IA	
A	B
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(5-trifluormetil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-trifluormetil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-2-(5-isopropoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-metilpentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-2-(7-fluor-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-metilpentan-2-ol	

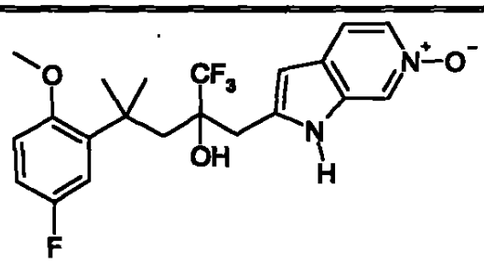
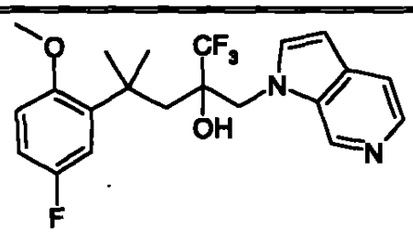
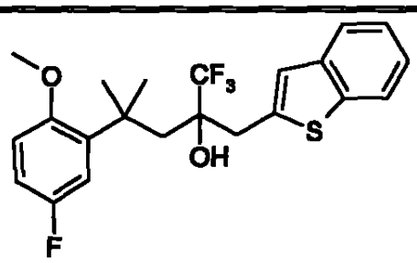
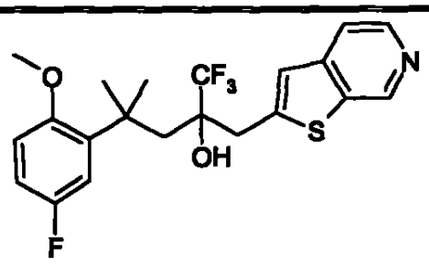
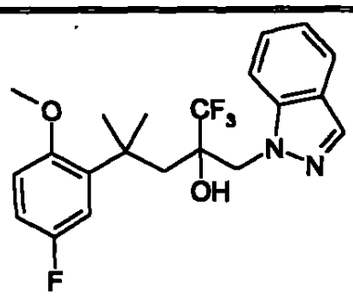
IA	
A	B
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(5-dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluor-4-metilpentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	

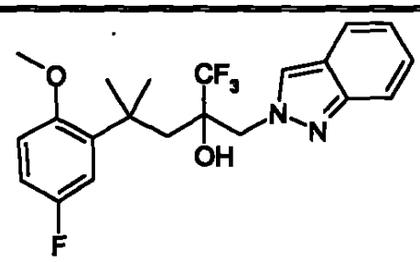
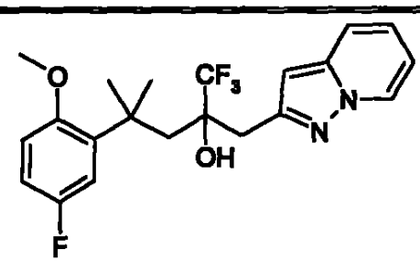
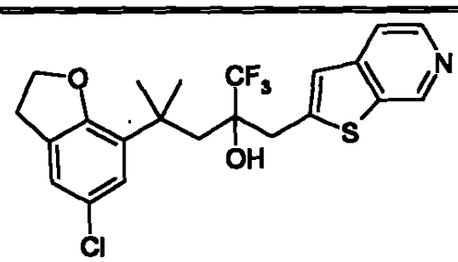
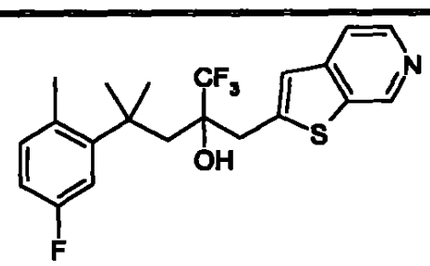
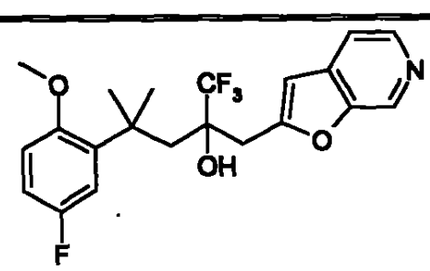
IA	
A	B
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(5-etoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluor-4-metilpentan-2-ol	
2-(5-Benciloxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metilfenil)-4-metilpentan-2-ol	

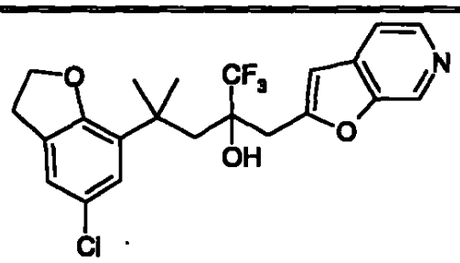
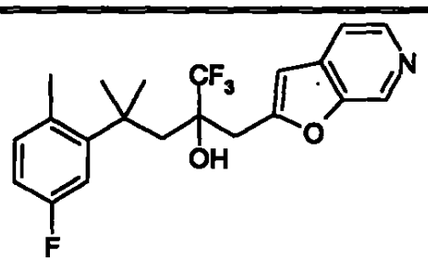
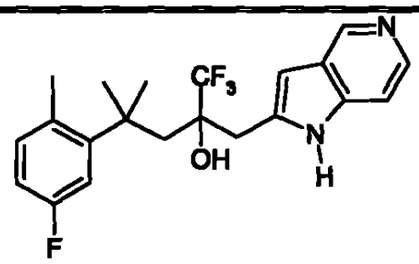
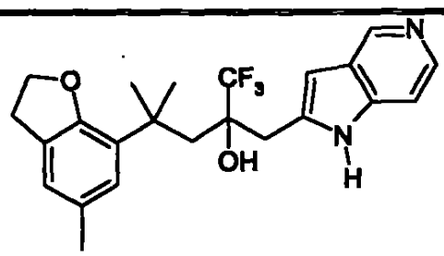
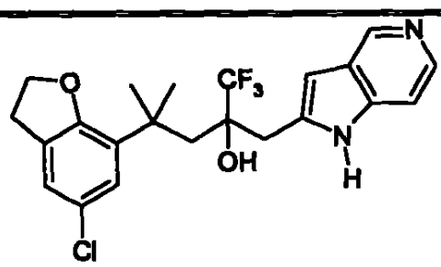
IA	
A	B
2-(5-Benciloxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-2-(5-cloro-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-[5-(metilamino)-1*H*-pirrolo[2,3-c]piridin-2-ilmetil]pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(5-amino-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	

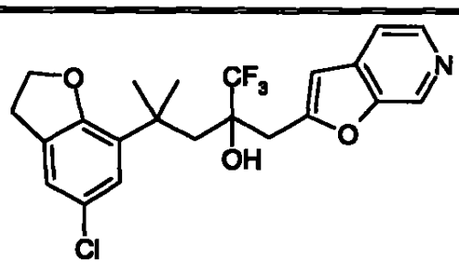
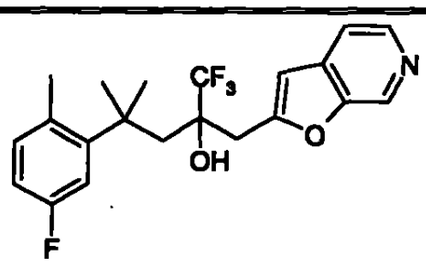
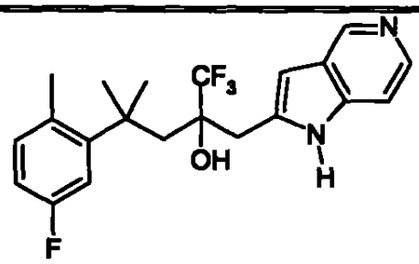
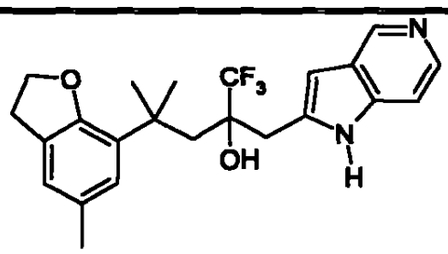
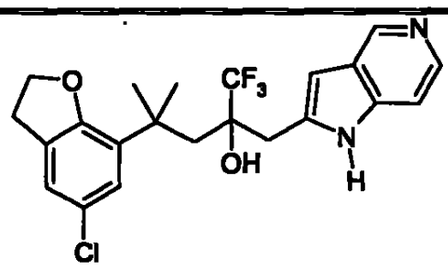
IA	
A	**B**
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(6-amino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-2-(5-amino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(5-metilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
Cloruro de 7-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[2,3-*b*]piridin-7-io	

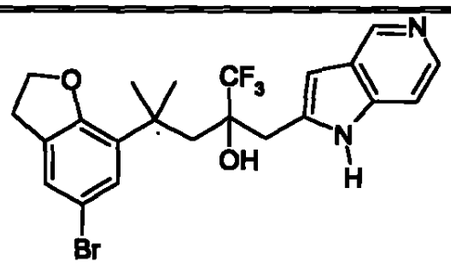
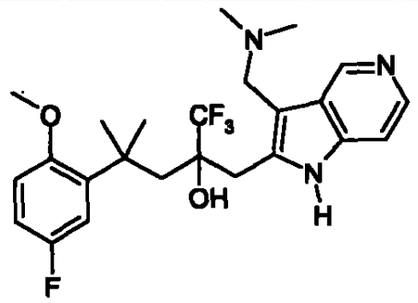
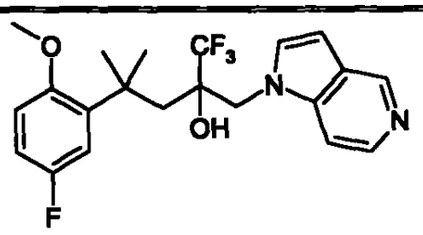
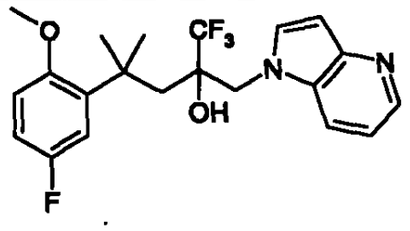
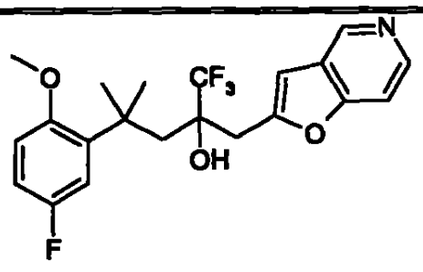
IA	
A	B
Cloruro de 6-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-2-metil-1*H*-pirrolo[2,3-*c*]piridin-6-io	
4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-(5-metil-2,3-dihidrobenzofuran-7-il)-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-pirrolo[2,3-*b*]piridin-1-ilmetilpentan-2-ol	

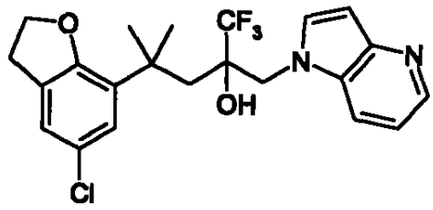
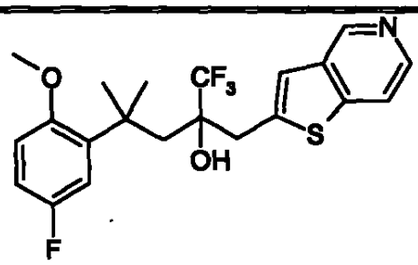
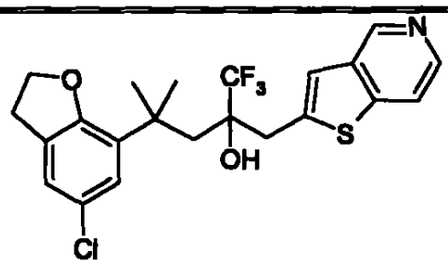
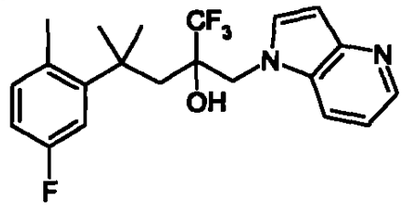
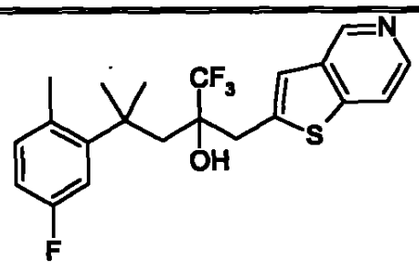
IA	
A	B
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(6-oxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-pirrolo[2,3-*c*]piridin-1-ilmetilpentan-2-ol	
2-Benzo[*b*]tiofen-2-ilmetil-1,1,1-trifluor-4-(5-fluor-2-metoxifenil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-tieno[2,3-*c*]piridin-2-ilmetilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-2-indazol-1-ilmetil-4-metilpentan-2-ol	

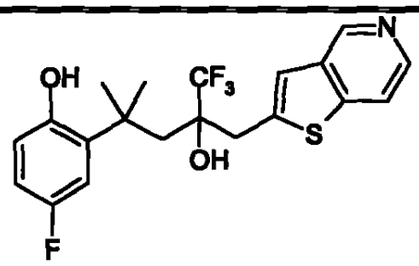
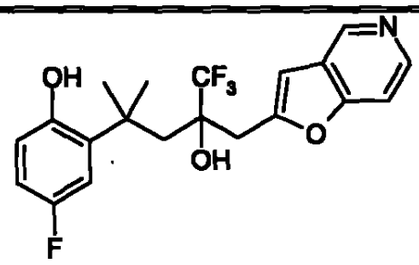
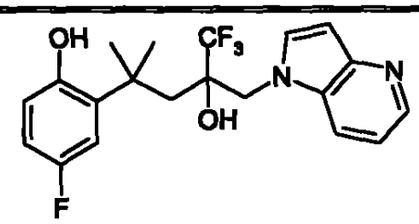
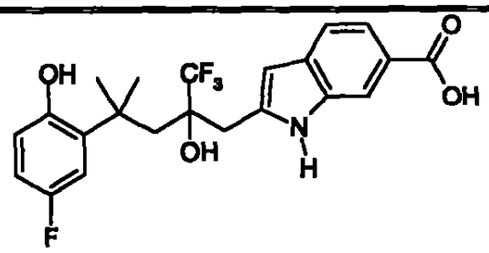
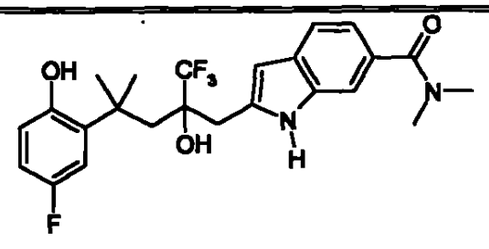
IA	
A	B
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-[4-((Z)propenil)-3-vinilpirazol-1-ilmetil]pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-pirazolo[1,5-a]piridin-2-ilmetilpentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,4-dimetil-1-tieno[2,3-c]piridin-2-ilpentan-2-ol	
4-(5-Fluor-2-metilfenil)-2,4-dimetil-1-tieno[2,3-c]piridin-2-ilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-2-furo[2,3-c]piridin-2-ilmetil-4-metilpentan-2-ol	

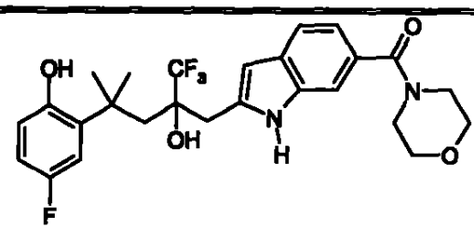
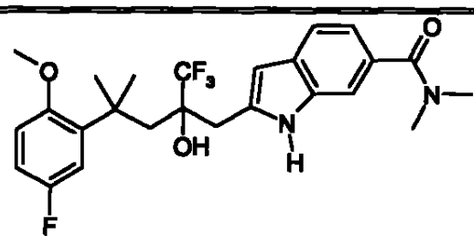
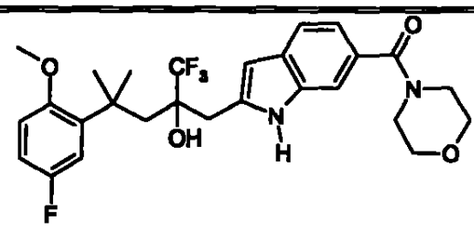
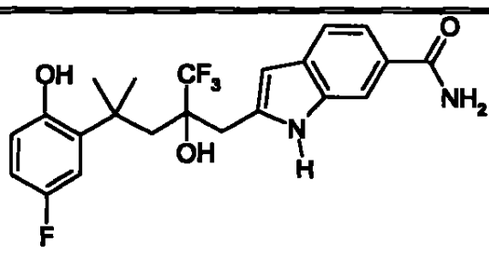
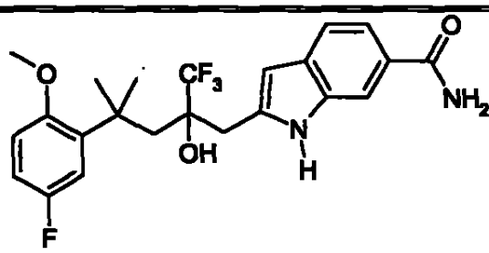
IA	
A	B
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1-furo[2,3-*c*]piridin-2-il-2,4-dimetilpentan-2-ol	
4-(5-Fluor-2-metilfenil)-1-furo[2,3-c]piridin-2-il-2,4-dimetilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-(5-metil-2,3-dihidrobenzofuran-7-il)-2-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol	

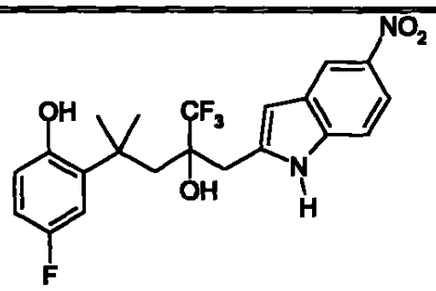
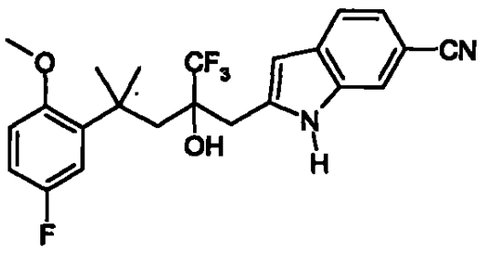
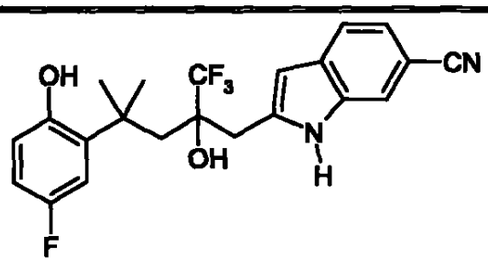
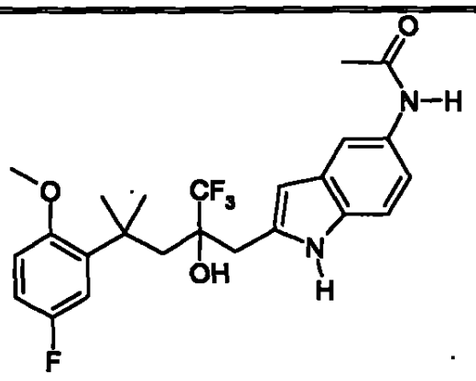
IA	
A	**B**
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1-furo[2,3-*c*]piridin-2-il-2,4-dimetilpentan-2-ol	
4-(5-Fluor-2-metilfenil)-1-furo[2,3-*c*]piridin-2-il-2,4-dimetilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-(5-metil-2,3-dihidrobenzofuran-7-il)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	

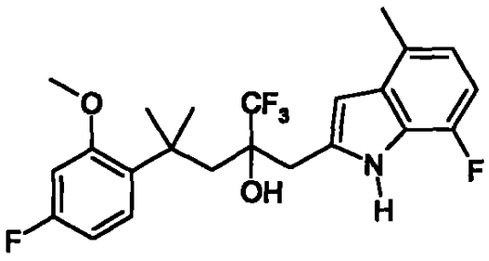
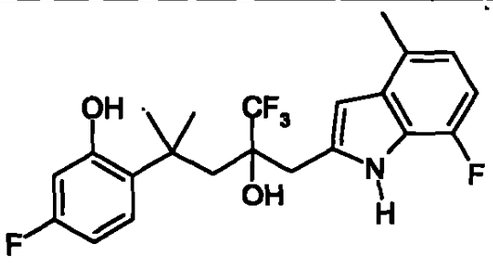
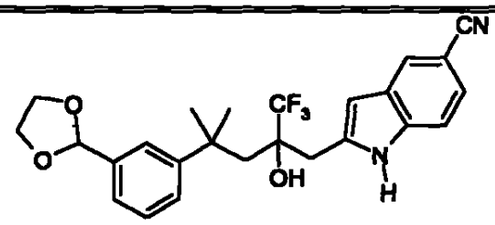
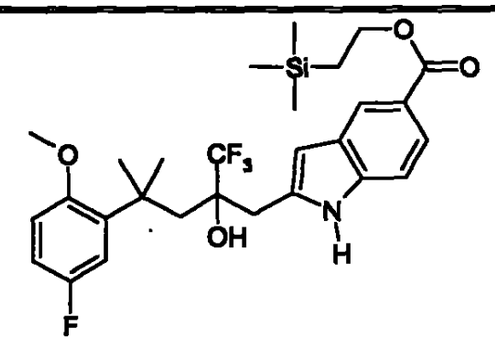
IA	
A	B
4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	
2-(3-Dimetilaminometil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metoxifenil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-pirrolo[3,2-*c*]piridin-1-ilmetilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-2-furo[3,2-*c*]piridin-2-ilmetil-4-metilpentan-2-ol	

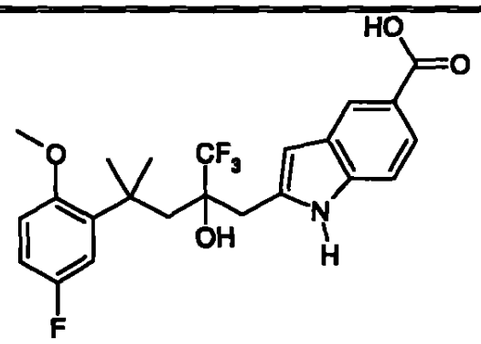
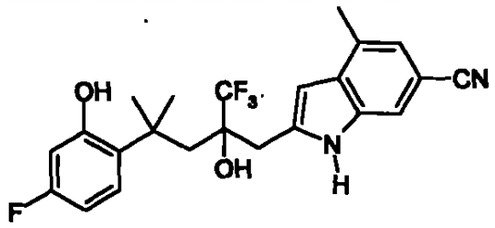
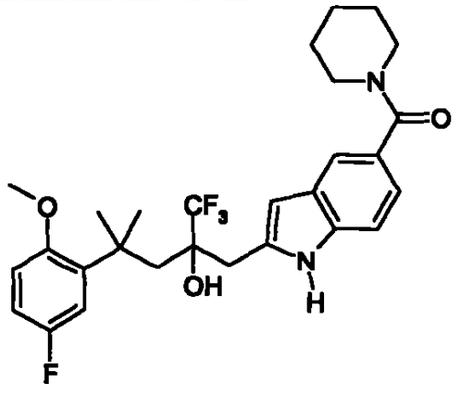
IA	
A	**B**
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-tieno[3,2-*c*]piridin-2-ilmetilpentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-tieno[3,2-*c*]piridin-2-ilmetilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-tieno[3,2-*c*]piridin-2-ilmetilpentan-2-ol	

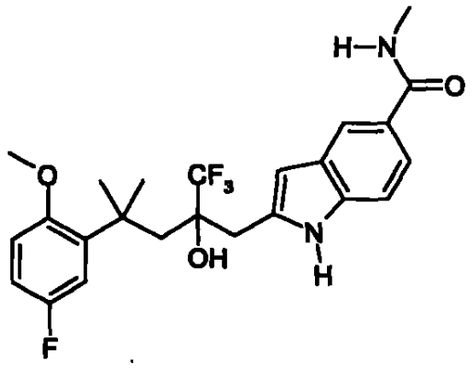
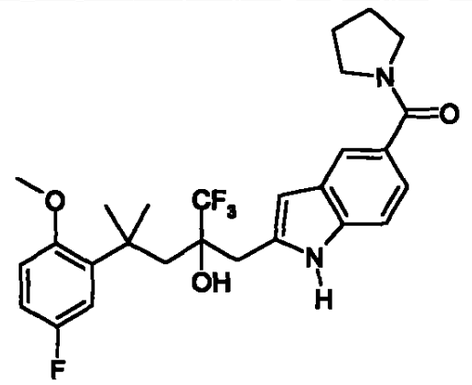
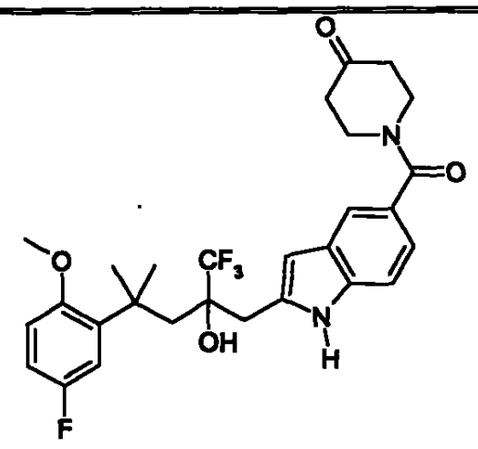
IA	
A	B
4-Fluor-2-(4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-tieno[3,2-*c*]piridin-2-ilmetilbutil)fenol	
4-Fluor-2-(4,4,4-trifluor-3-furo[3,2-*c*]piridin-2-ilmetil-3-hidroxi-1,1-dimetilbutil)fenol	
4-Fluor-2-(4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-pirrolo[3,2-*b*]piridin-1-ilmetilbutil)fenol	
ácido 2-[4-(5-fluor-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-6-carboxílico	
dimetilamida del ácido 2-[4-(5-fluor-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-6-carboxílico	

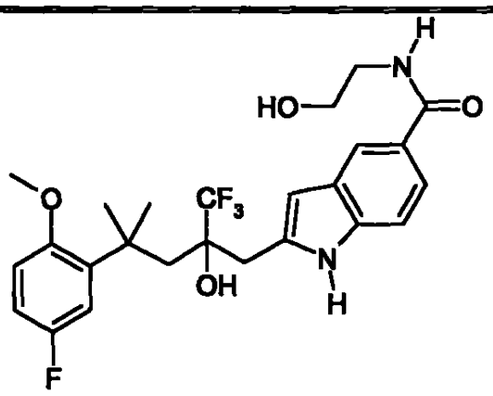
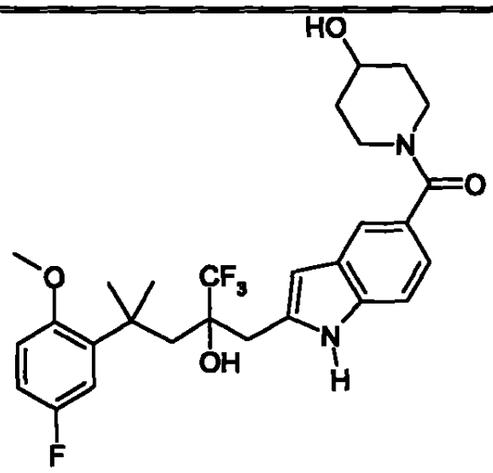
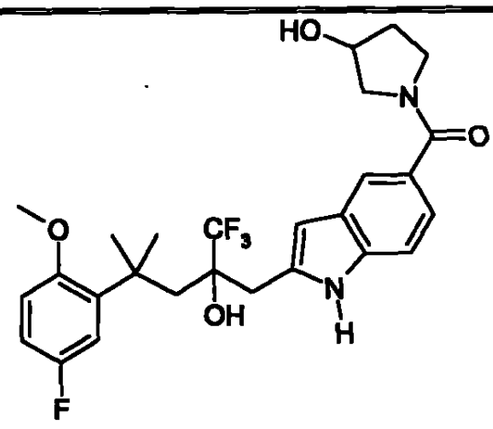
IA	
A	B
{2-[4-(5-Fluor-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-6-il}morfolin-4-ilmetanona	
dimetilamida del ácido 2-[4-(5-fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-6-carboxílico	
{2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-6-il}morfolin-4-ilmetanona	
amida del ácido 2-[4-(5-fluor-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-6-carboxílico	
amida del ácido 2-[4-(5-fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-6-carboxílico	

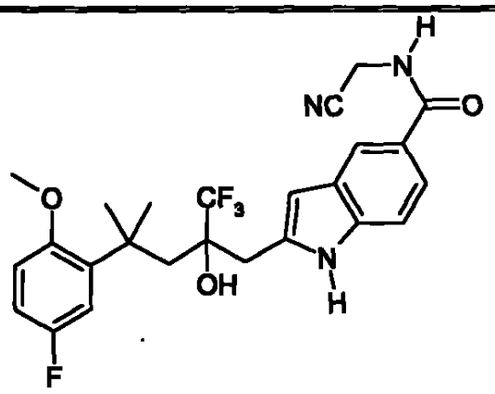
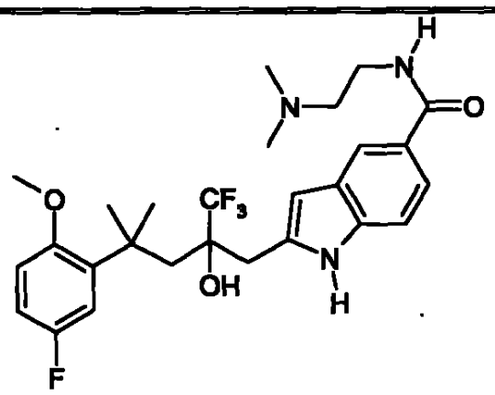
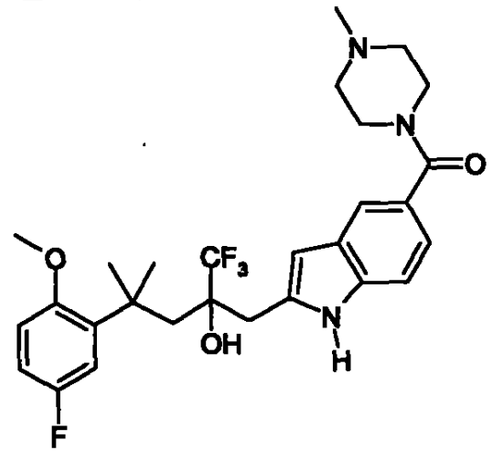
IA	
A	B
4-Fluor-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-nitro-1*H*-indol-2-ilmetil)butil]fenol	
2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-6-carbonitrilo	
2-[4-(5-Fluor-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-6-carbonitrilo	
N-{2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-il}acetamida	

IA	
A	B
1,1,1-Trifluor-4-(4-fluor-2-metoxifenil)-2-(7-fluor-4-metil-1*H*-indol-2-ilmetil)-4-metilpentan-2-ol	
5-Fluor-2-[4,4,4-trifluor-3-(7-fluor-4-metil-1*H*-indol-2-ilmetil)-3-hidroxi-1,1-dimetilbutil]fenol	
2-[4-(3-[1,3]Dioxolan-2-ilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carbonitrilo	
éster 2-trimetilsilaniletílico del ácido 2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carboxílico	

IA	
A	B
ácido 2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carboxílico	
2-[4-(4-Fluor-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-4-metil-1*H*-indol-6-carbonitrilo	
{2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-il}piperidin-1-ilmetanona	

IA	
A	B
metilamida del ácido 2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carboxílico	
{2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-il}pirrolidin-1-ilmetanona	
1-{2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carbonil}piperidin-4-ona	

IA	
A	B
(2-hidroxietil)amida del ácido 2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carboxílico	
{2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-il}(4-hidroxipiperidin-1-il)metanona	
{2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-il}(3-hidroxipirrolidin-1-il)metanona	

IA	
A	B
cianometilamida del ácido 2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carboxílico	
(2-dimetilaminoetil)amida del ácido 2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carboxílico	
{2-[4-(5-fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-il}(4-metilpiperazin-1-il)metanona	

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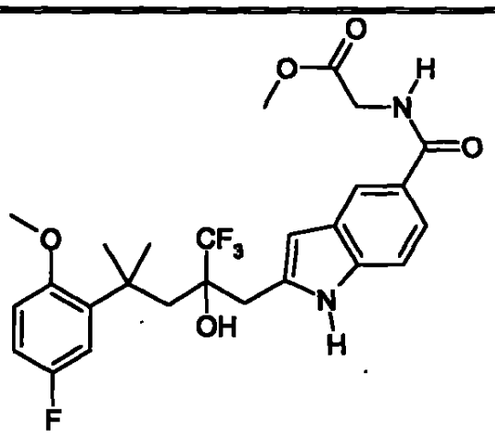
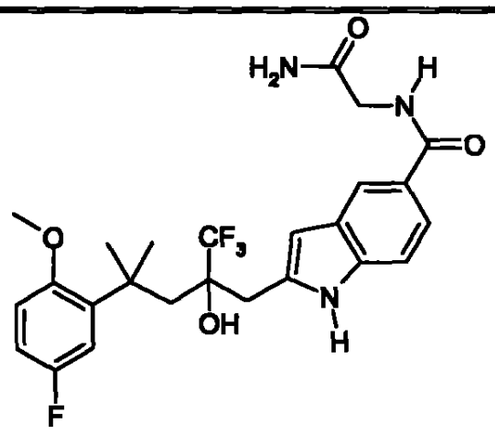
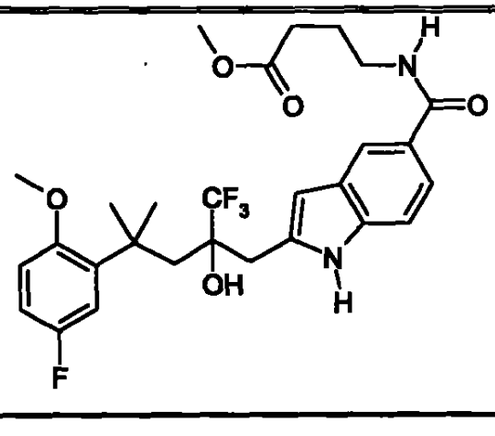
IA	
A	B
Éster metílico del ácido ({2-[4-(5-fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carbonil}amino)acético	
Carbamoilmetilamida del ácido 2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carboxílico	
éster metílico del ácido 4-({2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carbonil}amino)butírico	

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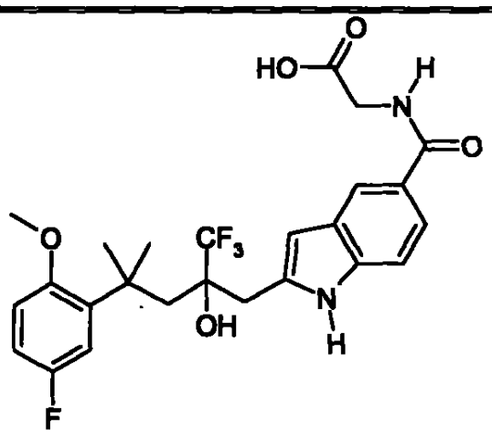
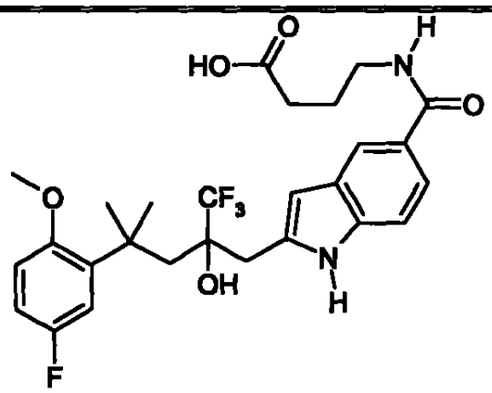
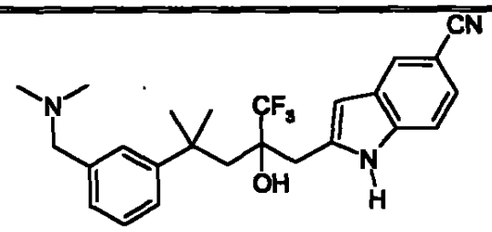
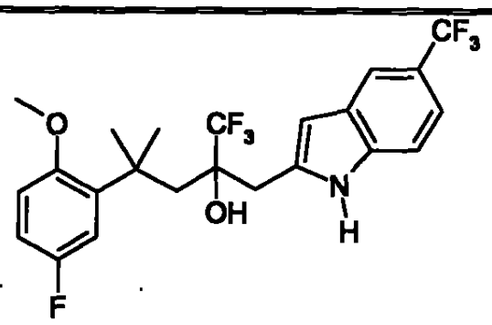
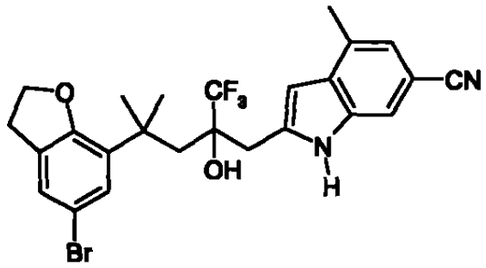
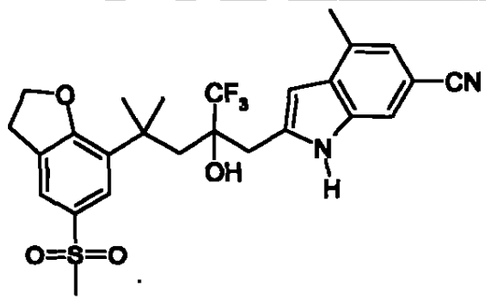
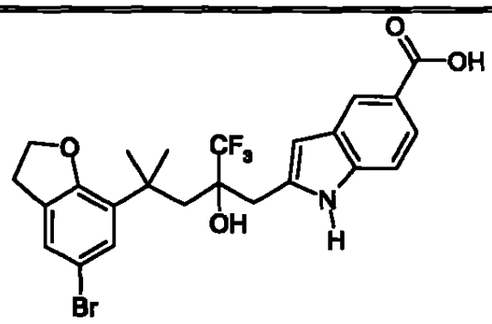
IA	
A	B
ácido ({2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carbonil}amino)acético	
ácido 4-({2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carbonil}amino)butírico	
2-[4-(3-Dimetilaminometilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carbonitrilo	

IA	
A	B
4-Fluor-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-trifluormetil-1*H*-indol-2-ilmetil)butil]fenol	
2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-4-metil-1*H*-indol-6-carbonitrilo	
2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluormetilpentil]-4-metil-1*H*-indol-6-carbonitrilo	
ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carboxílico	

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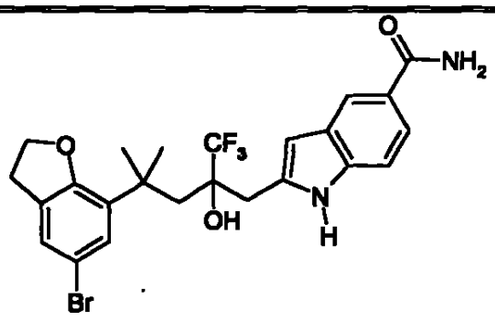
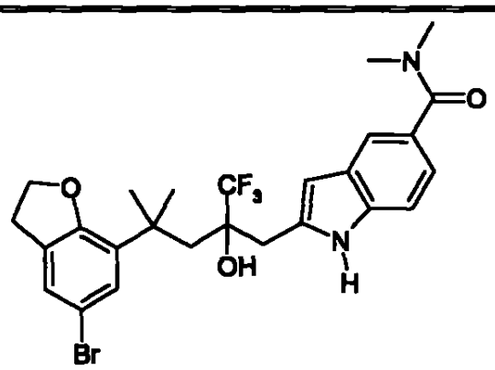
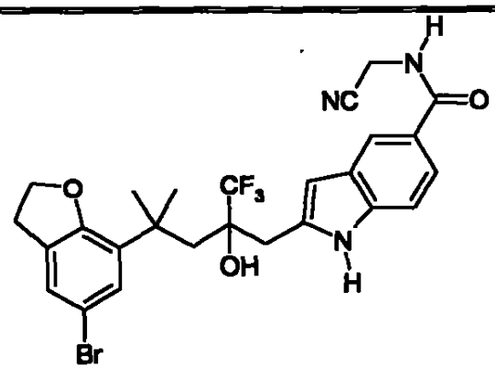
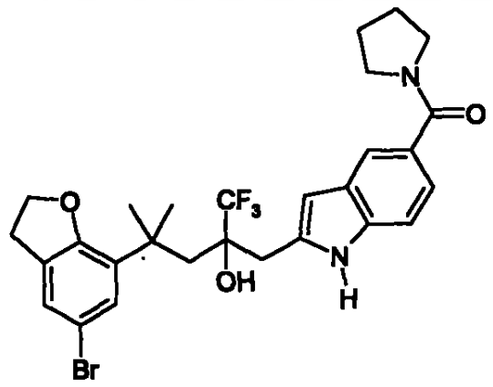
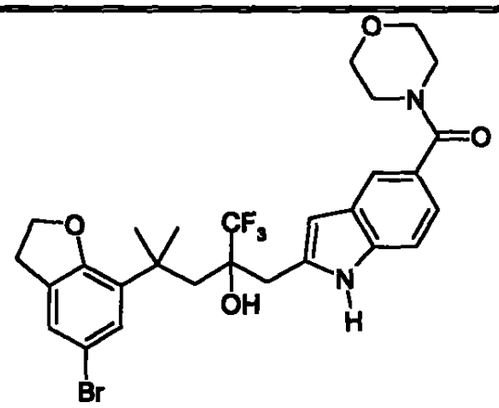
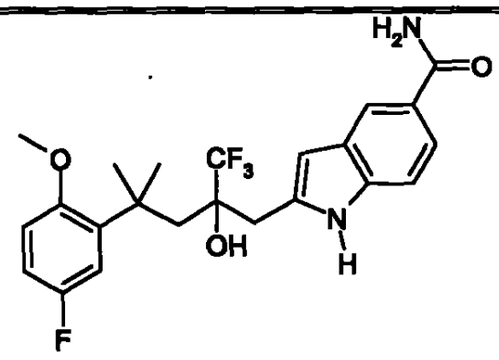
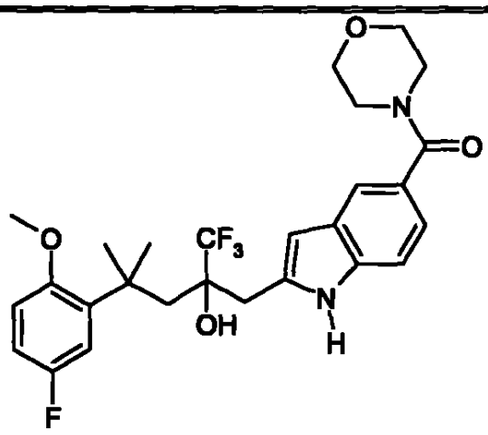
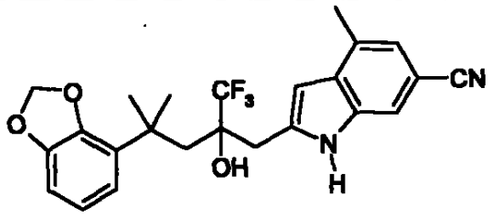
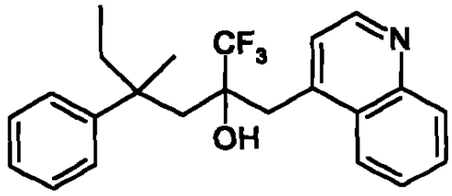
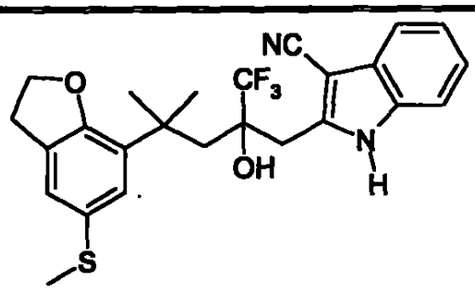
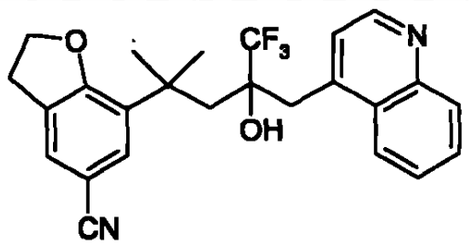
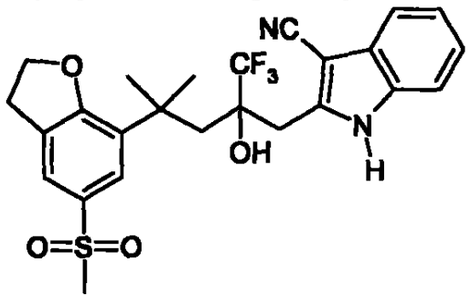
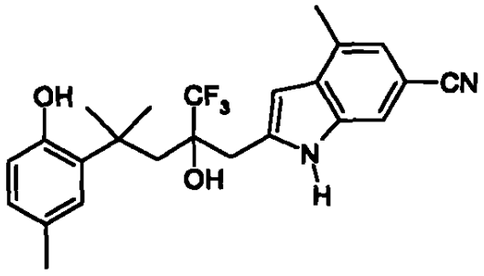
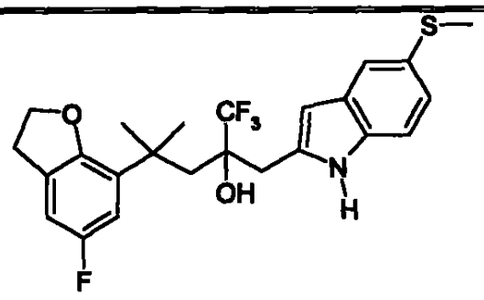
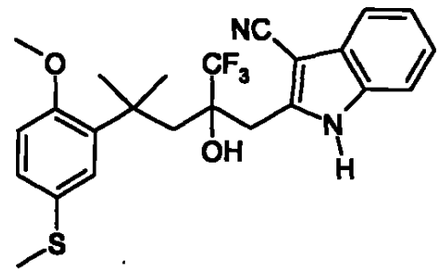
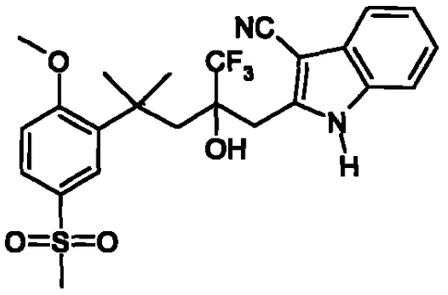
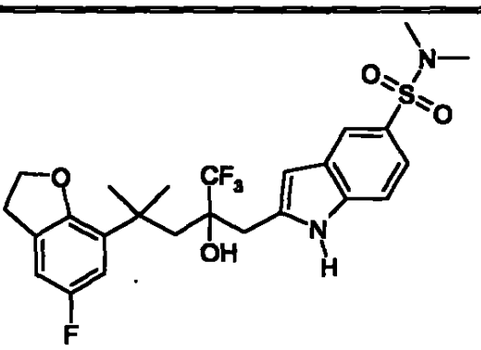
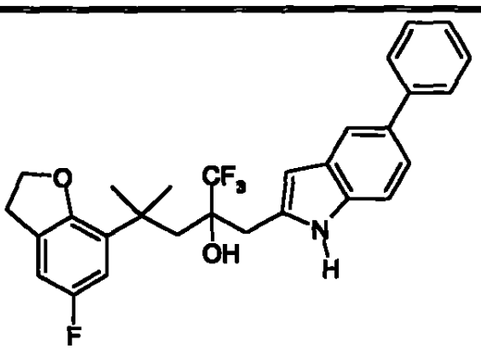
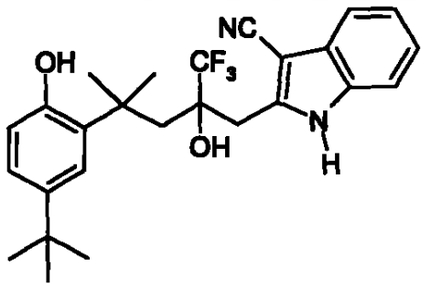
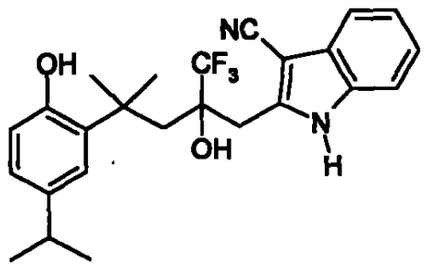
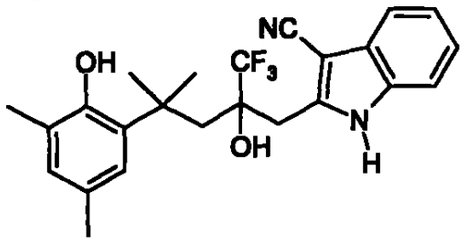
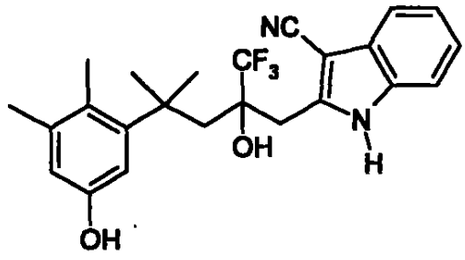
IA	
A	**B**
amida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carboxílico	
dimetilamida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carboxílico	
Cianometilamida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carboxílico	

IA	
A	B
{2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-il}pirrolidin-1-ilmetanona	
{2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-il}morfolin-4-ilmetanona	
amida del ácido 2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carboxílico	

IA	
A	B
{2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-il}morfolin-4-ilmetanona	
2-(4-Benzo[1,3]dioxol-4-il-2-hidroxi-4-metil-2-trifluormetilpentil)-4-metil-1*H*-indol-6-carbonitrilo	
1,1,1-Trifluor-4-metil-4-fenil-2-quinolin-4-ilmetilhexan-2-ol	
2-[2-Hidroxi-4-metil-4-(5-metilsulfanil-2,3-dihidrobenzofuran-7-il)-2-trifluormetilpentil]-1*H*-indol-3-carbonitrilo	

IA	
A	B
7-(4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)-2,3-dihidrobenzofuran-5-carbonitrilo	
2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluormetilpentil]-1*H*-indol-3-carbonitrilo	
2-[2-Hidroxi-4-(2-hidroxi-5-metilfenil)-4-metil-2-trifluormetilpentil]-4-metil-1*H*-indol-6-carbonitrilo	
1,1,1-Trifluor-4-(5-fluor-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-metilsulfanil-1*H*-indol-2-ilmetil)pentan-2-ol	

IA	
A	**B**
2-[2-Hidroxi-4-(2-metoxi-5-metilsulfanilfenil)-4-metil-2-trifluormetilpentil]-1*H*-indol-3-carbonitrilo	
2-[2-Hidroxi-4-(5-metansulfonil-2-metoxifenil)-4-metil-2-trifluormetilpentil]-1*H*-indol-3-carbonitrilo	
Dimetilamida del ácido 2-[4-(5-Fluor-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-sulfónico	
1,1,1-Trifluor-4-(5-fluor-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-fenil-1*H*-indol-2-ilmetil)pentan-2-ol	

IA	
A	B
2-[4-(5-*tert*-Butil-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-3-carbonitrilo	
2-[2-Hidroxi-4-(2-hidroxi-5-isopropilfenil)-4-metil-2-trifluormetilpentil]-1*H*-indol-3-carbonitrilo	
2-[2-Hidroxi-4-(2-hidroxi-3,5-dimetilfenil)-4-metil-2-trifluormetilpentil]-1*H*-indol-3-carbonitrilo	
2-[2-Hidroxi-4-(5-hidroxi-2,4-dimetilfenil)-4-metil-2-trifluormetilpentil]-1*H*-indol-3-carbonitrilo	

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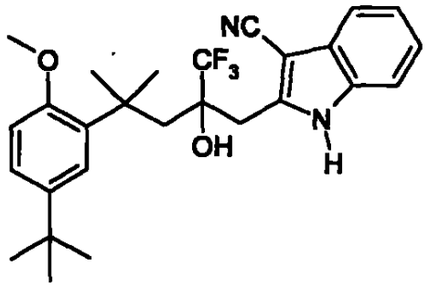
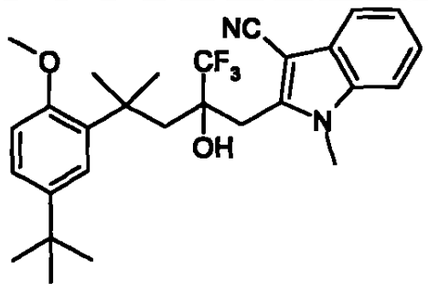
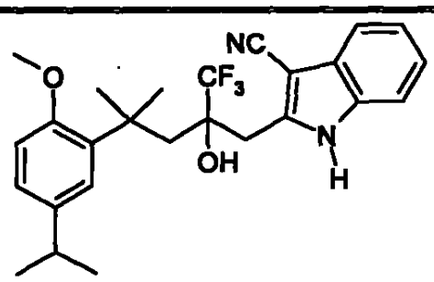
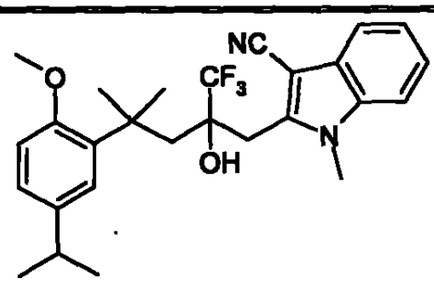
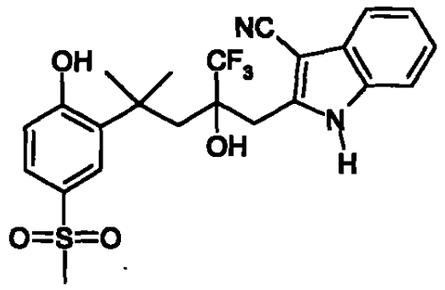
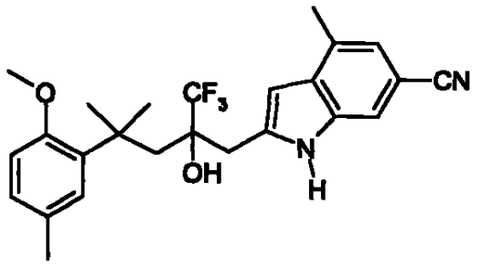
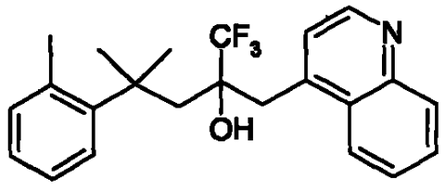
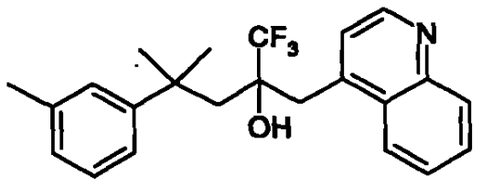
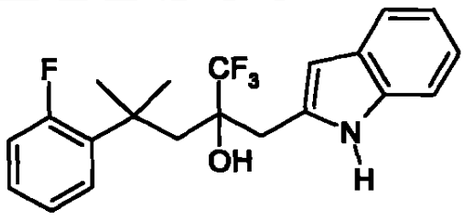
IA	
A	B
2-[4-(5-*tert*-Butil-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-3-carbonitrilo	
2-[4-(5-*tert*-Butil-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1-metil-1*H*-indol-3-carbonitrilo	
2-[2-Hidroxi-4-(5-isopropil-2-metoxifenil)-4-metil-2-trifluormetilpentil]-1*H*-indol-3-carbonitrilo	
2-[2-Hidroxi-4-(5-isopropil-2-metoxifenil)-4-metil-2-trifluormetilpentil]-1-metil-1*H*-indol-3-carbonitrilo	

IA	
A	B
2-[2-Hidroxi-4-(2-hidroxi-5-metansulfonilfenil)-4-metil-2-trifluormetilpentil]-1*H*-indol-3-carbonitrilo	
2-[2-Hidroxi-4-(2-metoxi-5-metilfenil)-4-metil-2-trifluormetilpentil]-4-metil-1*H*-indol-6-carbonitrilo	
1,1,1-Trifluor-4-metil-2-quinolin-4-ilmetil-4-*o*-tolilpentan-2-ol	
1,1,1-Trifluor-4-metil-2-quinolin-4-ilmetil-4-*m*-tolilpentan-2-ol	
1,1,1-Trifluor-4-(2-fluorfenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol	

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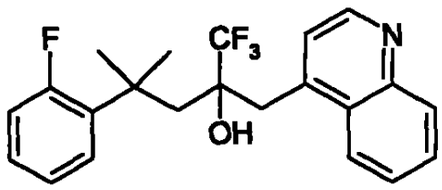
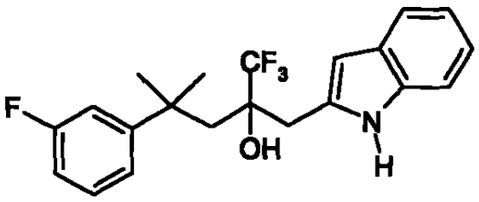
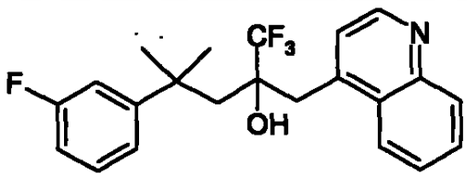
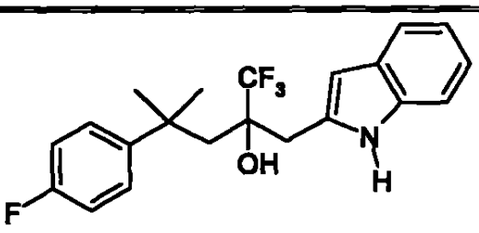
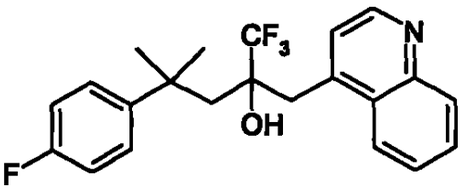
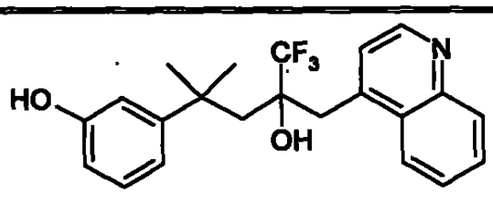
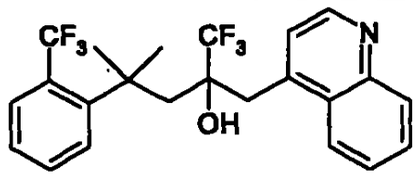
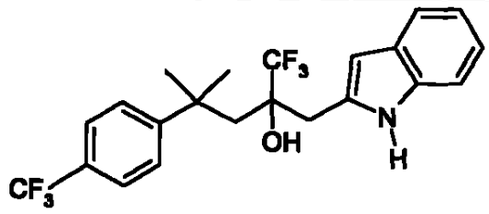
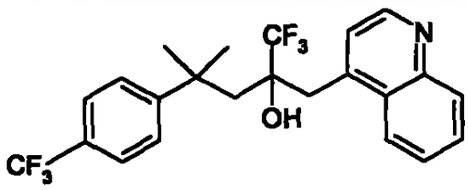
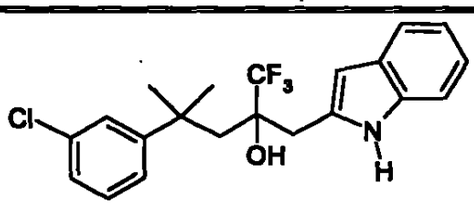
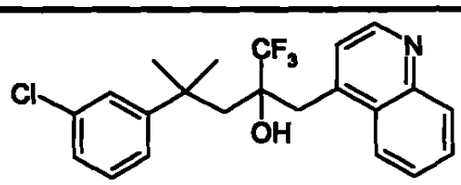
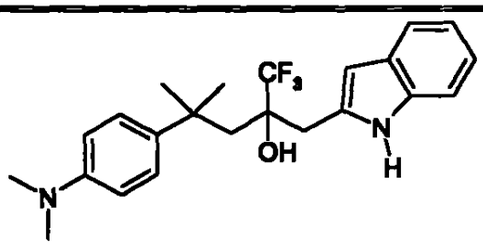
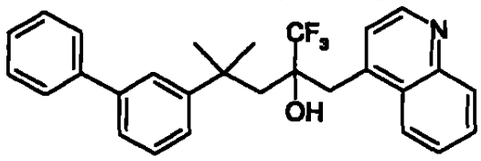
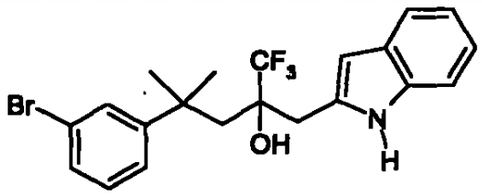
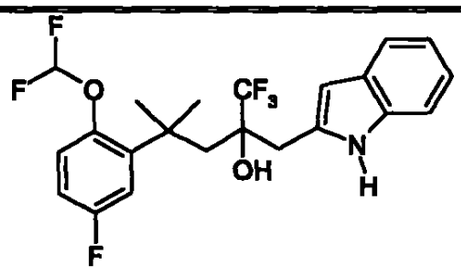
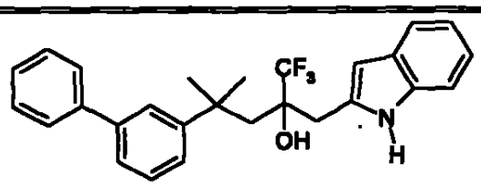
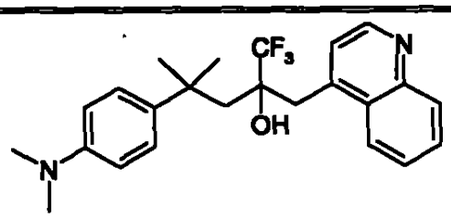
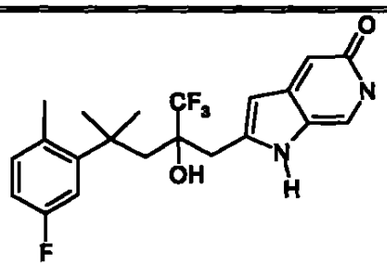
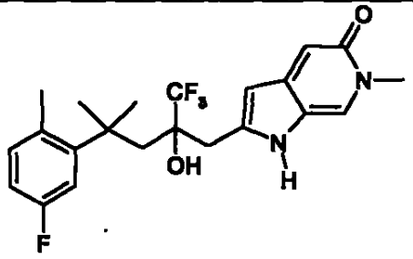
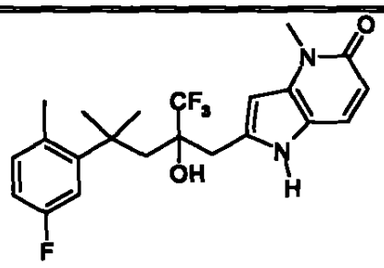
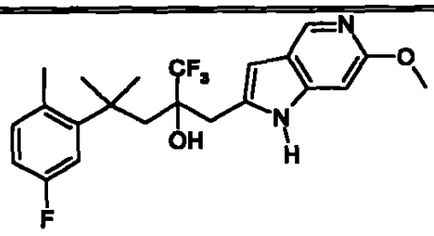
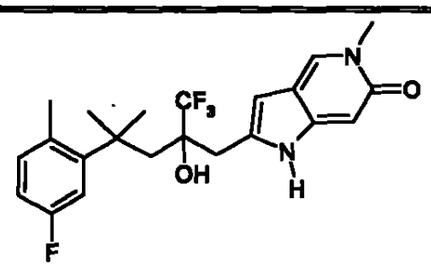
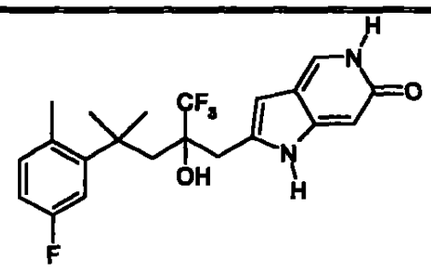
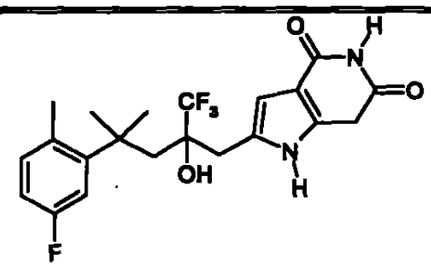
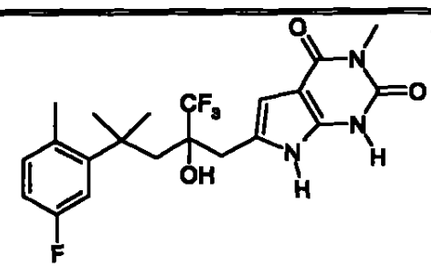
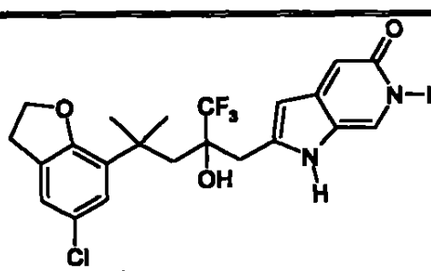
IA	
A	B
1,1,1-Trifluor-4-(2-fluorfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol	
1,1,1-Trifluor-4-(3-fluorfenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(3-fluorfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol	
1,1,1-Trifluor-4-(4-fluorfenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(4-fluorfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol	
3-(4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)fenol	

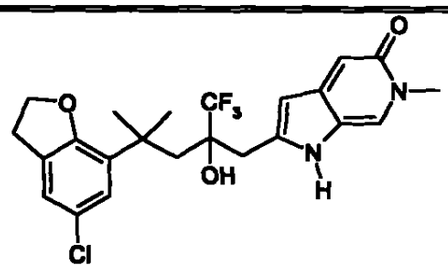
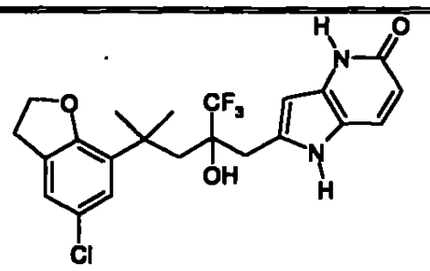
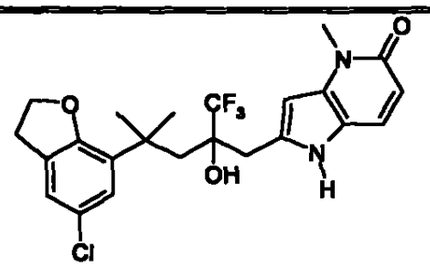
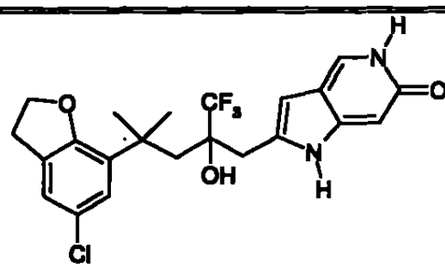
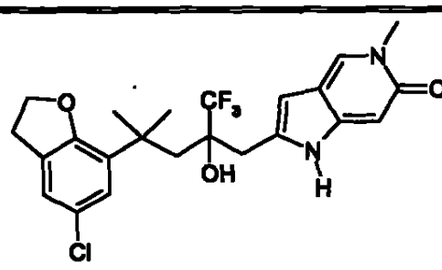
IA	
A	B
1,1,1-Trifluor-4-metil-2-quinolin-4-ilmetil-4-(2-trifluormetilfenil)pentan-2-ol	
1,1,1-Trifluor-2-(1*H*-indol-2-ilmetil)-4-metil-4-(4-trifluormetilfenil)pentan-2-ol	
1,1,1-Trifluor-4-metil-2-quinolin-4-ilmetil-4-(4-trifluormetilfenil)pentan-2-ol	
4-(3-Clorofenil)-1,1,1-trifluor-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol	
4-(3-Clorofenil)-1,1,1-trifluor-4-metil-2-quinolin-4-ilmetilpentan-2-ol	
4-(4-Dimetilaminofenil)-1,1,1-trifluor-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol	

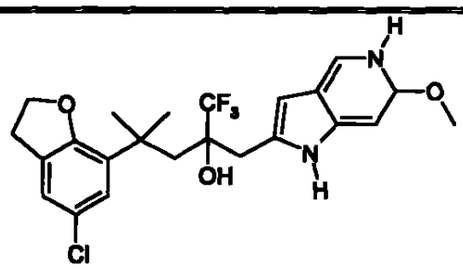
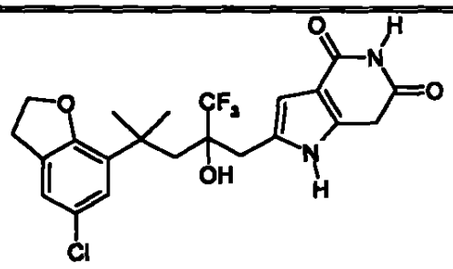
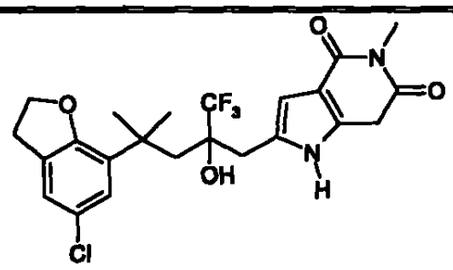
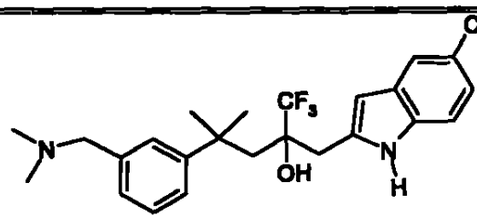
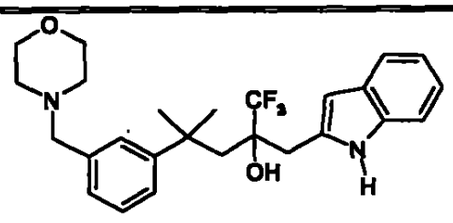
IA	
A	**B**
4-Bifenil-3-il-1,1,1-trifluor-4-metil-2-quinolin-4-ilmetilpentan-2-ol	
4-(3-Bromofenil)-1,1,1-trifluor-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol	
4-(2-Difluormetoxi-5-fluorfenil)-1,1,1-trifluor-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol	
4-Bifenil-3-il-1,1,1-trifluor-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol	
4-(4-Dimetilaminofenil)-1,1,1-trifluor-4-metil-2-quinolin-4-ilmetilpentan-2-ol	

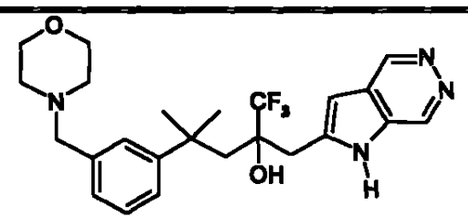
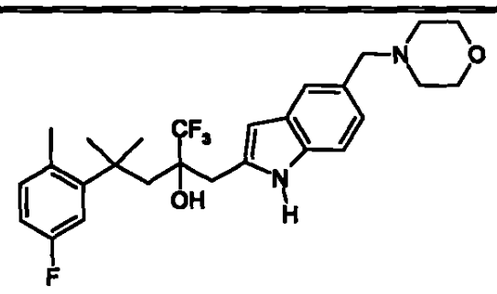
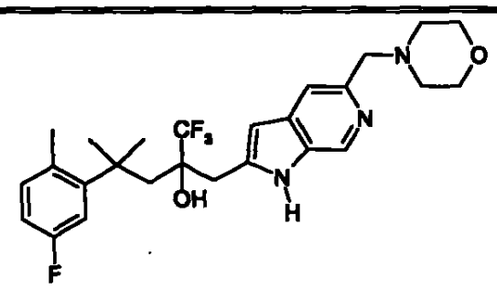
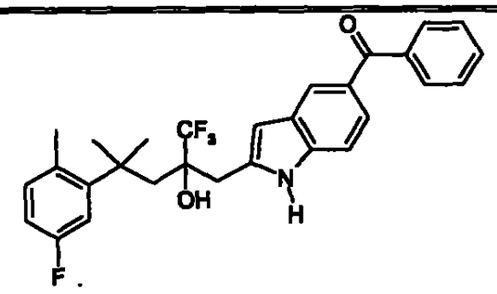
IA	
A	**B**
2-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1,6-dihidropirrolo[2,3-*c*]piridin-5-ona	
2-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-6-metil-1,6-dihidropirrolo[2,3-*c*]piridin-5-ona	
2-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-4-metil-1,4-dihidropirrolo[3,2-*b*]piridin-5-ona	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-2-(6-metoxi-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol	

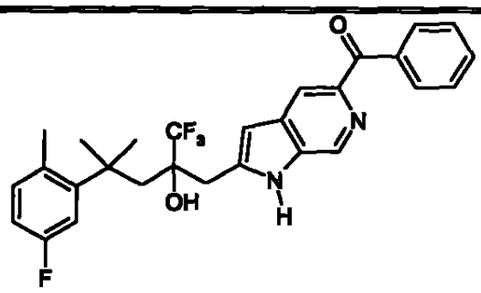
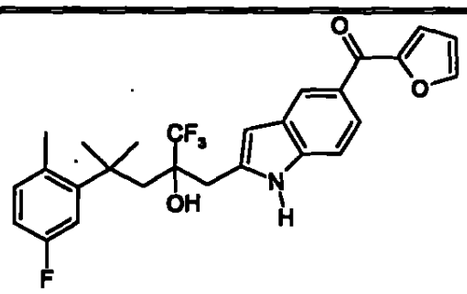
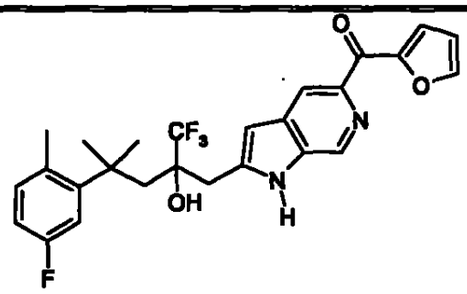
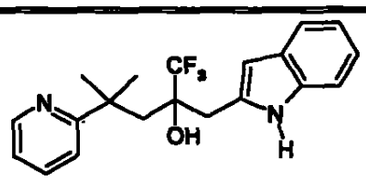
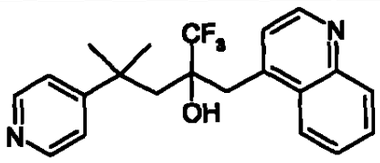
734

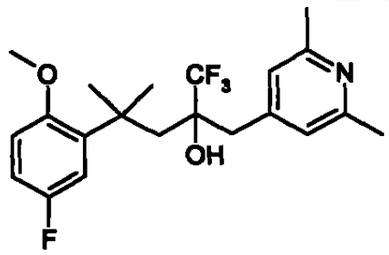
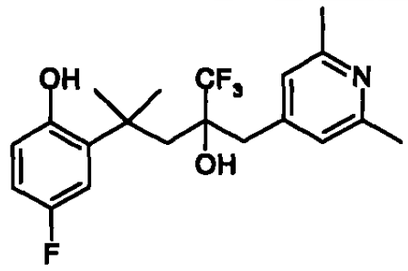
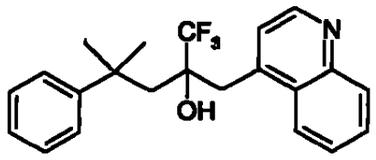
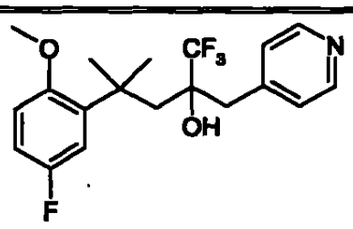
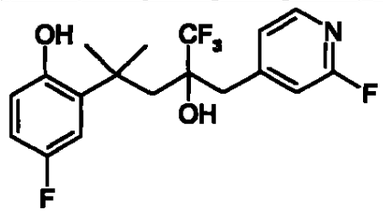
IA	
A	B
2-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-5-metil-1,5-dihidropirrolo[3,2-*c*]piridin-6-ona	
2-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1,3a-dihidropirrolo[3,2-*c*]piridin-6-ona	
2-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1,7-dihidropirrolo[3,2-*c*]piridin-4,6-diona	
6-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-3-metil-1,7-dihidropirrolo[2,3-*d*]pirimidine-2,4-diona	
2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1,6-dihidropirrolo[2,3-*c*]piridin-5-ona	

IA	
A	B
2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-6-metil-1,6-dihidropirrolo[2,3-*c*]piridin-5-ona	
2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1,4-dihidropirrolo[3,2-*b*]piridin-5-ona	
2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-4-metil-1,4-dihidropirrolo[3,2-*b*]piridin-5-ona	
2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1,5-dihidropirrolo[3,2-*c*]piridin-6-ona	
2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-5-metil-1,5-dihidropirrolo[3,2-*c*]piridin-6-ona	

IA	
A	**B**
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-2-(6-metoxi-5,6-dihidro-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol	
2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1,7-dihidropirrolo[3,2-*c*]piridin-4,6-diona	
6-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-3-metil-1,7-dihidropirrolo[2,3-*d*]pirimidine-2,4-diona	
2-[4-(3-Dimetilaminometilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carbonitrilo	
1,1,1-Trifluor-2-(1*H*-indol-2-ilmetil)-4-metil-4-(3-morfolin-4-ilmetilfenil)pentan-2-ol	

IA	
A	**B**
1,1,1-Trifluor-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(1*H*-pirrolo[2,3-*d*]piridazin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-morfolin-4-ilmetil-1*H*-indol-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-morfolin-4-ilmetil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
{2-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-il}fenilmetanona	

IA	
A	B
{2-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[2,3-*c*]piridin-5-il}fenilmetanona	
{2-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-il}furan-2-ilmetanona	
{2-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[2,3-*c*]piridin-5-il}furan-2-ilmetanona	
1,1,1-Trifluor-2-(1*H*-indol-2-ilmetil)-4-metil-4-piridin-2-ilpentan-2-ol	
1,1,1-Trifluor-4-metil-4-piridin-4-il-2-quinolin-4-ilmetilpentan-2-ol	

IA	
A	B
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metoxifenil)-4-metilpentan-2-ol	
2-[3-(2,6-Dimetilpiridin-4-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-fluorfenol	
1,1,1-Trifluor-4,4-dimetil-5-fenil-2-quinolin-4-ilmetilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-piridin-4-ilmetilpentan-2-ol	
4-Fluor-2-[4,4,4-trifluor-3-(2-fluorpiridin-4-ilmetil)-3-hidroxi-1,1-dimetilbutil]fenol	

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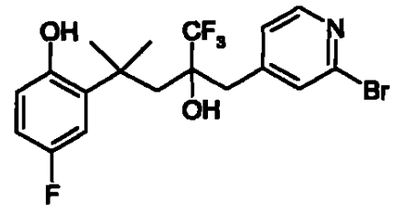
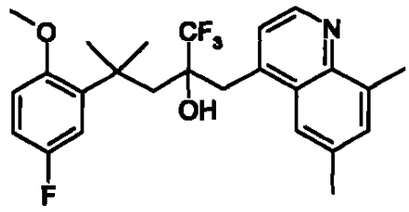
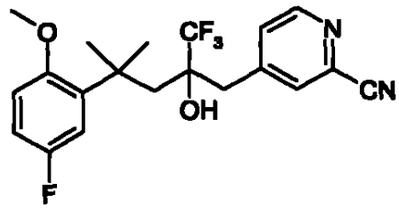
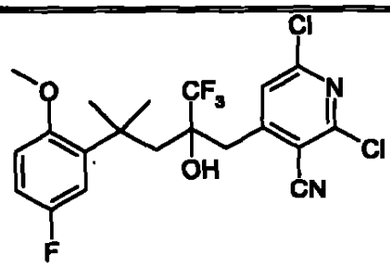
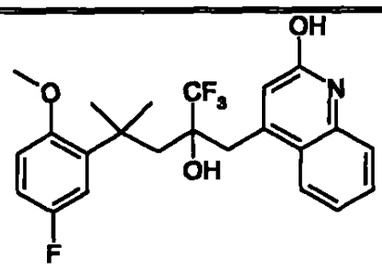
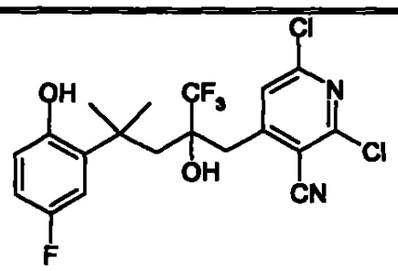
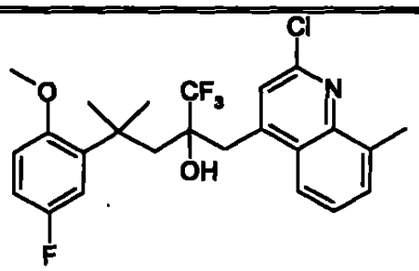
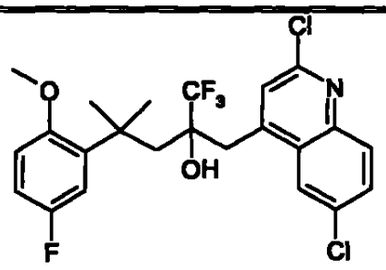
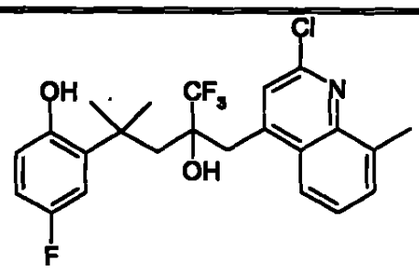
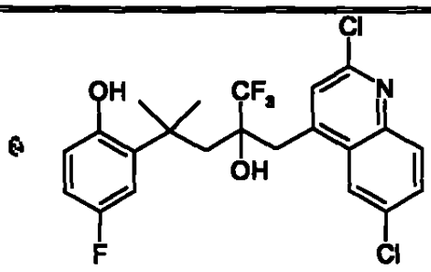
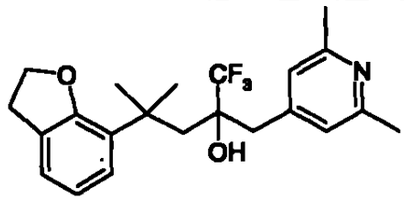
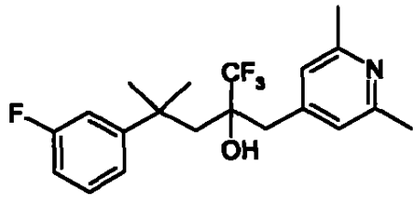
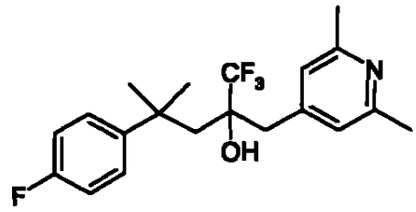
IA	
A	B
2-[3-(2-Bromopiridin-4-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-fluorfenol	
2-(6,8-Dimetilquinolin-4-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metoxifenil)-4-metilpentan-2-ol	
4-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]piridin-2-carbonitrilo	
2,6-Dicloro-4-[4-(5-fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]nicotinonitrilo	
4-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]quinolin-2-ol	

IA	
A	B
2,6-Dicloro-4-[4-(5-fluor-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]nicotinonitrilo	
2-(2-Cloro-8-metilquinolin-4-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metoxifenil)-4-metilpentan-2-ol	
2-(2,6-Dicloroquinolin-4-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metoxifenil)-4-metilpentan-2-ol	

IA	
A	B
2-[3-(2-Cloro-8-metilquinolin-4-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-fluorfenol	
2-[3-(2,6-Dicloroquinolin-4-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-fluorfenol	
4-(2,3-Dihidrobenzofuran-7-il)-2-(2,6-dimetilpiridin-4-ilmetil)-1,1,1-trifluor-4-metilpentan-2-ol	
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluor-4-(3-fluorfenil)-4-metilpentan-2-ol	
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluor-4-(4-fluorfenil)-4-metilpentan-2-ol	

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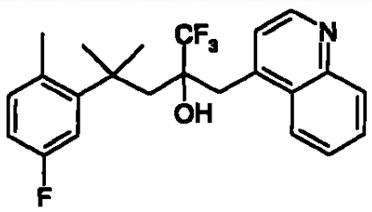
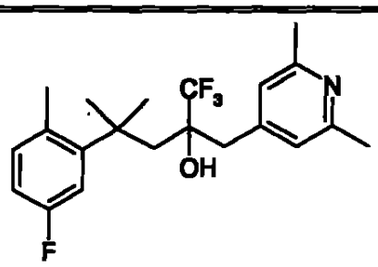
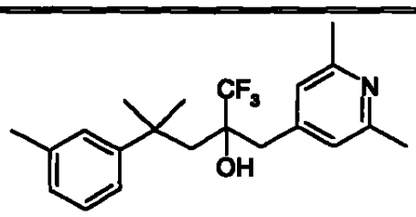
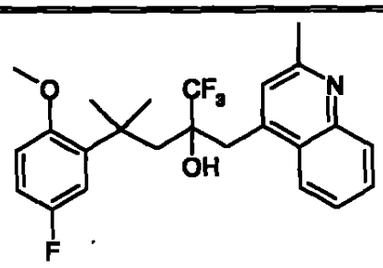
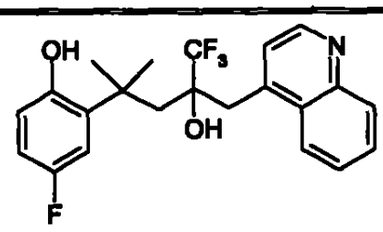
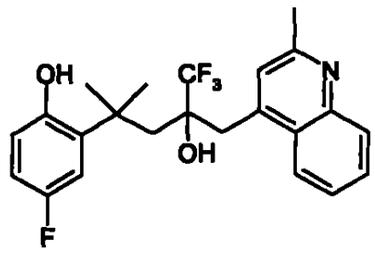
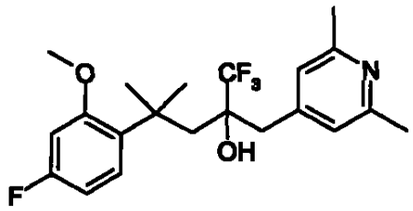
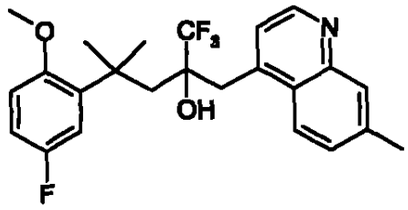
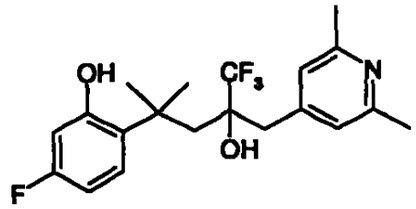
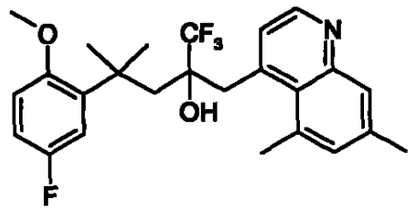
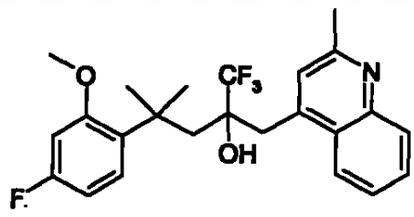
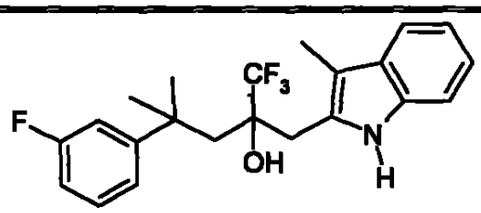
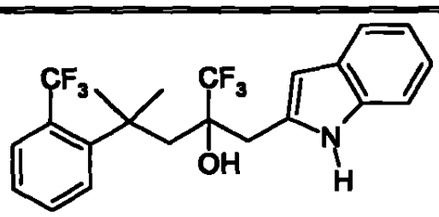
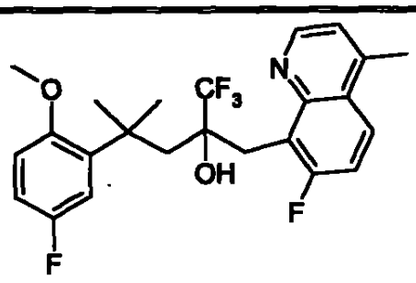
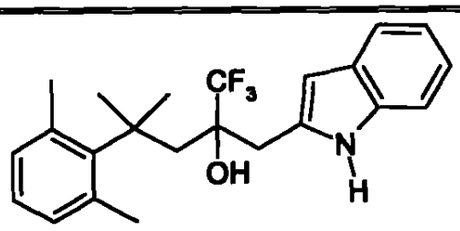
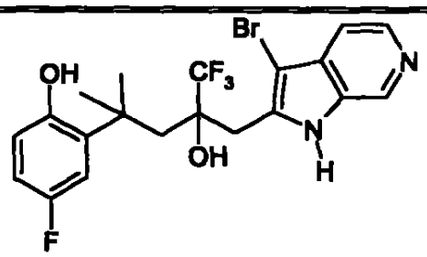
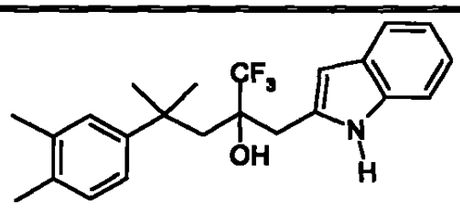
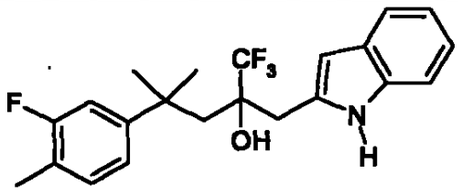
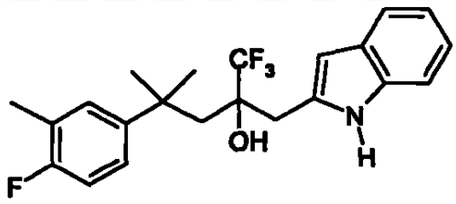
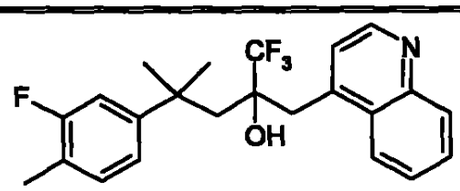
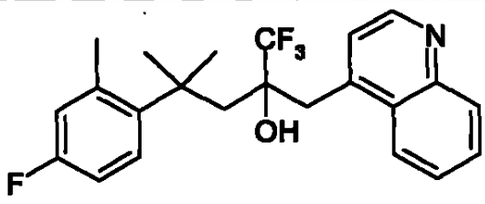
IA	
A	B
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol	
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metilfenil)-4-metilpentan-2-ol	
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluor-4-metil-4-*m*-tolilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(2-metilquinolin-4-ilmetil)pentan-2-ol	
4-Fluor-2-(4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)fenol	

IA	
A	B
4-Fluor-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(2-metilquinolin-4-ilmetil)butil]fenol	
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluor-4-(4-fluor-2-metoxifenil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(7-metilquinolin-4-ilmetil)pentan-2-ol	
2-[3-(2,6-Dimetilpiridin-4-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-5-fluorfenol	
2-(5,7-Dimetilquinolin-4-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metoxifenil)-4-metilpentan-2-ol	

IA	
A	**B**
1,1,1-Trifluor-4-(4-fluorfenil)-4-metil-2-(2-metilquinolin-4-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(3-fluorfenil)-4-metil-2-(3-metil-1*H*-indol-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-2-(1*H*-indol-2-ilmetil)-4-metil-4-(2-trifluormetilfenil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-2-(7-fluor-4-metilquinolin-8-il)-4-metilpentan-2-ol	
4-(2,6-Dimetilfenil)-1,1,1-trifluor-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol	

IA	
A	**B**
2-(3-Bromo-1*H*-indol-2-ilmetil)-1,1,1-trifluor-4-(3-fluorfenil)-4-metilpentan-2-ol	
4-(3,4-Dimetilfenil)-1,1,1-trifluor-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(3-fluor-4-metilfenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(4-fluor-3-metilfenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(3-fluor-4-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol	
1,1,1-Trifluor-4-(4-fluor-2-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol	

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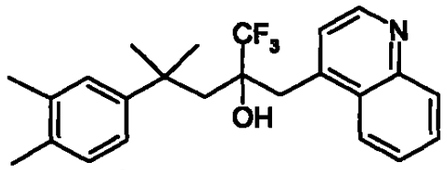
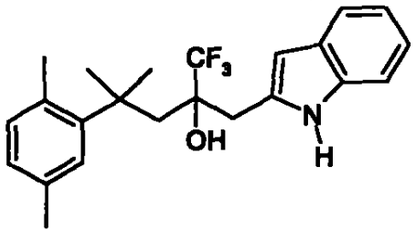
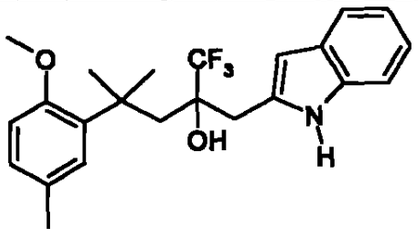
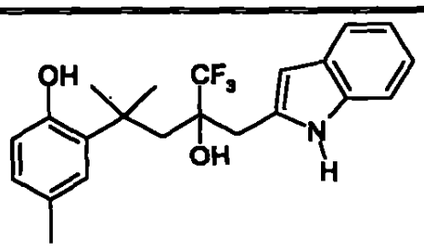
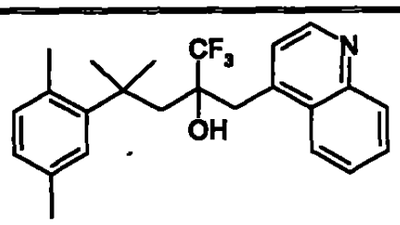
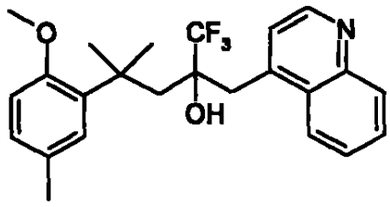
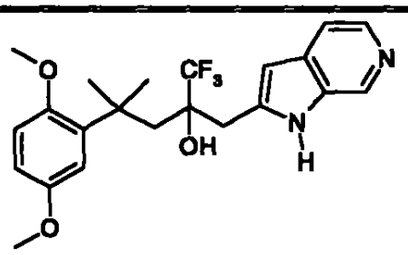
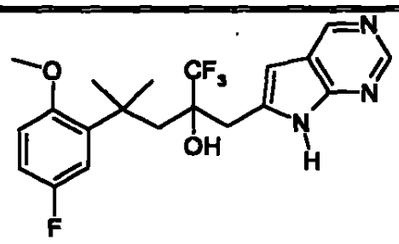
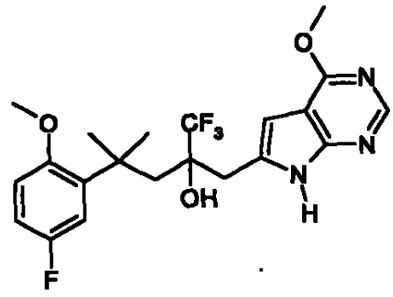
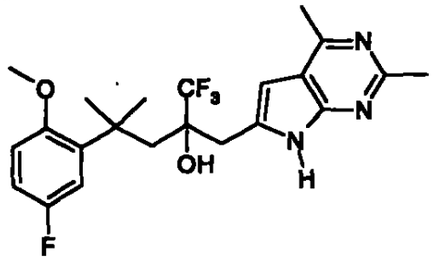
IA	
A	**B**
4-(3,4-Dimetilfenil)-1,1,1-trifluor-4-metil-2-quinolin-4-ilmetilpentan-2-ol	
4-(2,5-Dimetilfenil)-1,1,1-trifluor-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol	
1,1,1-Trifluor-2-(1*H*-indol-2-ilmetil)-4-(2-metoxi-5-metilfenil)-4-metilpentan-2-ol	
4-Metil-2-[4,4,4-trifluor-3-hidroxi-3-(1*H*-indol-2-ilmetil)-1,1-dimetilbutil]fenol	
4-(2,5-Dimetilfenil)-1,1,1-trifluor-4-metil-2-quinolin-4-ilmetilpentan-2-ol	

IA	
A	B
1,1,1-Trifluor-4-(2-metoxi-5-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol	
4-(2,5-Dimetoxifenil)-1,1,1-trifluor-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-2-(4-metoxi-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-4-metilpentan-2-ol	
2-(2,4-Dimetil-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metoxifenil)-4-metilpentan-2-ol	

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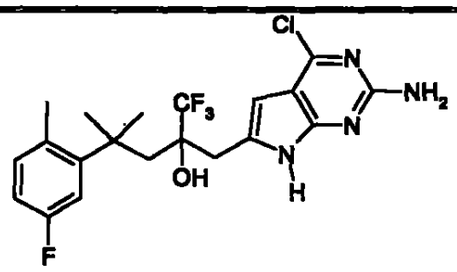
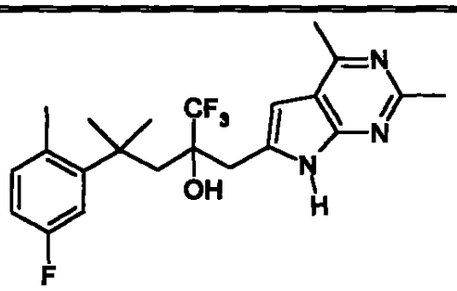
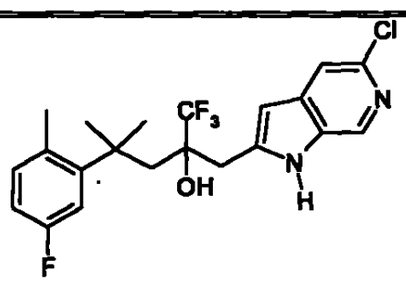
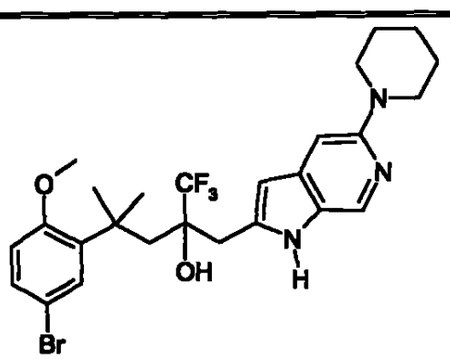
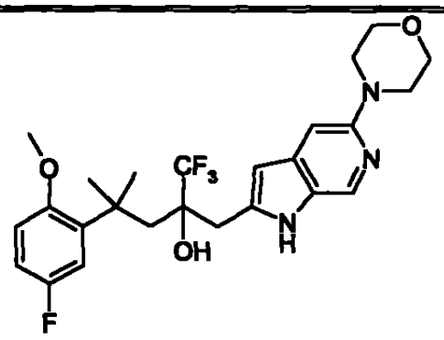
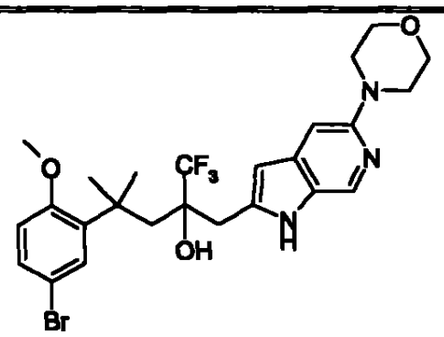
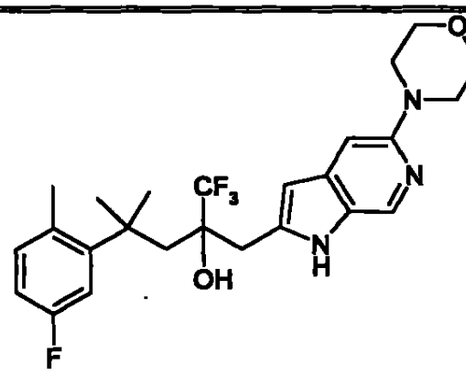
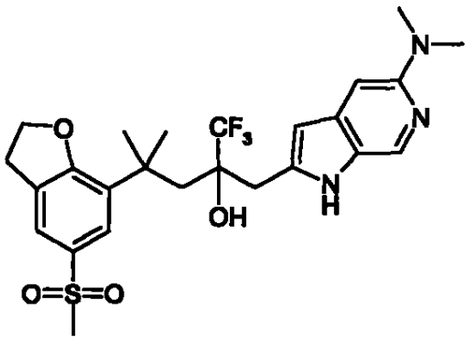
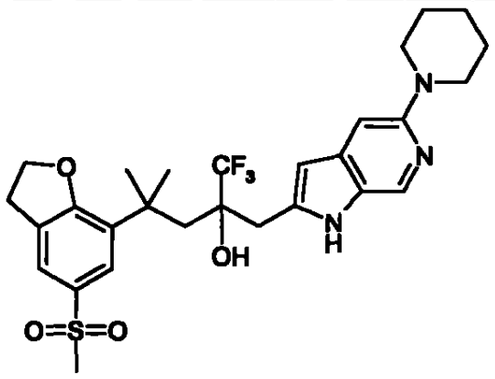
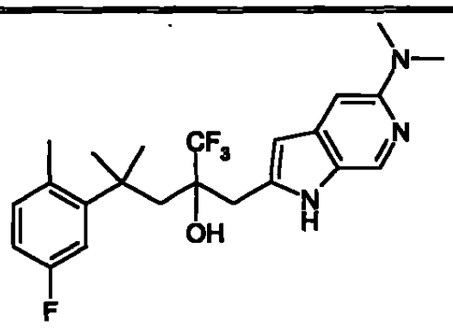
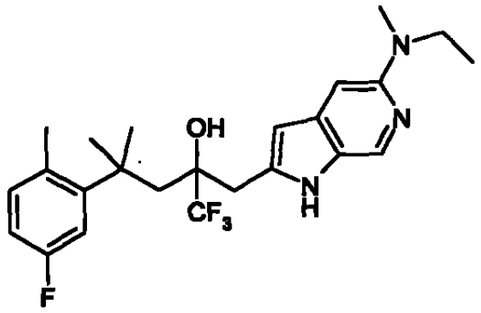
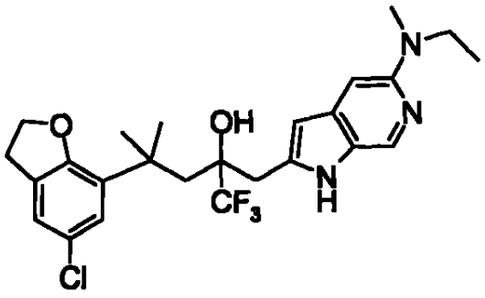
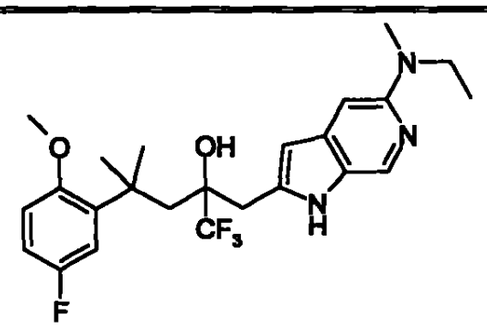
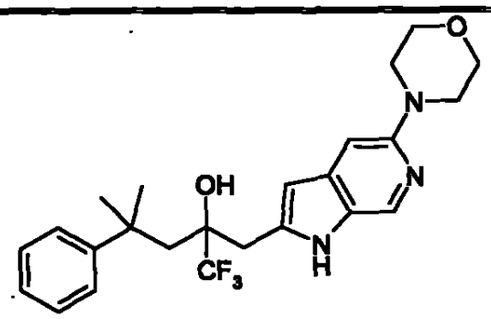
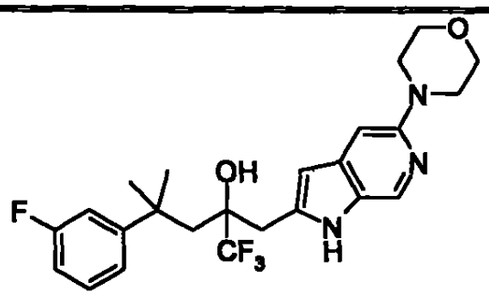
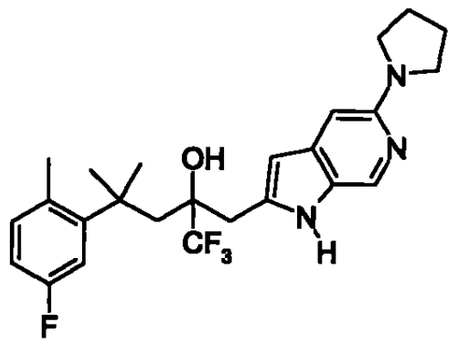
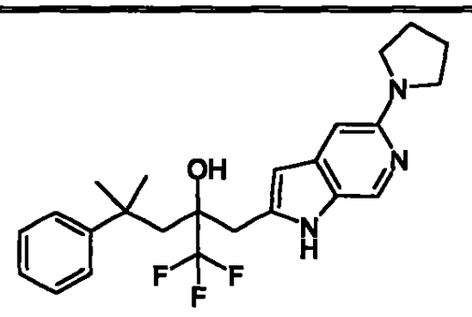
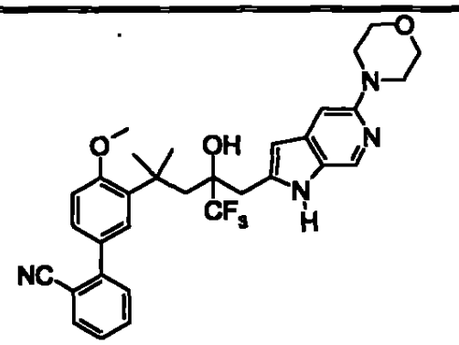
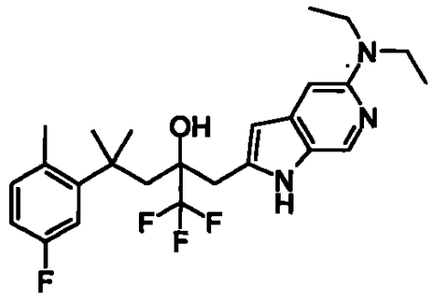
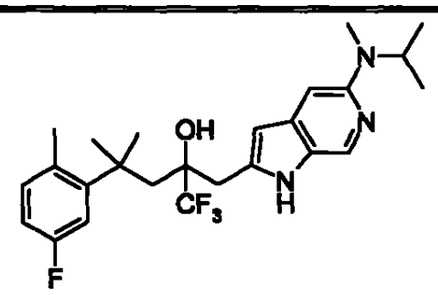
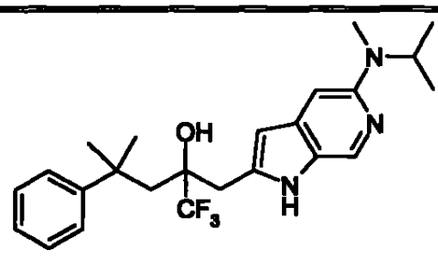
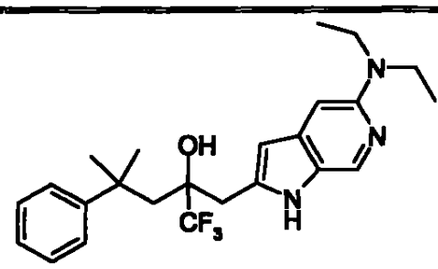
IA	
A	B
2-(2-Amino-4-cloro-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metoxifenil)-4-metilpentan-2-ol	
2-(2,4-Dimetil-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metilfenil)-4-metilpentan-2-ol	
2-(5-Cloro-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metilfenil)-4-metilpentan-2-ol	
4-(5-Bromo-2-metoxifenil)-1,1,1-trifluor-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	

