Industria y Comercio
SUPERINTENDENCIA

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FORMULARIO UNICO DE SOLICITUD DE PATENTE PCT
ENTRADA EN FASE NACIONAL

1 SOLICITUD DE:

☒ Patente de Invención. ☐ Patente de Modelo de Utilidad.

☐ Capítulo I. ☒ Capítulo II.

2 SOLICITANTE (71)	Nombre: **SYNAPTIC PHARMACEUTICAL CORPORATION** sociedad constituida y existente bajo las leyes del estado de New Jersey, Estados Unidos de América Dirección: 215 College Road, Paramus, New Jersey 07652 Estados Unidos de América Domicilio: New Jersey, Estados Unidos de América	**IDENTIFICACION** 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:: 217 92 11 E-mail: clientes@camyp.com. Domicilio: Bogotá, Colombia.	**IDENTIFICACION** C.C. ☒ NIT ☐ C.E. ☐ Otro ☐ Cual_____ Número: 438.019 T.P. 31.929

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2

(5) **PCT (86)**

Solicitud Internacional No. PCT/US02/21063 Fecha: 03 de julio de 2002

Publicación Interancional No. WO 03/004027 A1 Fecha: 16 de enero de 2003

(6) **Título (54)**

PIPERIDINAS ANÍLINICAS SUSTITUIDAS COMO ANTAGONISTAS SELECTIVOS DE LA HORMONA DE CONCENTRACIÓN DE MELANINA

(7) **Clasificación Internacional (51)** A61K 31/445

(8)

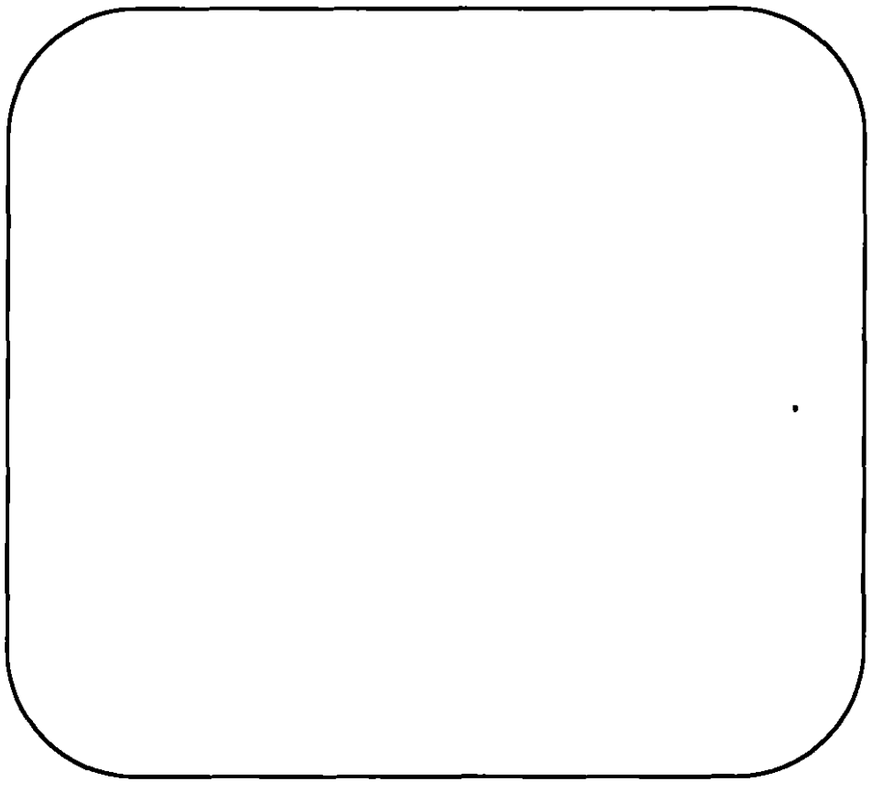
Prioridad	(33) País de Origen	(32) Fecha	(31) Número de Solicitud
SI ☒ NO ☐	US	05 de julio de 2001	09/899,794
	US	09 de enero de 2002	10/042,582

(9) **Comprobante de pago No.:** 04 – 23,596 **Fecha:** 19 de enero de 2004

(10) **Anexos:**

- ☒ Comprobante de pago de la tasa de presentación de la solicitud por $ 422.000.oo.
- ☐ Comprobante de pago por reivindicación de prioridad.
- ☒ Documento que acredita la existencia y representación legal cuando el solicitante sea persona jurídica.
- ☒ Poderes, si fuere el caso.
- ☐ Documento de cesión del inventor al solicitante o a su causante.
- ☐ Declaraciones.
- ☒ Copia de la solicitud internacional. (Resumen, descripción, reivindicaciones, dibujos)
- ☒ Traducción de la solicitud internacional al castellano. (Resumen, descripción, reivindicaciones, dibujos)
- ☒ Copia del examen preliminar efectuado por la IPEA.
- ☒ Traducción del examen preliminar efectuado por la IPEA.
- ☐ De ser el caso, copia del contrato de acceso.
- ☐ De ser el caso, documento que acredite la licencia o autorización de uso de conocimientos tradicionales de las comunidades indígenas.
- ☐ De ser el caso, certificado de depósito del material biológico.
- ☐ Arte final 12x12
- ☐ De ser el caso, información sobre otras solicitudes de patente o títulos obtenidos en el extranjero por el mismo titular o su causante, relacionadas parcial o totalmente con la invención de esta solicitud.
- ☐ Otros

11 **FIGURA CARACTERISTICA:**



12 Solicito la concesión de la patente, **NOMBRE:** EMILIO FERRERO

FIRMA :

C.C. 438.019 de Usaquén T.P. 31.929

DLM

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

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10/042,582 9 January 2002 (09.01.2002) US

(71) Applicant: SYNAPTIC PHARMACEUTICAL CORPORATION [US/US]; 215 College Road, Paramus, NJ 07652 (US).

(72) Inventors: MARZABADI, Mohammad R.; 153 Woodland Avenue, Ridgewood, NJ 07450 (US). WETZEL, John; 23-17 Morlot Avenue, Fairlawn, NJ 07410 (US). DELEON, John, E.; 7427 Boulevard East, Apt. 5, North Bergen, NJ 07047 (US). JIANG, Yu; 179 Manhattan Avenue, Apt. 7B, Jersey, City, NJ 07307 (US).

(74) Agent: WHITE, John, P.; Cooper & Dunham LLP, 1185 Avenue of the Americas, New York, NY 10036 (US).

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

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

Published:
— *with international search report*

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

WO 03/004027 A1

(54) Title: SUBSTITUTED ANILINIC PIPERIDINES AS MCH SELECTIVE ANTAGONISTS

(57) Abstract: This invention is directed to compounds which are selective antagonists for melanin concentrating hormone-1 (MCH1) receptors. The invention provides a pharmaceutical composition comprising a therapeutically effective amount of the compound of the invention and a pharmaceutically acceptable carrier. This invention provides a pharmaceutical composition made by combining a therapeutically effective amount of the compound of this invention and a pharmaceutically acceptable carrier. This invention further provides a process for making a pharmaceutical composition comprising combining a therapeutically effective amount of the compound of the invention and a pharmaceutically acceptable carrier.

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

ORGANIZACIÓN MUNDIAL DE LA PROPIEDAD INTELECTUAL
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(43) Fecha de publicación internacional:
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(51) Clasificación[7] de Patente Internacional: A6IK 31/445, CO7D 211/30, 211/94, 401/06, 401/12, 403/06, 403/12

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09/899,794	5 de julio del 2001 (05.07.2001)	US
10/042,582	9 de enero del 2002 (09.01.2002)	US

(71) Solicitante: SYNAPTIC PHARMACEUTICAL CORPORATION [US/US]; 215 College Road, Paramus, NJ 07652 (US).

(72) Inventores: MARZABADI, Mohammad R.; 153 Wood-land Avenue, Ridgewood, NJ 07450 (US). WETZEL, John; 23-47 Morlot Avenue. Fairlawn, NJ 07410 (US). DELEON, John, E.; 7427 Boulevard East, Apt. 5, North Bergen, NJ 07047 (US). JIANG, Yu; 179 Manhattan Avenue, Apt. 7B. Jersey, City, NJ 07307 (US).

(74) Agente: WHITE, John, P.; Cooper & Dunahm LLP, 1185 Avenue of the Americas, New York, NY 10036 (US).

(81) Estados designados (*nacional*); AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW.

(84) Estados Designados (*regional*); Patente ARIPO (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Patente Euroasiática (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), Patente Europea (AT, BE, CH, CY, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), Patente OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Publicada
- *sin el reporte de búsqueda internacional*
- *y para ser republicada al recibo de ese reporte*

- *Para códigos de dos letras y otras abreviaciones, se refiere a las "Notas Guía en Códigos y Abreviaciones" que aparecen al principio de cada emisión regular de la Gaceta del PCT.*

(54) Título: PIPERIDINAS ANÍLINICAS SUSTITUIDAS COMO ANTAGONISTAS SELECTIVOS DE MCH

(57) Resumen: Esta invención está dirigida a compuestos que son antagonistas selectivos para los receptores de la hormona-1 de concentración de melanina (MCH1). La invención proporciona una composición farmacéutica que comprende una cantidad terapéuticamente efectiva del compuesto de la invención y un portador farmacéuticamente aceptable. Esta invención proporciona una composición farmacéutica elaborada al combinar una cantidad terapéuticamente efectiva del compuesto de esta invención y un portador farmacéuticamente aceptable. Esta invención además proporciona un proceso para la manufactura de una composición farmacéutica que comprende combinar una cantidad terapéuticamente efectiva del compuesto de la invención y un portador farmacéuticamente aceptable.

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference *(if desired) (12 characters maximum)* 65369-B-PCT/JPW/ANX

Box No. I TITLE OF INVENTION

SUBSTITUTED ANILINIC PIPERIDINES AS MCH SELECTIVE ANTAGONISTS

Box No. II APPLICANT ☐ This person is also inventor

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

SYNAPTIC PHARMACEUTICAL CORPORATION
215 College Road
Paramus, New Jersey 07652
United States of America

Telephone No.: None

Facsimile No.: None

Teleprinter No.: None

Applicant's registration No. with the Office: None

State *(that is, country)* of nationality: United States of America

State *(that is, country)* of residence: United States of America

This person is applicant for the purposes of: ☒ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

MARZABADI, Mohammad R.
153 Woodland Avenue
Ridgewood, NJ 07450
United States of America

This person is:
☐ applicant only
☐ applicant and inventor
☒ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

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

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative

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.)*

WHITE, John P.
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United States of America

Telephone No.: (212) 278-0400

Facsimile No.: (212) 391-0526

Teleprinter No.: None

Agent's registration No. with the Office: 28,678

☐ 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.

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request.

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

WETZEL, John
16-08 Well Drive
Fairlawn, NJ 07410
United States of America

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office:

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

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This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office:

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

JIANG, Yu
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United States of America

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office:

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

CHEN, Chien-An
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United States of America

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office:

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on another continuation sheet.

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request.

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

LU, Kai
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Elmwood Park, NJ 07407
United States of America

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

LAGU, Bharat
41 Fisher Drive
Hillsborough, NJ 08844
United States of America

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No. V DESIGNATION OF STATES *Mark the applicable check-boxes below; at least one must be marked.*

The following designations are hereby made under Rule 4.9(a):

Regional Patent

☒ AP ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, MZ Mozambique, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZM Zambia, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT *(if other kind of protection or treatment desired, specify on dotted line)* .....

☒ EA Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT

☒ EP European Patent: AT Austria, BE Belgium, BG Bulgaria, CH & LI Switzerland and Liechtenstein, CY Cyprus, CZ Czech Republic, DE Germany, DK Denmark, EE Estonia, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, SK Slovakia, TR Turkey, and any other State which is a Contracting State of the European Patent Convention and of the PCT

☒ OA OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GQ Equatorial Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)* .....