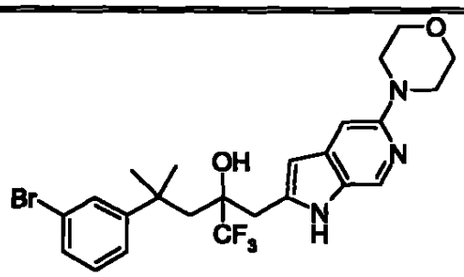
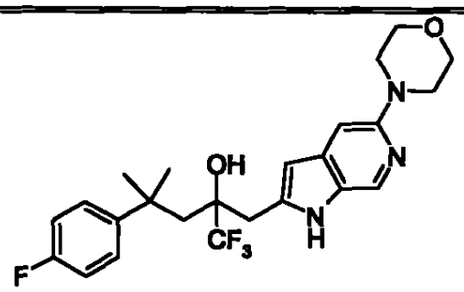
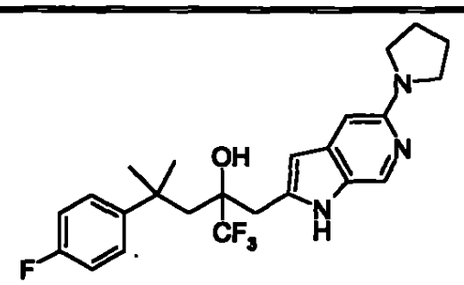
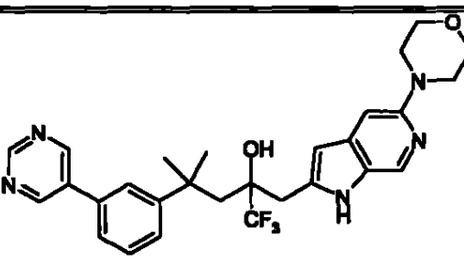
IA	
A	B
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
4-(5-Bromo-2-metoxifenil)-1,1,1-trifluor-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	

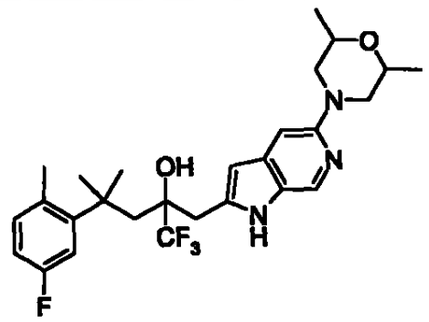
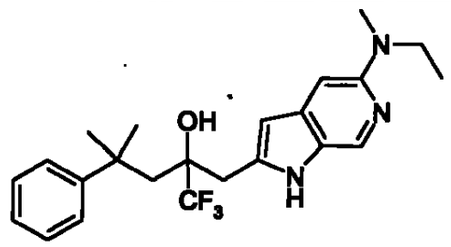
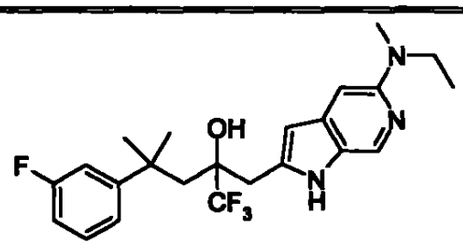
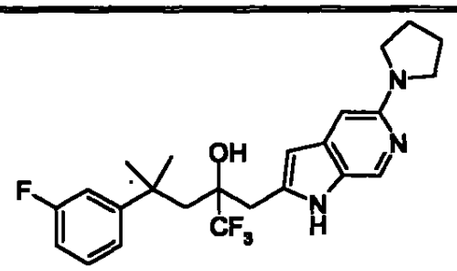
IA	
A	B
2-(5-Dimetilamino-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
2-(5-Dimetilamino-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metilfenil)-4-metilpentan-2-ol	

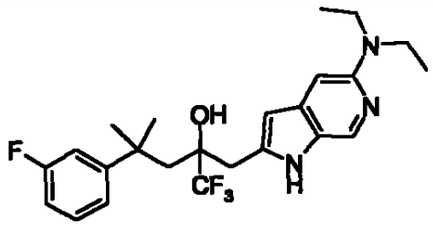
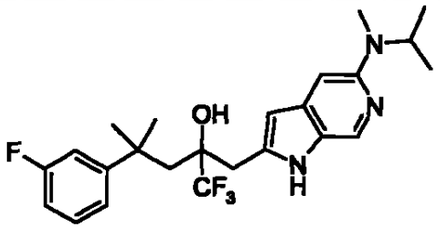
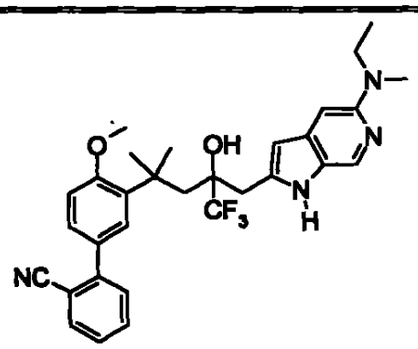
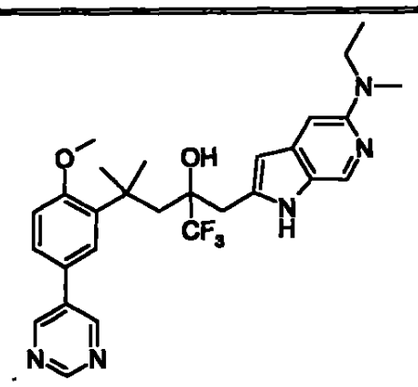
IA	
A	**B**
2-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluor-4-(5-fluor-2-metilfenil)-4-metilpentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-[5-(etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluor-4-metilpentan-2-ol	
2-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluor-4-(5-fluor-2-metoxifenil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-fenilpentan-2-ol	

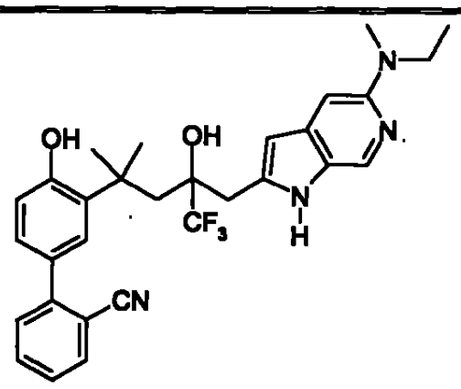
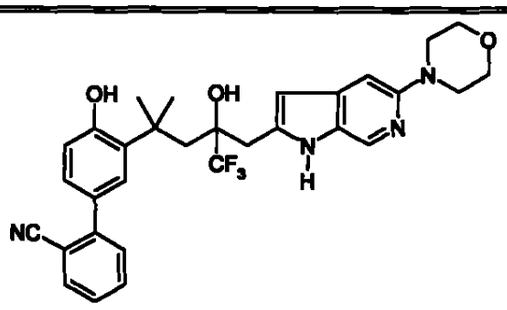
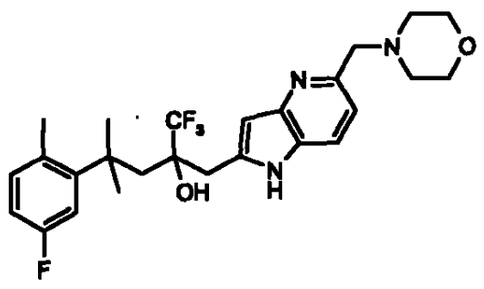
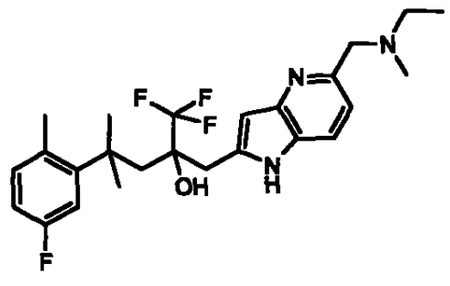
IA	
A	B
1,1,1-Trifluor-4-(3-fluorfenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-pirrolidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-fenil-2-(5-pirrolidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
4'-Metoxi-3'-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]bifenil-2-carbonitrilo	

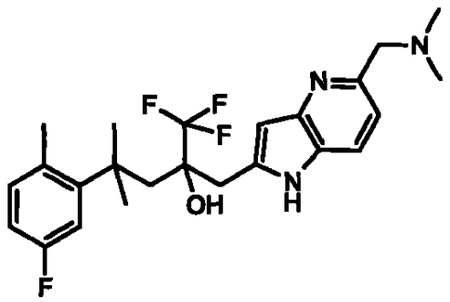
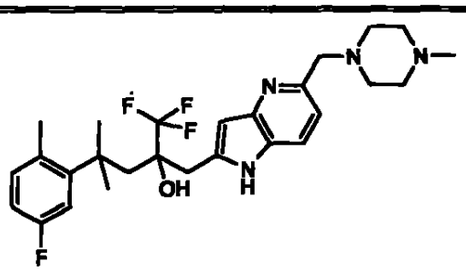
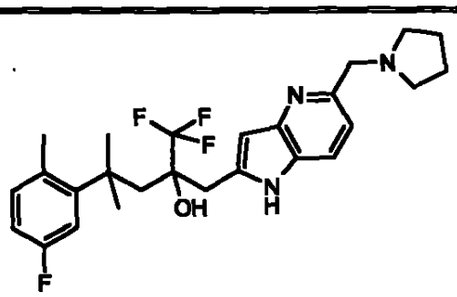
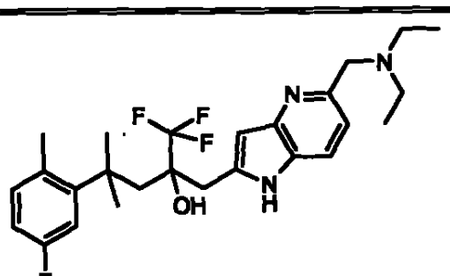
IA	
A	**B**
2-(5-Dietilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metilfenil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-2-[5-(isopropilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-4-metilpentan-2-ol	
1,1,1-Trifluor-2-[5-(isopropilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-4-metil-4-fenilpentan-2-ol	
2-(5-Dietilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluor-4-metil-4-fenilpentan-2-ol	

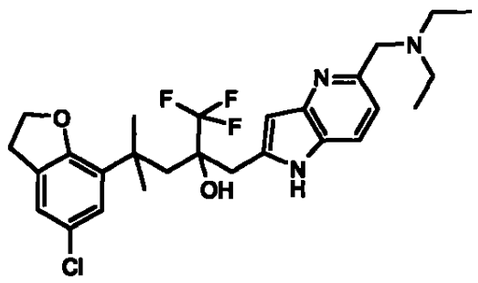
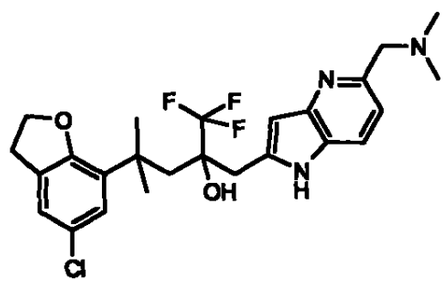
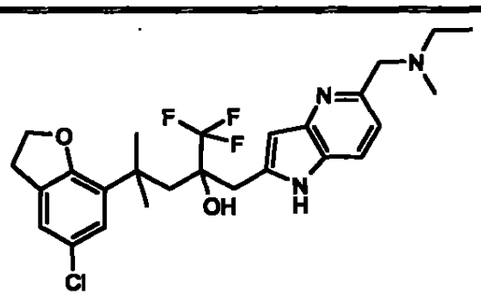
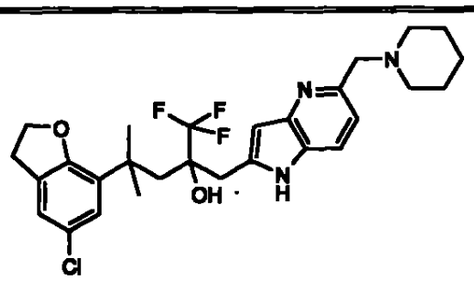
IA	
A	B
4-(3-Bromofenil)-1,1,1-trifluor-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(4-fluorfenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(4-fluorfenil)-4-metil-2-(5-pirrolidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-(3-pirimidin-5-ilfenil)pentan-2-ol	

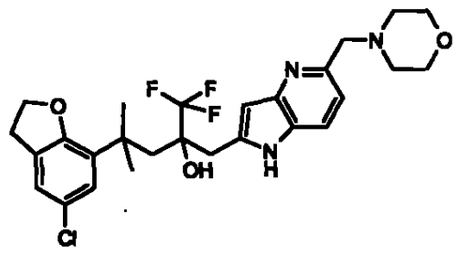
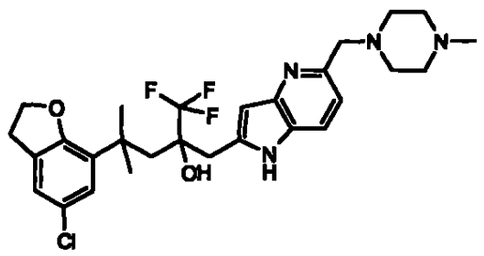
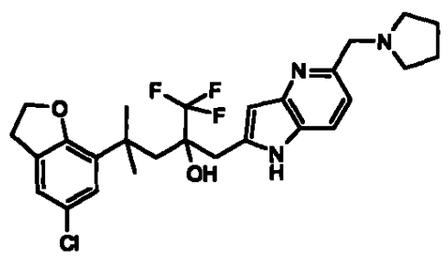
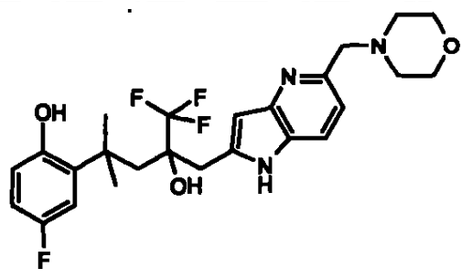
IA	
A	B
2-[5-(2,6-Dimetilmorfolin-4-il)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluor-4-(5-fluor-2-metilfenil)-4-metilpentan-2-ol	
2-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluor-4-metil-4-fenilpentan-2-ol	
2-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluor-4-(3-fluorfenil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(3-fluorfenil)-4-metil-2-(5-pirrolidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	

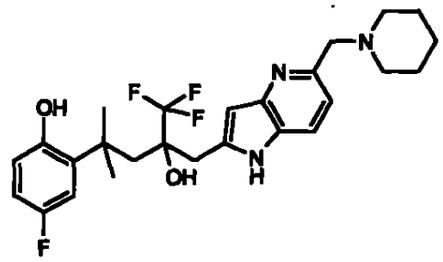
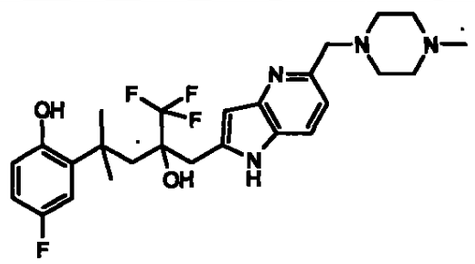
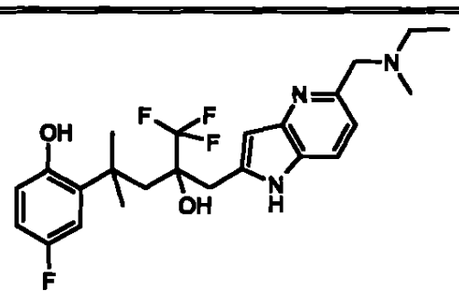
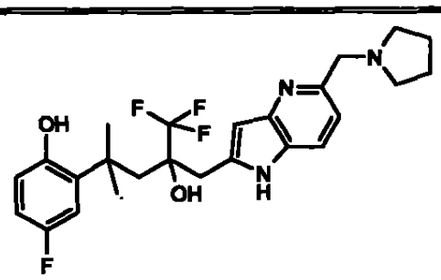
IA	
A	**B**
2-(5-Dietilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluor-4-(3-fluorfenil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(3-fluorfenil)-2-[5-(isopropilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-4-metilpentan-2-ol	
3'-{3-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil}-4'-metoxibifenil-2-carbonitrilo	
2-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluor-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metilpentan-2-ol	

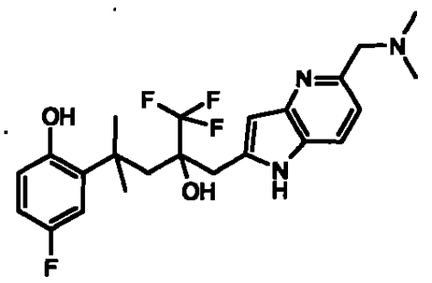
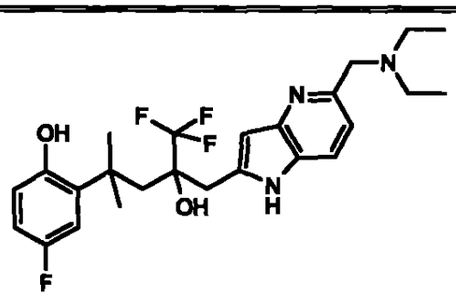
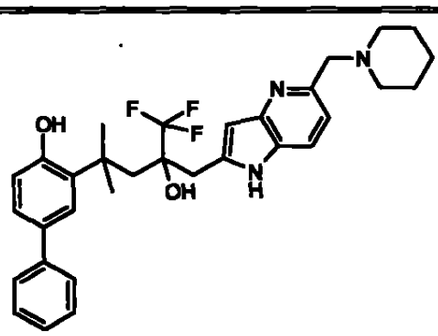
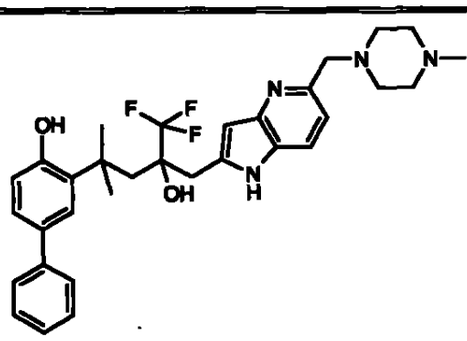
IA	
A	**B**
3'-{3-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-c]piridin-2-ilmetil]-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil}-4'-hidroxibifenil-2-carbonitrilo	
4'-Hidroxi-3'-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]bifenil-2-carbonitrilo	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-morfolin-4-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)pentan-2-ol	
2-{5-[(Etilmetilamino)metil]-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil}-1,1,1-trifluor-4-(5-fluor-2-metilfenil)-4-metilpentan-2-ol	

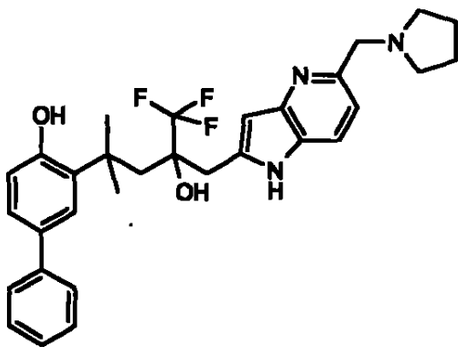
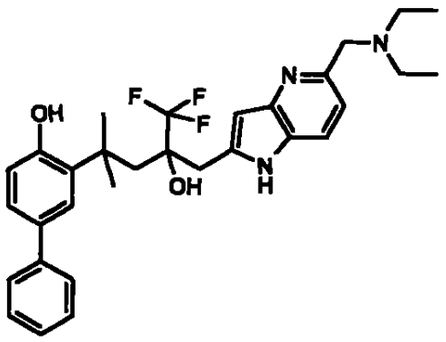
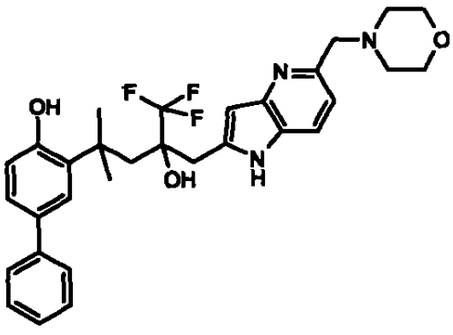
IA	
A	B
2-(5-Dimetilaminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metilfenil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-[5-(4-metilpiperazin-1-ilmetil)-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil]pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-pirrolidin-1-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)pentan-2-ol	
2-(5-Dietilaminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metilfenil)-4-metilpentan-2-ol	

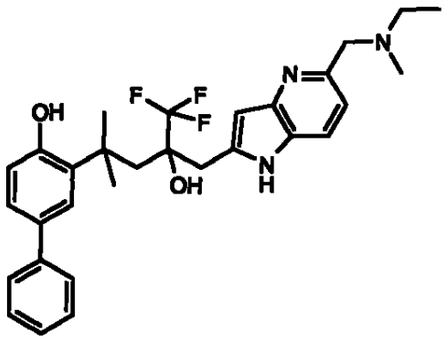
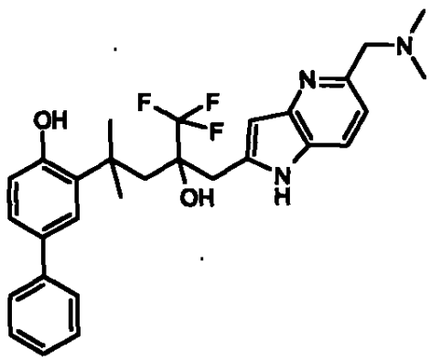
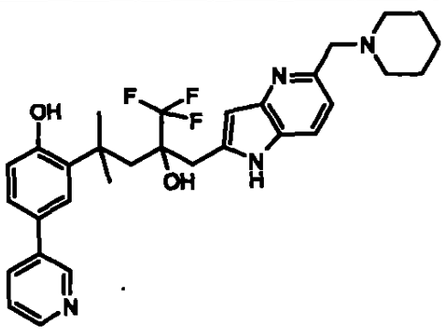
IA	
A	B
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(5-dietilaminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-1,1,1-trifluor-4-metilpentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(5-dimetilaminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-1,1,1-trifluor-4-metilpentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-{5-[(etilmetilamino)metil]-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil}-1,1,1-trifluor-4-metilpentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(5-piperidin-1-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)pentan-2-ol	

IA	
A	B
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(5-morfolin-4-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-[5-(4-metilpiperazin-1-ilmetil)-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil]pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(5-pirrolidin-1-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)pentan-2-ol	
4-Cloro-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)butil]fenol	

IA	
A	**B**
4-Fluor-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-piperidin-1-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)butil]fenol	
4-Fluor-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-[5-(4-metilpiperazin-1-ilmetil)-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil]butil]fenol	
2-(3-{5-[(Etilmetilamino)metil]-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil}-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil)-4-fluorfenol	
4-Fluor-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-pirrolidin-1-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)butil]fenol	

IA	
A	**B**
2-[3-(5-Dimetilaminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-fluorfenol	
2-[3-(5-Dietilaminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-fluorfenol	
3-[4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-(5-piperidin-1-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)butil]bifenil-4-ol	
3-{4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-[5-(4-metilpiperazin-1-ilmetil)-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil]butil}bifenil-4-ol	

IA	
A	**B**
3-[4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-(5-pirrolidin-1-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)butil]bifenil-4-ol	
3-[3-(5-Dietilaminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]bifenil-4-ol	
3-[4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)butil]bifenil-4-ol	

IA	
A	**B**
3-(3-(5-[(Etilmetilamino)metil]-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil)bifenil-4-ol	
3-[3-(5-Dimetilaminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]bifenil-4-ol	
4-Piridin-3-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-piperidin-1-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)butil]fenol	

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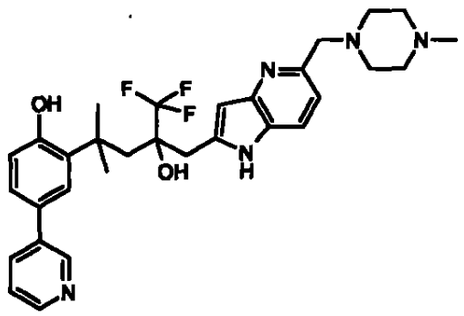
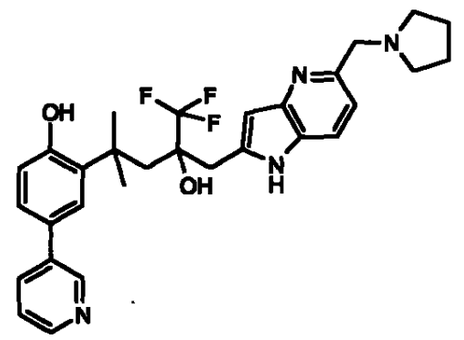
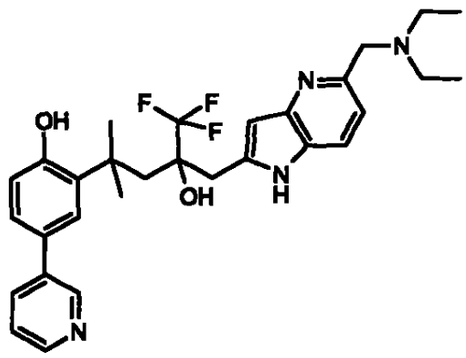
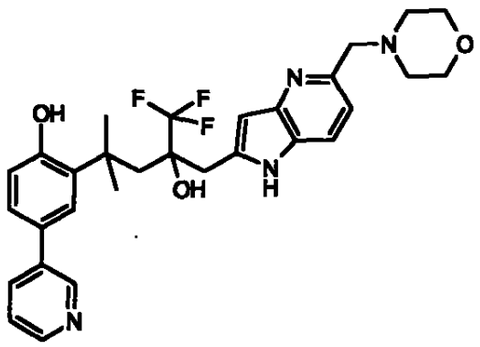
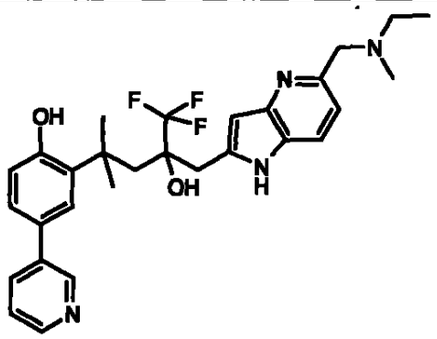
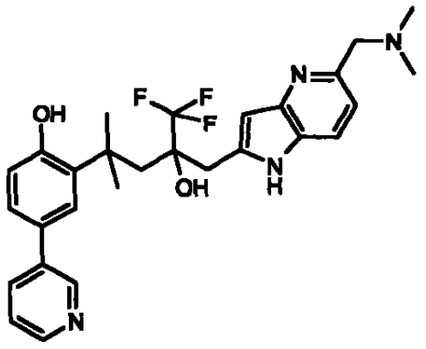
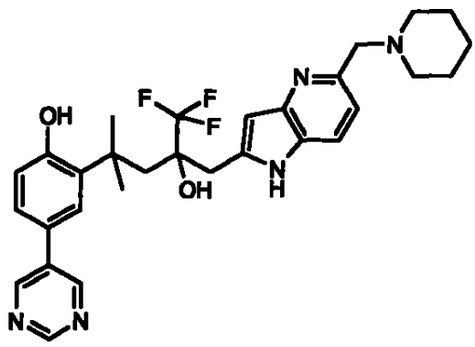
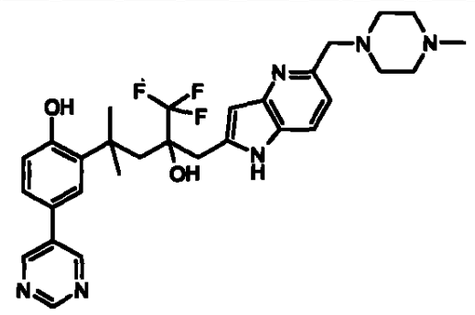
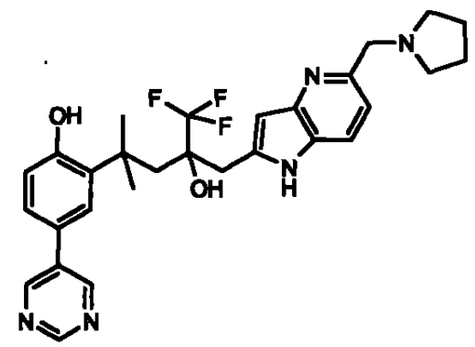
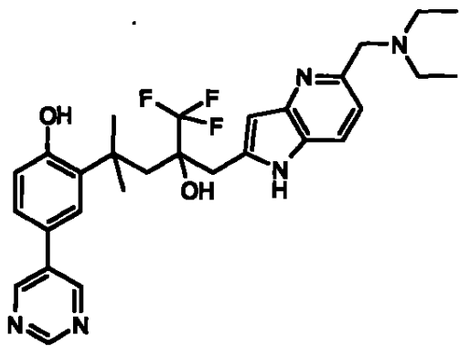
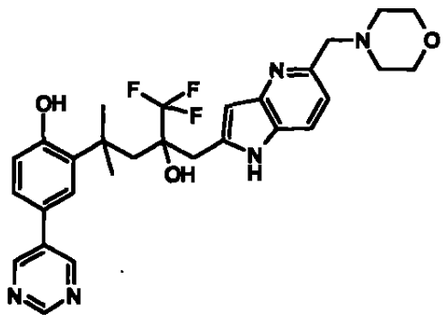
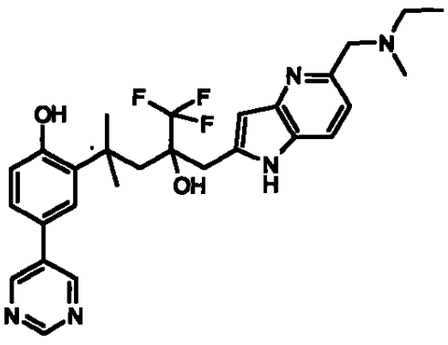
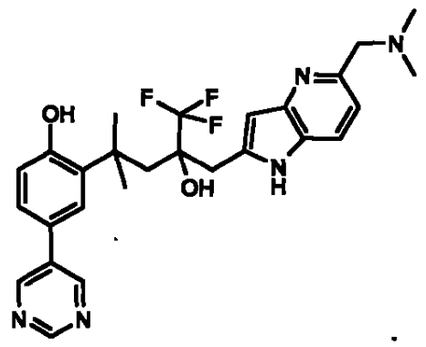
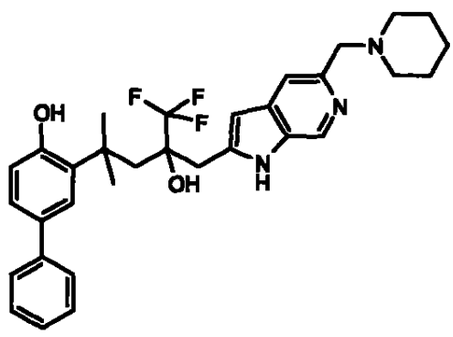
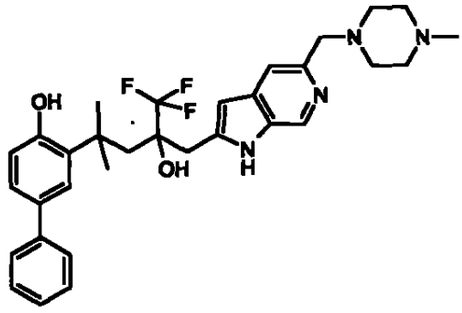
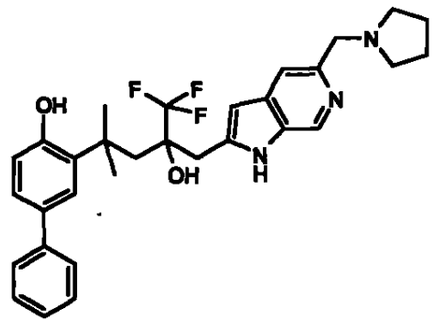
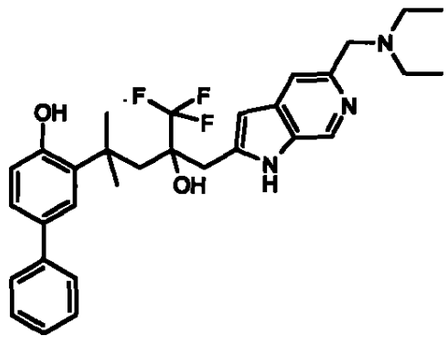
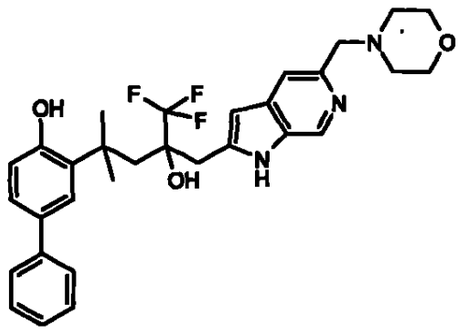
IA	
A	B
4-Piridin-3-il-2-{4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-[5-(4-metilpiperazin-1-ilmetil)-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil]butil}fenol	
4-Piridin-3-il-2-{4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-pirrolidin-1-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)butil]fenol	
2-[3-(5-Dietilaminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-piridin-3-ilfenol	

IA	
A	**B**
4-Piridin-3-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)butil]fenol	
2-(3-{5-[(Etilmetilamino)metil]-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil}-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil)-4-piridin-3-ilfenol	
2-[3-(5-Dimetilaminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-piridin-3-ilfenol	

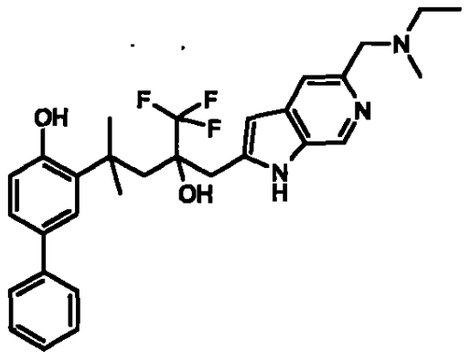
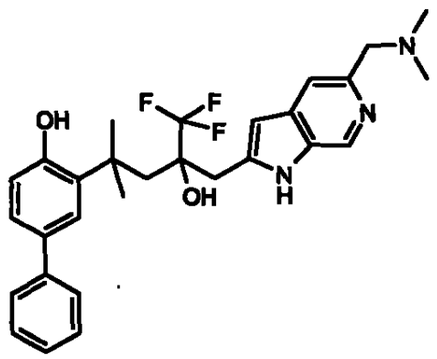
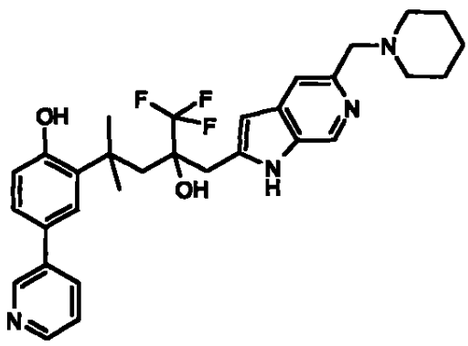
IA	
A	B
4-Pirimidin-5-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-piperidin-1-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)butil]fenol	
4-Pirimidin-5-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-[5-(4-metilpiperazin-1-ilmetil)-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil]butil]fenol	
4-Pirimidin-5-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-pirrolidin-1-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)butil]fenol	

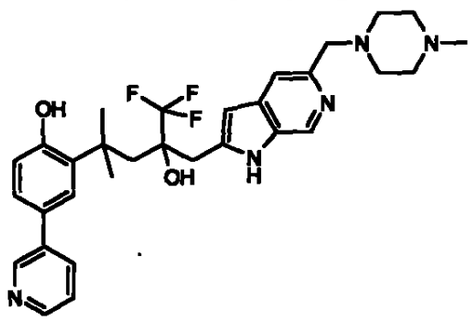
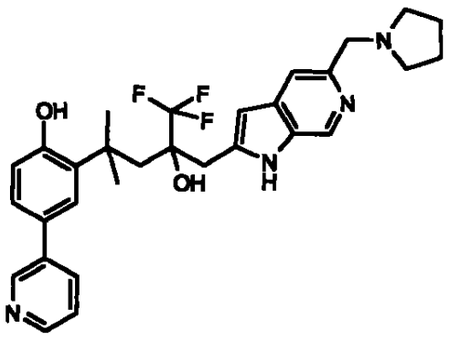
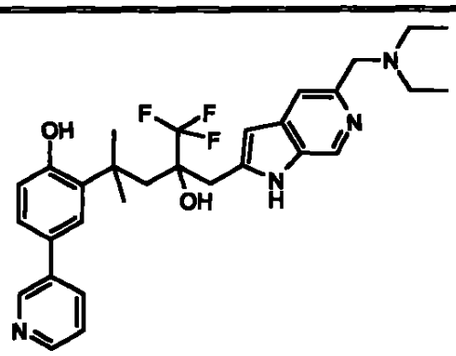
IA	
A	**B**
2-[3-(5-Dietilaminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-pirimidin-5-ilfenol	
4-Pirimidin-5-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)butil]fenol	
2-(3-[5-[(Etilmetilamino)metil]-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil}-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil)-4-pirimidin-5-ilfenol	

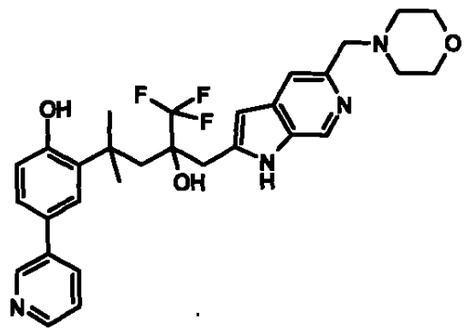
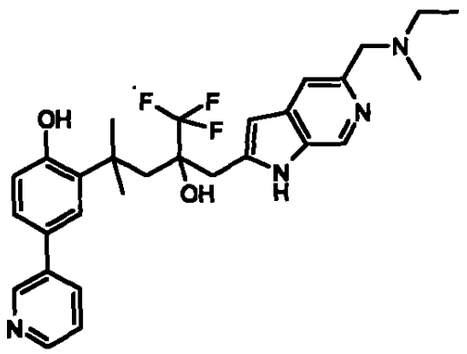
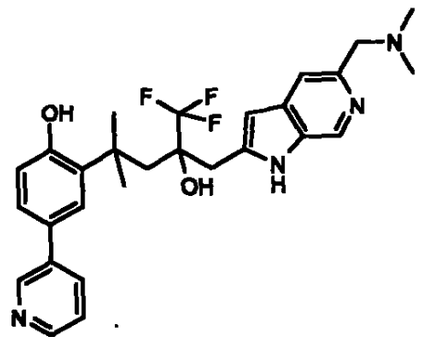
IA	
A	B
2-[3-(5-Dimetilaminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-pirimidin-5-ilfenol	
3-[4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-(5-piperidin-1-ilmetil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]bifenil-4-ol	
3-{4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-[5-(4-metilpiperazin-1-ilmetil)-1*H*-pirrolo[2,3-c]piridin-2-ilmetil]butil}bifenil-4-ol	

IA	
A	B
3-[4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-(5-pirrolidin-1-ilmetil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]bifenil-4-ol	
3-[3-(5-Dietilaminometil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]bifenil-4-ol	
3-[4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-ilmetil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]bifenil-4-ol	

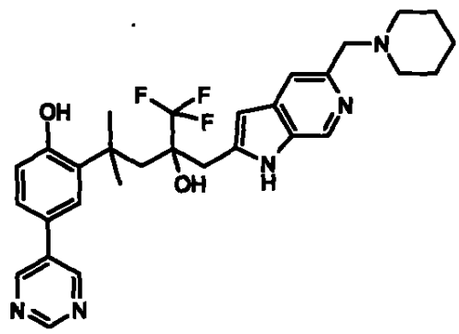
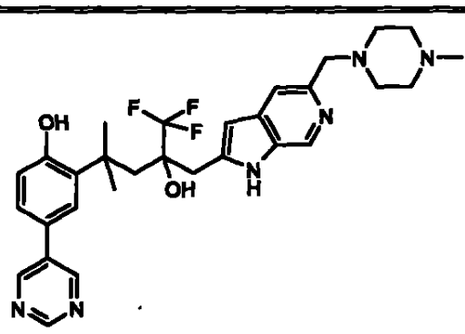
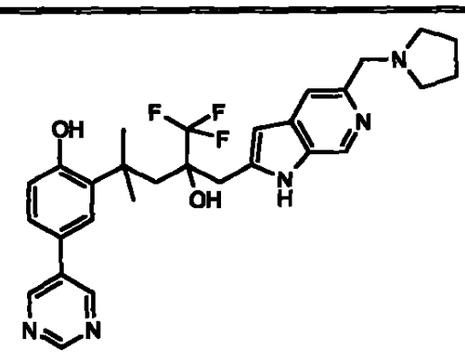
772

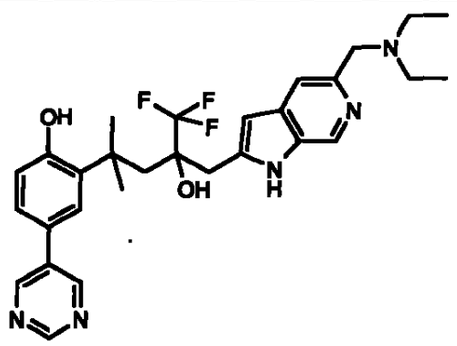
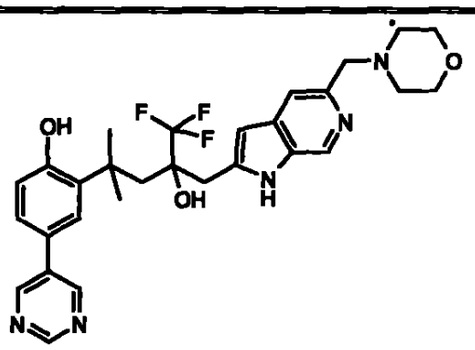
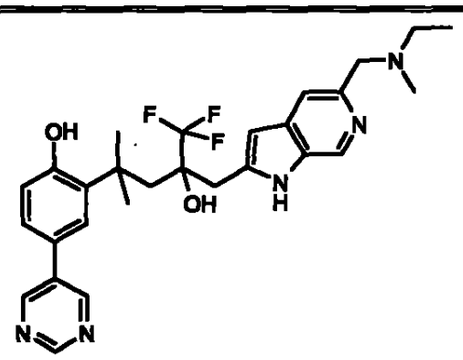
IA	
A	B
3-(3-{5-[(Etilmetilamino)metil]-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil}-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil)bifenil-4-ol	
3-[3-(5-Dimetilaminometil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]bifenil-4-ol	
4-Piridin-3-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-piperidin-1-ilmetil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]fenol	

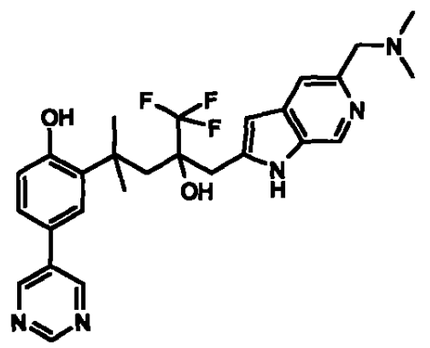
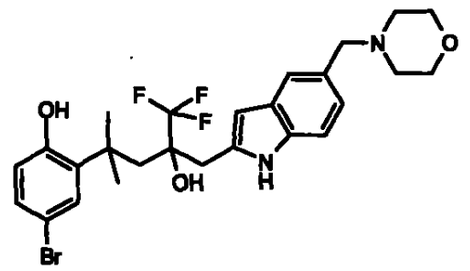
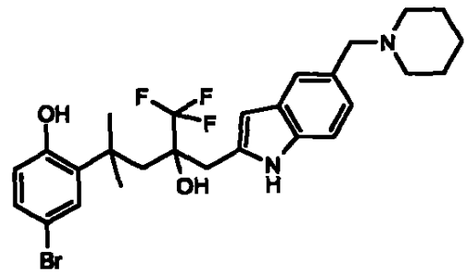
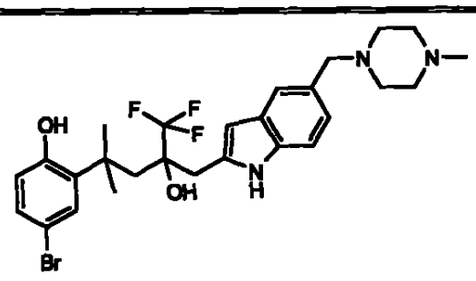
IA	
A	B
4-Piridin-3-il-2-{4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-[5-(4-metilpiperazin-1-ilmetil)-1*H*-pirrolo[2,3-c]piridin-2-ilmetil]butil}fenol	
4-Piridin-3-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-pirrolidin-1-ilmetil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]fenol	
2-[3-(5-Dietilaminometil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-piridin-3-ilfenol	

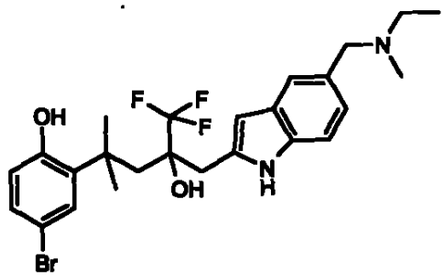
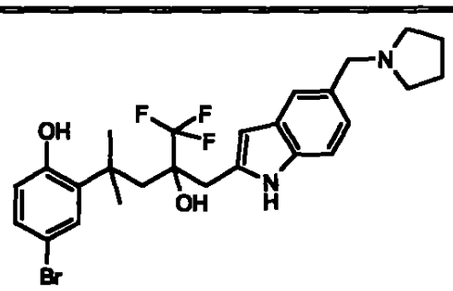
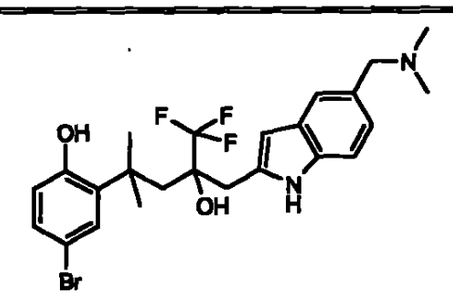
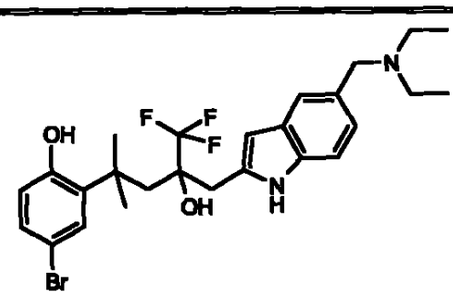
IA	
A	B
4-Piridin-3-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-ilmetil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]fenol	
2-(3-{5-[(Etilmetilamino)metil]-1*H*-pirrolo[2,3-c]piridin-2-ilmetil}-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil)-4-piridin-3-ilfenol	
2-[3-(5-Dimetilaminometil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-piridin-3-ilfenol	

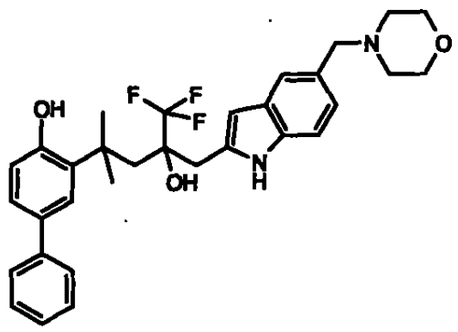
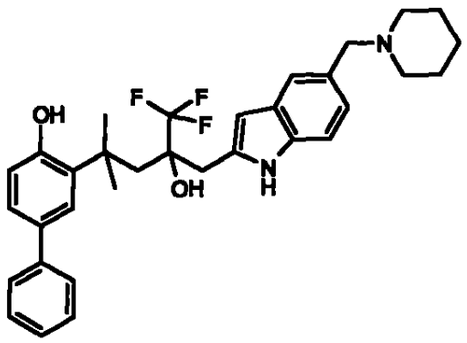
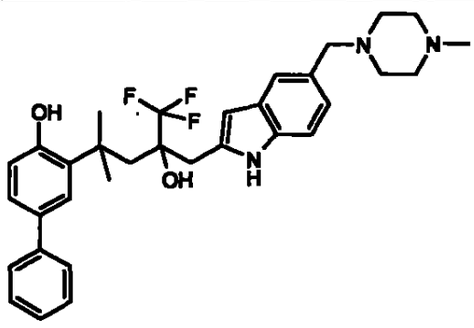
775

IA	
A	B
4-Pirimidin-5-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-piperidin-1-ilmetil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]fenol	
4-Pirimidin-5-il-2-{4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-[5-(4-metilpiperazin-1-ilmetil)-1*H*-pirrolo[2,3-c]piridin-2-ilmetil]butil}fenol	
4-Pirimidin-5-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-pirrolidin-1-ilmetil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]fenol	

IA	
A	**B**
2-[3-(5-Dietilaminometil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-pirimidin-5-ilfenol	
4-Pirimidin-5-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-ilmetil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]fenol	
2-(3-(5-[(Etilmetilamino)metil]-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil}-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil)-4-pirimidin-5-ilfenol	

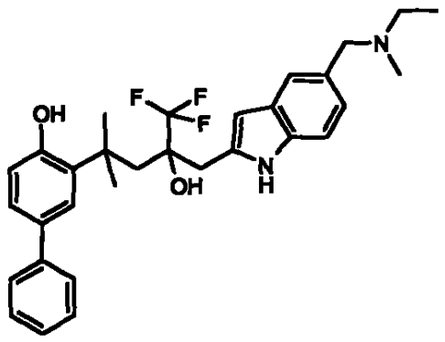
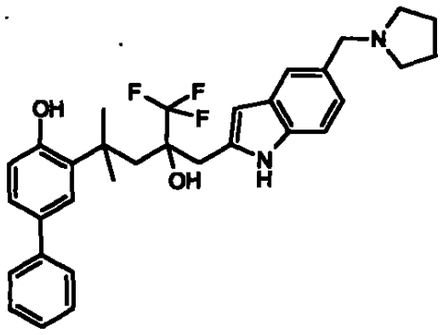
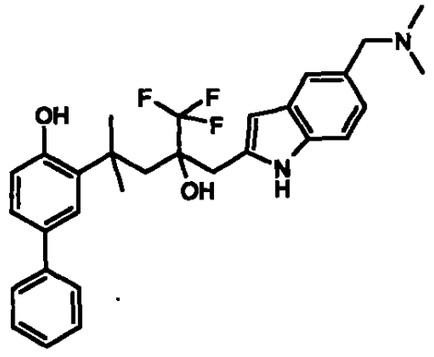
IA	
A	B
2-[3-(5-Dimetilaminometil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-pirimidin-5-ilfenol	
4-Bromo-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-ilmetil-1*H*-indol-2-ilmetil)butil]fenol	
4-Bromo-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-piperidin-1-ilmetil-1*H*-indol-2-ilmetil)butil]fenol	
4-Bromo-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-[5-(4-metilpiperazin-1-ilmetil)-1*H*-indol-2-ilmetil]butil]fenol	

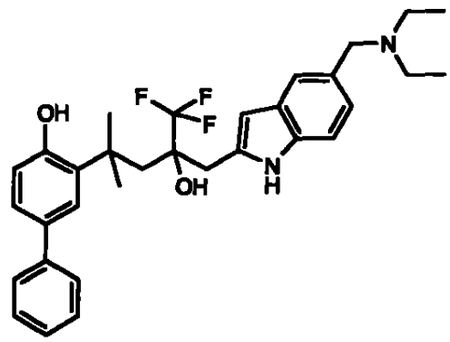
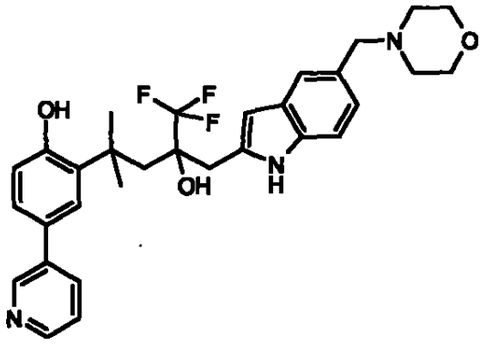
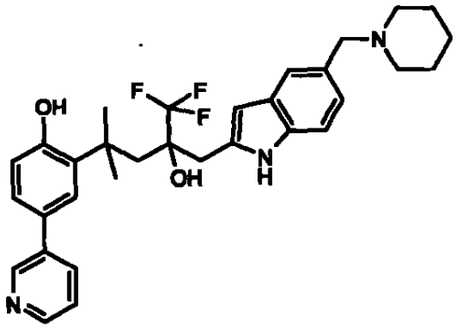
IA	
A	B
4-Bromo-2-{3-[5-[(etilmetilamino)metil]-1*H*-indol-2-ilmetil}-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil)fenol	
4-Bromo-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-pirrolidin-1-ilmetil-1*H*-indol-2-ilmetil)butil]fenol	
4-Bromo-2-[3-(5-dimetilaminometil-1*H*-indol-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]fenol	
4-Bromo-2-[3-(5-dietilaminometil-1*H*-indol-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]fenol	

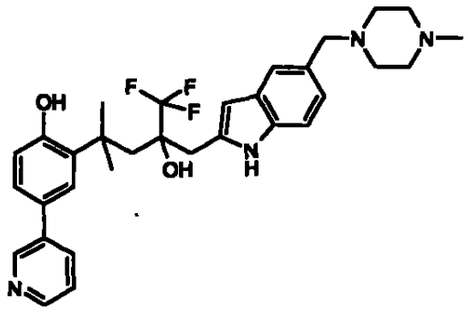
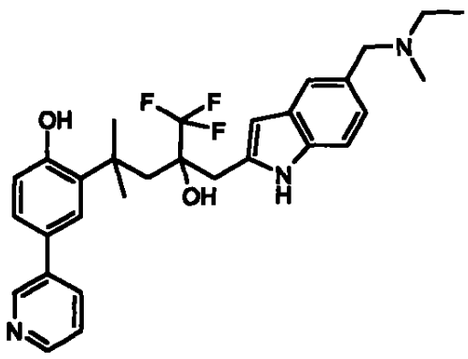
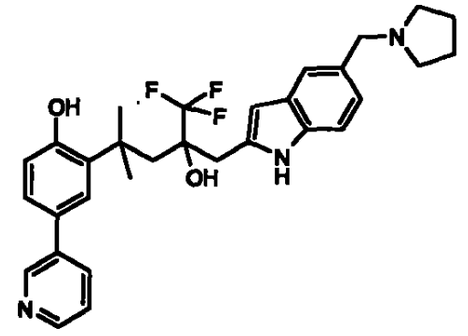
IA	
A	B
3-[4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-ilmetil-1*H*-indol-2-ilmetil)butil]bifenil-4-ol	
3-[4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-(5-piperidin-1-ilmetil-1*H*-indol-2-ilmetil)butil]bifenil-4-ol	
3-{4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-[5-(4-metilpiperazin-1-ilmetil)-1*H*-indol-2-ilmetil]butil}bifenil-4-ol	

760

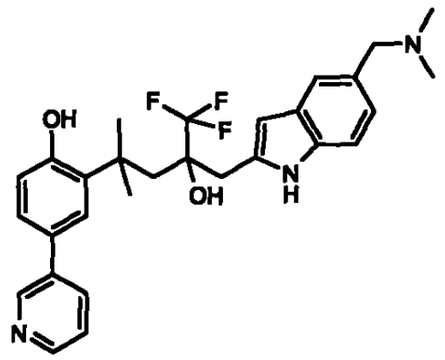
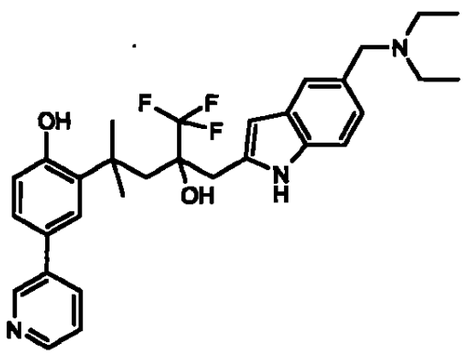
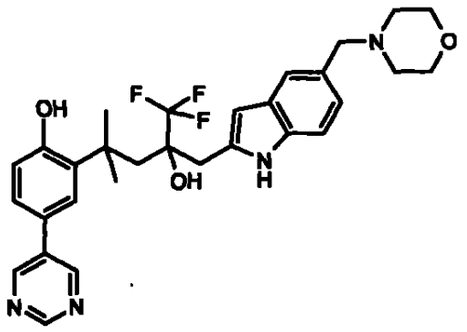
780

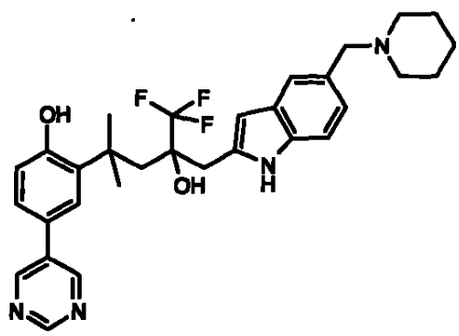
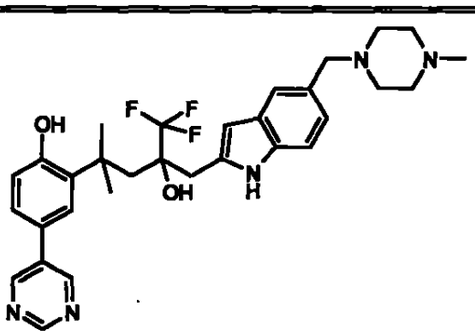
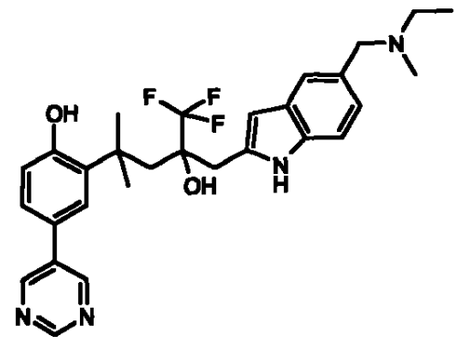
IA	
A	B
3-(3-{5-[(Etilmetilamino)metil]-1*H*-indol-2-ilmetil}-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil)bifenil-4-ol	
3-[4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-(5-pirolidin-1-ilmetil-1*H*-indol-2-ilmetil)butil]bifenil-4-ol	
3-[3-(5-Dimetilaminometil-1*H*-indol-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]bifenil-4-ol	

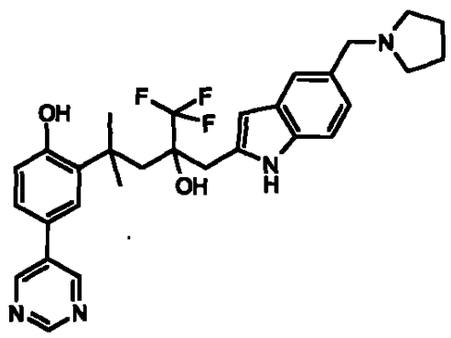
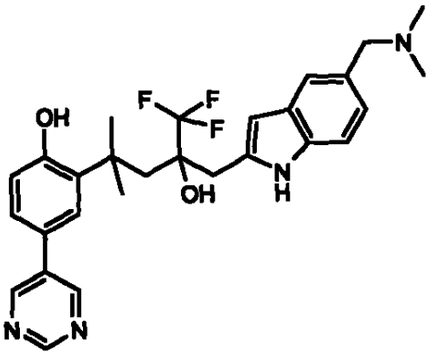
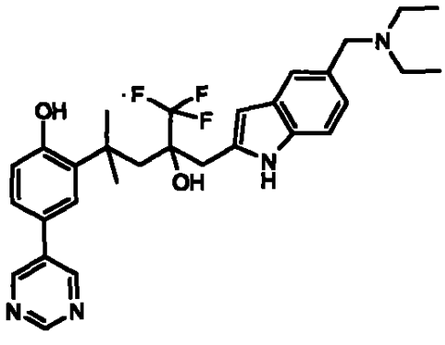
IA	
A	B
3-[3-(5-Dietilaminometil-1*H*-indol-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]bifenil-4-ol	
4-Piridin-3-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-ilmetil-1*H*-indol-2-ilmetil)butil]fenol	
4-Piridin-3-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-piperidin-1-ilmetil-1*H*-indol-2-ilmetil)butil]fenol	

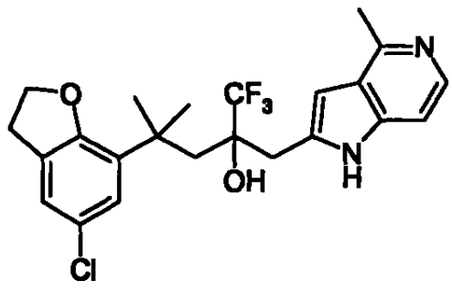
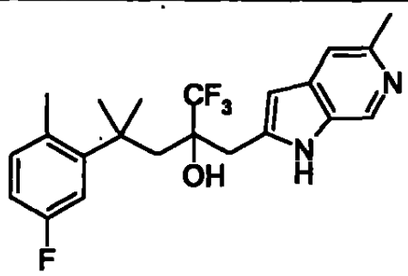
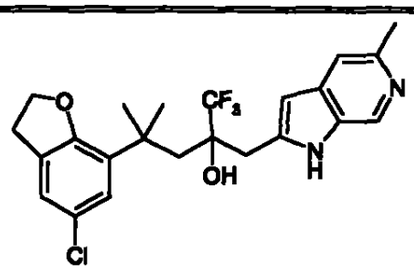
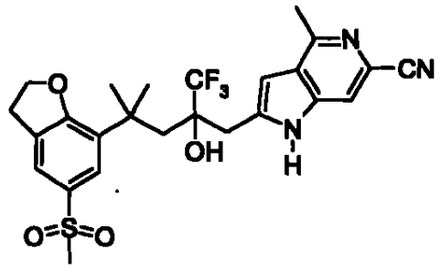
IA	
A	B
4-Piridin-3-il-2-{4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-[5-(4-metilpiperazin-1-ilmetil)-1*H*-indol-2-ilmetil]butil}fenol	
2-(3-{5-[(Etilmetilamino)metil]-1*H*-indol-2-ilmetil}-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil)-4-piridin-3-ilfenol	
4-Piridin-3-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-pirrolidin-1-ilmetil-1*H*-indol-2-ilmetil)butil]fenol	

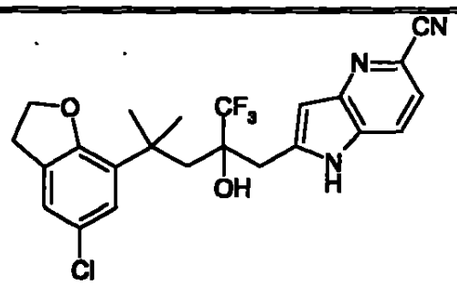
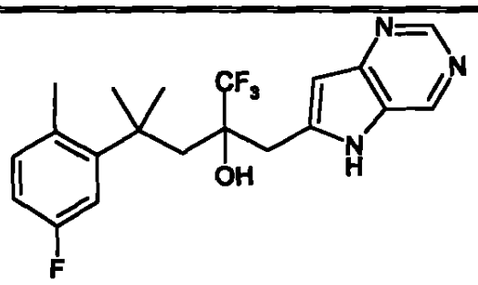
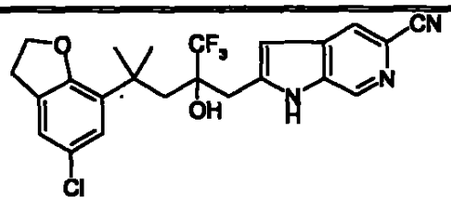
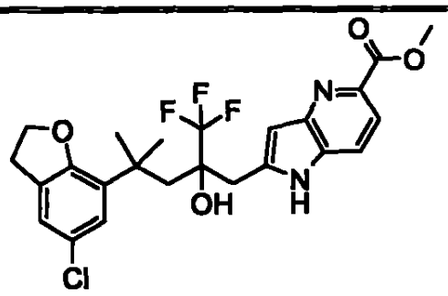
783

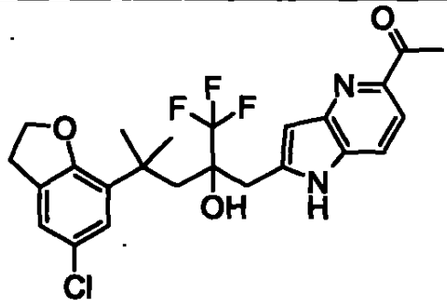
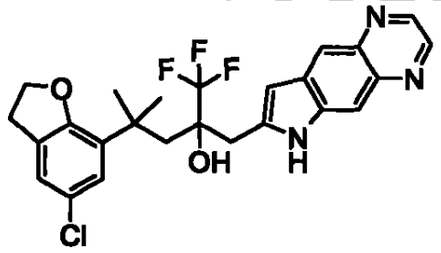
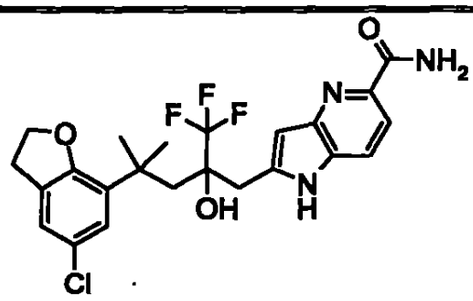
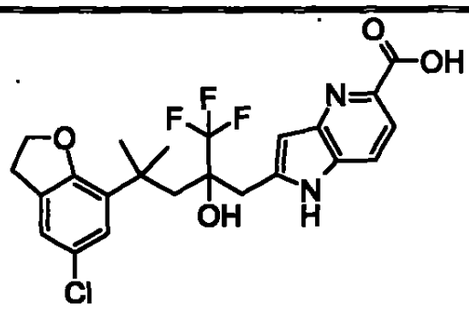
IA	
A	B
2-[3-(5-Dimetilaminometil-1*H*-indol-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-piridin-3-ilfenol	
2-[3-(5-Dietilaminometil-1*H*-indol-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-piridin-3-ilfenol	
4-Pirimidin-5-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-ilmetil-1*H*-indol-2-ilmetil)butil]fenol	

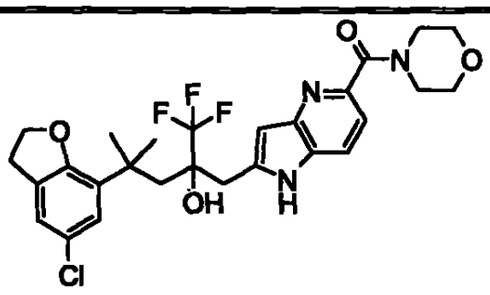
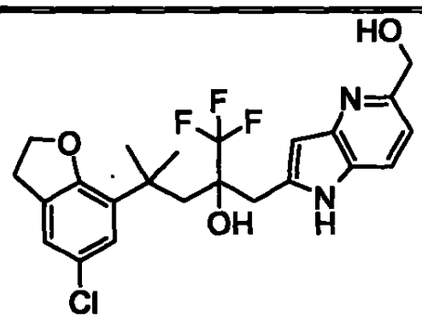
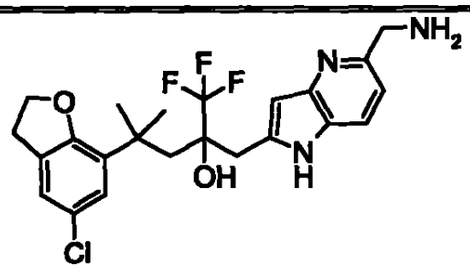
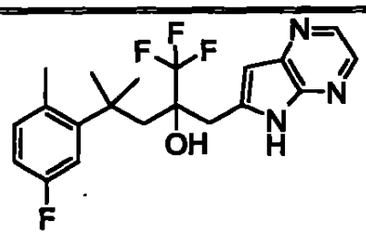
IA	
A	B
4-Pirimidin-5-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-piperidin-1-ilmetil-1*H*-indol-2-ilmetil)butil]fenol	
4-Pirimidin-5-il-2-{4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-[5-(4-metilpiperazin-1-ilmetil)-1*H*-indol-2-ilmetil]butil}fenol	
2-(3-{5-[(Etilmetilamino)metil]-1*H*-indol-2-ilmetil}-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil)-4-pirimidin-5-ilfenol	

IA	
A	B
4-Pirimidin-5-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-pirrolidin-1-ilmetil-1*H*-indol-2-ilmetil)butil]fenol	
2-[3-(5-Dimetilaminometil-1*H*-indol-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-pirimidin-5-ilfenol	
2-[3-(5-Dietilaminometil-1*H*-indol-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-pirimidin-5-ilfenol	

IA	
A	B
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(5-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluormetilpentil]-4-metil-1*H*-pirrolo[3,2-*c*]piridin-6-carbonitrilo	

IA	
A	**B**
2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-carbonitrilo	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol	
2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[2,3-*c*]piridin-5-carbonitrilo	
éster metílico del ácido 2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-carboxílico	

IA	
A	B
1-[2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il]etanona	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(6*H*-pirrolo[2,3-g]quinoxalin-7-ilmetil)pentan-2-ol	
amida del ácido 2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-carboxílico	
ácido 2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-carboxílico	

IA	
A	**B**
{2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il}morfolin-4-ilmetanona	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-2-(5-hidroximetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-metilpentan-2-ol	
2-(5-Aminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)pentan-2-ol	

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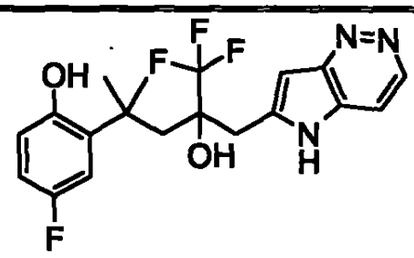
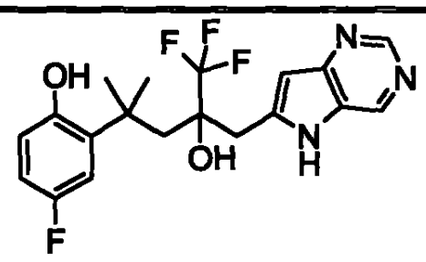
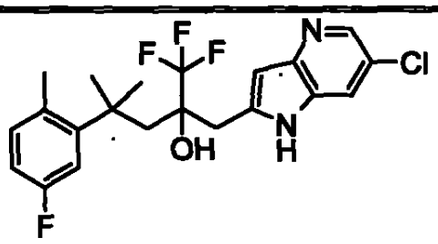
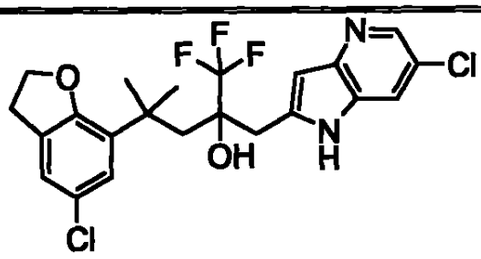
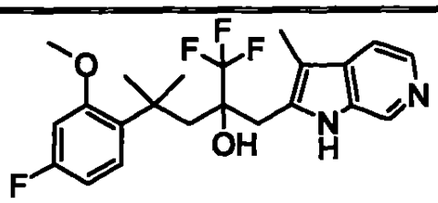
IA	
A	**B**
4-Fluor-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5*H*-pirrolo[3,2-c]piridazin-6-ilmetil)butil]fenol	
4-Fluor-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)butil]fenol	
2-(6-Cloro-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metilfenil)-4-metilpentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(6-cloro-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-1,1,1-trifluor-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(4-fluor-2-metoxifenil)-4-metil-2-(3-metil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	

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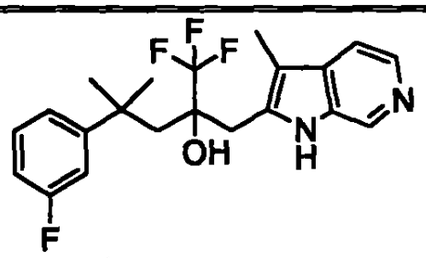
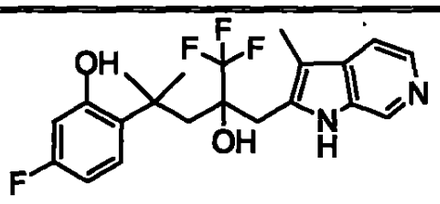
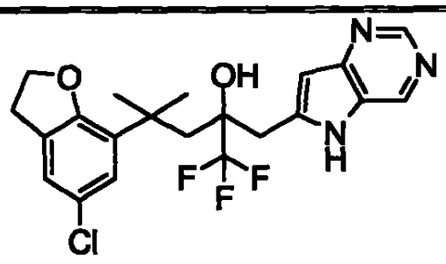
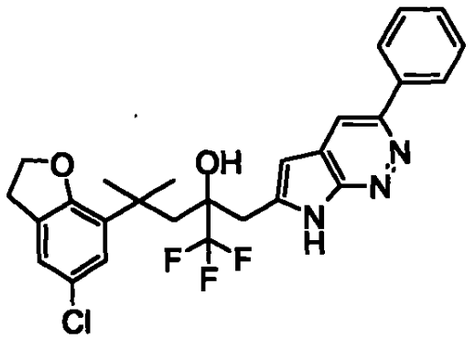
IA	
A	B
1,1,1-Trifluor-4-(3-fluorfenil)-4-metil-2-(3-metil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
5-Fluor-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(3-metil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]fenol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(3-fenil-7*H*-pirrolo[2,3-c]piridazin-6-ilmetil)pentan-2-ol	

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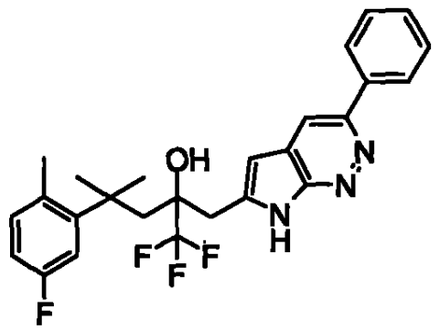
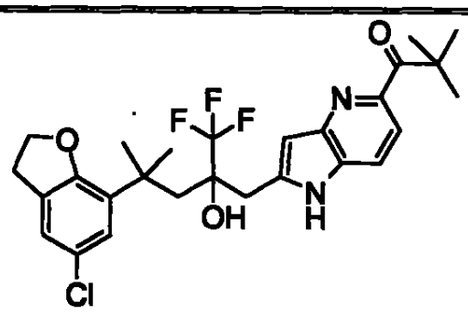
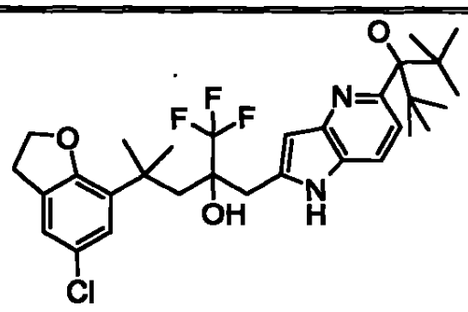
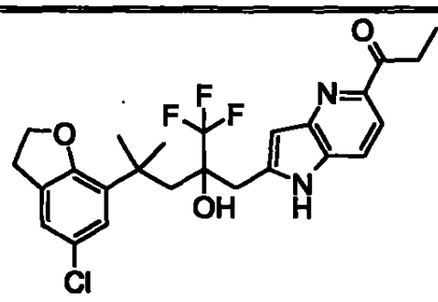
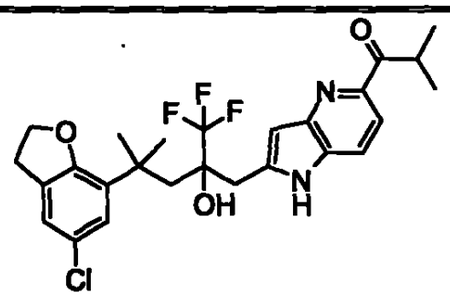
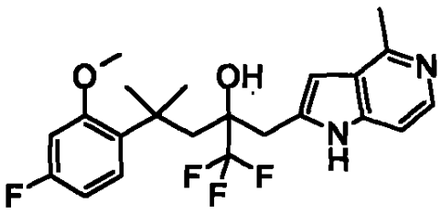
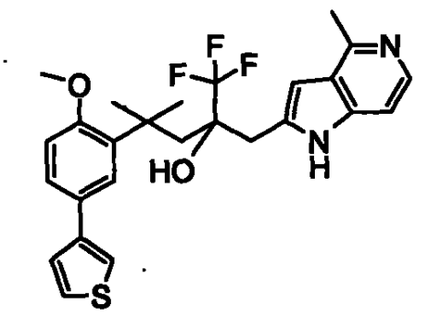
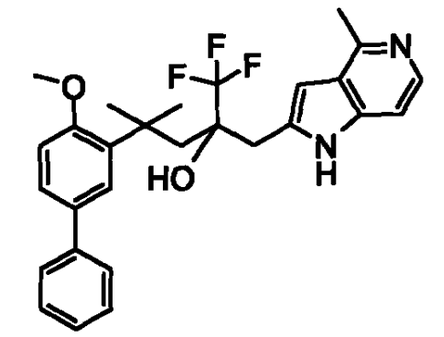
IA	
A	B
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(3-fenil-7*H*-pirrolo[2,3-*c*]piridazin-6-ilmetil)pentan-2-ol	
1-{2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il}-2,2-dimetilpropan-1-ona	
2-[5-(1-*tert*-Butil-1-hidroxi-2,2-dimetilpropil)-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil]-4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metilpentan-2-ol	
1-{2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il}propan-1-ona	

IA	
A	B
1-[2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il]-2-metilpropan-1-ona	
1,1,1-Trifluor-4-(4-fluor-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(2-metoxi-5-tiofen-3-ilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(4-metoxibifenil-3-il)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol	

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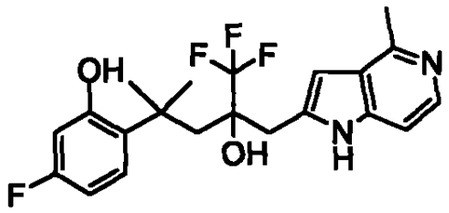
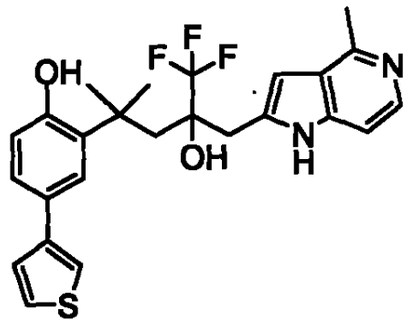
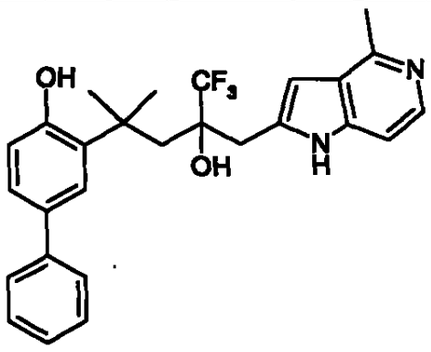
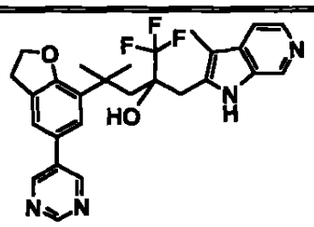
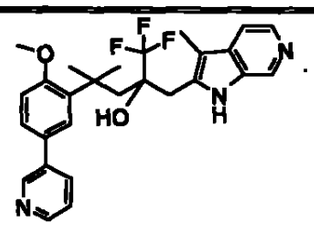
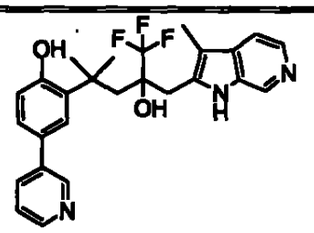
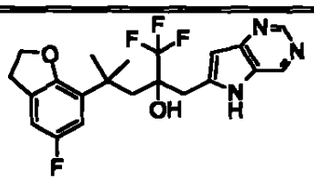
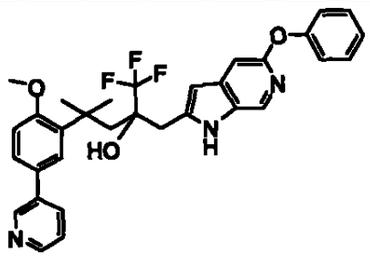
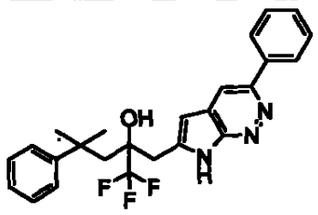
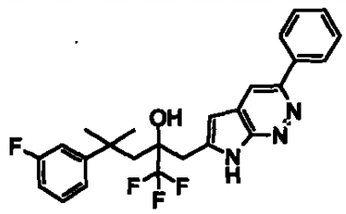
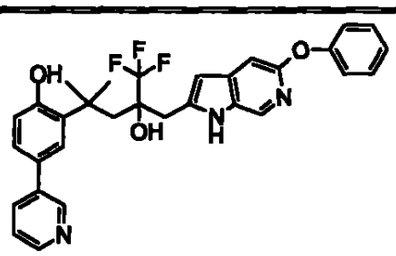
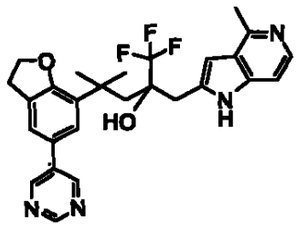
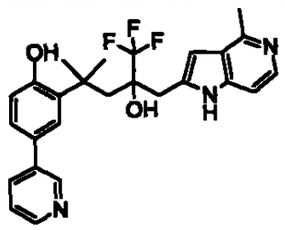
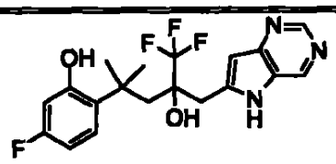
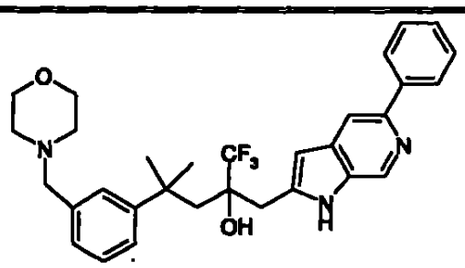
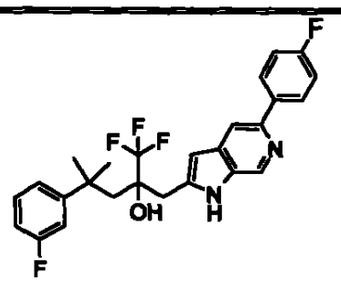
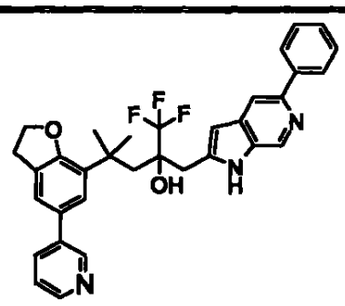
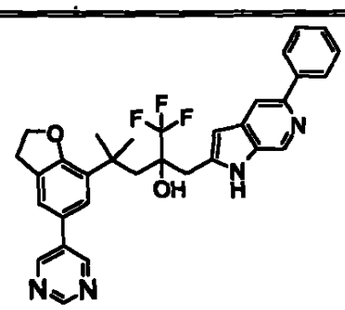
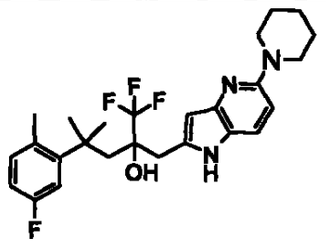
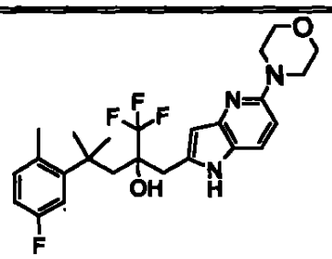
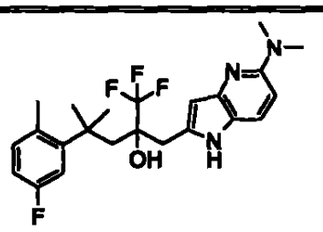
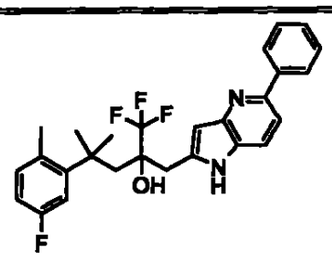
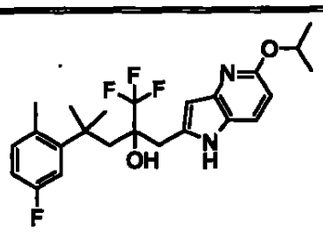
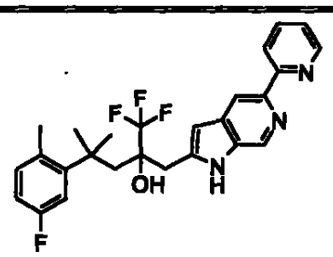
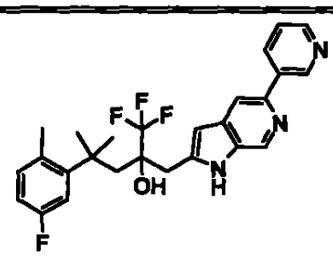
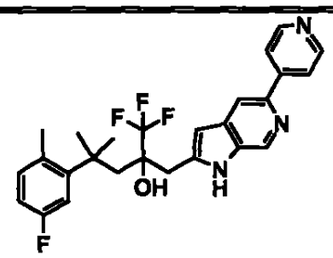
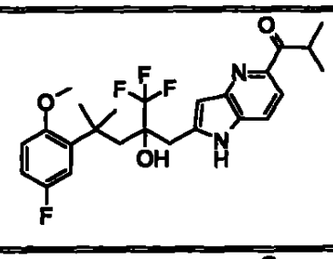
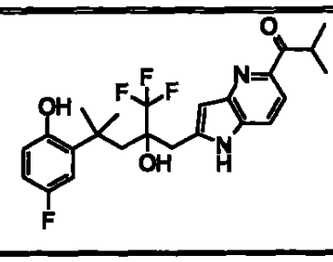
IA	
A	B
5-Fluor-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]fenol	
4-Tiofen-3-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]fenol	
3-[4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]bifenil-4-ol	
1,1,1-Trifluor-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-(5-pirimidin-5-il-2,3-dihidrobenzofuran-7-il)pentan-2-ol	

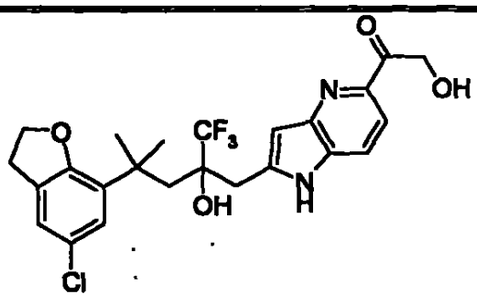
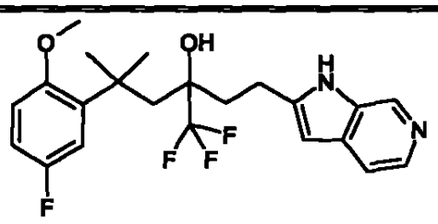
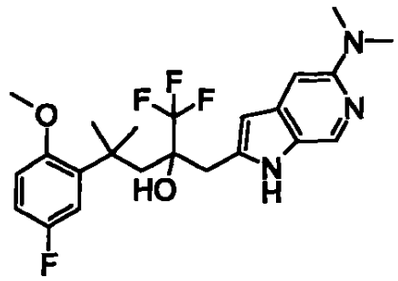
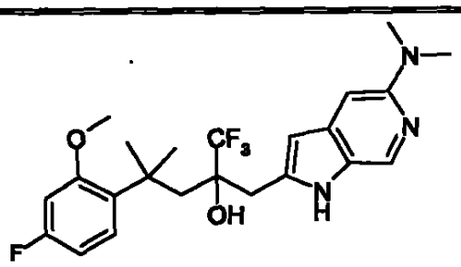
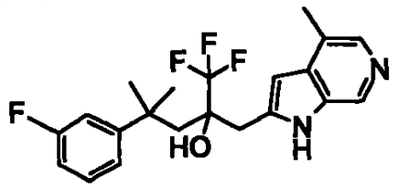
IA	
A	B
1,1,1-Trifluor-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
4-Piridin-3-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]fenol	
1,1,1-Trifluor-4-(5-fluor-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(5-fenoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-fenil-2-(3-fenil-7*H*-pirrolo[2,3-*c*]piridazin-6-ilmetil)pentan-2-ol	

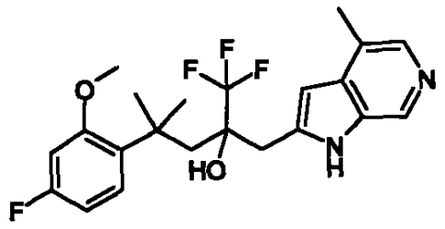
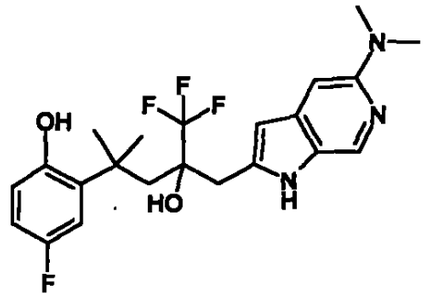
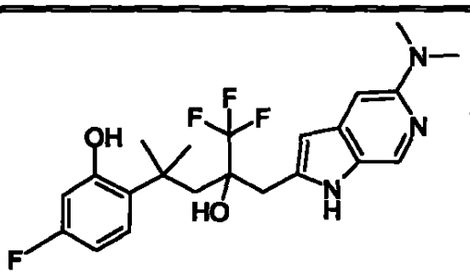
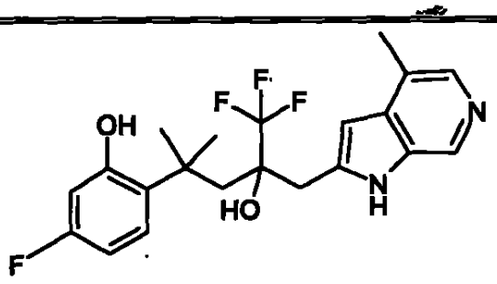
IA	
A	B
1,1,1-Trifluor-4-(3-fluorfenil)-4-metil-2-(3-fenil-7*H*-pirrolo[2,3-*c*]piridazin-6-ilmetil)pentan-2-ol	
4-Piridin-3-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-fenoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]fenol	
1,1,1-Trifluor-4-metil-2-(4-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)-4-(5-pirimidin-5-il-2,3-dihidrobenzofuran-7-il)pentan-2-ol	
4-Piridin-3-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]fenol	
5-Fluor-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)butil]fenol	

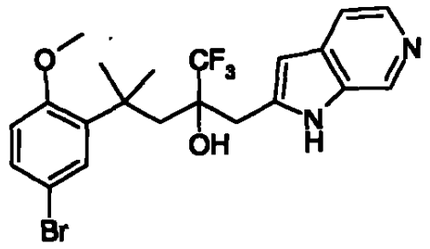
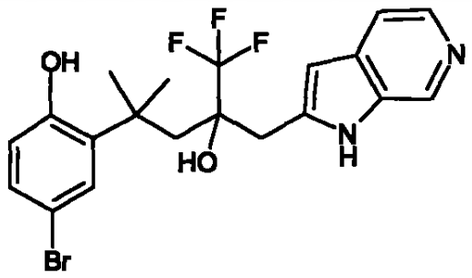
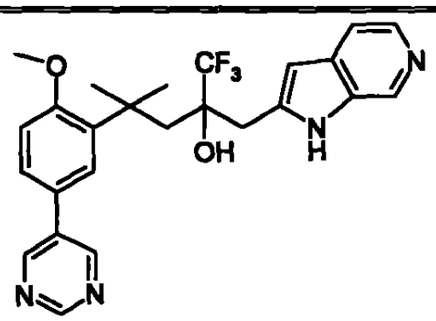
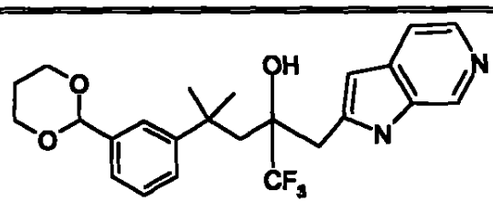
IA	
A	B
1,1,1-Trifluor-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(5-fenil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(3-fluorfenil)-2-[5-(4-fluorfenil)-1*H*-pirrolo[2,3-c]piridin-2-ilmetil]-4-metilpentan-2-ol	
1,1,1-Trifluor-4-metil-2-(5-fenil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-(5-piridin-3-il-2,3-dihidrobenzofuran-7-il)pentan-2-ol	
1,1,1-Trifluor-4-metil-2-(5-fenil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-(5-pirimidin-5-il-2,3-dihidrobenzofuran-7-il)pentan-2-ol	

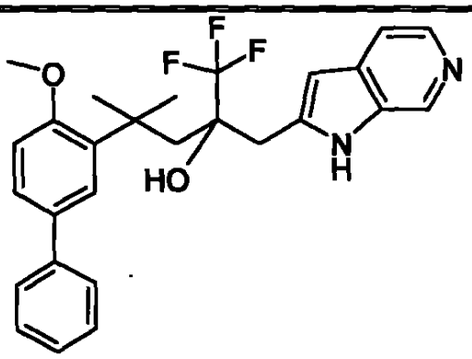
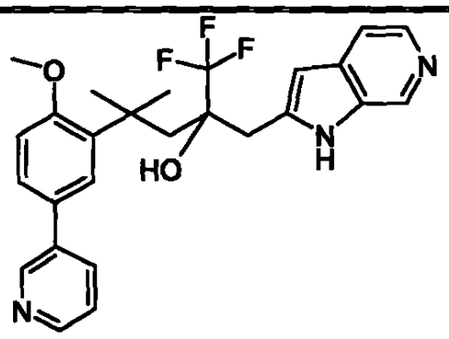
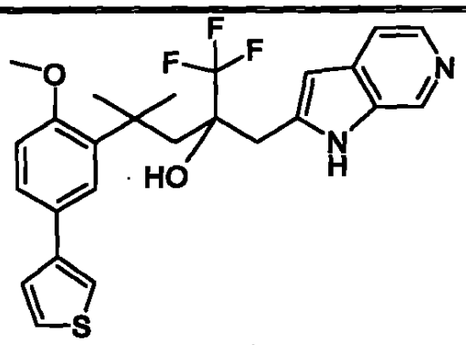
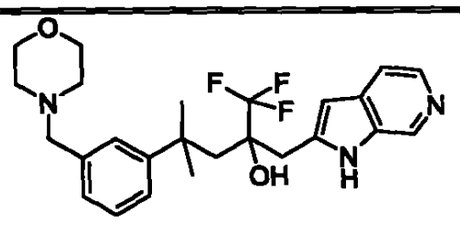
IA	
A	B
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)pentan-2-ol	
2-(5-Dimetilamino-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metilfenil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-fenil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-2-(5-isopropoxi-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-metilpentan-2-ol	

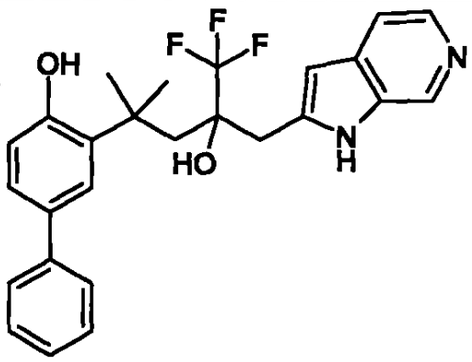
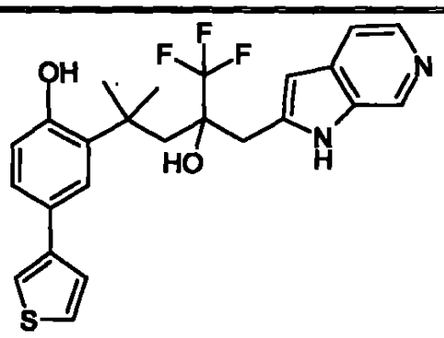
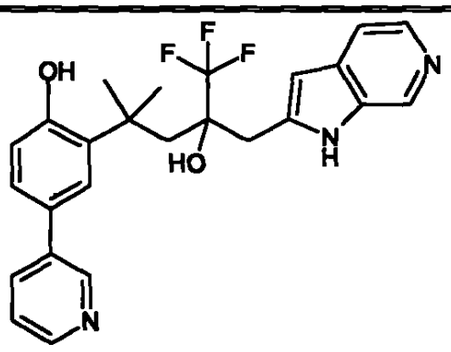
IA	
A	**B**
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-piridin-2-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-piridin-3-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-piridin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1-{2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il}-2-metilpropan-1-ona	
1-{2-[4-(5-Fluor-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il}-2-metilpropan-1-ona	

IA	
A	**B**
1-[2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il}-2-hidroxietanona	
5-(5-Fluor-2-metoxifenil)-5-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)-3-trifluormetilhexan-3-ol	
2-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metoxifenil)-4-metilpentan-2-ol	
2-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluor-4-(4-fluor-2-metoxifenil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(3-fluorfenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	

IA	
A	**B**
1,1,1-Trifluor-4-(4-fluor-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
2-[3-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-fluorfenol	
2-[3-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-5-fluorfenol	
5-Fluor-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]fenol	

IA	
A	B
4-(5-Bromo-2-metoxifenil)-1,1,1-trifluor-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
4-Bromo-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]fenol	
1,1,1-Trifluor-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
4-(3-[1,3]Dioxan-2-ilfenil)-1,1,1-trifluor-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	

IA	
A	B
1,1,1-Trifluor-4-(4-metoxibifenil-3-il)-4-metil-2-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(2-metoxi-5-tiofen-3-ilfenil)-4-metil-2-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	

IA	
A	B
3-[4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]bifenil-4-ol	
4-Tiofen-3-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]fenol	
4-Tiofen-3-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]fenol	

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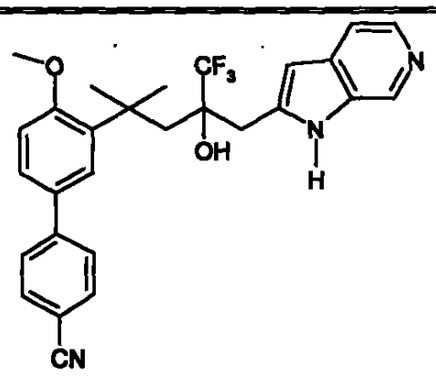
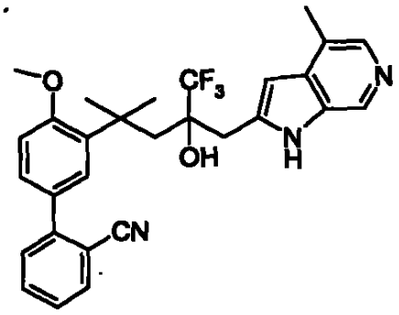
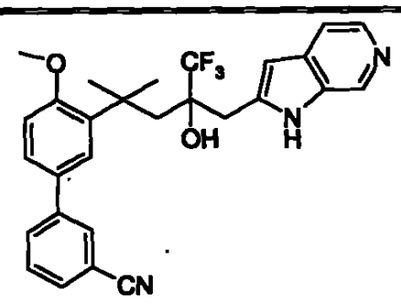
IA	
A	**B**
4-Tiofen-3-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]fenol	
4'-Metoxi-3'-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]bifenil-2-carbonitrilo	
4'-Metoxi-3'-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]bifenil-3-carbonitrilo	

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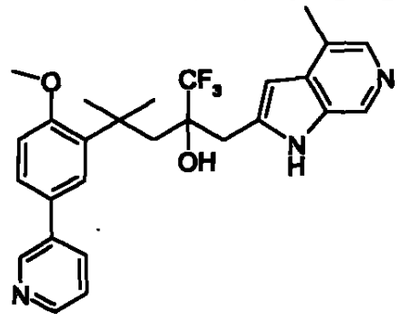
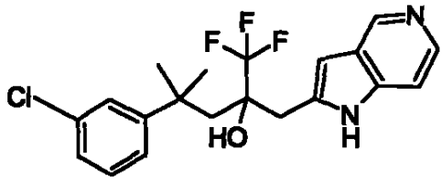
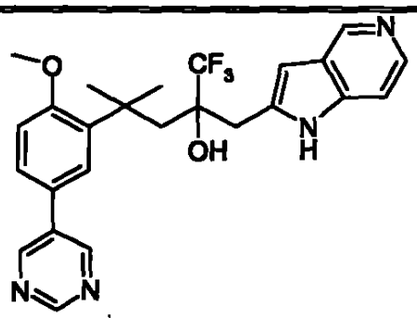
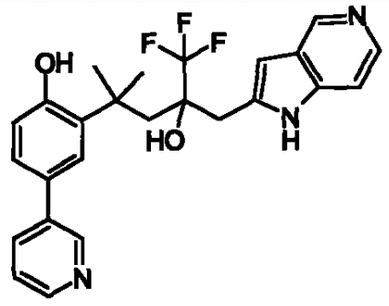
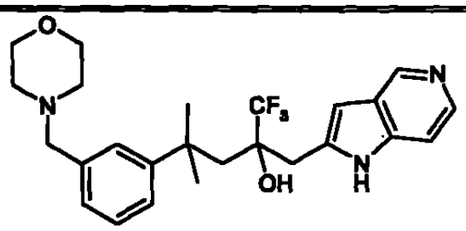
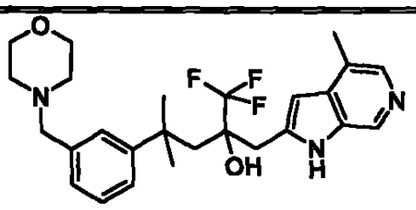
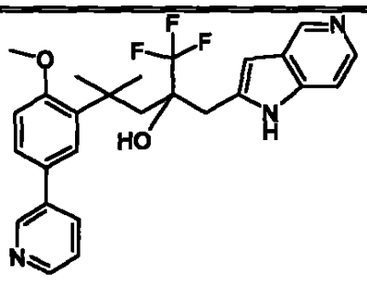
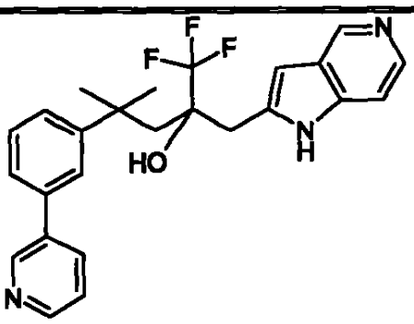
IA	
A	B
1,1,1-Trifluor-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
4-(3-Clorofenil)-1,1,1-trifluor-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	
4-Piridin-3-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]fenol	

IA	
A	B
1,1,1-Trifluor-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-(3-morfolin-4-ilmetilfenil)pentan-2-ol	
1,1,1-Trifluor-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-(3-piridin-3-ilfenil)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	

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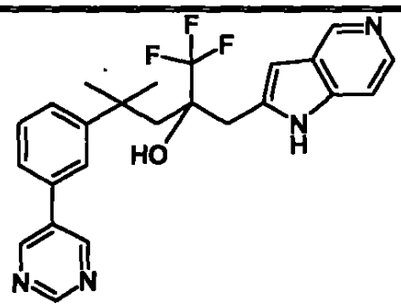
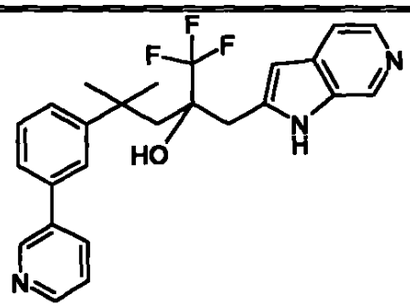
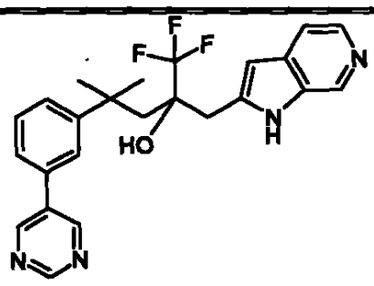
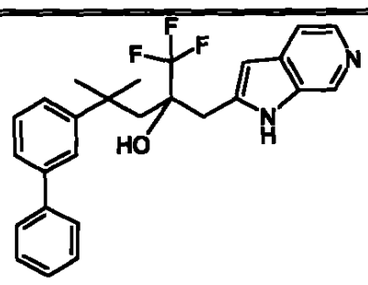
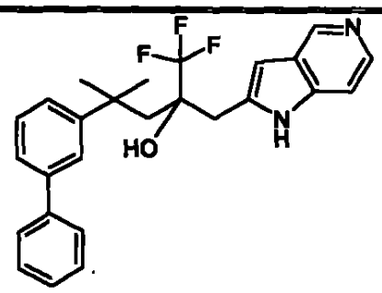
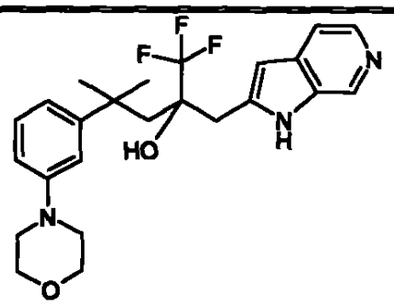
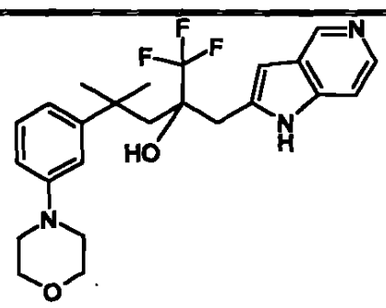
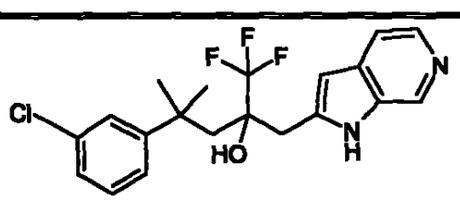
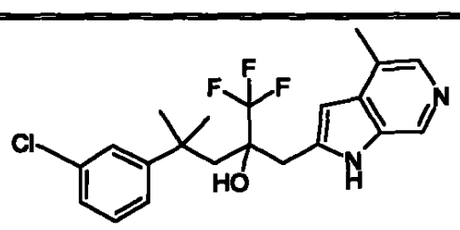
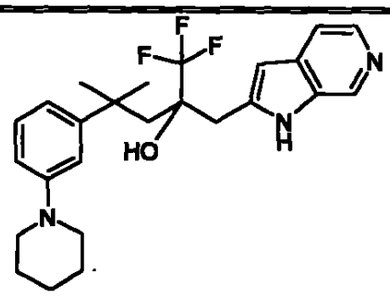
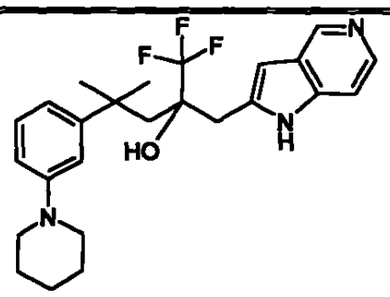
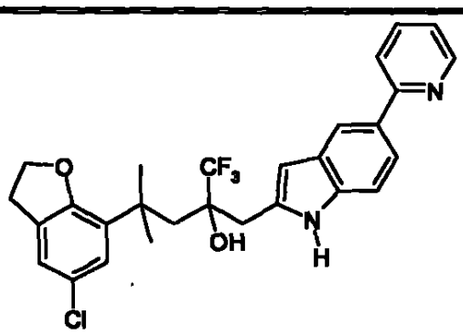
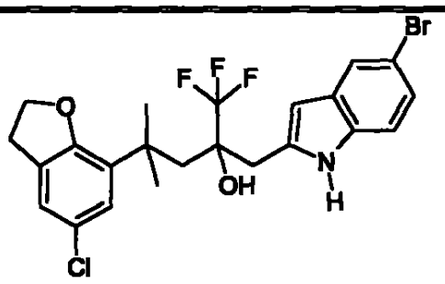
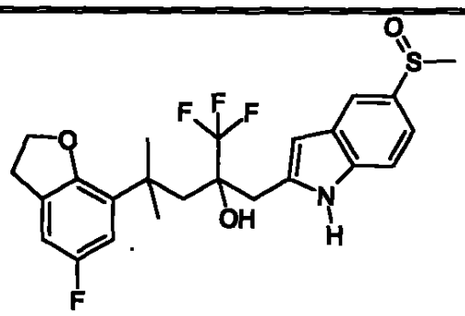
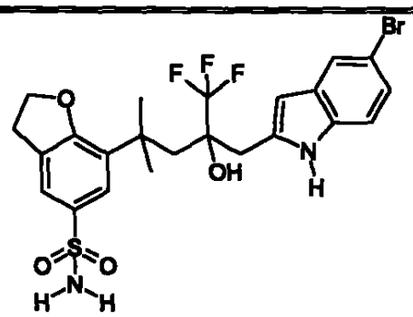
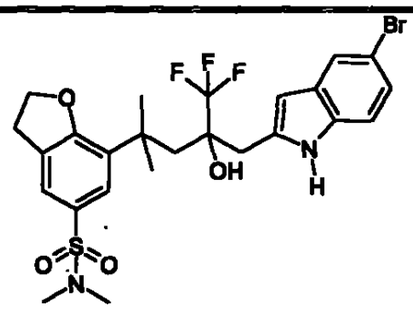
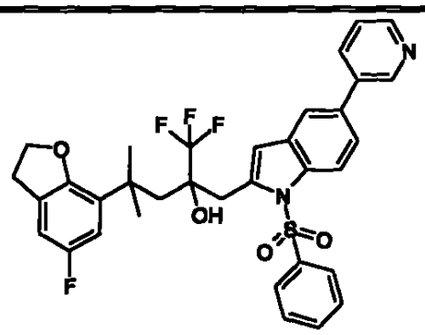
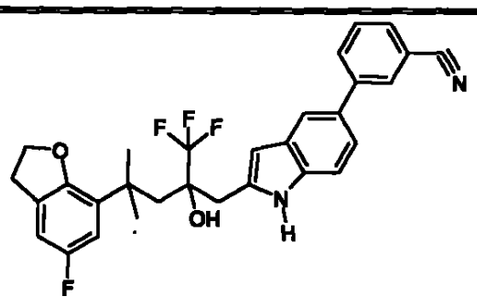
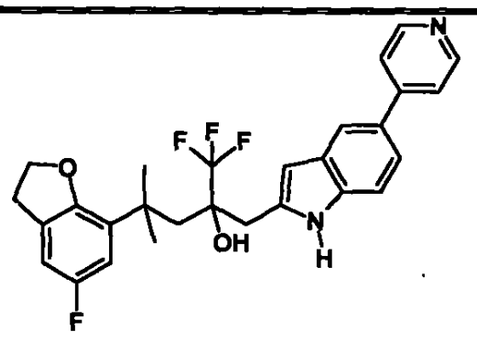
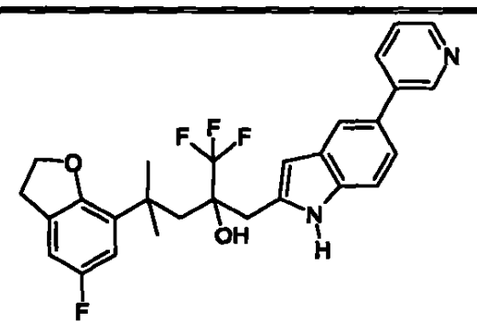
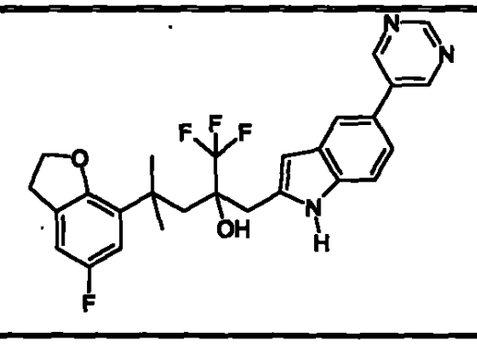
IA	
A	B
1,1,1-Trifluor-4-metil-4-(3-pirimidin-5-ilfenil)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-(3-piridin-3-ilfenil)-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-(3-pirimidin-5-ilfenil)-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
4-Bifenil-3-il-1,1,1-trifluor-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	

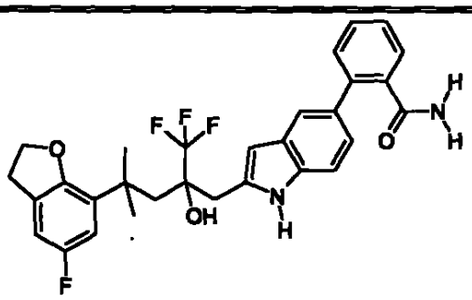
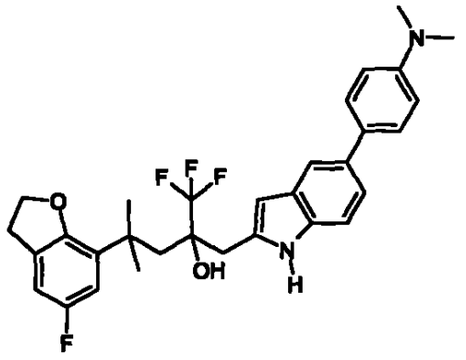
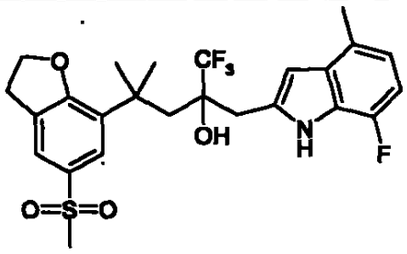
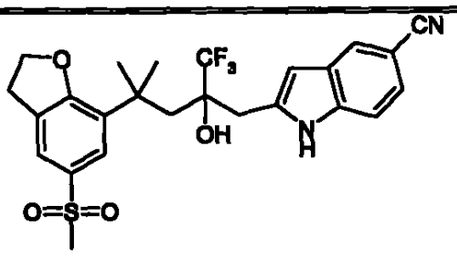
IA	
A	B
4-Bifenil-3-il-1,1,1-trifluor-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-(3-morfolin-4-ilfenil)-2-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-(3-morfolin-4-ilfenil)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	
4-(3-Clorofenil)-1,1,1-trifluor-4-metil-2-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
4-(3-Clorofenil)-1,1,1-trifluor-4-metil-2-(4-metil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	

IA	
A	B
1,1,1-Trifluor-4-metil-4-(3-piperidin-1-ilfenil)-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-(3-piperidin-1-ilfenil)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(5-piridin-2-il-1*H*-indol-2-ilmetil)pentan-2-ol	
2-(5-Bromo-1*H*-indol-2-ilmetil)-4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metilpentan-2-ol	

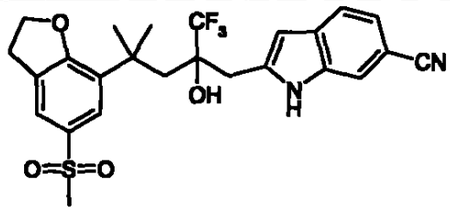
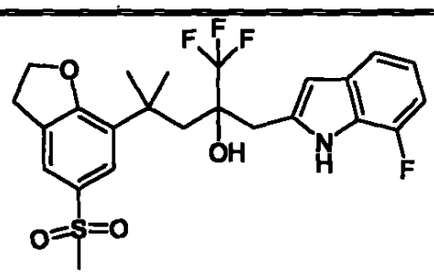
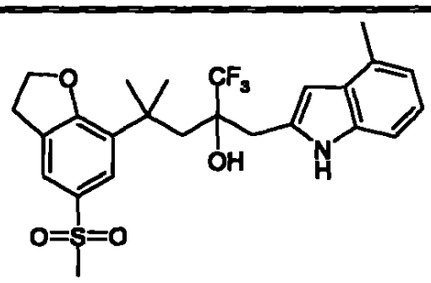
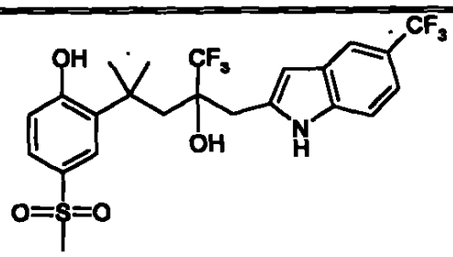
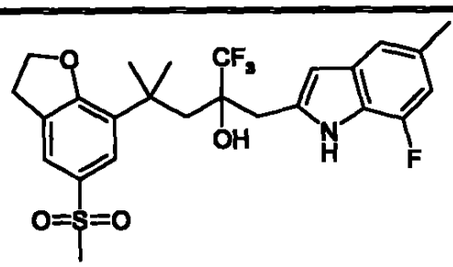
IA	
A	B
1,1,1-Trifluor-4-(5-fluor-2,3-dihidrobenzofuran-7-il)-2-(5-metansulfinil-1*H*-indol-2-ilmetil)-4-metilpentan-2-ol	
amida del ácido 7-[3-(5-Bromo-1*H*-indol-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-2,3-dihidrobenzofuran-5-sulfónico	
dimetilamida del ácido 7-[3-(5-Bromo-1*H*-indol-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-2,3-dihidrobenzofuran-5-sulfónico	
2-(1-Benzenesulfonil-5-piridin-3-il-1*H*-indol-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol	

812

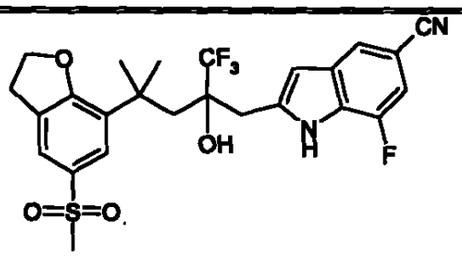
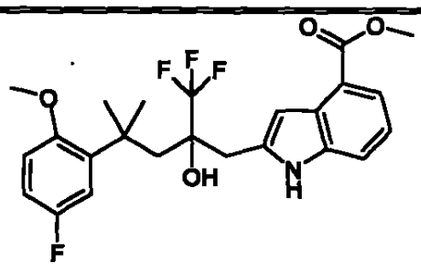
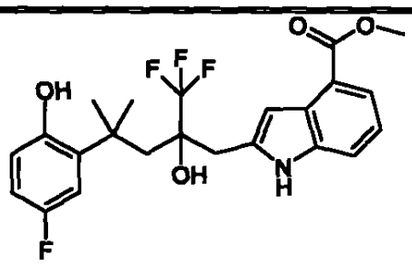
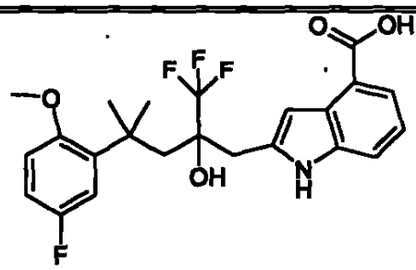
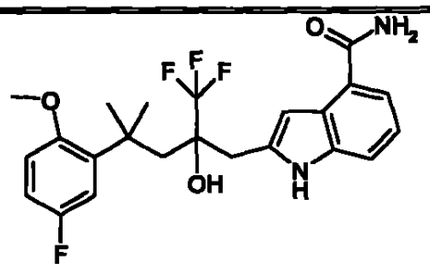
IA	
A	B
3-{2-[4-(5-Fluor-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-il}benzonitrilo	
1,1,1-Trifluor-4-(5-fluor-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-piridin-4-il-1*H*-indol-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-piridin-3-il-1*H*-indol-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-pirimidin-5-il-1*H*-indol-2-ilmetil)pentan-2-ol	

IA	
A	**B**
2-{2-[4-(5-Fluor-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-5-il}benzamida	
2-[5-(4-Dimetilaminofenil)-1*H*-indol-2-ilmetil]-1,1,1-trifluor-4-(5-fluor-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol	
1,1,1-Trifluor-2-(7-fluor-4-metil-1*H*-indol-2-ilmetil)-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol	
2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carbonitrilo	

814

IA	
A	B
2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluormetilpentil]-1*H*-indol-6-carbonitrilo	
1,1,1-Trifluor-2-(7-fluor-1*H*-indol-2-ilmetil)-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-(4-metil-1*H*-indol-2-ilmetil)pentan-2-ol	
4-Metansulfonil-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-trifluormetil-1*H*-indol-2-ilmetil)butil]fenol	
1,1,1-Trifluor-2-(7-fluor-5-metil-1*H*-indol-2-ilmetil)-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol	

815

IA	
A	B
7-Fluor-2-[2-hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluormetilpentil]-1*H*-indol-5-carbonitrilo	
éster metílico del ácido 2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-4-carboxílico	
éster metílico del ácido 2-[4-(5-Fluor-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-4-carboxílico	
ácido 2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-4-carboxílico	
amida del ácido 2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-4-carboxílico	

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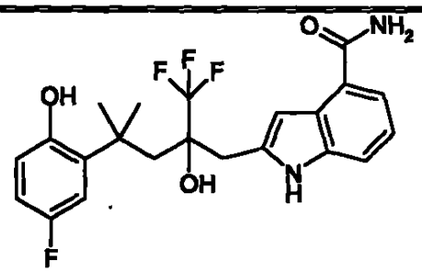
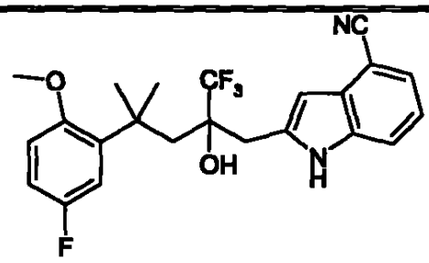
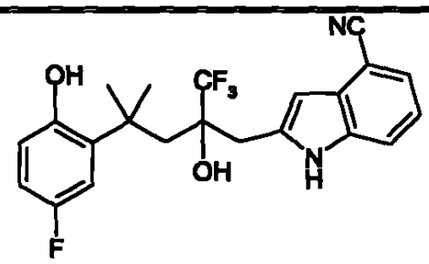
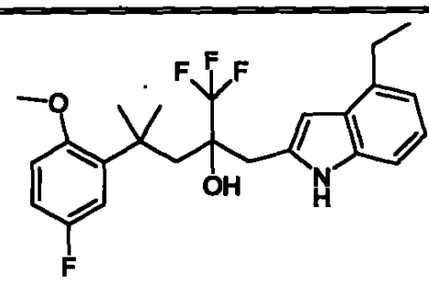
IA	
A	B
amida del ácido 2-[4-(5-Fluor-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-4-carboxílico	
2-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-4-carbonitrilo	
2-[4-(5-Fluor-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-indol-4-carbonitrilo	
2-(4-Etil-1*H*-indol-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metoxifenil)-4-metilpentan-2-ol	

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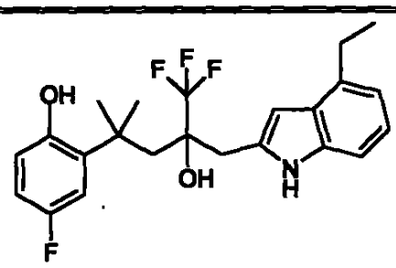
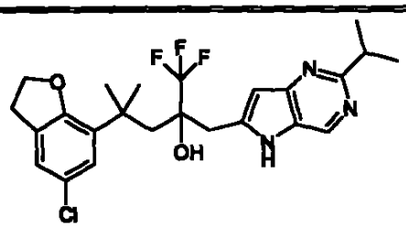
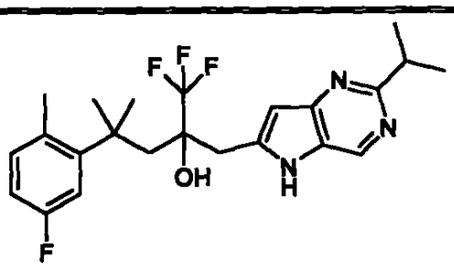
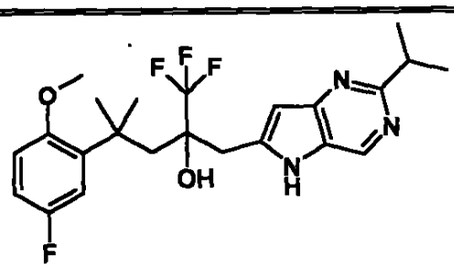
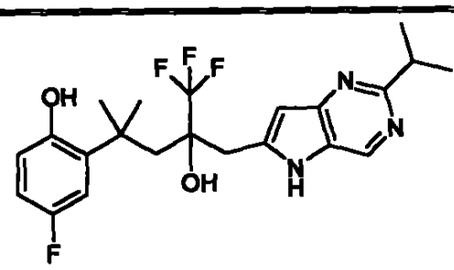
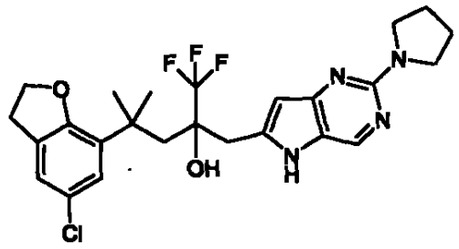
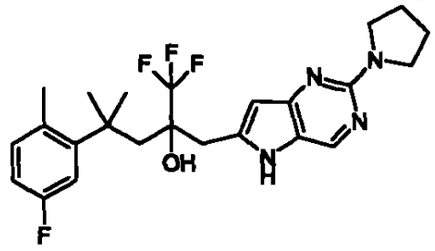
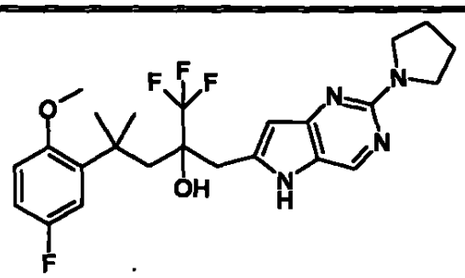
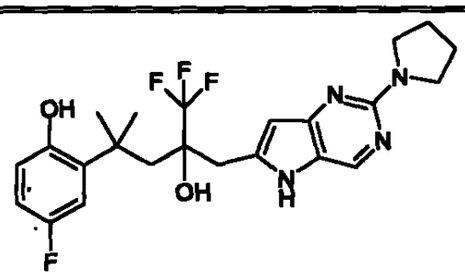
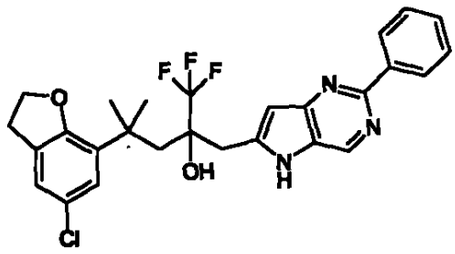
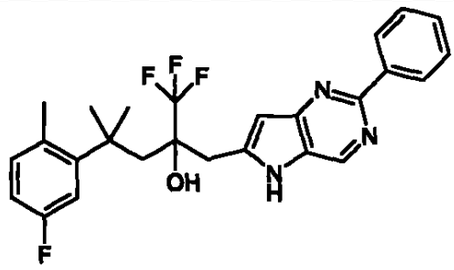
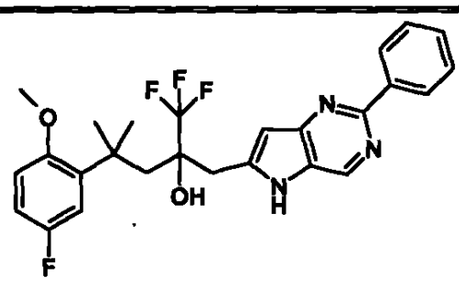
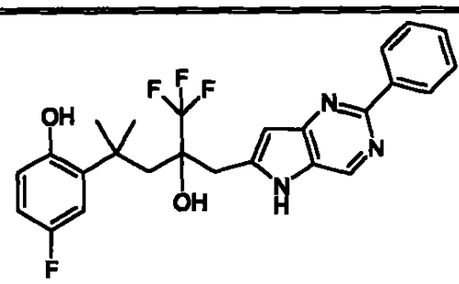
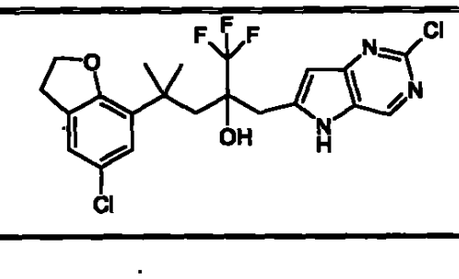
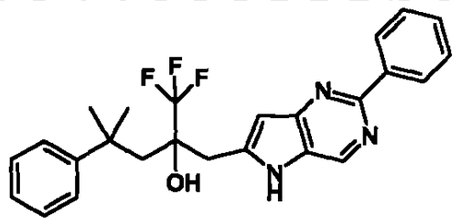
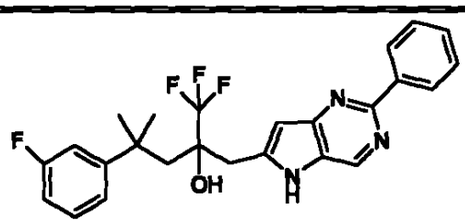
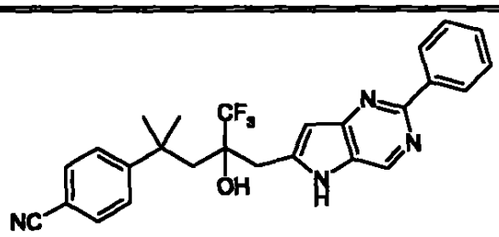
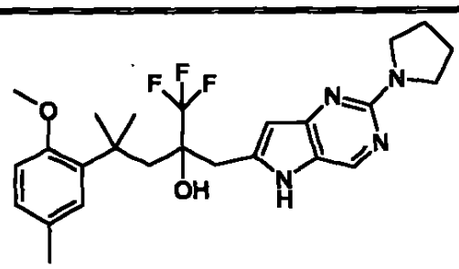
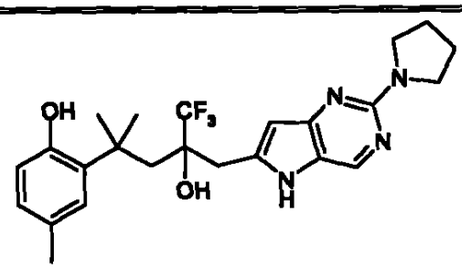
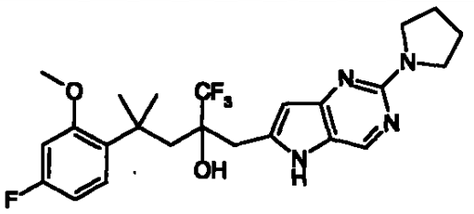
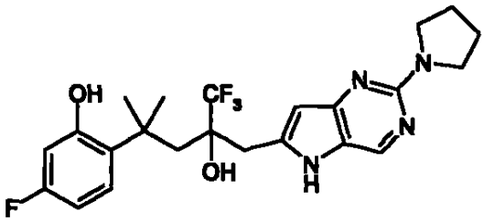
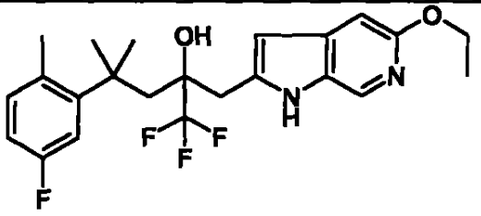
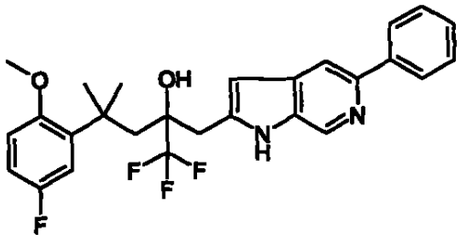
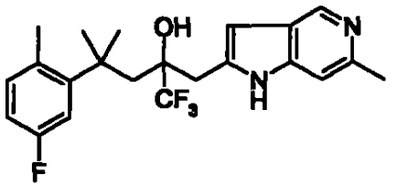
IA	
A	**B**
2-[3-(4-Etil-1*H*-indol-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-fluorfenol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-2-(2-isopropil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-2-(2-isopropil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-2-(2-isopropil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)-4-metilpentan-2-ol	
4-Fluor-2-[4,4,4-trifluor-3-hidroxi-3-(2-isopropil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)-1,1-dimetilbutil]fenol	

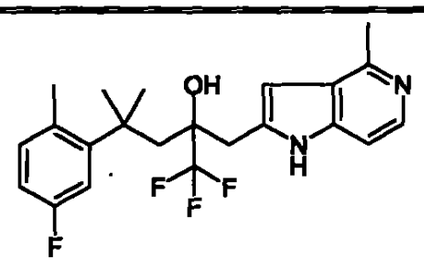
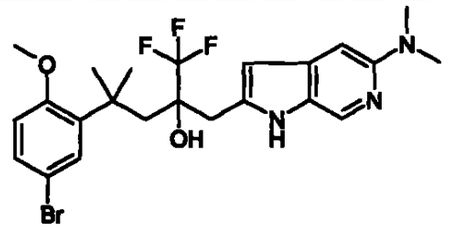
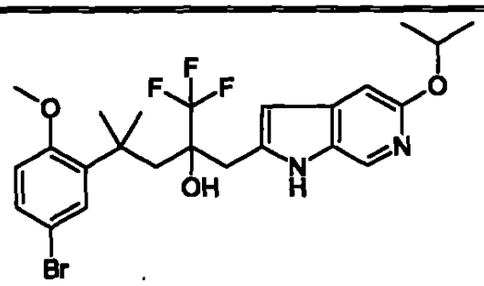
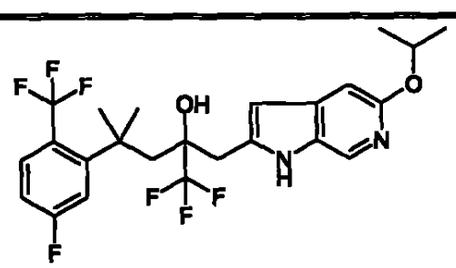
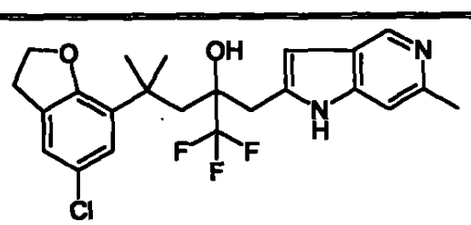
IA	
A	**B**
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol	
4-Fluor-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)butil]fenol	

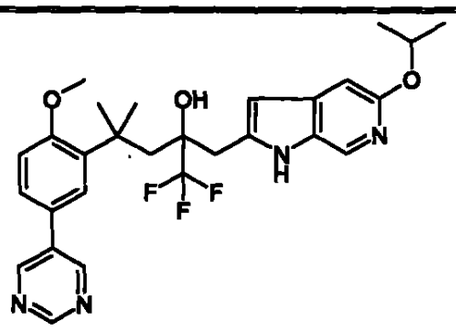
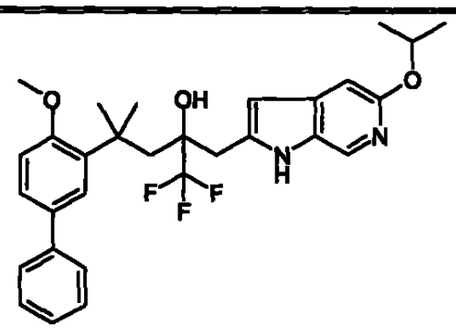
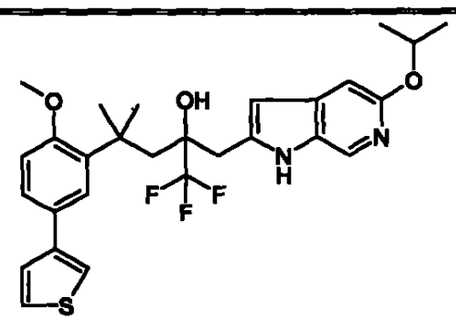
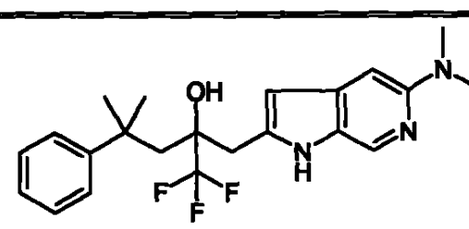
IA	
A	B
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(2-fenil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(2-fenil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(2-fenil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol	
4-Fluor-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(2-fenil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)butil]fenol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(2-cloro-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)-1,1,1-trifluor-4-metilpentan-2-ol	

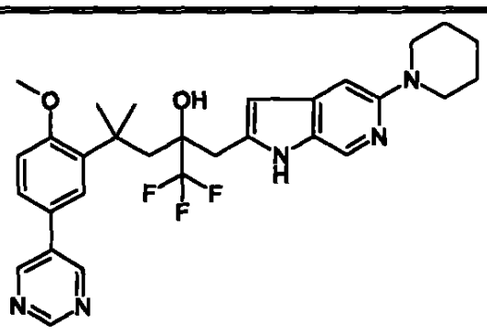
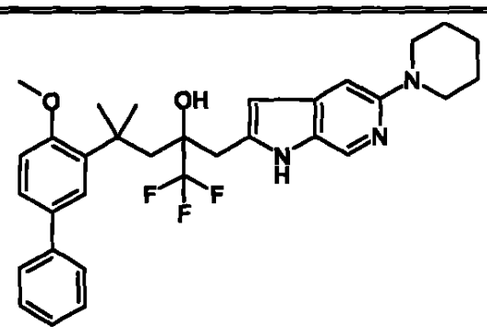
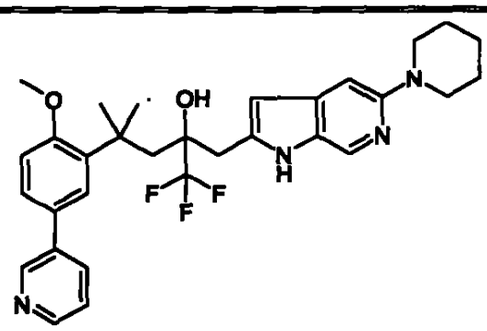
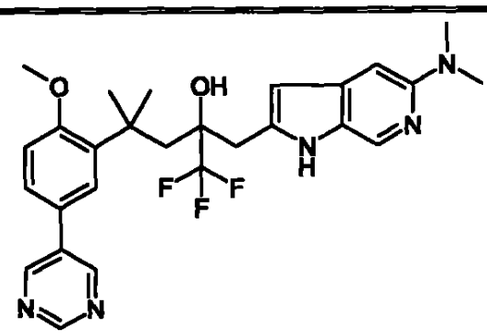
820

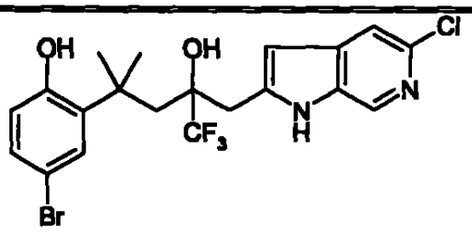
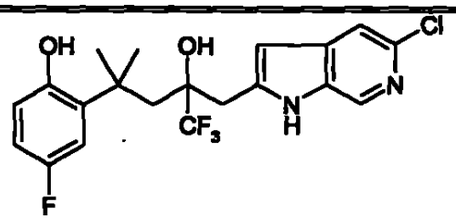
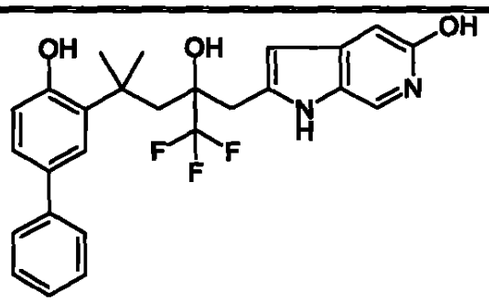
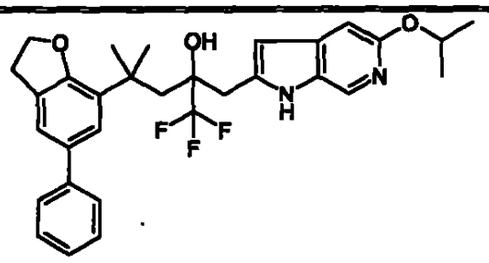
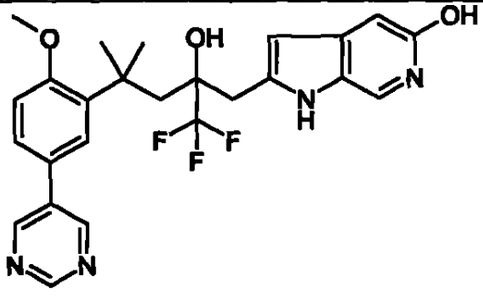
IA	
A	B
1,1,1-Trifluor-4-metil-4-fenil-2-(2-fenil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(3-fluorfenil)-4-metil-2-(2-fenil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol	
4-[4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-(2-fenil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)butil]benzonitrilo	
1,1,1-Trifluor-4-(2-metoxi-5-metilfenil)-4-metil-2-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(2-metoxi-5-metilfenil)-4-metil-2-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol	

IA	
A	B
1,1,1-Trifluor-4-(4-fluor-2-metoxifenil)-4-metil-2-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol	
5-Fluor-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)butil]fenol	
2-(5-Etoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metilfenil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(5-fenil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(6-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol	

IA	
A	B
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol	
4-(5-Bromo-2-metoxifenil)-2-(5-dimetilamino-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluor-4-metilpentan-2-ol	
4-(5-Bromo-2-metoxifenil)-1,1,1-trifluor-2-(5-isopropoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-trifluormetilfenil)-2-(5-isopropoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-metilpentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(6-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol	

IA	
A	**B**
1,1,1-Trifluor-2-(5-isopropoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metilpentan-2-ol	
1,1,1-Trifluor-2-(5-isopropoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-(4-metoxibifenil-3-il)-4-metilpentan-2-ol	
1,1,1-Trifluor-2-(5-isopropoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-(2-metoxi-5-tiofan-3-ilfenil)-4-metilpentan-2-ol	
2-(5-Dimetilamino-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluor-4-metil-4-fenilpentan-2-ol	

IA	
A	**B**
1,1,1-Trifluor-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(4-metoxibifenil-3-il)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
2-(5-Dimetilamino-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluor-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metilpentan-2-ol	

IA	
A	**B**
4-Bromo-2-[3-(5-cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]fenol	
2-[3-(5-Cloro-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-fluorfenol	
2-[2-Hidroxi-4-(4-hidroxibifenil-3-il)-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[2,3-c]piridin-5-ol	
1,1,1-Trifluor-2-(5-isopropoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-metil-4-(5-fenil-2,3-dihidrobenzofuran-7-il)pentan-2-ol	
2-[2-Hidroxi-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[2,3-c]piridin-5-ol	

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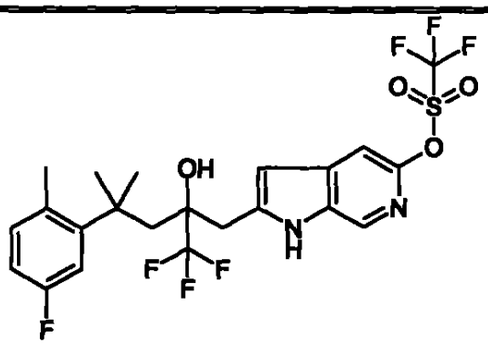
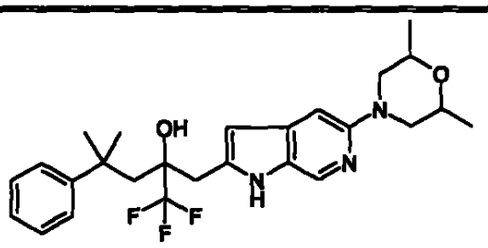
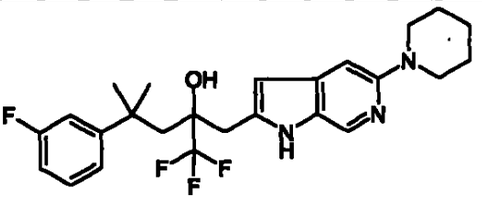
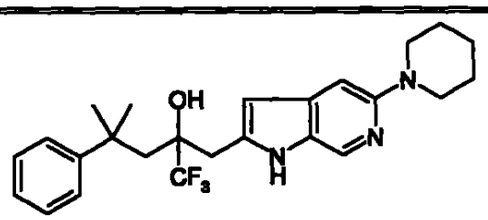
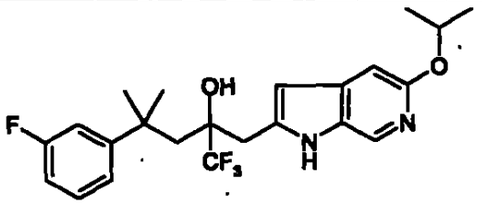
IA	
A	B
éster 2-[4-(5-fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[2,3-c]piridin-5-ílico del ácido trifluormetansulfónico	
2-[5-(2,6-Dimetilmorfolin-4-il)-1*H*-pirrolo[2,3-c]piridin-2-ilmetil]-1,1,1-trifluor-4-metil-4-fenilpentan-2-ol	
1,1,1-Trifluor-4-(3-fluorfenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-fenil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(3-fluorfenil)-2-(5-isopropoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-metilpentan-2-ol	

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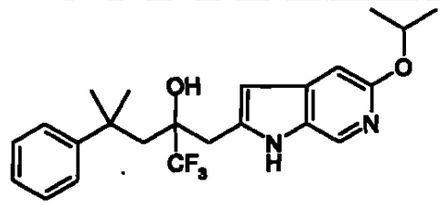
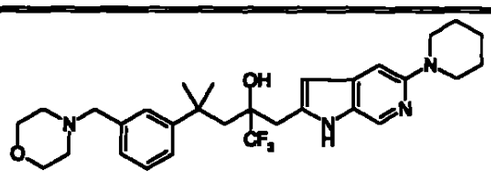
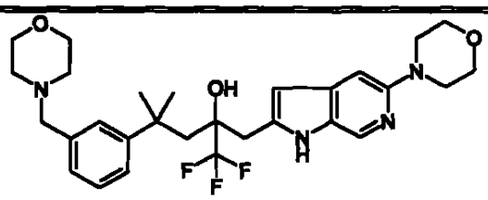
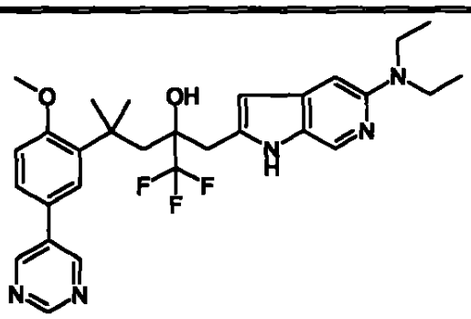
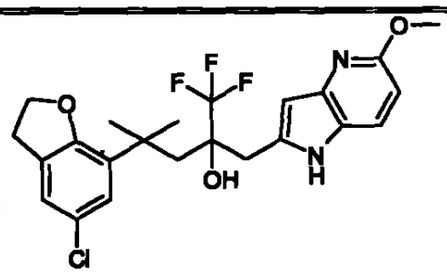
IA	
A	**B**
1,1,1-Trifluor-2-(5-isopropoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-metil-4-fenilpentan-2-ol	
1,1,1-Trifluor-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
2-(5-Dietilamino-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluor-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metilpentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-2-(5-metoxi-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-metilpentan-2-ol	

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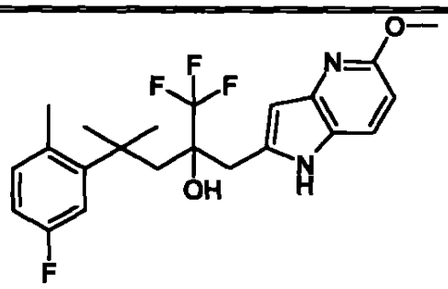
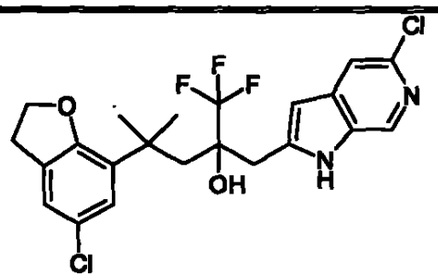
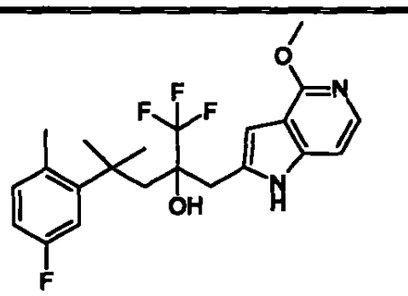
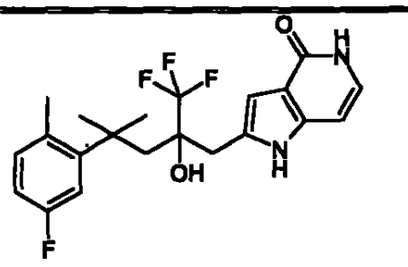
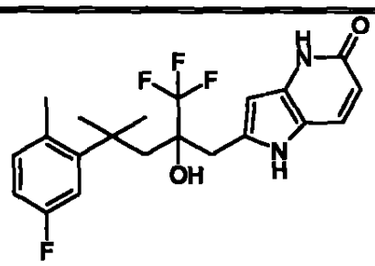
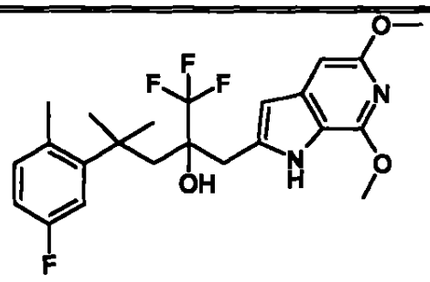
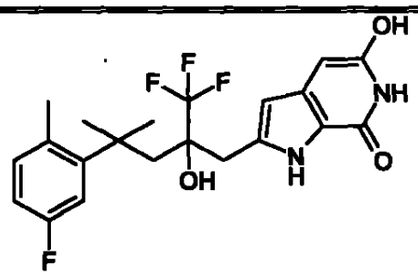
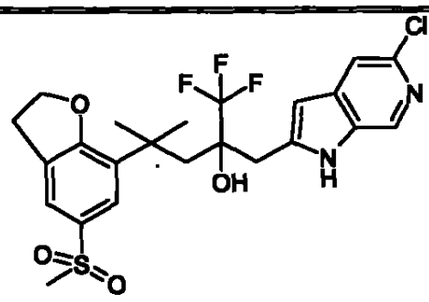
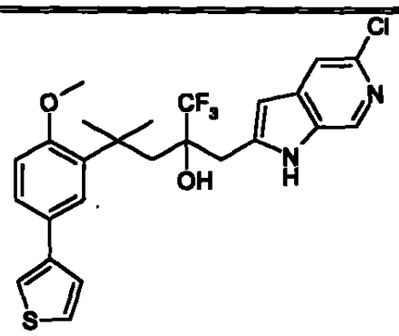
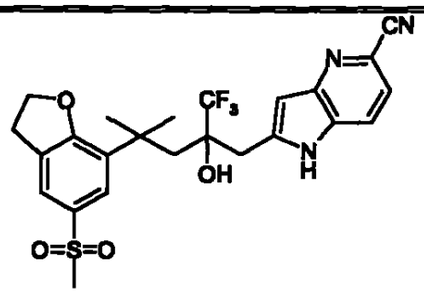
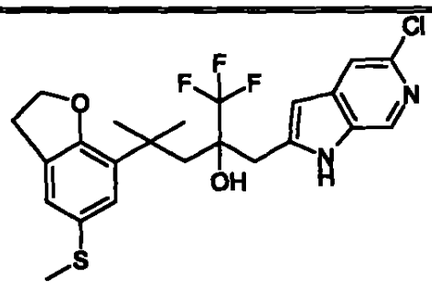
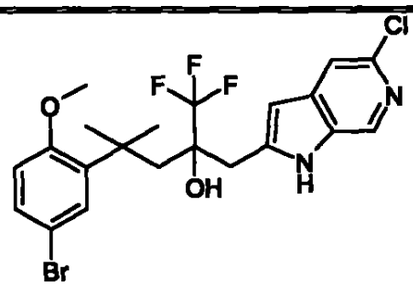
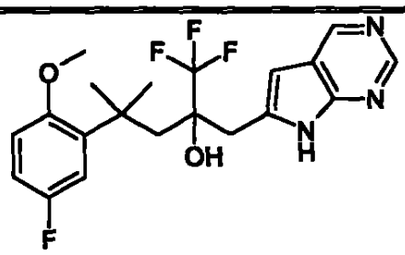
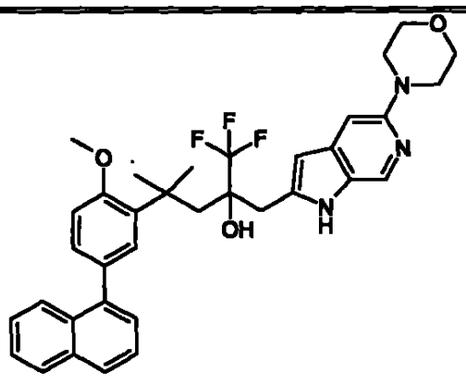
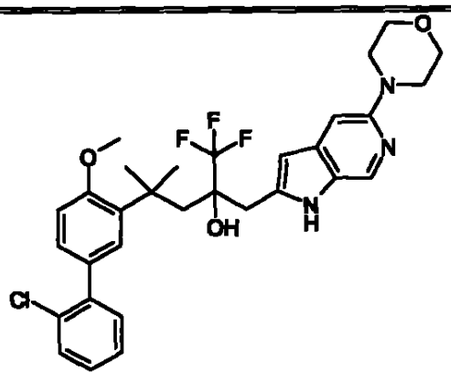
IA	
A	B
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-2-(5-metoxi-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-metilpentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(5-cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluor-4-metilpentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-2-(4-metoxi-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol	
2-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1,5-dihidropirrolo[3,2-*c*]piridin-4-ona	

IA	
A	B
2-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1,4-dihidropirrolo[3,2-*b*]piridin-5-ona	
2-(5,7-Dimetoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metilfenil)-4-metilpentan-2-ol	
2-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-5-hidroxi-1,6-dihidropirrolo[2,3-*c*]piridin-7-ona	
2-(5-Cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol	

IA	
A	B
2-(5-Cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluor-4-(2-metoxi-5-tiofen-3-ilfenil)-4-metilpentan-2-ol	
2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluormetilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-carbonitrilo	
2-(5-Cloro-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluor-4-metil-4-(5-metilsulfanil-2,3-dihidrobenzofuran-7-il)pentan-2-ol	
4-(5-Bromo-2-metoxifenil)-2-(5-cloro-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluor-4-metilpentan-2-ol	

IA	
A	B
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(2-metoxi-5-naftalen-1-ilfenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
4-(2'-Cloro-4-metoxibifenil-3-il)-1,1,1-trifluor-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	

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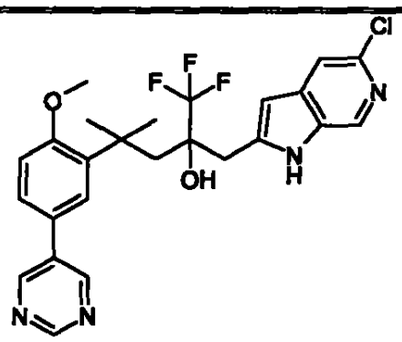
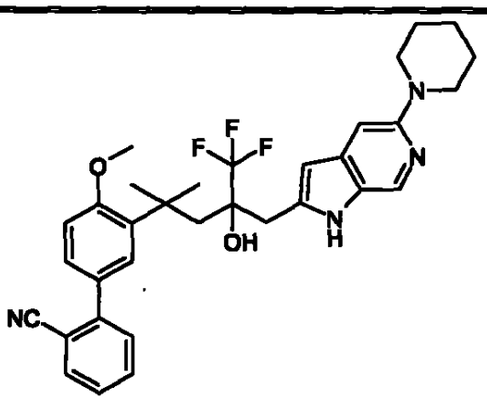
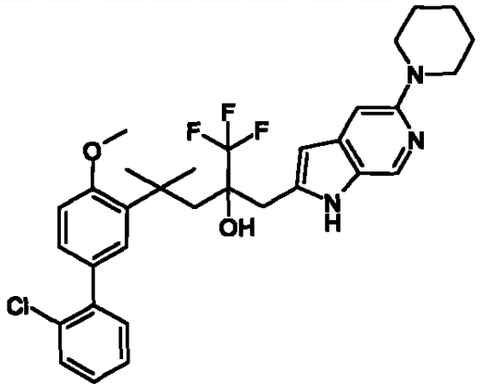
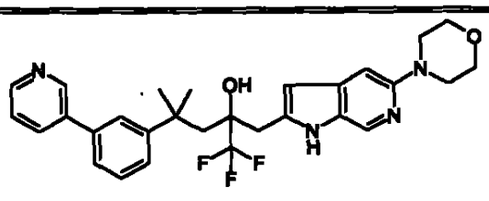
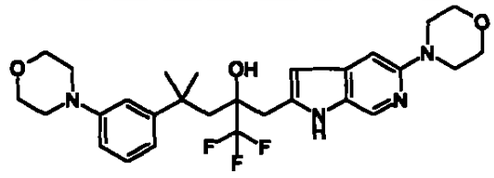
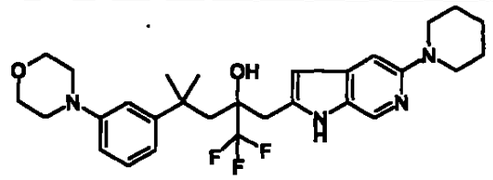
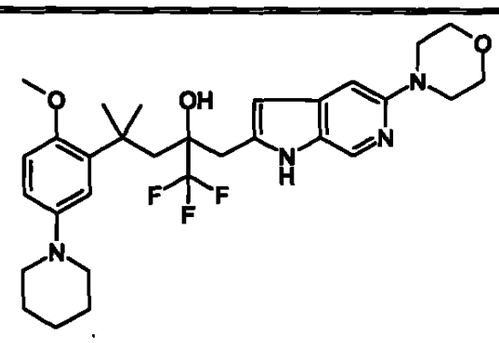
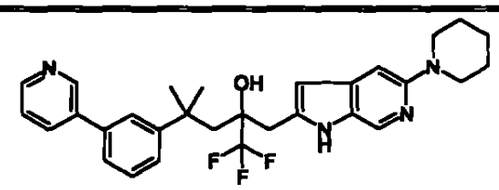
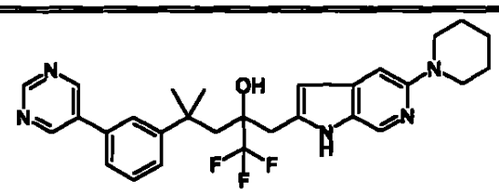
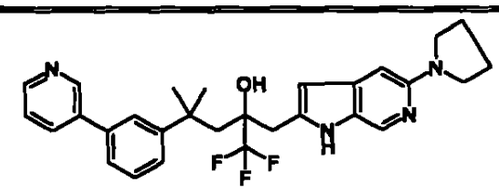
IA	
A	**B**
2-(5-Cloro-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluor-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metilpentan-2-ol	
4'-Metoxi-3'-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]bifenil-2-carbonitrilo	
4-(2'-Cloro-4-metoxibifenil-3-il)-1,1,1-trifluor-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-(3-piridin-3-ilfenil)pentan-2-ol	

IA	
A	B
1,1,1-Trifluor-4-metil-4-(3-morfolin-4-ilfenil)-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-(3-morfolin-4-ilfenil)-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(2-metoxi-5-piperidin-1-ilfenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-(3-piridin-3-ilfenil)pentan-2-ol	
1,1,1-Trifluor-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-(3-pirimidin-5-ilfenil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-(3-piridin-3-ilfenil)-2-(5-pirrolidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	

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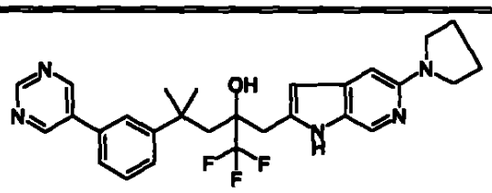
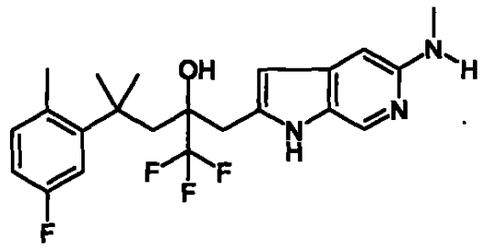
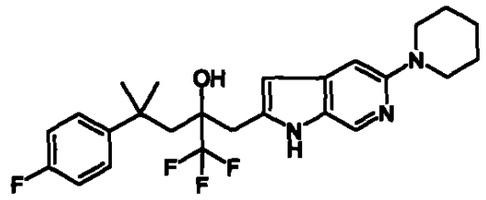
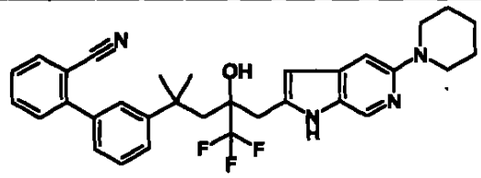
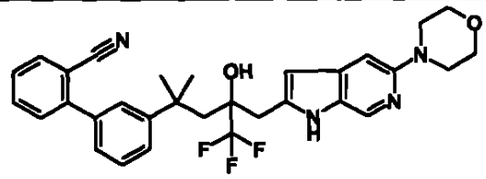
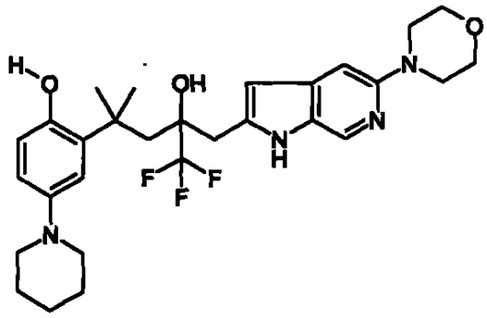
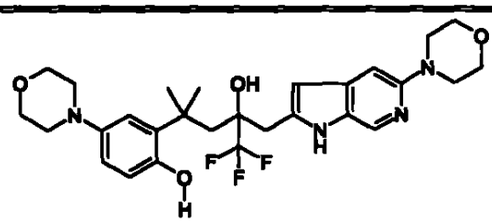
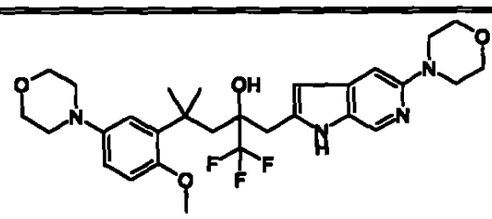
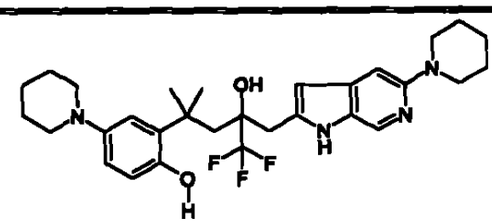
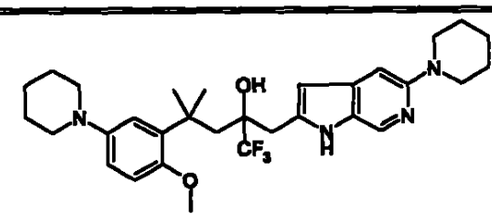
IA	
A	B
1,1,1-Trifluor-4-metil-4-(3-pirimidin-5-ilfenil)-2-(5-pirrolidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-metilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(4-fluorfenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
3'-[4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]bifenil-2-carbonitrilo	
3'-[4,4,4-Trifluor-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]bifenil-2-carbonitrilo	

835

IA	
A	B
4-Piperidin-1-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]fenol	
4-Morfolin-4-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]fenol	
1,1,1-Trifluor-4-(2-metoxi-5-morfolin-4-ilfenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
4-Piperidin-1-il-2-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]fenol	
1,1,1-Trifluor-4-(2-metoxi-5-piperidin-1-ilfenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	

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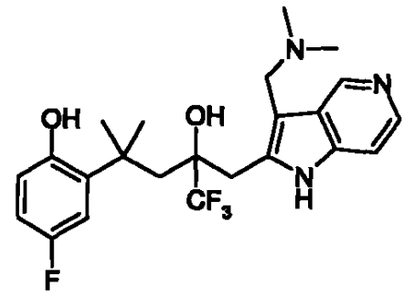
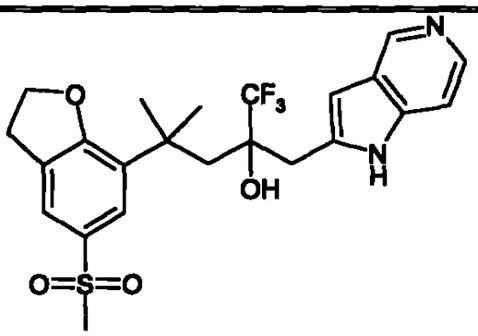
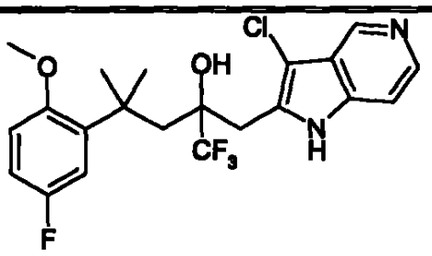
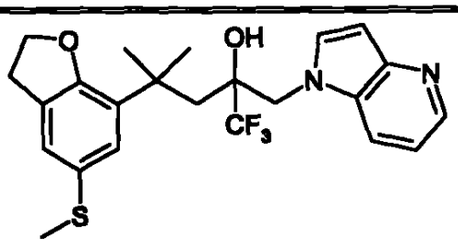
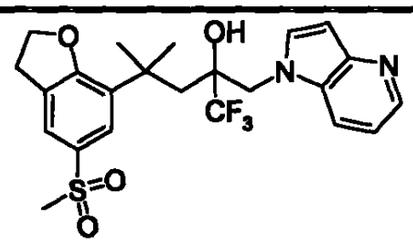
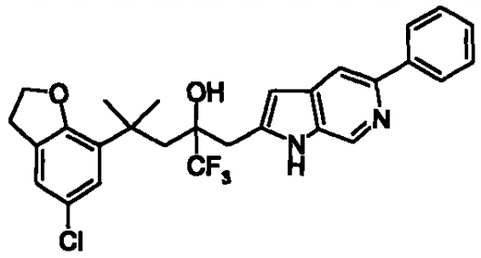
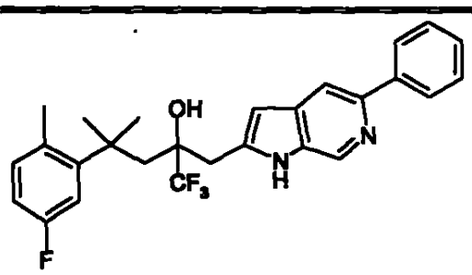
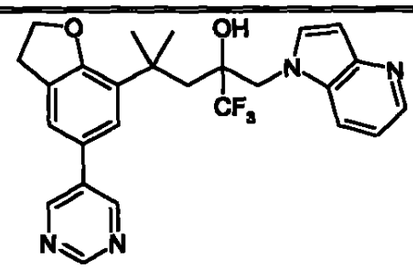
IA	
A	**B**
2-[3-(3-Dimetilaminometil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)-4,4,4-trifluor-3-hidroxi-1,1-dimetilbutil]-4-fluorfenol	
1,1,1-Trifluor-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol	
2-(3-Cloro-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)-1,1,1-trifluor-4-(5-fluor-2-metoxifenil)-4-metilpentan-2-ol	
1,1,1-Trifluor-4-metil-4-(5-metilsulfanil-2,3-dihidrobenzofuran-7-il)-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol	

IA	
A	**B**
1,1,1-Trifluor-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluor-4-metil-2-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-(5-fluor-2-metilfenil)-4-metil-2-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1,1,1-Trifluor-4-metil-4-(5-pirimidin-5-il-2,3-dihidrobenzofuran-7-il)-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol	

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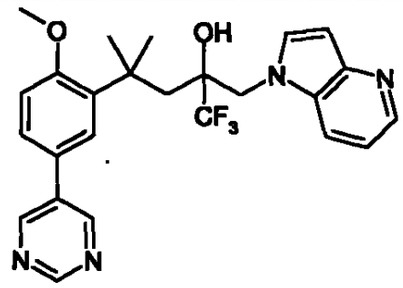
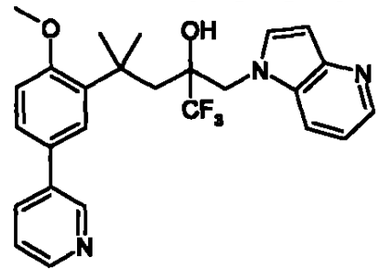
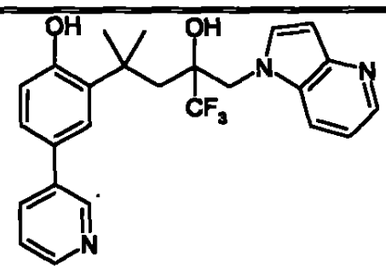
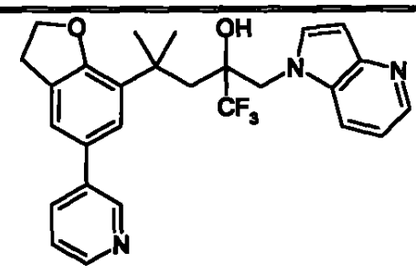
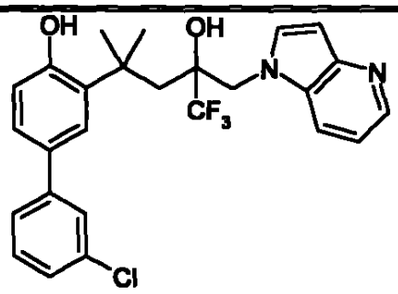
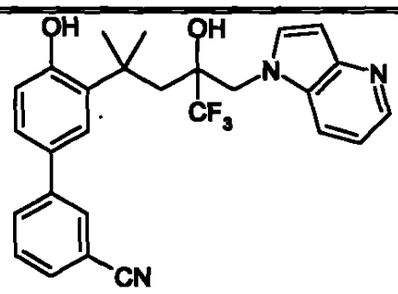
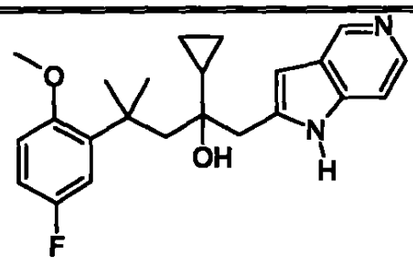
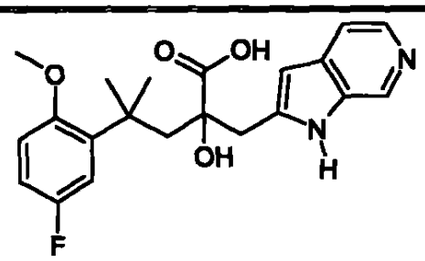
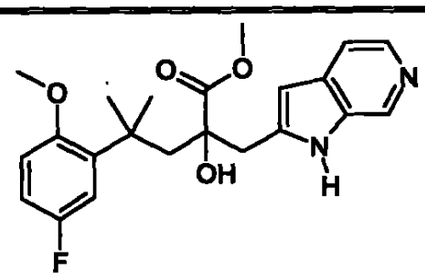
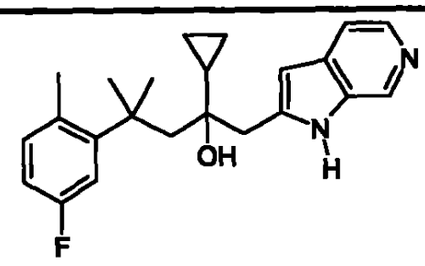
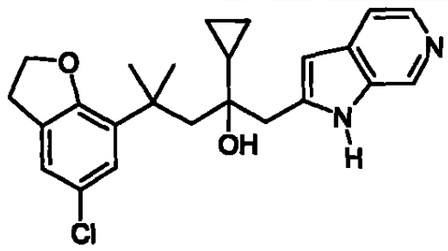
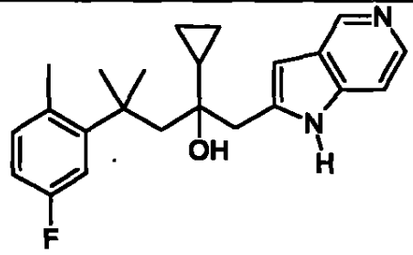
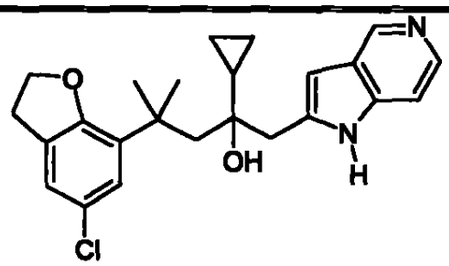
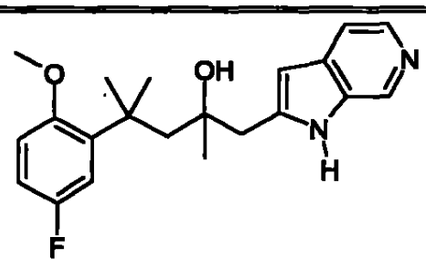
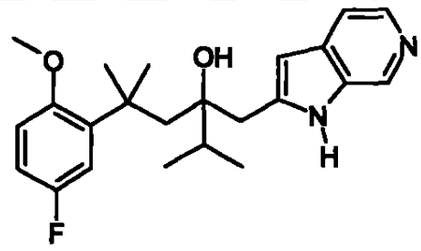
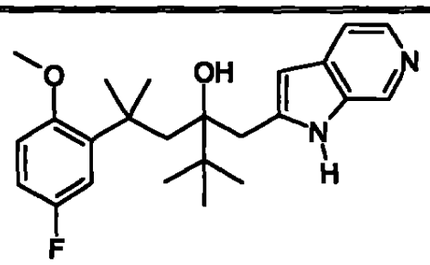
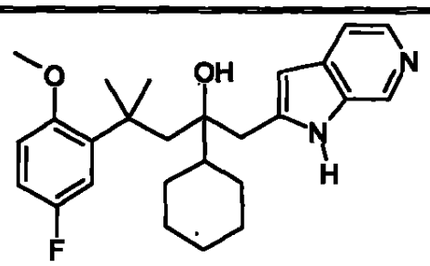
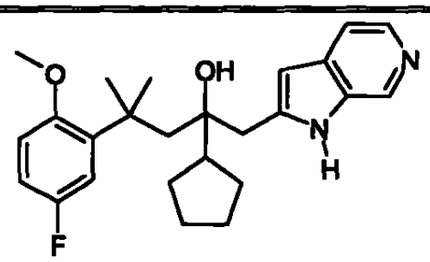
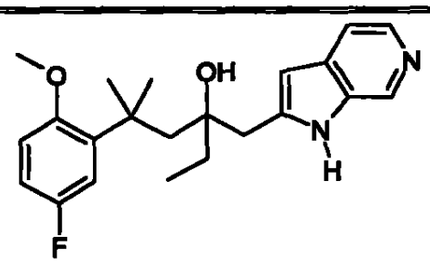
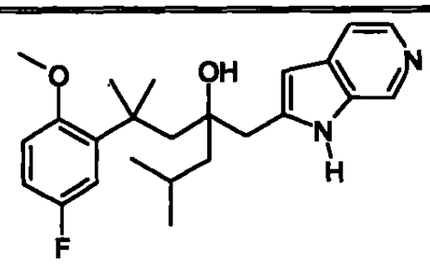
IA	
A	**B**
1,1,1-Trifluor-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol	
1,1,1-Trifluor-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol	
4-Piridin-3-il-2-(4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-pirrolo[3,2-*b*]piridin-1-ilmetilbutil)fenol	
1,1,1-Trifluor-4-metil-4-(5-piridin-3-il-2,3-dihidrobenzofuran-7-il)-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol	

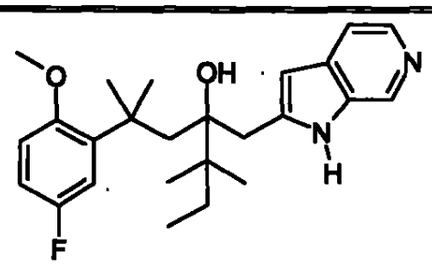
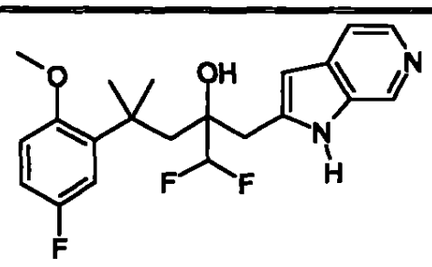
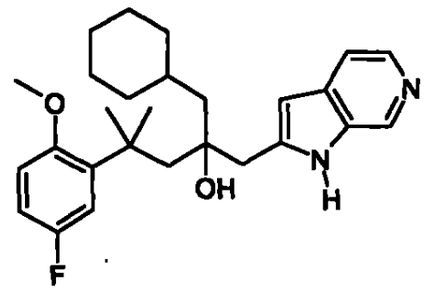
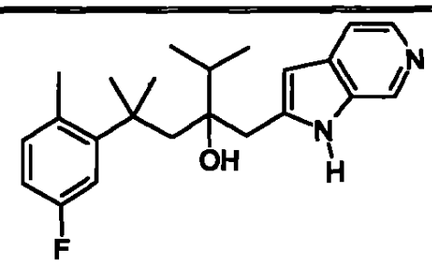
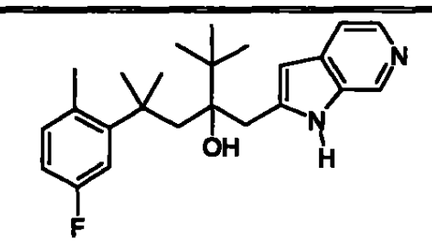
IA	
A	**B**
3'-Cloro-3-(4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-pirrolo[3,2-*b*]piridin-1-ilmetilbutil)bifenil-4-ol	
4'-Hidroxi-3'-(4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-pirrolo[3,2-*b*]piridin-1-ilmetilbutil)bifenil-3-carbonitrilo	
o un tautómero, prodroga, solvato o sal de los mismos.	

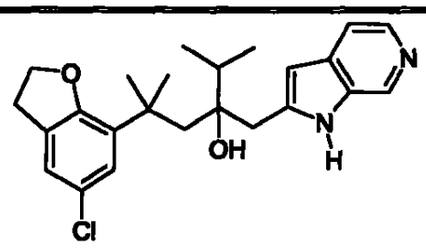
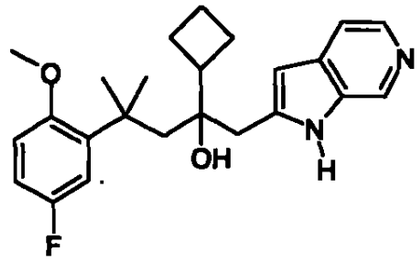
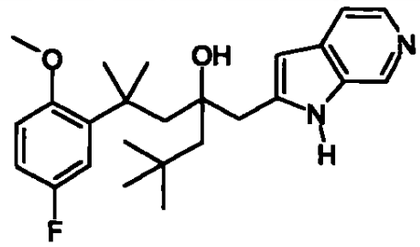
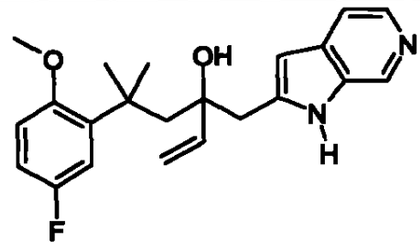
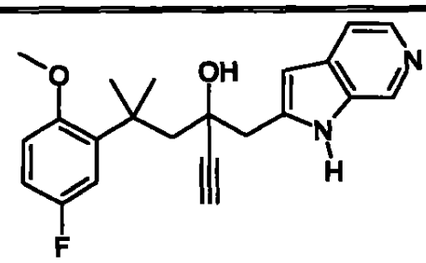
840

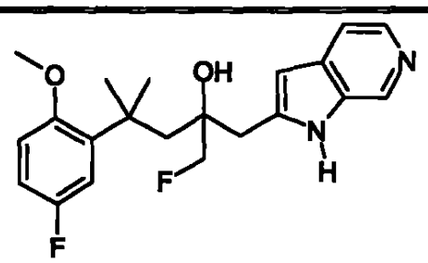
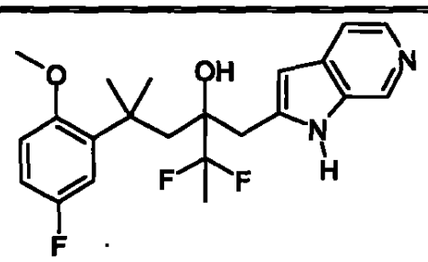
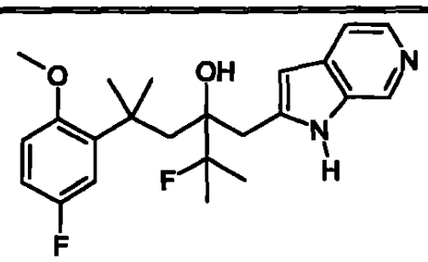
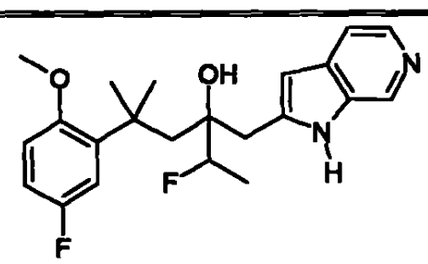
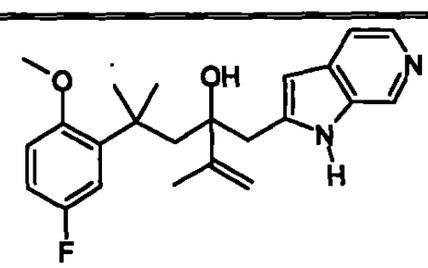
IB	
A	B
2-Ciclopropil-4-(5-fluor-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[3,2-*c*]piridin-2-il)pentan-2-ol	
ácido 4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentanoico	
éster metílico del ácido 4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentanoico	
2-Ciclopropil-4-(5-fluor-2-metilfenil)-4-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol	

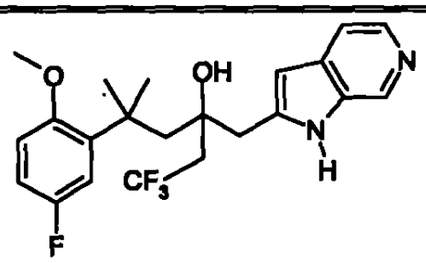
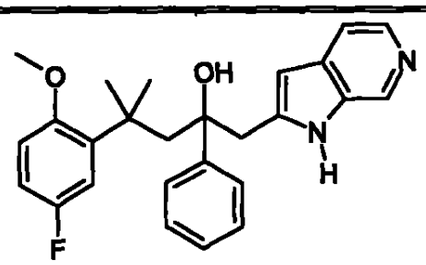
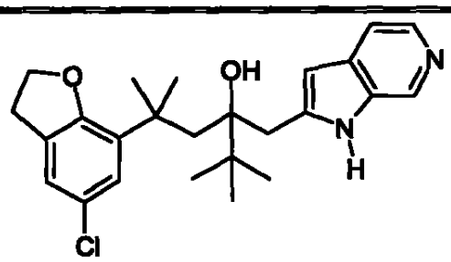
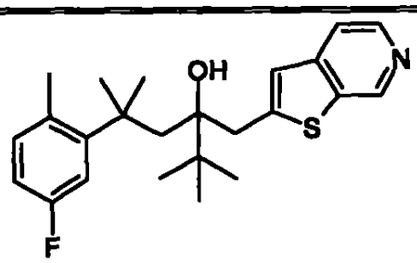
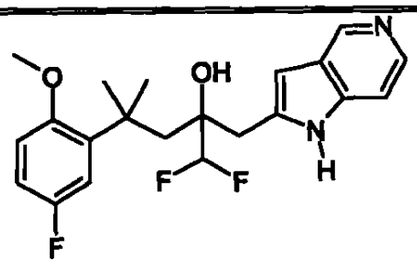
IB	
A	B
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-ciclopropil-4-metil-1-(1*H*-pirrolo[2,3-c]piridin-2-il)pentan-2-ol	
2-Ciclopropil-4-(5-fluor-2-metilfenil)-4-metil-1-(1*H*-pirrolo[3,2-c]piridin-2-il)pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-ciclopropil-4-metil-1-(1*H*-pirrolo[3,2-c]piridin-2-il)pentan-2-ol	
4-(5-Fluor-2-metoxifenil)-2,4-dimetil-1-(1*H*-pirrolo[2,3-c]piridin-2-il)pentan-2-ol	
5-(5-Fluor-2-metoxifenil)-2,5-dimetil-3-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol	

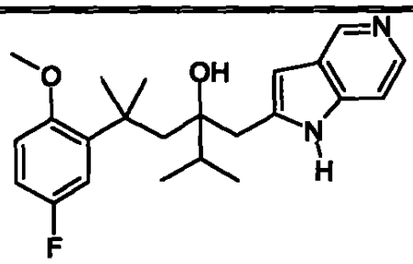
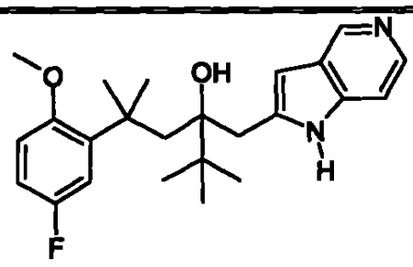
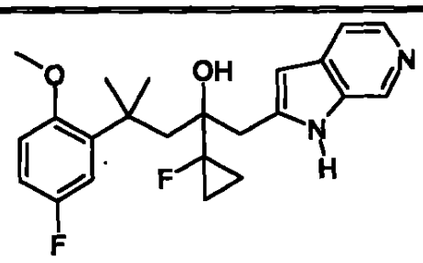
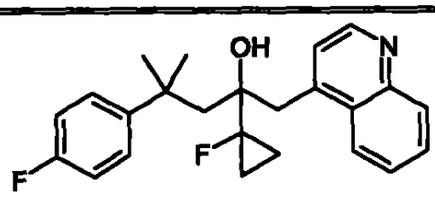
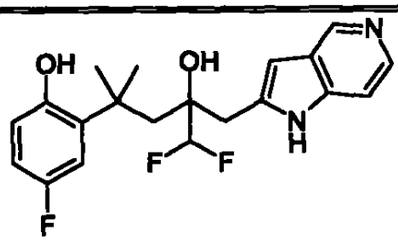
IB	
A	B
5-(5-Fluor-2-metoxifenil)-2,2,5-trimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)heksan-3-ol	
2-Ciklohekil-4-(5-fluor-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol	
2-Ciklopentil-4-(5-fluor-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol	
5-(5-Fluor-2-metoxifenil)-5-metil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)heksan-3-ol	
2-(5-Fluor-2-metoxifenil)-2,6-dimetil-4-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)heptan-4-ol	

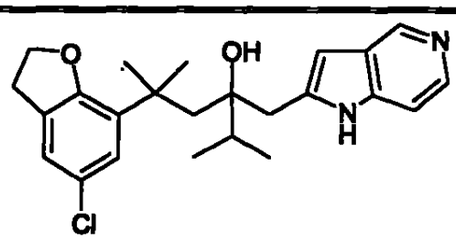
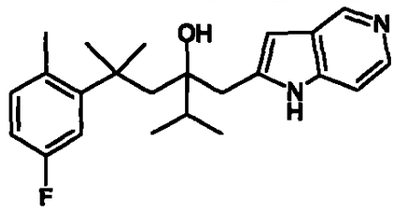
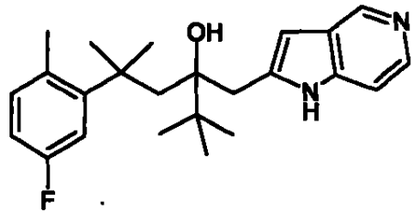
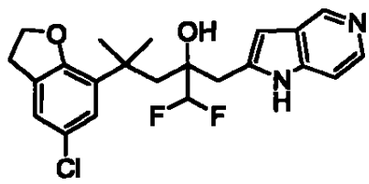
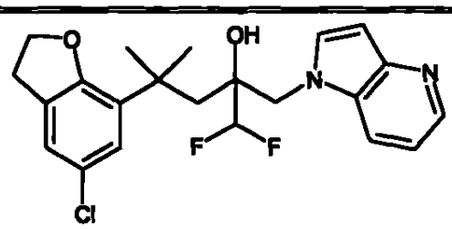
IB	
A	B
2-(5-Fluor-2-metoxifenil)-2,5,5-trimetil-4-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)heptan-4-ol	
1,1-Difluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
1-Ciclohexil-4-(5-fluor-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
5-(5-Fluor-2-metilfenil)-2,5-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol	
5-(5-Fluor-2-metilfenil)-2,2,5-trimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol	

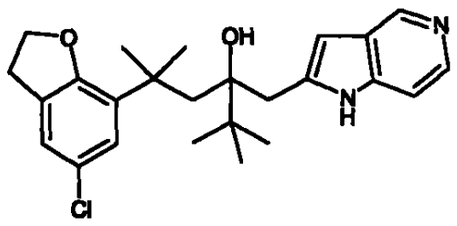
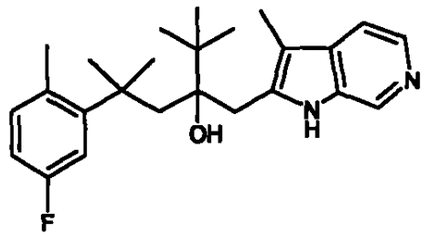
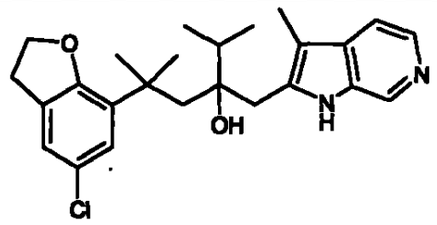
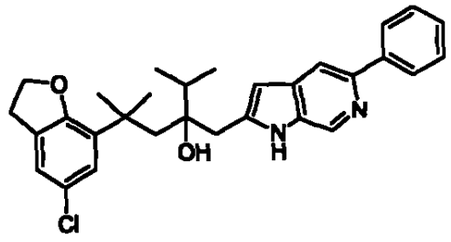
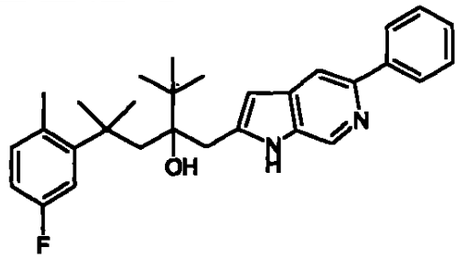
IB	
A	B
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol	
2-Ciclobutil-4-(5-fluor-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol	
2-(5-Fluor-2-metoxifenil)-2,6,6-trimetil-4-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)heptan-4-ol	
5-(5-Fluor-2-metoxifenil)-5-metil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hex-1-en-3-ol	
5-(5-Fluor-2-metoxifenil)-5-metil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hex-1-in-3-ol	

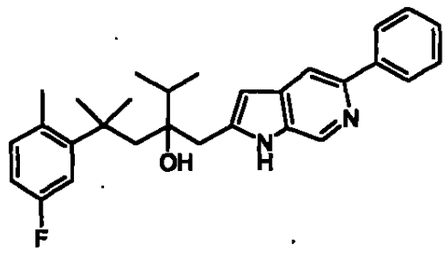
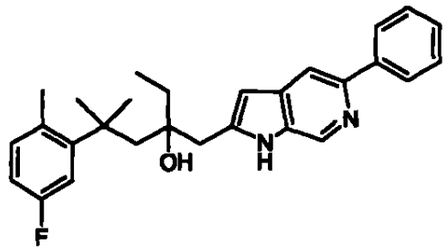
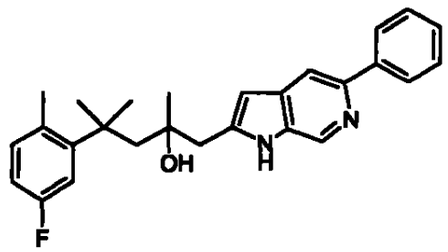
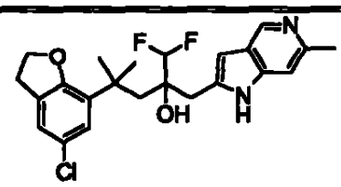
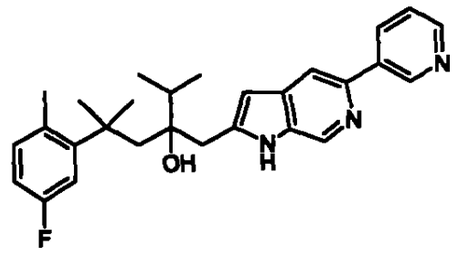
IB	
A	B
1-Fluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol	
2,2-Difluor-5-(5-fluor-2-metoxifenil)-5-metil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol	
2-Fluor-5-(5-fluor-2-metoxifenil)-2,5-dimetil-3-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol	
2-Fluor-5-(5-fluor-2-metoxifenil)-5-metil-3-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol	
5-(5-Fluor-2-metoxifenil)-2,5-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hex-1-en-3-ol	

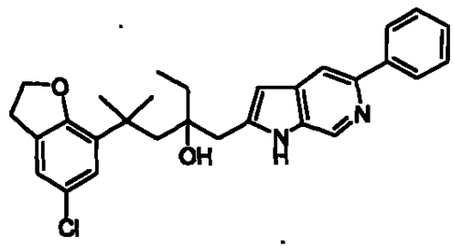
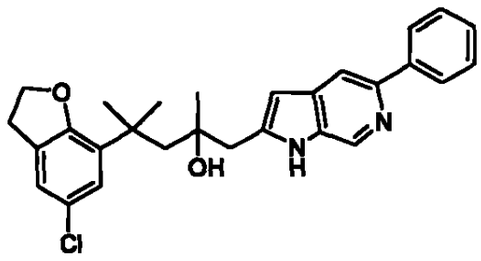
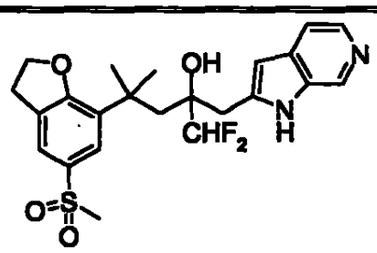
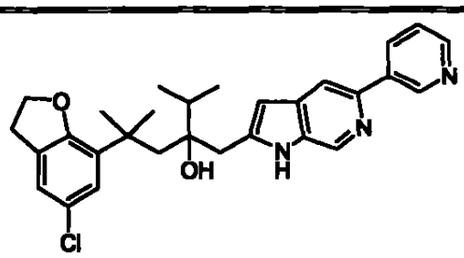
IB	
A	B
1,1,1-Trifluor-5-(5-fluor-2-metoxifenil)-5-metil-3-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol	
4-(5-Fluor-2-metoxifenil)-4-metil-2-fenil-1-(1*H*-pirrolo[2,3-c]piridin-2-il)pentan-2-ol	
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,2,5-trimetil-3-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol	
5-(5-Fluor-2-metilfenil)-2,2,5-trimetil-3-tieno[2,3-c]piridin-2-ilmetilhexan-3-ol	
1,1-Difluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol	

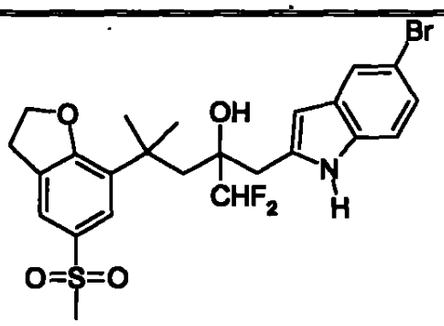
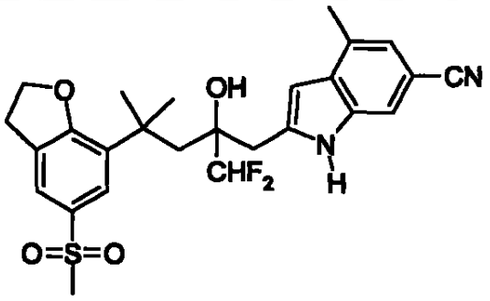
IB	
A	B
5-(5-Fluor-2-metoxifenil)-2,5-dimetil-3-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)hexan-3-ol	
5-(5-Fluor-2-metoxifenil)-2,2,5-trimetil-3-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)hexan-3-ol	
2-(1-Fluorciclopropil)-4-(5-fluor-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[2,3-c]piridin-2-il)pentan-2-ol	
2-(1-Fluorciclopropil)-4-(4-fluorfenil)-4-metil-1-quinolin-4-ilpentan-2-ol	
2-[4,4-Difluor-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)butil]-4-fluorfenol	

IB	
A	B
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol	
5-(5-Fluor-2-metilfenil)-2,5-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol	
5-(5-Fluor-2-metilfenil)-2,2,5-trimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluor-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluor-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol	

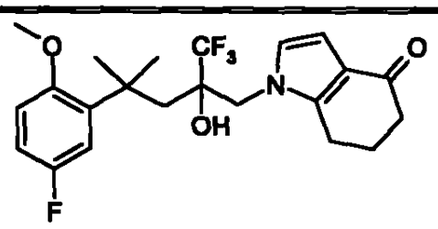
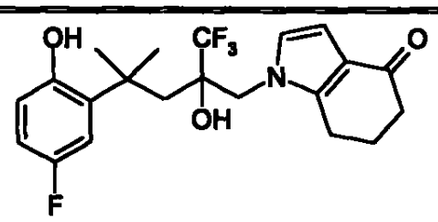
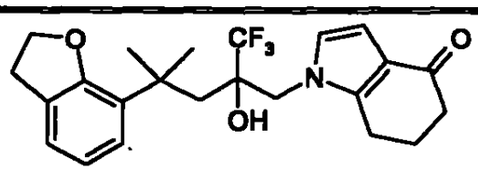
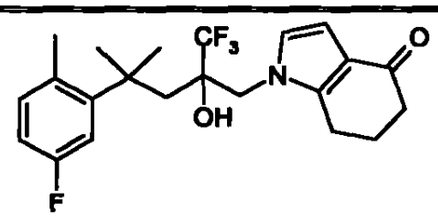
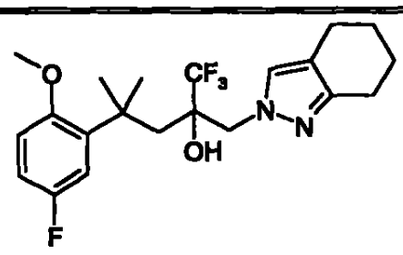
IB	
A	B
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,2,5-trimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol	
5-(5-Fluor-2-metilfenil)-2,2,5-trimetil-3-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol	
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol	
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol	
5-(5-Fluor-2-metilfenil)-2,2,5-trimetil-3-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol	

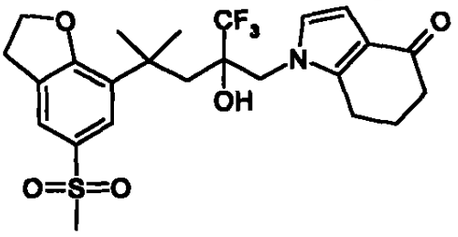
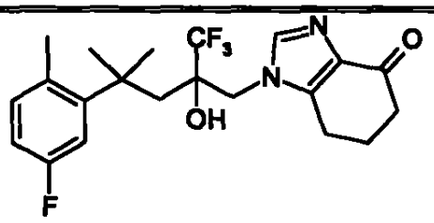
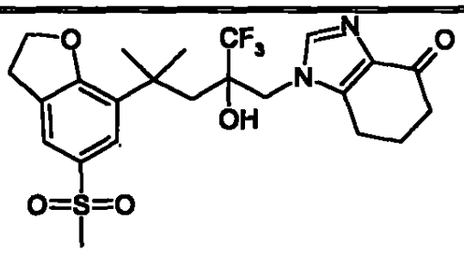
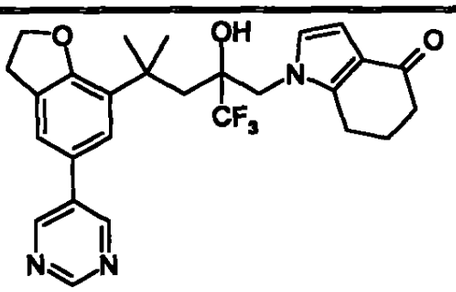
IB	
A	B
5-(5-Fluor-2-metilfenil)-2,5-dimetil-3-(5-fenil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol	
5-(5-Fluor-2-metilfenil)-5-metil-3-(5-fenil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)hexan-3-ol	
4-(5-Fluor-2-metilfenil)-2,4-dimetil-1-(5-fenil-1*H*-pirrolo[2,3-c]piridin-2-il)pentan-2-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluor-4-metil-2-(6-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol	
5-(5-Fluor-2-metilfenil)-2,5-dimetil-3-(5-piridin-3-il-1*H*-pirrolo [2,3-c]piridin-2-ilmetil)hexan-3-ol	

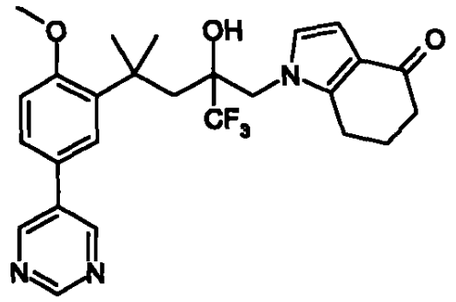
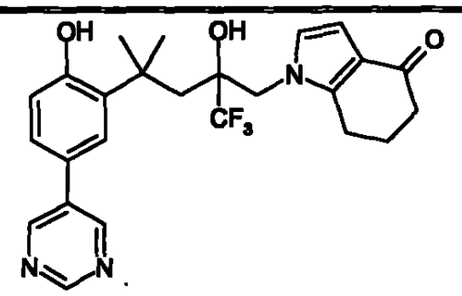
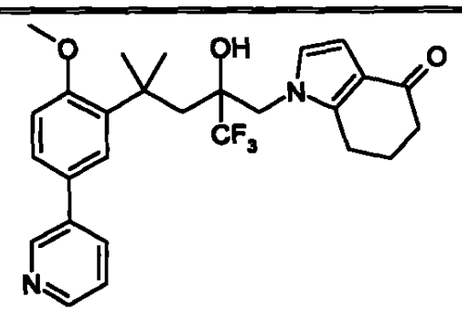
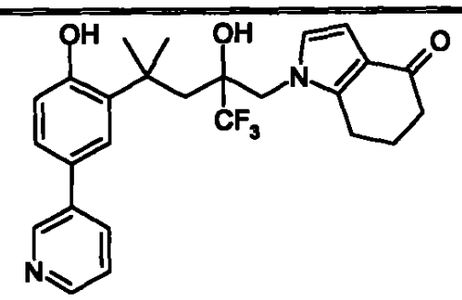
IB	
A	B
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-5-metil-3-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol	
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,4-dimetil-1-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol	
1,1-Difluor-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol	
5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(5-piridin-3-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol	

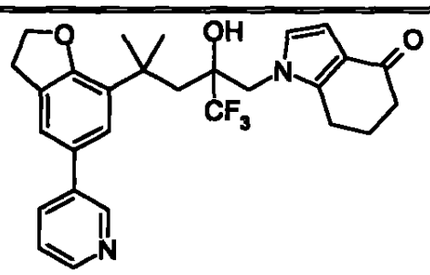
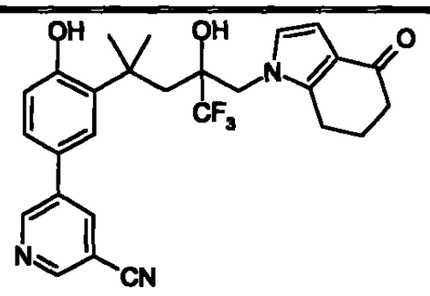
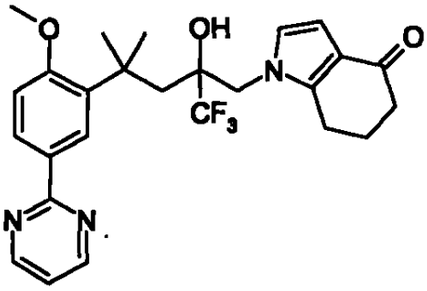
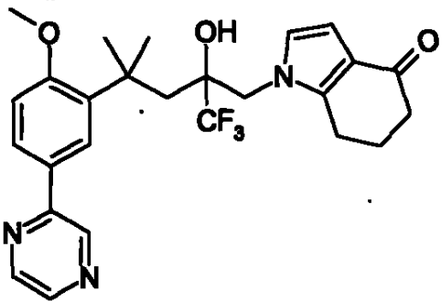
IB	
A	**B**
2-(5-Bromo-1*H*-indol-2-ilmetil)-1,1-difluor-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol	
2-[2-Difluormetil-2-hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentil]-4-metil-1*H*-indol-6-carbonitrilo	
o un tautómero, prodroga, solvato o sal de los mismos.	