National Patent *(if other kind of protection or treatment desired, specify on dotted line)*:

☒ AE United Arab Emirates	☒ GM Gambia	☒ NZ New Zealand
☒ AG Antigua and Barbuda	☒ HR Croatia	☒ OM Oman
☒ AL Albania	☒ HU Hungary	☒ PH Philippines
☒ AM Armenia	☒ ID Indonesia	☒ PL Poland
☒ AT Austria	☒ IL Israel	☒ PT Portugal
☒ AU Australia	☒ IN India	☒ RO Romania
☒ AZ Azerbaijan	☒ IS Iceland	☒ RU Russian Federation
☒ BA Bosnia and Herzegovina	☒ JP Japan	
☒ BB Barbados	☒ KE Kenya	☒ SD Sudan
☒ BG Bulgaria	☒ KG Kyrgyzstan	☒ SE Sweden
☒ BR Brazil	☒ KP Democratic People's Republic of Korea	☒ SG Singapore
☒ BY Belarus	☒ KR Republic of Korea	☒ SI Slovenia
☒ BZ Belize	☒ KZ Kazakhstan	☒ SK Slovakia
☒ CA Canada	☒ LC Saint Lucia	☒ SL Sierra Leone
☒ CH & LI Switzerland and Liechtenstein	☒ LK Sri Lanka	☒ TJ Tajikistan
☒ CN China	☒ LR Liberia	☒ TM Turkmenistan
☒ CO Colombia	☒ LS Lesotho	☒ TN Tunisia
☒ CR Costa Rica	☒ LT Lithuania	☒ TR Turkey
☒ CU Cuba	☒ LU Luxembourg	☒ TT Trinidad and Tobago
☒ CZ Czech Republic	☒ LV Latvia	☒ TZ United Republic of Tanzania
☒ DE Germany	☒ MA Morocco	☒ UA Ukraine
☒ DK Denmark	☒ MD Republic of Moldova	☒ UG Uganda
☒ DM Dominica		☐ US United States of America
☒ DZ Algeria	☒ MG Madagascar	
☒ EC Ecuador	☒ MK The former Yugoslav Republic of Macedonia	☒ UZ Uzbekistan
☒ EE Estonia	☒ MN Mongolia	☒ VN Viet Nam
☒ ES Spain	☒ MW Malawi	☒ YU Yugoslavia
☒ FI Finland	☒ MX Mexico	☒ ZA South Africa
☒ GB United Kingdom	☒ MZ Mozambique	☒ ZM Zambia
☒ GD Grenada	☒ NO Norway	☒ ZW Zimbabwe
☒ GE Georgia		
☒ GH Ghana		

Check-boxes below reserved for designating States which have become party to the PCT after issuance of this sheet:

☐ ..... ☐ ..... ☐ .....

☐ ..... ☐ ..... ☐ .....

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)*

Box No. VI PRIORITY CLAIM

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

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application:* regional Office	international application: receiving Office
item (1) (05.07.01) (05 July 2001)	09/899,794	US		
item (2) (09.01.02) (09 January 2002)	10/042,582	US		
item (3)				
item (4)				
item (5)				

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

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

☐ all items ☒ item (1) ☒ item (2) ☐ item (3) ☐ item (4) ☐ item (5) ☐ other, see Supplemental Box

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

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

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

ISA / US.....

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

Date *(day/month/year)* Number Country *(or regional Office)*

Box No. VIII DECLARATIONS

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

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

Box No. IX CHECK-LIST: LANGUAGE OF FILING

This international application contains:

(a) the following number of sheets in paper form:

request (including declaration sheets)	:	5
description (excluding sequence listing part)	:	749
claims	:	19
abstract	:	1
drawings	:	0
Sub-total number of sheets	:	774
sequence listing part of description *(actual number of sheets if filed in paper form, whether or not also filed in computer readable form; see (b) below)*	:	0
Total number of sheets	:	774

(b) sequence listing part of description filed in computer readable form

(i) ☐ only (under Section 801(a)(i))

(ii) ☐ in addition to being filed in paper form (under Section 801(a)(ii))

Type and number of carriers (diskette, CD-ROM, CD-R or other) on which the sequence listing part is contained *(additional copies to be indicated under item 9(ii), in right column)*: .....

This international application is accompanied by the following item(s) *(mark the applicable check-boxes below and indicate in right column the number of each item)*:

		Number of items
1. ☒ fee calculation sheet	:	1
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. ☐ priority document(s) identified in Box No. VI as item(s):	:	
7. ☐ translation of international application into (language):	:	
8. ☐ separate indications concerning deposited microorganism or other biological material	:	
9. ☐ sequence listing in computer readable form (indicate also type and number of carriers (diskette, CD-ROM, CD-R or other))		
(i) ☐ copy submitted for the purposes of international search under Rule 13*ter* only (and not as part of the international application)	:	
(ii) ☐ *(only where check-box (b)(i) or (b)(ii) is marked in left column)* additional copies including, where applicable, the copy for the purposes of international search under Rule 13*ter*	:	
(iii) ☐ together with relevant statement as to the identity of the copy or copies with the sequence listing part mentioned in left column	:	
10. ☒ other *(specify)*: Express Mail Certificate of Mailing dated July 3, 2002 bearing Express Mail Label No. EL398170469US	:	

Figure of the drawings which should accompany the abstract:

Language of filing of the international application: English

Box No. X 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 request).

SYNAPTIC PHARMACEUTICAL CORPORATION

Errol de Souza 10/10/02

NAME: Errol De Souza Date

TITLE: President and CEO

For receiving Office use only

1. Date of actual receipt of the purported international application:	2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority (if two or more are competent): ISA /	6. ☐ Transmittal of search copy delayed until search fee is paid

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

12 12

PCT

PETITORIO

El abajo firmante pide que la presente solicitud internacional sea tramitada de conformidad con el Tratado de Cooperación de Patentes

Para uso de la Oficina Receptora Únicamente

Solicitud Internacional No.