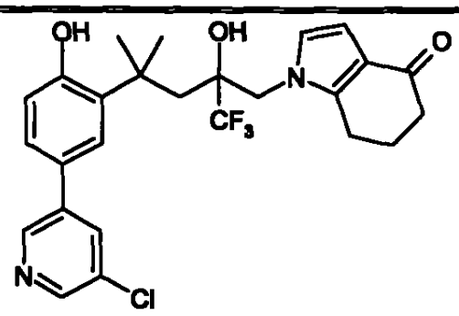
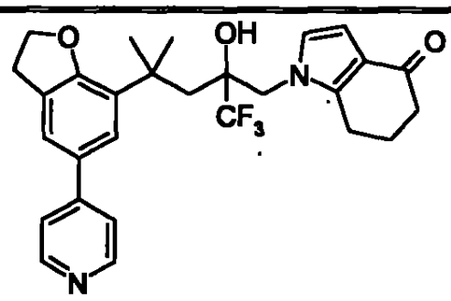
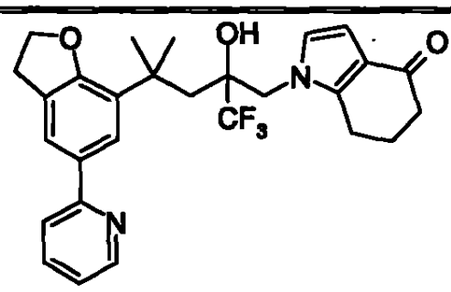
831
853

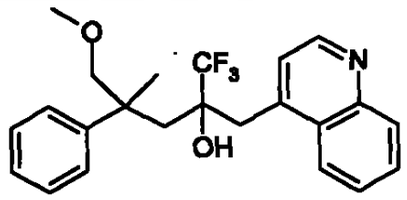
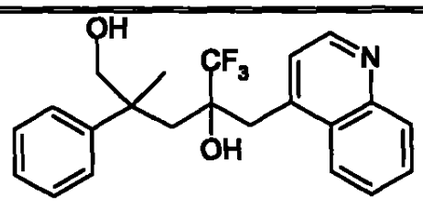
IC	
A	B
1-[4-(5-Fluor-2-metoxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1,5,6,7-tetrahidroindol-4-ona	
1-[4-(5-Fluor-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluormetilpentil-1,5,6,7-tetrahidroindol-4-ona	
1-[4-(2,3-Dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluormetilpentil]-1,5,6,7-tetrahidroindol-4-ona	
1-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1,5,6,7-tetrahidroindol-4-ona	
1,1,1-Trifluor-4-(5-fluor-2-metoxifenil)-4-metil-2-(4,5,6,7-tetrahidroindazol-2-ilmetil)pentan-2-ol	

IC	
A	B
1-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluormetilpentil]-1,5,6,7-tetrahidroindol-4-ona	
1-[4-(5-Fluor-2-metilfenil)-2-hidroxi-4-metil-2-trifluormetilpentil]-1,5,6,7-tetrahidrobenzoimidazol-4-ona	
1-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluormetilpentil]-1,5,6,7-tetrahidrobenzoimidazol-4-ona	
1-[2-Hidroxi-4-metil-4-(5-pirimidin-5-il-2,3-dihidrobenzofuran-7-il)-2-trifluormetilpentil]-1,5,6,7-tetrahidroindol-4-ona	

IC	
A	B
1-[2-Hidroxi-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-trifluormetilpentil]-1,5,6,7-tetrahidroindol-4-ona	
1-[2-Hidroxi-4-(2-hidroxi-5-pirimidin-5-ilfenil)-4-metil-2-trifluormetilpentil]-1,5,6,7-tetrahidroindol-4-ona	
1-[2-Hidroxi-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-trifluormetilpentil]-1,5,6,7-tetrahidroindol-4-ona	
1-[2-Hidroxi-4-(2-hidroxi-5-piridin-3-ilfenil)-4-metil-2-trifluormetilpentil]-1,5,6,7-tetrahidroindol-4-ona	

IC	
A	B
1-[2-Hidroxi-4-metil-4-(5-piridin-3-il-2,3-dihidrobenzofuran-7-il)-2-trifluormetilpentil]-1,5,6,7-tetrahidroindol-4-ona	
5-{4-Hidroxi-3-[4,4,4-trifluor-3-hidroxi-1,1-dimetil-3-(4-oxo-4,5,6,7-tetrahidroindol-1-ilmetil)butil]fenil}nicotinonitrilo	
1-[2-Hidroxi-4-(2-metoxi-5-pirimidin-2-ilfenil)-4-metil-2-trifluormetilpentil]-1,5,6,7-tetrahidroindol-4-ona	
1-[2-Hidroxi-4-(2-metoxi-5-pirazin-2-ilfenil)-4-metil-2-trifluormetilpentil]-1,5,6,7-tetrahidroindol-4-ona	

IC	
A	B
1-{4-[5-(5-Cloropiridin-3-il)-2-hidroxifenil]-2-hidroxi-4-metil-2-trifluormetilpentil}-1,5,6,7-tetrahidroindol-4-ona	
1-[2-Hidroxi-4-metil-4-(5-piridin-4-il-2,3-dihidrobenzofuran-7-il)-2-trifluormetilpentil]-1,5,6,7-tetrahidroindol-4-ona	
1-[2-Hidroxi-4-metil-4-(5-piridin-2-il-2,3-dihidrobenzofuran-7-il)-2-trifluormetilpentil]-1,5,6,7-tetrahidroindol-4-ona	
o un tautómero, prodroga, solvato o sal de los mismos.	

ID	
A	B
1,1,1-Trifluor-5-metoxi-4-metil-4-fenil-2-quinolin-4-ilmetilpentan-2-ol	
5,5,5-Trifluor-2-metil-2-fenil-4-quinolin-4-ilmetilpentano-1,4-diol	
o un tautómero, prodroga, solvato o sal de los mismos.	

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Descripción Detallada de la Invención

Definición de los Términos y Convenciones usados

A los términos no definidos específicamente aquí debe asignárseles el significado usual para aquel especialista en la técnica en vista de la revelación y el contexto. Como se utiliza en la memoria descriptiva y las reivindicaciones adjuntas, de todos modos y salvo especificación en contrario, los siguientes términos tienen el significado indicado y se agregan las siguientes convenciones.

A. Nomenclatura química, términos y convenciones

En los grupos, radicales o partes definidas a continuación, la cantidad de átomos de carbono con frecuencia se especifica a continuación del grupo, por ejemplo, alquilo C_1-C_{10} significa un grupo o radical alquilo con 1 a 10 átomos de carbono. El término "inferior" aplicado a cualquier grupo que contiene carbono significa un grupo que contiene de 1 a 8 átomos de carbono según corresponda al grupo (p.ej., un grupo cíclico debe presentar al menos 3 átomos para constituir un anillo). En general, para grupos que comprenden dos o más subgrupos, el grupo nombrado en último lugar es el punto de unión con el radical, por ejemplo, "alquilarilo" significa un radical monovalente de fórmula Alq-Ar-, mientras que "arilalquilo" significa un radical monovalente de fórmula Ar-Alq- (donde Alq es un grupo alquilo y Ar es un grupo arilo). Además, el uso de un término para designar un radical monovalente cuando corresponda un radical divalente se considerará que designa el respectivo radical divalente y vice versa. Salvo especificación en contrario, las definiciones convencionales de los términos control y valencias de átomos estables convencionales se presumen y se logran en todas las fórmulas y grupos.

Los términos "alquilo" o "grupo alquilo" significan un radical monovalente hidrocarbonado alifático saturado de cadena lineal o ramificada. Este término es ejemplificado por grupos tales como metilo, etilo, *n*-propilo, 1-metiletil (isopropil), *n*-butilo, *n*-pentilo, 1,1-dimetiletil (*ter*-butil) y similares. Puede abreviarse como "alq".

Los términos "alquenilo" o "grupo alquenilo" significan un radical monovalente hidrocarbonado alifático de cadena lineal o ramificada que presenta al menos una unión doble carbono-carbono. Este término es ejemplificado por grupos tales como etenilo, propenilo, *n*-butenilo, isobutenilo, 3-metilbut-2-enilo, *n*-pentenilo, heptenilo, octenilo, decenilo y similares.

Los términos "alquinilo" o "grupo alquinilo" significan un radical monovalente hidrocarbonado alifático de cadena lineal o ramificada que presenta al menos una unión triple carbono-carbono. Este término es ejemplificado por grupos tales como etinilo,

propinilo, *n*-butinilo, 2-butinilo, 3-metilbutinilo, *n*-pentinilo, heptinilo, octinilo, decinilo y similares.

Los términos "alquileno" o "grupo alquileno" significan un radical divalente hidrocarbonado alifático saturado de cadena lineal o ramificada que tiene la cantidad especificada de átomos de carbono. Este término es ejemplificado por grupos tales como metileno, etileno, propileno, *n*-butileno, y similares, y pueden en forma alternativa y equivalente indicarse en la presente como -(alquil)-.

Los términos "alquenileno" o "grupo alquenileno" significan un radical divalente hidrocarbonado alifático de cadena lineal o ramificada que presenta la cantidad especificada de átomos de carbono y al menos una unión doble carbono-carbono. Este término es ejemplificado por grupos tales como etenileno, propenileno, *n*-butenileno, y similares, y pueden en forma alternativa y equivalente indicarse aquí como -(alquilenil)-.

Los términos "alquinileno" o "alquinileno group" significan un radical divalente hidrocarbonado alifático de cadena lineal o ramificada que presenta al menos una unión triple carbono-carbono. Este término es ejemplificado por grupos tales como etinileno, propinileno, *n*-butinileno, 2-butinileno, 3-metilbutinileno, *n*-pentinileno, heptinileno, octinileno, decinileno, y similares, y pueden en forma alternativa y equivalente indicarse aquí como -(alquinil)-.

Los términos "alcoxi" o "grupo alcoxi" significan un radical monovalente de fórmula AlqO-, donde Alq es un grupo alquilo. Este término es ejemplificado por grupos tales como metoxi, etoxi, propoxi, isopropoxi, butoxi, *sec*-butoxi, *ter*-butoxi, pentoxi y similares.

Los términos "ariloxi", "grupo ariloxi", significan un radical monovalente de la fórmula ArO-, donde Ar es arilo. Este término es ejemplificado por grupos tales como fenoxi, naftoxi y similares.

El término "oxo" significa un radical oxígeno divalente de unión doble de la fórmula (=O), por ejemplo, un ejemplo de un grupo alquilo sustituido con un "oxo" sería un grupo de fórmula Alq-C(O)-Alq, donde cada Alq es un alquilo.

Los términos "alquilcarbonilo", "grupo alquilcarbonilo", "alcanoílo", o "grupo alcanoílo" significan un radical monovalente de fórmula AlqC(O)-, donde Alq es alquilo o hidrógeno.

Los términos "arilcarbonilo", "grupo arilcarbonilo", "aroílo" o "grupo aroílo" significan un radical monovalente de fórmula ArC(O)-, donde Ar es arilo.

Los términos "acilo" o "grupo acilo" significan un radical monovalente de la fórmula RC(O)-, donde R es un sustituyente seleccionado de hidrógeno o un sustituyente orgánico. Los sustituyentes ejemplares incluyen alquilo, arilo, arilalquilo, cicloalquilo,

heterociclilo, heteroarilo, heteroarilalquilo y similares. Como tales, los términos comprenden grupos alquilcarbonilo y grupos arilcarbonilo.

Los términos "acilamino" o "grupo acilamino" significan un radical monovalente de fórmula RC(O)N(R)-, donde cada R es un sustituyente seleccionado de hidrógeno o un grupo sustituyente.

Los términos "alcoxicarbonilo" o "grupo alcoxicarbonilo" significan un radical monovalente de la fórmula AlqO-C(O)-, donde Alq es alquilo. Los grupos alcoxicarbonilo ejemplares incluyen metoxicarbonilo, etoxicarbonilo, *ter*-butiloxicarbonilo, y similares.

Los términos "alquilaminocarboniloxi" o "grupo alquilaminocarboniloxi" significan un radical monovalente de fórmula $R_2NC(O)O$-, donde cada uno R es independientemente hidrógeno o alquilo inferior.

El término "alcoxicarbonilamino" o "grupo alcoxicarbonilamino" significan un radical monovalente de fórmula ROC(O)NH-, donde R es alquilo inferior.

Los términos "alquilcarbonilamino" o "grupo alquilcarbonilamino" o "alcanoilamino" o "grupos alcanoilamino" significan un radical monovalente de fórmula AlqC(O)NH-, donde Alq es alquilo. Los grupos alquilcarbonilamino ejemplares incluyen acetamida ($CH_3C(O)NH$-).

Los términos "alquilaminocarboniloxi" o "grupo alquilaminocarboniloxi" significan un radical monovalente de fórmula AlqNHC(O)O-, donde Alq es alquilo.

Los términos "amino" o "grupo amino" significan un grupo $-NH_2$.

Los términos "alquilamino" o "grupo alquilamino" significan un radical monovalente de fórmula (Alq)NH-, donde Alq es alquilo. Los grupos alquilamino ejemplares incluyen metilamino, etilamino, propilamino, butilamino, *ter*-butilamino y similares.

Los términos "dialquilamino" o "grupo dialquilamino" significan un radical monovalente de fórmula (Alq)(Alq)N-, donde cada Alq es independientemente alquilo. Los grupos dialquilamino ejemplares incluyen dimetilamino, metiletilamino, dietilamino, dipropilamino, etilpropilamino y similares.

Los términos "amino sustituido" o "grupo amino sustituido" significan un radical monovalente de la fórmula $-NR_2$, donde cada uno R es independientemente un sustituyente seleccionado de hidrógeno o los sustituyentes especificados (pero donde ambos Rs no pueden ser hidrógeno). Los sustituyentes ejemplares incluyen alquilo, alcanoilo, arilo, arilalquilo, cicloalquilo, heterociclilo, heteroarilo, heteroarilalquilo, y similares.

Los términos "alcoxicarbonilamino" o "grupo alcoxicarbonilamino" significan un radical monovalente de fórmula AlqOC(O)NH-, donde Alq es alquilo.

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Los términos "ureido" o "grupo ureido" significan un radical monovalente de fórmula $R_2NC(O)NH$-, donde cada uno R es independientemente hidrógeno o alquilo.

Los términos "halógeno" o "grupo halógeno" significan un grupo fluoro, cloro, bromo o yodo.

El término "halo" significa que uno o más átomos de hidrógeno del grupo son reemplazados por grupos halógeno.

Los términos "haloalquilo" o "grupo haloalquilo" significan un radical monovalente hidrocarbonado alifático saturado de cadena linaal o ramificada, donde uno o más átomos de hidrógeno del mismo son cada uno independientemente reemplazado con átomos de halógeno. Este término es ejemplificado por grupos tales como clorometilo, 1,2-dibromoetilo, 1,1,1-trifluoropropilo, 2-yodobutilo, 1-cloro-2-bromo-3-fluoropentilo, y similares.

Los términos "sulfanilo", "grupos sulfanilo", "tioéter", o "grupo tioéter" significan un radical divalente de fórmula -S-.

Los términos "alquiltio" o "grupo alquiltio" significan un radical monovalente de fórmula AlqS-, donde Alq es alquilo. Los grupos ejemplares incluyen metiltio, etiltio, *n*-propiltio, isopropiltio, *n*-butiltio y similares.

Los términos "sulfonilo" o "grupo sulfonilo" significan un radical divalente de la fórmula $-SO_2-$.

Los términos "sulfonilamino" o "grupo sulfonilamino" significan un radical divalente de la fórmula $-SO_2NR-$, donde R es un hidrógeno o un grupo sustituyente.

Los términos "aminosulfonilo" o "grupo aminosulfonilo" significan un radical monovalente de la fórmula NR_2SO_2-, donde R es cada uno independientemente un hidrógeno o un grupo sustituyente.

Los términos "carbocicio" o "grupo carbocíclico" significan un radical divalente o monovalente policíclico o monocíclico de 3-15 miembros alifático estable que consistesolamente de átomos de carbono e hidrógeno, que pueden comprender uno o más anillo(s) fusionados o puenteados, preferentemente un anillo bicíclico de 5 a 7 monocíclico o de 7 a 10 miembros bicíclico. Salvo especificación en contrario, el carbocicio puede estar unido a cualquier átomo de carbono que dé lugar a una estructura estable y, en caso de estar sustituido, puede estar sustituido en cualquier átomo de carbono que genere una estructura estable. El término comprende cicloalquilo (incluyendo espirocicloalquilo), cicloalquileno, cicloalquenilo, cicloalquenileno, cicloalquinilo, y cicloalquinileno y similares.

Los términos "cicloalquilo" o "grupo cicloalquilo" significan un radical monovalente policíclico o monocíclico de 3 a 15 miembros saturado alifático estable que consiste solamente en átomos de carbono e hidrógeno, que pueden comprender uno o más anillo(s) fusionados o puenteados, preferentemente un anillo bicíclico de 5 a 7 monocíclico o de 7 a 10 miembros bicíclico. Salvo especificación en contrario, el anillo cicloalquilo puede estar unido a cualquier átomo de carbono que genere una estructura estable y, en caso de estar sustituido, puede estar sustituido en cualquier átomo de carbono que genere una estructura estable. Los grupos cicloalquilo ejemplares incluyen ciclopropilo, ciclobutilo, ciclopentilo, ciclohexilo, cicloheptilo, ciclooctilo, ciclononilo, ciclodecilo, norbornanilo, adamantilo, tetrahidronaftilo (tetralina), 1-decalinilo, biciclo[2,2,2]octanilo, 1-metilciclopropilo, 2-metilciclopentilo, 2-metilciclooctilo, y similares.

Los términos "cicloalquenilo" o "grupo cicloalquenilo" significan un radical monovalente policíclico o monocíclico de 3 a 15 miembros alifático estable que presenta al menos una unión doble carbono-carbono y consiste solamente en átomos de carbono e hidrógeno, que pueden comprender uno o más anillo(s) fusionados o puenteados, preferentemente un anillo bicíclico de 5 a 7 monocíclico o de 7 a 10 miembros bicíclico. Salvo especificación en contrario, el anillo cicloalquenilo puede estar unido a cualquier átomo de carbono que genere una estructura estable y, en caso de estar sustituido, puede estar sustituido en cualquier átomo de carbono que genere una estructura estable. Los grupos cicloalquenilo ejemplares incluyen ciclopentenilo, ciclohexenilo, cicloheptenilo, ciclooctenilo, ciclononanilo, ciclodecenilo, norbornenilo, 2-metilciclopentenilo, 2-metilciclooctenilo y similares.

Los términos "cicloalquinilo" o "grupo cicloalquinilo" significan un radical monovalente policíclico o monocíclico de 8 a 15 miembros alifático estable que presenta al menos una triple unión carbono-carbono y que consiste solamente en átomos de carbono e hidrógeno, que pueden comprender uno o más anillo(s) fusionados o puenteados, preferentemente un anillo bicíclico de 8 a 10 monocíclico o de 12 a 15 miembros bicíclico. Salvo especificación en contrario, el anillo cicloalquinilo puede estar unido a cualquier átomo de carbono que genere una estructura estable y, en caso de estar sustituido, puede estar sustituido en cualquier átomo de carbono que genere una estructura estable. Los grupos cicloalquinilo incluyen, ciclooctinilo, ciclononinilo, ciclodecinilo, 2-metilciclooctinilo y similares.

Los términos "cicloalquileno" o "grupo cicloalquileno" significan un radical divalente monocíclico o policíclico de 3 a 15 miembors alifático saturado estable que consiste solamente en átomos de carbono e hidrógeno, que pueden comprender uno o más

anillo(s) fusionados o puenteados, preferentemente un anillo monocíclico de 5 a 7 miembros o bicíclico de 7 a 10 miembros. Salvo especificación en contrario, el carbociclo puede estar unido a cualquier átomo de carbono que resulte en una estructura estable y, en caso de estar sustituido, puede estar sustituido en cualquier átomo de carbono que resulte en una estructura estable. Los grupos cicloalquileno ejemplares incluyen ciclopentileno, y similares.

Los términos "cicloalquenileno" o "grupo cicloalquenileno" significan un radical divalente policíclico o monocíclico de 5 a 15 miembros alifático estable que presenta al menos una unión doble carbono-carbono y que consistesolamente de átomos de carbono e hidrógeno, que pueden comprender uno o más anillo(s) fusionados o puenteados, preferentemente un anillo monocíclico de 5 a 7 miembros o bicíclico de 7 a 10 miembros. Salvo especificación en contrario, el anillo cicloquenileno puede estar unido a cualquier átomo de carbono que genere una estructura estable y, en caso de estar sustituido, puede estar sustituido en cualquier átomo de carbono que genere una estructura estable. Los grupos cicloalquenileno ejemplares incluyen ciclopentenileno, ciclohexenileno, cicloheptenileno, ciclooctenileno, ciclononanileno, ciclodecenileno, norbomenileno, 2-metilciclopentenileno, 2-metilciclooctenileno y similares.

Los términos "cicloalquinileno" o "grupo cicloalquinileno" significan un radical divalente policíclico o monocíclico de 8 a 15 miembros alifático estable que presenta al menos una unión triple carbono-carbono y que consiste solamente en átomos de carbono e hidrógeno, que pueden comprender uno o más anillo(s) fusionados o puenteados, preferentemente un anillo monocíclico de 8 a 10 miembros o bicíclico de 12 a 15 miembros. Salvo especificación en contrario, el anillo cicloalquinileno puede estar unido a cualquier átomo de carbono que genere una estructura estable y, en caso de estar sustituido, puede estar sustituido en cualquier átomo de carbono que genere una estructura estable. Los grupos cicloalquinileno incluyen ciclooctinileno, ciclononinileno, ciclodecinileno, 2-metilciclooctinileno y similares.

Los términos "arilo" o "grupo arilo" significan un radical divalente o monovalente carbocíclico aromático de 6 a 14 átomos de carbono que presentan un anillo simple (p.ej., fenilo o fenileno) o anillos condensados múltiples (p.ej., naftilo o antranilo). Salvo especificación contraria, el anillo arilo puede estar unido a cualquier átomo de carbono adecuado que resulte en una estructura estable y, en caso de estar sustituido, puede estar sustituido en cualquier átomo de carbono que genere una estructura estable. Los grupos arilo ejemplares incluyen fenilo, naftilo, antrilo, fenantrilo, indanilo, indenilo, bifenilo y similares. Pueden abreviarse "Ar".

Los términos "heteroarilo" o "grupo heteroarilo" significan un radical divalente o monovalente, monocíclico o policíclico de 5 a 14 miembros, aromático estable que puede comprender uno o más anillo(s) fusionados o puenteados, preferentemente un radical monocíclico de 5 a 7 miembros o bicíclico de 7 a 10 miembros que presentan uno a cuatro heteroátomos en el/los anillo(s), independientemente seleccionados de nitrógeno, oxígeno y azufre, donde cualquiera de los heteroátomos de azufre puede opcionalmente estar oxidado y cualquier heteroátomo de nitrógeno puede opcionalmente estar oxidado o cuaternizado. Salvo especificación en contrario, el anillo heteroarilo puede estar unido a cualquier heteroátomo o átomo de carbono que genere una estructura estable y, en caso de estar sustituido, puede estar sustituido en cualquier heteroátomo o átomo de carbono que genere una estructura estable. Los heteroarilos preferidos ejemplares incluyen furanilo, tienilo, pirrolilo, oxazolilo, tiazolilo, imidazolilo, pirazolilo, isoxazolilo, isotiazolilo, oxadiazolilo, triazolilo, tetrazolilo, tiadiazolilo, piridinilo, piridazinilo, pirimidinilo, pirazinilo, triazinilo, indolizinilo, azaindolizinilo, indolilo, azaindolilo, diazaindolilo, dihidroindolilo, dihidroazaindolilo, isoindolilo, azaisoindolilo, benzofuranilo, furanopiridinilo, furanopirimidinilo, furanopirazinilo, furanopiridazinilo, dihidrobenzofuranilo, dihidrofuranopiridinilo, dihidrofuranopirimidinilo, benzodioxolanilo, benzotienilo, tienopiridinilo, tienopirimidinilo, tienopirazinilo, tienopiridazinilo, dihidrobenzotienilo, dihidrotienopiridinilo, dihidrotienopirimidinilo, indazolilo, azaindazolilo, diazaindazolilo, benzoimidazolilo, imidazopiridinilo, benzotiazolilo, tiazolopiridinilo, tiazolopirimidinilo, benzoxazolilo, oxazolopiridinilo, oxazolopirimidinilo, benzoisoxazolilo, purinilo, cromanilo, azacromanilo, quinolizinilo, quinolinilo, dihidroquinolinilo, tetrahidroquinolinilo, isoquinolinilo, dihidroisoquinolinilo, tetrahidroisoquinolinilo, cinnolinilo, azacinnolinilo, ftalazinilo, azaftalazinilo, quinazolinilo, azaquinazolinilo, quinoxalinilo, azaquinoxalinilo, naftiridinilo, dihidronaftiridinilo, tetrahidronaftiridinilo, pteridinilo, carbazolilo, acridinilo, fenazinilo, fenotiazinilo y fenoxazinilo, y similares.

Los términos "heterociclo", "grupo heterociclo", "heterociclilo", o "grupo heterociclilo" significan un anillo monovalente o divalente, monocíclico o policíclico, de 5 a 14 miembros no aromático estable que comprenden uno o más anillo(s) fusionados o puenteados, preferentemente un anillo monocíclico de 5 a 7 miembros o bicíclico de 7 a 10 miembros, que presenta de uno a tres heteroátomos en el/los anillos independientemente seleccionados de nitrógeno, oxígeno y azufre, donde cualquiera de los heteroátomos de azufre puede opcionalmente estar oxidado y cualquiero de los heteroátomos de nitrógeno puede opcionalmente estar oxidado o cuaternizado. Salvo especificación en contrario, el anillo heteroarilo puede estar unido a cualquier

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heteroátomo o átomo de carbono que resulte en una estructura estable y, en caso de estar sustituido, puede estar sustituido en cualquier heteroátomo o átomo de carbono que resulte en una estructura estable. Los heterocicios preferidos ejemplares incluyen pirrolinilo, pirrolidinilo, pirazolinilo, pirazolidinilo, piperidinilo, morfolinilo, tiomorfolinilo, piperazinilo, tetrahidropiranilo, tetrahidrotiopiranilo, tetrahidrofuranilo, hexahidropirimidinilo, hexahidropiridazinilo, y similares.

El término "compuestos de Fórmula (I)" y expresiones equivalentes abarcan compuestos de Fórmula (IA), compuestos de Fórmula (IB), compuestos de Fórmula (IC), y compuestos de Fórmula (ID), en forma individual, en alguna combinación o todos ellos, siempre que el contexto lo permita.

El término "compuestos de la invención" y expresiones equivalentes significa que abarcan compuestos de Fórmula (I) como los aquí descriptos, incluyendo los tautómeros, los profármacos, las sales, particularmente las sales aceptables para uso farmacéutico, y los solvatos e hidratos de los mismos, donde el contexto lo permita. En general y preferentemente, se entiende que los compuestos de la invención y las fórmulas que designan los compuestos de la invención solamente incluyen los compuestos estables de los mismos y excluyen los compuestos inestables, incluso si un compuesto inestable puede considerarse como literalmente incluido por el compuesto de la fórmula. En forma similar respecto de los intermediarios, estando o no ellos reivindicados, se entiende que se incluyen sus sales y solvatos, donde el contexto lo permita. A los efectos de la claridad, las instancias particulares están en ocasiones indicadas en el texto cuando el contexto lo permite, pero estas instancias son puramente ilustrativas y no se tiene la intención de excluir otras circunstancias cuando el contexto lo permita.

Los términos "opcional" u "opcionalmente" significan que los eventos o circunstancias descritas a continuación pueden o no ocurrir, y que la descripción incluye instancias, donde el evento o la circunstancia ocurre, e instancias, en las que no lo hace. Por ejemplo, "arilo opcionalmente sustituido" significa que el radical arilo puede o no estar sustituido y que la descripción incluye los radicales arilo sustituidos y los radicales arilo que no presentan sustitución.

Los términos "compuesto estable" o "estructura estable" significan un compuesto que es suficientemente fuerte para sobrevivir la aislación hasta un grado útil de pureza a partir de una mezcla de reacción, y la formulación en un agente terapéutico o de diagnóstico eficaz. Por ejemplo, un compuesto que tendría una "valencia cambiante" o es un carbanión no es un compuesto contemplado en esta invención.

El término "sustituido" significa que cualquiera o varios hidrógenos en un átomo de un grupo o resto, esté o no específicamente designado, está reemplazado con una selección de los grupos de sustituyentes indicados, siempre y cuando no se exceda la valencia normal del átomo y que la sustitución genere un compuesto estable. Si una unión a un sustituyente cruza la unión que conecta dos átomos en un anillo, entonces tal sustituyente puede unirse a cualquier átomo en el anillo. Cuando un sustituyente es enunciado sin indicar la vía del átomo por la cual tal sustituyente se une al resto del compuesto, entonces tal sustituyente puede unirse a través de cualquier átomo en tal sustituyente. Por ejemplo, cuando el sustituyente es piperazinilo, piperidinilo, o tetrazolilo, salvo especificación en contrario, tal grupo piperazinilo, piperidinilo o tetrazolilo puede estar unido al resto del compuesto de la invención a través de cualquier átomo en tal grupo piperazinilo, piperidinilo o tetrazolilo. Generalmente, cuando cualquier sustituyente o grupo se presenta más de una vez en cualquier constituyenbte o compuesto, la definición para cada caso es independiente de la definición de cualquier otro caso. Así, por ejemplo, un grupo aparece como sustituido con 0 a 2 R^5, entonces tal grupo está opcionalmente sustituido con hasta dos grupos R^5, y R^5 en cada caso se selecciona independientemente de la lista definida de posibles R^5. Tales combinaciones de sustituyentes y/o variables, de todos modos, sólo se permiten si tales combinaciones generan compuestos estables.

En una realización específica, el término "alrededor de" o "aproximadamente" significa dentro del 20%, preferentemente dentro del 10%, y de mayor preferencia dentro del 5% de un valor o rango dado.

El rendimiento de cada una de las reacciones aquí descriptas se expresa como un porcentaje del rendimiento teórico.

B. Términos y convenciones de Sales, Profármacos, Derivados y Solvatos

Los términos "profármaco" o "derivado de profármaco" significan un derivado o vehículo unido covalentemente del compuesto progenitor o la sustancia farmacéutica activa que se somete al menos a alguna biotransformación previo a presentar su/s efecto/s farmacológico/s. En general, tales profármacos presentan grupos que pueden disociarse metabólicamente y son rápidamente transformados *in vivo* para obtener el compuesto progenitor, por ejemplo por hidrólisis en sangre, y generalmente incluyen análogos de ésteres y amidas de los compuestos progenitores. El profármaco se formula con los objetivos de una estabilidad química mejorada, tolerancia y cumplimiento del paciente mejoradas, biodisponibilidad mejorada, duración prolongada del efecto,

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selectividad mejorada de órganos, formulación mejorada (p. ej. mayor hidrosolubilidad), y/o menores efectos colaterlaes (p. ej. toxicidad). En general, los profármacos mismos presentan una escasa o ninguna actividad biológica y son estables en condiciones usuales. Los profármacos pueden prepararse fácilmente a partir de compuestos progenitores utilizando métodos conocidos en la técnica, tales como los descriptos en A Textbook of Drug Design and Development, Krogsgaard-Larsen y H. Bundgaard (eds.), Gordon & Breach, 1991, particularmente en el capítulo 5: "Design and Applications of Prodrugs"; Design of Prodrugs, H. Bundgaard (ed.), Elsevier, 1985; Prodrugs: Topical and Ocular Drug Delivery, K.B. Sloan (ed.), Marcel Dekker, 1998; Methods in Enzymology, K. Widder *et al.* (eds.), Vol. 42, Academic Press, 1985, particularmente pp. 309-396; Burger's Medicinal Chemistry and Drug Discovery, 5ta. Ed., M. Wolff (ed.), John Wiley & Sons, 1995, particularmente Vol. 1 y pp. 172-178 y pp. 949-982; Pro-Drugs as Novel Delivery Systems, T. Higuchi y V. Stella (eds.), Am. Chem. Soc., 1975; Bioreversible Carriers in Drug Design, E.B. Roche (ed.), Elsevier, 1987, cada uno de los cuales se incorpora aquí en su totalidad a título de referencia.

El término "profármaco aceptable para uso farmacéutico" como se utiliza aquí significa un profármaco de un compuesto de la invención que está dentro del alcance del sano juicio médico, adecuado para su uso en contacto con los tejidos de humanos y animales inferiores sin desarrollar toxicidad, irritación, respuesta alérgica y similares, está en relación con un índice razonable de riesgo/beneficio, y es efectivo para el uso al que está destinado, como así también sus formas zwitteriónicas, cuando sea posible.

El término "sal" significa una forma iónica del compuesto progenitor o el producto de la reacción entre el compuesto progenitor con un ácido o una base adecuada para formar la sal ácida o la sal básica del compuesto progenitor. Las sales de los compuestos de la presente invención pueden ser sintetizadas a partir del compuesto progenitor que contiene una parte básica o ácida mediante métodos químicos convencionales. Generalmente, las sales se preparan por reacción de la base libre o el compuesto progenitor ácido con cantidades estequiométricas o con un exceso de la base o ácido orgánico o inorgánico formadores de sal, en un solvente adecuado o en diferentes combinaciones de solventes.

El término "sal aceptable para uso farmacéutico" significa una sal de un compuesto de la invención que es, dentro del alcance del sano juicio médico, adecuada para usar en contacto con los tejidos de humanos y animales inferiores sin producir toxicidad, irritación, respuesta alérgica y similares, está en relación con un índice razonable de riesgo/beneficio, generalmente es soluble o dispersable en agua o en aceite y es efectiva

para el uso al que está destinadas. El término incluye sales de adición con ácido aceptables para uso farmacéutico y sales de adición con base aceptables para uso farmacéutico. Dado que los compuestos de la presente invención son útiles en ambas formas, como sal y como base libre, en la práctica, el uso de la forma salina equipara el uso de la forma básica. Se encuentran listas de sales adecuadas en, p.ej., S.M. Birge *et al.*, J. Pharm. Sci., 1977, 66, pp. 1-19, que se incorpora aquí en su totalidad a título de referencia.

El término "sales de adición con ácidos aceptables para uso farmacéutico" significa aquellas sales que mantienen la efectividad biológica y las propiedades de las bases libres y que no son indeseables biológicamente o de algún otro modo, formadas con ácidos inorgánicos, tales como ácido clorhídrico, ácido bromhídrico, ácido yodhídrico, ácido sulfúrico, ácido sulfámico, ácido nítrico, ácido fosfórico y similares, y ácidos orgánicos, tales como ácido acético, ácido tricloroacético, ácido trifluoroacético, ácido adípico, ácido algínico, ácido ascórbico, ácido aspártico, ácido bencensulfónico, ácido benzoico, ácido 2-acetoxibenzoico, ácido butírico, ácido alcanfórico, ácido alcanforsulfónico, ácido cinámico, ácido cítrico, ácido diglucónico, ácido etansulfónico, ácido glutámico, ácido glicólico, ácido glicerofosfórico, ácido hemisúlfico, ácido heptanoico, ácido hexanoico, ácido fórmico, ácido fumárico, ácido 2-hidroxietansulfónico (ácido isetiónico), ácido láctico, ácido maleico, ácido hidroximaleico, ácido málico, ácido malónico, ácido mandélico, ácido mesitilensulfónico, ácido metansulfónico, ácido naftalensulfónico, ácido nicotínico, ácido 2-naftalensulfónico, ácido oxálico, ácido pamoico, ácido pectínico, ácido fenilacético, ácido 3-fenilpropiónico, ácido pícrico, ácido piválico, ácido propiónico, ácido pirúvico, ácido salicílico, ácido esteárico, ácido succínico, ácido sulfanílico, ácido tartárico, ácido *p*-toluensulfónico, ácido undecanoico y similares.

El término "sal de adición con bases de uso aceptable para uso farmacéutico" significa aquellas sales que mantienen la efectividad biológica y las propiedades de los ácidos libres y que no son indeseables biológicamente o de algún otro modo, formadas con bases inorgánicas, tales como amoníaco o hidróxido, carbonato, o bicarbonato de amonio o un catión metálico, tal como sodio, potasio, litio, calcio, magnesio, hierro, zinc, cobre, manganeso, aluminio y similares. Particularmente preferidas son las sales de amonio, potasio, sodio, calcio y magnesio. Las sales derivadas de bases no tóxicas orgánicas aceptables para uso farmacéutico de aminas primarias, secundarias y terciarias, compuestos de aminas cuaternarias, aminas sustituidas incluyendo aminas sustituidas de existencia natural, aminas cíclicas y resinas básicas de intercambio iónico,

tales como metilamina, dimetilamina, trimetilamina, etilamina, dietilamina, trietilamina, isopropilamina, tripropilamina, tributilamina, etanolamina, dietanolamina, 2-dimetilaminoetanol, 2-dietilaminoetanol, diciclohexilamina, lisina, arginina, histidina, cafeína, hidrabamina, colina, betaína, etilendiamina, glucosamina, metilglucamina, teobromina, purinas, piperazina, piperidina, *N*-etilpiperidina, compuestos de tetrametilamonio, compuestos de tetraetilamonio, piridina, *N,N*-dimetilanilina, *N*-metilpiperidina, *N*-metilmorfolina, diciclohexilamina, dibencilamina, *N,N*-dibencil-fenetilamina, 1-efenamina, *N,N'*-dibenciletilendiamina, resinas de poliamina y similares. Las bases no tóxicas orgánicas particularmente preferidas son isopropilamina, dietilamina, etanolamina, trimetilamina, diciclohexilamina, colina y cafeína.

El término "solvato" significa una asociación física de un compuesto con una o más moléculas de solvente o un complejo de estequiometría variable formado por un soluto (por ejemplo, un compuesto de Fórmula (I)) y un solvente, por ejemplo agua, etanol o ácido acético. Esta asociación física puede incluir diferentes grados de unión iónica y covalente, incluyendo una unión hidrógeno. En determinadas instancias, el solvato puede aislarse, por ejemplo cuando una o más moléculas de solvente se incorporan en la celda unitaria cristalina del sólido cristalino. En general, los solventes seleccionados no interfieren con la actividad biológica del soluto. Los solvatos incluyen la fase de solución y los solvatos aislables Los solvatos representativos incluyen hidratos, etanolatos, metanolatos y similares.

El término "hidrato" significa un solvato donde la/s molécula/s de solvente es/son H_2O.

Los compuestos de la presente invención explicados a continuación incluyen la base libre o el ácido de los mismos, sus sales, solvatos, y profármacos y pueden incluir átmos de azufre oxidados o átomos de nitrógeno cuaternizados en su estructura, aunque no se establezca o muestre explícitamente, particularmente las formas aceptables para uso farmacéutico de los mismos. Tales formas, particularmente las formas aceptables para uso farmacéutico, están destinadas a ser abarcadas por las reivindicaciones adjuntas.

C. Términos y Convenciones de Isómeros

El término "isómeros" significa compuestos con la misma cantidad y tipo de átomos, y por lo tanto el mismo peso molecular, pero que difieren respecto de la disposición o la configuración de los átomos en el espacio. El término incluye estereoisómeros e isómeros geométricos.

Los términos "estereoisómero" o "isómero óptico" significan un isómero estable, que presenta al menos un átomo quiral o rotación restringida, dando lugar a planos

disimétricos perpendiculares (p.ej., determinados compuestos bifenilos, alenos y espiro) y puede rotar el plano de la luz polarizada. Debido a los centros asimétricos y demás estructuras químicas existentes en los compuestos de la invención que pueden dar origen a estereoisomerismo, la invención incluye estereoisómeros y mezclas de los mismos. Los compuestos de la invención y sus sales incluyen átomos de carbono asimétricos y pueden así existir como estereoisómeros individuales, racematos, y como mezclas de enantiómeros y diastereómeros. Típicamente tales compuestos se preparan como mezcla racémica. Si se desea, de todos modos, tales compuestos pueden prepararse como estereoisómeros aislados o puros, p. ej. como enantiómeros o diastereómeros individuales, o como mezclas enriquecidas en stereoisómeros. Como se explica en mayor detalle a continuación, los estereoisómeros individuales de los compuestos se preparan mediante síntesis a partir de materiales de partida ópticamente activos que contienen los centros quirales deseados o mediante la preparación de mezclas de productos enantioméricos, seguida de separación o resolución, tal como conversión a una mezcla de diastereómeros seguida de separación o recristalización, técnicas cromatográficas, el uso de agentes de resolución quiral o la separación directa de los enantiómeros en columnas cromatográficas quirales. Los compuestos de partida de esteroquímica particular pueden obtenerse en el mercado o prepararse por los métodos descriptos a continuación y resolverse por técnicas bien conocidas en la técnica.

El término "enantiómeros" significa un par de estereoisómeros que son imágenes especulares no superponibles entre sí.

Los términos "diastereoisómeros" o "diastereómeros" significan isómeros ópticos que no son imágenes especulares uno del otro.

Los términos "mezcla racémica" o "racemato" significan una mezcla que contiene partes iguales de enantiómeros individuales.

El término "mezcla no racémica" significa una mezcla que contiene partes no iguales de enantiómeros individuales.

El término "isómero geométrico" significa un isómero estable que resulta de la libertad restringida de rotación alrededor de uniones dobles (p.ej., *cis*-2-buteno y *trans*-2-buteno) o en una estructura cíclica (p. ej. *cis*-1,3-diclorociclobutano y *trans*-1,3-diclorociclobutano). Debido a que pueden presentarse uniones dobles (olefínicas) carbono-carbono, uniones dobles C=N, estructuras cíclicas y similares en los compuestos de la invención, la invención contempla cada uno de los distintos isómeros geométricos estables y mezclas de los mismos, resultante s de las disposiciones de los sustituyentes alrededor de estas uniones dobles y en estas estructuras cíclicas. Los sustituyentes y los

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isómeros se designan usando la convención *cis/trans* o utilizando el sistema *E* o Z, donde el término "*E*" significa sustituyentes de orden superior en lados opuestos de la unión doble, y el término "*Z*" significa sustituyentes de orden superior en el mismo lado de la unión doble. Se ofrece una explicación del isomerismo *E* y *Z* en J. March, Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, 4ta. ed., John Wiley & Sons, 1992, que se incorpora aquí en su totalidad a título de referencia. Varios de los siguientes ejemplos representan isómeros *E* simples, isómeros *Z* simples, y mezclas de isómeros *E/Z*. La determinación de los isómeros *E* y *Z* puede efectuarse por métodos analíticos, tal como cristalografía por rayos X, ^{1}H-RMN, y ^{13}C-RMN.

Algunos de los compuestos de la invención pueden existir en más una forma tautomérica. Como se mencionó previamente, los compuestos de la invención incluyen todos aquellos tautómeros.

Es bien conocido en la técnica que la actividad biológica y farmacológica de un compuesto es sensible a la esteroquímica del compuesto. Así, por ejemplo, los enantiómeros con frecuencia presentan una actividad biológica marcadamente diferente incluyendo diferencias en las propiedades farmacocinéticas, incluyendo el metabolismo, la unión a proteínas y similares, y en las propiedades farmacológicas, incluyendo el tipo de actividad desplegada, el grado de actividad, toxicidad y similares. Así un especialista en la técnica apreciará que un enantiómero puede ser más activo o puede presentar efectos beneficiosos cuando está enriquecido respecto del otro enantiómero o cuando se separa del otro enantiómero. Además, un especialista en la técnica sabrá cómo separar, enriquecer o selectivamente preparar los enantiómeros de los compuestos de la invención a partir de esta revelación y el conocimiento de la técnica anterior.

Así, aunque puede usarse la forma racémica del fármaco, con frecuencia es menos efectivo que administrar una cantidad igual del fármaco enantioméricamente puro, aunque en algunos casos, un enantiómero puede ser farmacológicamente inactivo y solamente serviría como un simple diluyente. Por ejemplo, aunque el ibuprofeno se administró previamente como racemato, se demostró que sólo el isómero *S* del ibuprofeno es efectivo como agente anti-inflamatorio (en el caso del ibuprofeno, de todos modos, aunque el isómero *R* es inactivo, se convierte en vivo en el isómero *S*, aunque la rapidez de acción de la forma racémica del fármaco es menor que la del isómero *S* puro). Además, las actividades farmacológicas de enantiómeros pueden tener diferente actividad biológica. Por ejemplo, la *S*-penicilamina es un agente terapéutico para artritis crónica, mientras que la *R*-penicilamina es tóxica. Efectivamente, algunos enantiómeros purificados tienen ventajas sobre los racematos, ya que se informó que los isómeros

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individuales purificados presentan mayores índices de penetración transdérmica en comparación con la mezcla racémica. Véanse las Patentes Norteamericanas U.S. Nos. 5.114.946 y 4.818.541.

Así, si un enantiómero es farmacológicamente más activo, menos tóxico o presenta una disposición preferida en el cuerpo respecto del otro enantiómero, será más beneficioso terapéuticamente administrar ese enantiómero de modo preferencial. De este modo, el paciente sometido a tratamiento estaría expuesto a una dosis total menor del fármaco y a una menor dosis de un enantiómero que posiblemente es tóxico o un inhibidor del otro enantiómero.

La preparación de enantiómeros puros o mezclas del exceso enantiomérico (ee) deseado o la pureza enantiomérica se realiza por uno o varios de los muchos métodos de: (a) separación o resolución de enantiómeros, o (b) síntesis enantioselectivas conocidas por los especialistas en la técnica, o una combinación de las mismas. Estos métodos de resolución generalmente se basan en reconocimiento quiral e incluyen, por ejemplo, cromatografía usando fases estacionarias quirales, complejamiento enantioselectivo huésped-invitado, resolución o síntesis usando auxiliares quirales, síntesis enantioselectiva, resolución cinética enzimática o no enzimática, o cristalización enantioselectiva espontánea. Tales métodos se revelan en general en Chiral Separation Techniques: A Practical Approach (2da. Ed.), G. Subramanian (ed.), Wiley-VCH, 2000; T.E. Beesley y R.P.W. Scott, Chiral Chromatography, John Wiley & Sons, 1999; y Satinder Ahuja, Chiral Separations by Chromatography, Am. Chem. Soc., 2000. Además existen métodos que también son igualmente bien conocidos para la cuantificación de exceso o pureza enantiomérica, por ejemplo, CG, HPLC, CE, o RMN, y asignación de configuración y conformación absoluta, por ejemplo CD/ORD, cristalografía de rayos X o RMN.

En general, se incluyen todas las formas tautoméricas e isómericas y mezclas, ya sean isómeros geométricos individuales o estereoisómeros o mezclas racémicas o no racémicas, de una estructura o un compuesto químicos, salvo que la esteroquímica específica o forma isomérica se indique específicamente en el nombre o la estructura del compuesto. Generalmente se prefiere un enantiómero cuando se resuelve una mezcla racémica.

D. Administración Farmacéutica y Diagnóstica y Términos y Convenciones del Tratamiento

El término "paciente" incluye a mamíferos humanos y no humanos.

El término "cantidad efectiva" significa una cantidad de un compuesto de acuerdo ccon la invención que en el contexto en el que es administrado o usado, es suficiente para lograr el efecto o resultado deseados. Dependiendo del contexto, el término cantidad efectiva puede incluir o ser sinónimo de una cantidad farmacéuticamente efectiva o una cantidad diagnósticamente efectiva.

Los términos "cantidad farmacéuticamente efectiva" o "cantidad terapéuticamente efectiva" significa una cantidad de un compuesto de acuerdo con la invención que, cuando se administra a un paciente con necesidad del mismo, es suficiente para realizar un tratamiento para estados o cuadros patológicos o trastornos, para los cuales son de utilidad los compuestos. Tal cantidad será suficiente para lograr una respuesta biológica o médica de un tejido, un sistema o un paciente que sea esperado por un investigador o un médico. La cantidad de un compuesto de acuerdo con la invención que constituye una cantidad terapéuticamente efectiva variará dependiendo de factores tales como el compuesto y su actividad biológica, la composición utilizada para la administración, el tiempo de administración, la vía de administración, el índice de excreción del compuesto, la duración del tratamiento, el tipo de estado de enfermedad o trastorno que es sometido a tratamiento y su gravedad, los fármacos utilizados en combinación con o coincidentemente con los compuestos de la invención, y la edad, el peso corporal, el estado general de salud, el sexo y la dieta del paciente. Tal cantidad terapéuticamente efectiva puede determinarse rutinariamente por alguno de conocimiento general en la técnicasobre la base su conocimiento personal, la técnica previo y esta revelación.

El término "cantidad diagnósticamente efectiva" significa una cantidad de un compuesto de acuerdo con la invención que, cuando es usado en un método, dispositivo o ensayo de diagnóstico, es suficiente para lograr el efecto diagnóstico deseado o la actividad biológica deseada necesaria para el método, dispositivo o ensayo de diagnóstico. Una cantidad tal será suficiente para lograr el efecto diagnóstico deseado o la actividad biológica deseada necesaria para el método, dispositivo o ensayo de diagnóstico, que puede incluir una respuesta médica o biológica en un paciente en un sistema o tejido in vitro o in vivo, que puese ser esperada por un científico o un médico. La cantidad de un compuesto de acuerdo con la invención que constituye una cantidad diagnósticamente efectiva variará dependiendo de factores tales como el compuesto y su actividad biológica, el método, dispositivo o ensayo de diagnóstico usados, la composición utilizada par la administración, el tiempo de administración, la vía de administración, el índice de excreción del compuesto, la duración de la administración, los fármacos otros compuestos usados en combinación o conincidentemente con los

compuestos de la invención, y, si un paciente es el objetivo de la administración diagnóstica, la edad, el peso corporal, el estado general de salud, el sexo y la dieta del paciente. Tal cantidad diagnósticamente efectiva puede ser determinada rutinariamente por alguien con conocimiento general en la técnica sobre la base de su conocimiento personal, la técnica previa y esta revelación.

El término "modular" significa la capacidad de un compuesto de alterar la función del receptor de glucocorticoides, mediante, por ejemplo, la unión y estimulación o inhibición de las respuestas funcionales del receptor de glucocorticoides.

El término "modulador" en el contexto de la descripción de los compuestos de acuerdo con la invención significa un compuesto que modula la función del receptor de glucocorticoides. Como tales, los moduladores incluyen, pero sin limitación, a agonistas, agonistas parciales, antagonistas y antagonistas parciales.

El término "agonista" en el contexto de la descripción de los compuestos de acuerdo con la invención significa un compuesto que cuando está unido al receptor de glucocorticoides profundiza o aumenta la función del receptor de glucocorticoides. Como tales, los agonistas incluyen agonistas parciales y agonistas completos.

El término "agonista completo" en el contexto de la descripción de los compuestos de acuerdo con la invención significa un compuesto que provoca la máxima respuesta estimulatoria del receptor de glucocorticoides, inclusive cuando se está en presencia de receptores de glucocorticoides sobrantes (no ocupados).

El término "agonista parcial" en el contexto de la descripción de los compuestos de acuerdo con la invención. significa un compuesto que no puede provocar la máxima respuesta estimulatoria del receptor de glucocorticoides, incluso en concentraciones sufcientes para saturar los receptores de glucocorticoides presentes.

El término "antagonista" en el contexto de la descripción de los compuestos de acuerdo con la invención significa un compuesto que directa o indirectamente inhibe o reprime la función del receptor de glucocorticoides. Como tales, los antagonistas incluyen antagonistas parciales y antagonistas totales.

El término "antagonista total" en el contexto de la descripción de los compuestos de acuerdo con la invención significa un compuesto provoca la máxima respuesta inhibitoria del receptor de glucocorticoides, incluso cuando se está en presencia de receptores de glucocorticoides sobrantes (no ocupados).

El término "antagonista parcial" en el contexto de la descripción de los compuestos de acuerdo con la invención significa un compuesto que no puede provocar la máxima

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respuesta estimulatoria del receptor de glucocorticoides, incluso en concentraciones suficientes para saturar los receptores de glucocorticoides presentes.

Los términos "tratar" o "tratamiento" significan el tratamiento de un estado patológico en un paciente e incluyen:

(I) prevenir el estado patológico en un paciente, en particular, cuando tal paciente presente predisposición genética u otra para tal estado patológico, pero aún no se diagnosticó su presencia;

(II) inhibir o aliviar el estado patológico en un paciente, p. ej. frenando o lentificando su desarrollo, o

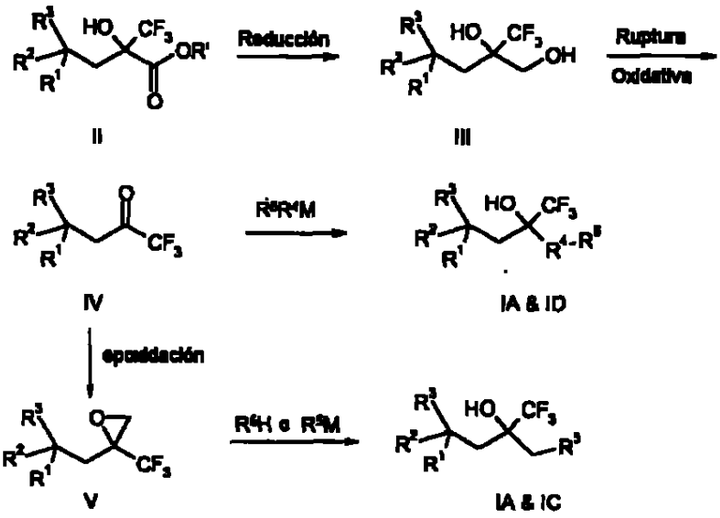
(III) suprimir el estado patológico en un paciente, p. ej. causando regresión o cura del estado patológico.

Métodos generales de síntesis para preparar compuestos de Fórmula (IA), Fórmula (IB), Fórmula (IC), y Fórmula (ID)

La invención asimismo provee procesos para preparar compuestos de Fórmula (IA), Fórmula (IB), Fórmula (IC) y Fórmula (ID). En todos los esquemas, salvo especificación contraria, R^1 a R^5 en las fórmulas a continuación pueden tener el significado de R^1 a R^5 de la fórmula (I) de la invención descrito previamente; y donde sea adecuado, R^1 a R^5 en las fórmulas a continuación pueden tener el significado de R^1 a R^5 de la fórmula (IB), Fórmula (IC) o Fórmula (ID) de la invención previamente descritos. Los intermediarios usados en la preparación de compuestos de la invención pueden obtenerse comercialmente o prepararse mediante métodos conocidos a aquellos especialistas en la técnica.

Las condiciones y tiempos de reacción óptimos pueden varias dependiendo de los reactivos particulares usados. Salvo especificación contraria, pueden ser seleccionados los solventes, las temperaturas, las presiones y otras condiciones de reacción por los especialistas en la técnica. Los procedimientos específicos se brindan en la sección de ejemplos experimentales. Típicamente, el avance de la reacción puede monitorearse mediante cromatografía en capa fina (TLC), si se desea, y los intermediarios y productos pueden purificarse mediante cromatografía en gel de sílice y/o por recristalización.

Pueden prepararse compuestos de Fórmula (IA), Fórmula (IC) y Fórmula (ID) por el método delinado en el Esquema I.



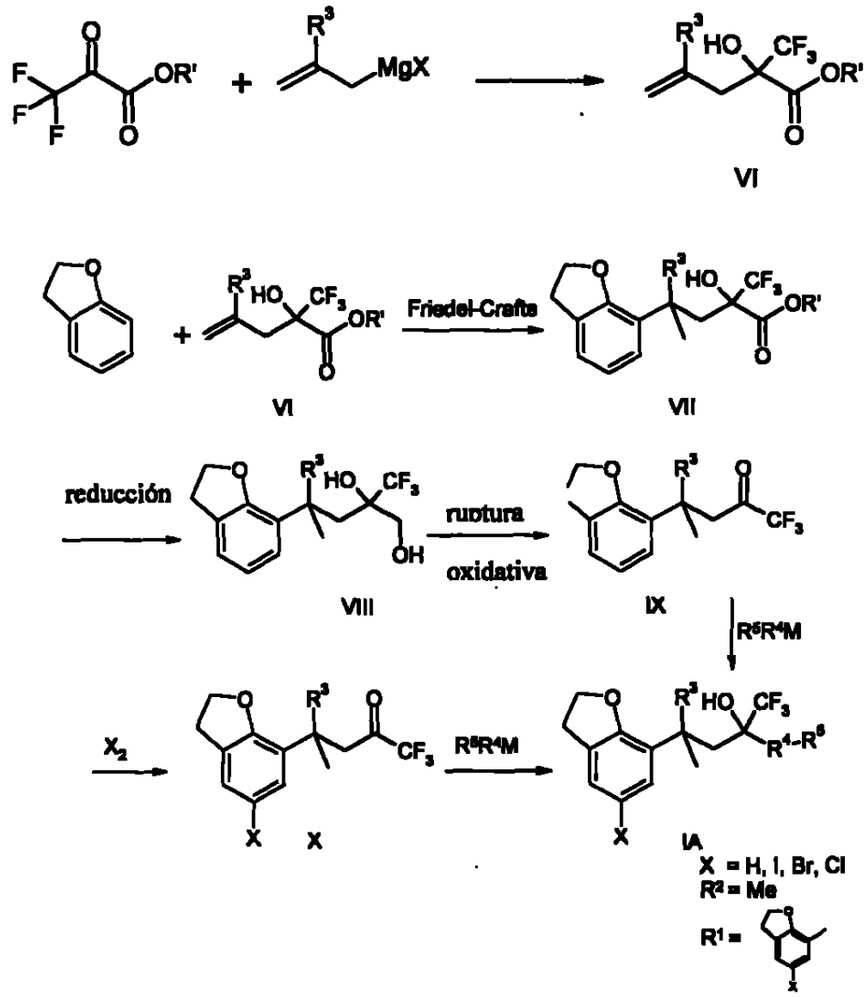
Esquema I

Como se ilustra en el Esquema I, un éster intermediario de Fórmula (II), donde R' es Me o Et, se reduce con un agente reductor adecuado, tal como hidruro de litio y aluminio, en un solvente adecuado, tal como THF o dietiléter, para producir el 1,2-diol de Fórmula (III). La ruptura oxidativa de 1,2-dioles es bien conocida en la técnica y puede realizarse con ácido periódico o tetraacetato de plomo, por ejemplo, en un solvente adecuado, tal como metanol, para dar la cetona (IV). La reacción de la cetona (IV) con un reactivo organometálico adecuado R^5R^4M, tal como un reactivo de Grignard (M es MgBr o MgCl) o un reactivo organolitio (M es Li), en un solvente adecuado tal como THF o dietiléter brinda el compuesto deseado de Fórmula (I). Tales reactivos organolitio o reactivos de Grignard son bien conocidos en la técnica, por ejemplo, los reactivos de Grignard se preparan fácilmente al hacer reaccionar los correspondientes haluros (R^5R^4X, donde X es Br o Cl) con magnesio metálico en un solvente adecuado, tal como dietiléter o THF, en condiciones anhidras. Los reactivos organolitio se preparan fácilmente al hacer reaccionar el R^5R^4H, donde R^5 es heteroarilo, con reactivos de alquillitio, tales como diisopropilamida de litio (LDA) en un solvente adecuado, tal como dietiléter o THF, en condiciones anhidras.

Alternativamente, se hace reaccionar la cetona (IV) con un reactivo adecuado para obtener epóxidos (V). La reacción del epóxido (V) con el R^5H o R^5M deseado (M es Na o Li), brinda el producto deseado de Fórmula (I). La reacción puede llevarse a cabo

calentando R^5H y el epóxido (V) en un solvente adecuado tal como DMF, calentando R^6H y el epóxido (V) juntos en un solvente en presencia de una base adecuada tal como etóxido de sodio en etanol, o haciendo reaccionar R^5M y el epóxido (V) en solventes adecuados tales como DMF o DMSO. Tales reactivos organometálicos pueden generarse mediante tratamiento de R^5H con NaH, LiH u otros reactivos o métodos conocidos por los especialistas en la técnica, en solventes adecuados tales como THF, DMF o DMSO.

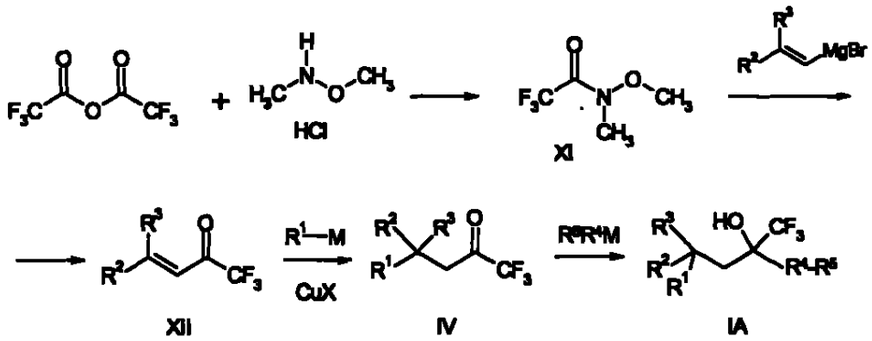
El esquema II delinea otro enfoque que puede usarse para obtener compuestos de Fórmula (IA).



Esquema II

En el esquema II, se hace reaccionar el trifluoropiruvato de etilo con un alil Grignard sustituido para dar una olefina (VI). La reacción de la olefina (VI) con 2,3-dihidrobenzofurano en presencia de un ácido de Lewis adecuado tal como $AlCl_3$, bien conocido en la técnica como la "alquilación Friedel-Craft", da el éster (VII). La reducción del éster (VII) con un agente reductor adecuado tal como hidruro de litio y aluminio (LAH) en un solvente tal como THF da el 1,2-diol (VIII). La ruptura oxidativa del 1,2-diol (VIII) puede efectuarse con peryodato de sodio o tetraacetato de plomo, por ejemplo, en un solvente adecuado, tal como metanol, para dar la cetona (IX). La reacción de la cetona (IX) con un halógeno adecuado (Cl_2, Br_2, o I_2) o reactivos halogenantes tales como *N*-bromosuccinimida (NBS), da la cetona (X). El tratamiento de las cetonas (IX) o (X) con un reactivo organometálico adecuado R^5R^4M, donde M es Li o MgX y X es Cl, Br o I, da el compuesto deseado de Fórmula (I), donde R^1 es un grupo 2,3-dihidrobenzofuranilo opcionalmente sustituido y R^1 es un grupo metilo.

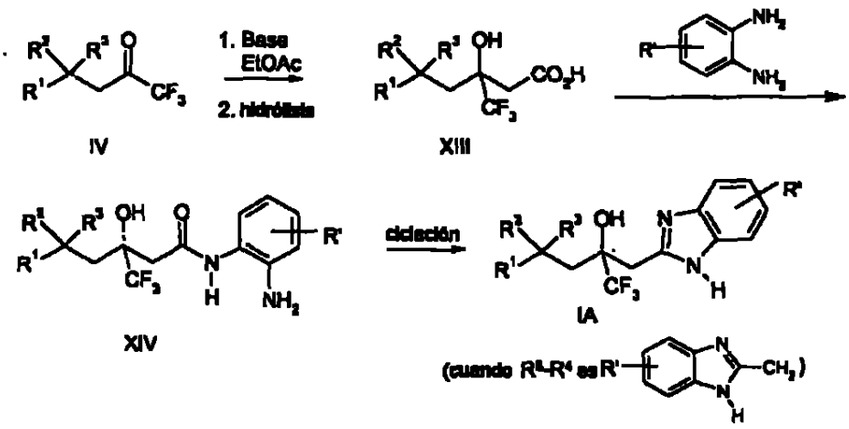
Los compuestos de Fórmula (IA) también pueden prepararse por el método delineado en el Esquema III.



Esquema III

En este enfoque, se acoplan el anhídrido trifluoroacético y el hidrocloruro de *N,O*-dimetilhidroxilamina en condiciones básicas para obtener la trifluoroacetamida (XI) (amida de Weinreb). La amida de Weinreb (XI) se hace reaccionar con un bromuro de vinil magnesio portador de R^2 y R^3 para obtener la trifluorometilenona intermediaria (XII). La trifluorometilenona intermediaria (XII) se trata con un reactivo organocuproso, derivado de un reactivo Grignard u organolitio por tratamiento con una sal de cobre, para obtener el producto de adición 1,4 (IV). Esta trifluorocetona intermediaria (IV) se hace reaccionar con un reactivo organometálico R^4R^5M (como se describe en el Esquema I) para obtener el compuesto deseado de Fórmula (IA).

Los compuestos de Fórmula (IA) donde R^4-R^5 es un grupo benzoimidazol-2-ilmetilo opcionalmente sustituido pueden prepararse mediante el procedimiento delineado

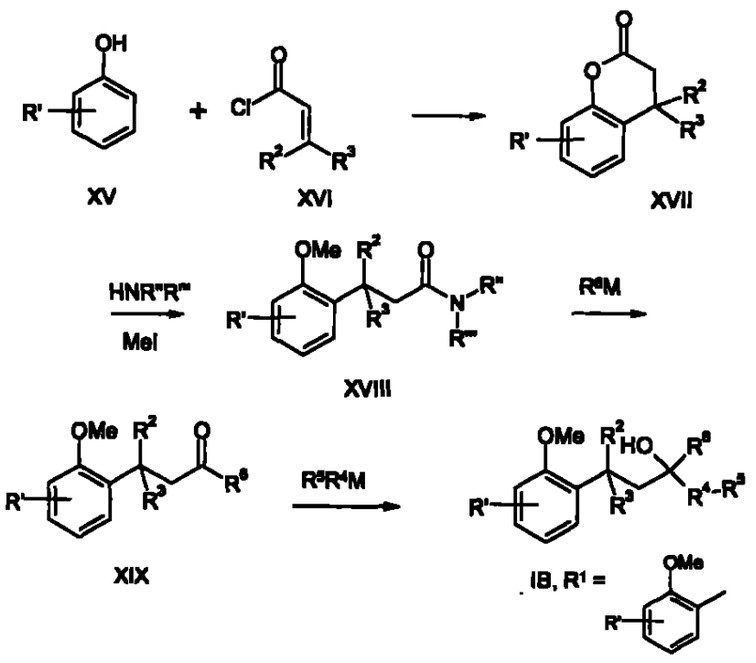


en el Esquema IV.

Esquema IV

Como se ilustra en el Esquema IV, se hace reaccionar la trifluorometilcetona (IV) con acetato de etilo en presencia de una base fuerte, tal como litio diisopropilamida (LDA) en un solvente adecuado tal como THF. El éster intermediario se hidroliza, por ejemplo, por tratamiento con una base acuosa, para obtener un ácido carboxílico intermediario (XIII). Este ácido carboxílico intermediario (XIII) se acopla luego con una fenilendiamina opcionalmente sustituida en condiciones de acoplamiento estándar conocidas en la técnica, por ejemplo por tratamiento con 1-(3-dimetilaminopropil)-3-etilcarbodiimida (EDC) en presencia de 1-hidroxibenzotriazol en un solvente adecuado tal como *N,N*-dimetilformamida (DMF), para obtener el compuesto (XIV). El cierre del anillo por métodos conocidos en la técnica, por ejemplo el cierre del anillo catalizado por ácidos por tratamiento con ácido polifosfórico, da el compuesto deseado de Fórmula (IA).

Los compuestos de Fórmula (IB) pueden prepararse mediante el procedimiento ilustrado en el Esquema V.

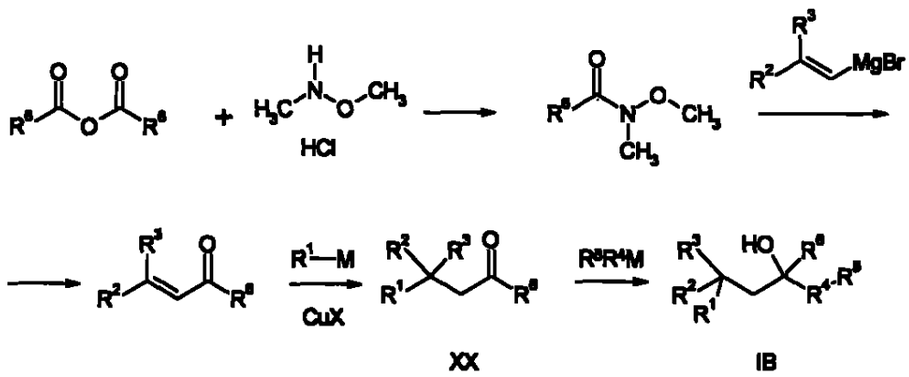


Esquema V

En el Esquema V, el fenol sustituido (XV) se hace reaccionar con cloruro de acriloílo portador de R^2 y R^3 (XVI) en presencia de una base adecuada, tal como trietilamina, para dar un éster intermediario que se cicla por tratamiento con un ácido de Lewis, tal como tricloruro de aluminio, en un solvente adecuado, tal como disufuro de carbono, para obtener la lactona (XVII). La lactona (XVII) se trata con una amina adecuada HNR"R'", tal como morfolina, de modo tal que en la amida resultante (XVIII), -NR"R'" funcionará como un grupo saliente en la posterior reacción. El fenol intermediario que se forma se protege, por ejemplo, por reacción con yoduro de metilo en presencia de una base adecuada tal como hidróxido de potasio para formar el fenol protegido (XVIII), presentando en este caso un grupo metoxi. Luego se hace reaccionar la amida (XVIII) con un reactivo organometálico (R^6M), tal como un reactivo de Grignard (M es MgBr o MgCl) o un reactivo organolítio (M es Li), en un solvente adecuado tal como THF o dietiléter, para dar la cetona (XIX). La reacción de la cetona (XIX) con R^5R^4M como se describe en el último paso del Esquema I brinda el compuesto deseado de Fórmula (IB) donde R^1 es un grupo metoxifenilo opcionalmente sustituido.

En un procedimiento más general, adecuado para una variedad de R^1, puede usarse un método análogo al descripto en el Esquema III. Como se ilustra en el Esquema VI, al utilizar una amida de Weinreb amida portadora de R^6 puede aplicarse el método

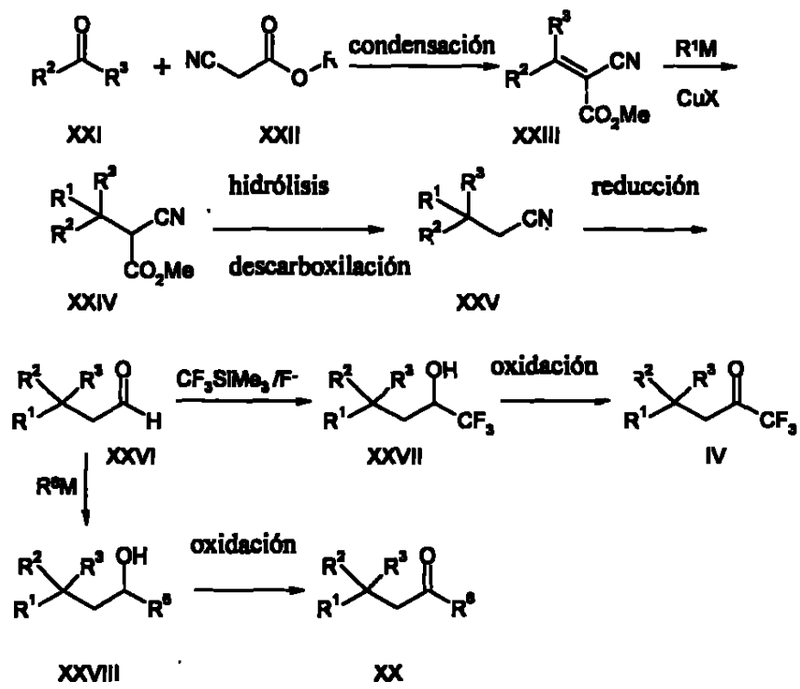
descripto en el Esquema III para preparar la cetona (XX) deseada y el compuesto de Fórmula (IB).



XX IB

Esquema VI

Un método alternativo para preparar un intermediario (IV) en los Esquemas I, III y V, así como la cetona (XX) del Esquema VI, se ilustra en el Esquema VII.



XXI XXII XXIII XXIV XXV XXVI XXVII IV XXVIII XX

Esquema VII

Como se ilustra en el Esquema VII, la cetona portadora de R^1 y R^2 (XXI) se condensa con el éster del ácido cianoacético (XXII), donde R' es Me o Et, en la reacción conocida en la técnica como condensación de Knoevenagel para dar la olefina (XXIII). De la reacción de la olefina (XXIII) con un reactivo organometálico adecuado, tal como R^1M,

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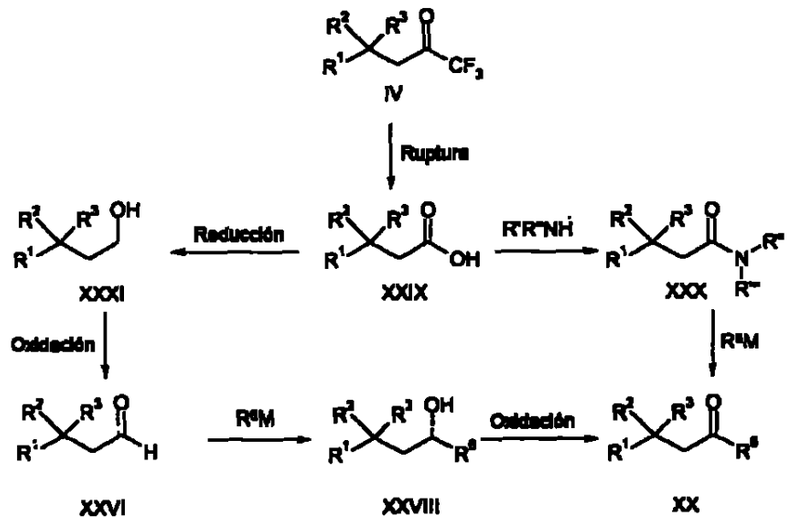
883
883

donde M es MgBr, MgCl, o Li, en presencia de una sal de cobre, tal como CuI, se obtiene el éster (XXIV). La hidrólisis del éster (XXIV) seguida de descarboxilación concomitante del ácido resultante en presencia de un reactivo adecuado, tal como cloruro de sodio, y en una mezcla adecuada de solventes, tal como DMSO y agua, brinda el correspondiente nitrilo (XXV). La reducción del nitrilo (XXV), por ejemplo mediante tratamiento con un agente reductor adecuado, tal como hidruro de diisobutilaluminio (DIBAL), en un solvente adecuado tal como diclorometano, da el aldehído (XXVI). El tratamiento del aldehído (XXVI) con trimetil(trifluorometil)silano en presencia de una adecuada fuente de fluoruro, tal como fluoruro de tetrabutilamonio, da el alcohol (XXVII). La oxidación del alcohol (XXVII) por métodos conocidos en la técnica, tal como el tratamiento con el reactivo periodinano de Dess-Martin, en un solvente adecuado, tal como diclorometano, da la cetona (IV).

Alternativamente, el aldehído (XXVI) se trata con un reactivo organometálico adecuado R^6M, tal como un reactivo de Grignard (M es MgBr o MgCl) o un reactivo organolitio (M es Li), en un solvente adecuado tal como THF o dietiléter para dar el alcohol (XXVIII). La posterior oxidación del alcohol (XXVIII) por un método bien conocido en la técnica da la cetona (XX).

Adicionalmente las cetonas (XX) del Esquema VII pueden prepararse a partir de la cetona (IV) como se describe en el Esquema VIII.

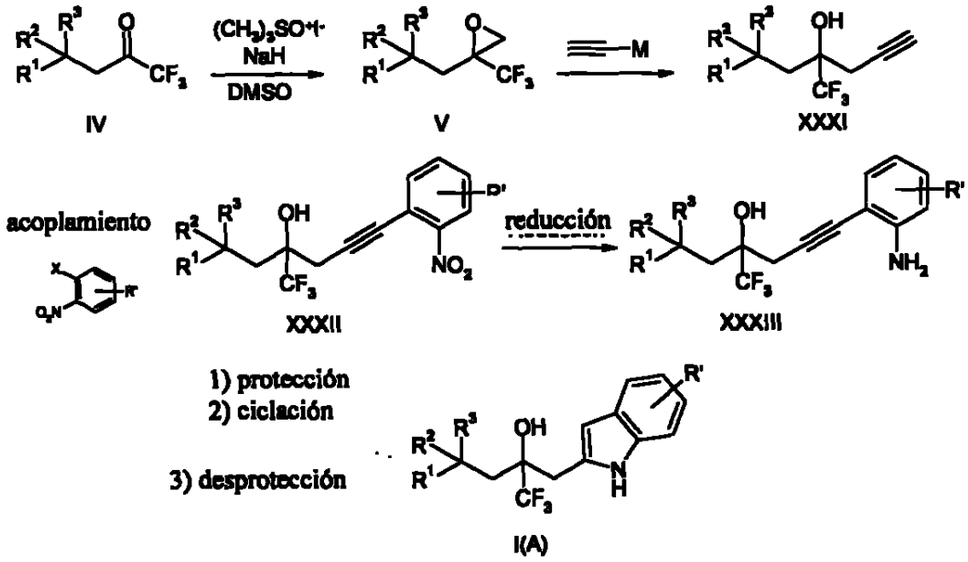


Esquema VIII

En el Esquema VIII, la cetona (IV) se escinde en presencia de una base adecuada, tal como NaOH, y en una mezcla de solventes adecuada, tal como una mezcla de agua y etanol, para dar el ácido (XXIX). El ácido (XXIX) se trata con una amina adecuada HNR"R"', tal como morfolina, de modo tal que -NR"R"' funcionará como un grupo saliente en la posterior reacción. La amida resultante (XXX), luego se hace reaccionar con un reactivo organometálico (R^6M), tal como un reactivo de Grignard (M es MgBr o MgCl) o un reactivo organolitio (M es Li), en un solvente adecuado, tal como THF o dietiléter, para dar la cetona (XX). Alternativamente, el ácido (XXIX) se trata con un agente reductor adecuado tal como hidruro de litio y aluminio (LAH) en un solvente tal como THF, de lo que resulta el alcohol (XXXI). La oxidación del alcohol (XXXI) conforme a métodos conocidos por los especialistas en la técnica, tal como el tratamiento con el reactivo periodinano de Dess-Martin, en un solvente adecuado, tal como diclorometano, proporciona el aldehído (XXVI).

Como se ilustró previamente en el Esquema VII, la reacción del aldehído (XXVI) con un reactivo organometálico adecuado R^6M (M es MgBr, MgCl o Li), en un solvente tal como THF o dietiléter da el alcohol (XXVIII), que se oxida al alcohol (XXVIII) por un método, tal como la oxidación de Swern o el tratamiento con periodinano de Dess-Martin, para dar la cetona (XX).

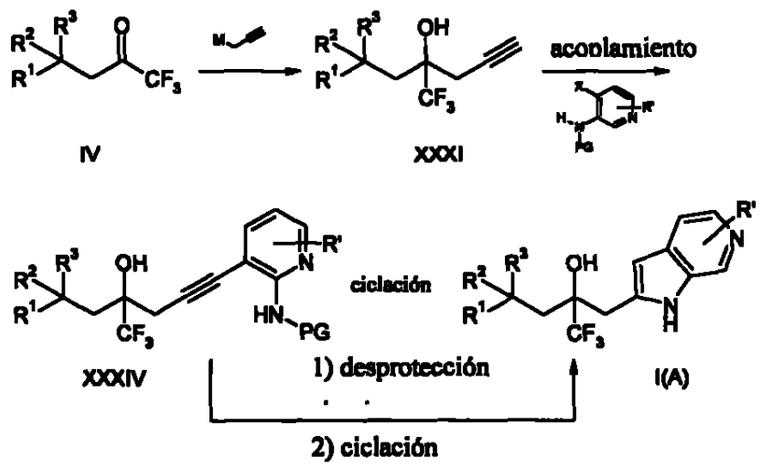
Los compuestos de Fórmula (IA) donde R^4-R^5 es un grupo indol-2-ilmetil opcionalmente sustituido pueden sintetizarse por el procedimiento del Esquema IX.



Esquema IX

Como se representa en el Esquema IX, la reacción de la cetona (IV) con iluro de azufre en un solvente adecuado, tal como DMSO, da el epóxido (V). La apertura del epóxido (V) con un acetiluro reactivo adecuado, tal como trimetilsililacetiluro de litio (M es Li) en un solvente adecuado, tal como DMSO, seguido de desprotección con una sal fluoruro en un solvente adecuado, proporciona el alquino (XXXI). El tratamiento del alquino (XXXI) con un compañero de acoplamiento adecuado, tal como anilina o nitrobenceno opcionalmente sustituidos (X es OTf, I, o Br) en presencia de catalizadores, bases y solventes adecuados (p.ej., diclorobis(trifenilfosfin)paladio (II), CuI, trietilamina, y DMF) proporciona el alquino (XXXII). La reducción del intermediario (XXXII) con un agente reductor metálico adecuado, tal como hierro, en un solvente adecuado, tal como ácido acético, da la anilina (XXXIII). La proteccion de la anilina (XXXIII) con un grupo protector adecuado, tal como trifluoroacetilo es bien conocida en la técnica y puede efectuarse mediante el tratamiento con anhídrido trifluoroacético en un solvente adecuado, tal como diclorometano. El intermediario resultante se cicla con una base adecuada, tal como 1,1,3,3-tetrametil guanidina, en un solvente adecuado, tal como metanol, dando el trifluoroacetil-indol protegido, que se somete a desprotección *in situ* del grupo acilo para dar el compuesto de Fórmula (IA).

Además, los compuestos de Fórmula (IA) donde R^4-R^8 es un grupo azaindol-2-ilmetilo opcionalmente sustituido pueden prepararse mediante el procedimiento ilustrado en el Esquema X.



Esquema X

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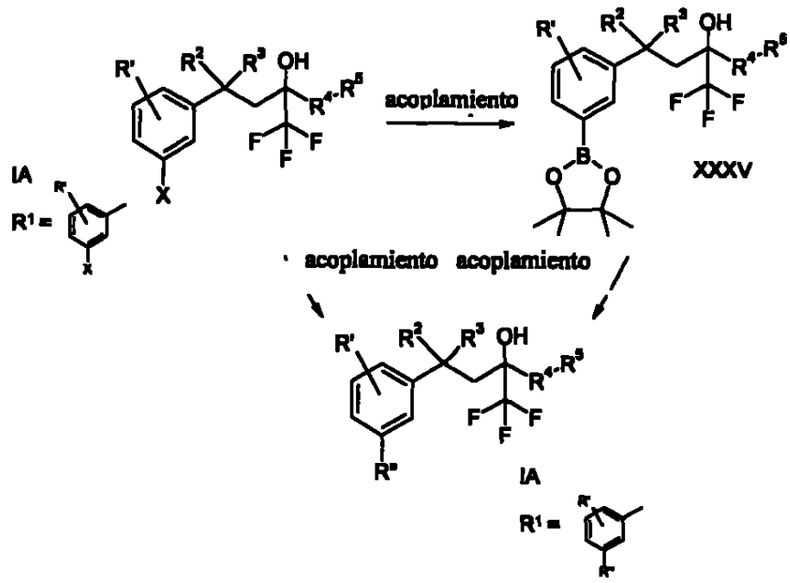
La cetona (IV) se trata con un agente de propargilación adecuado, tal como sesquibromuro de propargil aluminio (M es Al), en un solvente adecuado, tal como THF, para dar el alquino (XXXI). La reacción del alcohol homopropargílico (XXXI) con un compañero de acoplamiento adecuado, tal como amino piridinas protegidas y pirimidinas amono protegidas opcionalmentre sustituidas y piridazinas amino protegidas donde uno o dos átomos seleccionados de A, W, Y y Z son nitrógenos y los átomos restantes son carbonos, (X es I o Br y PG es H o BOC (*ter*-butoxicarbollo)) en presencia de catalizadores, bases y solventes adecuados (p.ej., diclorobis(trifenilfosfin)paladio (II), CuI, trietilamina y DMF) proporciona el alquino (XXXIV). El alquino (XXXIV), cuando PG es H, se convierte en el correspondiente azaindol o diazaindol opcionalmente protegido de Fórmula (IA) por tratamiento con la base adecuada tal como ter-butóxido de potasio, en un solvente adecuado, tal como *N*-metil pirrolidinona (NMP). Además, los alquinos (XXXIV) que contienen un grupo *N*-BOC se ciclan con una base adecuada, tal como 1,8-diazabiciclo[5,4,0]undec-7-eno (DBU), en una mezcla de solventes adecuada, tal como una mezcla de agua y metanol, para obtener el producto deseado de Fórmula (IA). Alternativamente, el grupo protector *N*-BOC del alquino (XXXIV) puede eliminarse por tratamiento con un ácido adecuado, tal como HCl, en un solvente adecuado, tal como acetato de etilo, para dar el correspondiene sal de amino, que se cicla en presencia de ter-butóxido de potasio en NMP para dar el compuesto de Fórmula (IA).

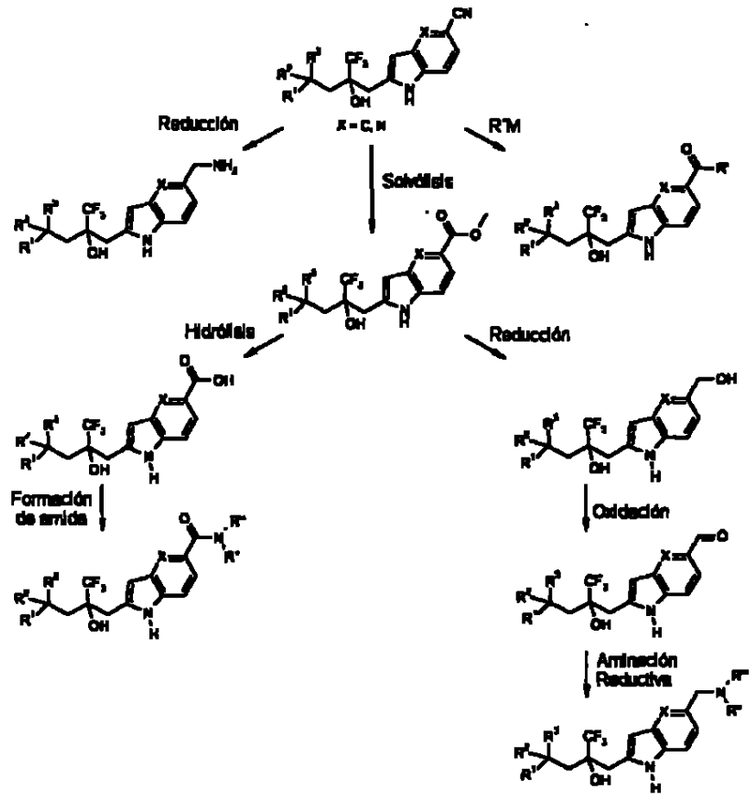
Además, los compuestos de Fórmula (I) en los cuales R^1 es un grupo arilo opcionalmente sustituido pueden convertirse mediante la secuencia ilustrada en el Esquema XI en compuestos de Fórmula (I) donde R^1, además, está opcionalmente funcionalizado.



Esquema XI

Como se delinea en el Esquema XI, los compuestos de Fórmula (I) en los cuales R^1 es un grupo arilo opcionalmente sustituido, en el cual uno de los sustituyentes es un grupo adecuado de acoplamiento, tal como Cl, Br, I u OTf, pueden tratarse con un compañero de acoplamiento adecuado, tal como un ácido borónico o un éster borónico, en un solvente adecuado o una mezcla de solventes, tal como una mezcla de DME, metanol y DMF, en presencia de un catalizador adecuado, tal como tetrakis(trifenilfosfina)paladio (0), con una base apropiada, tal como carbonato de potasio, a una temperatura adecuada y bajo un entorno atmosférico adecuado, tal como argón, para dar compuestos de Fórmula (I) donde R^1 está, además, opcionalmente funcionalizado. Alternativamente, compuestos de Fórmula (I) donde R^1 es un grupo arilo opcionalmente sustituido que contiene un grupo adecuado, tal como Cl, Br, I u OTf, se convierten en sus correspondientes ésteres borónicos (XXXV) reaccionando con un compañero de acoplamiento adecuado, tal como bis(pinacolato)diboro, en condiciones adecuadas, tal como calentamiento a 100°C en DME con carbonato de potasio y en presencia de [1,1'-bis(difenilfosfino)ferroceno]dicloropaladio (II). Posteriormente, el éster borónico de Fórmula (XXXV) puede convertirse en compuestos de Fórmula (I) donde R^1 está opcionalmente funcionalizado por tratamiento con un haluro de arilo adecuado, y en una condición de acoplamiento apropiada, indicada previamente. La elección entre los dos métodos descriptos depende de la disponibilidad comercial o sintética del compañero de acoplamiento, que queda a consideración del experto en la técnica.

Como se ilustra en el Esquema XII, los compuestos de Fórmula (IA) donde R^4R^5 es un azaindol-2-ilmetilo sustituido con ciano o un indol-2-ilmetilo sustituido con ciano pueden convertirse en un compuesto de Fórmula (IA) donde R^4R^5 está opcionalmente funcionalizado.

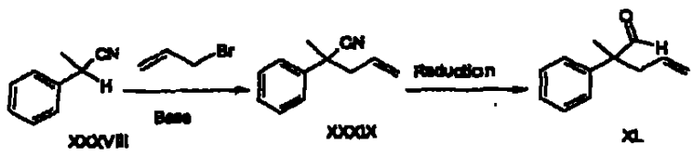


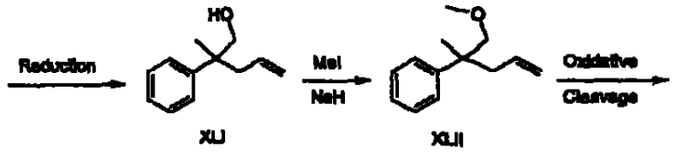
Esquema XII

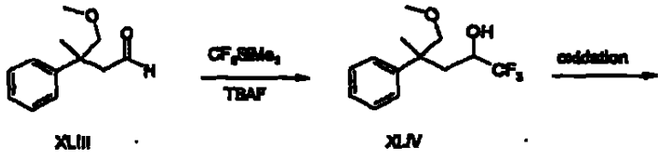
compuestos de Fórmula (IA) donde R^4R^5 es un azaindol-2-ilmetilo sustituido con ciano (X es nitrógeno Y es carbono, o X es un carbón y Y es un nitrógeno) o indol-2-ilmetilo sustituido con ciano (X y Y son carbonos), pueden convertirse en la correspondiente cetona por tratamiento con un reactivo organometálico adecuado tal como R'M, donde M es MgI, MgBr, MgCl, o LI y R' es alquilo, cicloalquilo, arilo, heteroarilo o heterociclilo. La reducción del grupo ciano con un agente reductor adecuado, tal como un complejo de borano-sulfuro de metilo en un solvente adecuado tal como THF, da un compuesto de Fórmula (IA) portador de un resto amino primario. Además, el compuesto de Fórmula (IA) portador de un grupo ciano puede tratarse con un alcohol, tal como metanol, en presencia de un catalizador ácido, tal como HCl, para dar el correspondiente

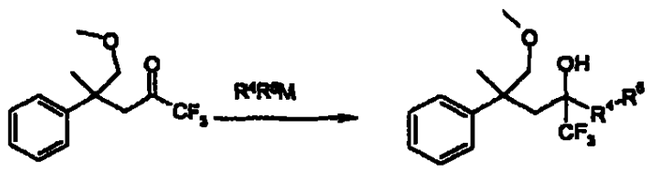
éster. El éster resultante puede hidrolizarse por tratamiento con una base adecuada, tal como hidróxido de litio en una mezcla de solventes adecuada, tal como una mezcla de THF, agua y metanol, para dr un compuesto de Fórmula (IA) que contiene un grupo ácido carboxílico. El ácido carboxílico resultante de Fórmula (IA) puede convertirse en una amida utilizando condiciones de acoplamiento estándar de péptidos conocidas por los especialistas en la técnica. Esta transformación puede efectuarse por tratamiento con una amina adecuada HNR"R"' y un reactivo activante adecuado, tal como 1,3-diciclohexilcarbodiimida (DCC), en presencia de una base adecuada, tal como *N,N*-diisopropiletil amina, en un solvente adecuado, tal como DMF o acetonitrilo. Alternativamente, el compuesto de Fórmula (IA) portador de un grupo éster puede reducirse por tratamiento con un agente reductor adecuado, tal como hidruro de litio y aluminio (LAH), en un solvente adecuado tal como THF, para dar el correspondiente alcohol. La oxidación del alcohol resultante con un agente oxidante adecuado, tal como óxido de manganeso (IV), en un solvente adecuado, tal como acetona, proporciona el compuesto deseado de Fórmula (IA) que contiene un grupo aldehído. Tal aldehído puede convertirse en la correspondiente amina por un método bien conocido en la técnica como la aminación reductiva. Esta inter-conversión de grupos funcionales puede llevarse a cabo por reacción de un aldehído con una amina adecuada HNR"R"' en presencia de un agente reductor adecuado, tal como triacetoxiborohidruro de sodio, y un catalizador ácido apropiado, tal como ácido acético, en un solvente adecuado, tal como 1,2-dicloroetano.

Compuestos de fórmula (ID) se pueden preparar de acuerdo al procedimiento mostrado en el esquema XIII.









XLV (ID)

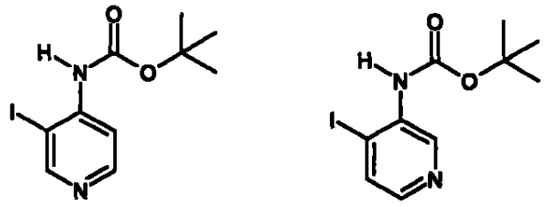
En el esquema XIII, el nitrilo (XXXVIII) se trata con bromuro de alil en presencia de una base adecuada tal como sodio bis (rimetilsilil) amida (NaHMDFS) en un solvente adecuado, tal como DMSO, para dar el correspondiente nitrilo (XXXXIX). Reducción del nitrilo (XXXIX) con un agente reductor adecuado tal como DIBAL en un solvente apropiado, tal como diclorometano, aldehído(XL). Aldehído (XL) es reducido posteriormente mediante reacción con un agente reductor adecuado como litiop aluminio hidrido (LAH) en un solvente adecuado como THF para dar alcohol (XLI). Reacción de alcohol (XLI) con loduro de metilo, en presencia de una base adecuada como hidrido de sodio (NaH) en un solvente apropiado como DMF se obtiene éter (XLII). Eter (XLII) se convierte a aldehído (XLIII) mediante métodos bien conocidos de clavaje oxidativo como tratamiento con ozono. La reaccipon del aldehído (XLIII) con un reactivo nucleofílico trifluorometilante como fluoruro de tetrabutilamonio (TBAF) da alcohol (XLIV). La subsecuente oxidación del alcohol (XLIV) con un reactivo oxidante adecuado como el reactivo de periodinano Dess_Martin, origina trifluorometil cetona (XLV). La reacción de la cetona (XLV) con un reactivo organometálico adecuado R^5R^4M donde M es Li o MgX y X es Cl, Br o I en unsolvente adecuado como THF, da el compuesto de fórmula (ID).

A los efectos de que esta invención sea entendida en su totalidad, se describen los siguientes ejemplos. Estos ejemplos cumplen la función de ilustrar las formas de realización de la presente invención y no deben considerarse limitativos del alcance de la invención en ningún modo ya que, como reconocerá un especialista en la técnica, determinados reactivos o condiciones pueden modificarse según sea necesario para compuestos individuales. Así, aunque los ejemplos ilustran la síntesis de determinados compuestos de la invención o de los intermediarios que pueden utilizarse para sintetizar compuestos de acuerdo con la invención, todos los compuestos aquí revelados pueden prepararse por uno o más métodos aquí revelados, como apreciará un especialista en la técnica. Los materiales de partida utilizados pueden obtenerse comercialmente o

prepararse fácilmente a partir de materiales comercialmente disponibles por parte de los expertos en la técnica.

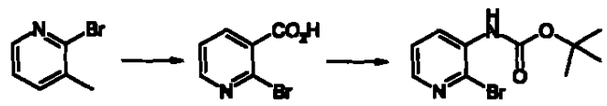
Ejemplos Experimentales

Ejemplo 1: Síntesis de *ter*-butiléster del ácido (3-yodopiridin-4-il)carbámico y *ter*-butiléster del ácido (4-yodopiridin-3-il)carbámico



Se prepararon los productos del título conforme al procedimiento descrito por T.A. Kelly *et al.*, J. Org. Chem., 1995, 60, p. 1875.

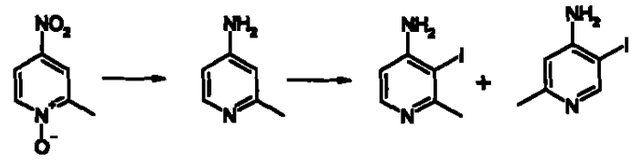
Ejemplo 2: Síntesis de *ter*-butiléster del ácido (2-Bromopiridin-3-il)carbámico



Se agregó 2-bromo-3-metilpiridina (25,0 ml, 213 mmol) a una solución de permanganato de potasio (87,7 g, 555 mmol) en 800 ml de agua y la mezcla se agitó a reflujo. Al cabo de 5 horas, se separaron por destilado 600 ml de agua y la suspensión remanentese filtró. El residuo se lavó con dos porciones de 50 ml de agua caliente y los filtrados combinados se acidificaron con HCl concentrado. El precipitado color blanco se filtró y se secó en un horno al vacío para dar 26,8 g de ácido 2-bromonicotínico (62% de rendimiento).

Se agregó difenilfosforilazida a una solución de ácido 2-bromonicotínico (15,0 g, 74,0 mmol) y trietilamina (11,4 ml, 81,4 mmol) en 140 ml de ter-butanol anhidro. La mezcla de reacción se agitó a reflujo durante 2 horas, se enfrió a temperatura ambiente, y se concentraron al vacío. El residuo se disolvió en 150 ml de acetato de etilo y se lavó con tres porciones de 50 ml de agua, tres porciones de 50 ml de bicarbonato de sodio acuoso saturado, y con dos porciones de 50 ml de salmuera. La capa orgánica se lavó sobre sulfato de magnesio ($MgSO_4$), se filtró, y se concentraron al vacío. El residuo cristalizó estando en reposo y resultaron 15,3 g del producto del título (76% de rendimiento).

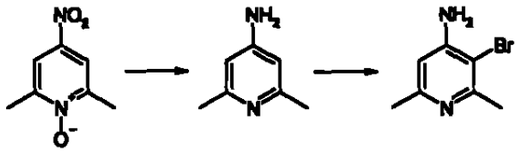
Ejemplo 3: Síntesis de 4-Amino-3-yodo-2-metilpiridina y 4-Amino-3-yodo-6-metilpiridina



Una solución de 2-metil-4-nitropiridina-*N*-óxido (3,80 g, 24,6 mmol) en 100 ml de ácido acético se calentó lentamente con hierro en polvo (6,89 g, 124 mmol) en un gran matraz (atención: la reacción se toma se torna muy exotérmica luego de volverse marrón). La suspensión resultante se calentó durante 2 horas a 80°C. El exceso de ácido acético se eliminó al vacío, el residuo se agregó a una solución acuosa de hidróxido de sodio al 20%, y se agregaron 100 ml de cloroformo ($CHCl_3$) y la mezcla se filtró a través del auxiliar filtrante de CELITE®. Se extrajo la fase acuosa con dos porciones de 200 ml de cloroformo. Las capas orgánicas combinadas se secaron sobre sulfato de magnesio, se filtró, y se concentraron al vacío. El producto en bruto (2,2 g, 83% de rendimiento) se usó sin ulterior purificación.

Una solución de KI (1,96 g, 11,9 mmol) y e_2 (1,87 g, 7,36 mmol) en 10 ml de agua se agregó a una solución a reflujo de 2-metilpiridin-4-ilamina (1,00 g, 9,25 mmol) y carbonato de sodio (683 mg, 6,44 mmol) en 5 ml de agua. La mezcla se calentó a reflujo durante 2 horas, se enfrió a temperatura ambiente, y se trató con 20 ml de acetato de etilo (EtOAc). Se separaron las fases y se extrajo la capa acuosa con tres porciones de 20 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con una solución acuosa saturada de tiosulfato de sodio ($Na_2S_2O_3$), se secaron sobre sulfato de magnesio y se concentraron al vacío. De la cromatografía flash (30% acetato de etilo en hexanos a 100% acetato de etilo, gradiente) del residuo resultante se obtuvo 4-amino-3-yodo-6-metilpiridina (primera elución: 226 mg, 11% de rendimiento) y 4-amino-3-yodo-2-metilpiridina (segunda elución: 116 mg; 5% de rendimiento).

Ejemplo 4: Síntesis de 4-Amino-3-bromo-2,6-dimetilpiridina



Una solución de 4-nitro-2,6-dimetilpiridina-*N*-óxido (11,0 g, 65,4 mmol) en 50 ml de ácido acético se trató con hierro en polvo (21,8 g, 390 mmol) en pequeñas porciones mientras la mezcla se agitó rápidamente y se calentó gradualmente a 50°C (atención: la reacción se toma muy exotérmica a esta temperatura). Al cabo de la reacción exotérmica, la mezcla se calentó durante una hora adicional a 80°C. La mezcla resultante solidificada

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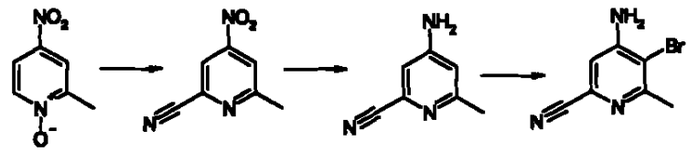
se trató con 50 ml de agua y la suspensión se filtró a través del auxiliar filtrante de CELITE®. El filtrado se trató con *ca.* 200 ml de solución de hidróxido de sodio 6 N hasta que el pH de la solución se tornó básico (>12). La suspensión verde resultante se extrajo con tres porciones de 300 ml de cloroformo. Se combinaron los extractos, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío de lo que resultaron cristales amarillentos (5,70 g, 71% de rendimiento).

Una solución de 2,6-dimetilpiridin-4-ilamina (2,00 g, 16,4 mmol) en 5 ml de ácido acético se trató gota a gota con una solución de bromo (0,84 ml, 16,3 mmol) en 2 ml de ácido acético a temperatura ambiente en un baño de agua durante un período de 10 minutos. Al cabo de 1 hora, La suspensión resultante se trató con 40 ml de una solución de hidróxido de sodio al 20% y se extrajo con tres porciones de 100 ml de diclorometano (CH_2Cl_2). Los extractos combinados se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. El sólido resultante (material de partida-producto deseado-subproducto dibromado (1:3:1)) se disolvió en 100 ml de hexanos calientes y en caliente se filtró para eliminar el material de partida insoluble. Se permitió el enfriamiento del filtrado a temperatura ambiente, para dar el producto del título como finas agujas blancas (1,30 g, 40% de rendimiento).

Ejemplo 5: Síntesis de 4-Amino-3-bromo-6-ciano-2-metilpiridina



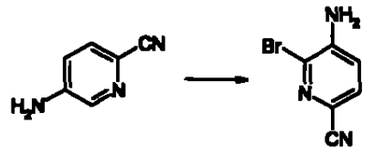
Se calentaron 4-Nitropicolina-*N*-óxido (10,0 g, 64,9 mmol) y sulfato de dimetilo (6,39 ml, 64,5 mmol) a 70°C durante 6 horas bajo una atmósfera de nitrógeno gaseoso (N_2). La mezcla marrón oscuro que solidificó luego de enfriarse a temperatura ambiente se disolvió en 20 ml de agua, se enfrió a -10°C mientras se agitó vigorosamente, y se trató gota a gota con una solución de KCN (5,04 g, 77,4 mmol) en 20 ml de agua. La mezcla se calentó a temperatura ambiente hasta el día siguiente. La mezcla heterogénea negra resultante se disolvió en 50 ml de acetato de etilo y 50 ml de agua. Se separaron las fases y se extrajo la capa acuosa con dos porciones de 50 ml de acetato de etilo. Las capas orgánicas combinadas se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. De la cromatografía flash (20% a 50% acetato de etilo en hexanos, gradiente) resultó el producto como un sólido marrón (2,80 g, 27% de rendimiento).

Se calentó 2-ciano-6-metil-4-nitropiridina (1,9 g, 11,6 mmol) en una mezcla de 50 ml de etanol y 15 ml de solución de cloruro de amonio saturado acuoso (NH_4Cl) con indio

en polvo (7,00 g, 60,9 mmol) a 60°C durante 3 días. Luego se agregó 20 ml de agua, y la suspensión se filtró a través del auxiliar filtrante de CELITE® y el lecho se lavó con metanol. El filtrado se concentró al vacío para remover los orgánicos volátiles y se extrajo con tres porciones de 20 ml de diclorometano. Los extractos combinados se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. De la cromatografía en SiO_2 (30% de acetato de etilo en hexanos a 100% de acetato de etilo, gradiente) resultó el producto como un sólido (580 mg, 27% de rendimiento).

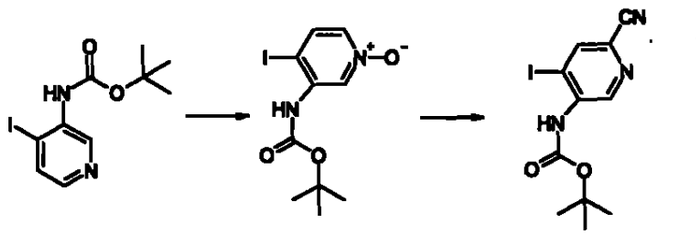
El 4-amino-6-metilpiridina-2-carbonitrilo se convirtió en el producto del título con un rendimiento del 57% conforme al procedimiento descrito para la preparación de 4-amino-3-bromo-2,6-dimetilpiridina.

Ejemplo 6: Síntesis de 5-Amino-6-bromopiridina-2-carbonitrilo



Se disolvió 5-aminopiridina-2-carbonitrilo (2,38 g, 20 mmol) en 6 ml de ácido acético glacial. Una solución de bromo (1 ml, 20 mmol) en 2,5 ml de ácido acético glacial se agregó gota a gota durante un período de 30 minutos mientras se mantuvo la temperatura ambiente con un baño de agua. La suspensión resultante se agitó durante 1 hora a temperatura ambiente, se trató con 50 ml de una solución acuosa de hidróxido de sodio al 20% y se extrajo con tres porciones de 160 ml de diclorometano. Las capas orgánicas combinadas se secaron sobre sulfato de sodio (Na_2SO_4), se filtraron y se concentraron al vacío. El residuo se purificó por cristalización de acetato de etilo-hexanos para dar 5-amino-6-bromopiridina-2-carbonitrilo (1,42 g, 35% de rendimiento).

Ejemplo 7: Síntesis de *ter*-butiléster del ácido (6-Ciano-4-yodopiridin-3-il)carbámico

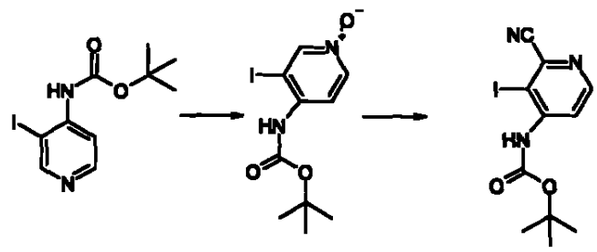


Se disolvió *ter*-butiléster del ácido (4-yodopiridin-3-il)carbámico (3,2 g, 10 mmol) en 100 ml de dimetoxietano a temperatura ambiente. Se agregó ácido *m*-cloroperoxibenzoico (77% en peso, 3,36 g, 15 mmol) y la reacción se agitó hasta el día siguiente a temperatura ambiente. La mezcla se concentraron al vacío, se redisolvió en 400 ml de acetato de etilo, y se lavó con dos porciones de 200 ml de solución saturada de

bicarbonato de sodio ($NaHCO_3$). Se separaron las fases y se extrajo la capa acuosa con dos porciones de 100 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. De la cristalización de acetato de etilo-hexanos se obtuvo el *ter*-butiléster del ácido (4-yodo-1-oxipiridin-3-il)carbámico (2,65 g, 79% de rendimiento).

Una mezcla de *ter*-butiléster del ácido (4-yodo-1-oxipiridin-3-il)carbámico (2,65 g, 7,6 mmol), cianuro de trimetilsililo (4 ml, 30 mmol), trietilamina (2,6 ml, 18,9 mmol), y 40 ml de acetonitrilo anhidro se calentó a 90°C durante 2,5 horas. La mezcla se concentraron al vacío, se diluyó con 500 ml de diclorometano, y se trató con una solución de carbonato de sodio saturada acuosa (Na_2CO_3) hasta que la capa acuosa se tornó básica. Después de haber separado las fases, la capa orgánica se lavó con salmuera, se secó sobre sulfato de sodio, se filtró, y se concentraron al vacío. De la cromatografía sobre SiO_2 (2:98 a 8:92 acetato de etilo-hexanos, gradiente) se obtuvo *ter*-butiléster del ácido (6-ciano-4-yodopiridin-3-il)carbámico (185 mg, 7% de rendimiento).

Ejemplo 8: Síntesis de *ter*-butiléster del ácido (2-Ciano-3-yodopiridin-4-il)carbámico

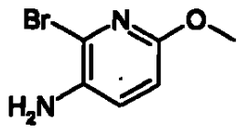


Se disolvió *ter*-butiléster del ácido (3-yodopiridin-4-il)carbámico (3,2 g, 10 mmol) en 100 ml de dimetoxietano a temperatura ambiente. Se agregó ácido *m*-Cloroperoxibenzoico (77% en peso, 3,36 g, 15 mmol) y la reacción se agitó hasta el día siguiente a temperatura ambiente. Al cabo de remover el solvente al vacío, el residuo se disolvió en 400 ml de acetato de etilo y se lavó con dos porciones de 200 ml de una solución de bicarbonato de sodio acuoso saturado. Se separaron las fases y se extrajo la capa acuosa con dos porciones de 100 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. De la cristalización de acetato de etilo-hexanos se obtuvo *ter*-butiléster del ácido (3-yodo-1-oxipiridin-4-il)carbámico (1,95 g, 58% de rendimiento).

Una mezcla de *ter*-butiléster del ácido (3-yodo-1-oxipiridin-4-il)carbámico (1,95 g, 5,79 mmol), cianuro de trimetilsililo (3 ml, 23 mmol), y trietilamina (2 ml, 14,5 mmol) en 30 ml de acetonitrilo anhidro se calentó a reflujo a 90°C durante 2,5 horas. El solvente luego se eliminó al vacío. El residuo se diluyó con 500 ml de diclorometano y se trató

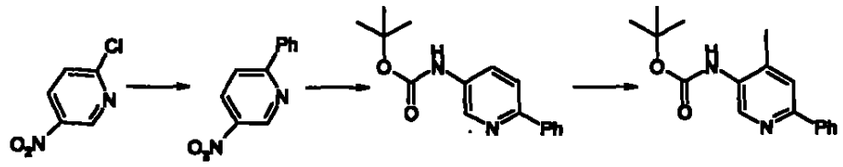
con una solución acuosa saturada de carbonato de sodio hasta que la capa acuosa se tornó básica. Se separaron las fases y la capa orgánica se lavó con salmuera, se secaron sobre sulfato de sodio, se filtró, y se concentraron al vacío. De la cromatografía sobre SiO_2 (2:98 a 8:92 acetato de etilo-hexanos, gradiente) se obtuvo *ter*-butiléster del ácido (2-ciano-3-yodopiridin-4-il)carbámico (1,22 g, 61% de rendimiento).

Ejemplo 9: Síntesis de 5-amino-6-bromo-2-metoxipiridina



Una mezcla agitada de 2-metoxi-5-aminopiridina (10 g, 0,081 mol, 1,0 equiv) y acetato de sodio (6,6 g, 0,081 mol, 1,0 equiv) en 60 ml de ácido acético se trató gota a gota con bromo (12,9 g, 0,081 mol, 1,0 equiv). Al cabo de 20 minutos, la mezcla de reacción se vertió en 1000 ml de una solución acuosa de hidróxido de sodio al 10% y se extrajo con tres porciones de 250 ml de acetato de etilo. Las capas orgánicas combinadas se secaron sobre sulfato de magnesio, se filtraron y se evaporaron a sequedad. De la cromatografía sobre SiO_2 (20% hexanos en diclorometano) se obtuvo 5-amino-6-bromo-2-metoxipiridina (6,5 g, 40% de rendimiento) como un sólido color púrpura.

Ejemplo 10: Síntesis de *ter*-butiléster del ácido (4-Yodo-6-fenilpiridin-3-il)carbámico



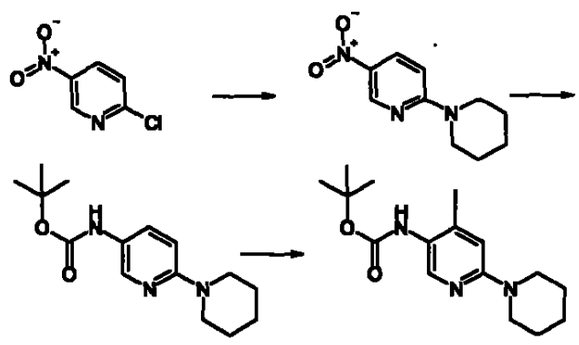
Una mezcla de $Pd(PPh_3)_4$ (354 mg, 1,58 mmol), 2-cloro-5-nitropiridina (5,00 g, 31,5 mmol), y ácido fenilborónico (4,61 g, 37,8 mmol) se gasificó y se llenó tres veces con gas nitrógeno. La mezcla se trató con 40 ml de DME y una solución de carbonato de potasio acuoso 2 M (80,0 mmol) y se calentó a reflujo. Al cabo de 4 horas, la mezcla de reacción se enfrió a temperatura ambiente y se diluyó con 100 ml de acetato de etilo y 50 ml de agua. Se separaron las fases y se extrajo la capa acuosa con tres porciones de 100 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con 100 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. De la cromatografía sobre SiO_2 (0% a 50% de acetato de etilo en hexanos, gradiente) se obtuvieron 4,60 g de 5-nitro-2-fenilpiridina (73% de rendimiento).

Una solución de 5-nitro-2-fenilpiridina (4,60 g, 23,0 mmol) y anhídrido BOC (15,0 g, 68,9 mmol) en una mezcla de 25 ml de metanol y 25 ml de acetato de etilo se trató con

paladio (10% sobre carbón, 500 mg). La mezcla resultante se agitó bajo 50 psi de hidrógeno gaseoso (H_2) a temperatura ambiente. Al cabo de 18 horas, la mezcla se diluyó con 20 ml de diclorometano, se filtró a través de un lecho del auxiliar filtrante de CELITE®, y se concentraron al vacío. El sólido resultante se trituró con acetato de etilo, se filtró y se secó para dar 5,54 g de *ter*-butiléster del ácido (6-fenilpiridin-3-il)carbámico como sólido blanco (89% de rendimiento).

Una solución de *ter*-butiléster del ácido (6-fenilpiridin-3-il)carbámico (5,54 g, 20,5 mmol) y TMEDA (6,49 ml, 43,0 mmol) en 100 ml de dietiléter anhidro se trató con *n*-BuLi a -78°C. Al cabo de 15 minutos a -78°C, la mezcla se calentó a -10°C y se agitó durante otras 3 horas. La mezcla de reacción luego se enfrió a -78°C y se agregó una solución de yodo en una mezcla de 10 ml de THF y 100 ml de dietiléter gota a gota. Al cabo de 2 horas a -78°C, se permitió a la mezcla calentarse a 0°C y se desactivó con 400 ml de una solución acuosa saturada de cloruro de amonio. La capa orgánica se lavó con cinco porciones de 100 ml de tiosulfato de sodio saturado acuoso. Las capas acuosas combinadas se extrajeron con tres porciones de 200 ml de acetato de etilo. Las capas orgánicas combinadas se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. De la cromatografía sobre SiO_2 (0% a 70% acetato de etilo en hexanos, gradiente) resultaron 900 mg del producto del título como aceite amarillo que se solidificó al cabo del tiempo (11% de rendimiento).

Ejemplo 11: Síntesis de *ter*-butiléster del ácido (4'-Yodo-3,4,5,6-tetrahidro-2*H*-[1,2']bipiridinil-5'-il)carbámico



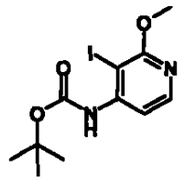
Se disolvió 2-cloro-5-nitropiridina (10 g, 63,3 mmol) en 150 ml de THF. Luego se agregó 20 ml de piperidina y la mezcla resultante se agitó durante 18 horas a temperatura ambiente. La mezcla de reacción con precipitado copioso luego se diluyó con 200 ml de agua y 100 ml de dietiléter. Las capas se mezclaron cuidadosamente y se separaron. La capa orgánica se lavó sobre sulfato de sodio y se concentraron al vacío. El sólido color amarillo brillantese redisolvió en 35 ml de diclorometano y, agitando vigorosamentese

agregaron hexanos hasta que el producto comenzó a precipitar. El sólido color amarillo brillantese colectó por filtración y se secó para obtener 12,5 g de 5'-nitro-3,4,5,6-tetrahidro-2*H*-[1,2']bipiridinilo.

Se suspendió 5'-nitro-3,4,5,6-tetrahidro-2*H*-[1,2']bipiridinilo (12,5 g, 60,4 mmol) en 125 ml de metanol en un agitador Parr y se agregaron 16 g de di-*ter*-butildicarbonato, seguido de 500 mg de óxido de platino. La mezcla resultante se agitó bajo 55 psi de hidrógeno gaseoso durante 2 horas, seguido de agitación bajo atmósfera de argón hasta el día siguiente. Al cabo de 16 horas, la mezcla se filtró a través de un lecho de tierra diatomea y se concentraron al vacío. El residuo en bruto se trituró con hexanos y se filtró La cromatografía en gel de sílice (100% diclorometano a 30% acetato de etilo en diclorometano, gradiente) proporcionó 6,9 g (41,2% de rendimiento) de *ter*-butiléster del ácido (3,4,5,6-tetrahidro-2*H*-[1,2']bipiridinil-5'-il)carbámico como un sólido color blanco.

El producto del título se preparó a partir de *ter*-butiléster del ácido (3,4,5,6-tetrahidro-2*H*-[1,2']bipiridinil-5'-il)carbámico del mismo modo que el descripto para la preparación del *ter*-butiléster del ácido (4-yodo-6-fenilpiridin-3-il)carbámico.

Ejemplo 12: Síntesis de 4-[(*ter*-Butoxicarbonil)amino]-3-yodo-2-metoxipiridina

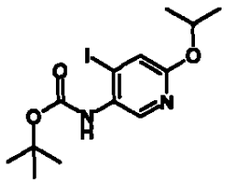


Se disolvió 4-amino-2-cloropiridina (15 g, 117 mmol, 1,0 equiv) en 100 ml de THF. Se gragó una solución de metóxido de sodio en metanol (1,0 M, 234 ml, 234 mmol, 2,0 equiv) la solución resultante se sometió a reflujo durante 16 horas. La mezcla de reacción se vertió en 500 ml de una solución saturada de bicarbonato de sodio agitada rápidamente. Se agregó 500 ml de acetato de etilo y se separaron las capas. La capa orgánica se lavó sobre sulfato de sodio, se decantó, y se concentró al vacío. De la cromatografía sobre SiO_2 (30% acetato de etilo en hexanos) se obtuvo el compuesto del título como un sólido amarillo (2,1 g).

Se disolvió 4-amino-2-metoxipiridina (2,1 g, 16,9 mmol, 1,0 equiv) en 35 ml de acetato de etilo. Se agregó BOC anhídrido (5,4 g, 25,4 mmol, 1,5 equiv) y la solución resultante se sometió a reflujo durante 3 horas. La reacción se enfrió y se concentraron al vacío. El residuo se trituró con 100 ml de hexanos para dar precipitado color blanquecino que se recogió y se secó al vacío para dar el producto del título (1,8 g).

Una solución de 4-[(*ter*-butoxicarbonil)amino]-2-metoxipiridina (1,8 g, 8,03 mmol, 1,0 equiv) en 100 ml de dietiléter anhidro se trató con 2,79 ml de *N,N,N',N'*-tetrametiletilenodiamina (18,5 mmol, 2,3 equiv) bajo una atmósfera inerte. La solución resultante se enfrió a -78°C, se trató con *n*-BuLi (2,5 M, 7,2 ml, 18,0 mmol, 2,24 equiv) y se calentó a -7°C. La reacción se agitó a -7°C a 0°C durante 3 horas, se enfrió a -78°C y se trató con una solución de yodo (3,05 g, 12 mmol) en 30 ml de THF anhidro. La mezcla resultante se agitó a temperatura ambiente durante 16 horas. Se agregaron 200 ml de una solución saturada de cloruro de amonio y 100 ml de dietiléter. Se separaron las fases y la capa orgánica se lavó con 100 ml de tiosulfato de sodio (solución acuosa al 10%), se secaron sobre sulfato de sodio, se decantó, y se concentraron al vacío. La cromatografía sobre SiO_2 (100% diclorometano a 5% de metanol en diclorometano, gradiente) proporcionó el producto del título (650 mg, 23% de rendimiento) como una cera blanca.

Ejemplo 13: Síntesis de 5-[(*ter*-Butoxicarbonil)amino]-4-yodo-2-(isopropoxi)piridina



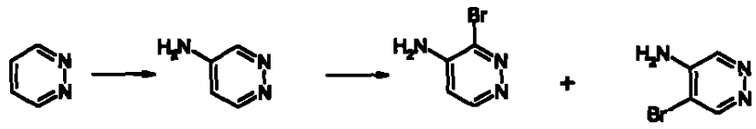
Una mezcla de 2-cloro-5-nitropiridina (15 g, 95 mmol) y 28 ml de alcohol isopropílico (366 mmol) en 100 ml de THF anhidro se agitó hasta disolver los sólidos. La solución resultante se enfrió en un baño helado y se trató gota a gota con ter-butóxido de potasio (1 M en THF, 115 ml, 115 mmol) durante 45 minutos. La reacción se desactivó con 75 ml de solución acuosa saturada de cloruro de amonio y se diluyó con 100 ml de acetato de etilo. Se separaron las fases y la capa orgánica se lavó sobre sulfato de magnesio, se filtraron y se concentraron al vacío. Este residuo se trituró con hexanos y se agitó a temperatura ambiente hasta el día siguiente. La mezcla se filtró y el filtrado se concentró al vacío para obtener 15,7 g de aceite color naranja oscuro, que se usó en el póximo paso sin otra purificación.

Se disolvió 5-nitro-2-isopropoxipiridina (15,7 g, 86 mmol) en 125 ml de metanol y se transfirió a un recipiente Parr. Se agregó paladio (10% sobre carbón, 1,57 g) y BOC anhídrido (28,2 g, 129 mmol). La mezcla resultante se agitó en un agitador Parr bajo 50 psi de hidrógeno gaseoso hasta el día siguiente. La mezcla se trató con 5 g del auxiliar filtrante de CELITE®, se filtró a través de un lecho del auxiliar filtrante de CELITE® y se concentraron al vacío. De la cromatografía sobre SiO_2 (hexanos-acetato de etilo (9:1)) se

obutvo un sólido rosado (16,1 g). Estesólido se disolvió en diclorometano, se trató con hexanos, y se filtró, para dar 13,7 g del producto del título como un sólido color blanco.

Una solución de 13,7 g de 5-[(*ter*-butoxicarbonil)amino]-2-(isopropoxi)piridina (54,3 mmol) y 16,1 ml de *N,N,N',N'*-tetrametiletilenodiamina (120 mmol) en 200 ml de dietiléter anhidro se enfrió a -78°C y se trató con *n*-BuLi (2,5 M en hexanos, 48 ml, 120 mmol) bajo una atmósfera inerte. La mezcla se colocó en un baño a -8°C durante 1 hora y se permitió calentar lentamente a temperatura ambiente. Al cabo de 40 minutos, se enfrió el matraz a -8°C y se agitó durante 4 horas. La mezcla luego se enfrió a -78°C, se trató con una solución de yodo (19,0 g, 75 mmol) en 100 ml de THF anhidro, y la mezcla resultante se agitó durante 16 horas mientras se permitió el calentamiento del baño a 11°C. La mezcla de reacción se vertió en una solución saturada de cloruro de amonio en agitación rápida (200 ml) y se diluyó con 100 ml de agua y 300 ml de dietiléter. Se separaron las fases y se extrajo la capa acuosa con 200 ml de dietiléter. Las capas orgánicas combinadas se lavaron con dos porciones de 200 ml de tiosulfato de sodio (solución acuosa al 10%), se secaron sobre sulfato de sodio, se decantó, y se concentraron al vacío. De la cromatografía sobre SiO_2 (10% a 50% acetato de etilo en hexanos, gradiente) se obtuvo el producto del título como un aceite, que se solidificó estando en reposo (13 g, 63% de rendimiento).

Ejemplo 14: Síntesis de 4-Amino-3-bromopiridazina y 4-Amino-5-bromopiridazina



Se condensaron 50 ml de amoníaco en un matraz de tres bocas de 200 ml, equipado con un refrigerante de hielo seco. Luego de agregar un cristal de $Fe(NO_3)_3$, se agegó potasio (468 mg, 12,0 mmol) en pequeños trozos, se enfrió a -78°C. Se retiró el baño refrigerante y la mezcla de color azul oscuro intenso se sometió a un suave reflujo hasta obtener una suspensión color gris claro. Luego de enfriar a -78°C, se agregaron 0,35 ml (4,80 mmol) de piridazina y la mezcla se agitó durante 10 minutos. Se agregó $KMnO_4$ (2,65 g, 16,8 mmol) sólido en pequeñas porciones, se retiró el baño refrigerante, y la mezcla se agitó durante 10 minutos. La reacción se desactivó cuidadosamente con 1,2 g de cloruro de amonio sólido. Se agregaron 20 ml de metanol y se dejó evaporar el amoníaco bajo campana. La mezcla negra se filtró a través del auxiliar filtrante de CELITE®, el filtrado se concentró al vacío, y el sólido negro resultante se purificó sobre SiO_2 (100% CH_2Cl_2 a 10% MeOH en CH_2Cl_2, gradiente) para obtener piridazin-4-ilamina como un sólido amarronado (380 mg; 83% de rendimiento).

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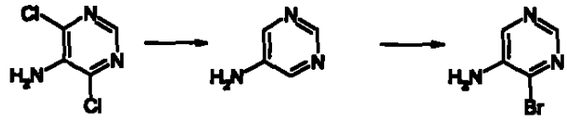
Se realizó la bromación de piridazin-4-ilamina del mismo modo que para la preparación de 4-amino-3-bromo-2,6-dimetilpiridina. De la cromatografía sobre SiO_2 (20% de acetato de etilo en hexanos a 100% acetato de etilo, gradiente, seguido de 2% de metanol en acetato de etilo) se obtuvo 4-amino-3-bromopiridazina (primera elución: 15% de rendimiento) y 4-amino-5-bromopiridazina (segunda elución: 5% de rendimiento) como sólidos tostados.

Ejemplo 15: Síntesis de 5-amino-4-bromopirimidina



Una solución de 5-amino-4,6-dicloropirimidina (5,0 g, 30,5 mmol) en 250 ml de dietiléter se trató con una solución de hidróxido de sodio (20,0 g, 0,50 mol, en 60 ml de agua) y paladio (10% sobre carbón, 400 mg). La mezcla se agitó a temperatura ambiente en un agitador Parr bajo 50 psi de hidrógeno gaseoso durante 20 horas. La mezcla se filtró a través del auxiliar filtrante de CELITE®. Se separaron las fases y se extrajo la capa acuosa con tres porciones de 100 ml de acetato de etilo. Las capas orgánicas combinadas se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. De la cristalización del producto en bruto a partir de acetato de etilo se obtuvo pirimidin-5-ilamina como un sólido cristalino color blanco (2,8 g, 95% de rendimiento).

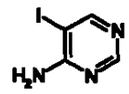
Se realizó la bromación de pirimidin-5-ilamina del mismo modo que para la preparación de 4-amino-3-bromo-2,6-dimetilpiridina. El producto en bruto resultante (300 mg, 35% de rendimiento) se consideró puro y se usó sin otra purificación.

Alternativamente, el 5-amino-4-bromopirimidina se puede sintetizar de acuerdo al siguiente procedimiento. Una solución de 4,6-dicloro-5-aminopirimidina (21 g, 128 mmol) en 250 ml de MeOH fur secuencialmente tratada con nformato de amonio (45 g, 714 mmol) y paladio (10% de carbón, 1g, 0.943 mmol) a 0°C. La mezclas se agito toda la noche a temperatura ambiente y luego filtrada a través de filtro CELITE. El filtrado se concentró para dar un sólido amamrillo. Se adicionaron 100 ml de agua y 250 ml de acetato de etilo.la fase orgánica se separó y la capa acuosa se extrajo con 8 porciones de 250 ml de etil acetato. Las capas orgánicas combinadas se secaron sobre sulfato de magnesio, filtradas y concentradas al vacío para un rendimiento de cristales blancos (8.1 g, 67%).

Una solución agitada de 5-aminopirimidina (3.0 g, 315 mmol) en 150 ml de diclorometano y 30 ml de metanol se enfriaron a 0C. se adicionó bencitrimetilamonio

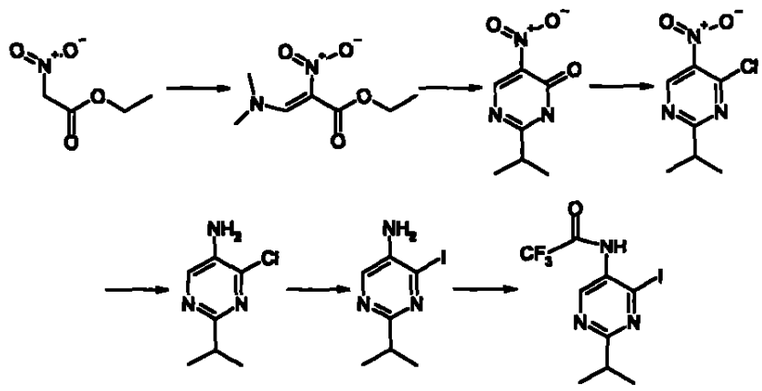
(13.5g, 34.7 mmol) en porciones por 10 minutos. La agitación continuó a 0°C por 15 minutos y a temperatura ambiente durante 90 minutos. La mexcla de reacción se trató soluciòin de bicarbonato de sodio acuoso hasta pH 8. la fase orgánica se separó y la fase acuosa se extrajo con tres prociones de 30 ml de etil acetato. Los extractos org´panicos combinados se secaron sobre sulfato de sodio, filtrados y concentrados al vacío. Se obtuvo un sólido blanco (2.8 g, 51%) el cusl se utilizó sin purificación adicional.

Ejemplo 16: Síntesis de 4-amino-5-yodopirimidina



Una solución de 4-aminopirimidina (0,970 g, 10,3 mmol) en 20 ml de ácido acético se trató con monocloruro de yodo (1,67 g, 10,3 mmol, 1,01 equiv), obteniéndose un copioso precipitado del *N*-yodo intermediario. La mezcla resultante se sometió a reflujo durante 3 horas bajo atmósfera de argón y se enfrió a alrededor de 10°C con un baño de agua. El precipitado formado se recolectó y se secó para dar el compuesto del título como un sólido amarilleno (1,4 g, 62% de rendimiento).

Ejemplo 17: Síntesis de 2,2,2-trifluoro-*N*-(4-yodo-2-isopropilpirimidin-5-il)acetamida



Se agregó lentamente nitroacetato de etilo (11,7 ml, 105 mmol) a una solución agitada de dimetil formamida dimetil acetal (29,2 ml, 220 mmol). La mezcla rojiza resultante se mantuvo a temperatura ambiente durante 2 horas, se calentó en un baño de aceite a 100°C for 90 minutos, y se enfrió a temperatura ambiente. La mezcla se concentraron al vacio a remove volatile organics y el residuo resultante se calentó a 60°C durante 1 hora. Se obtuvo un líquido naranja rojizo (18 g, ~100% de rendimiento), que se usó en el próximo paso sin purificación.

A una solución agitada del etil éster del ácido 3-dimetilamino-2-nitroacrílico (3,8 g, 20 mmol) en 50 ml de etanol anhidro se agregó hidrocloruro de isopropil amidina (3,1 g, 25 mmol) seguido de trietilamina (2,5 ml, 25 mmol). La mezcla resultante se calentó a 90°C for 6 horas. Al cabo del enfriado a temperatura ambiente, la mezcla se concentró al vacío y elproducto en bruto se purificó sobre SiO_2 (3% metanol en diclorometano) para dar 3,1 g de un aceite amarronado (84% de rendimiento).

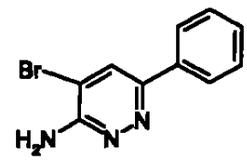
A suspensión de 2-isopropil-5-nitro-3*H*-pirimidin-4-ona (1,55 g, 8,5 mmol) y trietilamina (1,4 ml, 10 mmol) en 10 ml de diclorometano se enfrió en un baño helado. Una solución de oxicloruro de fósforo (1,9 ml, 20 mmol) en 5 ml de diclorometano se agregó lentamente durante un período de 5 minutos, y la mezcla resultante se agitó durante 90 minutos. La mezcla resultante se diluyó con diclorometano, se desactivó con hielo, en forma secuencial se lavó con una solución saturada de bicarbonato de sodio y agua, se secó sobre sulfato de sodio, se filtró y se concentraron al vacío para dar 0,7 g de aceite amarronado (41% de rendimiento), que se usó sin ulterior purificación.

Una solución agitada de 4-cloro-2-isopropil-5-nitropirimidina (0,7 g, 3,5 mmol) en 10 ml de alcohol absluto y 5 ml de ácido acético glacial se trató con hierro en polvo y la mezcla se calentó a 90°C durante 20 minutos. Al cabo del enfriamiento a temperatura ambiente, la mezcla de reacción se diluyó con 200 ml de diclorometano, en forma secuencial se lavó con una solución saturada de bicarbonato de sodio y agua, se secaron sobre sulfato de sodio, se filtró y se concentraron al vacío para dar 450 mg de aceite levemente amarronado que se usó sin ulterior purificación (75% de rendimiento).

Una mezcla agitada de 4-cloro-2-isopropilpirimidin-5-ilamina (450 mg, 2,6 mmol) en 10 ml de una solución de HI (40% acuosa) se trató con NaI (1,97 g, 13,1 mmol). La mezcla resultante se agitó a temperatura ambiente durante 2 horas y se vertió sobre diclorometano. Se separaron las fases. La capa orgánica se lavó con una solución acuosa de carbonato de sodio, una solución acuosa de bisulfito de sodio y agua, se secó sobre sulfato de sodio, se filtró y se concentraron al vacío para dar 600 mg de aceite amarronado que se usó sin ulterior purificación (87% de rendimiento).

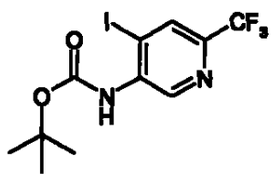
Una solución agitada de 4-yodo-2-isopropilpirimidin-5-ilamina (600 mg, 2,28 mmol) en 4 ml de diclorometano anhidro se trató con una solución de anhídrido trifluoroacético (0,43 ml, 3 mmol) en 2 ml de diclorometano a temperatura ambiente. Al cabo de 15 minutos, la mezcla se concentraron al vacío para dar 0,8 g de aceite amarronado que solidificó estando reposo y se usó sin ulterior purificación (rendimiento cuantitativo).

Ejemplo 18: Síntesis de 4-bromo-6-fenilpiridazin-3-ilamina



Se preparó 4-Bromo-6-fenilpiridazin-3-ilamina conforme al procedimiento descripto en M. Bourotte, N. Pellegrini, M. Schmitt, y J.-J. Bourguignon, Syn. Lett., 2003, 10, pp. 1482-1484.

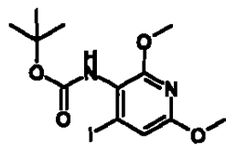
Ejemplo 19: Síntesis de *ter*-butiléster del ácido (4-yodo-6-trifluorometilpiridin-3-il)carbámico



Una solución de ácido 6-trifluorometilnicotínico (1,0 g, 5,23 mmol), difenilfosforilazida (1,36 ml, 6,3 mmol), y trietilamina (1,83 ml, 13,1 mmol) en 15 ml de ter-butanol anhidro se calentó a reflujo bajo gas nitrógeno durante 5 horas. La reacción se enfrió a temperatura ambiente y se concentraron al vacío. Se agregó 150 ml de agua y la mezcla se extrajo con dos porciones de 150 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con 150 ml de agua, 150 ml de una solución acuosa saturada de bicarbonato de sodio, se secó sobre sulfato de sodio, se filtró y se concentraron al vacío. La mezcla en bruto se purificó sobre SiO_2 (10% acetato de etilo en hexanos) proporcionó el producto del título (0,90 g, 66% de rendimiento).

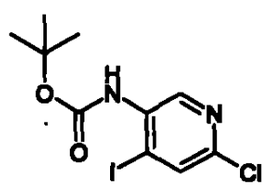
Una solución de *ter*-butiléster del ácido (6-trifluorometilpiridin-3-il)carbámico (0,90 g, 3,43 mmol) y *N,N,N',N'*-tetrametiletilenodiamina (1,29 ml, 8,55 mmol) en 25 ml de dietiléter anhidro se enfrió a -78°C bajo atmósfera de nitrógeno. La mezcla resultante se trató gota a gota con *n*-BuLi (2,5 M en hexanos, 3,42 ml, 8,55 mmol) durante 5 minutos, y la mezcla se permitió calentar a -10°C. Al cabo de 30 minutos, la mezcla se enfrió a -78°C y una solución de I_2 (1,14 g, 4,5 mmol) en 5 ml de THF anhidro se agregó rápidamente. La mezcla resultante se calentó a temperatura ambiente, se agitó durante 1 hora, y se desactivó con 50 ml de agua. La capa orgánica se lavó sobre sulfato de sodio, se filtró y se concentraron al vacío. La mezcla en bruto se purificó en SiO_2 (10% acetato de etilo en diclorometano) para obtener el compuesto del título (150 mg, 11,3% de rendimiento).

Ejemplo 20: Síntesis de *ter*-butiléster del ácido (4-Yodo-2,6-dimetoxipiridin-3-il)carbámico



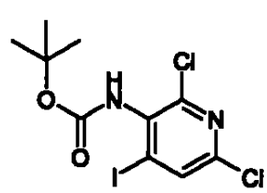
El producto del título se preparó a partir de ácido 2,6-dimetoxinicotínico del mismo modo que para la preparación del *ter*-butiléster del ácido (4-yodo-6-trifluorometilpiridin-3-il)carbámico.

Ejemplo 21: Síntesis de *ter*-butiléster del ácido (6-cloro-4-yodopiridin-3-il)carbámico



El producto del título se preparó a partir de ácido 6-cloronicotínico del mismo modo que para la preparación del *ter*-butiléster del ácido (4-yodo-6-trifluorometilpiridin-3-il)carbámico.

Ejemplo 22: Síntesis de *ter*-butiléster del ácido (2,6-dicloro-4-yodopiridin-3-il)carbámico

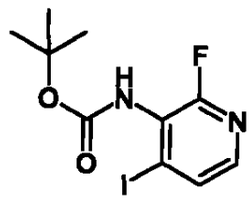


El producto del título se preparó a partir del ácido 2,6-dicloronicotínico del mismo modo que para la preparación de *ter*-butiléster del ácido (4-yodo-6-trifluorometilpiridin-3-il)carbámico.

Ejemplo 23: Síntesis de *ter*-butiléster del ácido (4-yodo-5-metilpiridin-3-il)carbámico

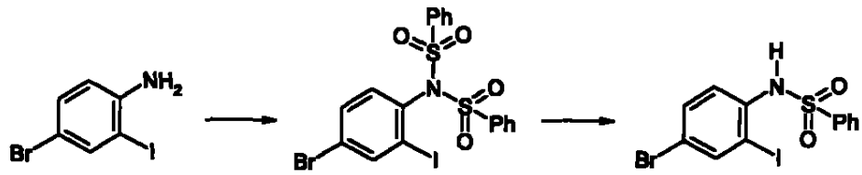
El producto del título se preparó a partir de ácido 5-metilnicotínico del mismo modo que para la preparación de *ter*-butiléster del ácido (4-yodo-6-trifluorometilpiridin-3-il)carbámico.

Ejemplo 24: Síntesis de *ter*-butiléster del ácido (2-fluoro-4-yodopiridin-3-il)-carbámico



El producto del título se preparó a partir de ácido 2-fluoronicotínico del mismo modo que para la preparación del *ter*-butiléster del ácido (4-yodo-6-trifluorometilpiridin-3-il)carbámico

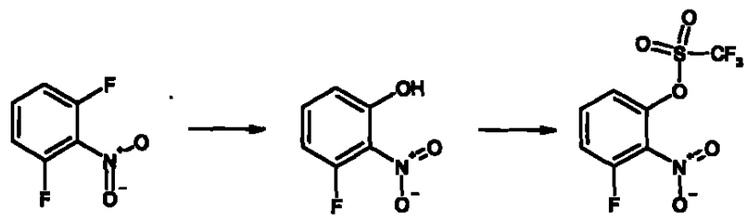
Ejemplo 25: Síntesis de *N*-(4-bromo-2-yodofenil)bencensulfonamida



Una solución de 4-bromo-2-yodoanilina (8,5 g, 28,5 mmol) en 200 ml de diclorometano en forma secuencial se trató con cloruro de bencensulfonilo (15 ml, 117,5 mmol) y trietilamina (25 ml, 179,6 mmol). Al cabo de 4 días, la mezcla se diluyó con 100 ml de solución acuosa saturada de bicarbonato de sodio y se extrajo con tres porciones de 100 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con 50 ml de salmuera, tres porciones de 60 ml de una solución acuosa saturada de cloruro de amonio, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. El producto en bruto se trituró con dietiléter para obtener 5,74 g (35% de rendimiento) de *N,N*-bisbencensulfonil-(4-bromo-2-yodoanilina).

Una solución de fluoruro de tetrabutilamonio (1 M en THF, 11 ml) en 30 ml de THF se trató con *N,N*-bisbencensulfonil-(4-bromo-2-yodoanilina) (5,78 g, 10 mmol) en varias porciones. Al cabo de 18 horas, la mezcla se diluyó con de 40 ml de acetato de etilo y 40 ml de 1 N HCl. Se separaron las fases y se extrajo la capa acuosa con dos porciones de 40 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con dos porciones de 20 ml de HCl 1 N, dos porciones de 20 ml de solución acuosa saturada de bicarbonato de sodio, 20 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío para dar 3,95 g (90% de rendimiento) del compuesto del título como un sólido, que se usó sin ulterior purificación.

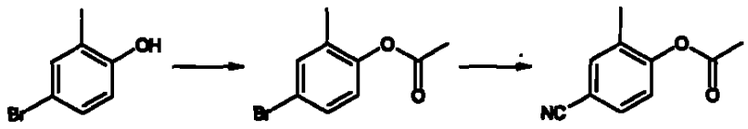
Ejemplo 26: Síntesis del 3-fluoro-2-nitrofenilléster del ácido trifluorometansulfónico

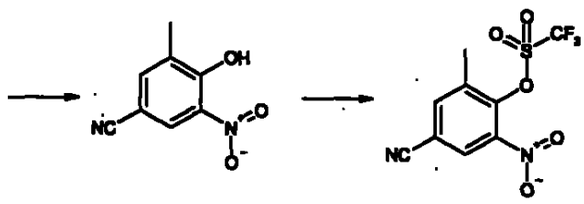


Una solución de ter-butóxido de potasio (1,23 g, 11 mmol) en 25 ml de DMSO anhidro se agitó a temperatura ambiente durante 30 minutos y se trató con 1,3-difluoro-2-nitrobenceno (1,59 g, 10 mmol). Al cabo de 18 horas, la mezcla se diluyó con 150 ml de ácido sulfúrico acuoso 1 N y se extrajo con tres porciones de 50 ml de dietiléter. Las capas orgánicas combinadas se lavaron con agua, se secaron sobre sulfato de sodio, se filtró, y se concentraron al vacío. El residuo se disolvió en 50 ml de ácido trifluoroacético. Al cabo de 30 minutos a temperatura ambiente, la mezcla se concentraron al vacío, se trató con 50 ml de hidróxido de sodio 1 N acuoso y se extrajo con tres porciones de 30 ml de dietiléter. La capa acuosa se acidificó con ácido sulfúrico acuoso 1 N y se extrajo con dos porciones de 50 ml de diclorometano. Las capas combinadas de diclorometano se lavaron con agua, se secaron sobre sulfato de sodio, se filtró, y se concentraron al vacío para dar 1,3 g de 3-fluoro-2-nitrofenol como aceite color naranja (61% de rendimiento).

Una solución de 3-fluoro-2-nitrofenol (1,13 g, 7,2 mmol) y piridina (0,65 ml, 8 mmol) en 15 ml de diclorometano anhidrose enfrió en un baño helado y se trató con una solución de anhídrido tríflico (1,33 ml, 7,9 mmol) en 3 ml de diclorometano anhidro. Al cabo de 4 horas, la mezcla de reacción se diluyó con 100 ml de diclorometano, se lavó con dos porciones de 30 ml de bicarbonato de sodio acuoso saturado, dos porciones de 30 ml de ácido sulfúrico 1 N acuoso, y dos porciones de 30 ml de agua, se secaron sobre sulfato de sodio, se filtró, y se concentró al vacío para dar 2 g del producto del título como un aceite color marrón claro (96% de rendimiento).

Ejemplo 27: Síntesis de 4-ciano-2-metil-6-nitrofenilléster del ácido trifluorometansulfónico





Una solución helada de 4-bromo-2-metilfenol (5,6 g, 30 mmol) y piridina (6,1 ml, 75 mmol) en 50 ml de diclorometano anhidro se trató con una solución de cloruro de acetilo (2,8 ml, 26 mmol) en 5 ml de diclorometano anhidro. Al cabo de 2 horas, la mezcla de reacción se concentró al vacío. El residuo resultante se trató con hielo picado, se diluyó con 150 ml de diclorometano, se lavó con agua, se secó sobre sulfato de sodio, se filtró, y se concentraron al vacío para dar 6,9 g de acetato de 4-bromo-2-metilfenilo como un aceite color marrón claro (rendimiento cuantitativo).

Una solución de acetato de 4-bromo-2-metilfenilo (6,9 g, 30 mol) en 75 ml de dimetil acetamida anhidra se trató con cianuro de zinc (3 g, 25,6 mmol) y tetrakis(trifenilfosfin)paladio(0) (4,5 g, 3,9 mmol). La mezcla de reacción se calentó a 100°C durante 2 horas, se enfrió a temperatura ambiente, y se trató con 300 ml de agua fría. El precipitado resultante se filtró, se lavó con agua, y se secó al aire. De la cromatografía sobre SiO_2 (100% diclorometano) resultó 5,2 g de acetato de 4-ciano-2-metilfenilo como un aceite incoloro (99% de rendimiento), que solidificó estando en reposo.

Una solución agitada de acetato de 4-ciano-2-metilfenilo (5,2 g, 29,7 mmol) en 75 ml de metanol se trató con una solución de carbonato de potasio (30 mmol, 4,15 g) en 25 ml de agua a temperatura ambiente. Al cabo de 30 minutos, la mezcla se concentraron al vacío y se trató con ácido sulfúrico 1 N. El precipitado resultante se filtró, se lavó con agua, y se secó para dar 3,1 g de 4-hidroxi-3-metilbenzonitrilo como un sólido color blanco (78% de rendimiento).

Una solución agitada de 4-hidroxi-3-metilbenzonitrilo (3,1 g, 23,3 mmol) en 60 ml de acetonitrilo anhidro se enfrió a -30°C y se trató con tetrafluoroborate de nitronio (3,4 g, 25,6 mmol) en porciones. Al cabo de 60 minutos, la mezcla de reacción se diluyó con 100 ml de agua. El precipitado resultante color amarillo claro se filtró, se lavó con agua, y se secó para dar 3,9 g de 4-hidroxi-3-metil-5-nitrobenzonitrilo (94% de rendimiento).

El 4-hidroxi-3-metil-5-nitrobenzonitrilo se convirtió en el producto del título conforme al procedimiento descrito para la preparación del 3-fluoro-2-nitrofenilléster del ácido trifluorometansulfónico.

Ejemplo 28: Síntesis de 3-fluoro-6-metil-2-nitrofenol

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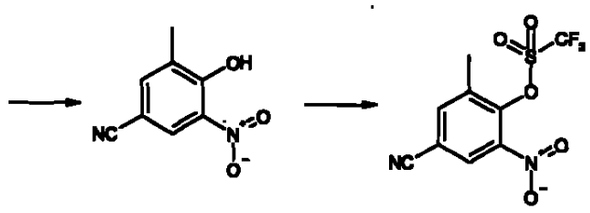


Una solución helada de 4-bromo-2-metilfenol (5,6 g, 30 mmol) y piridina (6,1 ml, 75 mmol) en 50 ml de diclorometano anhidro se trató con una solución de cloruro de acetilo (2,8 ml, 26 mmol) en 5 ml de diclorometano anhidro. Al cabo de 2 horas, la mezcla de reacción se concentró al vacío. El residuo resultante se trató con hielo picado, se diluyó con 150 ml de diclorometano, se lavó con agua, se secó sobre sulfato de sodio, se filtró, y se concentraron al vacío para dar 6,9 g de acetato de 4-bromo-2-metilfenilo como un aceite color marrón claro (rendimiento cuantitativo).

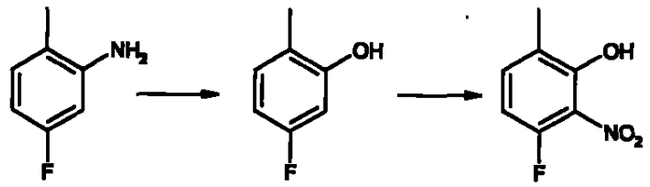
Una solución de acetato de 4-bromo-2-metilfenilo (6,9 g, 30 mol) en 75 ml de dimetil acetamida anhidra se trató con cianuro de zinc (3 g, 25,6 mmol) y tetrakis(trifenilfosfin)paladio(0) (4,5 g, 3,9 mmol). La mezcla de reacción se calentó a 100°C durante 2 horas, se enfrió a temperatura ambiente, y se trató con 300 ml de agua fría. El precipitado resultante se filtró, se lavó con agua, y se secó al aire. De la cromatografía sobre SiO_2 (100% diclorometano) resultó 5,2 g de acetato de 4-ciano-2-metilfenilo como un aceite incoloro (99% de rendimiento), que solidificó estando en reposo.

Una solución agitada de acetato de 4-ciano-2-metilfenilo (5,2 g, 29,7 mmol) en 75 ml de metanol se trató con una solución de carbonato de potasio (30 mmol, 4,15 g) en 25 ml de agua a temperatura ambiente. Al cabo de 30 minutos, la mezcla se concentraron al vacío y se trató con ácido sulfúrico 1 N. El precipitado resultante se filtró, se lavó con agua, y se secó para dar 3,1 g de 4-hidroxi-3-metilbenzonitrilo como un sólido color blanco (78% de rendimiento).

Una solución agitada de 4-hidroxi-3-metilbenzonitrilo (3,1 g, 23,3 mmol) en 60 ml de acetonitrilo anhidro se enfrió a -30°C y se trató con tetrafluoroborate de nitronio (3,4 g, 25,6 mmol) en porciones. Al cabo de 60 minutos, la mezcla de reacción se diluyó con 100 ml de agua. El precipitado resultante color amarillo claro se filtró, se lavó con agua, y se secó para dar 3,9 g de 4-hidroxi-3-metil-5-nitrobenzonitrilo (94% de rendimiento).

El 4-hidroxi-3-metil-5-nitrobenzonitrilo se convirtió en el producto del título conforme al procedimiento descrito para la preparación del 3-fluoro-2-nitrofeniléster del ácido trifluorometansulfónico.

Ejemplo 28: Síntesis de 3-fluoro-6-metil-2-nitrofenol

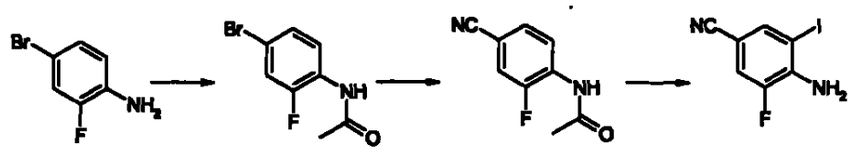


7 ml de una solución caliente de ácido sulfúrico en 21 ml de agua se agregó a 5-fluoro-2-metilfenilamina (5 g, 40 mmol). La mezcla se enfrió en un baño de hielo durante 30 minutos y se trató con una solución de nitrito de sodio (3,38 g, 48 mmol) en 10 ml de agua durante un período de 10 minutos. Al cabo de la agitación a 0°C durante 45 minutos, la reacción se diluyó con 20 ml de agua fría y se trató con 0,3 g de urea. La mezcla resultante se agregó a una solución agitada de 11 ml de ácido sulfúrico concentrado en 10 ml de agua que contiene 15 g de sulfato de sodio anhidro a 130°C durante 10 minutos. Al cabo de otros 5 minutos a 130°C, se permitió enfriar la reacción a temperatura ambiente y se extrajo con tres porciones de 100 ml de diclorometano. Las capas orgánicas combinadas se lavaron con dos porciones de 50 ml de agua y se concentraron al vacío. El aceite rojizo se disolvió en 250 ml de dietiléter y se lavó con tres porciones de 50 ml de hidróxido de sodio acuoso al 10%. Los extractos combinados de hidróxido de sodio acuosa se lavaron con dos porciones de 50 ml de dietiléter. La cpa básica se acidificó con HCl 1 N acuoso y se extrajo con tres porciones de 100 ml de diclorometano. Las capas combinadas de diclorometano se lavó con dos porciones de 50 ml de salmuera, se secaron sobre sulfato de sodio, se filtró, y se concentraron al vacío para dar un líquido rojizo claro. El producto en bruto se purificó mediante cromatografía en SiO_2 (10% acetato de etilo en hexanos) para dar 5 g de 5-fluoro-2-metilfenol como un aceite amarronado claro (99% de rendimiento).

Una solución agitada de 5-fluoro-2-metilfenol (640 mg, 5 mmol) en 20 ml de acetonitrilo anhidro se enfrió a -30°C a -40°C y se trató con tetrafluoroborate de nitronio (740 mg, 5,5 mmol). Al cabo de 45 minutos, la mezcla de reacción se diluyó con 100 ml de agua fría y se extrajo con tres porciones de 50 ml de diclorometano. Las capas orgánicas combinadas se lavaron con tres porciones de 25 ml de agua, se secaron sobre sulfato de sodio, y se concentraron al vacío para dar un sólido cristalino rojizo. La cromatografía sobre SiO_2 (5% acetato de etilo en hexanos) se obtuvo 0,58 g del producto del título como un sólido color amarillo brillante (68% de rendimiento).

El compuesto del título se convirtió en el correspondiente trifluorometansufonato conforme al procedimiento descripto en el Ejemplo 26.

Ejemplo 29: Síntesis de 4-amino-3-fluoro-5-yodobenzonitrilo



Una solución de 4-bromo-2-fluorofenilamina (10,9 g, 57,4 mmol) y piridina (9,4 ml, 115 mmol) en 50 ml de diclorometano anhidro se trató con cloruro de acetilo (3,33 ml, 63,1 mmol) a 0°C. Al cabo de 10 minutos a 0°C y 10 minutos a temperatura ambiente, la mezcla se concentraron al vacío y el residuo se trató con 300 ml de ácido sulfúrico 1 N acuoso. La capa orgánica se concentraron al vacío para dar 12,9 g de *N*-(4-bromo-2-fluorofenil)acetamida como un sólido grisáceo claro (97% de rendimiento).

Una solución de *N*-(4-bromo-2-fluorofenil)acetamida (12,9 g, 55,4 mmol) en 125 ml de dimetil acetamida anhidra se calentó en presencia de cianuro de zinc (5,53 g, 47,1 mmol) y tetrakis(trifenilfosfina)paladio (0) (5,2 g, 4,5 mmol) a 100°C durante 3 horas. La mezcla se diluyó con 300 ml de agua fría, el sólido resultante se filtró, se lavó con agua, y se secó. El filtrado se extrajo con tres porciones de 100 ml de acetato de etilo y los extractos combinados se secaron sobre sulfato de sodio, se filtraron y se concentraron al vacío. El residuo resultante se combinó con el sólido de la filtración. Este material combinado se filtró a través de una columna de gel de sílice (100% diclorometano seguido de 100% acetato de etilo) para dar 8,5 g de *N*-(4-ciano-2-fluorofenil)acetamida como un sólido color crema claro (86% de rendimiento).

Una solución de perborato de sodio (4,2 g, 27,3 mmols) y tungstato de sodio (450 mg, 1,4 mmol) en una mezcla de 20 ml de ácido acético glacial y 15 ml de anhídrido acético se trató con una solución de yoduro de potasio (2,3 g, 13,9 mmols) en 15 ml de agua. La mezcla se trató con 7,5 ml de ácido sulfúrico concentrado durante 15 minutos. Se agregó una suspensión de *N*-(4-ciano-2-fluorofenil)acetamida (1,79 g, 10 mmols) en 15 ml de ácido acético glacial y la mezcla resultante se calentó a 50°C. Al cabo de 1 hora, la mezcla se vertió en 300 ml de hielo picado y se trató con 100 ml de una solución saturada de tiosulfato de sodio seguido de 100 ml de una solución de bisulfito de sodio. La mezcla se extrajo con tres porciones de 100 ml de diclorometano y las capas orgánicas combinadas se lavaron con tres porciones de 50 ml de una solución de bicarbonato de sodio, tres porciones de 50 ml de agua, se secaron sobre sulfato de sodio, y se concentraron al vacío, para dar un sólido color marrón claro. De la cromatografía sobre SiO_2 (50% acetato de etilo en hexanos) resultaron 400 mg del producto del título como un sólido color amarronado claro (15% de rendimiento).

Ejemplo 30: Síntesis de 2-Fluoro-6-yodo-4-metilfenilamina

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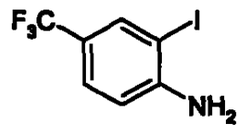
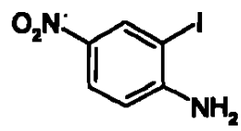
Una solución de 2-fluoro-4-metilfenilamina (1,25 g, 10 mmol) en 5 ml de metanol se trató con una solución de yodo (1,27 g, 5 mmol) en una mezcla de 25 ml de metanol y 3 ml de peróxido de hidrógeno durante un período de 15 minutos a temperatura ambiente. Al cabo de 18 horas, la mezcla de reacción se desactivó con 30 ml de solución acuosa saturada de tiosulfato de sodio y se extrajo con tres porciones de 50 ml de diclorometano. Las capas orgánicas combinadas se lavó con dos porciones de 30 ml de una solución saturada de bisulfito de sodio, tres porciones de 50 ml de agua, se secaron sobre sulfato de sodio, y se concentraron al vacío. De la cromatografía sobre SiO_2 (10% acetato de etilo en hexanos) se obtuvo 1,1 g del producto del título como un aceite amarronado claro (44% de rendimiento).

Ejemplo 31: Síntesis de 2-yodo-4-trifluorometilfenilamina



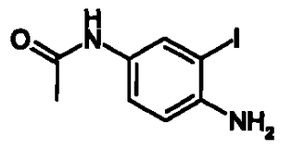
El compuesto del título se preparó del mismo modo que el indicado para la síntesis de 2-fluoro-6-yodo-4-metilfenilamina.

Ejemplo 32: Síntesis de 2-yodo-4-nitrofenilamina



El compuesto del título se preparó del mismo modo que el indicado para la síntesis de 2-fluoro-6-yodo-4-metilfenilamina.

Ejemplo 33: Síntesis de *N*-(4-amino-3-yodofenil)acetamida



El compuesto del título se preparó del mismo modo que el indicado para la síntesis de 2-fluoro-6-yodo-4-metilfenilamina.

Ejemplo 34: Síntesis de 2-etil-6-nitrofenol

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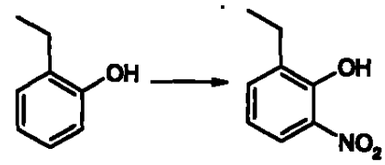
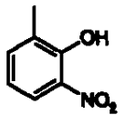


Una solución de 2-etilfenol (2,44 g, 20 mmol) en 80 ml de acetonitrilo anhidro se trató con tetrafluoroborato de nitronio (2,93 g, 22 mmols) en porciones durante un período de 5 minutos entre -30°C y -40°C. Al cabo de 20 minutos, la mezcla se desactivó con hielo, se trató con agua fría y se extrajo con tres porciones de 100 ml de diclorometano. Las capas orgánicas combinadas se lavaron con dos porciones 30 ml de agua, se secaron sobre sulfato de sodio, se filtraron y se concentraron al vacío. De la cromatografía sobre SiO_2 (20% acetato de etilo en hexanos) se obtuvo 2,0 g de 2-etil-6-nitrofenol como un aceite amarillo (60% de rendimiento).

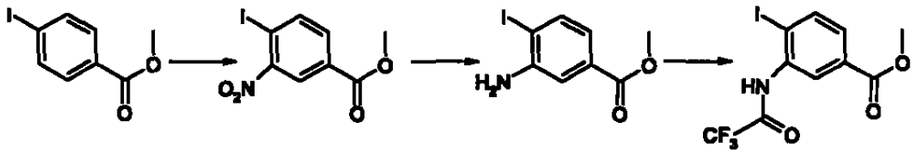
El compuesto del título se convirtió en el correspondiente trifluorometansulfonato de según el procedimiento descripto en Ejemplo 26.

Ejemplo 35: Síntesis de 2-metil-6-nitrofenol



El compuesto del título se preparó del mismo modo que el indicado para la síntesis de 2-etil-6-nitrofenol y se convirtió en el correspondiente trifluorometansulfonato según el procedimiento descripto en Ejemplo 26.

Ejemplo 36: Síntesis del metil éster del ácido 4-yodo-3-(2,2,2-trifluoroacetilamino) benzoico



Una solución de metil éster del ácido 4-yodobenzoico (5,24 g, 20,0 mmol) en ácido sulfúrico se trató con 1,43 ml de ácido nítrico concentrado en un agregado gota a gota a 0°C. Al cabo de 5 horas a temperatura ambiente, la mezcla de reacción se calentó a 40°C durante 1 hora. La solución color naranja resultante se agregó a 100 g de hielo, se trató con 200 ml de acetato de etilo, se agitó durante 30 minutos, y se filtró. Se separaron las fases y se extrajo la capa acuosa con 200 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con una solución saturada de bicarbonato de sodio y salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al

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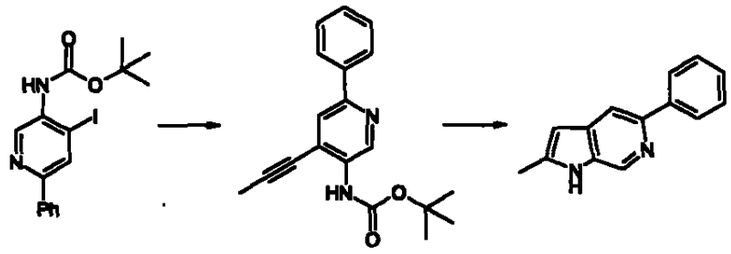
vacío. El residuo se pasó a través de una columna de gel de sílice (100% acetato de etilo) para dar 2,0 g de metil éster del ácido 4-yodo-3-nitrobenzoico como un sólido amarillo (33% de rendimiento).

Una solución de metil éster del ácido 4-yodo-3-nitrobenzoico (2,0 g, 6,50 mmol) en 25 ml de alcohol absoluto y 15 ml de ácido acético glacial se trató con hierro en polvo (3,6 g, 65,0 mmol) y la mezcla se calentó a 80°C. Al cabo de 1 hora, la mezcla de reacción se filtró a través de un lecho de sílice, se lavó con etanol, y se concentraron al vacío. El residuo se diluyó con una solución de carbonato de potasio y se extrajo con acetato de etilo. Las capas orgánicas combinadas se lavaron con salmuera, se secaron sobre sulfato de sodio, se filtró, y se concentraron al vacío para dar 1,6 g de metil éster del ácido 3-amino-4-yodobenzoico como un sólido color blanco (68% de rendimiento).

Una solución de metil éster del ácido 3-amino-4-yodobenzoico (1,59 g, 5,74 mmols) en 40 ml de diclorometano se hizo reaccionar con anhídrido trifluoroacético (3 ml, 21 mmol) a temperatura ambiente. Al cabo de 30 minutos, la mezcla de reacción se concentraron al vacío y el residuo se agregó a agua fría, se filtró, y se secó para dar 2,1 g del producto del título como un sólido blanquecino (rendimiento cuantitativo).

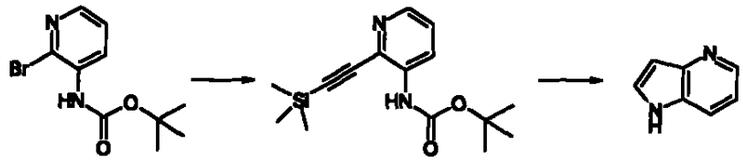
Ejemplo 37: Síntesis de 2-metil-5-fenil-1*H*-pirrolo[2,3-*c*]piridina



Se condensó propino (0,60 ml, 11,4 mmol) en un tubo de presión a -78°C. Se agregaron una solución del *ter*-butiléster del ácido (4-yodo-6-fenilpiridin-3-il)carbámico (900 mg, 2,27 mmol) en 2 ml de DMF, 6 ml de trietilamina, diclorobis(trifenilfosfin)paladio (II) (80,2 mg, 0,114 mmol) y CuI (43,0 mg, 0,227 mmol), se selló el tubo y la mezcla se agitó a temperatura ambiente hasta el día siguiente. La mezcla se enfrió a -78°C, el tubo sellado se abrió y se agregaron 20 ml de acetato de etilo y 10 ml de una solución de cloruro de amonio saturado acuoso. Se separaron las fases y se extrajo la capa acuosa con tres porciones de 10 ml de acetato de etilo. Las capas orgánicas combinadas se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. El producto en bruto se purificó sobre SiO_2 (0 a 40% de acetato de etilo en hexanos, gradiente) para dar 670 mg de *ter*-butiléster del ácido (6-fenil-4-prop-1-inilpiridin-3-il)carbámico (96% de rendimiento).

Una solución de *ter*-butiléster del ácido (6-fenil-4-prop-1-inilpiridin-3-il)carbámico (670 mg, 2,17 mmol) en una mezcla de 33 ml de metanol y 11 ml de agua se trató con DBU (2,0 ml, 13,4 mmol). La mezcla resultante se calentó a 60°C. Al cabo de 24 horas, la mezcla se concentró al vacío, se agregó 50 ml de agua, la mezcla se sonicó, y el sólido resultante se filtró. El sólido se secó sobre P_2O_5 al vacío para dar 450 mg del producto del título como un sólido amarillo (99% de rendimiento), que se usó sin ulterior purificación.

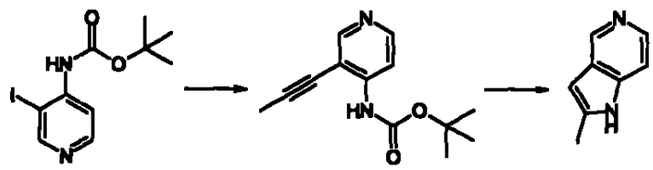
Ejemplo 38: Síntesis de 1*H*-pirrolo[3,2-*b*]piridina



Se agitaron *ter*-butiléster del ácido (2-bromopiridin-3-il)carbámico (1,09 mg, 4,00 mmol), (trimetilsilil)acetileno (2,83 ml, 20,0 mmol), CuI (75,8 mg, 0,400 mmol), y diclorobis(trifenilfosfina)paladio (II) (141 mg, 0,200 mmol) en una mezcla de 12 ml de trietilamina y 3,0 ml de DMF anhidra a temperatura ambiente hasta el día siguiente. La reacción se diluyó con 50 ml de dietiléter y se desactivó con 50 ml de una solución acuosa saturada de cloruro de amonio. La capa orgánica se lavó con 20 ml de solución acuosa saturada de cloruro de amonio y las capas acuosas combinadas se extrajeron con tres porciones de 20 ml de dietiléter. Las capas orgánicas combinadas luego se lavaron con 20 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. De la cromatografía sobre SiO_2 (20% a 30% acetato de etilo en hexanos, gradiente) se obtuvieron 500 mg de *ter*-butiléster del ácido (2-trimetilsililetinilpiridin-3-il)carbámico (43% de rendimiento).

Una mezcla de *ter*-butiléster del ácido (2-trimetilsililetinilpiridin-3-il)carbámico (500 mg, 1,72 mmol) en 5 ml de THF se trató con TBAF (1 M en THF, 10,3 ml) a temperatura ambiente. La mezcla se calentó a reflujo durante 8 horas, se enfrió a temperatura ambiente, se diluyó con 100 ml de dietiléter, y se desactivó con 100 ml de agua. Se extrajo la capa acuosa con tres porciones de 50 ml de dietiléter, y las capas orgánicas combinadas se lavaron con 500 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. De la cromatografía sobre SiO_2 (100% CH_2Cl_2 a 10% MeOH en CH_2Cl_2, gradiente) se obtuvieron 160 mg del producto del título como un sólido tostado (79% de rendimiento).

Ejemplo 39: Síntesis de 2-metil-1*H*-pirrolo[2,3-*c*]piridina



Se condensó propino (6,3 ml, 124 mmol) en n tubo a presión a -78°C. Se agregó una solución de *ter*-butiléster del ácido (3-yodopiridin-4-il)carbámico (7,98 g, 24,9 mmol) en 15 ml de DMF, 60 ml de trietilamina, diclorobis(trifenilfosfin)paladio (II) (877 mg, 1,25 mmol), y CuI (472 mg, 2,49 mmol), y se selló el tubo y se agitó a temperatura ambiente hasta el día siguiente: Se agregaron 200 ml de acetato de etilo y 100 ml de solución de cloruro de amonio saturado acuoso, se separaron las fases y se extrajo la capa acuosa con tres porciones de 100 ml de acetato de etilo. Las capas orgánicas combinadas se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. De la cromatografía sobre SiO_2 (25% a 40% acetato de etilo en hexanos, gradiente) resultaron 5,65 g de *ter*-butiléster del ácido (3-prop-1-inilpiridin-4-il)carbámico (98% de rendimiento).

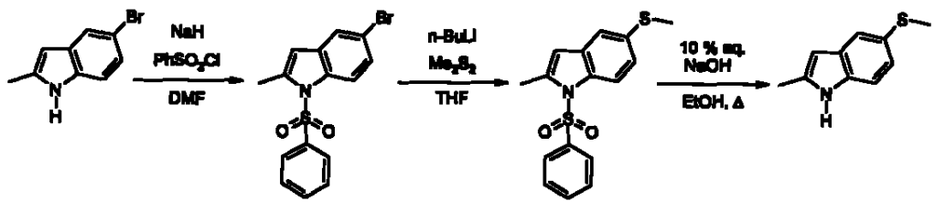
Se trató *ter*-butiléster del ácido (3-Prop-1-inilpiridin-4-il)carbámico (5,65 g, 24,3 mmol) con 30,4 ml de 4 M HCl en dioxano. La mezcla se sonicó hasta disolver completamente el compuesto. Al cabo de 15 horas, la mezcla se concentraron al vacío. El sólido márrón resultante (4,10 g) se disolvió en 65 ml de 1-metil-2-pirrolidinona (NMP) y se trató con *ter*-BuOK (7,08 g, 63,2 mmol) a temperatura ambiente. Al cabo de 18 horas, se agregaron 300 ml de acetato de etilo y 300 ml de agua. Se separaron las fases y se extrajo la capa acuosa con cinco porciones de 100 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con dos porciones de 20 ml de agua, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. De la cromatografía sobre SiO_2 (10% metanol en diclorometano) se obutvieron 2,85 g del producto del título como un sólido amarillo (89% de rendimiento).

Ejemplo 40: Síntesis de 2,3-dimetil-1*H*-pirrolo[2,3-*c*]piridina

En un tubo a presión, se trató una solución de yodopiridina (1,80 g, 8,18 mmol) en 20 ml de DMF con 2-butina (1,5 ml, 19,1 mmol), $Pd(dppf)_2Cl_2 \cdot CH_2Cl_2$ (357 mg, 0,438 mmol), cloruro de litio (367 mg, 8,71 mmol), y carbonato de sodio (1,82 g, 17,2 mmol). Se selló el tubo y se calentó a 90°C. Al cabo de 24 horas, el tubo se enfrió y se abrió. La mezcla resultante se diluyó con 20 ml de acetato de etilo y 20 ml de solución de cloruro

de amonio saturado acuoso. Se separaron las fases y se extrajo la capa acuosa con tres porciones de 50 ml de acetato de etilo. Las capas orgánicas combinadas se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. La cromatografía flash (CH_2Cl_2 a 10% de MeOH en CH_2Cl_2, gradiente) proporcionó el producto del título como un sólido marrón (920 mg, 77% de rendimiento).

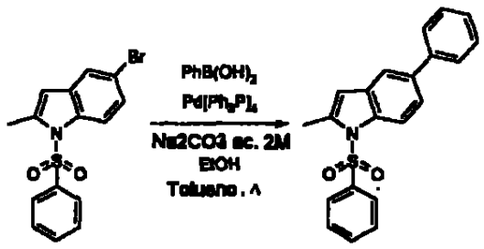
Ejemplo 41: Síntesis de 2-metil-5-metilsulfanil-1*H*-indol



A una solución de 5-bromo-2-metil-1*H*-indol (1,5 g, 7,14 mmol) en 10 ml de DMF se agregó 60% hidruro de sodio en aceite mineral (189 mg, 7,9 mmol). Después de cesado el desarrollo de hidrógeno gaseoso, la mezcla se agitó durante 10 minutos y luego se trató con 1 ml (7,83 mmol) de cloruro de bencensulfonilo. La reacción se monitoreó por TLC (acetato de etilo-hexanos (5:95)) para dar un producto levemente menos polar que el material de partida. Al cabo de 2 horas, la mezcla se vertió en 50 ml de una solución de cloruro de amonio saturada acuosa y se extrajo con tres porciones de 50 ml de acetato de etilo. Las capas orgánicas combinadas se lavó con cuatro porciones de 25 ml de salmuera, se secaron sobre sulfato de magnesio, se trató con carbón activado (NORIT A™), se filtró a través de tierra diatomea, y se concentraron al vacío. El residuo se absorbió en gel de sílice y se cromatografió en gel de sílice usando acetato de etilo-hexanos (1:99, luego 2:98, luego 3:97) para dar 1,71 g (68,4% de rendimiento) de 1-bencensulfonil-5-bromo-2-metil-1*H*-indol como un aceite claro.

A una solución helada de 1-bencensulfonil-5-bromo-2-metil-1*H*-indol (350 mg, 0,99 mmol) en 4 ml de THF se agregaron 440 µl (1,10 mmol) de *n*-BuLi (solución 2,5 M en hexanos), seguido de disufuro de dimetilo (100 µl, 1,11 mmol). La mezcla se agitó y se calentó a temperatura ambiente y luego se desactivó con cloruro de amonio y se extrajo con tres porciones 15 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con tres porciones de 15 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. El material en bruto se absorbió en gel de sílice y se cromatografió en gel de sílice usando acetato de etilo-hexanos (1:99, luego 2:98) para dar 156 mg (44,3% de rendimiento) de 1-bencensulfonil-2-metil-5-metilsulfanil-1*H*-indol como un aceite claro.

A una solución de 1-bencensulfonil-2-metil-5-metilsulfanil-1*H*-indol (156 mg, 0,49 mmol) en 10 ml de etanol se agregó 10 ml de una solución acuosa de hidróxido de sodio al 10%. La mezcla se calentó a reflujo durante 18 horas. La mezcla luego se diluyó con 10 ml de salmuera y se extrajo con tres porciones de 20 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con dos porciones 10 ml de una solución acuosa de hidróxido de sodio al 10%, dos porciones de 20 ml de cloruro de amonio saturado acuoso, dos porciones de 20 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. El producto en bruto se absorbió en gel de sílice y se cromatografió en gel de sílice usando acetato de etilo-hexanos (1:99, luego 2:98, luego



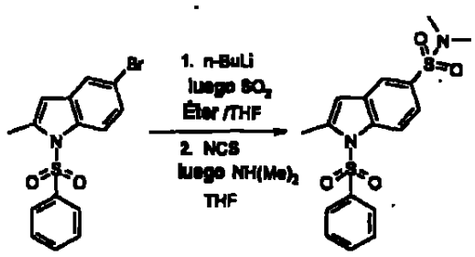
3:97, luego 5:96) para dar 62 mg (71,2% de rendimiento) de 2-metil-5-metilsulfanil-1*H*-indol.

Ejemplo 42: Síntesis de 1-bencensulfonil-2-metil-5-fenil-1*H*-indol

Una mezcla de 1-bencensulfonil-5-bromo-2-metil-1*H*-indol (810 mg, 2,31 mmol), ácido fenilborónico (850 mg, 6,97 mmol) y tetrakis(trifenilfosfin)paladio(0) (55 mg, 0,029 mmol) en 20 ml de tolueno, 10 ml de etanol, y 5 ml de carbonato de sodio 2 M se calentó a reflujo durante 4 horas. La reacción se monitoreó por TLC (acetato de etilo-hexanos (5:95), desarrollado 2 veces; y tolueno-hexanos (1:1)) indicando un producto ligeramente más polar. La mezcla se enfrió y se diluyó con una solución acuosa de hidróxido de amonio al 12% y se extrajo con tres porciones de 5 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con tres porciones de 15 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. La mezcla en bruto se absorbió sobre gel de sílice y se cromatografió en gel de sílice usando acetato de etilo-hexanos (1:99, luego 2:98, luego 3:97) para dar 731 mg (91% de rendimiento) de 1-bencensulfonil-2-metil-5-fenil-1*H*-indol.

La eliminación del grupo fenilsulfonilo como se describió en el Ejemplo 41 dio 2-metil-5-fenil-1*H*-indol.

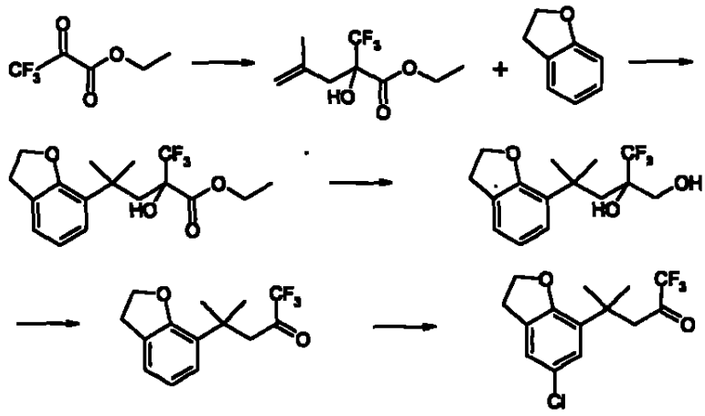
Ejemplo 43: Síntesis de dimetilamida del ácido 1-bencensulfonil-2-metil-1*H*-indol-5-sulfónico



A una solución helada (-78°C) de 1-bencensulfonil-5-bromo-2-metil-1*H*-indol (505 mg, 1,44 mmol) en 5 ml de dietiléter y 2 ml de THF se agregó 650 µL (1,63 mmol) de *n*-BuLi (solución 2,5 M en hexanos). La mezcla se agitó durante 10 minutos y luego se burbujeó gas de dióxido de azufre (SO_2) a través de la solución, resultando en un precipitado. La mezcla se calentó a temperatura ambiente y se filtró para dar 468 mg del sulfonato de litio. Este material se disolvió en 10 ml de THF y luego se agregó *N*-clorosuccinimida (200 mg, 1,49 mmol). La mezcla se agitó durante 15 minutos y luego se agregó 4 ml (8 mmol) de una solución 2 M de dimetilamina en THF. La mezcla luego se agitó durante 1 hora y se diluyó con una solución de cloruro de amonio saturado acuoso y se extrajo con tres porciones de 10 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con tres porciones de 10 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío para dar 365 mg de dimetilamida del ácido 1-bencensulfonil-2-metil-1*H*-indol-5-sulfónico.

De la eliminación del grupo fenilsulfonilo como se describe en Ejemplo 41 se obtuvo la dimetilamida del ácido 2-metil-1*H*-indol-5-sulfónico.

Ejemplo 44: Síntesis de 4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ona



Una solución de trifluoropiruvato de etilo (124,84 g, 0,734 mol) en 2,0 l de THF se trató con cloruro de metilalil magnesio (0,5 M en THF, 1,90 l, 0,954 mol) durante 4 horas mientras se mantuvo la temperatura interna inferior a -60°C. Se permitió calentar la mezcla de reacción a temperatura ambiente hasta el día siguiente, se concentró al vacío para remover THF, se desactivó con 1 l de solución saturada de cloruro de amonio, y se extrajo con tres porciones de 1 l de dietiléter. Las fases orgánicas combinadas se lavaron con 100 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. La destilación al vacío a 60 mmHg proporcionó 100,1 g de etil éster del ácido 2-hidroxi-4-metil-2-trifluorometilpent-4-enoico como un aceite claro (p.eb. 97°C-103°C, 60% de rendimiento).

Una solución del etil éster del ácido 2-hidroxi-4-metil-2-trifluorometilpent-4-enoico (100 g, 442 mmol) y 2,3-dihidrobenzofurano (57,7 g, 480 mmol) en 500 ml de dicloroetano se trató con $AlCl_3$ (87,8 g, 660 mmol) mientras se mantuvo la temperatura interna inferior a 10°C. Se permitió calentar la reacción a temperatura ambiente hasta el día siguiente y se desactivó con 1 l de HCl 1 N frío. La mezcla luego se extrajo con tres porciones de 1 l de acetato de etilo. Las capas orgánicas combinadas se lavaron con 1 l de una solución acuosa saturada de bicarbonato de sodio, 1 l de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. El residuo se purificó sobre SiO_2 (10% dietiléter en hexanos). El sólido resultante se recristalizó de hexanos calientes para dar 39,5 g de etiléster del ácido 4-(2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentanoico como un sólido blanco (26% de rendimiento).

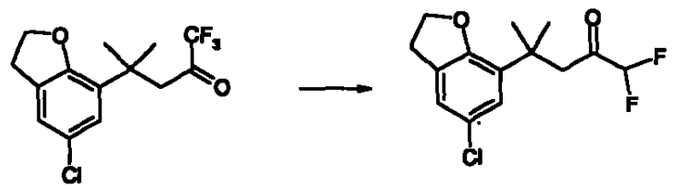
Una suspensión de LAH (4,52 g, 119 mmol) en 230 ml de THF se trató con una solución de etil éster del ácido 4-(2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentanoico (27,5 g, 79,4 mmol) en 40 ml de THF a 0°C durante 30 minutos. Luego de la agitación hasta el día siguiente, la reacción se enfrió a 0°C, se desactivó con 3 ml de agua, y se trató con 3 ml de una solución 4 M de hidróxido de sodio. Al cabo de 10 minutos, la mezcla se trató con una porción adicional de 18 ml de agua y la mezcla resultante se calentó a temperatura ambiente durante 4 horas. La mezcla se filtró y la torta del filtro se lavó con cinco porciones de 100 ml de dietiléter. El filtrado se concentró al vacío para dar 24,0 g de 4-(2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentan-1,2-diol como un aceite (99% de rendimiento).

Una solución de 4-(2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentan-1,2-diol (24,0 g, 78,9 mmol) y $NaIO_4$ (84,3 g, 394 mmol) en 360 ml de metanol se agitó a temperatura ambiente hasta el día siguiente. La mezcla resultante se filtró a través de un lecho del auxiliar filtrante de CELITE® y la torta del filtro se lavó con tres porciones de

100 ml de metanol. El filtrado se concentró al vacío, se mezció con hexanos, se filtró nuevamente, y se concentró al vacío para dar 21,4 g de 4-(2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ona como aceite incoloro (rendimiento cuantitativo), que se utilizó sin purificación.

Una solución de 4-(2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ona (20,8 g, 76,2 mmol) en 200 ml de ácido acético se trató con una solución de gas de cloro (Cl_2) en ácido acético (preparado mediante burbujeo de gas de cloro en ácido acético, ~1,19 M). La reacción se monitoreó por ^{1}H-RMN. El índice del material de partida del producto se determinó basándose en la integración de la señal CH_2 de las respectivas cetonas (material de partida: δ = 3,32 ppm; producto: δ = 3,32 ppm). La concentración de la solución de Cl_2 se recalculó basándose en los índices RMN y se agregó una porción adicional de solución de Cl_2 (este proceso se repitió hasta que el RMN mostró el consumo completo del material de partida). La mezcla se desactivó con 500 ml de agua y se agregó cuidadosamente bicarbonato de sodio sólido (~500 g) durante 1 hora. La mezcla se vertió sobre 500 ml de acetato de etilo. Se separaron las fases y se extrajo la capa acuosa con tres porciones de 500 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con dos porciones de 100 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío para dar 23,4 g del producto del título (rendimiento cuantitativo), que se utilizó sin purificación.

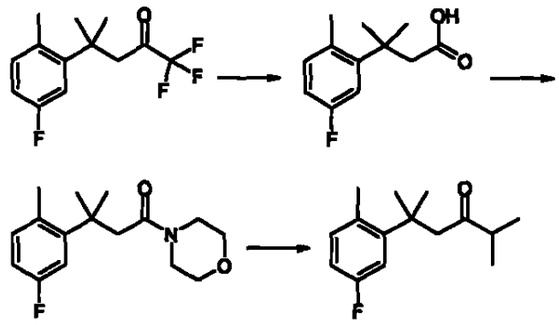
Ejemplo 45: Síntesis de 4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluoro-4-metilpentan-2-ona



Una mezcla de granallas de magnesio (204 mg, 8,40 mmol) y cloruro de trimetilsililo (2,13 ml, 16,8 mmol) en 10 ml de DMF se trató con 4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ona (1,23 g, 4,00 mmol) en 10 ml de DMF a 0°C. La mezcla resultante se agitó a temperatura ambiente hasta el día siguiente. La mezcla se filtró y se concentró al vacío. El residuo se suspendió en 20 ml de THF y se trató con TBAF (1 M en THF, 4,0 ml) a temperatura ambiente. Al cabo de 15 minutos, la reacción se desactivó con 25 ml de solución acuosa saturada de cloruro de amonio y se diluyó con 50 ml de dietiléter. Se separaron las fases y se extrajo la capa acuosa con tres porciones de 50 ml de dietiléter. Las capas orgánicas combinadas se

lavaron con salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. De la cromatografía sobre SiO_2 (100% hexanos a 10% dietiléter en hexanos, gradiente) se obtuvo 550 mg del producto del título (48% de rendimiento).

Ejemplo 46: Síntesis de 5-(5-Fluoro-2-metilfenil)-2,5-dimetilhexan-3-ona

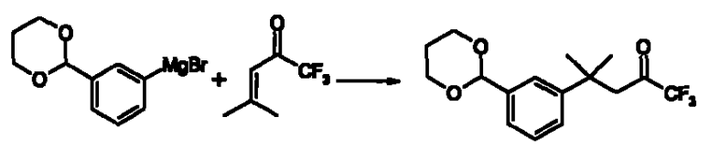


Una solución de 1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ona (4,88 g, 18,6 mmol) se trató con una solución de hidróxido de sodio (4 M en una mezcla de 30% agua en etanol, 40 ml) a temperatura ambiente. La mezcla se calentó a 80°C durante 1 hora. Al cabo del enfriado a temperatura ambiente, la mezcla se diluyó con 100 ml de agua y se extrajo con tres porciones de 100 ml de dietiléter. La capa acuosa se trató con 150 ml de acetato de etilo y la mezcla resultante se trató con HCl 6 M gota a gota hasta que la solución presentó un pH de 2. Se separaron las fases y se extrajo la capa acuosa con tres porciones de 100 ml de acetato de etilo. Las capas orgánicas combinadas se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío a para obtener 3,92 g de ácido 3-(5-fluoro-2-metilfenil)-3-metilbutírico en forma de aceite, que se solidificó estando en reposo y se usó sin ulterior purificación (rendimiento cuantitativo).

Una mezcla de ácido 3-(5-fluoro-2-metilfenil)-3-metilbutírico (3,80 g, 18,0 mmol) en 15 ml de diclorometano se trató con $SOCl_2$ (1,98 ml, 27,1 mmol) a 0°C. Al cabo de 30 minutos, una mezcla de morfolina (2,36 ml, 27,1 mmol) y piridina (4,4 ml, 54,2 mmol) en 10 ml de diclorometano se agregó a la mezcla de reacción a 0°C. Al cabo de otros 90 minutos, se agregaron 60 ml de solución acuosa de HCl 2 M, se separaron las fases y se extrajo la capa acuosa con tres porciones de 50 ml de diclorometano. Las fases orgánicas combinadas se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío de lo que resultaron 5,03 g de 3-(5-fluoro-2-metilfenil)-3-metil-1-morfolin-4-ilbutan-1-ona en forma de aceite, que se usó sin ulterior purificación (rendimiento cuantitativo).

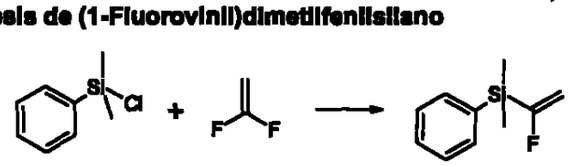
Una solución de 3-(5-fluoro-2-metilfenil)-3-metil-1-morfolin-4-ilbutan-1-ona (200 mg, 0,716 mmol) en 2 ml de THF se trató con *i*-PrLi (0,7 M en pentano, 1,28 ml) a -78°C. La mezcla de reacción se agitó a -78°C durante 1 hora, se permitió calentarse a temperatura ambiente, se desactivó con 1 ml de metanol y 5 ml de solución acuosa saturada de cloruro de amonio, y se extrajo con tres porciones de 50 ml de acetato de etilo. Las capas orgánicas combinadas se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. La cromatografía sobre SiO_2 (100% hexanos a 25% acetato de etilo en hexanos, gradiente) dio 80,4 mg del producto del título (48% de rendimiento).

Ejemplo 47: Síntesis de 4-(3-[1,3]Dioxan-2-ilfenil)-1,1,1-trifluoro-4-metilpentan-2-ona



Una solución del reactivo de Grignard (generada de la reacción de 2-(3-bromofenil)-[1,3]dioxano con granallas de magnesio en THF, 0,25 M, 52,6 ml, 13,1 mmol) se trató con yoduro de cobre (I) (2,5 g, 13,1 mmol) a 0°C. Al cabo de 45 minutos, se agregó 1,1,1-trifluoro-4-metilpent-3-en-2-ona (2 g, 13,1 mmol), y la mezcla de reacción lentamente se calentó a temperatura ambiente y se agitó hasta el día siguiente. La mezcla se desactivó con una solución acuosa saturada de cloruro de amonio y se extrajo con acetato de etilo. Las capas orgánicas combinadas se lavaron con solución acuosa saturada de cloruro de sodio, se secaron con sulfato de sodio, se filtraron, y se concentraron al vacío. El residuo se trituró con hexanos y se filtró. El filtrado se concentró al vacío, para dar 1,78 g del producto en bruto, que se utilizó sin purificación adicional.

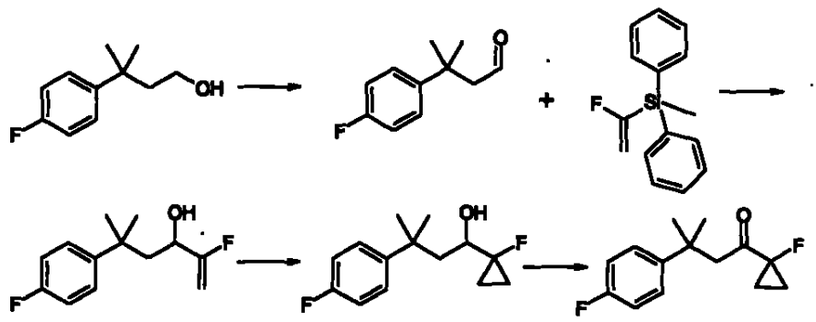
Ejemplo 48: Síntesis de (1-Fluorovinil)dimetilfenilsilano



Una suspensión de 4,4 g de alambre de litio cortado en pequeños trozos en 200 ml de THF anhidro se agitó bajo atmósfera de argón y se enfrió sobre hielo (temperatura interna <10°C) se agregó dimetilfenil- clorosilano en porciones de 5 ml durante 1 hora. El color rojo oscuro del reactivo de sililo litio se observó al cabo de aproximadamente 0,75 hora. La mezcla se agitó on hielo por otras 5 horas (temperatura interna se mantuvo entre 5°C y 10°C). La mezcla se enfrió en un baño de hielo seco/acetona y se introdujo 1,1-difluoroetileno llenando un balón conectado a la mezcla de reacción y el cilindro del

reactivo utilizando una válvula de tres vías. El balón se llenó con 1,1-difluoroetileno y se vació 10 veces en la mezcla de reacción. Se permitió a la mezcla calentarse a temperatura ambiente (se observó efervescencia, probablemente a partir de 1,1-difluoroetileno sin reaccionar). La mezcla se diluyó con 200 ml de hexanos y se filtró a través de un lecho de algodón. El filtrado se lavó con agua, se secó, se filtró, y se concentró al vacío. De cuatro destilaciones fraccionales al vacío a través de una columna de Vigreux se obtuvo 4,6 g del producto.

Ejemplo 49: Síntesis de 1-(1-fluorociclopropil)-3-(4-fluorofenil)-3-metilbutan-1-ona



Se diluyeron 12 ml de una solución de cloruro de oxalilo 2 M en diclorometano con 19 ml de diclorometano y se enfrió en un baño de hielo seco/acetona. A esta solución se agregó a gota a gota una solución de 3,6 ml de DMSO en 16 ml de diclorometano. Al cabo de 10 minutos, se agregó una solución de 3-(4-fluorofenil)-3-metilbutan-1-ol (3,6 g, 19,8 mmol) en 12 ml de diclorometano y la mezcla se agitó durante 15 minutos.Luego se agregaron 14 ml de trietilamina, se retiró el baño refrigerante, y se permitió calentarse a la mezcla de reacción a temperatura ambiente y se desactivó con agua y se diluyó con hexanos. La capa orgánica se separó, se lavó con agua, se secó, se filtró, y se concentró al vacío. El residuo se purificó mediante cromatografía sobre gel de sílice (eluyente: hexanos a hexanos-diclorometano (9:1), gradiente) de lo que resultaron 1,2 g de 3-(4-fluorofenil)-3-metilbutiraldehído en forma de aceite.

A una mezcla de 3-(4-fluorofenil)-3-metilbutiraldehído (1,2 g, 6,6 mmol) y (1-fluorovinil)metildifenilsilano en 5 ml de THF enfriada sobre hielo bajo nitrógeno gaseoso se agregó 1 ml de TBAF (1 M en THF). Se permitió a la mezcla calentarse a temperatura ambiente y se dejó hasta el día siguiente. El solvente se evaporó y el residuo se agregó a hexanos.El material soluble de hexanos se fraccionó sobre gel de sílice (eluyente: hexanos a hexanos-acetato de etilo (98:2)) para dar una fracción (3,1 g) que contiene el producto sililado junto con otros silanos. Esta fracción se disolvió en 5 ml de THF y se agregó 10 ml de solución TBAF (1 M en THF). La mezcla se dejó en reposo a

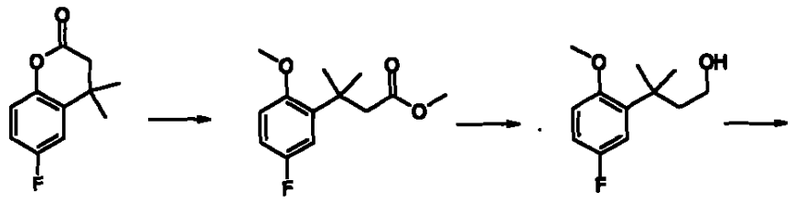
903
896
925

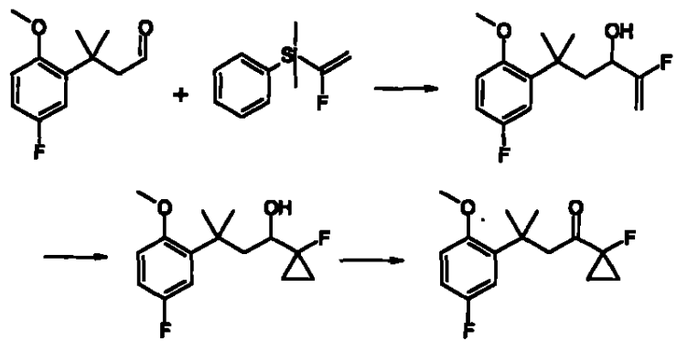
temperatura ambiente durante 20 minutos, se diluyó con hexanos-acetato de etilo, y se lavó con agua, se secó, se filtró, y se concentró al vacío. Del fraccionamiento del residuo sobre gel de sílice (eluyente: hexanos-acetato de etilo (99:1 a 9:1 gradiente)) se obtuvo 1,73 g del producto en bruto 2-fluoro-5-(4-fluorofenil)-5-metilhex-1-en-3-ol en forma de aceite que se utilizó sin purificación adicional .

El producto en bruto anterior 2-fluoro-5-(4-fluorofenil)-5-metilhex-1-en-3-ol (1,73 g, 7,65 mmol) agitado bajo gas nitrógeno y enfriado sobre hielo, se agregó dietil zinc (1,1 M en tolueno, 8,0 ml). Al cabo de 5 minutos, se agregó 1,0 ml de diyodometano gota a gota durante 20 minutos y la mezcla se agitó y se permitió tomar temperatura ambiente y luego se agitó a temperatura ambiente durante 4 días. Luego se agregó 0,5 ml de agua a la mezcla de reacción, seguido de acetato de etilo. La mezcla resultante luego se filtró a través de tierra diatomea y el solvente se eliminó al vacío y el residuo se fraccionó sobre gel de sílice (hexanos-diclorometano (1:1) a diclorometano gradiente) para dar 1-(1-fluorociclopropil)-3-(4-fluorofenil)-3-metilbutan-1-ol en forma de aceite.

2,2 ml de una solución de cloruro de oxalilo 2 M en diclorometano se diluyeron con 2,5 ml de diclorometano y se enfrió en un baño de hielo seco/acetona.A esta solución se agregó a gota a gota una solución de 0,7 ml de DMSO en 2,5 ml de diclorometano. Al cabo de 10 minutos, se agregó una solución del producto en bruto anterior 1-(1-fluorociclopropil)-3-(4-fluorofenil)-3-metilbutan-1-ol (0,72 g, 3,0 mmol) en 2 ml de diclorometano y la mezcla se agitó durante 15 minutos. Se agregaron 4 ml de trietilamina, se retiró el baño refrigerante, se permitió a la mezcla calentarse a temperatura ambiente y luego se desactivó con agua y se diluyó con hexanos. La capa orgánica se separó, se lavó con agua, se secó, se filtró, y se concentró al vacío. El residuo se purificó mediante cromatografía sobre gel de sílice (eluyente: hexanos a hexanos-diclorometano (4:1) gradiente) para dar 0,37 g del producto del título en forma de aceite.

Ejemplo 50: Síntesis de 1-(1-Fluorociclopropil)-3-(5-fluoro-2-metoxifenil)-3-metilbutan-1-ona





A una solución de 6-fluoro-4,4-dimetilcroman-2-ona en 40 ml de DMSO se agregó una solución de 5,5 g de hidróxido de sodio en 5 ml de agua durante 5 minutos (una reacción exotérmica). Al cabo de 20 minutos, se agregó yoduro de metilo (20 g) en porciones durante 15 minutos y la mezcla se agitó a temperatura ambiente hasta el día siguiente. La mezcla se diluyó con hexanos, se lavó con agua, se secó, se filtró, y se concentraron al vacío para dar 12,4 g del éster que se utilizó sin purificación adicional .

A una suspensión de LAH (1,64 g) en 100 ml de THF agitada bajo atmósfera de argón se agregó gota a gota durante 30 minutos una solución del anterior metil éster del ácido 3-(5-fluoro-2-metoxifenil)-3-metilbutírico en 10 ml de THF (reacción vigorosa). La mezcla se agitó a temperatura ambiente hasta el día siguiente. La reacción se diluyó con 200 ml de dietiléter y se desactivó por el agregado de 3 ml de agua (agregada cuidadosamente) y 3 ml de ácido acético. La mezcla se filtró a través de tierra diatomea y se lavó con dietiléter. De la evaporación del solvente se obtuvieron 10,8 g de 3-(5-fluoro-2-metoxifenil)-3-metilbutan-1-ol, que se utilizó sin purificación adicional .

Una solución de 3-(5-fluoro-2-metoxifenil)-3-metilbutan-1-ol (3,30 g, 15,5 mmol) en 40 ml de diclorometano se trató con clorocromato de piridinio (4,2 g, 19,5 mmol) en porciones durante 5 minutos. La mezcla se agitó durante 3 horas, se filtró a través de un lecho del auxiliar filtrante de CELITE® y el lecho se lavó con hexanos. El filtrado se concentró al vacío. De la cromatografía sobre SiO_2 (30% a 50% diclorometano en hexanos, gradiente) se obtuvieron 2,5 g de 3-(5-Fluoro-2-metoxifenil)-3-metilbutiraldehído en forma de aceite (77% de rendimiento).