Fecha de presentación internacional

Nombre de la Oficina receptora y "Solicitud Internacional PCT"

Referencia al expediente del solicitante o del mandatario *(si se desea) (como máximo 12 caracteres)*
65369-B-PCT/JPW/ANX

Recuadro No. I TITULO DE LA INVENCION

PIPERIDINAS ANILINICAS SUSTITUIDAS COMO ANTAGONISTAS SELECTIVOS DE MCH

Recuadro No. II SOLICITANTE ( ) esta persona es también un inventor

Nombre y dirección: *(Apellido seguido del nombre; en el caso de una persona jurídica, la descripción oficial completa. En la dirección deben figurar el código postal y el nombre del país). El país de la dirección indicada en este recuadro es el estado del solicitante (este es, país) de residencia, si no se indica ningún estado de residencia enseguida.)*

SYNAPTIC PHARMACEUTICAL CORPORATION
215 College Road
Paramus, New Jersey 07652
Estados Unidos de América

No. De teléfono
Ninguno

No. De Facsimile
Ninguno

No. De Impresora
Ninguno

Registro del Solicitante No. ante la Oficina
Ninguno

Estado de Nacionalidad:
Estados Unidos de América

Estado de residencia:
Estados Unidos de América

Esta persona es solicitante para:		Todos los estados designados		Todos los estados designados salvo los estados Unidos de América		Los Estados Unidos de América únicamente		Los estados indicados en el recuadro suplementario
	X							

Recuadro No. III OTRO(S) SOLICITANTE(S) Y/O OTRO(S) INVENTOR(ES)

Nombre y dirección: *(Apellido seguido del nombre; en el caso de una persona jurídica, la descripción oficial completa. En la dirección deben figurar el código postal y el nombre del país.). El país de la dirección indicada en este recuadro es el estado del solicitante (este es, país) de residencia, si no se indica ningún estado de residencia enseguida.)*

MARZABADI, Mohammad R.
153 Woodland Avenue
Ridgewood, NJ 07450
Estados Unidos de América

Esta persona es:
( ) solicitante únicamente
( ) solicitante e inventor
(x) inventor únicamente
(Si se marca esta casilla, no se debe rellenar lo que sigue)

Registro del Solicitante No. ante la Oficina

Estado de Nacionalidad:

Estado de residencia:

Esta persona es solicitante para:		Todos los estados designados		Todos los estados designados salvo los estados Unidos de América	X	Los Estados Unidos de América únicamente		Los estados indicados en el recuadro suplementario

X	Los demás solicitantes y/o (demás) inventores se indican en una hoja de continuación

Recuadro No. IV MANDATARIO O REPRESENTANTE COMÚN; O DIRECCIÓN PARA LA CORRESPONDENCIA

La persona abajo identificada se designa/ha sido designada para actuar en nombre del/de los solicitante(s) ante las administraciones internacional competentes como: (X) agente ( ) Representante común

Nombre y dirección: *(Apellido seguido del nombre; en el caso de una persona jurídica, la descripción oficial completa. En la dirección deben figurar el código postal y el nombre del país)*

WHITE, John P.
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
Estados Unidos de América

No. De Teléfono
(212) 278-0400

No. De Facsimile
(212) 391-0526

No. De Impresora Ninguna

Registro del Solicitante No. ante la Oficina
28,678

	Dirección para correspondencia: Márquese esta casilla cuando no se designe/se haya designado ningún mandatario o representante común y el espacio de arriba se utilice en su lugar para indicar una dirección especial a la que deba enviarse la correspondencia

12 13

Hoja No. 2

Continuación del recuadro No. III OTROS SOLICITANTES Y/O (OTROS) INVENTORES

Si no se ha de utilizar ninguno de estos subrecuadros, esta hoja no debe ser incluida en el petitorio.

Nombre y dirección: *(Apellido seguido del nombre; en el caso de una persona jurídica, la descripción oficial completa. En la dirección deben figurar el código postal y el nombre del país)*

WETZEL, John
16—08 Well Drive
Fairlawn, NJ 07410
Estados Unidos de América

Esta persona es:

( ) solicitante únicamente

( ) solicitante e inventor

(X) inventor únicamente
(Si se marca esta casilla, no se debe rellenar lo que sigue)

Registro del solicitante No. ante la Oficina

Estado de Nacionalidad:

Estado de residencia:

Esta persona es solicitante para: [ ] Todos los estados designados [ ] Todos los estados designados salvo los estados Unidos de América [ ] Los Estados Unidos de América únicamente [ ] Los estados indicados en el recuadro suplementario

Nombre y dirección: *(Apellido seguido del nombre; en el caso de una persona jurídica, la descripción oficial completa. En la dirección deben figurar el código postal y el nombre del país)*

DELEON, John E.
7427 Boulevard East
Apt. 5
North Bergen, NJ 07047
Estados Unidos de América

Esta persona es:

( ) solicitante únicamente

( ) solicitante e inventor

(X) inventor únicamente
(Si se marca esta casilla, no se debe rellenar lo que sigue)

Registro del solicitante No. ante la Oficina

Estado de Nacionalidad:

Estado de residencia:

Esta persona es solicitante para: [ ] Todos los estados designados [ ] Todos los estados designados salvo los estados Unidos de América [ ] Los Estados Unidos de América únicamente [ ] Los estados indicados en el recuadro suplementario

Nombre y dirección: *(Apellido seguido del nombre; en el caso de una persona jurídica, la descripción oficial completa. En la dirección deben figurar el código postal y el nombre del país)*

JIANG, Yu
179 Manhattan Avenue
Apt. 7B
Jersey City, NJ 07307
Estados Unidos de América

Esta persona es:

( ) solicitante únicamente

( ) solicitante e inventor

(X) inventor únicamente
(Si se marca esta casilla, no se debe rellenar lo que sigue)

Registro del solicitante No. ante la Oficina

Estado de Nacionalidad:

Estado de residencia:

Esta persona es solicitante para: [ ] Todos los estados designados [ ] Todos los estados designados salvo los estados Unidos de América [ ] Los Estados Unidos de América únicamente [ ] Los estados indicados en el recuadro suplementario

Nombre y dirección: *(Apellido seguido del nombre; en el caso de una persona jurídica, la descripción oficial completa. En la dirección deben figurar el código postal y el nombre del país)*

CHEN, Chien—An
4 9—02 196 Place
Fresh Meadows, NY 11365
Estados Unidos de América

Esta persona es:

( ) solicitante únicamente

( ) solicitante e inventor

(X) inventor únicamente
(Si se marca esta casilla, no se debe rellenar lo que sigue)

Registro del solicitante No. ante la Oficina

Estado de Nacionalidad:

Estado de residencia:

Esta persona es solicitante para: [ ] Todos los estados designados [ ] Todos los estados designados salvo los estados Unidos de América [ ] Los Estados Unidos de América únicamente [ ] Los estados indicados en el recuadro suplementario

(X) Los demás solicitantes y/o (demás) inventores se indican en otra hoja de continuación

Continuación del recuadro No. III OTROS SOLICITANTES Y/O (OTROS) INVENTORES

Si no se ha de utilizar ninguno de estos subrecuadros, esta hoja no debe ser incluida en el petitorio.