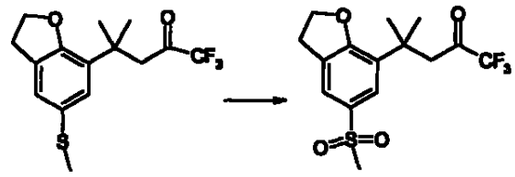
A una solución de 3-(5-fluoro-2-metoxifenil)-3-metilbutiraldehído (1,1 g, 5,2 mmol) y el anterior (1-fluorovinil)dimetilfenilsilano (2,2 g, 12,2 mmol) en 5 ml de THF se agregó 0,6 ml de fluoruro de tetrabutilamonio (1 M en THF) y la mezcla se agitó a temperatura ambiente hasta el día siguiente. TLC mostró una conversión parcial del producto. Se agregó fluoruro de cesio (0,22 g) y la mezcla se agitó a temperatura ambiente durante 3 días. Se agregaron 2 ml de agua y 2 ml de ácido acético y la mezcla se calentó a 60°C

durante 2 horas para efectuar la desilización de cualquier producto sililado. La mezcla se diluyó con acetato de etilo, se lavó con agua, se secó, se filtró y se concentró al vacío. Del fraccionamiento del residuo sobre gel de sílice (eluyente: hexanos-diclorometano (3:1 a 1:3 gradiente) se obtuvo 0,798 g (59,5% de rendimiento) de 2-fluoro-5-(5-fluoro-2-metoxifenil)-5-metilhex-1-en-3-ol en forma de aceite que se utilizó sin purificación adicional.

Al 2-fluoro-5-(5-fluoro-2-metoxifenil)-5-metilhex-1-en-3-ol, agitado bajo gas nitrógeno y enfriado sobre hielo, se agregó 8,0 ml de dietilo zinc (1,1 M en tolueno). Al cabo de 5 minutos, se agregó 1,0 ml de diyodometano gota a gota durante 20 minutos, y la mezcla se agitó y se permitió adquirir temperatura ambiente y luego se agitó a temperatura ambiente durante 2 días. Luego se agregaron 0,5 ml de agua, seguido de acetato de etilo, y la mezcla se filtró a través de tierra diatomea. El producto se concentró al vacío y el residuo se fraccionó sobre gel de sílice (hexanos-diclorometano (1:1) a diclorometano, gradiente) para dar 0,8 g de 1-(1-fluorociclopropil)-3-(5-fluoro-2-metoxifenil)-3-metilbutan-1-ol en forma de aceite que se utilizó sin purificación adicional.

6 ml de una solución 2 M de cloruro de oxalilo en diclorometano se diluyeron con 5 ml de diclorometano y se enfrió en un baño de hielo seco/acetona. A esta solución se agregó gota a gota una solución de 1,5 ml de DMSO en 5 ml de diclorometano. Al cabo de 10 minutos, se agregó una solución del producto en bruto 1-(1-fluorociclopropil)-3-(5-fluoro-2-metoxifenil)-3-metilbutan-1-ol (0,8 g, 3 mmol) en 4 ml de diclorometano se agregó y la mezcla se agitó durante 15 minutos. Se agregó 4 ml de trietilamina, se retiró el baño refrigerante, y se permitió a la mezcla de reacción calentarse a temperatura ambiente, se desactivó con agua, y se diluyó con hexanos. La capa orgánica se separó, se lavó con agua, se secó, se filtró, y se concentró al vacío. El residuo se purificó mediante cromatografía sobre gel de sílice (eluyente: hexanos a hexanos-acetato de etilo (10:1), gradiente) para dar 0,68 g del producto del título en forma de aceite que se utilizó sin purificación adicional.

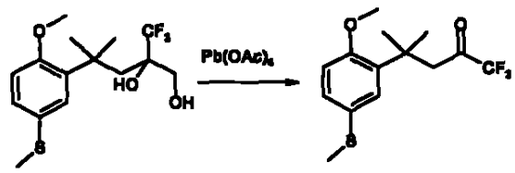
Ejemplo 51: Síntesis de 1,1,1-trifluoro-4-(5-metanosulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ona



Una solución agitada de 1,1,1-trifluoro-4-metil-4-(5-metilsulfanil-2,3-dihidrobenzofuran-7-il)pentan-2-ona (5,3 g, 16,7 mmol) en acetonitrilo se agregó

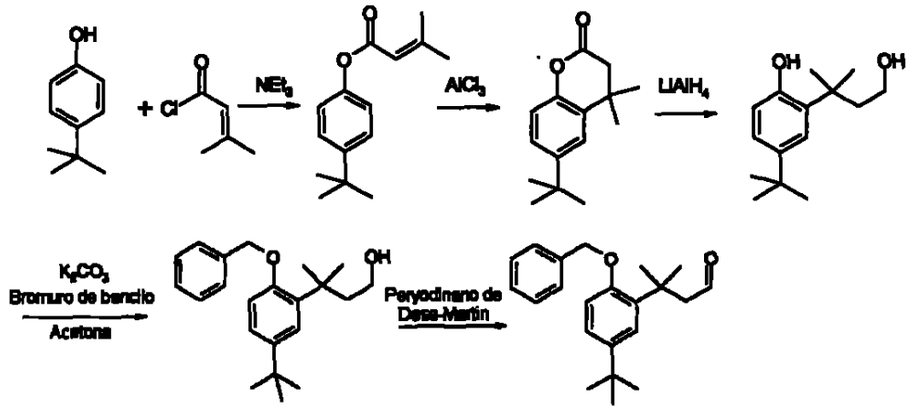
lentamente a una solución de $NaIO_4$ (10,7 g, 50 mmol) en 70 ml de agua. Al cabo de 10 minutos, se agregó $RuCl_3$ (50 mg, 0,24 mmol) y se continuó la agitación a temperatura ambiente durante 30 minutos. La mezcla se concentró al vacío, y el sólido grisáceo resultante se filtró, se lavó con agua, y se secó para dar 5,4 g del producto del título, que se usó sin ulterior purificación (93% de rendimiento).

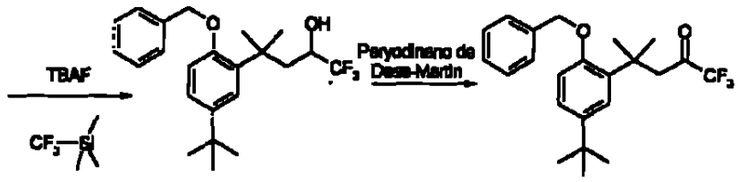
Ejemplo 52: Síntesis de 1,1,1-trifluoro-4-(2-metoxi-5-metilsulfanilfenil)-4-metilpentan-2-ona



A una solución de 4-(2-metoxi-5-metilsulfanilfenil)-4-metil-2-trifluorometilpentan-1,2-diol (1,5 g, 5,3 mmol) en 25 ml de metanol se agregó 2,4 g de acetato de plomo (IV) ($Pb(OAc)_4$) y la mezcla de reacción se agitó hasta que la TLC indicó que se había completado la reacción, al cabo de varias horas. La mezcla de reacción luego se filtró a través de un lecho de tierra diatomea y el filtrado se concentró al vacío para dar 1,12 g (83,8% de rendimiento) de 1,1,1-trifluoro-4-(2-metoxi-5-metilsulfanilfenil)-4-metilpentan-2-ona.

Ejemplo 53: Síntesis de 4-(2-Benciloxi-5-*ter*-butilfenil)-1,1,1-trifluoro-4-metilpentan-2-ona





A una solución helada de 4-*ter*-butilfenol (15 g, 100 mmol) y 11,12 ml de cloruro de 3-metilbut-2-enoilo en 200 ml de dietiléter a 0°C se agregó 13,9 ml de trietilamina mediante un embudo de adición. La mezcla de reacción se calentó a temperatura ambiente y se agitó hasta que la TLC indicó que se había completado la reacción. La mezcla de reacción luego se filtró a través de tierra diatomea, y la capa de dietiléter se lavó dos veces con agua, se lavó con salmuera, se secaron sobre sulfato de magnesio, y se concentró al vacío para producir 23 g de 4-*ter*-butilfeniléster del ácido 3-metilbut-2-enoico como aceite marrón que se cristalizó parcialmente estando en reposo

A una solución de 4-*ter*-butilfeniléster del ácido 3-metilbut-2-enoico (23 g, 99 mmol) en 50 ml de disulfuro de carbono (CS_2) se agregó 19,8 g de cloruro de aluminio ($AlCl_3$) en porciones en el transcurso de 1 hora, en una reacción muy exotérmica. Al cabo de agitar durante varias horas, TLC mostró que se había completado la reacción. La mezcla de reacción se concentró bajo un flujo de gas nitrógeno, y el residuo se vertió sobre hielo y se extrajo con acetato de etilo. Los orgánicos se combinaron, se secaron sobre sulfato de magnesio, y se concentraron al vacío. El residuo se purificó sobre un lecho de sílice (0% a 5% de acetato de etilo-hexanos) para dar 8,1 g de 6-*ter*-butil-4,4-dimetilcroman-2-ona en forma de aceite.

A una suspensión helada de 1,99 g de LAH en 60 ml de THF a 0°C se agregó una solución de 6-*ter*-butil-4,4-dimetilcroman-2-ona (8,1 g, 34,9 mmol) en 10 ml de THF por embudo de adición. La mezcla de reacción se calentó a temperatura ambiente y se agitó hasta que la TLC indicó que se había completado la reacción. Al cabo de 1 hora, la mezcla de reacción se enfrió en baño de hielo y se desactivó cuidadosamente con una cantidad mínima de agua. La mezcla de reacción luego se secó sobre sulfato de magnesio y se filtró a través de tierra diatomea. El filtrado se concentró al vacío, el residuo se agregó a hexanos, y los sólidos se aislaron por filtración para dar 5 g de 4-*ter*-butil-2-(3-hidroxi-1,1-dimetilpropil)fenol.

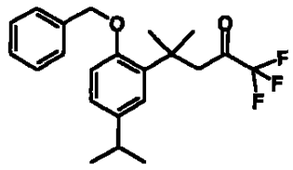
A una solución de 4-*ter*-butil-2-(3-hidroxi-1,1-dimetilpropil)fenol (2 g, 8,5 mmol) y 1,1 ml bromuro de bencilo en 10 ml de DMF se agregó 1,75 g de potasio carbonato (K_2CO_3) y la mezcla de reacción se agitó a temperatura ambiente hasta que la TLC indicó que se había completado la reacción. Al cabo de agitación hasta el día siguiente, la

mezcla de reacción se diluyó con hielo y se extrajo con dietiléter. Los orgánicos se combinaron, se lavó cuatro veces con agua, se lavó con salmuera, se secaron sobre sulfato de magnesio, y se concentraron al vacío. El residuo se purificó en el dispositivo COMBIFLASH® (0% a 30% acetato de etilo-hexanos) para dar 1,7 g de 3-(2-benciloxi-5-*ter*-butilfenil)-3-metilbutan-1-ol en forma de aceite.

A una solución de 3-(2-benciloxi-5-*ter*-butilfenil)-3-metilbutan-1-ol (1,7 g, 5,2 mmol) en 20 ml de diclorometano se agregó 3,27 g de peryodinano de Dess-Martin y la reacción se agitó hasta que la TLC indicó que se había completado la reacción. Al cabo de 2 horas, la mezcla de reacción se pasó a través de un lecho de sílica, se eluyó con 5% acetato de etilo-hexanos para dar 1,67 g de 3-(2-benciloxi-5-*ter*-butilfenil)-3-metilbutiraldehído en forma de aceite.

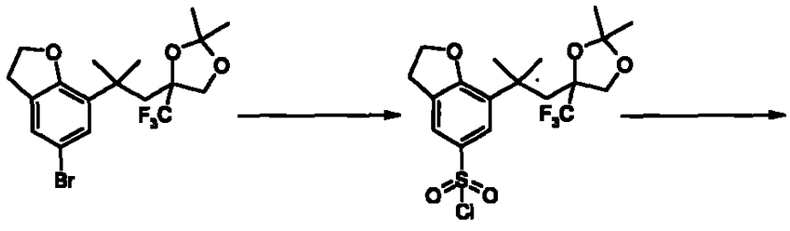
3-(2-Benciloxi-5-*ter*-butilfenil)-3-metilbutiraldehído se convirtió en 4-(2-benciloxi-5-*ter*-butilfenil)-1,1,1-trifluoro-4-metilpentan-2-ona usando procedimientos similares a los del Ejemplo 4 de la publicación de la solicitud de patente U.S. Nº 2004/0023999.

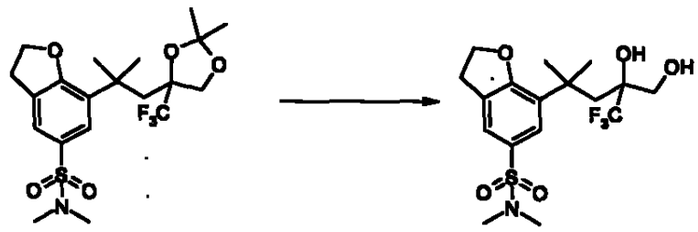
Ejemplo 54: Síntesis de 4-(2-Benciloxi-5-isopropilfenil)-1,1,1-trifluoro-4-metilpentan-2-ona



4-(2-Benciloxi-5-isopropilfenil)-1,1,1-trifluoro-4-metilpentan-2-ona se preparó a partir de 4-isopropilfenol del mismo modo como se describe en la síntesis de 4-(2-benciloxi-5-*ter*-butilfenil)-1,1,1-trifluoro-4-metilpentan-2-ona.

Ejemplo 55: Síntesis de dimetilamida del ácido 7-(4,4,4-Trifluoro-3-hidroxi-3-hidroximetil-1,1-dimetil-butil)-2,3-dihidrobenzofuran-5-sulfónico





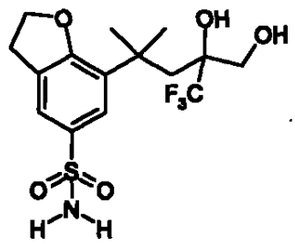
Una solución de 5-bromo-7-[2-(2,2-dimetil-4-trifluorometil-[1,3]dioxolan-4-il)-1,1-dimetiletil]-2,3-dihidrobenzofurano (4,0 g, 9,4 mmol) en 8 ml de THF se trató con *n*-BuLi (2,5 M en hexanos, 4,2 ml, 10,5 mmol) a -78°C. Al cabo de 15 minutos, se burbujeó un exceso de gas SO_2 en la mezcla y la reacción se monitoreó respecto de la desaparición del material de partida. A continuación, la mezcla de reacción se concentró bajo un flujo de gas nitrógeno, se diluyó con THF, y se trató con *N*-clorosuccinimida (1,48 g, 11,1 mmol). La mezcla se agitó durante 15 minutos y se dividió en tres porciones iguales. Una solución de stock de cloruro de sulfonilo (1/3 de la mezcla) en 8 ml de THF se trató con dimetilamina (2 M en THF, 10 ml, 20 mmol). Al cabo de 30 minutos, la mezcla se diluyó con 20 ml de solución acuosa saturada de cloruro de amonio y se extrajo con tres porciones de 10 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con tres porciones de 10 ml de solución acuosa saturada de cloruro de amonio, dos porciones de 10 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. El material en bruto se purificó en gel de sílice (3% a 30% acetato de etilo en hexanos, gradiente) para dar 1,18 g (83% de rendimiento) de dimetilamida del ácido 7-[2-(2,2-dimetil-4-trifluorometil-[1,3]dioxolan-4-il)-1,1-dimetil-etil]-2,3-dihidrobenzo-furan-5-sulfónico, que se usó sin ulterior purificación.

Una mezcla de 1,18 g (2,61 mmol) de dimetilamida del ácido 7-[2-(2,2-dimetil-4-trifluorometil-[1,3]dioxolan-4-il)-1,1-dimetil-etil]-2,3-dihidrobenzofuran-5-sulfónico y 303 mg (1,59 mmol) de monohidrato del ácido *p*-toluenosulfónico en 20 ml de metanol se calentó a reflujo durante 3 días. La mezcla luego se enfrió y se diluyó con 15 ml de bicarbonato de sodio acuoso saturado y se extrajo con tres porciones de 5 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con dos porciones de 5 ml de bicarbonato de sodio acuoso saturado, dos porciones de 5 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. El residuo se trituró con éter para dar 845 mg (78% de rendimiento) del compuesto del título como un sólido blanco.

Dimetilamida del ácido 7-(4,4,4-Trifluoro-3-hidroxi-3-hidroximetil-1,1-dimetil-butil)-2,3-dihidrobenzofuran-5-sulfónico se convirtió en la correspondiente trifluorometil cetona

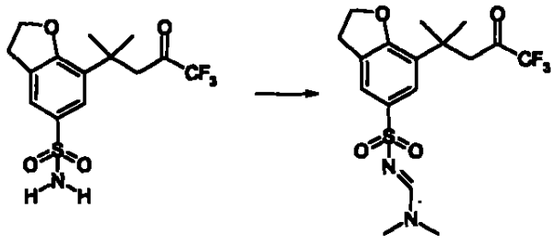
según el método revelado en la publicación de solicitud de patente U.S. Nº 2004/0029932, que se incorpora aquí a título de referencia.

Ejemplo 56: Síntesis de la amida del ácido 7-(4,4,4-Trifluoro-3-hidroxi-3-hidroximetil-1,1-dimetilbutil)-2,3-dihidrobenzofuran-5-sulfónico



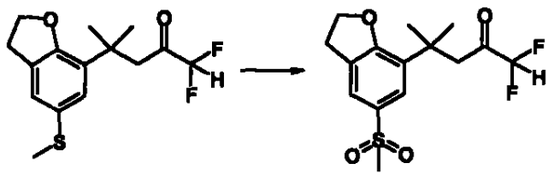
La amida del ácido 7-(4,4,4-Trifluoro-3-hidroxi-3-hidroximetil-1,1-dimetilbutil)-2,3-dihidrobenzofuran-5-sulfónico se preparó a partir de 5-bromo-7-[2-(2,2-dimetil-4-trifluorometil-[1,3]dioxolan-4-il)-1,1-dimetiletil]-2,3-dihidrobenzofurano del mismo modo que para la preparación de la dimetilamida del ácido 7-(4,4,4-trifluoro-3-hidroxi-3-hidroximetil-1,1-dimetilbutil)-2,3-dihidrobenzofuran-5-sulfónico.

Ejemplo 57: Síntesis de la 1-dimetilaminomet-(*E*)-ilidenamida del ácido 7-(4,4,4-Trifluoro-1,1-dimetil-3-oxobutil)-2,3-dihidrobenzofuran-5-sulfónico



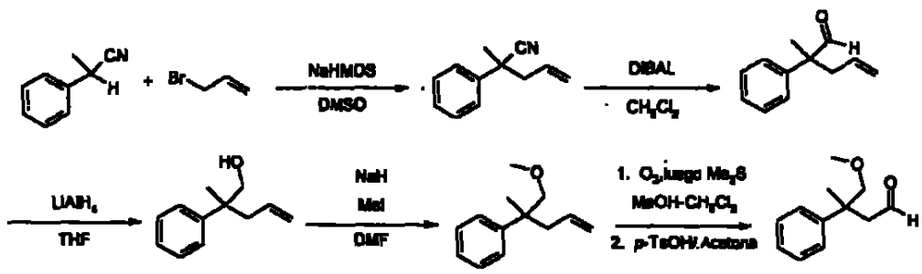
Una solución de la amida del ácido 7-(4,4,4-trifluoro-1,1-dimetil-3-oxobutil)-2,3-dihidrobenzofuran-5-sulfónico (870 mg, 2,47 mmol) en 30 ml de diclorometano se hizo reaccionar con *N,N*-dimetilformamida dimetil acetal (580 mg, 4,86 mmol). Al cabo de 30 minutos, la mezcla se concentró a sequedad al vacío. El sólido resultante se trituró con dietiléter y se recogió para dar 950 mg del compuesto del título (94% de rendimiento).

Ejemplo 58: Síntesis de 1,1-Difluoro-4-(5-metanosulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ona



A una solución de 1,1-difluoro-4-metil-4-(5-metilsulfanil-2,3-dihidrobenzofuran-7-il)pentan-2-ona (840 mg, 2,8 mmol) en 12 ml de MeCN y 4 ml de agua se agregó peryodato de sodio (1,79 g, 8,4 mmol) seguido de un cristal de hidrato de cloruro de rutenio (III). La reacción se monitoreó por TLC hasta que ya no resultó evidente el tioléter. Al cabo de 1 hora, la reacción se concentró al vacío, se diluyó con agua, y se extrajo con acetato de etilo. Las capas orgánicas combinadas se secaron sobre sulfato de magnesio, se trataron sobre carbón, se filtraron y se concentraron al vacío para dar 910 mg (98% de rendimiento) del compuesto del título como un sólido color blanco.

Ejemplo 59: Síntesis de 4-Metoxi-3-metil-3-fenilbutiraldehído



A una solución de 2-fenilpropionitrilo (4,04 g, 30,79 mmol) en 40 ml de DMSO se agregó 34 ml (34 mmol) de una solución 1 M de sodio bis(trimetilsilil)amida (NaHMDS) en THF en un plazo de 5 minutos. Al cabo de 10 minutos, se agregó bromuro de alilo (6 ml, 69,33 mmol) gota a gota (exotérmica). La mezcla se enfrió con un baño de hielo-agua. La mezcla se agitó durante 20 minutos, tomándose una masa sólida. Se agregaron otros 20 ml de DMSO. Al cabo de 10 minutos, la mezcla se diluyó con 200 ml de cloruro de amonio y se extrajo con tres porciones de 100 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con seis porciones de 5 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío para dar 5,25 g (99,5% de rendimiento) de 2-metil-2-fenilpent-4-enonitrilo como aceite amarillo que se usó sin ulterior purificación.

A una solución de 2-metil-2-fenilpent-4-enonitrilo (5,25 g, 30,65 mmol) en 150 ml de diclorometano se agregó una solución 1 M de hidruro de diisobutilaluminio (DIBAL) (38 ml, 38 mmol) en diclorometano durante un período de 15 minutos. La reacción se monitoreó por TLC; al cabo de 1 hora, la TLC (acetato de etilo-hexanos (1:9)) indicó un producto levemente menos polar. La reacción se vertió en HCl 1 N acuoso helado y se separó la capa de diclorometano. Se extrajo la capa acuosa con dos porciones de 50 ml de diclorometano. Las capas orgánicas combinadas se lavaron con 50 ml de salmuera, dos porciones de 50 ml de bicarbonato de sodio acuoso saturado, 50 ml de salmuera, se

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secaron sobre sulfato de magnesio, se filtraron a través de tierra diatomea, y se concentraron al vacío para dar 4,6 g (86,1% de rendimiento) de 2-metil-2-fenilpent-4-enal que se usó sin ulterior purificación.

A una solución de 2-metil-2-fenilpent-4-enal (4,6 g, 26,4 mmol) en 100 ml de THF se agregó hidruro de litio aluminio (LAH) (2,6 g, 68,51 mmol) en varias porciones. La mezcla se agitó durante 3 horas a temperatura ambiente y luego se sometió a reflujo durante 2 horas. La reacción se monitoreó por TLC con acetato de etilo-hexanos (1:9) donde se indicó un nuevo producto más polar. La reacción se enfrió, se eliminó el exceso de LAH y se desactivó cuidadosamente con agua gota a gota. La mezcla luego se diluyó con HCl 1 N acuoso y se extrajo con 100 ml de hexanos y dos porciones de 100 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con 50 ml de HCl 1 N acuoso , dos porciones de 50 ml de salmuera, dos porciones de 50 ml de bicarbonato de sodio acuoso saturado, 50 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. El material en bruto se cromatografió en gel de sílice usando hexanos para cargar la muestra y luego se eluyó con 1% a 15% de acetato de etilo-hexanos para dar 3,2 g (68,8) de 2-metil-2-fenilpent-4-en-1-ol.

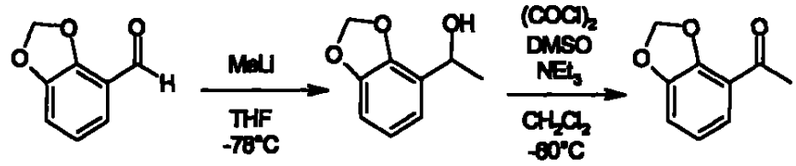
A una solución de 2-metil-2-fenilpent-4-en-1-ol (3,2 g, 18,15 mmol) en 17 ml de DMF se agregó hidruro de sodio (1,25 g, 31,25 mmol, 60% en aceite mineral). La mezcla se agitó hasta que cesó la espuma y luego se agregó yoduro de metilo (6 ml, 96 mmol). Al cabo de 2 horas, la mezcla se desactivó con 50 ml de solución acuosa saturada de cloruro de amonio y se extrajo con tres porciones de 50 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con 30 ml de solución acuosa saturada de cloruro de amonio, cinco porciones de 5 ml de salmuera, se secarpm sobre sulfato de magnesio, se filtraron y se concentraron al vacío para dar 3,4 g (98,4% de rendimiento) de (1-metoximetil-1-metilbut-3-enil)benceno que se usó sin ulterior purificación.

A una solución helada (-78°C) de (1-metoximetil-1-metilbut-3-enil)benceno (1,67 g, 8,77 mmol) en metanol-diclorometano se burbujeó gas de ozono hasta que la solución se tornó azul. Luego se purgó el exceso de ozono de la mezcla con oxígeno y luego se agregó sulfuro de dimetilo (5 ml, 68 mmol) y la mezcla se calentó a temperatura ambiente y se agitó hasta el día siguiente. La mezcla luego se concentró al vacío para remover el excedente de sulfuro de dimetilo y se diluyó con 20 ml de cloruro de amonio y se extrajo con tres porciones de 5 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con tres porciones de 5 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío para dar un aceite que correspondió al dimetil acetal por ^{1}H-RMN. El producto en bruto se diluyó con 40 ml de acetona y *p*-TsOH (300

mg, 1,57 mmol) se agregó y la mezcla se agitó a temperatura ambiente durante 2 horas. La reacción se monitoreó por ^{1}H-RMN, lo que indicó la presencia de aldehído y dimetil acetal. La reacción se sometió a reflujo durante 4 horas y se monitoreó por TLC (acetato de etilo-hexanos (1:9)) y luego se enfrió y se diluyó con una solución acuosa saturada de bicarbonato de sodio y se extrajo con tres porciones de 5 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con dos porciones de 10 ml de solución acuosa saturada de bicarbonato de sodio, dos porciones de 10 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vácío para dar 1,45 g (85,9% de rendimiento) de 4-metoxi-3-metil-3-fenilbutiraldehído.

El 4-metoxi-3-metil-3-fenilbutiraldehído se convirtió en 1,1,1-trifluoro-5-metoxi-4-metil-4-fenilpentan-2-ona como se describe previamente en el Ejemplo 26 de la publicación de solicitud de patente U.S. Nº 2004/0023999.

Ejemplo 60: Síntesis de 1-Benzo[1,3]dioxol-4-iletanona



A una solución de benzo[1,3]dioxol-4-carbaldehído (10 g, 66,7 mmol) en 200 ml THF a -78°C se agregó por embudo de adición 43,7 ml de una solución 1,6 M de MeLi en dietiléter. La reacción se calentó lentamente a temperatura ambiente y se agitó hasta el día siguiente. Una TLC de una alícuota mostró que se había completado la reacción. La reacción luego se enfrió a -78°C y se desactivó con cloruro de amonio saturado acuoso y se concentró al vacío. El residuo luego se extrajo con acetato de etilo. Los orgánicos se combinaron, se secaron sobre sulfato de magnesio, y se concentraron al vacío para dar 11 g (99,4% de rendimiento) de 1-benzo[1,3]dioxol-4-iletanol como un aceite marrón que se cristalizó estando en reposo.

A una solución de 1-benzo[1,3]dioxol-4-iletanol (11 g, 66,3 mmol) en 100 ml de THF se agregó 17,26 g de dióxido de manganeso (MnO_2) en una porción y la reacción se monitoreó por TLC. Al cabo de varias horas, la TLC mostró algo del producto pero con una cantidad significativa de alcohol. Se agregó más dióxido de manganeso y la solución se agitó La TLC luego mostró la mayoría del producto pero con una cantidad significativa de alcohol. La mezcla de reacción luego se filtró a través de un lecho de tierra diatomea y el filtrado se concentró al vacío para dar un aceite que cristalizó mayormente estando en reposo. A 9,24 ml de una solución de cloruro de oxalilo en 120 ml de diclorometano a -60°C se agregó una solución de 15 ml de DMSO en 20 ml de diclorometano. Al cabo de

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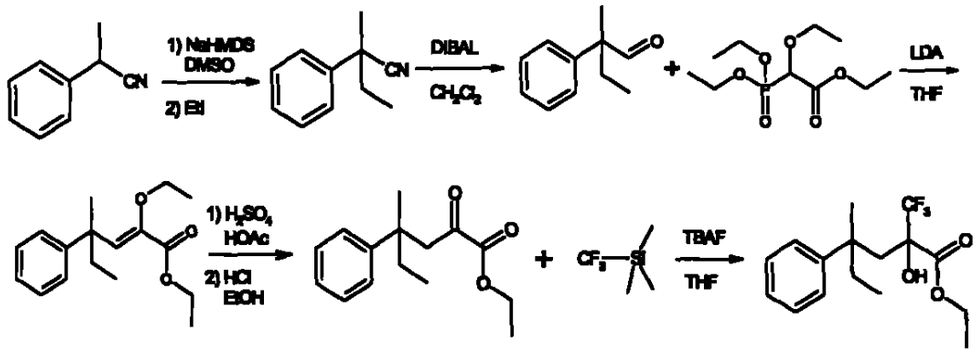
10 minutos, se agregó una solución de la mezcla anterior de alcohol/cetona (53 mmol) en 20 ml de diclorometano, seguidos 15 minutos más tarde de 44,3 ml de trietilamina. Se permitió que la reacción lentamente se calentara a temperatura ambiente hasta el día siguiente. La mezcla de reacción luego se vertió sobre hielo y la capa orgánica se lavó con cinco porciones de 100 ml de agua, luego salmuera, y luego se secaron sobre sulfato de magnesio. Los orgánicos se concentraron al vacío para obtener sólidos tostados, triturándose los sólidos con hexanos, se recolectaron por filtración, y se secaron para dar 9,33 g (85,8% de rendimiento) de 1-benzo[1,3]dioxol-4-iletanona.

La 1-benzo[1,3]dioxol-4-iletanona se convirtió en 4-benzo[1,3]dioxol-4-il-1,1,1-trifluoro-4-metilpentan-2-ona según el Ejemplo 26 de la publicación de solicitud de patente U.S. Nº 2004/0023999.

Ejemplo 61: Síntesis de etil ésteres del ácido 2-Hidroxi-4-metil-4-fenil-2-trifluorometilhexanoico



A una solución de 2-fenilpropionitrilo (5 g, 38 mmol) en 50 ml de DMSO se agregó 42 ml de una solución 1 M de THF y sodio bis(trimetilsilil)amida (NaHMDS). Al cabo de 15 minutos, la reacción se enfrió a 0°C y se agregaron 4,6 ml de yoduro de etilo. La reacción luego se agitó durante 30 minutos. Cuando la TLC mostró que se había completado la reacción, la mezcla de reacción se vertió en agua y se extrajo con dietiléter. Los orgánicos se combinaron, se lavó cuatro veces con agua, se lavó con salmuera, se secaron sobre sulfato de magnesio, y se concentraron al vacío para dar 6,1 g de 2-metil-2-fenilbutironitrilo en forma de aceite.

A una solución de 2-metil-2-fenilbutironitrilo (6,1 g, 38,3 mmol) en 50 ml de diclorometano a temperatura ambientese se agregó 57 ml de DIBAL 1 M en diclorometano mediante jeringa. La reacción se agitó durante 30 minutos, cuando la TLC de una alícuota mostró que se había completado la reacción La mezcla de reacción se vertió cuidadosamente en 100 ml de HCl 1 N y se separaron las capas. Los orgánicos se

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concentraron al vacío y se agregaron a dietiléter, se combinaron con la capa acuosa, y se extrajeron con dietiléter. Luego se combinaron los orgánicos, se secaron sobre sulfato de magnesio, y se concentraron al vacío. El residuo se purificó en una columna de gel de sílice (0% a 2% de acetato de etilo en hexanos) para dar 4,2 g de 2-metil-2-fenilbutiraldehído como aceite incoloro.

A una solución de etiléster del ácido (dietoxifosforil)etoxiacético (7,4 g, 27,6 mmol) en 30 ml de THF, a 0°C, se agregó 16 ml de LDA 1,8 M en heptano/THF/etilbenceno. La mezcla de reacción se agitó durante 30 minutos y luego se agregó una solución de 2-metil-2-fenilbutiraldehído (4,2 g, 25,9 mmol) en 30 ml de THF gota a gota mediante una jeringa. La mezcla de reacción luego se calentó a temperatura ambiente, se desactivó con solución acuosa saturada de cloruro de amonio, y se extrajo con dietiléter. Los orgánicos se combinaron, se secó sobre sulfato de magnesio y se concentraron al vacío para dar 8,3 g de una mezcla 2:1 de *E* y *Z* isómeros de etilésteres del ácido 2-etoxi-4-metil-4-fenilhex-2-enoico como aceite naranja.

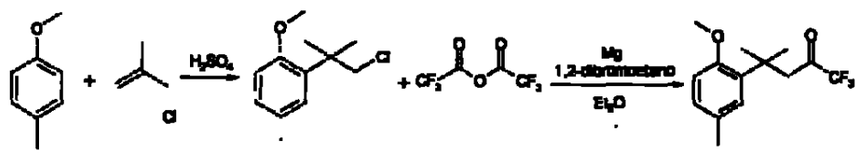
A una solución de etil éster del ácido 2-etoxi-4-metil-4-fenilhex-2-enoico (8,3 g, 30 mmol) en 25 ml de HOAc se agregó 116,5 ml de solución acuosa 1 M de ácido sulfúrico. La mezcla de reacción se agitó a temperatura ambiente durante varias horas. Como la TLC no mostró ninguna reacción, la mezcla de reacción se colocó en un baño de aceite a 100°C y se agitó hasta el día siguiente. Como la TLC continuó sin resultados, se agregaron 2 ml más de ácido sulfúrico 1 M acuoso y 20 ml de HOAc. Al cabo de 1 hora, la TLC de una alícuota mostró la consumición del isómero de la olefina (mancha más polar) principal y una mancha remanente del isómero menor (el producto puede correr junto con el isómero menor). La mezcla de reacción luego se enfrió a temperatura ambiente y se extrajo con dietiléter. Se combinaron los orgánicos, se lavaron con cuatro porciones de agua, se lavaron con salmuera, se secaron sobre sulfato de magnesio, y se concentraron al vacío para dar 2,5 g de un aceite naranja. La ^{1}H-RMN mostró una mezcla de 1:1 de un isómero menor y aldehído. Se extrajo la capa acuosa con acetato de etilo y se combinaron los extractos de acetato de etilo, se secaron sobre sulfato de magnesio, y se concentraron al vacío para obtener un líquido marrón. La ^{1}H-RMN mostró acetato de etilo significativo y HOAc y el producto deseado como cetoácido. La solución del cetoácido se agregó a 200 ml de etanol, se trató con 1 ml de HCl concentrado, y se calentó a reflujo hasta el día siguiente. La TLC luego mostró una nueva mancha menos polar. La mezcla de reacción se enfrió a temperatura ambiente y se concentró al vacío. El residuo luego se diluyó con agua y se extrajo con dietiléter. Los orgánicos se combinaron, se secaron sobre sulfato de magnesio, y se concentraron al vacío para

obtener etiléster del ácido 4,3 g de 4-metil-2-oxo-4-fenilhexanoico como un aceite color naranja.

A una solución del etil éster del ácido 4-metil-2-oxo-4-fenilhexanoico (4,3 g, 17,3 mmol) y 3,6 ml de trifluorometiltrimetilsilano en 50 ml de THF se agregó 1,5 ml (0,1 equiv) de una solución de TBAF 1 M y la reacción se agitó a temperatura ambiente hasta que el TLC mostró que el cetoéster se había consumido, alrededor de 30 minutos. Luego se agregó el resto de TBAF (17,5 ml) y la mezcla de reacción se agitó durante 1 hora. TLC luego mostró que se había completado la reacción. La mezcla de reacción se concentró al vacío, el residuo se diluyó con HCl 1 N y se extrajo con dietiléter. Los orgánicos se combinaron, se secaron sobre sulfato de magnesio, y se concentraron al vacío para obtener un aceite marrón. El aceite se agregó a hexanos (apariencia turbia), se agregó carbón activado, y la solución resultante se filtró a través de tierra diatomea y se concentró al vacío para obtener 3,8 g (83% de rendimiento) de una mezcla diaestereomérica de etiléstares del ácido 2-hidroxi-4-metil-4-fenil-2-trifluorometilhexanoico como un aceite verde claro.

La mezcla diaestereomérica de ésteres se convirtió en la correspondiente trifluorometil cetona según el Ejemplo 1 de la publicación de la solicitud de patente U.S. Nº 2004/0023999.

Ejemplo 62: Síntesis de 1,1,1-Trifluoro-4-(2-metoxi-5-metilfenil)-4-metilpentan-2-ona

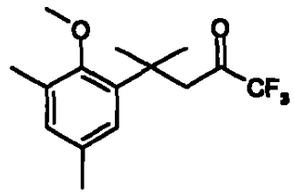


A una solución amarilla de 4-metilanisol (20 g, 183,5 mmol) y 1,7 ml de ácido sulfúrico concentrado se agregó 19,17 ml de 3-cloro-2-metilpropeno por embudo de adición. La reacción se calentó y se tomó púrpura oscuro. Al cabo de 20 minutos los sólidos comenzaron a precipitar. La TLC de una alícuota mostró algo de anisol inicial y la formación de una nueva mancha levemente menos polar. La mezcla de reacción se agitó hasta el día siguiente y la TLC luego mostró que se había completado la reacción. La mezcla de reacción se vertió sobre hielo y se extrajo con dietiléter. Los orgánicos se combinaron, se secaron sobre sulfato de magnesio, y se concentraron al vacío para obtener un aceite. El residuo se agregó a hexanos, se enfrió a -78°C, y los sólidos se colectaron por filtración para dar 14 g de 2-(2-cloro-1,1-dimetiletil)-1-metoxi-4-

metilbenceno en forma de aceite luego de calentarse. El filtrado se concentró al vacío para dar 15,5 g de una mezcla 4:1 del producto y el anisol inicial.

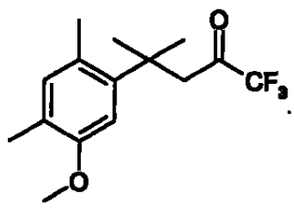
A una suspensión de granallas de magnesio (1,87 g) en 30 ml de dietiléter anhidro bajo atmósfera de argón en un baño de agua se agregó 1,62 ml de dibromoetano lentamente por jeringa de modo tal que la temperatura de reacción interna no exceda de 27°C. Una solución de 2-(2-cloro-1,1-dimetiletil)-1-metoxi-4-metilbenceno (4 g, 18,9 mmol) y dibromoetano adicional (1,62 ml) en 20 ml de dietiléter se agregó por embudo de adición en una proporción tal, que la temperatura interna se mantenga inferior a 25°C. La mezcla de reacción se torna verde y se formó un fino precipitado. Al cabo de 1 hora, la mezcla de reacción se enfrió a -78°C; los sólidos se aglomeran en el fondo de la mezcla de reacción y se detuvo la agitación. Una solución de 3,98 ml de anhidrirro trifluoroacético en 4 ml de dietiléter se agregó a la mezcla de reacción por embudo de adición mientras se agitaba manualmente la mezcla de reacción. La mezcla de reacción luego se calentó a temperatura ambiente, de la agitación resultó una temperatura superior a -40°C. La TLC de una alícuota mostró a una nueva mancha levemente más polar y material de partida. La mezcla de reacción luego se vertió sobre HCl 1 N frío y se extrajo con dietiléter. Los orgánicos se combinaron, se secaron sobre sulfato de magnesio, y se concentraron al vacío. El residuo se purificó en una columna de gel de sílice (0% a 5% acetato de etilo-hexanos) para dar 1,7 g (41% de rendimiento) de 1,1,1-trifluoro-4-(2-metoxi-5-metilfenil)-4-metilpentan-2-ona como un aceite claro.

Ejemplo 63: Síntesis de 1,1,1-Trifluoro-4-(2-metoxi-3,5-dimetilfenil)-4-metilpentan-2-ona



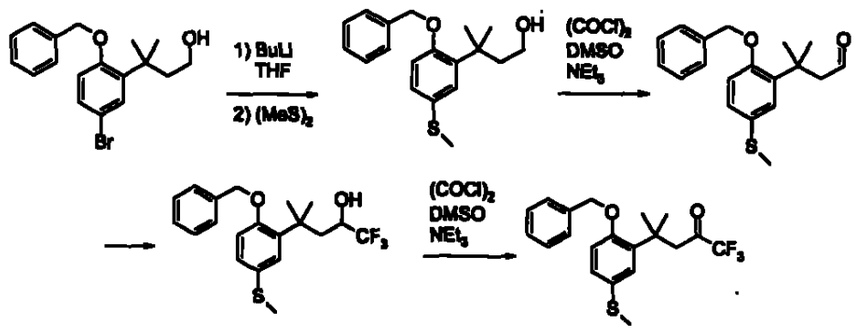
El producto del título se preparó a partir de 1-metoxi-2,4-dimetilbenceno según el mismo procedimiento descrito en la síntesis de 1,1,1-trifluoro-4-(2-metoxi-5-metilfenil)-4-metilpentan-2-ona.

Ejemplo 64: Síntesis de 1,1,1-Trifluoro-4-(5-metoxi-2,4-dimetilfenil)-4-metilpentan-2-ona



El producto del título se preparó a partir de 1-metoxi-2,4-dimetilbenceno según el mismo procedimiento descrito en la síntesis de 1,1,1-trifluoro-4-(2-metoxi-5-metilfenil)-4-metilpentan-2-ona.

Ejemplo 65: 4-(2-benciloxi-5-metilsulfanilfenil)-1,1,1-trifluoro-4-metilpentan-2-ona



A una solución de 3-(2-benciloxi-5-bromofenil)-3-metilbutan-1-ol (3 g, 8,6 mmol) en 50 ml de THF a -78°C se agregó 7,56 ml de *n*-BuLi (solución 2,5 M en hexanos) y la mezcla de reacción se agitó durante 10 minutos. Luego se agregó 1,55 ml de disulfuro de dimetilo y la mezcla de reacción se calentó a temperatura ambiente. Al cabo de 20 minutos, la TLC mostró una nueva mancha levemente más polar (mayor) con muy poco más. La mezcla de reacción luego se desactivó con solución acuosa saturada de cloruro de amonio y se extrajo con dietiléter. Los orgánicos se combinaron, se secaron sobre sulfato de magnesio, y se concentraron al vacío a 2,84 g de 3-(2-benciloxi-5-metilsulfanilfenil)-3-metilbutan-1-ol en forma de aceite.

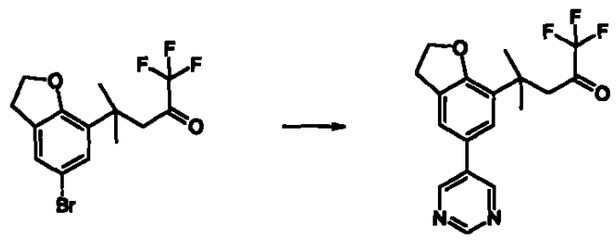
A una solución de 1,57 ml de cloruro de oxalilo en 15 ml de diclorometano a -60°C se agregó una solución de 2,55 ml de DMSO en 5 ml de diclorometano. Al cabo de 10 minutos, se agregó una solución de 3-(2-benciloxi-5-metilsulfanilfenil)-3-metilbutan-1-ol (2,84 g, 8,9 mmol) en 5 ml de diclorometano (los sólidos precipitaron rápidamente), seguido 15 minutos más tarde de 7,5 ml trietilamina y la mezcla de reacción se tornó muy espesa con los sólidos. La mezcla de reacción luego se calentó a temperatura ambiente y se monitoreó por TLC. Al cabo de 1 hora, la TLC de una alícuota mostró que se había completado la reacción, así se agregó agua a la mezcla de reacción y se separaron las capas resultantes. La capa acuosa se lavó con diclorometano y los orgánicos se

combinaron, se lavó cuatro veces con agua, se lavó con salmuera, se secaron sobre sulfato de magnesio, y se concentró al vacío para dar un aceite amarillo. El residuo se purificó sobre SiO_2 (0% a 10% de acetato de etilo-hexanos) para dar 2,2 g (78,7% de rendimiento) de 3-(2-benciloxi-5-metilsulfanilfenil)-3-metilbutiraldehído que un aceite incoloro que lentamente cristalizó estando en reposo.

El 3-(2-benciloxi-5-metilsulfanilfenil)-3-metilbutiraldehído se convirtió en 4-(2-benciloxi-5-metilsulfanilfenil)-1,1,1-trifluoro-4-metilpentan-2-ol como en el Ejemplo 26 de la publicación de la solicitud de patente U.S. Nº 2004/0023999.

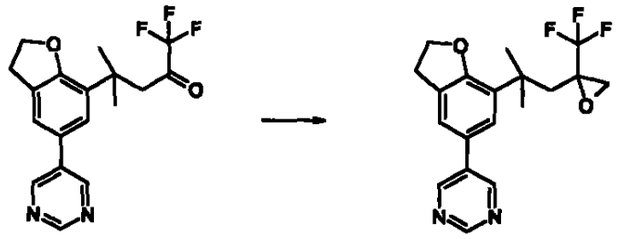
El 4-(2-benciloxi-5-metilsulfanilfenil)-1,1,1-trifluoro-4-metilpentan-2-ol se oxidó en 4-(2-benciloxi-5-metilsulfanilfenil)-1,1,1-trifluoro-4-metilpentan-2-ona aplicando condiciones de Swern como más arriba.

Ejemplo 66: Síntesis de 1,1,1-Trifluoro-4-metil-4-(5-pirimidin-5-il-2,3-dihidrobenzofuran-7-il)pentan-2-ona



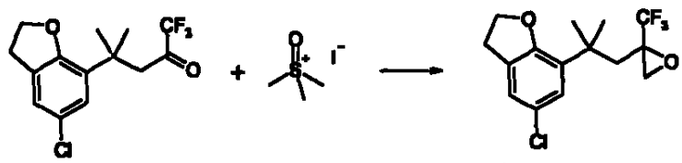
A una mezcla de 4-(5-bromo-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ona (1,00 g, 2,8 mmol), ácido pirimidin-5-borónico (529 mg, 4,3 mmol) y carbonato de potasio (787 mg) en un tubo sellado se agregó 20 ml de MeOH-DME-DMF (3:2:1). Al cabo de la agitación a temperatura ambiente durante 10 minutos, se agregó tetrakis(trifenilfosfin)paladio(0) (329 mg) y la mezcla de reacción se calentó a 120°C durante 40 minutos. Al cabo del enfriado a temperatura ambiente, la mezcla en bruto se filtró a través de un lecho de algodón con la ayuda de acetato de etilo. El filtrado se concentró al vacío para remover la mayoría del metanol, se redisolvió en 160 ml de acetato de etilo, y se lavó con 80 ml de una solución acuosa de hidróxido de sodio 1N, 80 ml de agua, y 80 ml de salmuera respectivamente. La fase orgánica se secó sobre sulfato de sodio anhidro, se filtró, y se concentró al vacío. La purificación por columna de cromatografía con 20% a 30% acetato de etilo-hexanos proporcionó 620 mg (62% de rendimiento) del compuesto del título.

Ejemplo 67: Síntesis de 5-[7-[1,1-Dimetil-2-(2-trifluorometiloxiranil)etil]-2,3-dihidrobenzofuran-5-il]pirimidina



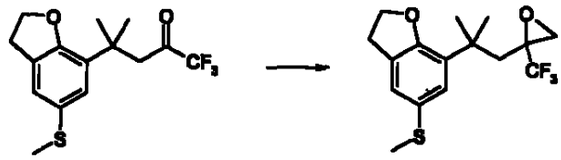
A una solución de 1,1,1-trifluoro-4-metil-4-(5-pirimidin-5-il-2,3-dihidrobenzofuran-7-il)pentan-2-ona (620 mg, 1,8 mmol) en 5 ml de DMSO anhidro-THF (1:1) se agregó 2,64 ml de una solución de iluro de trimetilsulfoxonio (solución de stock preparada por reacción de NaH (242 mg, 60% dispersion en aceite mineral) con yoduro de trimetilsulfoxonio (1,33 g, 6,0 mmol) en 7,50 ml de DMSO anhidro durante 30 minutos) gota a gota durante 5 minutos. Al cabo de agitación durante 2 hora a temperatura ambiente, la mezcla de reacción se vertió en 40 ml de agua y se extrajo con dietiléter (200 ml volumen total). Las fases orgánicas combinadas se lavaron con agua, salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío para dar 651 mg (99% de rendimiento) del compuesto del título como un aceite color amarillo claro que se usó sin ulterior purificación.

Ejemplo 68: Síntesis de 5-Cloro-7-[1,1-dimetil-2-(2-trifluorometiloxiranil)etil]-2,3-dihidrobenzofurano



A una solución de yoduro de trimetilsulfoxonio (343 mg, 1,56 mmol) en 3 ml de DMSO anhidro se trató con NaH (60% en aceite mineral, 66,0 mg, 1,65 mmol) en porciones y la mezcla se agitó a temperatura ambiente durante 30 minutos. La mezcla se transfirió a una solución de 4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ona (400 mg, 1,30 mmol) en 1 ml de DMSO anhidro durante 5 minutos y la mezcla resultante se agitó hasta el día siguiente. La mezcla se desactivó con agua y se extrajo con tres porciones de 20 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con dos porciones de 5 ml de agua, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío para dar 380 mg (91% de rendimiento) del producto del título como un aceite amarillo. El producto en bruto fue suficientemente puro y se usó sin otra purificación.

Ejemplo 69: Síntesis de 7-[1,1-Dimetil-2-(2-trifluorometiloxiranil)etil]-5-metilsulfanil-2,3-dihidrobenzofurano

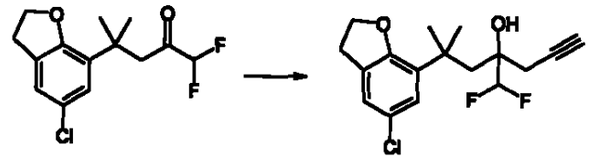


A una suspensión de yoduro de trimetilsulfoxonio (1,36 g, 6,1 mmol) en 7,7 ml de DMSO anhidro se agregó hidruro de sodio (60% dispersion en aceite mineral, 246 mg). La solución resultante se agitó a temperatura ambiente durante 30 minutos y luego se agregó gota a gota a una solución de 1,1,1-trifluoro-4-metil-4-(5-metilsulfanil-2,3-dihidrobenzofuran-7-il)pentan-2-ona (1,63 g, 6,2 mmol) en 6,5 ml de DMSO anhidro. Al cabo de 2 horas, se agregó 100 ml de agua y la mezcla resultante se extrajo con tres porciones de 100 ml de dietiléter. Las fases orgánicas combinadas se lavaron dos veces con agua, solución acuosa saturada de cloruro de sodio, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío para dar el compuesto del título, 1,64 g (95% de rendimiento) que se usó sin ulterior purificación.

Ejemplo 70: Síntesis de 7-[1,1-Dimetil-2-(2-trifluorometiloxiranil)etil]-5-metansulfonil-2,3-dihidrobenzofurano

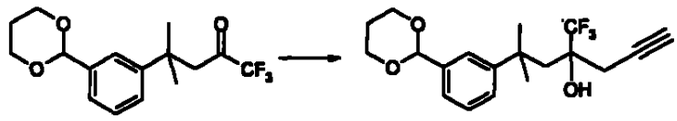
A una solución de 7-[1,1-dimetil-2-(2-trifluorometiloxiranil)etil]-5-metilsulfanil-2,3-dihidrobenzofurano (535 mg, 1,9 mmol) en 30 ml de acetonitrilo y 10 ml de agua se agregó peryodato de sodio (1,03 g, 4,8 mmol) seguido de cloruro de rutenio (III) (1 mg). Al cabo de 2 horas, la mezcla de reacción se diluyó con agua y se extrajo con acetato de etilo. Las fases orgánicas combinadas se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío para dar el compuesto del título como un sólido tostado , 568 mg (95% de rendimiento) que se usó sin ulterior purificación.

Ejemplo 71: Síntesis de 6-(5-Cloro-2,3-dihidrobenzofuran-7-il)-4-difluorometil-6-metilhept-1-in-4-ol



Se agitó vigorosamente lámina de aluminio (108 mg, 4,00 mmol) y cloruro mercúrico (aprox. 1 mg, 0,01 mmol) en 3,5 ml de THF anhidro durante 20 minutos. Se agregó lentamente bromuro de propargilo (80% en tolueno, 0,45 ml, 4,00 mmol) (la mezcla de reacción se calentó) y la mezcla resultante se agitó a 40°C durante 1 hora. La solución color gris oscuro de sesquibromuro de propargil aluminio se agregó a una solución de 4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluoro-4-metilpentan-2-ona (380 mg, 1,32 mmol) en 10 ml de THF anhidro a 0°C y se permitió a la reacción calentar lentamente a temperatura ambiente y se agitó hasta el día siguiente. La mezcla se concentró al vacío, se desactivó con hielo y agua, y se extrajo la capa acuosa con acetato de etilo. Los extractos orgánicos combinados se secaron sobre sulfato de magnesio y se concentraron al vacío para dar 420 mg del producto del título en forma de aceite (97% de rendimiento), que se usó sin ulterior purificación.

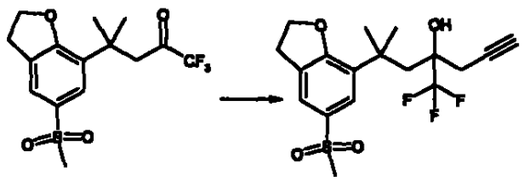
Ejemplo 72: Síntesis de 6-(3-[1,3]Dioxan-2-ilfenil)-6-metil-4-trifluorometilhept-1-in-4-ol



Se preparó amalgama de aluminio a partir de lámina de aluminio (1,16 g, 14,4 mmol) y cloruro mercúrico (12 mg, cantidad catalítica) en 20 ml de THF anhidro y se agitó vigorosamente la mezcla a temperatura ambiente durante 1 hora bajo una atmósfera nitrogenada. Una solución de bromuro de propargilo (4,80 ml, 80% en peso en tolueno, 43,1 mmol) en 25 ml de THF anhidro se agregó lentamente a la suspensión agitada manteniendo una temperatura de 30°C-40°C, y al cabo del agregado, se continuó la agitación a 40°C hasta obtener una solución color gris oscuro (aprox. 1 hora). La solución de sesquibromuro de propargil aluminio se agregó a una solución de 4-(3-[1,3]dioxan-2-ilfenil)-1,1,1-trifluoro-4-metilpentan-2-ona (5,6 g, 14,2 mmol) en 100 ml de dietiléter anhidro a -78°C. La mezcla de reacción se agitó a esta temperatura durante 3 horas, y luego se permitió calentarse a temperatura ambiente, al tiempo que se agitó durante 12 horas. La mezcla de reacción luego se vertió en 20 ml de hielo-agua y se extrajo con cuatro porciones de 30 ml de dietiléter. Los extractos combinados se lavaron con 20 ml de salmuera, se secaron sobre sulfato de magnesio, y se concentraron al vacío. La

cromatografía en gel de sílice (100% hexanos a 40% acetato de etilo en hexanos, gradiente) proporcionó 2,5 g del compuesto del título en forma de aceite (50% de rendimiento).

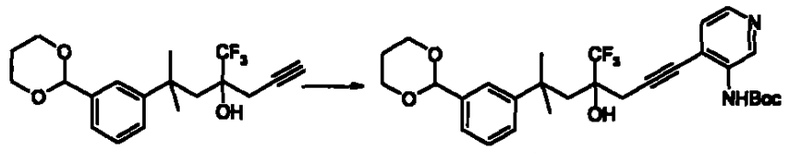
Ejemplo 73: Síntesis de 6-(5-Metanosulfonil-2,3-dihidrobenzofuran-7-il)-6-metil-4-trifluorometilhept-1-in-4-ol



40 ml de THF anhidro se agregaron a una mezcla de lámina de aluminio (1,25 g, 4,6 mmol) y cloruro mercúrico (100 mg, 0,37 mmol). La mezcla resultante se agitó vigorosamente durante 1 hora, se enfrió en un baño helado, y se trató con bromuro de propargilo (80% en peso de solución en tolueno, 62,9 mmol, 7 ml). La mezcla de reacción se agitó a 0°C durante 1 hora y a temperatura ambiente durante 30 minutos.

Una solución de 1,1,1-trifluoro-4-(5-metanosulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ona (5,4 g, 15,4 mmol) en una mezcla de 10 ml de dietiléter anhidro y 10 ml de THF anhidro se trató con el reactivo de organoaluminio a -78°C. Al cabo de 1 hora a -78°C y 1 hora a temperatura ambiente, la mezcla de reacción se desactivó con una solución saturada de cloruro de amonio y se diluyó con agua. Se extrajo la capa acuosa con tres porciones de 100 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con salmuera, se secaron sobre sulfato de sodio, se filtraron y se concentraron al vacío para dar 6,3 g del producto del título como un sólido, que se usó sin ulterior purificación (rendimiento cuantitativo).

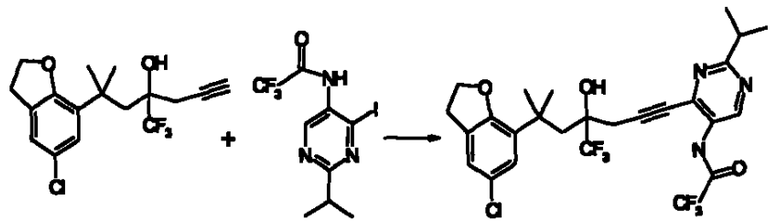
Ejemplo 74: Síntesis de *ter*-butil éster del ácido {4-[6-(3-[1,3]Dioxan-2-ilfenil)-4-hidroxi-6-metil-4-trifluorometilhept-1-inil]piridin-3-il}carbámico



Una mezcla de 6-(3-[1,3]dioxan-2-ilfenil)-6-metil-4-trifluorometilhept-1-in-4-ol (300 mg, 0,84 mmol), *ter*-butiléster del ácido (4-yodopiridin-3-il)carbámico (270 mg, 0,84 mmol), catalizador cloruro de bis(trifenilfosfina)paladio(II) (29,6 mg, 0,04 mmol) y yoduro de cobre (I) (16 mg, 0,08 mmol) en 4 ml de trietilamina ahidra y 1 ml de DMF anhidro se agitó a temperatura ambiente durante 12 horas. La mezcla de reacción luego se diluyó con 30 ml de dietiléter y se lavó con 20 ml de una solución acuosa saturada de cloruro

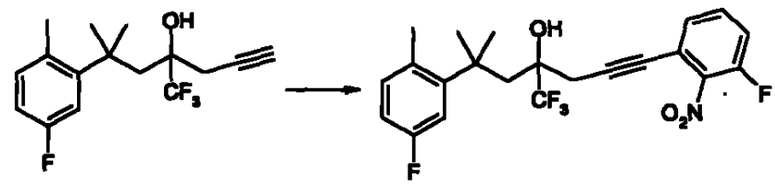
de amonio y 20 ml de salmuera. La capa orgánica se lavó sobre sulfato de magnesio y se concentró al vacío. La cromatografía en columna de gel de sílice con hexanos-acetato de etilo (5:1 a 1:1) proporcionó 250 mg del compuesto del título como una espuma (54% de rendimiento).

Ejemplo 75: Síntesis de *N*-(4-[6-(5-Cloro-2,3-dihidrobenzofuran-7-il)-4-hidroxi-6-metil-4-trifluorometilhept-1-inil]-2-isopropilpirimidin-5-il)-2,2,2-trifluoroacetamida



Una mezcla de clorodihidrobenzofuran alquino (185 mg, 0,533 mmol), yodopirimidina (144 mg, 0,4 mmol), yoduro de cobre (I) (9,5 mg, 0,05 mmol), y diclorobis(trifenilfosfina)paladio (II) (17,5 mg, 0,025 mmol) en 0,8 ml de acetonitrilo anhidro y 0,25 ml de trietilamina anhidra se agitó a temperatura ambiente. Al cabo de 1 hora, LC-MS indicó ninguna alquina inicial, pero mostró un mayor pico a M+H = 578 correspondiendo al compuesto deseado y un menor pico del dímero a M+H = 691. La mezcla de reacción en bruto se purificó en una columna de gel de sílice. La cromatografía se eluyó con un gradiente de 0%-25% acetato de etilo en hexanos para dar el compuesto del título como un aceite amarronado, (120 mg, 52% de rendimiento), M+H = 577.

Ejemplo 76: Síntesis de 6-(5-Fluoro-2-metilfenil)-1-(3-fluoro-2-nitrofenil)-6-metil-4-trifluorometilhept-1-in-4-ol

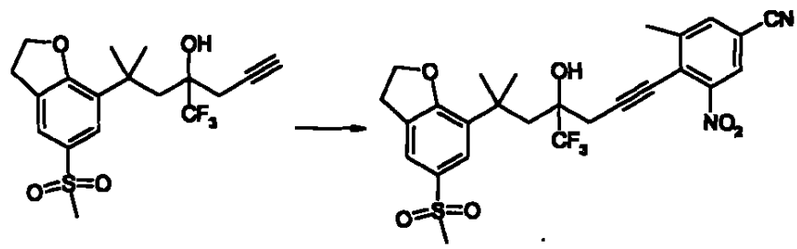


Una mezcla de 3-fluoro-2-nitrofenil éster del ácido trifluorometansulfónico (149 mg, 0,52 mmol), diclorobis(trifenilfosfina)paladio (II) (20 mg, 0,028 mmol), yoduro de cobre (I) (14 mg, 0,074 mmol), yoduro de tetrabutil amonio (200 mg, 0,54 mmol), 0,25 ml de trietilamina anhidra, 0,5 ml de acetonitrilo anhidro, y 0,5 ml de tetrahidrofurano anhidro se agitó a temperatura ambiente durante 30 minutos. La mezcla resultante se trató con 6-(5-fluoro-2-metilfenil)-6-metil-4-trifluorometilhept-1-in-4-ol (145 mg, 0,48 mmol) y se agitó a temperatura ambiente durante 18 horas. El producto en bruto se purificó mediante

925
918
947

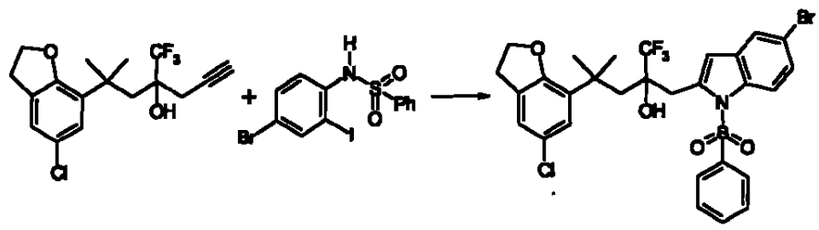
cromatografía en SiO_2 (50% hexanos en diclorometano) para dar 96 mg del producto del título como un aceite color amarillo claro, (45% de rendimiento).

Ejemplo 77: Síntesis de 4-[4-Hidroxi-6-(5-metanosulfonil-2,3-dihidrobenzofuran-7-il)-6-metil-4-trifluorometilhept-1-inil]-3-metil-5-nitrobenzonitrilo



Una mezcla de 4-ciano-2-metil-6-nitrofeniléster del ácido trifluorometanosulfónico (217 mg, 0,7 mmol), diclorobis(trifenilfosfina)paladio (II) (24,6 mg, 0,035 mmol), yoduro de cobre (I) (13,3 mg, 0,7 mmol), y 6-(5-metanosulfonil-2,3-dihidrobenzofuran-7-il)-6-metil-4-trifluorometilhept-1-in-4-ol (273 mg, 0,7 mmol) en una mezcla de 0,8 ml de tolueno anhidro y 0,3 ml de trietilamina anhidra se calentó en un horno a microondas a 60°C durante 10 minutos. La mezcla de reacción se aplicó a una columna de SiO_2 (50% acetato de etilo en hexanos) para dar 165 mg del producto del título como un aceite color amarillo claro (43% de rendimiento).

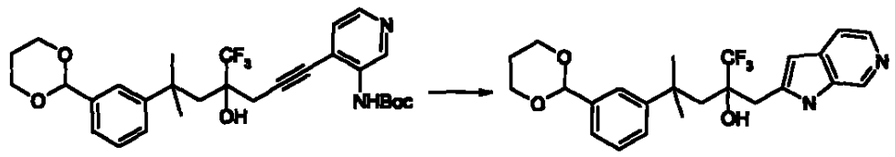
Ejemplo 78: Síntesis de 2-(1-Bencenosulfonil-5-bromo-1*H*-indol-2-ilmetil)-4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ol



Una mezcla de 6-(5-cloro-2,3-dihidrobenzofuran-7-il)-6-metil-4-trifluorometilhept-1-in-4-ol (170 mg, 0,49 mmol), *N*-(4-bromo-2-yodofenil)bencenosulfonamida (220 mg, 0,50 mmol), diclorobis(trifenilfosfina)paladio (II) (20 mg, 0,03 mmol), y yoduro de cobre (I) (10 mg, 0,05 mmol) en 1 ml de DMF y 0,7 ml de trietilamina se calentó a 70°C. Al cabo de 45 minutos, la mezcla se enfrió y se diluyó con 7 ml de solución acuosa saturada de cloruro de amonio y se extrajo con tres porciones de 7 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con dos porciones de 7 ml de solución acuosa saturada de cloruro de amonio, cuatro porciones de 7 ml de salmuera, se secaron sobre sulfato de magnesio, se filtró y se concentraron al vacío. El residuo en bruto se purificó en gel de

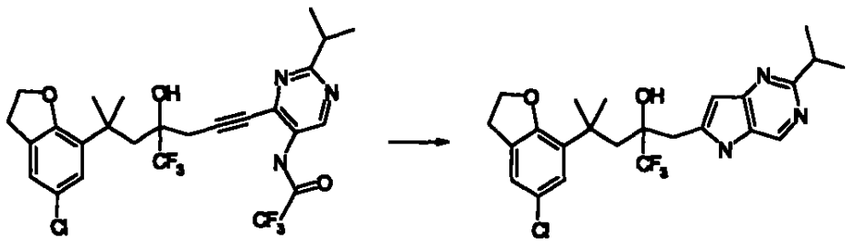
sílice se eluyó con acetato de etilo-hexanos (0-30% gradiente) para dar 126 mg (39% de rendimiento) del compuesto del título.

Ejemplo 79: Síntesis de 4-(3-[1,3]dioxan-2-ilfenil)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol



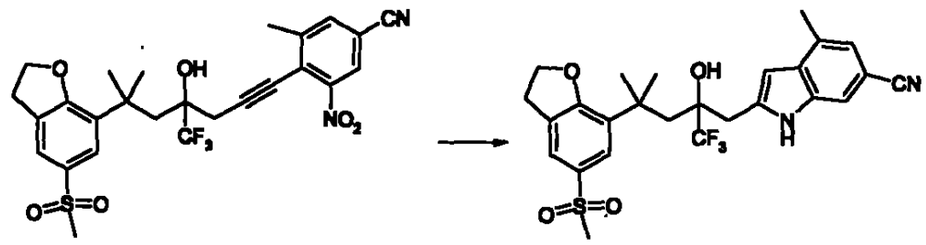
A una solución de *ter*-butil éster del ácido {4-[6-(3-[1,3]dioxan-2-ilfenil)-4-hidroxi-6-metil-4-trifluorometilhept-1-inil]piridin-3-il}carbámico (250 mg, 0,46 mmol) en 5 ml de metanol-agua (4:1) se agregó DBU (0,7 ml, 4,6 mmol) y la mezcla de reacción se calentó a 65°C durante 2 hora. La solución se concentraron al vacío y el producto se precipitó de agua. Se filtró el precipitado y se secó para dar 176 mg del compuesto del título como un sólido color blanco (86% de rendimiento).

Ejemplo 80: Síntesis de 4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(2-isopropil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)-4-metilpentan-2-ol



A una solución de *N*-{4-[6-(5-cloro-2,3-dihidrobenzofuran-7-il)-4-hidroxi-6-metil-4-trifluorometilhept-1-inil]-2-isopropilpirimidin-5-il}-2,2,2-trifluoroacetamida (58 mg, 0,1 mmol) en 1 ml de dioxano anhidro se agregó tetrametilguanidina (0,05 ml, 0,4 mmol) y la mezcla de reacción se agitó y se calentó en un baño de aceite mantenido a 100°C durante 1 hora. La purificación por TLC preparativa en gel de sílice se eluyó con 5% metanol en diclorometano proporcionó el compuesto del título como un sólido color crema claro, (25 mg, 52% de rendimiento) M+H = 482.

Ejemplo 81: Síntesis de 2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo

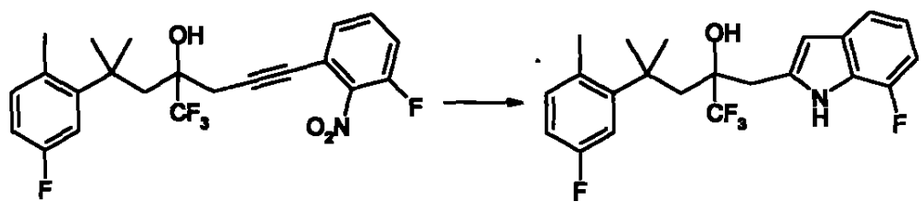


Una solución agitada de 4-[4-hidroxi-6-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-6-metil-4-trifluorometilhept-1-inil]-3-metil-5-nitrobenzonitrilo. (165 mg, 0,3 mmol) en 6 ml de etanol absoluto se trató con 4 ml de ácido acético glacial y hierro en polvo (335 mg, 6 mmol). La mezcla resultante se calentó a 90°C durante 30 minutos, se enfrió a temperatura ambiente, se diluyó con 200 ml de diclorometano, y se filtró a través de un lecho del auxiliar filtrante de CELITE®. El filtrado se lavó con tres porciones de 50 ml de solución acuosa saturada de carbonato de sodio y dos porciones de 5 ml de salmuera, se secaron sobre sulfato de sodio, se filtró, y se concentró al vacío para dar 140 mg de 3-amino-4-[4-hidroxi-6-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-6-metil-4-trifluorometilhept-1-inil]-5-metilbenzonitrilo como un aceite levemente amarronado (90% de rendimiento).

Una solución agitada de 3-amino-4-[4-hidroxi-6-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-6-metil-4-trifluorometilhept-1-inil]-5-metilbenzonitrilo (140 mg, 0,27 mmol) en 5 ml de diclorometano anhidro se enfrió en un baño helado y se trató con anhídrido trifluoroacético (0,075 ml, 0,54 mmol). Al cabo de 5 minutos, la mezcla se concentró al vacío. De la cromatografía sobre SiO_2 (100% diclorometano) se obtuvo 155 mg de *N*-(5-ciano-2-[4-hidroxi-6-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-6-metil-4-trifluorometilhept-1-inil]-3-metilfenil)-2,2,2-trifluoroacetamida como un aceite levemente amarronado (93% de rendimiento).

Una solución de *N*-(5-ciano-2-[4-hidroxi-6-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-6-metil-4-trifluorometilhept-1-inil]-3-metilfenil)-2,2,2-trifluoroacetamida (154 mg, 0,25 mmol) en 0,6 ml de DMSO anhidro se calentó en presencia de 1,1,3,3-tetrametilguanidina (0,094 ml, 0,75 mmol) en un horno a microondas a 140°C durante 10 minutos. La reacción se desactivó con una mezcla de ácido sulfúrico 1 N y 10 ml de hielo picado. El precipitado resultante se filtró, se lavó con agua, y se secó. De la TLC preparativa cromatografía (50% acetato de etilo en hexanos, seguido de 15% acetato de etilo en diclorometano) se obtuvo 23 mg del producto del título como un sólido blanquecino (18% de rendimiento).

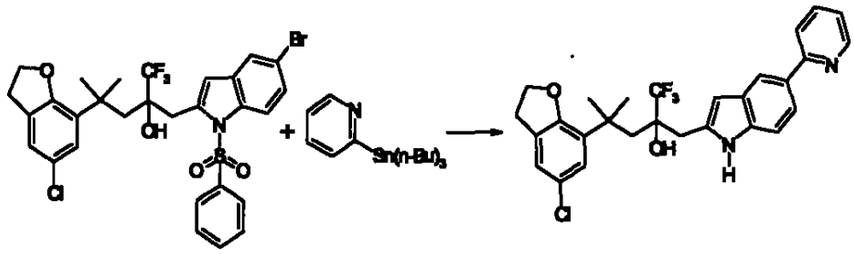
Ejemplo 82: Síntesis de 1,1,1-Trifluoro-2-(7-fluoro-1*H*-indol-2-ilmetil)-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol



Una solución agitada de 6-(5-fluoro-2-metilfenil)-1-(3-fluoro-2-nitrofenil)-6-metil-4-trifluorometilhept-1-in-4-ol (1,05 g, 2,4 mmol) en 6 ml de etanol absoluto y 2 ml de ácido acético glacial se trató con hierro en polvo (800 mg, 14,3 mmol). La mezcla resultante se calentó a 80°C durante 2 horas, se enfrió a temperatura ambiente, se diluyó con dietiléter, se filtró a través de un lecho del auxiliar filtrante de CELITE®, y se concentró al vacío. El residuo se disolvió en dietiléter, se trató con carbonato de potasio anhidro, se filtró, y se concentró al vacío para dar 900 mg de 1-(2-amino-3-fluorofenil)-6-(5-fluoro-2-metilfenil)-6-metil-4-trifluorometilhept-1-in-4-ol como un aceite ligeramente amarronado (92% de rendimiento), que se utilizó sin purificación adicional.

Una solución de 1-(2-amino-3-fluorofenil)-6-(5-fluoro-2-metilfenil)-6-metil-4-trifluorometilhept-1-in-4-ol (900 mg, 2,2 mmol) en 10 ml de dioxano anhidro se trató con diclorobis(trifenilfosfin)paladio (II) (250 mg, 0,36 mmol) y la mezcla se calentó a 100°C durante 60 horas. La mezcla en bruto de reacción se purificó en SiO_2 (20% diclorometano en hexanos) para dar 700 mg del producto del título como un aceite amarillo (78% de rendimiento).

Ejemplo 83: Síntesis de 4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-piridin-2-il-1*H*-indol-2-ilmetil)pentan-2-ol

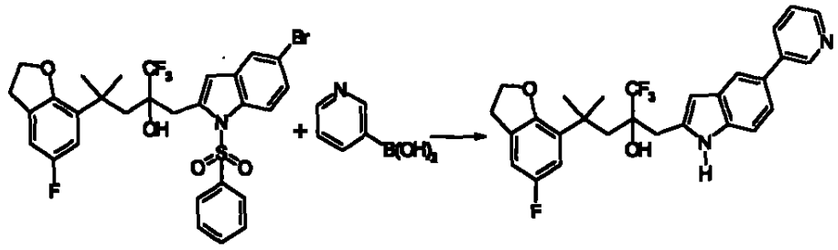


Una mezcla de 2-(1-bencensulfonil-5-bromo-1*H*-indol-2-ilmetil)-4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ol (30 mg, 0,046 mmol), 2-tributilstannanilpiridina (72 mg, 0,196 mmol) y diclorobis(trifenilfosfin)paladio (II) (10 mg) se calentó a reflujo durante 2 horas. La mezcla luego se enfrió y se diluyó con dietiléter,

se agregaron algunas gotas de DBU, y la mezcla se diluyó con agua y se extrajo con acetato de etilo. El material en bruto se purificó parcialmente en gel de sílice por TLC preparativa se eluyó con acetato de etilo-hexanos (35:65) para dar un producto parcialmente purificado contaminado con subproductos de estaño.

Una mezcla de 2-(1-bencensulfonil-5-piridin-2-il-1*H*-indol-2-ilmetil)-4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ol anterior (30,1 mg, 0,046 mmol, máximo teórico de arriba) en 5 ml de metanol y 5 ml de una solución acuosa de hidróxido de sodio al 10% se calentaron a reflujo. Al cabo de 4 horas, la mezcla se diluyó con 7 ml de salmuera y se extrajo con tres porciones de 5 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con tres porciones de 5 ml de solución acuosa saturada de bicarbonato de sodio, 5 ml de salmuera, dos porciones de 5 ml de solución acuosa saturada de cloruro de amonio, 5 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. El material en bruto se purificó por gel de sílice en TLC preparativa usando acetato de etilo-hexanos (1:1). El material de la placa de TLC preparativa se concentró al vacío a partir de dietiléter-hexanos dio 10 mg (42% de rendimiento) del compuesto del título.

Ejemplo 84: Síntesis de 1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-piridin-3-il-1*H*-indol-2-ilmetil)pentan-2-ol

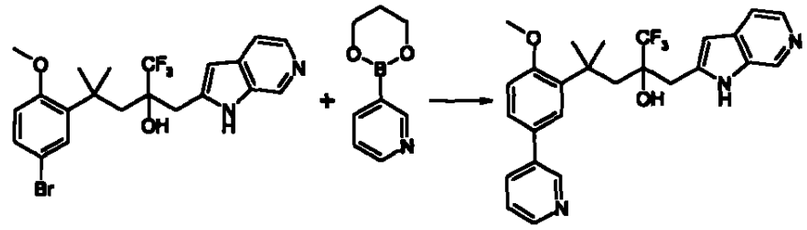


Una mezcla de 2-(1-bencensulfonil-5-bromo-1*H*-indol-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol (100 mg, 0,156 mmol), ácido piridin-3-borónico (80 mg, 0,65 mmol), y tetrakis(trifenilfosfina)paladio (0) (25 mg, 0,022 mmol) en 6 ml de tolueno, 3 ml de etanol, y 1,5 ml de solución acuosa de carbonato de sodio 2 M se calentó a reflujo. La reacción se monitoreó por TLC (acetato de etilo-hexanos (6:4)). La mezcla luego se diluyó con solución acuosa saturada de cloruro de amonio y se extrajo con tres porciones de 10 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con tres porciones de 10 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. El material en bruto se purificó en gel de sílice usando acetato de etilo-hexanos (gradiente 10-60%) para dar 88 mg (88% de rendimiento) de material. La cristalización de dietiléter -hexanos proporcionó 76 mg (76%

de rendimiento) de 2-(1-bencensulfonil-5-piridin-3-il-1*H*-indol-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol.

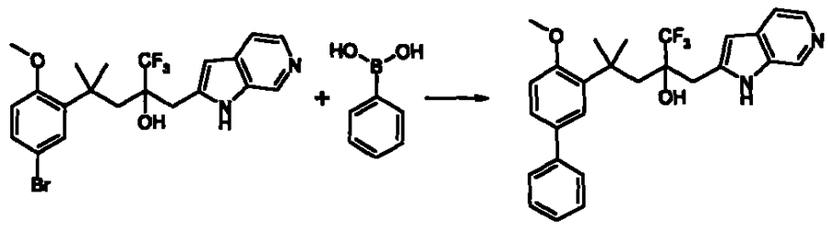
A una solución del anterior 2-(1-bencensulfonil-5-piridin-3-il-1*H*-indol-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol (71 mg, 0,11 mmol) en 5 ml de THF se agregó una solución 1 M de fluoruro de tetrabutilamonio (0,5 ml, 0,5 mmol) en THF y la mezcla se calentó a 80°C. Al cabo de 18 horas, la mezcla se concentró al vacío y se diluyó con una solución acuosa 1 N de hidróxido de sodio y se extrajo con tres porciones de 5 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con dos porciones de 5 ml de una solución acuosa 1 N de hidróxido de sodio, 5 ml de salmuera, tres porciones de 5 ml de solución acuosa saturada de cloruro de amonio, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. El residuo se purificó en gel de sílice se eluyó con metanol-diclorometano (0:100, luego 0,5:99,5, luego 1:99) para dar 46 mg (83% de rendimiento) del compuesto del título.

Ejemplo 85: Síntesis de 1,1,1-Trifluoro-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol



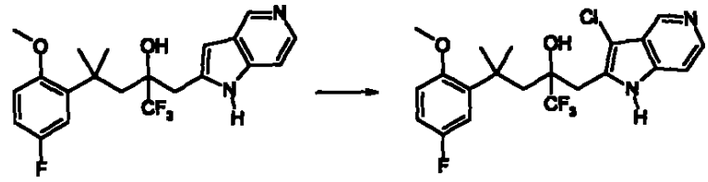
Una mezcla de 4-(5-bromo-2-metoxifenil)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol (188 mg, 0,4 mmol), éster cíclico 1,3-propandiol del ácido piridin-3-borónico (89 mg, 0,6 mmol), carbonato de potasio (K_2CO_3; 166 mg, 1,2 mmol), y $Pd(PPh_3)_4$ (46,2 mg, 0,04 mmol) en 3,0 ml de DME-MeOH-DMF (1:1,5:0,5) se colocó en microondas durante 20 minutos a 120°C, se enfrió a temperatura ambiente, se diluyó con 20 ml de acetato de etilo y se filtró a través de tierra diatomea. El filtrado se lavó con 5 ml de una solución acuosa 1,0 M de hidróxido de sodio, agua, y salmuera, se secaron sobre sulfato de magnesio, y se concentró al vacío. El residuo se purificó por gel de sílice. La cromatografía proporcionó 90 mg (48% de rendimiento) del compuesto del título como espuma blanca.

Ejemplo 86: Síntesis de 1,1,1-Trifluoro-4-(4-metoxibifenil-3-il)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol



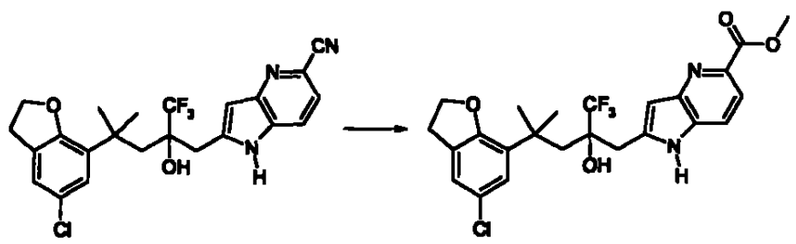
Una mezcla de 4-(5-bromo-2-metoxifenil)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol (188 mg, 0,4 mmol), $Pd(OAc)_2$ (9 mg, 0,04 mmol), DCyBPP ((2-diciclohexilfosfin)bifenilo, 28 mg, 0,08 mmol), y KF (93 mg, 1,6 mmol) en 3 ml de THF a temperatura ambiente se trató con ácido fenilborónico (74 mg, 0,6 mmol). La mezcla de reacción se colocó en microondas durante 20 minutos a 120°C, se enfrió a temperatura ambiente, se diluyó con 20 ml de acetato de etilo y se filtró a través de tierra diatomea. El filtrado se lavó con 5 ml de una solución acuosa 1;0 M de hidróxido de sodio, agua, y 5 ml de salmuera. La fase orgánica se secó sobre sulfato de magnesio, se filtró y el solvente se evaporó al vacío. El residuo se purificó en gel de silice La cromatografía proporcionó 75 mg (40% de rendimiento) del compuesto del título como un sólido color blanco.

Ejemplo 87: Síntesis de 2-(3-Cloro-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol



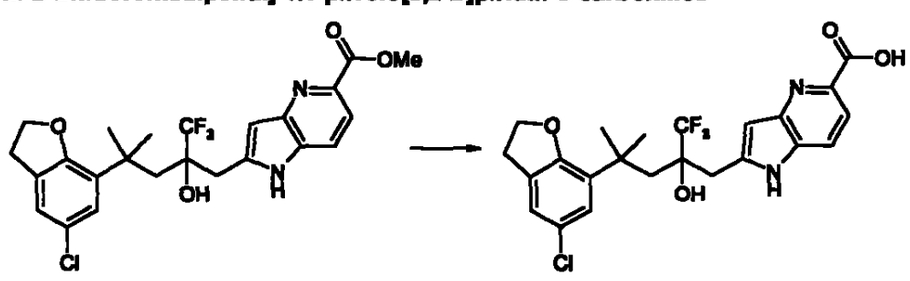
Una solución de cloruro de tricloroacetilo (0,045 ml, 0,403 mmol) en 0,5 ml de DMF se trató con una solución de 1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol (33,0 mg, 0,081 mmol) en 0,5 ml de DMF a temperatura ambiente. Al cabo de 2 días, la reacción se desactivó con 2 ml de hielo-agua y 2 ml de solución fría 1 N de hidróxido de sodio. La mezcla resultante se extrajo con tres porciones de 5 ml de acetato de etilo. Las capas orgánicas combinadas se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. De la cromatografía sobre SiO_2 (100% de diclorometano a 10% de metanol en diclorometano, gradiente) se obtuvo 20,0 mg del producto del título (56% de rendimiento).

Ejemplo 88: Síntesis de metil éster del ácido 2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carboxílico



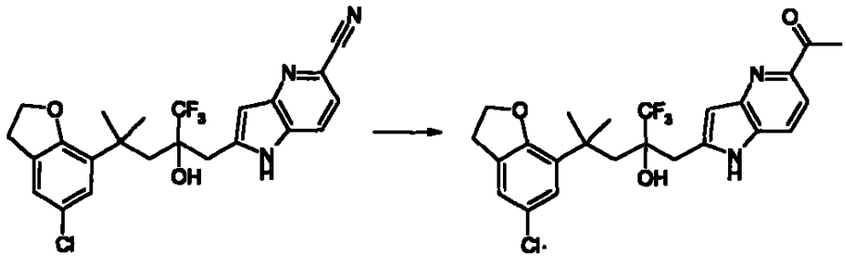
Se disolvió 2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo (300 mg, 0,65 mmol) en 10 ml de metanol a temperatura ambiente. Se introdujo gas HCl durante 2 minutos. La mezcla se calentó a reflujo hasta el día siguiente. El solvente se eliminó al vacío. El residuo se diluyó con 50 ml de acetato de etilo y se neutralizó con 30 ml de una solución saturada de carbonato de sodio. La capa orgánica se separó. Se extrajo la capa acuosa con tres porciones de 50 ml de acetato de etilo. Se combinaron las capas orgánicas, se lavó con salmuera, se secaron sobre sulfato de sodio, y el solvente se eliminó al vacío. El residuo se purificó por cromatografía flash (SiO_2 desactivado con 2% de trietilamina, eluyendo con CH_2Cl_2 hasta CH_2Cl_2-MeOH (95:5)) para dar el compuesto del título (263 mg, 82% de rendimiento).

Ejemplo 89: Síntesis del ácido 2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-carboxílico



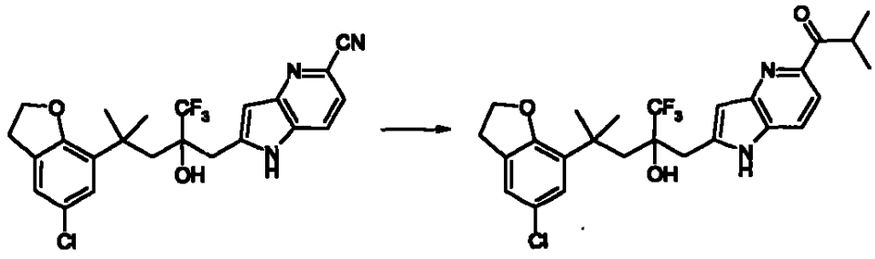
Se disolvió metil éster del ácido 2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-carboxílico (100 mg, 0,2 mmol) en 2 ml de THF-MeOH-agua (3:1:1). Se agregó monohidrato de hidróxido de litio (25 mg, 0,6 mmol) La reacción se agitó a temperatura ambiente durante 4 horas. La mezcla se diluyó con 5 ml de agua y se usó una solución de HCl 6 N para ajustar el pH hasta alrededor de 2. El orgánico se extrajo con tres porciones de 50 ml de acetato de etilo, se lavó con salmuera, y se secaron sobre sulfato de sodio anhidro. El solvente se eliminó al vacío para dar el compuesto del título (13,5 mg, 14% de rendimiento).

Ejemplo 90: Síntesis de 1-(2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il)etanona



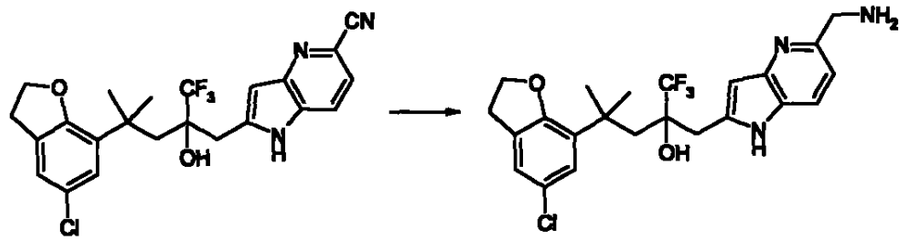
Se disolvió 2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-carbonitrilo (100 mg, 0,22 mmol) en 6 ml de THF. La solución se enfrió a -78°C. Se agregó yoduro de metil magnesio (3 M en dietiléter, 1,2 ml, 3,6 mmol). La reacción se agitó hasta el día siguiente y se permitió a la temperatura adquirir temperatura ambiente. La reacción se desactivó con 10 ml de solución acuosa saturada de cloruro de amonio y se extrajo con tres porciones de 50 ml de acetato de etilo. Se combinaron las capas orgánicas y se secaron sobre sulfato de magnesio. El solvente se eliminó al vacío. El residuo se purificó por cromatografía flash (se eluyó con CH_2Cl_2 hasta 95:5 CH_2Cl_2-MeOH) para dar el compuesto del título (36 mg, 35% de rendimiento).

Ejemplo 91: Síntesis de 1-[2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il]-2-metilpropan-1-ona



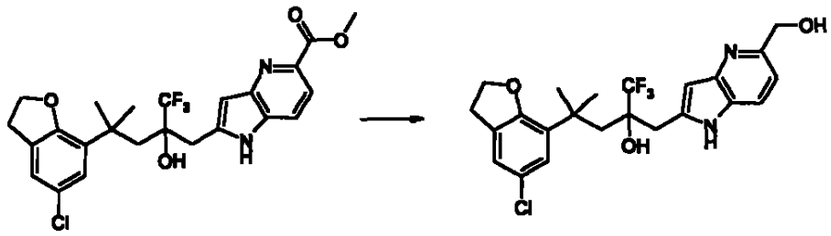
Se disolvió 2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo (50 mg, 0,11 mmol) en 3 ml de THF. Se agregó cloruro de isopropil magnesio (2 M en THF, 0,15 ml, 0,3 mmol) seguido de CuBr (7 mg, 0,05 mmol). La reacción se agitó a reflujo (75°C) durante 30 minutos. La mezcla se enfrió a temperatura ambiente. La reacción se desactivó con 1 ml de agua, seguido de 3 gotas de HCl concentrado. La mezcla se agitó durante 10 minutos, y se neutralizó con una solución saturada de carbonato de sodio hasta que el pH fue 8. La mezcla de reacción se extrajo con acetato de etilo y se lavó con salmuera. El solvente se eliminó al vacío. El residuo se purificó por HPLC preparativa (condición polar del medio) para dar el compuesto del título (39 mg, 70% de rendimiento).

Ejemplo 92: Síntesis de 2-(5-Aminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ol



Se disolvió 2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-carbonitrilo (100 mg, 0,22 mmol) se disolvió en 3 ml de THF y se agregó borano-sulfuro de metilo (10 M, 0,065 ml, 0,648 mmol) . La reacción se calentó a reflujo durante 1 hora y luego se enfrió a temperatura ambiente. Luego se agregó 1 ml de una solución de HCl 6 N. La reacción se calentó a reflujo hasta el día siguiente. La reacción se enfrió a temperatura ambiente, se diluyó con 50 ml de acetato de etilo, y luego se desactivó con solución saturada de carbonato de sodio hasta que el pH fue 12. La capa orgánica se separó y la capa acuosa se extrajo con tres porciones de 50 ml de acetato de etilo. Las fracciones orgánicas fraccionadas se secaron sobre sulfato de sodio y el solvente se eliminó al vacío. El residuo se purificó por HPLC preparativa (condición polar) para dar el compuesto del título (49 mg, 49% de rendimiento).

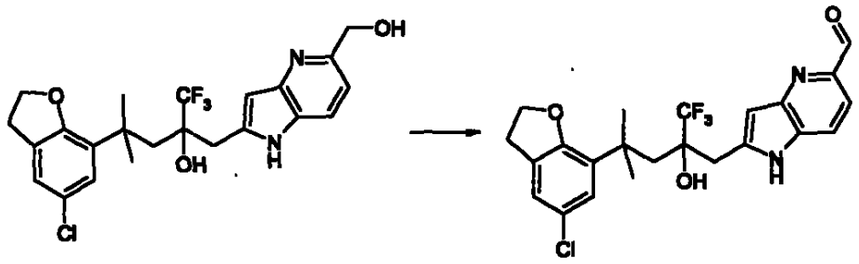
Ejemplo 93: Síntesis de 4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(5-hidroximetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-metilpentan-2-ol



A una solución del éster de partida (0,995 g, 2,00 mmol) en 35,0 ml de THF se agregó hidruro de litio aluminio (2,40 ml, 2,40 mmol) gota a gota a 0°C. Se permitió a la reacción adquirir temperatura ambiente, luego se agitó durante 2 horas. Los análisis por TLC (5% MeOH-CH_2Cl_2, 0,5% NH_4OH) mostró la apariencia de un producto en mancha y la consumición de todo el material de partida. La solución se diluyó con 50 ml de THF y se desactivó con una solución de agua-THF (3,0 ml de agua y 50 ml de THF). Se agregó este sulfato de magnesio y la suspensión resultante se agitó durante 30 minutos. La

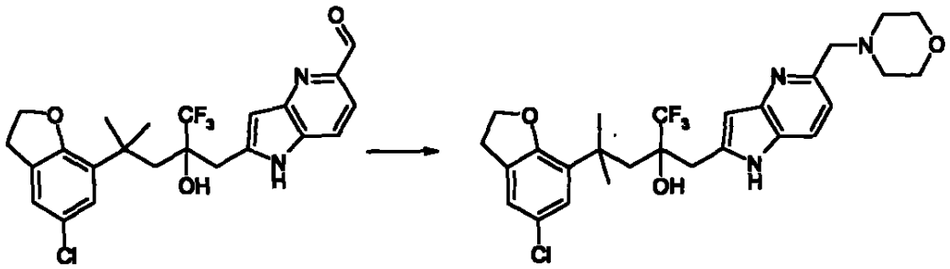
suspensión se filtró a través de tierra diatomea y el THF se evaporó para dar el compuesto del título como una espuma amarilla (0,882 g, 94,0% de rendimiento).

Ejemplo 94: Síntesis de 2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-carbaldehído



A una solución del alcohol del Ejemplo 93 (0,882 g, 1,88 mmol) en 25 ml de acetona se agregó óxido de manganeso (IV) (3,99 g, 9,41 mmol). La suspensión negra se agitó a temperatura ambiente durante 1 hora. La solución se filtró a través de tierra diatomea y the acetona se evaporó al vacío para dar el compuesto del título (0,625 g, 74,0% de rendimiento) como una espuma amarilla.

Ejemplo 95: Síntesis de 4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-morfolin-4-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)pentan-2-ol



A una solución del aldehído de Ejemplo 94 (0,050 g, 0,107 mmol) y 0,078 ml de ácido acético en 3,0 ml de dicloroetano se agregó morfolina (0,233 ml, 2,68 mmol) a 0°C. Se permitió a la reacción adquirir temperatura ambiente agitando durante 30 minutos. A esta solución amarilla se agregó borohidruro de triacetoxi sodio (0,057 mg, 0,268 mmol), luego se continuó agitando a temperatura ambiente durante 14 horas. La mezcla de reacción se diluyó con 10 ml de acetato de etilo y 2 ml de solución de hidróxido de amonio al 3%. Se separó el sistema bifásico y se extrajo la fase acuosa con acetato de etilo. Las capas orgánicas combinadas se lavaron con tres porciones de 20 ml de agua, salmuera, se secaron sobre sulfato de sodio, se filtró y el solvente se evaporó al vacío para dar aceite amarillo. Este material en bruto se aplicó en una columna flash y se eluyo

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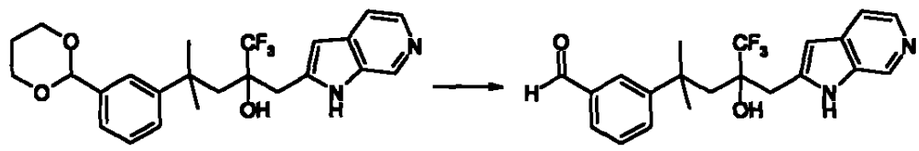
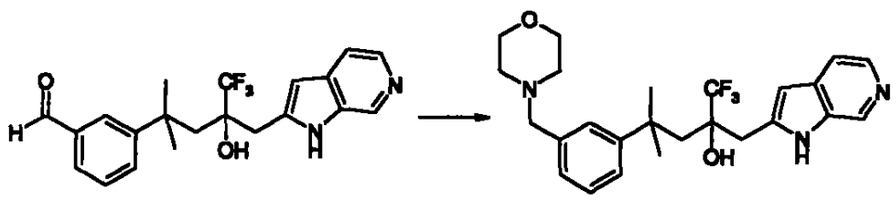
con 5% MeOH-CH_2Cl_2, 0,5% NH_4OH, para dar el compuesto del título (0,018 g, 32,0% de rendimiento) como una espuma blanca.

Ejemplo 96: Síntesis de 3-[4,4,4-Trifluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]benzaldehído



Una mezcla de 4-(3-[1,3]dioxan-2-ilfenil)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol (160 mg, 0,36 mmol), 2 ml de etanol, 1 ml de agua, y piridinio *p*-toluenosulfónico (200 mg, 0,8 mmol) se agitó a temperatura ambiente durante 14 horas y luego se concentró al vacío para remover el etanol. El residuo se diluyó con acetato de etilo y agua. Se extrajo la capa acuosa con acetato de etilo. Las capas orgánicas combinadas se lavaron con una solución acuosa saturada de bicarbonato de sodio y salmuera, y se secaron sobre sulfato de sodio. La eliminación del solvente al vacío proporcionó 134 mg (95% de rendimiento) del compuesto del título.

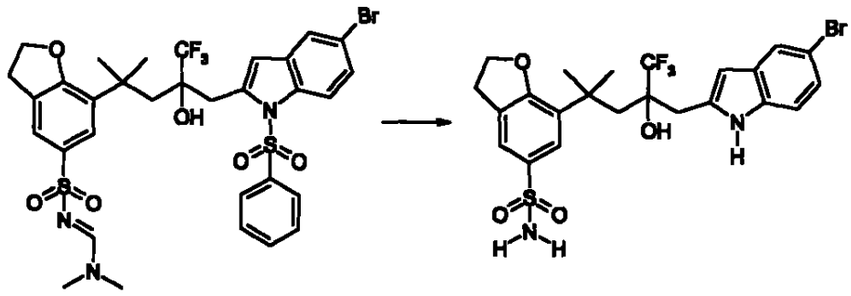
Ejemplo 97: Síntesis de 1,1,1-Trifluoro-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol



A una solución de 3-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]benzaldehído (50 mg, 0,13 mmol), 3 ml de dicloroetano, y ácido acético (0,1 ml, 1,6 mmol) en un baño helado se agregó morfolina (0,28 ml, 3,20 mmol) en un lote. La solución se calentó a temperatura ambiente y se agitó durante 0,5 horas. Se agregó borohidruro de triacetoxi sodio (68 g, 0,32 mmol) se agregó en una sola porción y la reacción se agitó a temperatura ambiente durante 3,0 horas. La solución se diluyó con acetato de etilo y se agregaron 3 ml de una solución de hidróxido de amonio al 3%. El sistema bifásico se transfirió a un embudo de separación, se eliminó la capa acuosa y se extrajo de retorno con acetato de etilo. Las capas orgánicas combinadas se lavaron con salmuera, se secaron sobre sulfato de magnesio, se filtraron y el solvente se evaporó al vacío. El producto se eluyó de una columna de cromatografía flash con diclorometano-

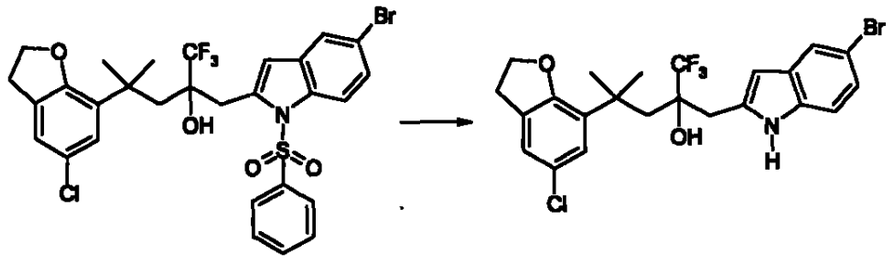
metanol, y la evaporación del solvente al vacío proporcionó el compuesto del título (27 mg, 45% de rendimiento).

Ejemplo 98: Síntesis de amida del ácido 7-[3-(5-Bromo-1*H*-indol-2-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-2,3-dihidrobenzofuran-5-sulfónico



Una mezcla de 1-dimetilaminometil(*E*)-ilidenamida del ácido 7-[3-(1-bencensulfonil-5-bromo-1*H*-indol-2-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-2,3-dihidrobenzofuran-5-sulfónico (167 mg, 0,22 mmol) en 10 ml de metanol y 3 ml de una solución acuosa de hidróxido de sodio al 10% se calentó a reflujo. Al cabo de 24 horas, la mezcla se diluyó con 10 ml de salmuera y se extrajo con tres porciones de 10 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con dos porciones de 5 ml de una solución de bicarbonato de sodio acuoso saturado, 5 ml de salmuera, tres porciones de 5 ml de solución acuosa saturada de cloruro de amonio, 5 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. El material en bruto se cromatografió en gel de sílice usando acetato de etilo-hexanos (0-50% gradiente) y luego se trituró con dietiléter -hexanos para dar 79 mg (64% de rendimiento) del compuesto del título.

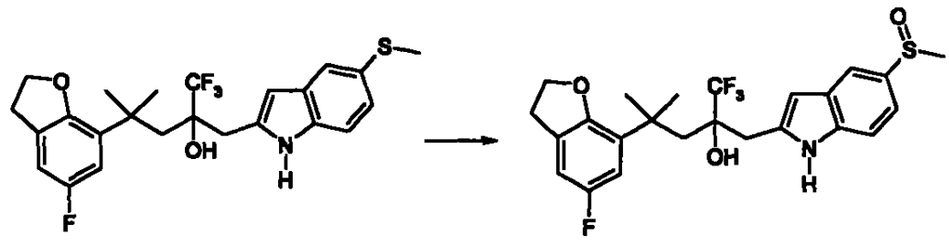
Ejemplo 99: Síntesis de 2-(5-Bromo-1*H*-indol-2-ilmetil)-4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ol



Una mezcla de 2-(1-bencensulfonil-5-bromo-1*H*-indol-2-ilmetil)-4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ol (30 mg, 0,046 mmol) en 5 ml de metanol y 5 ml de una solución acuosa de hidróxido de sodio al 10% se calentó a reflujo.