Nombre y dirección: *(Apellido seguido del nombre; en el caso de una persona jurídica, la descripción oficial completa. En la dirección deben figurar el código postal y el nombre del país)*

LU, Kai
67A Glenwood Avenue
Elmwood Park, NJ 07407
Estados Unidos de América

Esta persona es:

( ) solicitante únicamente

( ) solicitante e inventor

(X) inventor únicamente
(Si se marca esta casilla, no se debe rellenar lo que sigue)

Registro del solicitante No. ante la Oficina

Estado de Nacionalidad:

Estado de residencia:

Esta persona es solicitante para: [ ] Todos los estados designados [ ] Todos los estados designados salvo los estados Unidos de América [ ] Los Estados Unidos de América únicamente [ ] Los estados indicados en el recuadro suplementario

Nombre y dirección: *(Apellido seguido del nombre; en el caso de una persona jurídica, la descripción oficial completa. En la dirección deben figurar el código postal y el nombre del país)*

LAGU, Bharat
41 Fisher Drive
Hillsborough, NJ 08844
Estados Unidos de América

Esta persona es:

( ) solicitante únicamente

( ) solicitante e inventor

(X) inventor únicamente
(Si se marca esta casilla, no se debe rellenar lo que sigue)

Registro del solicitante No. ante la Oficina

Estado de Nacionalidad:

Estado de residencia:

Esta persona es solicitante para: [ ] Todos los estados designados [ ] Todos los estados designados salvo los estados Unidos de América [ ] Los Estados Unidos de América únicamente [ ] Los estados indicados en el recuadro suplementario

Nombre y dirección: *(Apellido seguido del nombre; en el caso de una persona jurídica, la descripción oficial completa. En la dirección deben figurar el código postal y el nombre del país)*

Esta persona es:

( ) solicitante únicamente

( ) solicitante e inventor

( ) inventor únicamente
(Si se marca esta casilla, no se debe rellenar lo que sigue)

Registro del solicitante No. ante la Oficina

Estado de Nacionalidad:

Estado de residencia:

Esta persona es solicitante para: [ ] Todos los estados designados [ ] Todos los estados designados salvo los estados Unidos de América [ ] Los Estados Unidos de América únicamente [ ] Los estados indicados en el recuadro suplementario

Nombre y dirección: *(Apellido seguido del nombre; en el caso de una persona jurídica, la descripción oficial completa. En la dirección deben figurar el código postal y el nombre del país)*

Esta persona es:

( ) solicitante únicamente

( ) solicitante e inventor

( ) inventor únicamente
(Si se marca esta casilla, no se debe rellenar lo que sigue)

Registro del solicitante No. ante la Oficina

Estado de Nacionalidad:

Estado de residencia:

Esta persona es solicitante para: [ ] Todos los estados designados [ ] Todos los estados designados salvo los estados Unidos de América [ ] Los Estados Unidos de América únicamente [ ] Los estados indicados en el recuadro suplementario

( ) Los demás solicitantes y/o (demás) inventores se indican en otra hoja de continuación

~~15~~ 15

Recuadro No. V DESIGNACION DE ESTADOS Marcar los recuadros de verificación aplicables; al menos uno debe de ser marcado

A continuación se hacen las designaciones siguientes en virtud de la regla 4.9 a)

Patente Regional

X	AP	PATENTE ARIPO: GH Ghana, GM Gambia, KE Kenia, LS Lesotho, MW Malawi, MZ Mozambique, SD Sudán, SL Sierra Leona,SZ Swazilandia, TZ República Unida de Tanzania, UG Uganda, ZM Zambia, ZW Zimbabwe y cualquier otro Estado contratante del Protocolo de Harare y del PCT *(si se desean otras formas de protección o de tramitación, especifíquense en la línea de puntos)*.....
X	EA	PATENTE Euroasiática: AM Armenia, AZ Azerbayan, BY Belarus, KG Kirguistán, KZ Kazajstán, MD República de Moldova, RU Federación Rusa, TJ Tayikistán, TM Turkmenistán y cualquier otro Estado que sea Estado contratante de la Convención de Patentes Euroasiática y del PCT
X	EP	PATENTE Europea: AT Austria, BE Bélgica, CH y LI Suiza y Liechtenstein, CY Chipre, DE Alemania, DK Dinamarca, ES España, FI Finlandia, FR Francia, GB ReinoUnido, GR Grecia, IE Irlanda, IT Italia, LU Luxemburgo, MC Mónaco, NL Países Bajos, PT Portugal, SE Suecia, TR Turquía, y cualquier otro Estado Contratante del Convenio sobre la Patente Europea y del PCT
X	OA	PATENTE OAPI: BF Burkina Faso, BJ Benín, CF República Centroafricana, CG Congo, CI Costa de Marfil, CM Camerún, GA Gabón, GN Guinea, GQ Guinea Ecuatorial, GW Guinea-Bissau, ML Malí, MR Mauritania, NE Nigeria, SN Senegal, TD Chad, TG Togo y cualquier otro Estado que sea estado miembro de la OAPI y que sea un Estado contratante del PCT *(si se desea otra forma de protección o de tramitación, especifíquese en la línea de puntos)*.....1.....

Patente Nacional *(si se desea otra forma de protección o de tramitación, especifíquese en la línea de puntos)*

X	AE	Emiratos Arabes Unidos	X	KP	República Democrática Coreana
X	AG	Antigua y Barbuda	X	KR	República de Corea
X	AL	Albania	X	KZ	Kazajstán
X	AM	Armenia	X	LC	Santa Lucía
X	AT	Austria	X	LK	Sri Lanka
X	AU	Australia	X	LR	Liberia
X	AZ	Azerbayán	X	LS	Lesotho
X	BA	Bosnia y Herzegovina	X	LT	Lituania
X	BB	Barbados	X	LU	Luxemburgo
X	BG	Bulgaria	X	LV	Letonia
X	BR	Brasil	X	MA	Marruecos
X	BY	Belarús	X	MD	República de Moldova
X	BZ	Belice	X	MG	Madagascar
X	CA	Canadá	X	MK	La antigua República Yugoslava de Macedonia
X	CH y LI	Suiza y Liechtenstein	X	MN	Mongolia
X	CN	China	X	MW	Malawi
X	CO	Colombia	X	MX	México
X	CR	Costa Rica	X	MZ	Mozambique
X	CU	Cuba	X	NO	Noruega
X	CZ	República Checa	X	NZ	Nueva Zelanda
X	DE	Alemania	X	OM	Omán
X	DK	Dinamarca	X	PH	Filipinas
X	DM	Dominica	X	PL	Polonia
X	DZ	Argelia	X	PT	Portugal
X	EC	Ecuador	X	RO	Rumania
X	EE	Estonia	X	RU	Federación Rusa
X	ES	España	X	SD	Sudán
X	FI	Finlandia	X	SE	Suecia
X	GB	Reino Unido	X	SG	Singapur
X	GD	Granada	X	SI	Slovenia
X	GE	Georgia	X	SK	Slovakia
X	GH	Ghana	X	SL	Sierra Leona
X	GM	Gambia	X	TJ	Tajikistán
X	HR	Croacia	X	TM	Turkmenistán
X	HU	Hungría	X	TN	Tunisia
X	ID	Indonesia	X	TR	Turquía
X	IL	Israel	X	TT	Trinidad y Tobago
X	IN	India	X	TZ	República Unida de Tanzania
X	IS	Islandia	X	UA	Ucrania
X	JP	Japón	X	UG	Uganda
X	KE	Kenia		US	Estados Unidos de América
X	KG	Kirguistán	X	UZ	Uzbekistán
			X	VN	Viet Nam
			X	YU	Yugoslavia
			X	ZA	África del Sur
			X	ZM	Zambia
			X	ZW	Zimbabwe

Recuadros de verificación reservados para Estados designados que formarán parte del PCT después de la expedición de esta hoja.

(X) .....( ) .....( ).....

( ) .....( ) .....( ).....

Declaración de designaciones Precautorias: Además de las designaciones arriba efectuadas, el solicitante efectuará también, en virtud de la Regla 4.9 b), todas las designaciones que estén permitidas con arreglo al PCT, salvo la designación o designaciones indicadas en el recuadro suplementario que estén excluidas del alcance de esta Declaración. El solicitante declara que esas designaciones adicionales están sujetas a confirmación y que cualquier designación que no se confirme antes de que expiren los 15 meses a partir de la fecha de prioridad se considerará retirada por el solicitante al expirar dicho plazo. *(La confirmación(incluyendo las tasas) deberá llegar a la Oficina receptora dentro de un plazo de 15 meses).*

Hoja No. 4

Recuadro No. VI REIVINDICACION DE PRIORIDAD

Se reclama la prioridad de las siguientes solicitud(es) básica(s):

Fecha de presentación De solicitud anterior (día/mes/año)	Número de solicitud Anterior	En donde la solicitud anterior es: solicitud nacional: país	solicitud regional:* Oficina regional	solicitud internacional: Oficina receptora
Item (1) (05.07.01) (05 Julio 2001)	09/899,794	US		
Item (2) (09.01.02) (09 Enero 2002)	10/042,582	US		
Item (3)				
Item (4)				
Item (5)				

( ) Reivindicación de proridades adicionales están indicadas en el recuadro suplementario.

_ Se solicita a la Oficina receptora que prepare y transmita a la Oficina Internacional una copia certificada de la(s) solicitud(es) anterior(es) (solamente si la solicitud anterior fue presentada ante la Oficina que para los propósitos de la presente solicitud internacional es la Oficina receptora) identificada(s) anteriormente como:

( ) todos los items (X) item (1) (X)item (2) ( )item (3) ( )item (4) ( )item(5) ( )otros, ver recuadro suplementario

* En donde la solicitud anterior es una solicitud ARIPO, es determinante indicar en el Recuadro Complementario por lo menos un país que es parte de la Convención de París para la Protección de la Propiedad Industrial para la cual aquella solicitud anterior fue presentada (Regla 4.10(b)(ii))

Recuadro No. VII. AUTORIDAD DE BUSQUEDA INTERNACIONAL

Elección de Autoridad de Búsqueda Internacional (ISA)
(si dos o más Autoridades de Búsqueda Internacional son competentes para llevar a cabo la búsqueda internacional, indique la autoridad escogida; se puede utilizar el código de dos letras):
ISA/ .....

Petición para utilizar los resultados de búsqueda anterior; referencia a aquella búsqueda (si se llevó a cabo una búsqueda anterior por o se ha solicitado de la Autoridad de Búsqueda Internacional):
Fecha (día/mes/año) No. País (u oficina regional)

Recuadro No. VIII DECLARACIONES

Las siguientes declaraciones están contenidas en los recuadros Nos. VIII (i) a (v) (señalar los recuadros de verificación aplicables enseguida e indicar en la columna derecha el número de cada tipo de declaración):		Número de declaraciones
( ) Recuadro No. VIII (i)	Declaraciones en cuanto a la identificación del inventor	
( ) Recuadro No. VIII (ii)	Declaración en cuanto el derecho del solicitante, como a la fecha de presentación internacional, para solicitar para y ser concedida una patente:	
( ) Recuadro No. VIII (iii)	Declaración en cuanto el derecho del solicitante, como a la fecha de presentación internacional, para reclamar la prioridad de la solicitud básica:	
( ) Recuadro No. VIII (iv)	Declaración del inventor (solamente para los propósitos de la designación de los Estados Unidos de América)	
( ) Recuadro No. VIII (v)	Declaración en cuanto descripciones no perjudicial o excepciones a carencia de novedad	