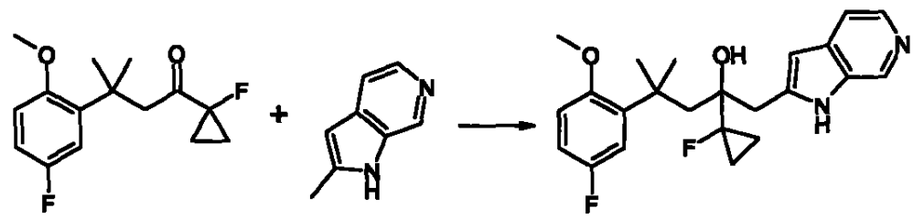
Al cabo de 18 horas, la mezcla se diluyó con salmuera y se extrajo con tres porciones de 7 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con tres porciones de 5 ml de salmuera, tres porciones de 5 ml de solución acuosa saturada de cloruro de amonio, 5 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. El material en bruto se purificó por TLC preparativa (1 mm, gel de sílice, acetato de etilo-hexanos (3:7)) para dar 15 mg (63% de rendimiento) del compuesto del título.

Ejemplo 100: Síntesis de 1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-2-(5-metanosulfinil-1*H*-indol-2-ilmetil)-4-metilpentan-2-ol



A una solución de 1,1,1-trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-metilsulfanil-1*H*-indol-2-ilmetil)pentan-2-ol (25 mg, 0,053 mmol) en 10 ml de metanol se agregó peryodato de sodio (150 mg, 0,70 mmol). Al cabo de 1 hora, la mezcla se diluyó con salmuera y se extrajo con tres porciones de 10 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con tres porciones de 7 ml de salmuera, se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. El residuo en bruto se purificó por TLC preparativa en gel de sílice se eluyó con acetato de etilo para dar 19,8 mg (77% de rendimiento) del compuesto del título.

Ejemplo 101: Síntesis de 2-(1-Fluorociclopropil)-4-(5-fluoro-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[2,3-c]piridin-2-il)pentan-2-ol

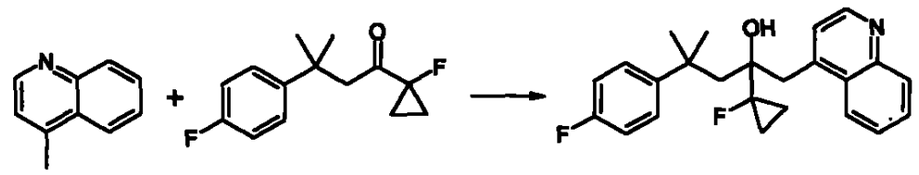


A una solución de 2-metil-1*H*-pirrolo[2,3-c]piridina (80,0 mg, 0,605 mmol) en 2 ml de THF se enfrió a -78°C se agregó 0,70 ml de *n*-BuLi (1,6 M en hexanos). Al cabo de 5 minutos, *ter*-BuOK (1 M en THF, 0,75 ml) se agregó y la mezcla se calentó a temperatura ambiente durante 1 hora. La mezcla se enfrió a -78°C y the arriba 1-(1-fluorociclopropil)-3-(5-fluoro-2-metoxifenil)-3-metilbutan-1-ona (150 mg, 0,600 mmol) se agregó como una

959
932
961

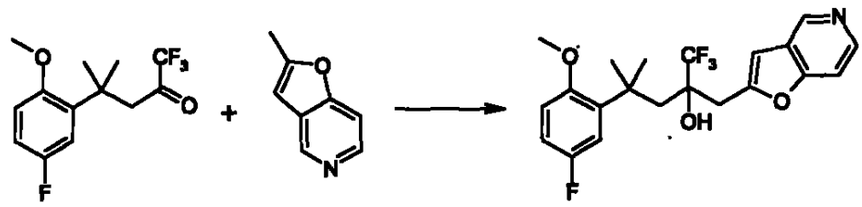
solución en 0,5 ml de THF. La mezcla se agitó durante 30 minutos a -78°C y se calentó a temperatura ambiente. 5 ml de acetato de etilo se agregó y la fase orgánica se lavó con agua, se secó, se filtró, y se evaporó. De la cromatografía de fase preparativa (activador: diclorometano-etanol (95:5)) se obtuvo 100 mg del compuesto del título en forma de aceite que solidificó estando en reposo (45% de rendimiento).

Ejemplo 102: Síntesis de 2-(1-Fluorociclopropil)-4-(4-fluorofenil)-4-metil-1-quinolin-4-ilpentan-2-ol



A una solución de 4-metilquinolina (69 mg, 0,482 mmol) en THF enfriada sobre hielo seco/acetona se agregó 0,4 ml de diisopropilamidade litio (1,5 M en hexanos). La mezcla se colocó en un baño frío entre -20°C y -30°C durante 15 minutos y luego se enfrió a -78°C. Se agregó 1-(1-fluorociclopropil)-3-(4-fluorofenil)-3-metilbutan-1-ona (49 mg, 0,206 mmol) gota a gota como una solución en 0,5 ml de THF. Luego se remitró el baño frío y la mezcla se agitó durante 1 hora. La reacción se desactivó mediante el agregado de 0,5 ml de agua y se diluyó con acetato de etilo. La fase orgánica se separó, se lavó con agua, se secó, se filtró, y el solvente se evaporó al vacío. Del fraccionamiento del residuo por cromatografía de fase preparativa (activante: acetato de etilo-hexanos (2:1)) se obtuvo el compuesto del título (0,019 g, 24% de rendimiento) (levemente menos polar que la lepidina) en forma de aceite que cristalizó estando en reposo en hexanos, p.f. 152°C-155°C.

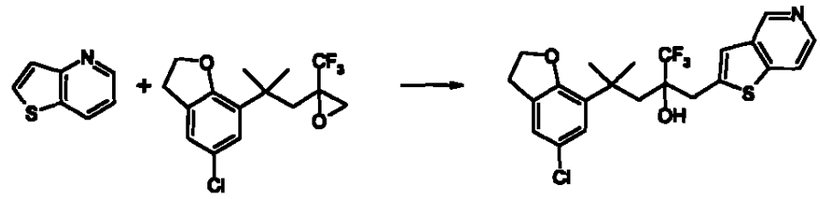
Ejemplo 103: Síntesis de 1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-furo[3,2-c]piridin-2-ilmetil-4-metilpentan-2-ol



Una solución de 2-metilfuro[3,2-c]piridina (preparada según el procedimiento de T. Kitamura, K. Tsuda, y Y. Fujiwara, Tetrahedron Lett. 1998, 39, pp. 5375-5376) (26,0 mg, 0,195 mmol) en 2 ml de THF se trató con diisopropilamida de litio (LDA; 1,5 M en ciclohexano, 195 µl) gota a gota a -78°C. La mezcla se agitó durante 30 minutos (el color

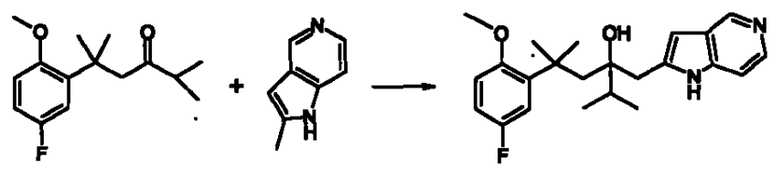
cambió de amarillo rojo anaranjado) y lentamente se trató con una solución de 1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ona (61,5 mg, 0,293 mmol) en 1 ml de THF. La reacción se agitó a -78°C durante 4,5 horas, se desactivó con 5 ml de solución saturada de cloruro de amonio, y se diluyó con 20 ml de acetato de etilo. Se separaron las fases y se extrajo la capa acuosa con tres porciones de 10 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con salmuera, se secaron sobre sulfato de magnesio, y se concentraron al vacío. De la cromatografía flash (acetato de etilo-hexanos, 5% a 50% gradiente) se obtuvo 36,0 mg (45% de rendimiento) del producto del título como un aceite claro.

Ejemplo 104: Síntesis de 4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-tieno[3,2-c]piridin-2-ilmetilpentan-2-ol



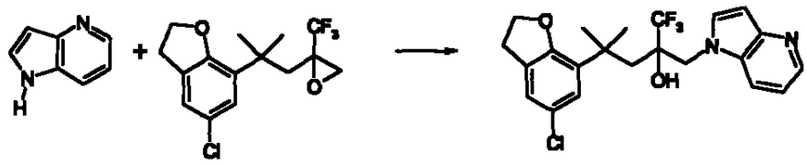
Una solución de tieno[3,2-*c*]piridina (preparada según el procedimiento de J.H. Wikel, M.L. Denney, y R.T.J. Vasileff, Heterocíclic Chem. 1993, 30, pp. 289-290) (152 mg, 1,12 mmol) en 2 ml de THF se trató con 450 µl de *n*-BuLi (2,5 M en hexanos) en un modo gota a gota a -78°C. La mezcla de reacción oscura resultante se agitó durante 30 minutos y se trató con una solución de 5-cloro-7-[1,1-dimetil-2-(2-trifluorometiloxiranil)etil]-2,3-dihidrobenzofurano (180 mg, 0,561 mmol) en 0,5 ml de THF. Se permitió a la reacción calentar a temperatura ambiente hasta el día siguiente y se desactivó con una mezcla de 5 ml de una solución saturada de cloruro de amonio y 10 ml de acetato de etilo. Se separaron las fases y se extrajo la capa acuosa con tres porciones de 10 ml de acetato de etilo. Las capas orgánicas combinadas se lavaron con salmuera, se secaron sobre sulfato de magnesio, y se concentraron al vacío. De la cromatografía flash (acetato de etilo-hexanos, 20%-30% gradiente) se obtuvo 33,5 mg (13% de rendimiento) del producto del título como espuma amarilla.

Ejemplo 105: Síntesis de 5-(5-Fluoro-2-metoxifenil)-2,5-dimetil-3-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)hexan-3-ol



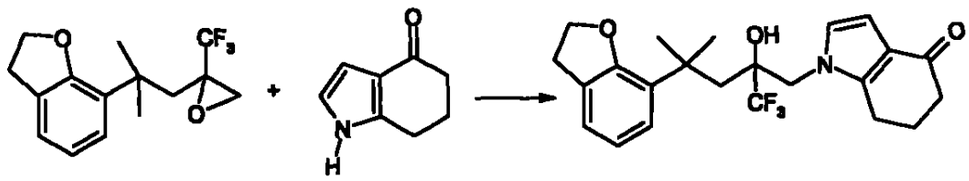
Una solución de 2-metil-1*H*-pirrolo[3,2-c]piridina (69 mg, 0,52 mmol) en 4 ml de THF se trató con 610 µL de *n*-BuLI (2,5 M en hexanos) a -78°C. Al cabo de 5 minutos, *ter*-BuOK (1 M en THF, 1,0 ml) se agregó y la mezcla se calentó a temperatura ambiente durante 1,5 horas. La mezcla de reacción color naranja se enfrió a -78°C y 5-(5-fluoro-2-metoxifenil)-2,5-dimetilhexan-3-ona (110 mg, 0,436 mmol) en 2 ml de THF se agregó gota a gota. La mezcla se agitó a -78°C durante 30 minutos, se calentó a temperatura ambiente, se desactivó con 10 ml de slución saturada de cloruro de amonio, y se diluyó con 20 ml de acetato de etilo. Se separaron las fases y se extrajo la capa acuosa con dos porciones de 10 ml de acetato de etilo. Las capas orgánicas combinadas se secaron sobre sulfato de magnesio y se concentraron al vacío. De la cromatografía sobre SiO_2 (MeOH en CH_2Cl_2, gradiente, 0% a 10%) se obtuvo 71,4 mg (43% de rendimiento) del producto como un sólido color blanco.

Ejemplo 106: Síntesis de 4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol



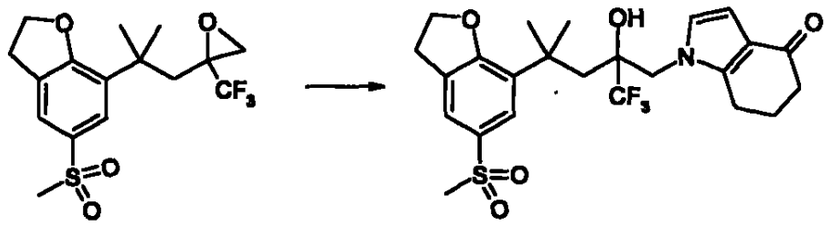
Una solución de 1*H*-pirrolo[3,2-*b*]piridina (33,0 mg, 0,279 mmol) en 4 ml de DMF se trató con NaH (60% en aceite mineral, 16,8 mg, 0,419 mmol) a temperatura ambiente. Al cabo de 30 minutos, se agregó 5-cloro-7-[1,1-dimetil-2-(2-trifluorometiloxiranil)etil]-2,3-dihidrobenzofurano (188 mg, 0,558 mmol) y la mezcla resultante se agitó hasta el día siguiente. La reacción luego se diluyó con 5 ml de acetato de etilo y se desactivó con 5 ml de solución saturada de cloruro de amonio. Se extrajo la capa acuosa con 5 ml de acetato de etilo. Las capas orgánicas combinadas se secaron sobre sulfato de magnesio, se filtraron y se concentraron al vacío. El residuo se trituró con dietiléter para dar 55,0 mg (45% de rendimiento) del producto del título como sólido blanco.

Ejemplo 107: Síntesis de 1-[4-(2,3-Dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona



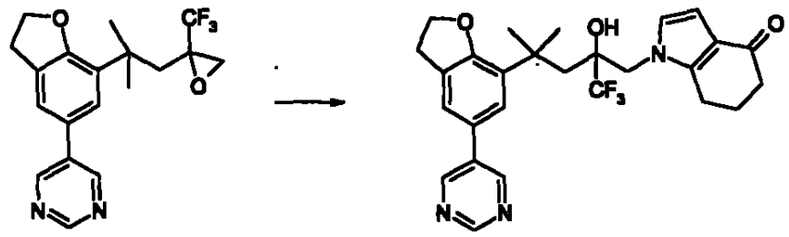
A una suspensión de 7-[1,1-dimetil-2-(2-trifluorometiloxiranil)etil]-2,3-dihidrobenzofurano (59,2 mg, 0,21 mmol) y 1,5,6,7-tetrahidroindol-4-ona (56,0 mg, 0,41 mmol) en 0,4 ml de etanol anhidro se agregó 0,077 ml de solución de etóxido de sodio (21 % en peso en etanol). La mezcla de reacción luego se calentó a 85°C durante 16 horas. La mezcla resultante se vertió en bicarbonato de sodio parcialmente saturado y se extrajo con acetato de etilo. Las fases orgánicas combinadas se secaron sobre sulfato de sodio, se filtró, y se concentraron al vacío. El residuo se purificó por gel de sílice. De la cromatografía (eluido con 35% acetato de etilo-hexanos) resultaron 58,4 mg (66% de rendimiento) del compuesto del título como un sólido color blanco, p.f. 145°C-146°C.

Ejemplo 108: Síntesis de 1-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona



A una suspensión de 7-[1,1-dimetil-2-(2-trifluorometiloxiranil)etil]-5-metansulfonil-2,3-dihidrobenzofurano (101 mg, 0,33 mmol) y 1,5,6,7-tetrahidroindol-4-ona (74,9 mg, 0,56 mmol) en 0,75 ml de etanol anhidro se agregó etóxido de sodio (solución 21% en peso en etanol, 103 µl). Luego de calentar a 85°C durante 16 horas, la mezcla de reacción se diluyó con acetato de etilo, se secaron sobre sulfato de sodio, se filtró, y se concentraron al vacío. El residuo se purificó por cromatografía en columna de gel de sílice (eluido con 50% a 60% acetato de etilo-hexanos) para dar 80,0 mg (58% de rendimiento) del compuesto del título como un sólido color blanco, p.f. 207°C-208°C.

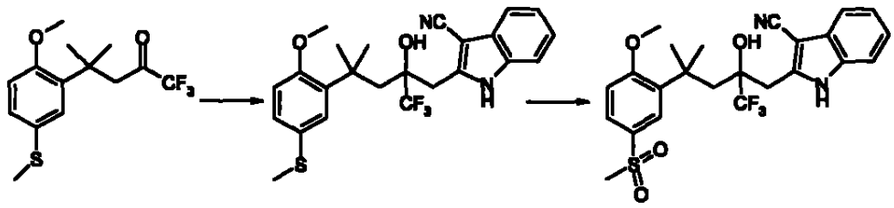
Ejemplo 109: Síntesis de 1-[2-Hidroxi-4-metil-4-(5-pirimidin-5-il-2,3-dihidrobenzofuran-7-il)-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona



A una suspensión de 5-[7-[1,1-dimetil-2-(2-trifluorometiloxiranil)etil]-2,3-dihidrobenzofuran-5-il]pirimidina (56,0 mg, 0,15 mmol) y 1,5,6,7-tetrahidroindol-4-ona

(41,6 mg, 0,31 mmol) en 1,0 ml de etanol anhidro se agregó una solución de etóxido de sodio (0,057 ml, 21 % en peso en etanol). La mezcla de reacción se calentó a 85°C durante 15 horas. Al cabo del enfriado a temperatura ambiente, la mezcla de reacción se concentró sobre gel de sílice (para carga seca) y se purificó por gel de sílice mediante cromatografía (eluido con 40% a 70% de acetato de etilo-hexanos) para dar 42,0 mg (55% de rendimiento) del compuesto del título como un sólido color blanco, p.f. 213°C-214°C.

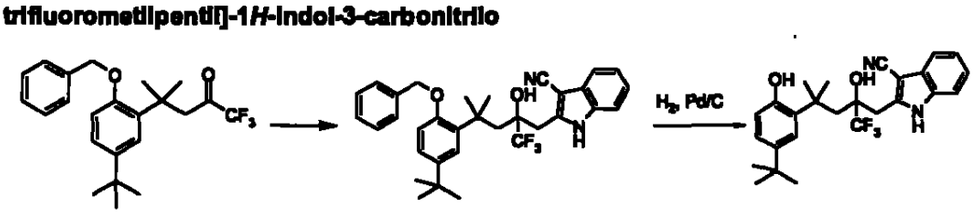
Ejemplo 110: 2-[2-Hidroxi-4-(5-metansulfonil-2-metoxifenil)-4-metil-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo



1,1,1-Trifluoro-4-(2-metoxi-5-metilsulfanilfenil)-4-metilpentan-2-ona se convirtió en 2-[2-Hidroxi-4-(2-metoxi-5-metilsulfanilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo en un modo similar al Ejemplo 4 de la publicación de la solicitud de patente U.S. Nº 2004/0023999.

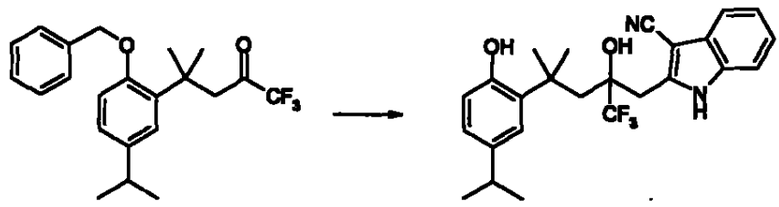
Se oxidó 2-[2-hidroxi-4-(2-metoxi-5-metilsulfanilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo en 2-[2-hidroxi-4-(5-metansulfonil-2-metoxifenil)-4-metil-2-trifluoro-metilpentil]-1*H*-indol-3-carbonitrilo según Ejemplo 4 de la publicación de la solicitud de patente U.S. Nº 2004/0023999.

Ejemplo 111: Síntesis de 2-[4-(5-*ter*-butil-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo



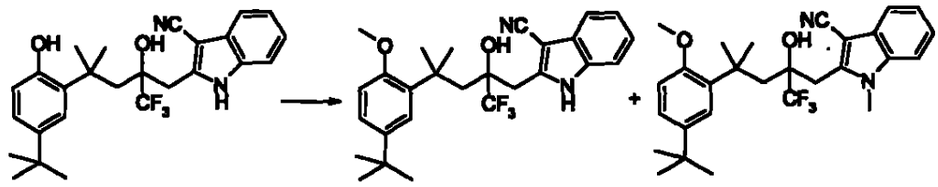
La 4-(2-Benciloxi-5-*ter*-butilfenil)-1,1,1-trifluoro-4-metilpentan-2-ona se convirtió en 2-[4-(5-*ter*-butil-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo usando procedimientos similares al del Ejemplo 4 de la publicación de la solicitud de patente U.S. Nº 2004/0023999.

Ejemplo 112: Síntesis de 2-[2-Hidroxi-4-(2-hidroxi-5-isopropilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo



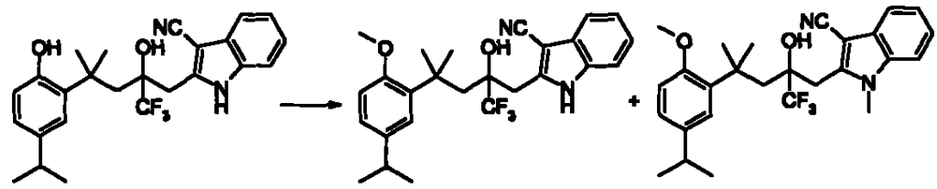
La 4-(2-Benciloxi-5-isopropilfenil)-1,1,1-trifluoro-4-metilpentan-2-ona se convirtió en 2-[2-hidroxi-4-(2-hidroxi-5-isopropilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo usando un procedimiento similar al descripto en la síntesis de 2-[4-(5-*ter*-butil-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo.

Ejemplo 113: Síntesis de 2-[4-(5-*ter*-Butil-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo y 2-[4-(5-*ter*-Butil-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1-metil-1*H*-indol-3-carbonitrilo



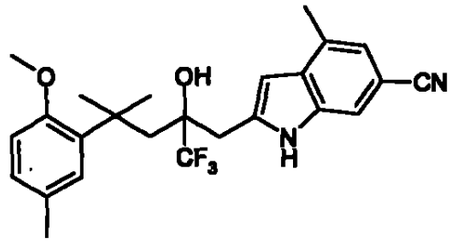
Se alquiló el 2-[4-(5-*ter*-Butil-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo para dar 2-[4-(5-*ter*-butil-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo y 2-[4-(5-*ter*-butil-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1-metil-1*H*-indol-3-carbonitrilo de un modo similar al descripto para la alquilación de 3-(2-benciloxi-5-*ter*-butilfenil)-3-metilbutan-1-ol en Ejemplo 53.

Ejemplo 114: Síntesis de 2-[2-Hidroxi-4-(5-isopropil-2-metoxifenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo y 2-[2-Hidroxi-4-(5-isopropil-2-metoxifenil)-4-metil-2-trifluorometilpentil]-1-metil-1*H*-indol-3-carbonitrilo



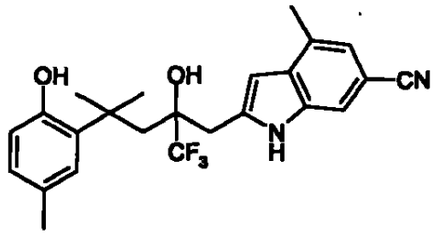
Se alquiló el 2-[2-Hidroxi-4-(2-hidroxi-5-isopropilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo para dar 2-[2-hidroxi-4-(5-isopropil-2-metoxifenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo y 2-[2-Hidroxi-4-(5-isopropil-2-metoxifenil)-4-metil-2-trifluorometilpentil]-1-metil-1*H*-indol-3-carbonitrilo de un modo similar al descripto para la alquilación de 3-(2-benciloxi-5-*ter*-butilfenil)-3-metilbutan-1-ol en Ejemplo 53.

Ejemplo 115: Síntesis de 2-[2-Hidroxi-4-(2-metoxi-5-metilfenil)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo



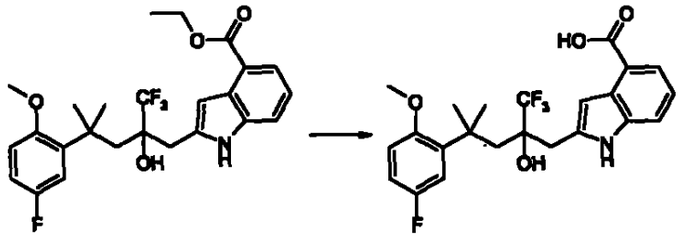
La 1,1,1-trifluoro-4-(2-metoxi-5-metilfenil)-4-metilpentan-2-ona se convirtió en 2-[2-hidroxi-4-(2-metoxi-5-metilfenil)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo como en Ejemplo 8 de la publicación de la solicitud de patente U.S. Nº 2004/0023999.

Ejemplo 116: Síntesis de 2-[2-Hidroxi-4-(2-hidroxi-5-metilfenil)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo



El 2-[2-Hidroxi-4-(2-metoxi-5-metilfenil)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo se convirtió en 2-[2-hidroxi-4-(2-hidroxi-5-metilfenil)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo como en el Ejemplo 8 de la publicación de la solicitud de patente U.S. Nº 2004/0023999.

Ejemplo 117: Síntesis del ácido 2-[4-(5-fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-4-carboxílico



Una solución de etil éster del ácido 2-[4-(5-fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-4-carboxílico (220 mg, 0,470 mmol) en 10 ml de metanol se trató con una solución de hidróxido de potasio (85 mg, 1,5 mmol) en 3 ml de agua. La

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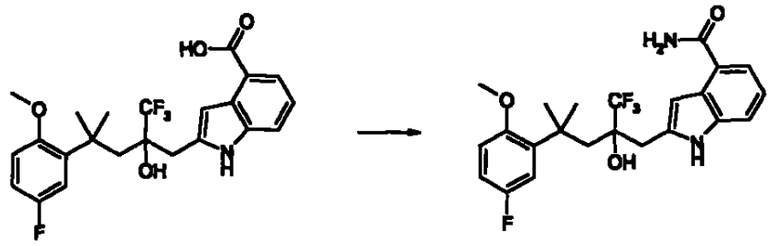
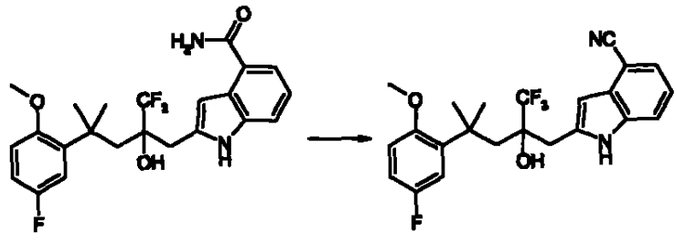
mezcla resultante se agitó a temperatura ambiente durante 4 horas, se sometió a reflujo durante 6 horas, se enfrió a temperatura ambiente, y se concentraron al vacío. El residuo se trató con ácido sulfúrico 1 N frío y se extrajo con tres porciones de 30 ml de diclorometano. Las capas orgánicas combinadas se lavaron con agua, se secaron sobre sulfato de sodio, se filtraron y se concentraron al vacío para dar 190 mg del producto del título como un sólido color crema claro (89% de rendimiento).

Ejemplo 118: Síntesis de la amida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-4-carboxílico



Una solución de 2-[4-(5-fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-4-carboxílico (170 mg, 0,375 mmol) en 2 ml de acetonitrilo se trató con 105 ml de trietilamina y TBTU (133 mg, 0,413 mmol). Al cabo de 15 minutos, se agregaron 53,6 ml de solución de hidróxido de amonio. La mezcla de reacción resultante se diluyó con agua y se extrajo con diclorometano. La capa orgánica se lavó sobre sulfato de sodio, se filtró, y se concentró al vacío. De la cromatografía sobre SiO_2 (50% acetato de etilo en hexanos) se obtuvo 170 mg del producto del título como un sólido blanquecino (rendimiento cuantitativo).

Ejemplo 119: Síntesis de 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-4-carbonitrilo



Una solución de la amida del ácido 2-[4-(5-fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-4-carboxílico (95 mg, 0,21 mmol) en 1 ml de DMF se hizo reaccionar con cloruro cianúrico (46 mg, 0,25 mmol). Al cabo de 3 horas, la mezcla se trató con bicarbonato de sodio, se extrajo con diclorometano. La capa orgánica se lavó

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sobre sulfato de sodio, se filtró, y se concentró al vacío para dar 33 mg del producto del título como un sólido color blanquerino (36% de rendimiento).

La resolución a los enantiómeros (+) y (-) se realizó mediante HPLC quiral en una columna CHIRALCEL™ OD, eluyendo con 15% a 25% de isopropanol-hexanos.

Evaluación de Propiedades Biológicas

Los compuestos de la invención se evaluaron respecto de la capacidad de unión al receptor esteroide mediante un ensayo de unión competitiva de polarización de fluorescencia. Las descripciones detalladas para la preparación del complejo del receptor de glucocorticoides recombinante (GR) utilizado en este ensayo se describe en la Solicitud de Patente publicada U.S. Nº 2003/0017503, que se incorpora aquí en su totalidad como referencia. Se realizó la preparación de la sonda de dexametasona marcada con tetrametil rodamina (TAMRA) usando un procedimiento estándar de la literatura (M. Pons *et al.*, J. Steroid Biochem., 1985, 22, pp. 267-273).

A. Ensayo de unión competitiva del receptor de glucocorticoides

Paso 1. Caracterización de la muestra fluorescente

Las longitudes de onda para la excitación y emisión máxima de la sonda fluorescente deben medirse en primer lugar. Un ejemplo de una sonda tal es la dexametasona marcada con rodamina (TAMRA).

La afinidad de la muestra para el receptor esteroide se determinó luego en un experimento de titulación. El valor de la polarización de fluorescencia de la muestra en el buffer de ensayo se midió en un fluorómetro SLM-8100 usando los valores máximos de emisión previamente descriptos. Se sumaron las alícuotas del vector de expresión del lisado y se midió la polarización de la fluorescencia al cabo de cada adición hasta que no se observó ningún otro cambio en el valor de la polarización. Se utilizó análisis de regresión no lineal por cuadrados mínimos para calcular la constante de disociación de la sonda respecto de los valores de polarización obtenidos para la unión de lisados a la sonda.

Paso 2. Verificación de inhibidores de uniones en la muestra

En este ensayo se utiliza polarización de fluorescencia (FP) para cuantificar la propiedad de los compuestos de ensayo para competir con la dexametasona marcada con tetrametil rodamina (TAMRA) para unirse a un complejo de receptor de glucocorticoides (GR) humanos preparados a partir de un sistema de expresión de insectos. El buffer de ensayo fue: TES 10 mM, KCl 50 mM, $Na_2MoO_4 \cdot 2H_2O$ 20 mM, EDTA 1,5 mM, 0,04% w/v CHAPS, 10% v/v glicerol, 1 mM ditiotreitol, pH 7,4. Los compuestos de ensayo se disolvieron en concentración 1 mM en DMSO puro y luego se diluyeron a

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una concentración de ensayo 10x en buffer de ensayo suplementado con 10% v/v de DMSO. Los compuestos de ensayo se diluyeron serialmente en concentraciones de ensayo 10x en buffer que contenía 10% de DMSO en placas de polipropileno de 96 cavidades. Se prepararon mezclas de reacción para la unión en placas de microtitulación Dynex negras de 96 cavidades por adición secuencial de los siguientes componentes del ensayo en cada cavidad: 15 µl de solución del compuesto de ensayo 10x, 85 µl de lisado de baculovirus que contenía GR diluido 1:170 en buffer de ensayo, y 50 µl de dexametasona 15 nM marcada con TAMRA. Los controles positivos fueron mezclas de reacción que no contenían el compuesto de ensayo; los controles negativos (blancos) fueron mezclas de reacción que contenían 0,7 µM a 2 µM de dexametasona. Las reacciones de unión se incubaron durante 1 hora a temperatura ambiente y luego se leyó la polarización de fluorescencia en el LJL Analist fijado en una excitación de 550 nm y una emisión de 580 nm, con el espejo dicroico de Rodamina 561 instalado. Se determinaron los valores de IC_{50} por ajuste de la curva no lineal iterativa de los datos de la señal FP a una ecuación logística de 4 parámetros.

Los compuestos que se encontró se unen al receptor de glucocorticoides pueden evaluarse respecto de la unión con el receptor de progesterona (PR), el receptor de estrógenos (ER), y los receptores de mineralocorticoides (MR) para evaluar la selectividad del compuesto por los GR. Los protocolos para PR y MR son idénticos al método de GR indicado previamente, con las siguientes excepciones: el lisado de células PR de insecto se diluyó 1:7,1 y el lisado MR se diluyó 1:9,4. La muestra PR es mifepristone marcado con TAMRA, usado a una concentración final de 5 nM en el ensayo, y los controles negativos (blancos) fueron reacciones que contenían mifepristone de 0,7 µM a 2 µM.

El protocolo de ER es similar a protocolos anteriores, pero emplea un receptor del kit PanVera, una muestra con marcado fluorescente. Los componentes del ensayo se realizan con el mismo volumen que el anterior, para producir concentraciones finales de ensayo para las muestras de ER de 15 nM y de ES2 de 1 nM. Además, se modifica el orden de adición de los componentes respecto de los ensayos anteriores: la sonda se agrega primero a la placa, seguido del receptor y del compuesto de ensayo. Las placas se leen en el LJL Analist ajustado con una excitación de 485 nm y una emisión de 530 nm, con el espejo dicroico Fluorescein 505 instalado.

Los compuestos que se encontró se unen al receptor de glucocorticoides pueden ser evaluados respecto de la disociación de la transactivación y la transrepresión en los ensayos citados en los antecedentes de la invención (C.M. Bamberger y H.M. Schulte,

Eur. J. Clin. Invest., 2000, 30 (suppl. 3) pp. 6-9) o en los ensayos descritos a continuación.

B: Ensayos con células de receptores de glucocorticoides

1. Inducción de Aromatasa en Fibroblastos (Ensayo celular para transactivación)

La dexametasona, un ligando sintético del receptor de glucocorticoides (GR), induce la expresión de aromatasa en células fibroblastos de prepucio humano. La actividad de la aromatasa se mide por conversión de testosterona a estradiol en medio de cultivo. Los compuestos que presentan una unión a GR son evaluados respecto de su capacidad para inducir la actividad de aromatasa en fibroblastos de prepucio humano.

Las células de fibroblastos de prepucio humano (ATCC Cat. Nº CRL-2429, designación CCD112SK) se colocan en placas de 96 cavidades a razón de 50.000 células por cavidad 5 días previo a su uso, en Medio de Iscove Modificado de Dulbecco (GibcoBRL Life Technologies Cat Nº 12440-053) suplementado con FBS al 10% filtrado con carbón (Clonetech Cat Nº SH30068) y gentamicina (GibcoBRL Life Technologies Cat. Nº 15710-064). El día del experimento, se reemplazó el medio en las cavidades por medio fresco. Las células se trataron con compuestos de ensayo en concentraciones finales de 10^{-6} M a 10^{-5} M, y testosterona con una concentración final de 300 ng/ml. Cada cavidad presenta un volumen total de 100 µl. Las muestras se realizaron por duplicado. El control de las cavidades incluye: (a) cavidades que sólo reciben testosterona, y (b) cavidades que reciben testosterona más 2 µM de dexametasona para dar la máxima inducción de aromatasa. Las placas se incubaron a 37°C hasta el día siguiente (15 a 18 horas), y los sobrenadantes se cosecharon al final de la incubación. Se midió el estradiol en los sobrenandantes usando kits ELISA para estradiol (producidos por ALPCO, obtenidos de American Laboratory Productos Cat. Nº 020-DR-2693) según las instrucciones del fabricante. La cantidad de estradiol es inversamente proporcional a las señales de ELISA en cada cavidad. El nivel de inducción de la aromatasa en los compuestos de ensayo se expresa como un porcentaje relativo de dexametasona. Los valores de EC_{50} de los compuestos de ensayo se derivan por ajuste de curvas no lineales.

2. Inhibición de la producción de IL-6 en fibroblastos (Ensayo celular para transrepresión)

Las células fibroblastos de prepucio humano producen IL-6 en respuesta a la estimulación mediante la citoquina IL-1 proinflamatoria. Esta repuesta inflamatoria, medida mediante la producción de IL-6, puede inhibirse efectivamente por la dexametasona, un ligando sintético del receptor de glucocorticoides (GR). Los

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compuestos que exhiben una unión a GR son evaluados respecto de su capacidad de inhibir la producción de IL-6 en fibroblastos de prepucio humano.

Las celulas fibroblastos de prepucio humano (ATCC Cat. Nº CRL-2429) se colocan en placas de 96 cavidades a razón de 5.000 células por cavidad el día previo a su uso, en Medio de Iscove Modificado de Dulbecco (GibcoBRL Life Technologies Cat. Nº 12440-053) suplementado con 10% de FBS filtrado por carbón (Clonetech Cat. Nº SH30068) y gentamicina (GibcoBRL Life Technologies Cat. Nº 15710-064). Al día siguiente se reemplazó el medio en las cavidades por medio fresco. Las células se trataron con IL-1 (rhIL-1α, R&D Systems Cat. Nº 200-LA) con una concentración final de 1 ng/ml, y con compuestos de ensayo con concentraciones finales de 10^{-5} M a 10^{-8} M, con un volumen total de 200 µl por cavidad. Las muestras se realizaron por duplicado. El control de trasfondo de las cavidades no recibe compuestos de ensayo o IL-1. Las cavidades de control positivo reciben sólo IL-1 y representa un máximo (o 100%) de la cantidad de la producción de IL-6. Las placas se incubaron a 37°C hasta el día siguiente (15 a 18 horas), y los sobrenadantes se cosecharon al final de la incubación. Se midieron los niveles de IL-6 en los sobrenandantes usando kits ELISA para IL-6 (MedSystems Diagnostics GmbH, Vienna, Austria, Cat. Nº BMS213TEN) según las instrucciones del fabricante. La extensión de la inhibición de IL-6 para compuestos de ensayo se expresa en porcentajes en relación a los controles positivos. Los valores de IC_{50} de los compuestos de ensayo se derivan por ajuste de curvas no lineales.

Puede determinarse la evaluación de la actividad agonista o antagonista que forma una unión con el receptor de glucocorticoides por cualquiera de los ensayos.

3. Modulación de la Inducción de la Tirosina aminotransferasa (TAT) en células de hepatoma de ratas

Evaluación de los compuestos respecto de la actividad agonista y antagonista en la inducción de la tirosina aminotransferasa (TAT) en células de hepatoma de rata.

Se incubaron células H4-II-E-C3 hasta el día siguiente en placas de 96 cavidades (20.000 células/100 µl/cavidad) en medio MEM que contenía un 10% de FBS inactivado por calor y 1% de aminoácidos no esenciales. Al día siguiente, las células fueron estimuladas con las concentraciones indicadas de dexametasona o compuesto de ensayo (disuelto en DMSO, concentración final de DMSO 0,2%) durante 18 horas. El control de células se trató con DMSO 0,2%. Al cabo de 18 horas, las células se lisaron en un buffer que contenía 0,1% de Triton X-100 y la actividad TAT se midió en un ensayo fotométrico usando tirosina y alfa-cetoglutarato como sustratos.

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Para medir la actividad antagonista, se preestimularon las células de hepatoma mediante el agregado de dexametasona (la concentración oscila entre 3×10^{-9} M a 3×10^{-6} M) un breve lapso antes de que el compuesto de ensayo se aplicara a las células. El antagonista esteroidal no selectivo GR/PR mifepristona se utilizó como control.

4. Modulación de la inducción de MMTV-Luc en células HeLa

Verificación de compuestos respecto de actividad agonista o antagonista en estimulación del promotor de MMTV-(virus tumoral mamario de ratón) en células HeLa.

Se transfectaron células HeLa en forma estable con el plásmido pHHLuc que contenía un fragmento de MMTV-LTR (-200 a +100 respecto del punto de inicio de la transcripción) clonado frente al gen luciferasa (Norden, 1988) y el plásmido pcDNA3,1 (Invitrogen) expresando constitutivamente la resistencia respecto del antibiótico selectivo GENETICIN®. Se seleccionaron clones con la mejor inducción del promotor MMTV y se utilizaron para otros experimentos.

Se cultivaron las células hasta el día siguiente en medio DMEM sin rojo fenol, suplementado con 3% de CCS (suero bovino tratado con carbón) y luego se transfirieron a placas de 96 cavidades (15.000 células/100 µl/cavidad). Al día siguiente, se estimuló la activación del promotor MMTV por adición de compuesto de ensayo o dexametasona disuelta en DMSO (concentración final 0,2%). El control de células se trató sólo con DMSO. Al cabo de 18 horas, las células fueron lisadas con reactivo de lisado celular (Promega, Cat. Nº E1531), se agregó reactivo de ensayo de luciferasa (Promega, Cat. Nº E1501) y se midió la luminiscencia brillante usando un luminómetro (BMG, Offenburg).

Para medir la actividad antagonista, el promotor MMTV fue preestimulado mediante el agregado de dexametasona (3×10^{-9} M a 3×10^{-8} M) poco antes de que el compuesto de ensayo fuera aplicado a las células. El antagonista esteroidal no selectivo GR/PR mifepristona se utilizó como control.

5. Modulación de la producción de IL-8 en células U937

Verificación de compuestos respecto de la actividad agonista o antagonista en la inhibición mediada por GR de la secreción de IL-8 inducida por LPS en células U-937.

Se incubaron células U-937 durante 2 a 4 días en medio RPMI1640 que contenía 10% CCS (suero bovino tratado con carbón). Las células fueron transferidas a placas de 96 cavidades (40.000 células/100 µl/cavidad) y estimuladas con 1 µg/ml de LPS (disuelto en PBS) en presencia o ausencia de dexametasona o compuesto de ensayo (disuelto en DMSO, concentración final 0,2%). El control de células se trató con DMSO 0,2%. Al cabo de 18 horas, la concentración de IL-8 en el sobrenadante celular se midió por ELISA, usando el "OptEIA human IL-8 set" (Pharmingen, Cat. Nº 2654KI).

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Para la medición de la actividad antagonista, la secreción de IL-8 inducida por LPS fue inhibida por agregado de dexametasona (3×10^{-9} M a 3×10^{-8} M) poco antes de que el compuesto de ensayo fuera aplicado a las células. Se utilizó como control el antagonista esteroidal no selectivo GR/PR mifepristona.

6. Modulación de la expresión de ICAM-Luc en células HeLa

Verificación de compuestos respecto de la actividad agonista o antagonista en la inhibición de la activación de inducida por TNFalfa del promotor ICAM en células HeLa.

Las células HeLa fueron co-transfectadas en forma estable con un plásmido que contenía un fragmento de 1,3 kb del promotor ICAM humano (-1353 a -9 respecto al punto de inicio de la transcripción, Ledebur y Parks, 1995) clonado frente al gen de la luciferasa y el plásmido pcDNA3,1 (Invitrogen) que constitutivamente expresan la resistencia al antibiótico GENETICIN®. Se seleccionaron los clones con la mejor inducción del promotor ICAM y se usaron para otros experimentos. Las células fueron transferidas a placas de 96 cavidades (15.000 células/100 µl/cavidad) en medio DMEM suplementado con 3% de CCS. Al día siguiente se indujo la activación del promotor ICAM mediante el agregado de 10 ng/ml de TNF-alfa recombinante (R&D System, Cat. Nº 210-TA). Simultáneamente las células se trataron con el compuesto de ensayo o dexametasona (disuelto en DMSO, concentración final 0,2%). El control de células se trató sólo con DMSO. Al cabo de 18 horas, las células fueron lisadas con reactivo de lisado de células (Promega, Cat. Nº E1531), se agregó el reactivo del ensayo de luciferasa (Promega, Cat. Nº E1501) y la luminiscencia brillante se midió usando un luminómetro (BMG, Offenburg).

Para la medición de la actividad antagonista, la activación del promotor ICAM inducida por TNF alfa se inhibió agregando dexametasona (3×10^{-9} M a 3×10^{-8} M) un breve tiempo antes de que el compuesto del ensayo se aplicara a las células. El antagonista GR/PR esteroidal no selectivo mifepristone se utilizó como control.

En general el rango de potencia preferido en los ensayos anteriores se ubica entre 0,1 nM y 10 µM, el rango de potencia de mayor preferencia es 0,1 nM a 1 µM, y el rango de potencia de máxima preferencia es 0,1 nM a 100 nM.

Se ensayaron compuestos representativos de la invención y mostraron actividad como modulares de la función de los receptores glucorticoides en uno o más de los ensayos anteriores. Por ejemplo, los siguientes compuestos de la invención de Fórmula (IA) demostraron una intensa actividad en el ensayo de unión de GR.

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(3-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(4,6-Dimetil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(6-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-pirrolo[3,2-*c*]piridina-6-carbonitrilo;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-*c*]piridina-5-carbonitrilo;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*c*]piridina-4-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-tieno[2,3-*d*]piridazin-2-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5*H*-pirrolo[3,2-c]piridazin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(2-metil-5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(1*H*-pirrolo[2,3-*d*]piridazin-2-ilmetil)pentan-2-ol;

2-(4,6-Dimetil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(4,6-dimetil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(6-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(6-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol;

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2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;

2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(7-fluoro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(5,7-Dicloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5-trifluorometil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(5-metoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(5-metoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(5-metoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(7-fluoro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-trifluorometil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(5-cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(5-metil-2,3-dihidrobenzofuran-7-il)-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-pirrolo[2,3-*b*]piridin-1-ilmetilpentan-2-ol;

2-Benzo[*b*]tiofen-2-ilmetil-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-tieno[2,3c]piridin-2-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-[4-((*Z*)propenil)-3-vinilpirazol-1-ilmetil]pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,4-dimetil-1-tieno[2,3-*c*]piridin-2-ilpentan-2-ol;

4-(5-Fluoro-2-metilfenil)-2,4-dimetil-1-tieno[2,3-*c*]piridin-2-ilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(5-metil-2,3-dihidrobenzofuran-7-il)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(3-Dimetilaminometil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-pirrolo[3,2-*c*]piridin-1-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-furo[3,2-*c*]piridin-2-ilmetil-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;

1,1-Difluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-tieno[3,2-*c*]piridin-2-ilmetilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-tieno[3,2-c]piridin-2-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-tieno[3,2-*c*]piridin-2-ilmetilpentan-2-ol;

dimetilamida del ácido 2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carboxílico;

{2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-il}morfolin-4-ilmetanona;

dimetilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carboxílico;

dimetilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-il}morfolin-4-ilmetanona;

2-[4-(2,3-Dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

amida del ácido 2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carboxílico;

amida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carboxílico;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-nitro-1*H*-indol-2-ilmetil)butil]fenol;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carbonitrilo;

2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carbonitrilo;

N-{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}acetamida;

1,1,1-Trifluoro-4-(4-fluoro-2-metoxifenil)-2-(7-fluoro-4-metil-1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-(7-fluoro-4-metil-1*H*-indol-2-ilmetil)-3-hidroxi-1,1-dimetilbutil]fenol;

2-[4-(3-[1,3]Dioxolan-2-ilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonitrilo;

2-Trimetilsilaniletil éster del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

2-[4-(4-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

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{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}piperidin-1-ilmetanona;

Metilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}pirrolidin-1-ilmetanona;

1-{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}piperidin-4-ona;

(2-Hidroxietil)amida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}(4-hidroxipiperidin-1-il)metanona;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}(3-hidroxipirrolidin-1-il)metanona;

Cianometilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Metil éster del ácido ({2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}amino)acético ;

Carbamoilmetilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Metil éster del ácido 4-({2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometil-pentil]-1*H*-indol-5-carbonil}amino)butírico;

Ácido ({2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}amino)acético ;

Ácido 4-({2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}amino)butírico;

2-[4-(3-Dimetilaminometilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonitrilo;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-trifluorometil-1*H*-indol-2-ilmetil)butil]fenol;

2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

Ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Amida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Dimetilamida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Cianometilamida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}pirrolidin-1-ilmetanona;

{2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}morfolin-4-ilmetanona;

Amida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}morfolin-4-ilmetanona;

2-(4-Benzo[1,3]dioxol-4-il-2-hidroxi-4-metil-2-trifluorometilpentil)-4-metil-1*H*-indol-6-carbonitrilo;

1,1,1-Trifluoro-4-metil-4-fenil-2-quinolin-4-ilmetilhexan-2-ol;

2-[2-Hidroxi-4-metil-4-(5-metilsulfanil-2,3-dihidrobenzofuran-7-il)-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

7-(4,4,4-Trifluoro-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)-2,3-dihidrobenzofuran-5-carbonitrilo;

2-[2-Hidroxi-4-(2-hidroxi-5-metilfenil)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-metilsulfanil-1*H*-indol-2-ilmetil)pentan-2-ol;

2-[2-Hidroxi-4-(5-metansulfonil-2-metoxifenil)-4-metil-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-fenil-1*H*-indol-2-ilmetil)pentan-2-ol;

2-[4-(5-*ter*-Butil-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(2-hidroxi-5-isopropilfenil)-4-metil-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(2-hidroxi-3,5-dimetilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(5-hidroxi-2,4-dimetilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[4-(5-*ter*-Butil-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(5-isopropil-2-metoxifenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(2-metoxi-5-metilfenil)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*o*-tolilpentan-2-ol;

1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*m*-tolilpentan-2-ol;

1,1,1-Trifluoro-4-(2-fluorofenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(2-fluorofenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorofenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorofenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

3-(4,4,4-Trifluoro-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)fenol;

1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-(2-trifluorometilfenil)pentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-(4-trifluorometilfenil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-(4-trifluorometilfenil)pentan-2-ol;

4-(3-Clorofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

4-(3-Clorofenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

4-(4-Dimetilaminofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

4-Bifenil-3-il-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

4-(3-Bromofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

4-(2-Difluorometoxi-5-fluorofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

4-Bifenil-3-il-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

4-(4-Dimetilaminofenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,6-dihidropirrolo[2,3-c]piridin-5-ona;

2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-6-metil-1,6-dihidropirrolo[2,3-c]piridin-5-ona;

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1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(5-metoxi-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-metilpentan-2-ol;

2-[4-(3-Dimetilaminometilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonitrilo;

1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-piridin-2-ilpentan-2-ol;

1,1,1-Trifluoro-4-metil-4-piridin-4-il-2-quinolin-4-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*o*-tolilpentan-2-ol;

1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*m*-tolilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-piridin-4-ilmetilpentan-2-ol;

4-Fluoro-2-[4,4,4-trifluoro-3-(2-fluoropiridin-4-ilmetil)-3-hidroxi-1,1-dimetilbutil]fenol;

2-[3-(2-Bromopiridin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;

2-(6,8-Dimetilquinolin-4-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

4-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]piridina-2-carbonitrilo;

2,6-Dicloro-4-[4-(5-fluoro-2-metoxifenil)-2-hidroxi-4-metil-2trifluorometilpentil]nicotinonitrilo;

2,6-Dicloro-4-[4-(5-fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2trifluorometilpentil]nicotinonitrilo;

2-(2,6-Dicloroquinolin-4-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

2-[3-(2-Cloro-8-metilquinolin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;

2-[3-(2,6-Dicloroquinolin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;

4-(2,3-Dihidrobenzofuran-7-il)-2-(2,6-dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(3-fluorofenil)-4-metilpentan-2-ol;

2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(4-fluorofenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;

2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-metil-4-*m*-tolilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(2-metilquinolin-4-ilmetil)pentan-2-ol;

4-Fluoro-2-(4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)fenol;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(2-metilquinolin-4-ilmetil)butil]fenol;

2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(4-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(7-metilquinolin-4-ilmetil)pentan-2-ol;

2-[3-(2,6-Dimetilpiridin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-5-fluorofenol;

1,1,1-Trifluoro-4-(4-fluorofenil)-4-metil-2-(2-metilquinolin-4-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(3-metil-1*H*-indol-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-(2-trifluorometilfenil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(7-fluoro-4-metilquinolin-8-il)-4-metilpentan-2-ol;
4-(2,6-Dimetilfenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
2-(3-Bromo-1*H*-indol-2-ilmetil)-1,1,1-trifluoro-4-(3-fluorofenil)-4-metilpentan-2-ol;
4-(3,4-Dimetilfenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(3-fluoro-4-metilfenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(4-fluoro-3-metilfenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(3-fluoro-4-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(4-fluoro-2-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(3,4-Dimetilfenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(2,5-Dimetilfenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-(2-metoxi-5-metilfenil)-4-metilpentan-2-ol;
4-Metil-2-[4,4,4-trifluoro-3-hidroxi-3-(1*H*-indol-2-ilmetil)-1,1-dimetilbutil]fenol;
4-(2,5-Dimetilfenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(2-metoxi-5-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(2,5-Dimetoxifenil)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-(2-trifluorometilfenil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(4-metoxi-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-4-metilpentan-2-ol;
2-(2,4-Dimetil-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
2-(2-Amino-4-cloro-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol; y
2-(5-Cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol,
o un tautómero, un profármaco, un solvato o sal de los mismos.

Además, se estudiaron los siguientes compuestos de la invención de Fórmula (IA) y presentaron actividad como agonistas potentes de la función del receptor glucocorticoide en uno o más de los ensayos anteriores:

4-pirimidin-5-il-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(1H-pirrolo[2,3-c]piridin-2-ilmetil)butil]fenol
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(3-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(4,6-Dimetil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-pirrolo[3,2-*c*]piridina-6-carbonitrilo;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-*c*]piridina-5-carbonitrilo;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*c*]piridina-4-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-tieno[2,3-*d*]piridazin-2-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(1*H*-pirrolo[2,3-*d*]piridazin-2-ilmetil)pentan-2-ol;

2-(4,6-Dimetil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(4,6-dimetil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;

2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(7-fluoro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(5,7-Dicloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5-trifluorometil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(5-metoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(5-isopropoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(5-metoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(5-metoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(7-fluoro-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-trifluorometil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

2-(5-Dimetilamino-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

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1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(5-cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(5-metil-2,3-dihidrobenzofuran-7-il)-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-tieno[2,3c]piridin-2-ilmetilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,4-dimetil-1-tieno[2,3-*c*]piridin-2-ilpentan-2-ol;

4-(5-Fluoro-2-metilfenil)-2,4-dimetil-1-tieno[2,3-*c*]piridin-2-ilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(5-metil-2,3-dihidrobenzofuran-7-il)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(3-Dimetilaminometil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;

1,1-Difluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-tieno[3,2-*c*]piridin-2-ilmetilpentan-2-ol;

2-[4-(2,3-Dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-nitro-1*H*-indol-2-ilmetil)butil]fenol;

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carbonitrilo;

2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carbonitrilo;

N-[2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il]acetamida;

1,1,1-Trifluoro-4-(4-fluoro-2-metoxifenil)-2-(7-fluoro-4-metil-1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;

5-Fluoro-2-[4,4,4-trifluoro-3-(7-fluoro-4-metil-1*H*-indol-2-ilmetil)-3-hidroxi-1,1-dimetilbutil]fenol;

2-[4-(3-[1,3]Dioxolan-2-ilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonitrilo;

2-[4-(4-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

metilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}pirrolidin-1-ilmetanona;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}(3-hidroxipirrolidin-1-il)metanona;

cianometilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Metil éster del ácido ({2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}amino)acético;

Carbamoilmetilamida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Metil éster del ácido 4-({2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonil}amino)butírico;

4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-trifluorometil-1*H*-indol-2 ilmetil)butil]fenol;

2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

Amida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Dimetilamida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Cianometilamida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}pirrolidin-1-ilmetanona;

{2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}morfolin-4-ilmetanona;

Amida del ácido 2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}morfolin-4-ilmetanona;

2-(4-Benzo[1,3]dioxol-4-il-2-hidroxi-4-metil-2-trifluorometilpentil)-4-metil-1*H*-indol-6-carbonitrilo;

1,1,1-Trifluoro-4-metil-4-fenil-2-quinolin-4-ilmetilhexan-2-ol;

2-[2-Hidroxi-4-metil-4-(5-metilsulfanil-2,3-dihidrobenzofuran-7-il)-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

7-(4,4,4-Trifluoro-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)-2,3-dihidrobenzofuran-5-carbonitrilo;

2-[2-Hidroxi-4-(2-hidroxi-5-metilfenil)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-metilsulfanil-1*H*-indol-2-ilmetil)pentan-2-ol;

2-[2-Hidroxi-4-(5-metansulfonil-2-metoxifenil)-4-metil-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo;

2-[4-(5-*ter*-Butil-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(2-hidroxi-5-isopropilfenil)-4-metil-2-trifluorometil-pentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(2-hidroxi-3,5-dimetilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(5-hidroxi-2,4-dimetilfenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[4-(5-*ter*-Butil-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

2-[2-Hidroxi-4-(5-isopropil-2-metoxifenil)-4-metil-2-trifluorometilpentil]-1*H*-indol-3-carbonitrilo;

1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*o*-tolilpentan-2-ol;

1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*m*-tolilpentan-2-ol;

1,1,1-Trifluoro-4-(2-fluorofenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(2-fluorofenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(3-fluorofenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(4-fluorofenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(4-fluorofenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
3-(4,4,4-Trifluoro-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)fenol;
1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-(2-trifluorometilfenil)pentan-2-ol;
1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-(4-trifluorometilfenil)pentan-2-ol;
4-(3-Clorofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
4-(3-Clorofenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-Bifenil-3-il-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(3-Bromofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
4-(2-Difluorometoxi-5-fluorofenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
4-(4-Dimetilaminofenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(5-metoxi-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-metilpentan-2-ol;
2-[4-(3-Dimetilaminometilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonitrilo;
1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-piridin-2-ilpentan-2-ol;
1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*o*-tolilpentan-2-ol;
1,1,1-Trifluoro-4-metil-2-quinolin-4-ilmetil-4-*m*-tolilpentan-2-ol;
4-Fluoro-2-[4,4,4-trifluoro-3-(2-fluoropiridin-4-ilmetil)-3-hidroxi-1,1-dimetilbutil]fenol;
2-[3-(2-Bromopiridin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;
2-(6,8-Dimetilquinolin-4-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
4-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]piridina-2-carbonitrilo;
2,6-Dicloro-4-[4-(5-fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil] nicotinonitrilo;
2,6-Dicloro-4-[4-(5-fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil] nicotinonitrilo;
2-[3-(2,6-Dicloroquinolin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;
4-(2,3-Dihidrobenzofuran-7-il)-2-(2,6-dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(3-fluorofenil)-4-metilpentan-2-ol;
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(4-fluorofenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-metil-4-*m*-tolilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(2-metilquinolin-4-ilmetil)pentan-2-ol;
4-Fluoro-2-(4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-quinolin-4-ilmetilbutil)fenol;
4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(2-metilquinolin-4-ilmetil)butil]fenol;
2-(2,6-Dimetilpiridin-4-ilmetil)-1,1,1-trifluoro-4-(4-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(7-metilquinolin-4-ilmetil)pentan-2-ol;
2-[3-(2,6-Dimetilpiridin-4-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-5-fluorofenol;
1,1,1-Trifluoro-4-(4-fluorofenil)-4-metil-2-(2-metilquinolin-4-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(3-metil-1*H*-indol-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-(2-trifluorometilfenil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(7-fluoro-4-metilquinolin-8-il)-4-metilpentan-2-ol;
4-(2,6-Dimetilfenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
2-(3-Bromo-1*H*-indol-2-ilmetil)-1,1,1-trifluoro-4-(3-fluorofenil)-4-metilpentan-2-ol;
4-(3,4-Dimetilfenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(3-fluoro-4-metilfenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(4-fluoro-3-metilfenil)-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(3-fluoro-4-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(4-fluoro-2-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(3,4-Dimetilfenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(2,5-Dimetilfenil)-1,1,1-trifluoro-2-(1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-(2-metoxi-5-metilfenil)-4-metilpentan-2-ol;
4-Metil-2-[4,4,4-trifluoro-3-hidroxi-3-(1*H*-indol-2-ilmetil)-1,1-dimetilbutil]fenol;
4-(2,5-Dimetilfenil)-1,1,1-trifluoro-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(2-metoxi-5-metilfenil)-4-metil-2-quinolin-4-ilmetilpentan-2-ol;
4-(2,5-Dimetoxifenil)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-2-(1*H*-indol-2-ilmetil)-4-metil-4-(2-trifluorometilfenil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(4-metoxi-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-4-metilpentan-2-ol;
2-(2,4-Dimetil-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

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2-(2-Amino-4-cloro-7*H*-pirrolo[2,3-*d*]pirimidin-6-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

2-(5-Cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

4-(5-Bromo-2-metoxifenil)-1,1,1-trifluoro-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Bromo-2-metoxifenil)-1,1,1-trifluoro-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

2-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-[5-(etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluoro-4-metilpentan-2-ol;

2-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-fenilpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5-pirrolidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4'-Metoxi-3'-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]bifenil-2-carbonitrilo;

2-(5-Dietilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-[5-(isopropilmetilamino)-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil]-4-metilpentan-2-ol;

4-(3-Bromofenil)-1,1,1-trifluoro-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(4-fluorofenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-(3-pirimidin-5-ilfenil)pentan-2-ol;

3'-{3-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-c]piridin-2-ilmetil]-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil}-4'-hidroxibifenil-2-carbonitrilo;

4'-Hidroxi-3'-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]bifenil-2-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5-morfolin-4-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-morfolin-4-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)pentan-2-ol;

4-Cloro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-morfolin-4-ilmetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)butil]fenol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-pirrolo[3,2-*c*]piridina-6-carbonitrilo;

2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)pentan-2-ol;

2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-c]piridina-5-carbonitrilo;

1-[2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il]etanona;

Amida del ácido 2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridina-5-carboxílico;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(5-hidroximetil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-metilpentan-2-ol;

2-(5-Aminometil-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5*H*-pirrolo[3,2-c]piridazin-6-

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ilmetil)pentan-2-ol;
4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5*H*-pirrolo[3,2-*c*]piridazin-6-ilmetil)butil]fenol;
4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)butil]fenol;
1,1,1-Trifluoro-4-(4-fluoro-2-metoxifenil)-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
5-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]fenol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5*H*-pirrolo[3,2-*d*]pirimidin-6-ilmetil)pentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(3-fenil-7*H*-pirrolo[2,3-*c*]piridazin-6-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(3-fenil-7*H*-pirrolo[2,3-*c*]piridazin-6-ilmetil)pentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
1-{2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il}propan-1-ona;
1-{2-[4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[3,2-*b*]piridin-5-il}-2-metilpropan-1-ona;
1,1,1-Trifluoro-4-(4-fluoro-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(2-metoxi-5-tiofen-3-ilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(4-metoxibifenil-3-il)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
5-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]fenol;
4-Tiofen-3-il-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]fenol;
3-[4,4,4-Trifluoro-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]bifenil-4-ol;

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1,1,1-Trifluoro-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-(5-pirimidin-5-il-2,3-dihidrobenzofuran-7-il)pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-Piridin-3-il-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]fenol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(5-fenoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-fenil-2-(3-fenil-7*H*-pirrolo[2,3-c]piridazin-6-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(3-fenil-7*H*-pirrolo[2,3-c]piridazin-6-ilmetil)pentan-2-ol;

4-Piridin-3-il-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-fenoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]fenol;

1,1,1-Trifluoro-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-4-(5-pirimidin-5-il-2,3-dihidrobenzofuran-7-il)pentan-2-ol;

4-Piridin-3-il-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)butil]fenol;

5-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)butil]fenol;

1,1,1-Trifluoro-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(5-fenil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-2-[5-(4-fluorofenil)-1*H*-pirrolo[2,3-c]piridin-2-ilmetil]-4-metilpentan-2-ol;

2-(5-Dimetilamino-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

2-(5-Dimetilamino-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluoro-4-(4-fluoro-2-metoxifenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(4-fluoro-2-metoxifenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

2-[3-(5-Dimetilamino-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;

2-[3-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-5-fluorofenol;

5-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]fenol;

4-(5-Bromo-2-metoxifenil)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-Bromo-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]fenol;

1,1,1-Trifluoro-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(3-[1,3]Dioxan-2-ilfenil)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(4-metoxibifenil-3-il)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-tiofen-3-ilfenil)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

3-[4,4,4-Trifluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]bifenil-4-ol;

4-Tiofen-3-il-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]fenol;

4-Tiofen-3-il-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]fenol;

4-Tiofen-3-il-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]fenol;

4'-Metoxi-3'-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]bifenil-2-carbonitrilo;

4'-Metoxi-3'-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)butil]bifenil-3-carbonitrilo;

1,1,1-Trifluoro-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(3-Clorofenil)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-

ilmetil)pentan-2-ol;
4-Piridin-3-il-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]fenol;
1,1,1-Trifluoro-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-metil-4-(3-piridin-3-ilfenil)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-metil-4-(3-pirimidin-5-ilfenil)-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-piridin-2-il-1*H*-indol-2-ilmetil)pentan-2-ol;
2-(5-Bromo-1*H*-indol-2-ilmetil)-4-(5-cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-2-(5-metansulfinil-1*H*-indol-2-ilmetil)-4-metilpentan-2-ol;
3-{2-[4-(5-Fluoro-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}benzonitrilo;
1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-piridin-4-il-1*H*-indol-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-piridin-3-il-1*H*-indol-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-pirimidin-5-il-1*H*-indol-2-ilmetil)pentan-2-ol;
2-[5-(4-Dimetilaminofenil)-1*H*-indol-2-ilmetil]-1,1,1-trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol;
1,1,1-Trifluoro-2-(7-fluoro-4-metil-1*H*-indol-2-ilmetil)-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentan-2-ol;
2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carbonitrilo;
2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-1*H*-indol-6-carbonitrilo;
1,1,1-Trifluoro-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-(4-metil-1*H*-indol-2-ilmetil)pentan-2-ol;
2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-4-

carbonitrilo;
2-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-4-carbonitrilo;
2-(4-Etil-1*H*-indol-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(2-isopropil-5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-2-(2-isopropil-5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)-4-metilpentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)pentan-2-ol;
4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)butil]fenol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(2-fenil-5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(2-fenil-5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(2-fenil-5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)pentan-2-ol;
4-Fluoro-2-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(2-fenil-5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)butil]fenol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(2-cloro-5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-metil-4-fenil-2-(2-fenil-5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(2-fenil-5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(2-metoxi-5-metilfenil)-4-metil-2-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(2-metoxi-5-metilfenil)-4-metil-2-(2-pirrolidin-1-il-5*H*-pirrolo[3,2-d]pirimidin-6-ilmetil)pentan-2-ol;
2-(5-Etoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5-fenil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(4-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Bromo-2-metoxifenil)-2-(5-dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

4-(5-Bromo-2-metoxifenil)-1,1,1-trifluoro-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-trifluorometilfenil)-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metilpentan-2-ol;

1,1,1-Trifluoro-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-(4-metoxibifenil-3-il)-4-metilpentan-2-ol;

1,1,1-Trifluoro-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-(2-metoxi-5-tiofen-3-ilfenil)-4-metilpentan-2-ol;

2-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metil-4-fenilpentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(4-metoxibifenil-3-il)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-(5-Dimetilamino-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metilpentan-2-ol;

4-Bromo-2-[3-(5-cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]fenol;

2-[3-(5-Cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;

2-[2-Hidroxi-4-(4-hidroxibifenil-3-il)-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-*c*]piridin-5-ol;

1,1,1-Trifluoro-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metil-4-(5-fenil-2,3-

dihidrobenzofuran-7-il)pentan-2-ol;
2-[2-Hidroxi-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-*c*]piridin-5-ol;
2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-*c*]piridin-5-il éster del ácido trifluorometansulfónico;
1,1,1-Trifluoro-4-(3-fluorofenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-metil-4-fenil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(3-fluorofenil)-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-2-(5-isopropoxi-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-4-metil-4-fenilpentan-2-ol;
1,1,1-Trifluoro-4-metil-4-(3-morfolin-4-ilmetilfenil)-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(5-metoxi-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(5-metoxi-1*H*-pirrolo[3,2-*b*]piridin-2-ilmetil)-4-metilpentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(5-cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-2-(4-metoxi-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-4-metilpentan-2-ol;
2-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,4-dihidropirrolo[3,2-*b*]piridin-5-ona;
2-(5-Cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(2-metoxi-5-tiofen-3-ilfenil)-4-metilpentan-2-ol;
2-(5-Cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metil-4-(5-metilsulfanil-2,3-dihidrobenzofuran-7-il)pentan-2-ol;
4-(5-Bromo-2-metoxifenil)-2-(5-cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(7*H*-pirrolo[2,3-d]pirimidin-6-ilmetil)pentan-2-ol;
1,1,1-Trifluoro-4-(2-metoxi-5-naftalen-1-ilfenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
4-(2'-Cloro-4-metoxibifenil-3-il)-1,1,1-trifluoro-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-

c]piridin-2-ilmetil)pentan-2-ol;
2-(5-Cloro-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metilpentan-2-ol;
4'-Metoxi-3'-[4,4,4-trifluoro-3-hidroxi-1,1-dimetil-3-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)butil]bifenil-2-carbonitrilo;
4-(2'-Cloro-4-metoxibifenil-3-il)-1,1,1-trifluoro-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;
2-[3-(3-Dimetilaminometil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;
1,1,1-Trifluoro-4-(5-metanosulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;
2-(3-Cloro-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-(5-fluoro-2-metoxifenil)-4-metilpentan-2-ol;
1,1,1-Trifluoro-4-metil-4-(5-metilsulfanil-2,3-dihidrobenzofuran-7-il)-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;
1,1,1-Trifluoro-4-(5-metanosulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol; y
1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol,
o un tautómero, un profármaco, un solvato o sal de los mismos.

Los siguientes compuestos de la invención de Fórmula (IB) fueron ensayados y presentaron actividad como agonistas de la función del receptor de glucocorticoides en uno o más de los ensayos anteriores:
2-Ciclopropil-4-(5-fluoro-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[3,2-*c*]piridin-2-il)pentan-2-ol;
2-Ciclopropil-4-(5-fluoro-2-metilfenil)-4-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-ciclopropil-4-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol;
2-Ciclopropil-4-(5-fluoro-2-metilfenil)-4-metil-1-(1*H*-pirrolo[3,2-*c*]piridin-2-il)pentan-2-ol;
4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-ciclopropil-4-metil-1-(1*H*-pirrolo[3,2-*c*]piridin-2-il)pentan-2-ol;
5-(5-Fluoro-2-metoxifenil)-2,5-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;
5-(5-Fluoro-2-metoxifenil)-2,2,5-trimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;
2-(5-Fluoro-2-metoxifenil)-2,5,5-trimetil-4-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)heptan-4-ol;

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1,1-Difluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

5-(5-Fluoro-2-metilfenil)-2,5-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metilfenil)-2,2,5-trimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

1,1-Difluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

5-(5-Fluoro-2-metoxifenil)-2,5-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metoxifenil)-2,2,5-trimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;

2-(1-Fluorociclopropil)-4-(5-fluoro-2-metoxifenil)-4-metil-1-(1*H*-pirrolo[2,3-*c*]piridin-2-il)pentan-2-ol;

2-[4,4-Difluoro-3-hidroxi-1,1-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)butil]-4-fluorofenol;

5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metilfenil)-2,5-dimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metilfenil)-2,2,5-trimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluoro-4-metil-2-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluoro-4-metil-2-pirrolo[3,2-*b*]piridin-1-ilmetilpentan-2-ol;

5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,2,5-trimetil-3-(1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metilfenil)-2,2,5-trimetil-3-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(3-metil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2,5-dimetil-3-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metilfenil)-2,2,5-trimetil-3-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

5-(5-Fluoro-2-metilfenil)-2,5-dimetil-3-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)hexan-3-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1-difluoro-4-metil-2-(6-metil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)pentan-2-ol; y

2-[2-Difluorometil-2-hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metilpentil]-4-metil-1*H*-indol-6-carbonitrilo.

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o un tautómero, un profármaco, un solvato o sal de los mismos.

Los siguientes compuestos de la invención de Fórmula (IC) fueron ensayados y mostraron actividad como agonistas de la función del receptor de glucocorticoides en uno o más de los ensayos anteriores:

1-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[4-(5-Fluoro-2-hidroxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil1,5,6,7-tetrahidroindol-4-ona;

1-[4-(2,3-Dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[4-(5-Fluoro-2-metilfenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[2-Hidroxi-4-metil-4-(5-pirimidin-5-il-2,3-dihidrobenzofuran-7-il)-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[2-Hidroxi-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[2-Hidroxi-4-(2-hidroxi-5-pirimidin-5-ilfenil)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona;

1-[2-Hidroxi-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona; y

1-[2-Hidroxi-4-(2-hidroxi-5-piridin-3-ilfenil)-4-metil-2-trifluorometilpentil]-1,5,6,7-tetrahidroindol-4-ona,

o un tautómero, un profármaco, un solvato o sal de los mismos.

El siguiente compuesto de la invención de Fórmula (ID) fue ensayado y mostró actividad como agonista de la función del receptor de glucocorticoides en uno o más de los ensayos anteriores:

5,5,5-Trifluoro-2-metil-2-fenil-4-quinolin-4-ilmetilpentan-1,4-diol, o un tautómero, profármaco, solvato o una sal del mismo.

La invención asimismo ofrece métodos para modular la función del receptor de glucocorticoides en un paciente, que comprende administrar a un paciente un compuesto de acuerdo con la invención. Si el propósito de modular la función del receptor de glucocorticoides en un paciente es tratar un estado o cuadro patológico, la administración de preferencia comprende una cantidad terapéutica o farmacéuticamente efectiva de un compuestos aceptable para uso farmacéutico de acuerdo con la invención. Si el propósito de modular la función del receptor de glucocorticoides en un paciente es a los fines del

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diagnóstico u otros (p.ej., para determinar si la terapia es adecuada para el paciente o la sensibilidad a diversas dosis subterapéuticas de los compuestos conforme la invención), la administración de preferencia comprende una cantidad efectiva de un compuesto de acuerdo con la invención, ello es, la cantidad necesaria para obtener el efecto o el grado de modulación deseados.

7. Inhibción de la producción de osteocalcina a partir de la línea celular de osteoblastos MG-63

Se colocan células de osteosarcoma humano MG-63 (ATCC, Cat. Nº CRL-1427) en placas de 96 cavidades a razón de 20.000 células por cavidad, el día previo al uso en 200 µl de medio de D-MEM/F-12 99% (Gibco-Invitrogen, Cat. Nº 11039-021), suplementado con 1% de penicilina y estreptomicina (Gibco-Invitrogen, Cat. Nº 15140-122), 10 µg/ml de vitamina C (Sigma, Cat. Nº A-4544), y 1% de suero bovino fetal filtrado a través de carbón (HyClone, Cat. Nº SH30068,02). Al día siguiente, se reemplaza el medio en las cavidades. Las células se tratan con vitamina D (Sigma, Cat. Nº D1530) hasta una concentración final de 10 nM, y con los compuestos de ensayo en concentraciones de 10^{-6} M a 10^{-9} M, en un volumen total de 200 µl por cavidad. Las muestras se realizan por duplicado. Las cavidades de control de fondo no reciben vitamina D o compuestos. Las cavidades de control positivo sólo reciben vitamina D, sin compuestos, y representan la cantidad máxima (100%) de producción de osteocalcina. Las placas se incuban a 37ºC durante 48 horas y se cosechan los sobrenadantes al final de la incubación. Se determina la cantidad de osteocalcina en los sobrenadantes mediante el kit Glype osteocalcin ELISA (Zymed, Cat. Nº 99-0054) de acuerdo al protocolo del fabricante. La inhibición de la osteocalcina por los compuestos de ensayo se expresa en porcentaje en relación a los controles positivos. Los valores de IC_{50} de los compuestos de ensayo se derivan por ajuste a una curva no lineal.

Los siguientes compuestos de Fórmula (IA) inhiben la producción de osteocalcina estimulada por vitamina D:

2-[4-(5-Fluoro-2-metoxifenil)-2-hidroxi-4-metil-2-trifluorometilpentil]-4-metil-1*H*-pirrolo[3,2-*c*]piridina-6-carbonitrilo;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(1*H*-pirrolo[2,3-d]piridazin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-(4,6-dimetil-1*H*-pirrolo[3,2-*c*]piridin-2-ilmetil)-1,1,1-trifluoro-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-2-(5-metoxi-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-metilpentan-2-ol;

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1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

2-[2-Hidroxi-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-trifluorometilpentil]-4-metil-1*H*-indol-6-carbonitrilo;

Amida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

Ciclometilamida del ácido 2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-carboxílico;

{2-[4-(5-Bromo-2,3-dihidrobenzofuran-7-il)-2-hidroxi-4-metil-2-trifluorometilpentil]-1*H*-indol-5-il}pirrolidin-1-ilmetanona;

1,1,1-Trifluoro-4,4-dimetil-5-fenil-2-quinolin-4-ilmetilpentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-metansulfonil-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

2-[5-(Etilmetilamino)-1*H*-pirrolo[2,3-c]piridin-2-ilmetil]-1,1,1-trifluoro-4-(5-fluoro-2-metilfenil)-4-metilpentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-2-[5-(etilmetilamino)-1*H*-pirrolo[2,3-c]piridin-2-ilmetil]-1,1,1-trifluoro-4-metilpentan-2-ol;

4-(3-Bromofenil)-1,1,1-trifluoro-4-metil-2-(5-morfolin-4-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(4-metil-1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-metil-2-(3-metil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4-(5-pirimidin-5-il-2,3-dihidrobenzofuran-7-il)pentan-2-ol;

2-[3-(5-Dimetilamino-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)-4,4,4-trifluoro-3-hidroxi-1,1-dimetilbutil]-4-fluorofenol;

4-(3-Clorofenil)-1,1,1-trifluoro-4-metil-2-(1*H*-pirrolo[3,2-c]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2,3-dihidrobenzofuran-7-il)-4-metil-2-(5-piridin-3-il-1*H*-indol-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(5-fluoro-2-metoxifenil)-4-metil-2-(5-fenil-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

1,1,1-Trifluoro-4-(2-metoxi-5-pirimidin-5-ilfenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-c]piridin-2-ilmetil)pentan-2-ol;

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1,1,1-Trifluoro-4-(2-metoxi-5-piridin-3-ilfenil)-4-metil-2-(5-piperidin-1-il-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol;

2-[2-Hidroxi-4-(4-hidroxibifenil-3-il)-4-metil-2-trifluorometilpentil]-1*H*-pirrolo[2,3-*c*]piridin-5-ol;

4-(5-Cloro-2,3-dihidrobenzofuran-7-il)-1,1,1-trifluoro-4-metil-2-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol; y

1,1,1-Trifluoro-4-(5-fluoro-2-metilfenil)-4-metil-2-(5-fenil-1*H*-pirrolo[2,3-*c*]piridin-2-ilmetil)pentan-2-ol,

o un tautómero, un profármaco, un solvato o sal de los mismos.

Métodos de uso terapéutico

Como se señaló más arriba, los compuestos de la invención son útiles para modular la función del receptor de glucocorticoides. Debido a ello, estos compuestos presentan utilidad terapéutica para tratar estados y cuadros patológicos mediados por la función del receptor de glucocorticoides o que se beneficiarían de la modulación de la función del receptor de glucocorticoides.

Dado que los compuestos de la invención modulan la función del receptor de glucocorticoides, presentan una muy útil actividad anti-inflamatoria y antialérgica, de inmunosupresión y anti-proliferativa y pueden usarse en pacientes como fármacos, particularmente en forma de composiciones farmacéuticas como se indica a continuación, para el tratamiento de estos estados y cuadros patológicos.

Los compuestos agonistas de acuerdo con la invención pueden usarse en pacientes como medicamentos para el tratamiento de los siguientes estados patológicos o indicaciones que son acompañadas por procesos inflamatorios, alérgicos y/o proliferativos:

(i) Enfermedades pulmonares: crónicas, enfermedades pulmonatres obstructivas de cualquier génesis, particularmente asma bronquial, enfermedad pulmonar obstructiva crónica (COPD); síndrome de distrés respiratorio de adultos (ARDS); bronquiestasis; bronquitis de diferentes génesis; todas las formas de enfermedades pulmonares restrictivas, particularmente alveolitis alérgica; todas las formas de edema pulmonar, particularmente edema pulmonar tóxico; todas las formas de infermedades pulmonares intersticiales de cualquier génesis, p.ej., pneumonitis por radiación; y sarcoidosis y granulomatosis, particularmente enfermedad de Boeck.

(ii) Enfermedades reumáticas o autoinmunes o enfermedades adjuntas: todas las formas de enfermedades reumáticas, especialmente artritis reumatoidea, fiebre

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reumática grave y polimialgia reumática; artritis reactiva; enfermedades reumáticas de tejido blando; enfermedades inflamatorias de tejido blando de otras génesis; síntomas de artritis en enfermedades adjuntas degenerativas (artrosis); artritis traumática; colagenosis de cualquier génesis, p.ej. lupus eritematoso sistémico, esclerodermia, polimiositis, dermatomiositis, síndrome de Sjögren, enfermedad de Still y síndrome de Felty;

(iii) Enfermedades alérgicas: todas las formas de reacciones alérgicas, p.ej., edema angioneurótico, fiebre deheno, picaduras de insectos, reacciones alérgicas a medicamentos, derivados de sangre, agentes de contraste, etc., shock anafiláctico (anafilaxis), urticaria, edema angioneurótico y dermatitis por contacto;

(iv) Enfermedades vasculares: panartritis nodosa, pollartritis nodosa, artritis temporalis, granulomatosis de Wegner, artritis de células gigantes y eritema nodoso;

(v) Enfermedades dermatológicas: dermatitis atópica, particularmente en niños; psoriasis; pitiriasis rubra pilaris; enfermedades eritematosas disparadas por diferentes agentes nocivos, p.ej. rayos, productos químicos, quemaduras, etc.; dermatosis bullosa; enfermedades del complejo liquenoide; prurito (p.ej. de génesis alérgica); dermatitis seborreica; rosácea; pénfigo común; eritema multiforme exudativo; balanitis; vulvitis; pérdida de pelo, tal como occurre en alopecía areata; y linfomas de células T cutáneas;

(vi) Enfermedades renales: síndrome nefrótico; y todos los tipos de nefritis, p.ej. glomerulonefritis;

(vii) Enfermedades hepáticas: desintegración grave de células hepáticas; hepatitis grave de diferentes génesis, p.ej., viral, tóxica, inducida por medicamentos; y hepatitis crónicamente agresiva y/o crónicamente intermitente;

(viii) Enfermedades gastrointestinales: enfermedades intestinales inflamtorias, p.ej., enteritis regional (enfermedad de Crohn), colitis ulcerosa; gastritis; esofagitis péptica (esofagitis de reflujo); y gastroenteritis de otras génesis, p.ej., esprue no trópico;

(ix) Enfermedades proctológicas: eczema anal; fisuras; hemorroides; y proctitis idiopática;

(x) Enfermedades de los ojos: keratitis alérgica, uveitis, o iritis; conjuntivitis; blefaritis; neuritis del nervio óptico; coroiditis; y oftalmia simpatética;

(xi) Enfermedades del área de nariz, garanganta y oídos (ENT): rinitis alérgica o fiebre de heno; otitis externa, p.ej., causada por eczema de contacto, infección, etc.; y otitis media;

(xii) Enfermedades neurológicas: edema cerebral, particularmente edema cerebral relacionada con tumores; multiple esclerosis; encefalomielitis grave; meningitis; lesión del cordón agudoespinal; apoplejía; y diferentes formas de convulsiones, p.ej. espasmos nodding;

(xiii) Enfermedades de la sangre: anemia hemolítica adquirida; y trombocitopenia idiopática;

(xiv) Enfermedades tumorales: leucemia linfática aguda; linfoma maligno; linfogranulomatosis; linfosarcoma; metastasis extensiva, particularmente en carcinomas mamario, bronquial y prostático;

(xv) Enfermeades endócrinas: oftalmopatía endócrina; orbitopatía endócrina; crisis tirotóxica; tiroiditis de Quervain; tiroiditis de Hashimoto; Morbus Basedow; tiroiditis granulomatosa; struma linfomatosa; y enfermedad de Grave;

(xvi) Enfermedades de trasplantes de órganos y tejidos e injerto-versus-huésped;

(xvii) Estados graves de shock, p.ej., shock séptico, shock anafiláctico, y síndrome de respuesta inflamatoria sistémica (SIRS);

(xviii) Terapia de sustitución en: insuficiencia adrenal primaria congénita, p.ej., síndrome adrenogenital; insuficiencia adrenal primaria adquirida, p.ej. enfermedad de Addison, adrenalitis autoinmune, post-infección, tumores, metástasis, etc.; insuficiencia adrenal secundaria congénita, p.ej. hipopituitarismo congénito; e insuficiencia adrenal secundaria adquirida, p.ej. post-infección, tumores, metastasis, etc.;

(xix) Dolores de génesis inflamatoria, p.ej. lumbago; y

(xx) Otros estados o cuadros patológicos diferentes que incluyen diabetes tipo I (diabetes insulino-dependiente), osteoartritis, síndrome de Guillain-Barre, restenosis como consecuencia de angioplastia coronaria transluminal percutánea, enfermedad de Alzheimer, dolor grave y crónico, aterosclerosis, lesión por reperfusión, enfermedades de resorción ósea, falla cardíaca congestiva, infarto del miocardio, lesión térmal, lesión orgánica múltiple secundaria a trauma, meningitis purulenta grave, enterocolitis necrotizante y síndromes asociados con hemodiálisis, leucoferesis, y transfusión de granulocitos.

Además, los compuestos de acuerdo con la invención pueden usarse para el tratamiento de otros estados o cuadros de enfermedad no mencionados previamente que

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no fueron tratados, no son tratados o serán tratados con glucocorticoides sintéticos (véase, p.ej., H.J. Hatz, Glucocorticoide: Immunologische Grundlagen, Pharmakologie und Therapierichtlinien [Glucocorticoids: Immunological Fundamentals, Pharmacology, and Therapeutic Guidelines], Stuttgart: Verlagsgesellschaft mbH, 1998, que se incorpora aquí en su totalidad a título de referencia). La mayoría o todas las indicaciones (i) a (xx) previamente mencionadas se describen en detalle en H.J. Hatz, Glucocorticoide: Immunologische Grundlagen, Pharmakologie und Therapierichtlinien. Además los compuestos de la invención también puede usarse para tratar trastornos diferentes a los antes eunciados o los mencionados o discutidos, incluidos en el alcance de la invención.

Los compuestos antagonistas según la invención, ya sea antagonistas totales o parciales, puede usarse en pacientes como medicmaentos para el tratamiento de los estados o enfermedades, sin constituir limitación: diabetes tipo II (diabetes no insulinodecendiente); obesidad; enfermedades cardiovasculares; hipertensión; arterioscleroeis; enfermedades neurológicas, tal como psicosis y depresión; tumores adrenales y pituitarios; glaucoma; y sóindrome de Cushing basado en tumor con secreción de ACTH como adenoma pituitario. En particular, los compuestos de la invención son útiles para el tratamiento de la obesidad y todos los estados de enfermedad e indicaciones relacionada con un metabolisma de ácidos grasos desregulados, tal como hipertensión, ateroscleroeis, y otras enfermedades cardiovasculares. Usando los compuestos de la invención que son antagonistas de GR, puede ser posible antagonizar al metabolismo de carbohidratos y al metabolismo de los ácidos grasos. Así, los compuestos antagonistas de la invención son útiles para tratar todos los estados y los cuadros patológicos que incluyen un metabolismo aumentado de carbohidratos, proteínas y lípidos y pueden incluir estados y enfermedades que generan un catabolismo, como fragilidad muscular (como ejemplo del metabolismo de proteínas).

Métodos de uso diagnóstico

Los compuestos de la invención pueden usarse asimismo en aplicaciones de diagnóstico y a los fines comerciales y otros como estándares en ensayos de unión competitiva. En tales usos, los compuestos de la invención pueden usarse en forma de los compuestos mismos o pueden modificarse adjuntando un marcador radioisótopo, de luminiscencia, fluorescente o similar, a los efectos de obtener una sonda radioisotópica, luminiscente o fluorescente, como es de conocimiento por un especialista en la técnica y como se delinea en Handbook of Fluorescent Probes and Research Chemicals, 6ta. Edición, R.P. Haugland (ed.), Eugene: Molecular Probes, 1996; Fluorescence and Luminescence Probes for Biological Activity, W.T. Mason (ed.), San Diego: Academic

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Press, 1993; Receptor-Ligand Interaction, A Practical Approach, E.C. Hulme (ed.), Oxford: IRL Press, 1992, cada uno de los cuales se incorporan a la presente a título de referencia en su totalidad.

Administración general y composiciones farmacéuticas

Cuando son usados como productos farmacéuticos, los compuestos de la invención se administran usualmente en forma de una composición farmacéutica. Tales composiciones puede prepararse utilizando procedimientos bien conocidos en la técnica farmacéutico y comprenden al menos un compuesto de la invención. Los compuestos de la invención también puede ser administrados solos o en combinación con adyuvantes que aumentan la estabilidad de los compuestos de la invención, facilitan la administración de composiciones farmacéuticas que los contienen en determinadas formas de realización, brindan una mayor disolución o dispersión, aumentada actividad inhibitoria, proveen un tratamiento adjunto, y similares. Los compuestos de acuerdo con la invención pueden usarse solos o conjuntamente con otras sustancias activas según la invención, por lo tanto en forma opcional junto con otras sustancias farmacológicamente activas. En general, los compuestos de esta invención son administrados en una cantidad terapéuticamente o farmacéuticamente efectiva, pero pueden administrarse en cantidas menores a los fines de diagnóstico u otros.

En particular, los compuestos de la invención son útiles en combinación con glucocorticoides o corticosteroides. Como antes indicado, el tratamiento estándar para una cantidad de trastornos inmunes e inflamatorios, incluyen la administración de corticosteroides, que presentan la propiedad de reprimir respuestos inmunológicas e inflamatorias (A.P. Truhan *et al.*, Annals of Allergy, 1989, 62, pp. 375-391; J.D. Baxter, Hospital Practice, 1992, 27, pp. 111-134; R.P. Kimberly, Curr. Opin. Rheumatol., 1992, 4, pp. 325-331; M.H. Weisman, Curr. Opin. Rheumatol., 1995, 7, pp. 183-190; W. Sterry, Arch. Dermatol. Res., 1992, 284 (Suppl.), pp. S27-S29). Mientras sea de beneficio terapéutico, de todos modos el uso de corticosteroides está asociado a una cantidad de efectos colaterales, desde un leve o posible peligro de vida, especialmente en caso de usar un esteroide en dosis altas y/o por tiempo prolongado. De modo concordante, soerían altamente deseables los métodos y las composiciones que permitieran el uso de una dosis efectiva inferior de corticosteroides (denominado "steroid sparing effect") para evitar tales efectos colaterales no deseados. Los compuestos de la invención aportan tal efecto "steroid sparing" por lograr el deseado efecto terapéutico mientras permitan el uso de dosis más bajas y una administración menos frecuente de glucocorticoides o corticosteroides.

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La administración de los compuestos de la invención, en forma pura o en una composición farmacéutica adecuada, puede ser llevada a cabo usando cualquier de las formas de administración adecuadas de composiciones farmacéuticas. Así, la administración puede ser, por ejemplo, por vía oral, bucal (p.ej., sublingual), nasal, parenteral, topical, transdermal, vaginal, o rectal, en en forma de polvo sólido, semi-sólido, polvo liofilizado, o formas de presentación líquidas, tales como, por ejemplo, comprimidos, supositorios, píldoras, cápsulas de gelatina dura y blandas elásticas, en polvos, soluciones, suspensiones o aerosoles, o similares, preferentemente en formas de dosificación unitaria adecuadas para la administración simple de dosis precisas. Las composiciones farmacéuticas generalmente incluyen un vehículo o excipiente convencional y un compuesto de la invención como el/un agente activo, y adicionalmente pueden incluir otros agentes médicos, farmacéuticos, vehículos, adyuvantes, diluyentes, vehículos o combinaciones de los mismos. Tales excipientes, vehículos o aditivos, así como los métodos para preparar composiciones farmacéuticas para diversos modos o administración son bien conocidos por los especialistas en la técnica. El estado de la técnica se evidencia, p.ej., por Remington: The Science and Practice of Pharmacy, 20ma. Edición, A. Gennaro (ed.), Lippincott Williams & Wilkins, 2000; Handbook of Pharmaceutical Additives, Michael & Irene Ash (eds.), Gower, 1995; Handbook of Pharmaceutical Excipients, A.H. Kibbe (ed.), American Pharmaceutical Ass'n, 2000; H.C. Ansel y N.G. Popovish, Pharmaceutical Dosage Forms and Drug Delivery Systems, 5ta. ed., Lea y Febiger, 1990; cada uno de los cuales se incorpora a la presente en su totalidad como referencia para una mejor descripción del estado de la técnica.

Como debe esperar un especialista en la técnica, las formas de los compuestos de la invención utilizadas en una particular formulación farmacéutica serán seleccionadas (p.ej., sales) de modo que dispongan de propiedades físicas adecuadas (p.ej., solubilidad en agua) que se requiere para que la formulación sea eficaz.

Las composiciones farmacéuticas adecuadas para administración bucal (sub-lingual) incluyen pastillas que comprenden un compuesto de la presente invención en una base aromatizada, usualmente sacarosa y acacia o tragacanto, y comprimidos que comprenden el compuesto en una base inerte, tal como gelatina y glicerina o sacarosa y acacia.

Las composiciones farmacéuticas adecuadas para administración parenteral comprenden preparaciones estériles acuosas de un compuesto de la presente invención. Estas preparaciones son preferentemente administradas en forma endovenosa, aunque la administración también puede realizarse mediante una inyección subcutánea,

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intramuscular o intradérmica. Las formulaciones farmacéuticas inyectables en general se basan en solución salina estéril inyectable, solución salina bufferizada con fosfato, suspensiones oleaginosas u otros vehículos inyectables conocidos en la técnica y generalmente se producen en forma estéril e isotónica con la sangre. Las formulaciones farmacéuticas inyectables pueden así ser proporcionadas como una solución o suspensión estéril inyectable en un diluyente o solvente no tóxico parenteralmente adecuado, incluyendo 1,3-butanodiol, agua, solución de Ringer, solución isotónica de cloruro de sodio, aceites fijos, tales como mono- o diglicéridos fijos, ácidos grasos, tales como ácido oleico, y similares. Tales formulaciones farmacéuticas inyectables son formuladas según se conoce en la técnica, usando agentes adecuados de dispersión o fijación y agentes de suspensión. Las composiciones inyectables generalmente contendrán de 0,1 a 5% p/p de un compuesto de la invención.

Las formas de presentación sólidas para administración oral de los compuestos incluyen cápsulas, comprimidos, píldoras, polvos y gránulos. Para tal administración oral, se forma una composición farmacéutica adecuada que contiene un/unos compuesto(s) de la invención por la incorporación de cualquiera de los excipientes usualmente empleados, tales como, por ejemplo, grados farmacéuticos de manitol, lactosa, almidón, almidón pregelatinizado, estearato de magnesio, sacarina sódica, talco, derivados de éteres de celulosa, glucosa, gelatina, sacarosa, citrato, propilgalato, y similares. Tales formulaciones farmacéuticas sólidas puede incluir formulaciones, como son conocidas en la técnica, para dar una entrega prolongada o sostenida del medicamento al tracto gastrointestinal a través de cualquier número de mecanismos, que incluyen, pero sin limitación, entrega sensible al pH de la forma de presentación basada en el pH cambiante del intestino delgado, la lenta erosión de un comprimido o cápsula, la retención en el estómago basado en las propiedades físicas de la formulación, la bioadhesión de la forma de dosificación o la mucosa del tracto intestinal, o la entrega enzimática del principio activo de la forma de dosificación.

Las formas de presentación líquidas para administración oral de los compuestos incluyen emulsiones, microemulsiones, soluciones, suspensiones, jarabes y elixires, opcionalmente contien adyuvantes farmacéuticos en un vehículo, tales como, por ejemplo, agua, solución salina, dextrosa acuosa, glicerol, etanol y similares. Estas composiciones también pueden contener adyuvantes tales como agentes humectantes, emulsionantes, de suspensión, edulcorantes, saborizantes y perfumes.

Las formas de presentación tópicas de los compuestos incluyen ungüentos, pastas, cremas, lociones, geles, polvos, soluciones, rociadores, inhalantes ungüentos

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para ojos, gotas para los ojos u oídos, vendajes impregnados y aerosoles, y pueden contener aditivos convencionales, tales como conservantes, solventes que ayuden a la penetración del medicamento y emolientes en ungüentos y cremas. La aplicación tópica puede realizarse una vez al día o más de una vez, dependiendo de las consideraciones médicas usuales. Además, los compuestos preferidos de la presente invención pueden administrarse en forma intranasal a través del uso tópico de vehículos intranasales adecuados. Las formulaciones también pueden contener vehículos convencionales compatibles tal como bases para cremas o ungüentos y etanol u oleil alcohol para lociones. Tales vehículos pueden presentarse constituyendo de alrededor de 1% hasta alrededor de 98% de la formulación, con mayor frecuencia constituirán desde alrededor del 80% de la formulación.

También es posible la administración transdérmica. Las composiciones farmacéuticas adecuadas para administración transdérmica pueden presentarse como parches discretos adpatados para mantenerse en contacto íntimo con la epidermis del receptor por un período prolongado de. Para ser administrada en forma de un sistema de entrega transdérmica, la dosis de administración será, por supuesto, continua en lugar de intermitente a lo largo del regimen de dosificación. Tales parches adecuadamente contienen un compuesto de la invención en una solución acuosa, opcionalmente bufferizada, disuelta y/o dispersa en un adhesivo, o dispersa en un polímero. Una adecuada concentración del compuesto activo es alrededor de 1% a 35%, preferentemente alrededor de 3% a 15%.

Para la administración por inhalación, los compuestos de la invención son convenientemente entregados en forma de un rociado en aerosol desde un dispositivo de bomba rociadora que no requiere gas propelente o desde un envase presurizado o un nebulizador con el uso del propelente adecuado, p.ej. diclorodifluorometano, triclorofluorometano, diclorotetrafluoroetano, tetrafluoroetano, heptafluoropropano, dióxido de carbono u otro gas adecuado. En cualquier caso, la unidad de dosis del rociador en aerosol puede determinarse mediante la provisión de una válvula o para entregar una cantidad determinada, de modo tal que la dosis determinada resultante para inhalar (MDI) se usa para administrar los compuestos de la invención de un modo reproducible y controlado. Tales dispositivos para inhalar, nebulizar o atomizar son conocidos en la técnica previa, por ejemplo en la Publicación Internacional PCT N° WO 97/12687 (particularmente la Figura 6 de la misma, que es la base para el nebulizador comercial RESPIMAT®); WO 94/07607; WO 97/12683; y WO 97/20590, a las que se hace referencia aquí y donde cada uno se incorpora en su totalidad a título de referencia.

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La administración rectal puede realizarse usando supositorios de dosis única, en los que el compuesto es mezclado con sólidos no solubles o solubles en agua de bajo punto de fusión, tal como grasas, manteca de cacao, gelatina glicerinada, aceites vegetales hidrogenados, mezclas de polietilenglicoles de diversos pesos moleculares, o ésteres de ácidos grasos de polietilenglicoles o similares. El compuesto activo es usualmente un componente menor, con frecuencia de alrededor de 0,05 a 10% en peso, siendo que el resto constituye el componente básico.

En todas las composiciones farmacéuticas anteriores, los compuestos de la invención son formulados con un vehículo o un excipiente adecuados. Los vehículos o excipientes utilizados deben ser, por supuestos adecuados en el sentido de ser compatibles con los demás ingredientes de la composición y no deben ser nocivos para el paciente. El vehículo o excipiente puede ser un sólido o un líquido, o ambos, y es preferentemente formulado con el compuesto de la invención como una composición de dosis única, por ejemplo, un comprimido, que puede contener desde 0,05% a 95% en peso del principio activo. Tales vehículos o excipientes incluyen diluyentes o rellenos, aglutinantes, lubricantes, agentes desintegrantes, retardadores de disolución, aceleradores de resorción, agentes de absorción y agentes colorantes. Los aglutinantes aceptables incluyen almidón, gelatina, azúcares naturales, tales como glucosa o β-lactosa, edulcorantes de maíz, gomas naturales y sintéticas, tales como acacia, tragacanto o alginato de sodio, carboximetilcelulosa, polietilenglicol, ceras, y similares. Los lubricantes incluyen oleato de sodio, estearato de sodio, estearato de magnesio, benzoato de sodio, acetato de sodio, cloruro de sodio, y similares. Los desintegradores incluyen almidón, metilcelulosa, agar, bentonita, goma xántica y similares.

Generalmente, una dosis diaria terapéuticamente efectiva es de alrededor de 0,001 mg a alrededor de 15 mg/kg de peso corporal por día de un compuesto de la invención; preferentemente, desde alrededor de 0,1 mg a alrededor de 10 mg/kg de peso corporal por día ; y de mayor preferencia, desde alrededor de 0,1 mg a alrededor de 1,5 mg/kg de peso corporal por día . Por ejemplo, para la administración a una persona de 70 kg, la dosis será desde alrededor de 0,07 mg a alrededor de 1050 mg por día de un compuesto de la invención, preferentemente desde alrededor de 7,0 mg a alrededor de 700 mg por día, y de mayor preferencia de alrededor de 7,0 mg a alrededor de 105 mg por día. Podría requerirse algún grado de rutina para optimizar la dosis a los efectos de determinar un nivel óptimo de dosis y de modelo.

Los vehículos y excipientes aceptables para uso farmacéutico incluyen todos los aditivos y similares anteriores.

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Ejemplos de Formulaciones Farmacéuticas

A. COMPRIMIDOS	
Componente	Cantidad por comprimido (mg)
sustancia activa	100
lactosa	140
almidón de maíz	240
polivinilpirrolidona	15
estearato de magnesio	5
TOTAL	500

La sustancia activa finamente molida, lactosa, y una cantidad de almidón de maíz se mezclan. La mezcla se tamiza, luego se humedece con una solución de polivinilpirrolidona en agua, se amasa, se granula en húmedo y se seca. Los gránulos, el almidón de maíz restante y el estearato de magnesio se tamizan y se mezclan entre sí. La mezcla se comprime para preparar comprimidos de adecuada forma y tamaño.

B. COMPRIMIDOS	
Componente	Cantidad por comprimido (mg)
sustancia activa	80
lactosa	55
almidón de maíz	190
polivinilpirrolidona	15
estearato de magnesio	2
celulosa microcristalina	35
carboximetil almidón sódico	23
TOTAL	400

La sustancia activa finamente molida, el almidón de maíz, lactosa, celulosa microcristalina y la polivinilpirrolidona se mezclan, la mezcla es tamizada y procesada con el almidón de maíz remanente y agua, para formar un granulado que se seca y tamiza. Se agrega el carboximetil almidón sódico y el estearato de magnesio, se mezcla y dicha mezcla se comprime para preparar comprimidos de adecuada forma y tamaño.

C. COMPRIMIDOS RECUBIERTOS	
Componente	Cantidad por comprimido (mg)
sustancia activa	5
lactosa	30
almidón de maíz	41,5
polivinilpirrolidona	3
estearato de magnesio	0,5
TOTAL	90

La sustancia activa,almidón de maíz, lactosa, y polivinilpirrolidona se mezclan cuidadosamente y se humedecen con agua. La masa húmeda es empujada a través de un tamiz con un tamaño de malla de 1 mm, se seca a alrededor de 45°C y los gránulos son luego pasados a través del mismo tamiz. Luego de haber mezclado el estearato de magnesio, se fabrican núcleos de comprimidos convexos con un diámetro de 6 mm en una máquina para producir comprimidos. Los núcleos de comprimidos así producidos se recubren de un modo conocido con una cubierta que esencialmente consiste en azúcar y talco. Los comprimidos recubiertos terminados se pulen con cera.