Recuadro No. IX LISTA DE VERIFICACION: IDIOMA DE PRESENTACION

Esta solicitud internacional contiene:		Esta solicitud internacional está acompañada por el(los) siguiente(s) item(s) (marcar los recuadros de verificación aplicables enseguida e indicar en la columna derecha el número de cada ítem):	Número de items
(a)el siguiente número de hojas en forma de papel:			
Petitorio (incluyendo hojas de declaración):	5	1. (X) hoja de cálculo de pago:	1
Descripción (excluyendo parte del listado de secuencias):	749	2. ( ) poder original por separado	
Reivindicaciones:	193	3. ( ) poder de apoderado general original:	
Extracto:	1	4. ( ) copia del poder general; número de referencia, si existe: GF 1519/2001 ... :	
Dibujos:	0		
Número subtotal de hojas:	774	5. ( ) declaración que explica carencia de firma	
Parte del listado de secuencias de la descripción (número real de hojas si se presentó en forma de papel, si sí o no también presentada en forma leíble por computadora; ver (b) enseguida):	0	6. ( ) documento(s) de prioridad identificados en el recuadro VI como ítem(s): SIGUEN :	
	——	7. ( ) traducción de la solicitud internacional en (idioma):	
Total de número de hojas:	774	8. ( ) indicaciones separadas concernientes a microorganismos depositados u otro material biológico:	
(b) Parte del listado de secuencias de la descripción presentada en forma leíble por computadora		9. ( ) listado de secuencias en forma leíble por computadora (indicar también el tipo y número de portadores (disquete, CD-ROM, CD-R u otro))	
(i) ( ) solamente (bajo sección 801 (a) (i))		(i) ( ) copia presentada para los propósitos de búsqueda internacional bajo la Regla 13ter solamente (y no como parte de la solicitud internacional	
(ii) ( ) además a ser presentada en forma de papel (bajo sección 801 (a) (ii))			
Tipo y número de portadores (disquete, CD-ROM, CD-R u otro) en los cuales la parte del listado de secuencias está contenido (copias adicionales a ser indicadas bajo el item 9 (ii), en la columna derecha):		(ii) ( ) (solamente en donde el recuadro de verificación (b) (i) o (b) (ii) es marcado en la columna izquierda) copias adicionales incluyendo, en donde sea aplicable, la copia para los propósitos de búsqueda internacional bajo la Regla 13ter	
		(iii) ( ) junto con declaración relevante para identificar la copia o copias con la parte del listado de secuencias mencionada en la columna izquierda	
		10. (X) otros (especifique): Certificado por Correo Express EL398170469US	

Figura de los dibujos la cual deberá acompañar al resumen :	Idioma de presentación de la solicitud Internacional : Inglés

Recuadro No. X FIRMA DE LA SOLICITANTE, AGENTE O REPRESENTANTE COMUN

Enseguida de cada firma, indique el nombre de la persona que firma y la capacidad en la cual firma (si tal capacidad no es obvia de la lectura del petitorio).

SYNAPTIC PHARMACEUTICAL CORPORATION

RUBRICA 10/10/02

NOMBRE: Errol De Souza
TITULO: Presidente y CEO

Fecha

Para uso de la Oficina receptora solamente

1. Fecha del recibo real de la solicitud internacional alegada:	2. Dibujos ☐ recibidos: ☐ no recibidos:
3. Fecha corregida del vencimiento del recibo real a los documentos o dibujos recibidos posteriormente pero a tiempo que complementan la solicitud internacional alegada:	
4. Fecha del recibo a tiempo de las correcciones requeridas bajo el artículo 11(2) del PCT:	
5. Autoridad de Búsqueda Internacional (si dos o más son competentes): ISA/	6. ☐ Transmisión de copia de búsqueda retardada hasta que la tasa de búsqueda sea pagada

Para uso de la Oficina Internacional solamente

Fecha del recibo de la copia de registro por la Oficina Internacional:

Dkt. 65369-B-PCT/JPW/JCC

IN THE UNITED STATES RECEIVING OFFICE (RO/US)

Applicant	:	Synaptic Pharmaceutical Corporation
PCT International Application No.	:	PCT/US02/21063
International Filing Date	:	03 July 2002
For	:	Substituted Anilinic Piperidines As MCH Selective Antagonists

1185 Ave. of the Americas
New York, New York 10036
October 1, 2003

The International Bureau of WIPO
PCT Receiving Office Section
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized Officer Mougamadou Abidine:

FACSIMILE CERTIFICATE OF TRANSMISSION IN CONNECTION WITH THE ABOVE-IDENTIFIED APPLICATION

Date of Facsimile: October 1, 2003

I hereby certify that this paper or fee is being transmitted by facsimile on the date indicated above and is addressed to the The International Bureau of WIPO, 34 chemin des Colombettes, 1211 Geneva 20, Switzerland

Printed Name: Jeffrey C. Chu

Respectfully submitted,

John P. White
Registration No. 28,678
Attorney for Applicant
Cooper & Dunham LLP
1185 Ave. of the Americas
New York, New York 10036
(212) 278-0400

Dkt. 65369-B-PCT/JPW/JCC 19

IN THE UNITED STATES RECEIVING OFFICE (RO/US)

Applicant	:	Synaptic Pharmaceutical Corporation
PCT International Application No.	:	PCT/US02/21063
International Filing Date	:	03 July 2002
For	:	Substituted Anilinic Piperidines As MCH Selective Antagonists

1185 Ave. of the Americas
New York, New York 10036
October 1, 2003

BY FACSIMILE/ CONFIRMATION BY FEDERAL EXPRESS
The International Bureau of WIPO
PCT Receiving Office Section
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized Officer Mougamadou Abidine:

REQUEST UNDER RULE 92 *bis*.1(a) TO RECORD A CHANGE OF INVENTORS

Applicant respectfully request the addition of three (3) second inventor's names under Rule 92 *bis*.1(a) on the Request Form for the subject International Application.