D. CÁPSULAS	
Componente	Cantidad por cápsula (mg)
sustancia activa	50
almidón de maíz	268,5
estearato de magnesio	1,5
TOTAL	320

La sustancia y el almidón de maíz se mezclan y humedecen con agua. La masa húmeda es tamizada y secada. Los gránulos secos se tamizan y mezclan con estearato de magnesio. La mezcla terminada se envasa en cápsulas de gelatina dura tamaño 1.

E. SOLUCIÓN EN AMPOLLA	
Componente	Cantidad por ampolla
sustancia activa	50 mg
cloruro de sodio	50 mg
agua para iny.	5 ml

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La sustancia activa se disuelve en agua a su propio pH u opcionalmente a un valor de pH de 5,5 a 6,5 y se agrega cloruro de sodio para tornarla isotónica. La solución obtenida se filtra libre de pirógenos y el filtrado se transfiere en condiciones asépticas a ampollas que son luego esterilizadas y selladas por fusión. Las ampollas contienen 5 mg, 25 mg, y 50 mg de sustancia activa.

F. SUPOSITORIOS	
Componente	Cantidad por supositorio (mg)
Sustancia activa	50
grasa sólida	1650
TOTAL	1700

La grasa sólida se funde. A 40°C, la sustancia activa molida se dispersa homogénamente en ella. La mezcla se enfría a 38°C y se vierte en moldes de supositorios levemente enfriados.

G. AEROSOL DOSIFICADOR	
Componente	Cantidad
sustancia activa	0,005
trioleato de sorbitano	0,1
monofluorotriclorometano y difluorodiclorometano (2:3)	hasta 100

La suspensión se transfiere a un contenedor convencional para aerosol con una válvula dosificadora. Preferentemente se dispensan 50 µl de suspensión por rociado. La sustancia activa también puede dosificarse en dosis mayores si se desea (p.ej., 0,02% en peso).

H. POLVO PARA INHALACIÓN	
Componente	Cantidad
sustancia activa	1,0 mg
monohidrato de lactosa	hasta 25 mg

I. POLVO PARA INHALACIÓN	
Componente	Cantidad
sustancia activa	2,0 mg
monohidrato de lactosa	hasta 25 mg

J. POLVO PARA INHALACIÓN	
Componente	Cantidad
sustancia activa	1,0 mg
monohidrato de lactosa	hasta 5 mg

K. POLVO PARA INHALACIÓN	
Componente	Cantidad
sustancia activa	2,0 mg
monohidrato de lactosa	hasta 5 mg

En los ejemplos H, I, J y K, el povo para inhalación se produce del modo habitual mezclando los ingredientes individuales entre sí.

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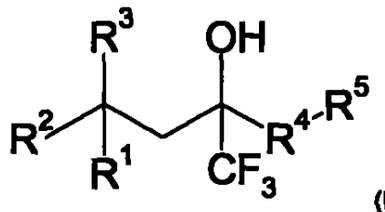
REIVINDICACIONES

1. Un compuesto de Fórmula (IA)



(IA)

en el cual:

R^1 es un grupo arilo o heteroarilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_5, alquenilo C_2-C_5, alquinilo C_2-C_5, cicloalquilo C_3-C_8, heterociclilo, arilo, heteroarilo, alcoxi C_1-C_5, alqueniloxi C_2-C_5, alquiniloxi C_2-C_5, ariloxi, acilo, alcoxicarbonilo C_1-C_5, alcanoiloxi C_1-C_5, alcanoilo C_1-C_5, aroilo, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilaminocarboniloxi C_1-C_5, dialquilaminocarboniloxi C_1-C_5, alcanoilamino C_1-C_5, alcoxicarbonilamino C_1-C_5, alquilsulfonilamino C_1-C_5, aminosulfonilo, alquilaminosulfonilo C_1-C_5, dialquilaminosulfonilo C_1-C_5, halógeno, hidroxi, carboxi, ciano, trifluorometilo, trifluorometoxi, nitro, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_5 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_5; o alquiltio C_1-C_5 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^1 está independientemente sustituido en forma opcional con uno a tres grupos sustituyentes seleccionados de metilo, metoxi, halógeno, hidroxi, oxo, ciano, heteroarilo, heterociclilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_5 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_5;

R^2 y R^3 son cada uno independientemente hidrógeno o alquilo C_1-C_5, o R^2 y R^3 junto con el átomo de carbono al que están unidos usualmente forman un anillo espiro cicloalquilo C_3-C_8;

R^4 es alquilo C_1-C_5, alquenilo C_2-C_5, o alquinilo C_2-C_5, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

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donde cada grupo sustituyente de R^4 es independientemente alquilo C_1-C_3, hidroxi, halógeno, amino u oxo; y

R^5 es un grupo heteroarilo independientemente sustituido en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, cicloalquilo C_3-C_8, heterociclilo, arilo, heteroarilo, alcoxi C_1-C_8, alqueniloxi C_2-C_8, alquiniloxi C_2-C_8, ariloxi, acilo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_8, heterociclilcarbonilo, aroilo, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilamino-carboniloxi C_1-C_8, dialquilaminocarboniloxi C_1-C_8, alcanoilamino C_1-C_8, alcoxicarbonilamino C_1-C_8, alquilsulfonilamino C_1-C_8, aminosulfonilo, alquilaminosulfonilo C_1-C_8, dialquilaminosulfonilo C_1-C_8, halógeno, hidroxi, carboxi, ciano, trifluorometilo, trifluorometoxi, trifluorometiltio, nitro o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_8; o alquiltio C_1-C_8 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^5 está independientemente sustituido en forma opcional con uno a tres grupos sustituyentes seleccionados de alquilo C_1-C_3, alcoxi C_1-C_3, acilo, silaniloxi C_1-C_3, alcoxicarbonilo C_1-C_3, carboxi, halógeno, hidroxi, oxo, ciano, arilo, heteroarilo, heterociclilo o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_8, o trifluorometilo,

o un tautómero, un profármaco, un solvato o sal del mismo.

2. El compuesto de Fórmula (IA) de acuerdo con la reivindicación 1, en el cual:

R^1 es tienilo, fenilo, naftilo, dihidrobenzofuranilo, benzofuranilo, cromanilo, dihidroindolilo, indolilo, dihidrobenzotienilo, benzotienilo, benzodioxolanilo, dihidrobenzoxazolilo, benzoxazolilo, benzoisoxazolilo, benzopirazolilo, benzoimidazolilo, tienilo, quinolinilo, piridinilo, pirimidinilo o pirazinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, heterociclilo, trifluorometilo, trifluorometoxi, nitro, amino donde el átomo de nitrógeno en forma opcional

está independientemente mono- o di-sustituido con alquilo C_1-C_5 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_5, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^1 está sustituido independientemente en forma opcional con un grupo sustituyente seleccionado de metilo, metoxi, halógeno, hidroxi, oxo, ciano o amino;

R^2 y R^3 son cada uno independientemente hidrógeno o alquilo C_1-C_3, o R^2 y R^3 junto con el átomo de carbono al que están unidos usualmente forman un anillo espiro cicloalquilo C_3-C_6;

R^4 es CH_2; y

R^5 es un grupo imidazolilo, piridilo, indolilo, indazolilo, azaindolilo, diazaindolilo, benzofuranilo, furanopiridinilo, furanopirimidinilo, imidazolopirimidinilo, imidazolopiridazinilo, imidazolopirazinilo, benzotienilo, tienopiridinilo, tienopirimidinilo, tienopiridazinilo, benzoxazolilo, oxazolopiridinilo, benzotiazolilo, tiazolopiridinilo, benzoimidazolilo, imidazolopiridinilo, quinolinilo o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes;

donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, fenilo, alcoxi C_1-C_3, metoxicarbonilo, aminocarbonilo, alquilaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, heterociclilcarbonilo, hidroxi, oxo, fluoro, cloro, bromo, ciano, trifluorometilo, amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_5 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_5, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^5 está sustituido independientemente en forma opcional con un grupo sustituyente seleccionado de metilo, metoxi, fluoro, cloro, bromo, oxo, o trifluorometilo, hidroxi, ciano, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_5 o arilo,

o un tautómero, un profármaco, un solvato o sal del mismo.

3. El compuesto de Fórmula (IA) de acuerdo con la reivindicación 1, en el cual:

R^1 es fenilo, naftilo, piridilo, cromanilo, dihidrobenzofuranilo o benzofuranilo, cada uno sustituido independientemente en forma opcional con uno o dos grupos sustituyentes,

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donde cada grupo sustituyente de R^1 es independientemente metilo, etilo, metoxi, etoxi, fluoro, cloro, bromo, hidroxi, trifluorometilo, trifluorometoxi, ciano o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona;

R^2 y R^3 son cada uno independientemente metilo o etilo, o R^2 y R^3 junto con el átomo de carbono al que están unidos usualmente forman un anillo espiro ciclopropilo;

R^4 es CH_2; y

R^5 es un grupo piridilo, indolilo, azaindolilo, diazaindolilo, benzofuranilo, furanopiridinilo, tienopiridinilo, benzoxazolilo, benzoimidazolilo, quinolinilo, o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente metilo, fenilo, metoxi, etoxi, isopropoxi, metoxicarbonilo, aminocarbonilo, metilaminocarbonilo, dimetilaminocarbonilo, morfolinilcarbonilo, morfolinilo, piperidinilo, trifluorometilo, fluoro, cloro, bromo, hidroxi, ciano o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo o trifluorometilo,

o un tautómero, un profármaco, un solvato o sal del mismo.

4. El compuesto de Fórmula (IA) de acuerdo con la reivindicación 1, en el cual R^2 y R^3 junto con el átomo de carbono al que están unidos usualmente para formar un anillo espiro cicloalquilo C_3-C_8.

5. El compuesto de Fórmula (IA) de acuerdo con la reivindicación 1, en el cual R^2 y R^3 son cada uno independientemente hidrógeno o alquilo C_1-C_6.

6. El compuesto de Fórmula (IA) de acuerdo con la reivindicación 1, en el cual:

R^1 es fenilo, dihidrobenzofuranilo, o benzofuranilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente C_1-C_3 alquilo, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona; y

R^2 y R^3 son cada uno independientemente hidrógeno o alquilo C_1-C_3,

o un tautómero, un profármaco, un solvato o sal del mismo.

7. El compuesto de Fórmula (IA) de acuerdo con la reivindicación 1, en el cual:

R^5 es un grupo piridilo, indolilo, azaindolilo, diazaindolilo, benzofuranilo, furanopiridinilo, tienopiridinilo, benzoxazolilo, benzoimidazolilo, quinolinilo, o isoquinolinilo,

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cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

o un tautómero, un profármaco, un solvato o sal del mismo.

8. El compuesto de Fórmula (IA) de acuerdo con la reivindicación 1, en el cual:

R^1 es tienilo, fenilo, naftilo, dihidrobenzofuranilo, benzofuranilo, cromanilo, dihidroindolilo, indolilo, dihidrobenzotienilo, benzotienilo, benzodioxolilo, dihidrobenzoxazolilo, benzoxazolilo, benzoisoxazolilo, benzopirazolilo, bencimidazolilo, tienilo, quinolinilo, piridinilo, pirimidinilo, o pirazinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, arilo, heteroarilo, halógeno, hidroxi, carboxi, ciano, heterociclilo, trifluorometilo, trifluorometoxi, nitro, aminosulfonilo, dialquilaminosulfonilo, amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_6, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^1 está sustituido independientemente en forma opcional con uno o dos grupos sustituyentes seleccionados de metilo, metoxi, halógeno, hidroxi, oxo, ciano, morfolinilo o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6;

R^2 y R^3 son cada uno independientemente hidrógeno o alquilo C_1-C_3, o R^2 y R^3 junto con el átomo de carbono al que están unidos usualmente forman un anillo espiro cicloalquilo C_3-C_6;

R^4 es CH_2; y

R^5 es un grupo imidazolilo, piridilo, indolilo, indazolilo, azaindolilo, diazaindolilo, benzofuranilo, furanopiridinilo, furanopirimidinilo, imidazolopirimidinilo, imidazolopiridazinilo, imidazolopirazinilo, benzotienilo, tienopiridinilo, tienopirimidinilo, tienopiridazinilo, benzoxazolilo, oxazolopiridinilo, benzotiazolilo, tiazolopiridinilo, benzoimidazolilo, imidazolopiridinilo, quinolinilo o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, fenilo, heteroarilo, heterociclilo, acilo, dialquilaminosulfonilo, alcoxi C_1-C_3, metoxicarbonilo, aminocarbonilo, alquilaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-

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C_3, heterociclilcarbonilo, hidroxi, oxo, fluoro, cloro, bromo, ciano, trifluorometilo, amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_6; o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^5 está independientemente en forma opcional sustituido con uno o dos grupos sustituyentes seleccionados de metilo, metoxi, fluoro, cloro, bromo, oxo, trifluorometilo, hidroxi, ciano, morfolinilo, pirrolidinilo o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo,

o un tautómero, un profármaco, un solvato o sal del mismo.

9. El compuesto de Fórmula (IA) de acuerdo con la reivindicación 1, en el cual:

R^1 es tienilo, fenilo, naftilo, piridilo, cromanilo, benzodioxolilo, dihidrobenzofuranilo, o benzofuranilo, cada uno sustituido independientemente en forma opcional con uno o dos grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente metilo, etilo, metoxi, etoxi, fluoro, cloro, bromo, hidroxi, trifluorometilo, trifluorometoxi, morfolinilmetilo, dimetilaminometilo, aminosulfonilo, dimetilaminosulfonilo, fenilo, pirimidinilo, piridinilo, tienilo, naftalenilo, morfolinilo, piperidinilo, ciano, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^1 está independientemente en forma opcional sustituido con uno o dos grupos seleccionados de ciano, cloro, bromo o fluoro;

R^2 y R^3 son cada uno independientemente metilo o etilo, o R^2 y R^3 junto con el átomo de carbono al que están unidos usualmente forman un anillo espiro ciclopropilo;

R^4 es CH_2; y

R^5 es un grupo piridilo, indolilo, azaindolilo, diazaindolilo, benzofuranilo, tienopiridazinilo, furanopiridinilo, tienopiridinilo, benzoxazolilo, benzoimidazolilo, quinolinilo o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente metilo, fenilo, metoxi, etoxi, isopropoxi, metoxicarbonilo, aminocarbonilo, metilaminocarbonilo, dimetilaminocarbonilo, morfolinilcarbonilo, morfolinilo, piperidinilo, fenoxi, pirrolidinilo, acetilo, pivaloilo, etilcarbonilo, isopropilcarbonilo, piridinilo, pirimidinilo, trifluorometilo, fluoro, cloro, bromo, hidroxi, ciano o amino donde el átomo de nitrógeno en forma

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opcional está independientemente mono- o di-sustituido con C_1-C_8 alquilo o arilo o trifluorometilo,

donde cada grupo sustituyente de R^5 está independientemente en forma opcional sustituido con uno o dos grupos sustituyentes seleccionados de ciano, halógeno, metilo, dimetilamino, morfolinilo, pirrolidinilo, o piperidinilo,

o un tautómero, un profármaco, un solvato o sal del mismo.

10. El compuesto de Fórmula (IA) de acuerdo con la reivindicación 1, en el cual:

R^1 es fenilo, dihidrobenzofuranilo o benzofuranilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona; y

R^2 y R^3 son cada uno independientemente hidrógeno o alquilo C_1-C_3,

o un tautómero, un profármaco, un solvato o sal del mismo.

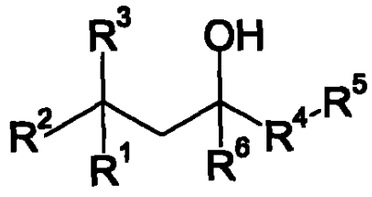
11. El compuesto de Fórmula (IA) de acuerdo con la reivindicación 1, en el cual:

R^5 es un grupo piridilo, indolilo, azaindolilo, diazaindolilo, benzofuranilo, tienopiridazinilo furanopiridinilo, tienopiridinilo, benzoxazolilo, benzoimidazolilo, quinolinilo o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

o un tautómero, un profármaco, un solvato o sal del mismo.

12. Una composición farmáceutica que comprende una cantidad efectiva de un compuesto de acuerdo con una de las reivindicaciones 1 a 11, o un tautómero, profármaco, solvato o una sal del mismo, y un excipiente o vehículo aceptables para uso farmacéutico.

13. Un compuesto de Fórmula (IB)



(IB)

en el cual:

R^1 es un grupo arilo o heteroarilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

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donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, cicloalquilo C_3-C_8, heterocicilo, arilo, heteroarilo, alcoxi C_1-C_8, alqueniloxi C_2-C_8, alquiniloxi C_2-C_8, ariloxi, acilo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_8, alcanoilo C_1-C_8, aroilo, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilaminocarboniloxi C_1-C_8, dialquilaminocarboniloxi C_1-C_8, alcanoilamino C_1-C_8, alcoxicarbonilamino C_1-C_8, alquilsulfonilamino C_1-C_8, aminosulfonilo, alquilaminosulfonilo C_1-C_8, dialquilaminosulfonilo C_1-C_8, halógeno, hidroxi, carboxi, ciano, trifluorometilo, trifluorometoxi, nitro, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_8; o alquiltio C_1-C_8 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^1 está sustituido independientemente en forma opcional con uno a tres grupos sustituyentes seleccionados de metilo, metoxi, halógeno, hidroxi, oxo, ciano, heteroarilo, heterocicilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_8;

R^2 y R^3 son cada uno independientemente alquilo C_1-C_8,

R^4 es alquilo C_1-C_8, alquenilo C_2-C_8, o alquinilo C_2-C_8, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^4 es independientemente alquilo C_1-C_3, hidroxi, halógeno, amino, u oxo; y

R^5 es un grupo heteroarilo independientemente sustituido en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, cicloalquilo C_3-C_8, heterocicilo, arilo, heteroarilo, alcoxi C_1-C_8, alqueniloxi C_2-C_8, alquiniloxi C_2-C_8, ariloxi, acilo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_8, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilamino-carboniloxi C_1-C_8, dialquilaminocarboniloxi C_1-C_8, alcanoilamino C_1-C_8, alcoxicarbonilamino C_1-C_8, alquilsulfonilamino C_1-C_8, aminosulfonilo, alquilaminosulfonilo C_1-C_8, dialquilaminosulfonilo C_1-C_8, halógeno, hidroxi, carboxi, ciano, trifluorometilo, trifluorometoxi, trifluorometiltio, nitro o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8; o ureido

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donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_6; o alquiltio C_1-C_6 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^5 está independientemente sustituido en forma opcional con uno a tres grupos sustituyentes seleccionados de alquilo C_1-C_3, alcoxi C_1-C_3, halógeno, hidroxi, oxo, ciano, arilo, heteroarilo, heterociclilo o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_3, o trifluorometilo,

R^6 es hidrógeno, alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, carbociclo, heterociclilo, arilo, heteroarilo, carbociclo-alquilo C_1-C_8, carboxi, alcoxicarbonilo, aril-alquilo C_1-C_8, aril-haloalquilo C_1-C_8, heterociclil-alquilo C_1-C_8, heteroaril-alquilo C_1-C_8, carbociclo-alquenilo C_2-C_8, aril-alquenilo C_2-C_8, heterociclil-alquenilo C_2-C_8, o heteroaril-alquenilo C_2-C_8, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^6 es independientemente alquilo C_1-C_6, alquenilo C_2-C_6, alquinilo C_2-C_6, cicloalquilo C_3-C_8, fenilo, alcoxi C_1-C_6, fenoxi, alcanoílo C_1-C_3, aroílo, alcoxicarbonilo C_1-C_6, alcanoíloxi C_1-C_6, aminocarboniloxi, alquilaminocarboniloxi C_1-C_6, dialquilaminocarboniloxi C_1-C_6, aminocarbonilo, alquilaminocarbonilo C_1-C_6, dialquilaminocarbonilo C_1-C_6, alcanoilamino C_1-C_6, alcoxicarbonilamino C_1-C_6, alquilsulfonilamino C_1-C_6, alquilaminosulfonilo C_1-C_6, dialquilaminosulfonilo C_1-C_6, halógeno, hidroxi, carboxi, ciano, oxo, trifluorometilo, nitro, amino en donde el átomo de nitrógeno en forma opcional es independientemente mono- o di-sustituido con alquilo C_1-C_6; o ureido en donde el átomo de nitrógeno en forma opcional es independientemente sustituido con alquilo C_1-C_6; o alquiltio C_1-C_6 en donde el átomo de azufre en forma opcional es oxidado a un sulfóxido o una sulfona,

en donde R^6 no puede ser trifluorometilo,

o un tautómero, un profármaco, un solvato o sal del mismo.

14. El compuesto de Fórmula (IB) de acuerdo con la reivindicación 13, en el cual:

R^1 es tienilo, fenilo, naftilo, dihidrobenzofuranilo, benzofuranilo, cromanilo, dihidroindolilo, indolilo, dihidrobenzotienilo, benzotienilo, benzodioxolanilo, benzoxazolilo, benzoisoxazolilo, benzopirazolilo, bencimidazolilo, tienilo, quinolinilo, piridinilo, pirimidinilo, o pirazinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

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en donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoílo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoíloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3 en donde el átomo de azufre en forma opcional es oxidado a un sulfóxido o una sulfona,

en donde cada grupo sustituyente de R^1 está sustituido independientemente en forma opcional con un grupo sustituyente seleccionado de metilo, metoxi, halógeno, hidroxi, oxo, ciano, heteroarilo, heterocicilo, o amino en donde el átomo de nitrógeno en forma opcional es independientemente mono- o di-sustituido con alquilo C_1-C_5 o arilo;

R^2 y R^3 son cada uno independientemente alquilo C_1-C_3;

R^4 es CH_2;

R^5 es un grupo imidazolilo, piridilo, indolilo, azaindolilo, diazaindolilo, benzofuranilo, furanopiridinilo, furanopirimidinilo, benzotienilo, tienopiridinilo, tienopirimidinilo, benzoxazolilo, oxazolopiridinilo, benzotiazolilo, tiazolopiridinilo, bencimidazolilo, imidazolopiridinilo, imidazolopirimidinilo, imidazolopiridazinilo, imidazolopirazinilo, quinolinilo, o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, fenilo, alcoxi C_1-C_3, metoxicarbonilo, aminocarbonilo, alquilaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, heterocicilcarbonilo, hidroxi, fluoro, cloro, bromo, ciano, trifluorometilo, o alquiltio C_1-C_3 en donde el átomo de azufre en forma opcional es oxidado a un sulfóxido o una sulfona,

en donde cada grupo sustituyente de R^6 está sustituido independientemente en forma opcional con un grupo sustituyente seleccionado de metilo, metoxi, fluoro, cloro, bromo, trifluorometilo, heteroarilo, heterocicilo, o amino en donde el átomo de nitrógeno en forma opcional es independientemente mono- o di-sustituido con alquilo C_1-C_5 o arilo; y

R^6 es alquilo C_1-C_5, alquenilo C_2-C_5, cicloalquilo C_3-C_8, fenilo, cicloalquil-C_3-C_8-alquilo C_1-C_3, fenilo alquilo C_1-C_3, fenil-haloalquilo C_1-C_3, cicloalquil-C_3-C_8-alquenilo C_2-C_3, fenil-alquenilo C_2-C_3, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^6 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, aminocarbonilo, C_1-C_3, alquilaminocarbonilo C_1-C_3 dialquilaminocarbonilo, halógeno, hidroxi, oxo, carboxi, ciano, trifluorometilo, nitro, o

alquiltio C_1-C_3 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

o un tautómero, un profármaco, un solvato o sal del mismo.

15. El compuesto de Fórmula (IB) de acuerdo con la reivindicación 13, en el cual:

R^1 es tienilo, fenilo, naftilo, piridilo, cromanilo, dihidrobenzofuranilo, o benzofuranilo, cada uno independientemente en forma opcional sustituido con uno o dos grupos sustituyentes,

en donde cada grupo sustituyente de R^1 es independientemente metilo, etilo, metoxi, etoxi, fluoro, cloro, bromo, hidroxi, trifluorometilo, ciano, o alquiltio C_1-C_3 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona;

R^2 y R^3 son cada uno metilo;

R^4 es CH_2;

R^5 es un grupo piridilo, indolilo, azaindolilo, diazaindolilo, benzofuranilo, furanopiridinilo, tienopiridinilo, benzoxazolilo, bencimidazolilo, quinolinilo, o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^5 es independientemente metilo, fenilo, metoxicarbonilo, aminocarbonilo, metilaminocarbonilo, dimetilaminoa-minocarbonilo, morfolinilcarbonilo, hidroxi, fluoro, cloro, bromo, ciano, o trifluorometilo; y

R^6 es alquilo C_1-C_3, cicloalquilo C_3-C_6, cicloalquilmetilo C_3-C_6 o bencilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^6 es independientemente metilo, metoxi, fluoro, cloro, bromo, ciano, trifluorometilo, o hidroxi,

o un tautómero, un profármaco, un solvato o sal del mismo.

16. El compuesto de Fórmula (IB) de acuerdo con la reivindicación 13, en el cual:

R^1 es tienilo, fenilo, dihidrobenzofuranilo, o benzofuranilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona; y

R^2 y R^3 son cada uno independientemente alquilo C_1-C_3,

o un tautómero, un profármaco, un solvato o sal del mismo.

17. El compuesto de Fórmula (IB) de acuerdo con la reivindicación 13, en el cual:

R^1 es tienilo, fenilo, naftilo, piridilo, cromanilo, dihidrobenzofuranilo, o benzofuranilo, cada uno independientemente sustituido en forma opcional con uno o dos grupos sustituyentes,

en el cual cada grupo sustituyente de R^1 es independientemente metilo, etilo, metoxi, etoxi, fluoro, cloro, bromo, hidroxi, trifluorometilo, ciano, o alquiltio C_1-C_5 en el cual el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona;

R^2 y R^3 son cada uno metilo;

R^4 es CH_2;

R^5 es un grupo piridilo, indolilo, azaindolilo, diazaindolilo, benzofuranilo, furanopiridinilo, tienopiridinilo, benzoxazolilo, benzoimidazolilo, quinolinilo, o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en el cual cada grupo sustituyente de R^5 es independientemente metilo, fenilo, metoxicarbonilo, aminocarbonilo, metilaminocarbonilo, dimetilaminoaminocarbonilo, morfolinilcarbonilo, piridinilo, hidroxi, fluoro, cloro, bromo, ciano, o trifluorometilo; y

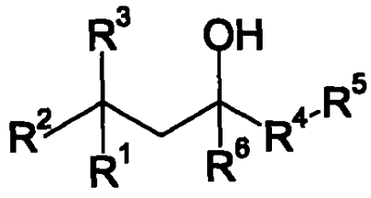
R^6 es alquilo C_1-C_5, cicloalquilo C_3-C_6, cicloalquilmetilo C_3-C_6 o bencilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^6 es independientemente metilo, metoxi, fluoro, cloro, bromo, ciano, trifluorometilo, o hidroxi,

o un tautómero, un profármaco, un solvato o sal del mismo.

18. Una composición farmacéutica que comprende una cantidad efectiva de un compuesto según una de las reivindicaciones 13 a 17 o un tautómero, profármaco, solvato o una sal del mismo, y un excipiente o vehículo aceptables para uso farmacéutico.

19. Un compuesto de Fórmula (IC)



(IC)

en el cual:

R^1 es un grupo arilo o heteroarilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

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donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, cicloalquilo C_3-C_8, heterociclilo, arilo, heteroarilo, alcoxi C_1-C_8, alqueniloxi C_2-C_8, alquiniloxi C_2-C_8, ariloxi, acilo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_8, alcanoílo C_1-C_8, aroílo, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilaminocarboniloxi C_1-C_8, dialquilaminocarboniloxi C_1-C_8, alcanoilamino C_1-C_8, alcoxicarbonilamino C_1-C_8, alquilsulfonilamino C_1-C_8, aminosulfonilo, alquilaminosulfonilo C_1-C_8, dialquilaminosulfonilo C_1-C_8, halógeno, hidroxi, carboxi, ciano, trifluorometilo, trifluorometoxi, nitro, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_8; o alquiltio C_1-C_8 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^1 está independientemente sustituido en forma opcional con uno a tres grupos sustituyentes seleccionados de metilo, metoxi, halógeno, hidroxi, oxo, ciano, heteroarilo, heterociclilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_8;

R^2 y R^3 son cada uno independientemente alquilo C_1-C_6;

R^4 es alquilo C_1-C_8, alquenilo C_2-C_8, o alquinilo C_2-C_8, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^4 es independientemente alquilo C_1-C_3, hidroxi, halógeno, amino, u oxo; y

R^5 es un grupo heteroarilo independientemente sustituido en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, cicloalquilo C_3-C_8, heterociclilo, arilo, heteroarilo, alcoxi C_1-C_8, alqueniloxi C_2-C_8, alquiniloxi C_2-C_8, ariloxi, acilo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_8, heterociclilcarbonilo, aroílo, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilamino-carboniloxi C_1-C_8, dialquilaminocarboniloxi C_1-C_8, alcanoilamino C_1-C_8, alcoxicarbonilamino C_1-C_8, alquilsulfonilamino C_1-C_8, aminosulfonilo, alquilaminosulfonilo C_1-C_8, dialquilaminosulfonilo C_1-C_8, halógeno, hidroxi, carboxi, ciano, trifluorometilo, trifluorometoxi, trifluorometiltio, nitro o amino donde el átomo de nitrógeno en forma

opcional está independientemente mono- o di-sustituido con alquilo C_1-C_5; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_5; o alquiltio C_1-C_8 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

donde cada grupo sustituyente de R^5 está independientemente sustituido en forma opcional con uno a tres grupos sustituyentes seleccionados de alquilo C_1-C_3, alcoxi C_1-C_3, acilo, silaniloxi C_1-C_3, alcoxicarbonilo C_1-C_6, carboxi, halógeno, hidroxi, oxo, ciano, arilo, heteroarilo, heterociclilo o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_5 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_3, o trifluorometilo,

R^6 es hidrógeno, alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, carbociclo, heterociclilo, arilo, heteroarilo, carbociclo-alquilo C_1-C_8, carboxi, trifluorometilo, alcoxicarbonilo, aril-alquilo C_1-C_8, aril-haloalquilo C_1-C_8, heterociclil-alquilo C_1-C_8, heteroaril-alquilo C_1-C_8, carbociclo-alquenilo C_2-C_8, aril-alquenilo C_2-C_8, heterociclil-alquenilo C_2-C_8, o heteroaril-alquenilo C_2-C_8, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^6 es independientemente alquilo C_1-C_5, alquenilo C_2-C_5, alquinilo C_2-C_5, cicloalquilo C_3-C_8, fenilo, alcoxi C_1-C_5, fenoxi, alcanoilo C_1-C_5, aroilo, alcoxicarbonilo C_1-C_5, alcanoiloxi C_1-C_5, aminocarboniloxi, alquilaminocarboniloxi C_1-C_5, dialquilaminocarboniloxi C_1-C_5, aminocarbonilo, alquilaminocarbonilo C_1-C_5, dialquilaminocarbonilo C_1-C_5, alcanoilamino C_1-C_5, alcoxicarbonilamino C_1-C_5, alquilsulfonilamino C_1-C_5, alquilaminosulfonilo C_1-C_5, dialquilaminosulfonilo C_1-C_5, halógeno, hidroxi, carboxi, ciano, oxo, trifluorometilo, nitro, amino en donde el átomo de nitrógeno en forma opcional es independientemente mono- o di-sustituido con alquilo C_1-C_5; o ureido en donde el átomo de nitrógeno en forma opcional es independientemente sustituido con alquilo C_1-C_5; o alquiltio C_1-C_8 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

o un tautómero, un profármaco, un solvato o sal del mismo.

20. El compuesto de Fórmula (IC) de acuerdo con la reivindicación 19, en el cual:

R^1 es tienilo, fenilo, naftilo, dihidrobenzofuranilo, benzofuranilo, cromanilo, dihidroindolilo, indolilo, dihidrobenzotienilo, benzotienilo, benzodioxolanilo, benzoxazolilo, bencisoxazolilo, benzpirazolilo, bencimidazolilo, tienilo, quinolinilo, piridinilo, pirimidinilo, o pirazinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

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en donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

en donde cada grupo sustituyente de R^1 está independientemente sustituido en forma opcional con un grupo sustituyente seleccionado de metilo, metoxi, halógeno, hidroxi, oxo, ciano, heteroarilo, heterociclilo, o amino en donde el átomo de nitrógeno en forma opcional está independientemente monó- o di-sustituido con alquilo C_1-C_6 o arilo;

R^2 y R^3 son cada uno independientemente alquilo C_1-C_3;

R^4 es CH_2;

R^5 es un heteroarilo unido a N con un anillo carbocíclico saturado de 5-7 miembros fusionado en forma opcional e independientemente sustituido con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, fenilo, alcoxi C_1-C_3, metoxicarbonilo, aminocarbonilo, alquilaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, heterociclilcarbonilo, fluoro, cloro, bromo, ciano, trifluorometilo, hidroxilo, oxo, o alquiltio C_1-C_3 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

en donde cada grupo sustituyente de R^5 está independientemente sustituido en forma opcional con un grupo sustituyente seleccionado de metilo, metoxi, fluoro, cloro, bromo, trifluorometilo, heteroarilo, heterociclilo, o amino en donde el átomo de nitrógeno en forma opcional es independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; y

R^6 es alquilo C_1-C_6, alquenilo C_2-C_5, cicloalquilo C_3-C_8, trifluorometilo, fenilo, cicloalquil-C_3-C_8-alquilo C_1-C_3, fenil-alquilo C_1-C_3, fenil-haloalquilo C_1-C_3, cicloalquil-C_3-C_8 alquenilo C_2-C_3, fenil-alquenilo C_2-C_3, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^6 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, aminocarbonilo, alquilaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3, en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

o un tautómero, un profármaco, un solvato o sal del mismo.

21. El compuesto de Fórmula (IC) de acuerdo con la reivindicación 19, en el cual:

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R^1 es tienilo, fenilo, naftilo, piridilo, cromanilo, dihidrobenzofuranilo, o benzofuranilo, cada uno independientemente en forma opcional sustituido con uno o dos grupos sustituyentes,

en donde cada grupo sustituyente de R^1 es independientemente metilo, etilo, metoxi, etoxi, fluoro, cloro, bromo, hidroxi, trifluorometilo, piridinilo, pirimidinilo, pirazinilo, ciano, o alquiltio C_1-C_3 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona;

R^2 y R^3 son cada uno metilo;

R^4 es CH_2;

R^5 es un pirrol, pirazol o imidazol unido por N, fusionado con un anillo carbocíclico saturado de 5-7 miembros en forma opcional e independientemente sustituido con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^5 es independientemente metilo, fenilo, metoxicarbonilo, aminocarbonilo, metilaminocarbonilo, dimetilaminoamino-carbonilo, morfolinilcarbonilo, fluoro, cloro, bromo, ciano, hidroxi, oxo, o trifluorometilo; y

R^6 es alquilo C_1-C_6, cicloalquilo C_3-C_6, trifluorometilo, cicloalquilmetilo C_3-C_6, o bencilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^6 es independientemente metilo, metoxi, fluoro, cloro, bromo, ciano, trifluorometilo, o hidroxi,

o un tautómero, un profármaco, un solvato o sal del mismo.

22. El compuesto de Fórmula (IC) de acuerdo con la reivindicación 19, en el cual:

R^1 es tienilo, fenilo, naftilo, dihidrobenzofuranilo, benzofuranilo, cromanilo, dihidroindolilo, indolilo, dihidrobenzotienilo, benzotienilo, benzodioxolanilo, benzoxazolilo, benzoisoxazolilo, benzopirazolilo, benzoimidazolilo, tienilo, quinolinilo, piridinilo, pirimidinilo, o pirazinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoílo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

en donde cada grupo sustituyente de R^1 es en forma opcional independientemente sustituido con un grupo sustituyente seleccionado de metilo, metoxi, halógeno, hidroxi,

oxo, ciano, heteroarilo, heterociclilo, o amino en donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo;

R^2 y R^3 son cada uno independientemente alquilo C_1-C_3;

R^4 es CH_2;

R^5 es un heteroarilo unido por el N con un anillo carbocíclico saturado de 5-7 miembros fusionado en forma opcional e independientemente sustituido con uno a tres grupos sustituyentes.

en donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, fenilo, alcoxi C_1-C_3, metoxicarbonilo, aminocarbonilo, alquilaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, heterociclilcarbonilo, fluoro, cloro, bromo, ciano, trifluorometilo, hidroxilo, oxo, o alquiltio C_1-C_3 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

en donde cada grupo sustituyente de R^5 está independientemente sustituido en forma opcional con un grupo sustituyente seleccionado de metilo, metoxi, fluoro, cloro, bromo, trifluorometilo, heteroarilo, heterociclilo, o amino en donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo; y

R^6 es alquilo C_1-C_8, alquenilo C_2-C_8, cicloalquilo C_3-C_8, trifluorometilo, fenilo, cicloalquil-C_3-C_8-alquilo C_1-C_3, fenil-alquilo C_1-C_3, fenil-haloalquilo C_1-C_3, cicloalquil-C_3-C_8 alquenilo C_2-C_3, fenil-alquenilo C_2-C_3, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^6 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, aminocarbonilo, alquilaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3, en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

o un tautómero, un profármaco, un solvato o sal del mismo.

23. El compuesto de Fórmula (IC) de acuerdo con la reivindicación 19, en el cual:

R^1 es tienilo, fenilo, naftilo, piridilo, cromanilo, dihidrobenzofuranilo, o benzofuranilo, cada uno independientemente en forma opcional sustituido con uno o dos grupos sustituyentes,

en donde cada grupo sustituyente de R^1 es independientemente metilo, etilo, metoxi, etoxi, fluoro, cloro, bromo, hidroxi, trifluorometilo, ciano, o alquiltio C_1-C_6 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona;

R^2 y R^3 son cada uno metilo;

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R^4 es CH_2;

R^5 es un pirrol, pirazol o imidazol unido por el N, fusionado a un anillo carbocíclico saturado de 5-7 miembros, en forma opcional e independientemente sustituido con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^5 es independientemente metilo, fenilo, metoxicarbonilo, aminocarbonilo, metilaminocarbonilo, dimetilamino-aminocarbonilo, morfolinilcarbonilo, fluoro, cloro, bromo, ciano, hidroxi, oxo, o trifluorometilo; y

R^6 es alquilo C_1-C_6, cicloalquilo C_3-C_6, trifluorometilo, fenilo, cicloalquilmetilo C_3-C_6 o bencilo cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes

en donde cada grupo sustituyente de R^6 es independientemente metilo, metoxi, fluoro, cloro, bromo, ciano, trifluorometilo, o hidroxi,

o un tautómero, un profármaco, un solvato o sal del mismo.

24. El compuesto de fórmula (IC) de acuerdo a la reivindicación 19, donde:

R^1 es tienil, fenil, naftil, piridil, cromanil, dihidrobenzofuranil o benzofuranil cada uno sustituido independientemente con uno o dos grupos sustituyentes, donde cada grupo sustituyente de R1 es independientemente metil, etil, metoxi, etoxi, fluor, cloro, bromo, hidroxi, trifluorometil, furanil, tienil, pirrolil,pirrolidinil,oxazolil,tiazolil,imidazolil,pirazolil,pirazolidinil,isozazolil,isotiazolil,oxadiazolil,triazolil,tiadiazolil,piridinil,piperidinil,morfolinil,tiomorfolinil,piridazinil,pirimidinil,pirazinil,piperazinil,indolil,benzofuranil,benzotienil,indazolil,benzimidazolil,ciano, o C1-C5 alquiltio donde átomo de sulfuro es opcionalmente oxidado a sulfoxido o sulfona;

Donde cada grupo sustituyente de R^1 es opcionalmente independientemente sustituido con un grupo sustituyente seleccionado de C^1-C^5 alcoxi, C^1-C^5 alcoxicarbonil, acil, aminocarbonil, C^1-C^5 alquilaminocarbonil, C^1-C^5 dialquilaminocarboni, C^1-C^5alcanoilamino, hidroxil, ciano, halógeno o amino donde el átomo de nitrógeno es opcionalmente independiente mono o disustituido por C^1-C^5 alquil,

R^2 y R^3 son cada uno metilo;

R^4 es CH^2;

R^5 es un pirrolo unido a N, pirazol o imidazol fusionado a un anillo carboxílico saturado de 5-7 miembros opcionalmente e independientemente sustituido con uno a tres grupos sustituyentes,

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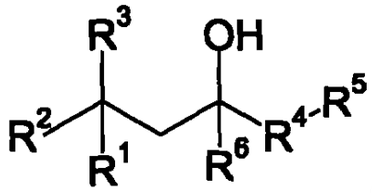
Donde cada grupo sustituyente de R^5 es independientemente metilo, fenil,metoxicarbonil,aminocarbonil,metilaminocarbonil,dimetilaminocarbonil,morfolinilcarbonil,fluor,cloro,bromo,ciano,hidroxi,oxo o trifluorometil; y

R^6 es C^1-C^5 alquil, C^3-C^6 cicloalquil, trifluorometil, C^3-C^6 cicloalquilmetil o bencil, cada uno opcionalmente independientemente sustituido con uno a tres grupos sustituyentes donde cada grupo sustituyente de R^6 es independientemente metilo, metoxi, fluor, cloro, bromo, ciano, trifluorometil o hidroxi o un tautómero, profármaco, solvato o sal del mismo.

25. Una composición farmacéutica que comprende una cantidad efectiva de un compuesto de acuerdo con una de las reivindicaciones 19 a 24 o un tautómero, profármaco, solvato o una sal del mismo, y a un excipiente o vehículo aceptables para uso farmacéutico.

26. Un compuesto de Fórmula (ID)



(ID)

en el cual:

R^1 es un grupo arilo o heteroarilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, cicloalquilo C_3-C_8, heterocicilo, arilo, heteroarilo, alcoxi C_1-C_8, alqueniloxi C_2-C_8, alquiniloxi C_2-C_8, ariloxi, acilo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_8, alcanoilo C_1-C_8, aroilo, aminocarbonilo, alquilaminocarbonilo C_1-C_8, dialquilaminocarbonilo, aminocarboniloxi, alquilaminocarboniloxi C_1-C_8, dialquilaminocarboniloxi C_1-C_8, alcanoilamino C_1-C_8, alcoxicarbonilamino C_1-C_8, alquilsulfonilamino C_1-C_8, aminosulfonilo, alquilaminosulfonilo C_1-C_8, dialquilaminosulfonilo C_1-C_8, halógeno, hidroxi, carboxi, ciano, trifluorometilo, trifluorometoxi, nitro, o amino en donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo; o ureido en donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_8; o alquiltio C_1-C_8 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

en donde cada grupo sustituyente de R^1 está independientemente sustituido en forma opcional con uno a tres grupos sustituyentes seleccionados de metilo, metoxi, halógeno, hidroxi, oxo, ciano, heteroarilo, heterociclilo, o amino en donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo; o ureido en donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_8;

R^2 y R^3 son cada uno independientemente alquilo C_1-C_8, en donde uno o ambos están independientemente sustituidos con hidroxi, alcoxi C_1-C_8, alquiltio C_1-C_8 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona, amino en donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo;

R^4 es alquilo C_1-C_8, alquenilo C_2-C_8, o alquinilo C_2-C_8, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^4 es independientemente alquilo C_1-C_3, hidroxi, halógeno, u oxo;

R^5 es un grupo heteroarilo independientemente sustituido en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, cicloalquilo C_3-C_8, heterociclilo, arilo, heteroarilo, alcoxi C_1-C_8, alqueniloxi C_2-C_8, alquiniloxi C_2-C_8, arilioxi, acilo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_8, heterociclilcarbonilo, aroilo, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilaminocarboniloxi C_1-C_8, dialquilaminocarboniloxi C_1-C_8, alcanoilamino C_1-C_8, alcoxicarbonilamino C_1-C_8, alquilsulfonilamino C_1-C_8, aminosulfonilo, alquilaminosulfonilo C_1-C_8, dialquilaminosulfonilo C_1-C_8, halógeno, hidroxi, carboxi, ciano, trifluorometilo, trifluorometoxi, trifluorometiltio, nitro, o amino en donde el átomo de nitrógeno en forma opcional es independientemente mono- o di-sustituido con alquilo C_1-C_8; o ureido en donde el átomo de nitrógeno en forma opcional es independientemente sustituido con alquilo C_1-C_8; o alquiltio C_1-C_8 en donde el átomo de azufre en forma opcional es oxidado a un sulfóxido o una sulfona,

en donde cada grupo sustituyente de R^5 está sustituido independientemente en forma opcional con uno a tres grupos sustituyentes seleccionados de alquilo C_1-C_3, alcoxi C_1-C_3, acilo, silaniloxi C_1-C_3, alcoxicarbonilo C_1-C_8, carboxi, halógeno, hidroxi, oxo, ciano, arilo, heteroarilo, heterociclilo, o amino en donde el átomo de nitrógeno en forma opcional es independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo; o ureido en donde

el átomo de nitrógeno en forma opcional es independientemente sustituido con alquilo C_1-C_6, o trifluorometilo,

R^8 es hidrógeno, alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, carbociclo, heterociclilo, arilo, heteroarilo, carbociclo-alquilo C_1-C_8, carboxi, alcoxicarbonilo, aril-alquilo C_1-C_8, aril-haloalquilo C_1-C_8, heterocicil-alquilo C_1-C_8, heteroaril-alquilo C_1-C_8, carbociclo-alquenilo C_2-C_8, aril-alquenilo C_2-C_8, heterocicil-alquenilo C_2-C_8, o heteroaril-alquenilo C_2-C_8, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes

en donde cada grupo sustituyente de R^8 es independientemente alquilo C_1-C_6, alquenilo C_2-C_6, alquinilo C_2-C_6, cicloalquilo C_3-C_8, fenilo, alcoxi C_1-C_6, fenoxi, alcanoilo C_1-C_8, aroílo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_5, aminocarboniloxi, alquilaminocarboniloxi C_1-C_5, dialquilaminocarboniloxi C_1-C_5, aminocarbonilo, alquilaminocarbonilo C_1-C_5, dialquilaminocarbonilo C_1-C_5, alcanoilamino C_1-C_5, alcoxicarbonilamino C_1-C_5, alquilsulfonilamino C_1-C_5, alquilaminosulfonilo C_1-C_5, dialquilaminosulfonilo C_1-C_5, halógeno, hidroxi, carboxi, ciano, oxo, trifluorometilo, nitro, amino en donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_5; o ureido en donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_5; o alquiltio C_1-C_5 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

o un tautómero, un profármaco, un solvato o sal del mismo.

27. El compuesto de Fórmula (ID) según reivindicación 26, en el cual:

R^1 es tienilo, fenilo, naftilo, dihidrobenzofuranilo, benzofuranilo, cromanilo, dihidroindolilo, indolilo, dihidrobenzotienilo, benzotienilo, benzodioxolanilo, benzoxazolilo, benzoisoxazolilo, benzopirazolilo, benzoimidazolilo, tienilo, quinolinilo, piridinilo, pirimidinilo, o pirazinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoílo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

en donde cada grupo sustituyente de R^1 está sustituido independientementen forma opcional e con un grupo sustituyente seleccionado de metilo, metoxi, halógeno, hidroxi, oxo, ciano, heteroarilo, heterociclilo, o amino en donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_6 o arilo;

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R^2 y R^3 son cada uno independientemente alquilo C_1-C_3, en donde uno o ambos están independientemente sustituidos con hidroxi, alcoxi C_1-C_5;

R^4 es CH_2;

R^5 es un grupo imidazolilo, piridilo, indolilo, azaindolilo, diazaindolilo, benzofuranilo, furanopiridinilo, furanopirimidinilo, benzotienilo, tienopiridinilo, tienopirimidinilo, benzoxazolilo, oxazolopiridinilo, benzotiazolilo, tiazolopiridinilo, bencimidazolilo, imidazolopiridinilo, imidazolopirimidinilo, imidazolopiridazinilo, imidazolopirazinilo, quinolinilo, o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, fenilo, alcoxi C_1-C_3, metoxicarbonilo, aminocarbonilo, alquilaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, heterociclilcarbonilo, fluoro, cloro, bromo, ciano, trifluorometilo, hidroxilo, oxo, o alquiltio C_1-C_3 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

en donde cada grupo sustituyente de R^5 está sustituido independientemente en forma opcional con un grupo sustituyente seleccionado de metilo, metoxi, fluoro, cloro, bromo, trifluorometilo, heteroarilo, heterociclilo, o amino en donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_5 o arilo; y

R^6 es alquilo C_1-C_6, alquenilo C_2-C_6, cicloalquilo C_3-C_6, trifluorometilo, fenilo, cicloalquil-C_3-C_6-alquilo C_1-C_3, fenil-alquilo C_1-C_3, fenil-haloalquilo C_1-C_3, cicloalquil-C_3-C_6 alquenilo C_2-C_3, fenil-alquenilo C_2-C_3, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^6 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, aminocarbonilo, alquilaminocarbonilo C_1-C_3, dialquilaminocarbonilo C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3, en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona,

o un tautómero, un profármaco, un solvato o sal del mismo.

28. El compuesto de Fórmula (ID) de acuerdo con la reivindicación 26, en el cual:

R^1 es tienilo, fenilo, naftilo, piridilo, cromanilo, dihidrobenzofuranilo, o benzofuranilo, cada uno independientemente en forma opcional sustituido con uno o dos grupos sustituyentes,

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en donde cada grupo sustituyente de R^1 es independientemente metilo, etilo, metoxi, etoxi, fluoro, cloro, bromo, hidroxi, trifluorometilo, ciano, o alquiltio C_1-C_6 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona;

R^2 y R^3 son cada uno metilo, en donde uno o ambos están independientemente sustituidos con hidroxi o metoxi;

R^4 es CH_2;

R^5 es un grupo piridilo, indolilo, azaindolilo, benzofuranilo, furanopiridinilo, tienopiridinilo, benzoxazolilo, benzoimidazolilo, quinolinilo, o isoquinolinilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^5 es independientemente metilo, fenilo, metoxicarbonilo, aminocarbonilo, metilaminocarbonilo, dimetilaminoamino-carbonilo, morfolinilcarbonilo, fluoro, cloro, bromo, ciano, o trifluorometilo; y

R^6 es alquilo C_1-C_6, cicloalquilo C_3-C_6, cicloalquilmetilo C_3-C_6, trifluorometilo, o bencilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^6 es independientemente metilo, metoxi, fluoro, cloro, bromo, ciano, trifluorometilo, o hidroxi,

o un tautómero, un profármaco, un solvato o sal del mismo.

29. El compuesto de Fórmula (ID) de acuerdo con la reivindicación 26, en el cual:

R^1 es fenilo, dihidrobenzofuranilo o benzofuranilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

en donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_3, alquenilo C_2-C_3, alquinilo C_2-C_3, alcoxi C_1-C_3, alqueniloxi C_2-C_3, alcanoilo C_1-C_3, alcoxicarbonilo C_1-C_3, alcanoiloxi C_1-C_3, halógeno, hidroxi, carboxi, ciano, trifluorometilo, nitro, o alquiltio C_1-C_3 en donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona, y

R^2 y R^3 son cada uno independientemente alquilo C_1-C_3 cada uno sustituido independientemente en forma opcional con hidroxi, alcoxi C_1-C_3,

o un tautómero, un profármaco, un solvato o sal del mismos.

30. Una composición farmacéutica que comprende una cantidad efectiva de un compuesto de acuerdo con una de las reivindicaciones 26 a 29, o un tautómero, profármaco, solvato o una sal del mismo, y a un excipiente o vehículo aceptables para uso farmacéutico.

31. Un método de modulación de la función del receptor de glucocorticoides en un paciente, comprendiendo el método administrar a un paciente una cantidad efectiva de un

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compuesto aceptable para uso farmacéutico de acuerdo con una de las reivindicaciones 1 a 11, 13 a 17, 19 a 24 o 26 a 29, o un tautómero, profármaco, solvato o una sal de los mismos.

32. Un método para tratar un estado o un cuadro patológico mediado por la función del receptor de glucocorticoides en un paciente con necesidad de tal tratamiento, comprendiendo el método administrar a un paciente una cantidad efectiva de un compuesto de uso farmacéuticamente aceptable de acuerdo con una de las reivindicaciones 1 a 11, 13 a 17, 19 a 24 o 26 a 29,, o un tautómero, profármaco, solvato o una sal del mismo.

33. Un método para tratar un estado o un cuadro patológico seleccionado de: diabetes tipo II, obesidad, enfermedades cardiovasculares, hipertensión, arterioesclerosis, enfermedades neurológicas, tumores adrenales o pituitarios y glaucoma, en un paciente con necesidad de tal tratamiento, comprendiendo el método administrar a un paciente una cantidad efectiva de un compuesto farmacéuticamente aceptable de acuerdo con una de las reivindicaciones 1 a 11, 13 a 17, 19 a 24 o 26 a 29, o un tautómero, profármaco, solvato o una sal del mismo.

34. Un método para tratar una enfermedad caracterizada por procesos inflamatorios, alérgicos o proliferativos, en un paciente con necesidad de tal tratamiento, comprendiendo el método administrar a un paciente una cantidad efectiva de un compuesto aceptable para uso farmacéutico de acuerdo con una de las reivindicaciones 1 a 11, 13 a 17, 19 a 24 o 26 a 29,, o un tautómero, profármaco, solvato o una sal del mismo.

35. El método según reivindicación 34, en el cual la enfermedad se selecciona de: (i) enfermedades pulmonares; (ii) enfermedades reumáticas/enfermedades autoinmunes/enfermedades articulares; (iii) enfermedades alérgicas; (iv) enfermedades vasculares; (v) enfermedades dermatológicas; (vi) enfermedades renales; (vii) enfermedades hepáticas; (viii) enfermedades gastrointestinales; (ix) enfermedades proctológicas; (x) enfermedades oculares; (xi) enfermedades del área de garaganta, nariz y oídos (ENT); (xii) enfermedades neurológicas; (xiii) enfermedades de la sangre; (xiv) enfermedades tumorales; (xv) enfermedades endocrinas; (xvi) transplantes de órganos y tejidos y enfermedades injerto-versus-huésped; (xvii) estados graves de shock; (xviii) terapia de sustitución; y (xix) dolor de génesis inflamatoria.

36. El método de acuerdo con la reivindicación 34, en el cual la enfermedad se selecciona de: diabetes tipo I, osteoartritis, síndrome de Guillain-Barre, restenosis luego de angioplastía coronaria transluminal percutánea, enfermedad de Alzheimer, dolores

graves y crónicos, ateroesclerosis, lesión de reperfusión, enfermedades de resorción ósea, falla cardiaca congestiva, infarto de miocardio, lesión térmica, lesión orgánica múltiple como consecuencia de traumas, meningitis grave purulenta, enterocolitis necrotizante, y síndromes asociados con hemodiálisis, leucoferesis y transfusión de granulocitos.

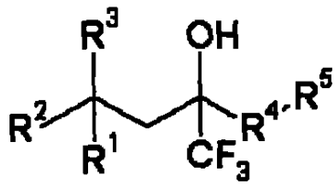
37. Un método para tratar un estado o un cuadro patológico mediado por la función del receptor de glucocorticoides en un paciente con necesidad de tal tratamiento, comprendiendo el método administrar en forma secuencial o simultánea al paciente: (a) una cantidad efectiva de un compuesto farmacéuticamente aceptable de acuerdo con una de las reivindicaciones 1 a 11, 13 a 17, 19 a 24 o 26 a 29, o un tautómero, profármaco, solvato o una sal del mismo; y (b) un glucocorticoide farmacéuticamente aceptable.

38. Un kit para la determinación diagnóstica *in vitro* de la función del receptor de glucocorticoides en una muestra que comprende:

(a) una cantidad efectiva con fines diagnósticos de un compuesto de acuerdo con una de las reivindicaciones 1, 13, 19 o 26, o un tautómero, profármaco, solvato o una sal del mismo; y

(b) instrucciones para el uso del kit de diagnóstico.

39. Un método para preparar un compuesto de Fórmula (IA)

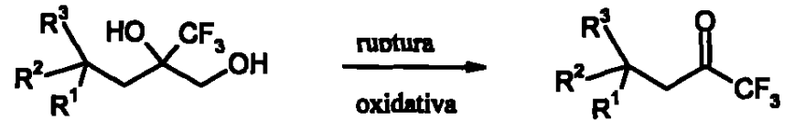


en el cual R^1, R^2, R^3, R^4 y R^5 son como se definió en la reivindicación 1, comprendiendo el método:

(a) hacer reaccionar un éster de Fórmula (II) con un agente reductor adecuado en un solvente adecuado para formar un diol de Fórmula (III)

II III

(b) hacer reaccionar el diol de Fórmula (III) en condiciones adecuadas de ruptura oxidativa para formar una cetona de Fórmula (IV)

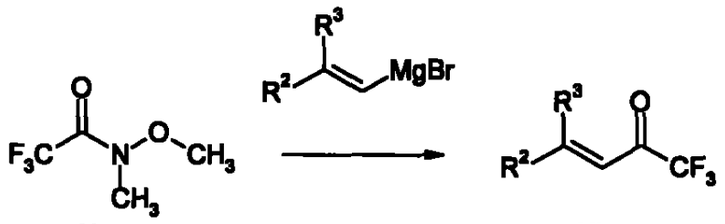


III IV ; y

(c) hacer reaccionar la cetona de Fórmula (IV) con un reactivo organometálico adecuado R^5R^4M en donde M es Li o MgX y X es Cl, Br, o I, en un solvente adecuado para formar el compuesto de Fórmula (IA)

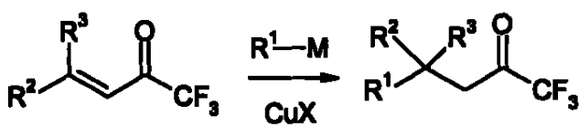
IV IA ; o

(a') hacer reaccionar la trifluoroacetamida de Fórmula (X) con un bromuro de vinil magnesio portador de R^2 y R^3 en un solvente adecuado para obtener la trifluorometilenona de Fórmula (XI)



X XI ;

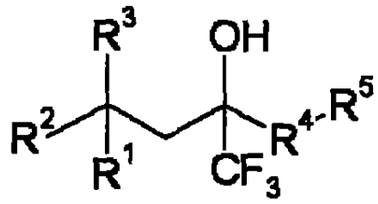
(b') hacer reaccionar la trifluorometilenona de Fórmula (XI) con un reactivo organocuproso adecuado producido a partir de un reactivo organometálico R^5R^4M, en donde M es Li o MgX y una sal de cobre CuX, en donde X es Cl, Br o I, en un solvente adecuado para formar la cetona de Fórmula (IV)



XI IV ; y

llevar a cabo el paso (c) como se indicó anteriormente.

40. Un método para preparar un compuesto de Fórmula (IA)

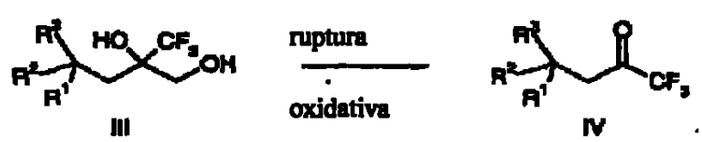


en donde R^1, R^2, R^3, R^4, y R^5 son como se definió en la reivindicación 1, comprendiendo el método:

(a") hacer reaccionar un éster de Fórmula (II) con un agente reductor adecuado en un solvente adecuado para formar un diol de Fórmula (III)

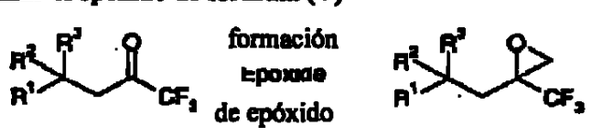
II III ;

(b'') hacer reaccionar el diol de Fórmula (III) en condiciones adecuadas de ruptura oxidativa para formar una cetona de Fórmula (IV)



III IV

(c'') **hacer reaccionar la cetona de Fórmula (IV) con un adecuado agente de epoxidación, tal como un iluro de azufre adecuado, en un solvente adecuado para formar el epóxido de fórmula (V)**

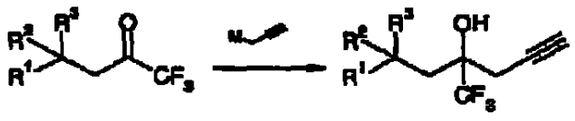


IV V ;

(d1'') hacer reaccionar el epóxido de Fórmula (V) con un reactivo acetiluro metálico adecuado, donde M es un metal adecuado y PG es un grupo protector adecuado, en un solvente adecuado para obtener un alquino intermediario protegido, seguido de eliminación del grupo protector para formar un alquino de Fórmula (XXXI)

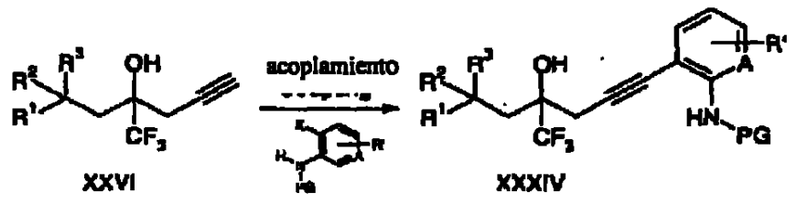
V XXXI

(d2'') hacer reaccionar la cetona de Fórmula (IV) con un reactivo de propargilo adecuado en un solvente adecuado para formar el alquino de Fórmula (XXXI)



IV XXXI

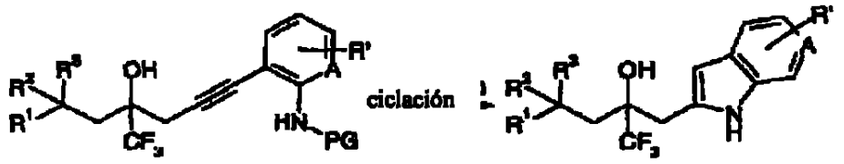
(e") hacer reaccionar el alquino de Fórmula (XXXI) con un compañero de acoplamiento adecuado, tal como anilinas o amino piridinas protegidas opcionalmente sustituidas, en las cuales R' es un sustituyente R^6 como se definió en la reivindicación 1, A es C o N, X es I o Br, y PG es H o un grupo protector adecuado, en presencia de catalizadores, bases y solventes adecuados para formar el alquino de Fórmula (XXXIV)



XXVI XXXIV

;y

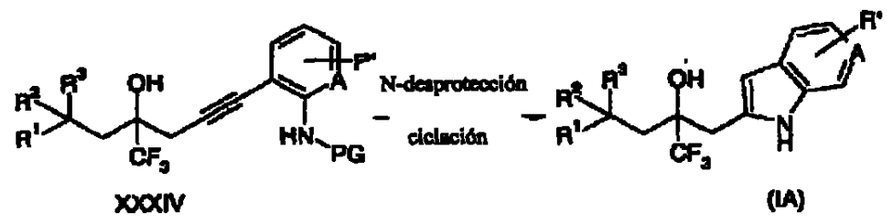
(f1") ciclar el alquino de Fórmula (XXXIV) en presencia de una base adecuada y en un solvente adecuado para formar el compuesto de Fórmula (IA)



XXXIV (IA)

o

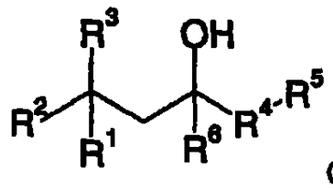
(f2") N-desproteger el compuesto de Fórmula (XXXIV) por reacción con un ácido adecuado en un solvente adecuado para formar una sal de amina, seguida de la ciclación de la sal de amina en presencia de una base adecuada y en un solvente adecuado para formar el compuesto de Fórmula (IA)



XXXIV (IA)

1047

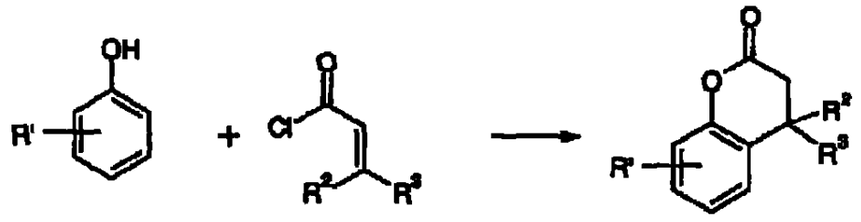
41. Un método para preparar un compuesto de Fórmula (IB)



(IB)

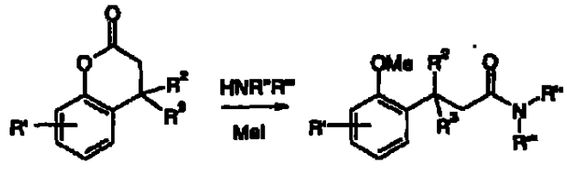
en el cual R^1, R^2, R^3, R^4, R^5, y R^6 son como se definió en la reivindicación 13, comprendiendo el método:

(a) hacer reaccionar un fenol opcionalmente sustituido de Fórmula (XV) con un cloruro de acriloílo de Fórmula (XVI) en presencia de una base adecuada, seguido de ciclación del éster intermediario por tratamiento con un ácido de Lewis adecuado para formar una lactona de Fórmula (XVII)



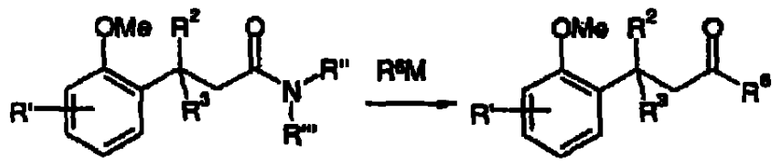
XV XVI XVII ;

(b) hacer reaccionar la lactona de Fórmula (XVII) con una amina HNR'R" adecuada, seguido del tratamiento del fenol intermediario con yoduro de metilo en presencia de una base adecuada para formar una amida de Fórmula (XVIII)



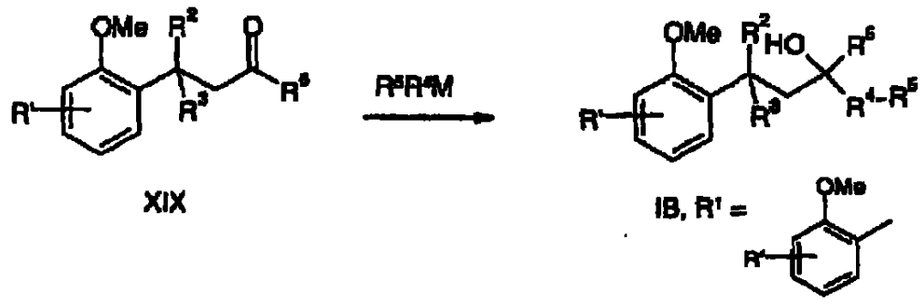
XVII XVIII ;

(c) hacer reaccionar la amida de Fórmula (XVIII) con un reactivo organometálico adecuado R^6M, donde M es Li o MgX y X es Cl, Br, o I, en un solvente adecuado para formar una cetona de Fórmula (XIX)



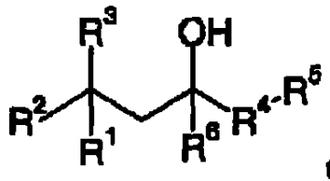
XVIII XIX

(d) hacer reaccionar la cetona de Fórmula (XIX) con un reactivo organometálico adecuado R^5R^4M, donde M es Li o MgX y X es Cl, Br, o I, en un solvente adecuado para formar el compuesto de Fórmula (IB)



XIX IB, R^1 =

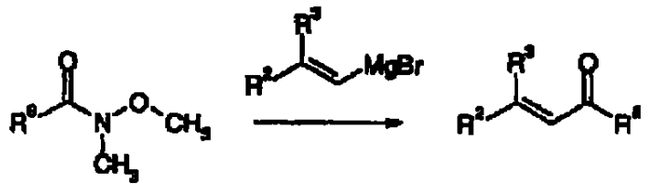
42. Un método para preparar un compuesto de Fórmula (IB)



(IB)

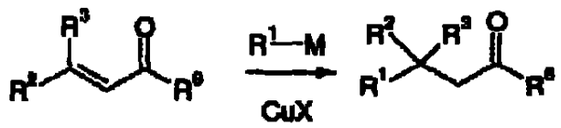
donde R^1, R^2, R^3, R^4, R^5, y R^6 son como se definió en la reivindicación 13, comprendiendo el método:

(a') hacer reaccionar una amida de Fórmula (XXXVI) con un compuesto bromuro de vinil magnesio portador de R^2 y R^3 en un solvente adecuado para obtener una enona de Fórmula (XXXVII)



XXXVI XXXVII ;

(b') hacer reaccionar la enona de Fórmula (XXXVII) con un reactivo organocuproso adecuado producido a partir de un reactivo organometálico R^1M, donde M es Li o MgX, y una sal de cobre CuX, donde X es Cl, Br o I, en un solvente adecuado para formar una cetona de Fórmula (XX)



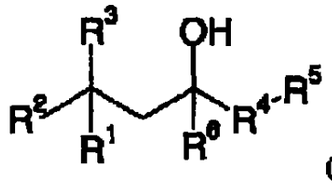
XXXVII XX

y

(c') hacer reaccionar la cetona de Fórmula (XX) con un reactivo organometálico adecuado R^5R^4M, donde M es Li o MgX, y X es Cl, Br o I, en un solvente adecuado para formar el compuesto de Fórmula (IB)

XX IB

43. Un método para preparar un compuesto de Fórmula (IB)



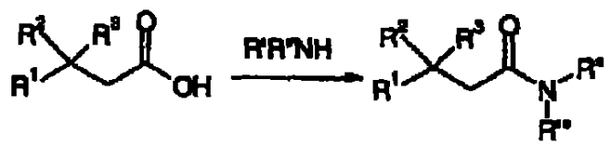
(IB)

donde R^1, R^2, R^3, R^4, R^5, y R^6 son como se definió en la reivindicación 13, comprendiendo el método:

(a") hacer reaccionar una cetona de Fórmula (IV) con una base adecuada y en una mezcla de solventes adecuada para obtener un ácido de Fórmula (XXIX)

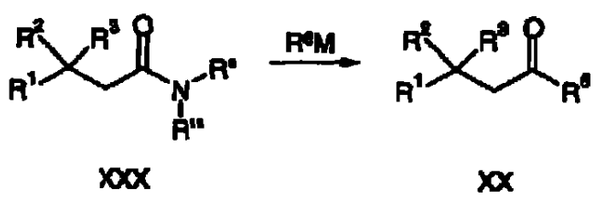
;

(b") hacer reaccionar el ácido de Fórmula (XXIX) con una amina adecuada $HNR^{n}R^{m}$, de modo que $-NR^{n}R^{m}$ funcionará como grupo saliente en la siguiente reacción, en condiciones de acoplamiento adecuadas para formar la amida de Fórmula (XXX)



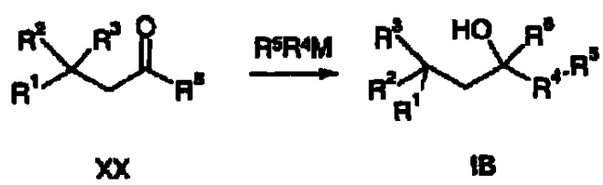
;

(c") hacer reaccionar la amida de Fórmula (XXX) con un reactivo organometálico adecuado, tal como un reactivo de Grignard, donde M es MgBr o MgCl, o un reactivo organolitio, donde M es Li, en un solvente adecuado para obtener una cetona de Fórmula (XX)

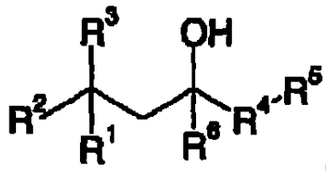


y

(d") hacer reaccionar la cetona de Fórmula (XX) con un reactivo organometálico adecuado R^5R^4M, donde M es Li o MgX, y X es Cl, Br o I, en un solvente adecuado para formar el compuesto de Fórmula (IB)



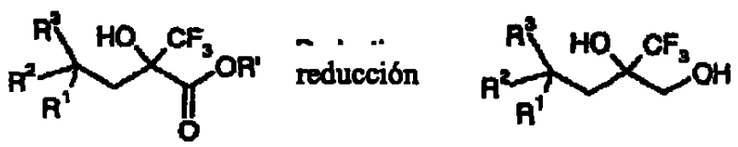
44. Un método para preparar un compuesto de Fórmula (IC)



(IC)

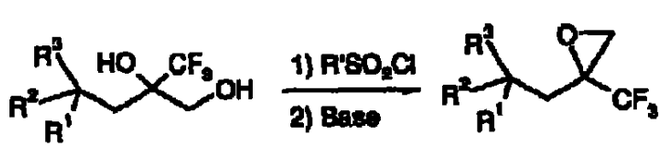
donde R^1, R^2, R^3, R^4, R^5, y R^6 son como se definió en la reivindicación 19, comprendiendo el método:

(a) hacer reaccionar un éster de Fórmula (II) con un agente reductor adecuado en un solvente adecuado para formar un diol de Fórmula (III)



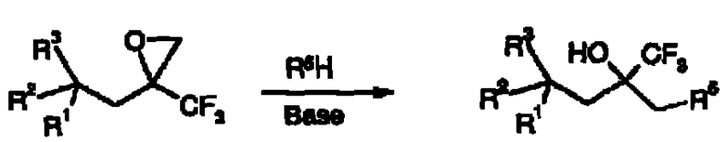
II III

(b) hacer reaccionar el diol de Fórmula (III) con un reactivo cloruro de alquil o arilsulfonilo adecuado, de modo tal que $R'SO_2O$ actúe como grupo saliente en el próximo paso, seguido de la reacción del intermediario resultante con una base adecuada para obtener un epóxido de Fórmula (V)



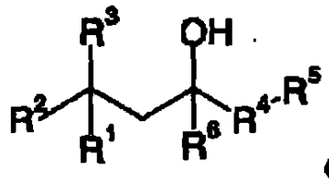
III V

(c) hacer reaccionar el epóxido de Fórmula (V) con un nucléofilo adecuado R^6H, en presencia de una base adecuada, para obtener el compuesto de Fórmula (IC)



V IC

45. Un método para preparar un compuesto de Fórmula (IC)



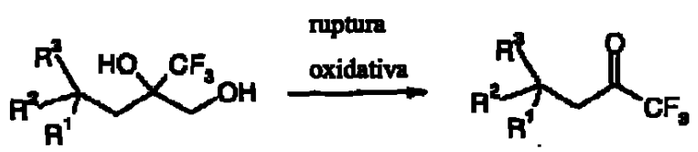
(IC)

donde R^1, R^2, R^3, R^4, R^5, y R^6 son como se definió en la reivindicación 19, comprendiendo el método:

(a') hacer reaccionar un éster de Fórmula (II) con un agente reductor adecuado en un solvente adecuado para formar un diol de Fórmula (III)

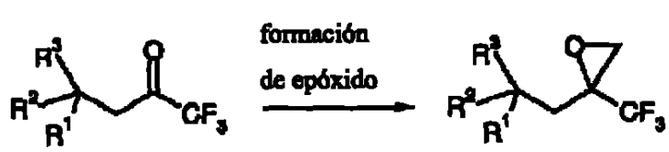
II III ;

(b') hacer reaccionar el diol de Fórmula (III) en condiciones adecuadas de ruptura oxidativa para formar una cetona de Fórmula (IV)



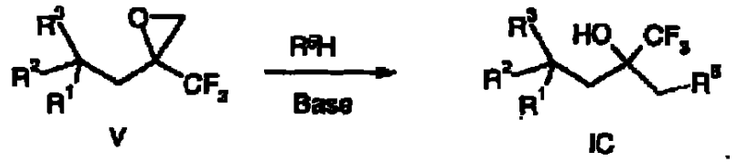
III IV ;

(c') hacer reaccionar la cetona de Fórmula (IV) con un agente de epoxidación adecuado, tal como un iluro de azufre adecuado, en un solvente adecuado para obtener un epóxido de Fórmula (V)



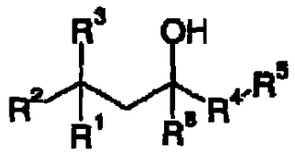
y

(d') hacer reaccionar el epóxido de Fórmula (V) con un nucleófilo apropiado R^5H, en presencia de una base adecuada, para obtener el compuesto de Fórmula (IC).



V IC

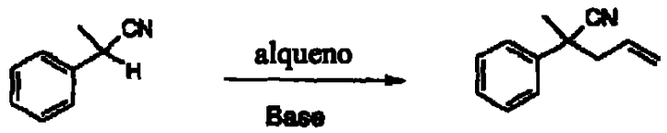
46. Un método para preparar un compuesto de Fórmula (ID)



(ID)

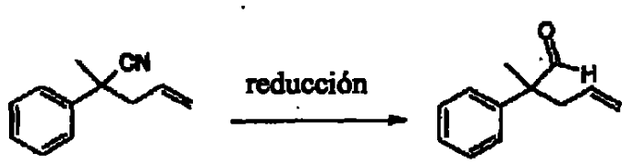
donde R^1, R^2, R^3, R^4, R^5, y R^6 son como se definió en la reivindicación 26, comprendiendo el método:

(a) hacer reaccionar un ciano compuesto de Fórmula (XXXVIII) con un alqueno adecuado en presencia de una base adecuada para obtener un alqueno de Fórmula (XXXIX)



XXXVIII XXXIX ;

(b) hacer reaccionar el alqueno de Fórmula (XXXIX) con un agente reductor adecuado para obtener un aldehído de Fórmula (XXXX)



XXXIX XXXX ;

(c) hacer reaccionar el aldehído de Fórmula (XXXX) con un agente reductor adecuado

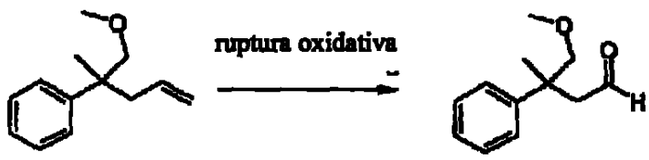
para obtener un alcohol de Fórmula (XXXXI)

XXXX XXXXI .

(d) hacer reaccionar el alcohol de Fórmula (XXXXI) con un agente alquilante adecuado en presencia de una base adecuada para obtener un éter de Fórmula (XXXXII)

XXXXI XXXXII ;

(e) hacer reaccionar el éter de Fórmula (XXXXII) en condiciones de ruptura adecuadas para obtener un aldehído de Fórmula (XXXXIII)



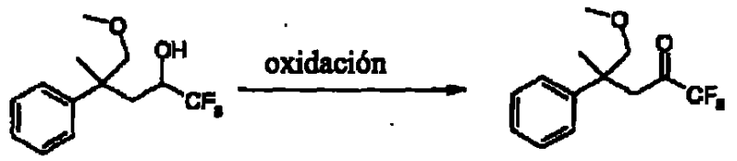
XXXXII XXXXIII ;

(f) hacer reaccionar el aldehído de Fórmula (XXXXIII) con un reactivo nucleofílico de trifluorometilación para obtener el trifluorometil alcohol de Fórmula (XXXXIV)

XXXXIII XXXXIV :

1055

(g) hacer reaccionar el trifluorometil alcohol de Fórmula (XXXXIV) con un reactivo oxidante adecuado para obtener la trifluorometilcetona de Fórmula (XXXXV)



XXXXIV XXXXV

(h) hacer reaccionar la cetona de Fórmula (XXXXV) con un reactivo organometálico adecuado R^5R^4M, donde M es Li o MgX, y X es Cl, Br o I, en un solvente adecuado para formar el compuesto de Fórmula (ID)

XXXXV ID

1034
1029
1056

PCT/US2004/031009

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JAN 31 2006
PATENT SECTION

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

To:

RAYMOND, Robert, P.
Boehringer Ingelheim Corporation
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877-0368
United States of America

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

Date of mailing (day/month/year)	
19 January 2006 (19.01.2006)	
Applicant's or agent's file reference: 9-289PCT	IMPORTANT NOTIFICATION
International application No.: PCT/US2004/031009	International filing date (day/month/year): 22 September 2004 (22.09.2004)

1. The following indications appeared on record concerning:
[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address	State of Nationality	State of Residence
BETAGERI, Rajashekar		
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:
[ ] the person [X] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address	State of Nationality	State of Residence
BETAGERI, Rajashekhar		
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

3. Further observations, if necessary:
The request for recording of the above change was received by the International Bureau between 20 and 30 months from the priority date.

4. A copy of this notification has been sent to:
[X] the receiving Office
[ ] the International Searching Authority
[X] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer T. Vernhes (Fax 338-8965)
Facsimile No. (41-22) 338.89.85	Telephone No. (41-22) 338 8938

Form PCT/IB/306 (March 1994)

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PCT/US2004/031009

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

RAYMOND, Robert, P.
Boehringer Ingelheim Corporation
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877-0368
United States of America

Date of mailing (day/month/year): 19 January 2006 (19.01.2006)	
Applicant's or agent's file reference: 9-289PCT	IMPORTANT NOTIFICATION
International application No.: PCT/US2004/031009	International filing date (day/month/year): 22 September 2004 (22.09.2004)

1. The following indications appeared on record concerning:
[X] the applicant [X] the inventor [ ] the agent [ ] the common representative

Name and Address: HARCKEN, Hanka, Justus, Joachim

State of Nationality | State of Residence
Telephone No.
Facsimile No.
Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:
[ ] the person [X] the name [ ] the address [ ] the nationality [ ] the residence

Name and Address: HARCKEN, Christian, H.J.J.

State of Nationality | State of Residence
Telephone No.
Facsimile No.
Teleprinter No.

3. Further observations, if necessary:
The request for recording of the above change was received by the International Bureau between 20 and 30 months from the priority date.

4. A copy of this notification has been sent to:
[X] the receiving Office
[ ] the International Searching Authority
[X] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No. (41-22) 338.88.85

Authorized officer: T. Vernhes (Fax 338-8995)
Telephone No. (41-22) 338 8838

Form PCT/IB/306 (March 1994) 000666160

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
9-289PCT		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US2004/031009	22/09/2004	24/09/2003
Applicant		
BOEHRINGER INGELHEIM PHARMACEUTICALS, INC.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
      [ ] The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
   b. [ ] With regard to any nucleotide and/or amino acid sequence disclosed in the international application, see Box No. I.

2. [ ] Certain claims were found unsearchable (See Box II).

3. [ ] Unity of invention is lacking (see Box III).

4. With regard to the title,
   [ ] the text is approved as submitted by the applicant.
   [X] the text has been established by this Authority to read as follows:

   1,1,1-TRIFLUORO-4-PHENYL-4-METHYL-2-(1H-PYRROLO'2,3-C|PYRIDIN-2-YLMETHYL) PENTAN-2-OL DERIVATIVES AND RELATED COMPOUNDS AS GLUCOCORTICOID LIGANDS FOR THE TREATME NT OF INFLAMMATORY DISEASES AND DIABETES

5. With regard to the abstract,
   [X] the text is approved as submitted by the applicant.
   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the drawings,
   a. the figure of the drawings to be published with the abstract is Figure No. _____
      [ ] as suggested by the applicant.
      [ ] as selected by this Authority, because the applicant failed to suggest a figure.
      [ ] as selected by this Authority, because this figure better characterizes the invention.
   b. [ ] none of the figures is to be published with the abstract.

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/4745 A61K31/52 C07D471/04 C07D487/04 C07D495/04
C07D491/04 C07D405/10 C07D307/79 A61P5/44 A61P5/46

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

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B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C07D A61P

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

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

EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 03/059899 A1 (BOEHRINGER INGELHEIM PHARMACEUTICALS INC (US)) 24 July 2003 (2003-07-24) the whole document	1-46
P,X	WO 03/082280 A1 (BOEHRINGER INGELHEIM PHARMACEUTICALS INC (US)) 9 October 2003 (2003-10-09) the whole document	1-46
P,X	WO 03/082787 A1 (BOEHRINGER INGELHEIM PHARMACEUTICALS INC (US)) 9 October 2003 (2003-10-09) the whole document	1-46
P,X	WO 2004/063163 A1 (BOEHRINGER INGELHEIM PHARMACEUTICALS INC (US)) 29 July 2004 (2004-07-29) the whole document	1-46

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

☒ Patent family members are listed in annex.

* Special categories of cited documents :

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

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

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

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

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
26 January 2005	03/02/2005

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

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INTERNATIONAL SEARCH REPORT

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

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: 1060

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

Although claims 31-37 are directed to a method of treatment of the human body, the search has been carried out and based on the alleged effects of the compounds.

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

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

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

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

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

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

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

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

Remark on Protest

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

[ ] No protest accompanied the payment of additional search fees.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 03059899 A1	24-07-2003	CA 2472746 A1	24-07-2003
		EP 1467982 A1	20-10-2004
		US 2003232823 A1	18-12-2003
WO 03082280 A1	09-10-2003	BR 0308784 A	11-01-2005
		CA 2478156 A1	09-10-2003
		EP 1490062 A1	29-12-2004
		US 2004023999 A1	05-02-2004
WO 03082787 A1	09-10-2003	CA 2477764 A1	09-10-2003
		EP 1490317 A1	29-12-2004
		US 2004029932 A1	12-02-2004
WO 2004063163 A1	29-07-2004	US 2004162321 A1	19-08-2004

From the
INTERNATIONAL SEARCHING AUTHORITY

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To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2004/031009	22.09.2004	24.09.2003

International Patent Classification (IPC) or both national classification and IPC
A61K31/4745, A61K31/52, C07D471/04, C07D487/04, C07D495/04, C07D491/04, C07D405/10, C07D307/79,

Applicant
BOEHRINGER INGELHEIM PHARMACEUTICALS, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Cortés, J Telephone No. +49 89 2399-8206

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☐ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 31-37

because:

☒ the said international application, or the said claims Nos. 31-37 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-46
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-46
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-30, 38-46
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 31-37 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion with regard to the industrial applicability will be formulated for these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The following documents have been cited in the International Search Report:

D1: WO 03/059899 A1 (BOEHRINGER INGELHEIM PHARMACEUTICALS INC (US)) 24 July 2003 (2003-07-24)

Novelty (Article 33(2) PCT)

The present compounds differ from the compounds in D1 in the group R4. The present claim set is therefore novel.

Inventive Step (Article 33(3) PCT)

D1 discloses glucocorticoid ligands and could be regarded as the closest prior art.

The problem of the invention was the provision of new glucocorticoid ligands.

The present compounds are not suggested by D1. The present in invention is therefore based on an inventive step.

Clarity (Article 6 PCT)

Many of the examples in the description are not encompassed by the claims (e.g. examples 1-73, 76, etc., p. 324, 1st compound, etc.)

Re Item VI
Certain documents cited

Reference is made to the following P-documents:

D2: WO 03/082280 A1 (BOEHRINGER INGELHEIM PHARMACEUTICALS INC (US)) 9 October 2003 (2003-10-09)

D3: WO 03/082787 A1 (BOEHRINGER INGELHEIM PHARMACEUTICALS INC (US)) 9 October 2003 (2003-10-09)

D4: WO 2004/063163 A1 (BOEHRINGER INGELHEIM PHARMACEUTICALS INC (US)) 29 July 2004 (2004-07-29)

The priority documents pertaining to the present application were not available at the time of establishing this report. Hence, it is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct, the P-documents cited in the international search report could become relevant to asses whether the present claims satisfy the criteria set forth in Article 33(1) PCT.

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

IPEA/ EPO

PCT

CHAPTER II

DEMAND

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

For International Preliminary Examining Authority use only

Identification of IPEA	Date of receipt of DEMAND

Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION

Applicant's or agent's file reference: 9-289PCT

International application No.	International filing date (day/month/year)	(Earliest) Priority date (day/month/year)
PCT/US2004/031009	22 Sep 2004	24 Sep 2003

Title of invention: Glucocorticoid Mimetics, Methods of Making Them, Pharmaceutical Compositions and Uses Thereof

Box No. II APPLICANT(S)

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

BOEHRINGER INGELHEIM PHARMACEUTICALS, INC.
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

Telephone No.: 203-798-9988
Facsimile No.: 203-798-4408
Teleprinter No.:
Applicant's registration No. with the Office:

State *(that is, country)* of nationality: US
State *(that is, country)* of residence: US

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

BEKKALI, Younes
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality: CA
State *(that is, country)* of residence: US

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

BETAGERI, Rajashehar
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900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality: IN
State *(that is, country)* of residence: US

[X] Further applicants are indicated on a continuation sheet.

International application No.
PCT/US2004/031009

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Continuation of Box No. II APPLICANT(S)

If none of the following sub-boxes is used, this sheet should not be included in the demand.

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

EMMANUEL, Michael, J.
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
HT	US

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

HAMMACH, Abdelhakim
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
US	US

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

HARCKEN, Hanke, Justus, Joachim
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
DE	US

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

KIRRANE, Thomas, Martin
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
US	US

☒ Further applicants are indicated on another continuation sheet.

International application No.
PCT/US2004/031009

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Continuation of Box No. II APPLICANT(S)

If none of the following sub-boxes is used, this sheet should not be included in the demand.

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

KUZMICH, Daniel
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900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
US	US

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

LEE, Thomas, Wai-Ho
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900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
US	US

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

LIU, Pingrong
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
CN	US

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

PATEL, Usha, R.
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
US	US

☒ Further applicants are indicated on another continuation sheet.

International application No.
PCT/US2004/031009

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Continuation of Box No. II APPLICANT(S)

If none of the following sub-boxes is used, this sheet should not be included in the demand.

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

RAZAVI, Hossein
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
IR	US

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

REITHER, Doris
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
AT	US

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

TAKAHASHI, Hidenori
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
JP	US

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

THOMSON, David, S.
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
GB	US

☒ Further applicants are indicated on another continuation sheet.

International application No.
PCT/US2004/031009

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1073

Continuation of Box No. II APPLICANT(S)

If none of the following sub-boxes is used, this sheet should not be included in the demand.

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

WANG, Ji
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
CN	US

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

ZINDELL, Renee
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
US	US

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

PROUDFOOT, John, Robert
Boehringer Ingelheim Pharmaceuticals, Inc.
900 Ridgebury Road
P.O. Box 368
Ridgefield, Connecticut 06877 USA

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
IE	US

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

State *(that is, country)* of nationality:	State *(that is, country)* of residence:

☐ Further applicants are indicated on another continuation sheet.

International application No.
PCT/US2004/031009

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

The following person is ☒ agent ☐ common representative

and ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.

☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.

☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

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

MORRIS, Michael P.; DEVLIN, Mary-Ellen M.; STEMPEL, Alan, R.; WITKOWSKI, Timothy, X.; BOTTINO, Anthony, P.; DATLOW, Philip, I.; POCCHIARI, Susan, K.; DOW, David, A.; SMALL, Andrea, D.; BLANKINSHIP, Thomas, C.
Boehringer Ingelheim Corp.
900 Ridgebury Road, P.O. Box 368
Ridgefield, CT 06877-0368

Telephone No.
203-798-9988

Facsimile No.
203-798-4408

Teleprinter No.

Agent's registration No. with the Office

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

Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION

Statement concerning amendments:*

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

☒ the international application as originally filed

the description
☒ as originally filed
☐ as amended under Article 34

the claims
☒ as originally filed
☐ as amended under Article 19 (together with any accompanying statement)
☐ as amended under Article 34

the drawings
☐ as originally filed
☐ as amended under Article 34

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

3. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of the applicable time limit under Rule 69.1(d).

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

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

Language for the purposes of international preliminary examination: English

☒ which is the language in which the international application was filed.
☐ which is the language of a translation furnished for the purposes of international search.
☐ which is the language of publication of the international application.
☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.

Box No. V ELECTION OF STATES

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

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Sheet No. 7.

International application No.
PCT/US2004/031009

Box No. VI CHECK LIST

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

			For International Preliminary Examining Authority use only: received	not received
1. translation of international application	:	sheets	☐	☐
2. amendments under Article 34	:	sheets	☐	☐
3. copy (or, where required, translation) of amendments under Article 19	:	sheets	☐	☐
4. copy (or, where required, translation) of statement under Article 19	:	sheets	☐	☐
5. letter	:	sheets	☐	☐
6. other *(specify)*	:	sheets	☐	☐

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

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

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

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

Timothy Witkowski

Timothy X. Witkowski, Agent

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:

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

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

For International Bureau use only

Demand received from IPEA on:

[redacted]

F RMATO DE DIGITALIZACIO
RELACION DE ANEXOS

Royal Technologies S.A.

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Item		Expediente No 06038137	No de Folio
		No de unidades	√
1	CD		
2	DVD		
3	REVISTA		
4	LIBRO		
5	PERIODICO		
6	DISQUETES		
7	SOBRE DE MANILA		
8	SOBRE BLANCO TAMAÑO CARTA X	1	
9	SOBRE BLANCO TAMAÑO OFICIO		
10	OTROS:		

Observaciones:

Arte final

1077

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

RECIBO OFICIAL DE CAJA : 06 - 19,913
FECHA : MARZO 13 DE 2006

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
Rad: 06-038137- -00000-0000 Fec: 2006-04-21 18:05:56
Dep: 2020 NUECREACIONES
Tra: 11 PATENTEIYII Eva 379 FASENACIONALII
Act 411 PRESENTACION Folios: 1051

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

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
CAVELIER ABOGADOS	CONSIGNACION	BANCO POPULAR	050-00110-6	49935721	13/03/2006	38,686,520.00

C O N C E P T O

CANT.	REMTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01 SOLICITUDES	1 TRAMITES DE SOL. DE PATENTE DE IN	463,000.00
		TOTAL : $	463,000.00

SON: CUATROCIENTOS SESENTA Y TRES MIL PESOS

RESPONSABLE : _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No. _____

Cobo 07612-891-02-3

1052.1078

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
Rad: 06-038137- -00000-0000 Fec: 2006-04-21 16:05:56
Dep: 2020 NUECREACIONES
Tra: 11 PATENTEYII Eve 379 FASENACIONALII
Act 411 PRESENTACION Folios: 1051

Industria y Comercio

SUPERINTENDENCIA

Delegatura de Propiedad Industrial
División de Nuevas Creaciones

REQUISITOS NECESARIOS PARA PRESENTACIÓN Y AGILIZACIÓN DEL TRAMITE

PEI

	USUARIO	RADICADOR
PATENTE DE INVENCIÓN ( ) MODELO DE UTILIDAD ( )	( )	( )
-Indicación de que se solicita la concesión de una patente.	( )	(X)
-Datos de identificación del solicitante o de la persona que se presenta la solicitud.	( )	(X)
-Descripción de la invención.	( )	(X)
-Dibujos de ser estos pertinentes.	( )	(X)
-Comprobante de Pago de las tasas establecidas.	( )	(X)
COMPLETA (X) INCOMPLETA ( )	( )	( )
DISEÑO INDUSTRIAL ( )		
-Indicación de que se solicita el registro de Diseño Industrial.	( )	( )
-Datos de identificación del solicitante o de la persona que se 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 ( )		
-Indicación de que se solicita el registro de Diseño Industrial.	( )	( )
-Datos de identificación del solicitante o de la persona que se presenta la solicitud.	( )	( )
-Representación gráfica del Esquema Trazado.	( )	( )
-Comprobante de Pago de las tasas establecidas.	( )	( )
COMPLETA ( ) INCOMPLETA ( )	( )	( )

Firma Responsable: _____

Fecha: _____

1079

Industria y Comercio
SUPERINTENDENCIA

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

(21) N° de solicitud: 06-38137

22) Fecha de solicitud: 2006-04-21

(30) Prioridad (31) 60/505,456 (32) 24/09/2003 (33) US
60/507,079 29/09/2003 US

(51) Int Cl: A61K 31/475 , 31/52, C07D471/04, 487/04, 495/04, 491/04, 405/10, 307/79, A61P5/44, 5/46

(71)Solicitante(s) BOEHRINGER INGELHEIM PHARMACEUTICALS, INC

(72) Inventor(es) YOUNES BEKKALI
Y OTROS

(74) Apoderado: EMILIO FERRERO

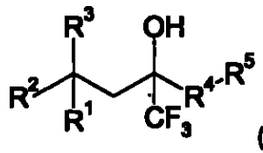
(85) Fecha límite inicio fase nacional: 24/04/2003
(86) Datos relativos a la presentación de la solicitud PCT
Fecha de presentación de la solicitud: 22/09/2004
No. de solicitud PCT/US2004/031009

(87) Publicación Internacional
Fecha: 07/04/2005
N° publicación: WO 2005/030213 A1

(54) Título: **MIMETICOS DE GLUCOCORTICOIDES, METODOS DE PREPARACION, COMPOSICIONES FARMACEUTICAS Y USOS DE LOS MISMOS**

REIVINDICACIONES

1. Un compuesto de Fórmula (IA)



(IA)

en el cual:

R^1 es un grupo arilo o heteroarilo, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^1 es independientemente alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, cicloalquilo C_3-C_8, heterociclilo, arilo, heteroarilo, alcoxi C_1-C_8, alqueniloxi C_2-C_8, alquiniloxi C_2-C_8, ariloxi, acilo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_8, alcanoilo C_1-C_8, arolio, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilaminocarboniloxi C_1-C_8, dialquilaminocarboniloxi C_1-C_8, alcanoilamino C_1-C_8, alcoxicarbonilamino C_1-C_8, alquilsulfonilamino C_1-C_8, aminosulfonilo, alquilaminosulfonilo C_1-C_8, dialquilaminosulfonilo C_1-C_8, halógeno, hidroxi, carboxi, ciano, trifluorometilo, trifluorometoxi, nitro, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_8; o alquiltio C_1-C_8 donde el átomo de azufre en forma opcional está oxidado a sulfóxido o sulfona, donde cada grupo sustituyente de R^1 está independientemente sustituido en forma opcional con uno a tres grupos sustituyentes seleccionados de metilo, metoxi, halógeno, hidroxi, oxo, ciano, heteroarilo, heterociclilo, o amino donde el átomo de nitrógeno en forma opcional está independientemente mono- o di-sustituido con alquilo C_1-C_8 o arilo; o ureido donde el átomo de nitrógeno en forma opcional está independientemente sustituido con alquilo C_1-C_8;

R^2 y R^3 son cada uno independientemente hidrógeno o alquilo C_1-C_8, o R^2 y R^3 junto con el átomo de carbono al que están unidos usualmente forman un anillo espiro cicloalquilo C_3-C_8;

R^4 es alquilo C_1-C_8, alquenilo C_2-C_8, o alquinilo C_2-C_8, cada uno sustituido independientemente en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^4 es independientemente alquilo C_1-C_8, hidroxi, halógeno, amino u oxo; y

R^5 es un grupo heteroarilo independientemente sustituido en forma opcional con uno a tres grupos sustituyentes,

donde cada grupo sustituyente de R^5 es independientemente alquilo C_1-C_8, alquenilo C_2-C_8, alquinilo C_2-C_8, cicloalquilo C_3-C_8, heterociclilo, arilo, heteroarilo, alcoxi C_1-C_8, alqueniloxi C_2-C_8, alquiniloxi C_2-C_8, ariloxi, acilo, alcoxicarbonilo C_1-C_8, alcanoiloxi C_1-C_8, heterociclilcarbonilo, arolio, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aminocarboniloxi, alquilamino-carboniloxi C_1-C_8,

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(86) PCT

Solicitud Internacional No. PCT/US2004/031009 Fecha: 22 de septiembre de 2004

Publicación Internacional No. WO 2005/030213 A1 Fecha: 7 de abril de 2005

(54) Título

MIMETICOS DE GLUCOCORTICOIDES, METODOS DE PREPARACION, COMPOSICIONES FARMACEUTICAS Y USOS DE LOS MISMOS

(51) Clasificación Internacional: A61K 31/475, 31/52, C01D471/04, 471/04, 495/04, 491/04, 405/10, 307/79, A61P5/44, 5/26

(30) Prioridad	(33) País de Origen	(32) Fecha	(31) Número de Solicitud
SI☒ NO☐	US	24 de septiembre de 2003	60/505.456
	US	29 de septiembre de 2003	60/507.078

(19) Comprobante de pago No.: 06-19.913 Fecha: marzo 13 de 2006

Industria y Comercio
SUPERINTENDENCIA

PETITORIO

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
Rad 06-038137 -00000-0000 Fec 2006-04-21 18:05:58
Dep. 2020 NUECREACIONES
Tra. 11 PATENTEIYII Eve 379 FASENACIONALII
Act 411 PRESENTACION Folios: 1061

FORMULARIO UNICO DE SOLICITUD DE PATENTE
PCT
ENTRADA EN FASE NACIONAL 24-04-2006

1 SOLICITUD DE

☒ Patente de Invención ☐ Patente de Modelo de Utilidad
☐ Capítulo I ☒ Capítulo II

2 SOLICITANTE (71)

Nombre. BOEHRINGER INGELHEIM PHARMACEUTICALS INC
sociedad constituida y existente bajo las leyes del Estado de Delaware Estados Unidos de América.

Dirección 900 Ridgebury Road
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Connecticut 06877-0368
Estados Unidos de América

Domicilio Ridgefield
Connecticut 06877-0368
Estados Unidos de América

IDENTIFICACIÓN
C C ☐ NIT ☐
C E ☐ Otro ☐
Cual
Número

3 REPRESENTANTE O APODERADO

Nombre EMILIO FERRERO
Dirección Carrera 4ª No 72-35
Teléfono 347 36 11
Fax 211 86 50
E-mail clientes@camyp.com.
Domicilio Bogotá Colombia

IDENTIFICACIÓN
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C E ☐ Otro ☐
Cual
Numero 438 019 T P 31.929

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1053
1082

REPUBLICA DE COLOMBIA
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

Bogotá,
2020

Doctor(a)
FERRERO EMILIO
Apoderado(a) y/o Representante de
BOEHRINGER INGELHEIM PHARMACEUTICALS INC

REFERENCIA	Radicación No.	06 38137
	Solicitud internacional	US2004/031009
	Fecha inicio fase nacional	24/04/2006
	Trámite	11
	Evento	379
	Actuación	430
	Oficio No.	8442

Como resultado del examen de forma, realizado con fundamento en el artículo 38 de la Decisión 486 de la Comisión de la Comunidad Andina, artículo 27 del Tratado de Cooperación en Materia de Patentes (PCT), regla 51 bis del Reglamento y Circular Única de la Superintendencia de Industria y Comercio, se le comunica que:

1. Si fuere el caso, el solicitante debe adjuntar la traducción de los anexos del reporte de examen preliminar internacional (Art. 36.2.b) del tratado PCT.

En cumplimiento de lo dispuesto por el artículo 39 de la Decisión 486, se le requiere para que dentro del término de dos meses siguientes a la fecha de notificación del presente oficio, complete los requisitos anteriormente enunciados. En caso de no dar cumplimiento al presente requerimiento, la solicitud se considerará abandonada y perderá su prelación.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Unica No.10 de 2001.

ALIX CARMENZA CESPEDES DE VERGEL
Jefe de la división de Nuevas Creaciones

El anterior requerimiento fue notificado por fijación en lista de fecha 04 AGO. 2006
jramos

04-09-06