Specifically, on page 2 (Box No. III) of the Request Form, please add the following inventor:

CHEN, Chien-An
49-02 196 Place
Fresh Meadows, New York 11365
United States of America

Also, on page 2a (Continuation of Box No. III) of the Request Form, please add the following inventors:

LU, Kai
67A Glenwood Avenue
Elmwood Park, New Jersey 07407
United States of America

LAGU, Bharat
41 Fisher Drive
Hillsborough, NJ 08844
United State of America

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20

Therefore, pursuant to Rule 92 *bis*.1(a), please record that the inventors have changed and the current, correct inventors are:

1) MARZABADI, Mohammad R.
153 Woodland Avenue
Ridgewood, New Jersey 07450
United States of America

2) WETZEL, John
16-08 Well Drive
Fairlawn, New Jersey 07410
United States of America

3) DELEON, John E.
7427 Boulevard East, Apt. 5
North Bergen, New Jersey 07047
United States of America

4) JIANG, Yu
179 Manhattan Avenue, Apt. 7-B
Jersey City, New Jersey 07307
United States of America

5) CHEN, Chien-An
49-02 196 Place
Fresh Meadows, New York 11365
United States of America

6) LU, Kai
67A Glenwood Avenue
Elmwood Park, New Jersey 07407
United States of America

7) LAGU, Bharat
41 Fisher Drive
Hillsborough, NJ 08844
United States of America

Applicant attaches hereto as **Exhibit A** a PCT Request Form, including the additional inventors and replacement pages 1-5, signed on behalf of Synaptic Pharmaceutical Corporation by an authorized officer thereof. Therefore, the undersigned now has the authorization to request the change of inventors under Rule 92 *bis*.1(a) on the Request Form for the subject International Application.

2 of 21

In light of the foregoing, applicants respectfully submit that this Request is in compliance with Rule 92 *bis* 1(a) and should be granted.

Respectfully submitted,

John P. White
Registration No. 28,678
Attorney for Applicant
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
(212) 278-0400

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference *(if desired) (12 characters maximum)* 65369-B-PCT/JPW/ANK

Box No. I TITLE OF INVENTION

SUBSTITUTED ANILINIC PIPERIDINES AS MCH SELECTIVE ANTAGONISTS

Box No. II APPLICANT ☐ This person is also inventor

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

SYNAPTIC PHARMACEUTICAL CORPORATION
215 College Road
Paramus, New Jersey 07652
United States of America

Telephone No.: None

Facsimile No.: None

Teleprinter No.: None

Applicant's registration No. with the Office: None

State *(that is, country)* of nationality: United States of America

State *(that is, country)* of residence: United States of America

This person is applicant for the purposes of: ☒ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

MARZABADI, Mohammad R.
153 Woodland Avenue
Ridgewood, NJ 07450
United States of America

This person is:
☐ applicant only
☐ applicant and inventor
☒ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office:

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

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

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative

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.)*

WHITE, John P.
Cooper & Dunham LLP
1185 Avenue of the Americas
New York, New York 10036
United States of America

Telephone No.: (212) 278-0400

Facsimile No.: (212) 391-0526

Teleprinter No.: None

Agent's registration No. with the Office: 28,678

☐ 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.

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13

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request.

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

WETZEL, John
16-08 Well Drive
Fairlawn, NJ 07410
United States of America

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

DELEON, John E.
7427 Boulevard East
Apt. 5
North Bergen, NJ 07047
United States of America

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

JIANG, Yu
179 Manhattan Avenue
Apt. 7B
Jersey City, NJ 07307
United States of America

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

CHEN, Chien-An
49-02 196 Place
Fresh Meadows, NY 11365
United States of America

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on another continuation sheet.

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Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request.

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

LU, Kai
67A Glenwood Avenue
Elmwood Park, NJ 07407
United States of America

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

LAGU, Bharat
41 Fisher Drive
Hillsborough, NJ 08844
United States of America

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☒ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.

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Box No. V DESIGNATION OF STATES *Mark the applicable check-boxes below; at least one must be marked.*

The following designations are hereby made under Rule 4.9(a):

Regional Patent

☒ **AP** ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, MZ Mozambique, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZM Zambia, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT *(If other kind of protection or treatment desired, specify on dotted line)* .....

☒ **EA** Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT

☒ **EP** European Patent: AT Austria, BE Belgium, BG Bulgaria, CH & LI Switzerland and Liechtenstein, CY Cyprus, CZ Czech Republic, DE Germany, DK Denmark, EE Estonia, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, SK Slovakia, TR Turkey, and any other State which is a Contracting State of the European Patent Convention and of the PCT

☒ **OA** OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GQ Equatorial Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(If other kind of protection or treatment desired, specify on dotted line)* .....

National Patent *(If other kind of protection or treatment desired, specify on dotted line)*:

☒ AE United Arab Emirates	☒ GM Gambia	☒ NZ New Zealand
☒ AG Antigua and Barbuda	☒ HR Croatia	☒ OM Oman
☒ AL Albania	☒ HU Hungary	☒ PH Philippines
☒ AM Armenia	☒ ID Indonesia	☒ PL Poland
☒ AT Austria	☒ IL Israel	☒ PT Portugal
☒ AU Australia	☒ IN India	☒ RO Romania
☒ AZ Azerbaijan	☒ IS Iceland	☒ RU Russian Federation
☒ BA Bosnia and Herzegovina	☒ JP Japan	
☒ BB Barbados	☒ KE Kenya	☒ SD Sudan
☒ BG Bulgaria	☒ KG Kyrgyzstan	☒ SE Sweden
☒ BR Brazil	☒ KP Democratic People's Republic of Korea	☒ SG Singapore
☒ BY Belarus	☒ KR Republic of Korea	☒ SI Slovenia
☒ BZ Belize	☒ KZ Kazakhstan	☒ SK Slovakia
☒ CA Canada	☒ LC Saint Lucia	☒ SL Sierra Leone
☒ CH & LI Switzerland and Liechtenstein	☒ LK Sri Lanka	☒ TJ Tajikistan
☒ CN China	☒ LR Liberia	☒ TM Turkmenistan
☒ CO Colombia	☒ LS Lesotho	☒ TN Tunisia
☒ CR Costa Rica	☒ LT Lithuania	☒ TR Turkey
☒ CU Cuba	☒ LU Luxembourg	☒ TT Trinidad and Tobago
☒ CZ Czech Republic	☒ LV Latvia	☒ TZ United Republic of Tanzania
☒ DE Germany	☒ MA Morocco	☒ UA Ukraine
☒ DK Denmark	☒ MD Republic of Moldova	☒ UG Uganda
☒ DM Dominica		☐ US United States of America
☒ DZ Algeria	☒ MG Madagascar	
☒ EC Ecuador	☒ MK The former Yugoslav Republic of Macedonia	☒ UZ Uzbekistan
☒ EE Estonia		☒ VN Viet Nam
☒ ES Spain	☒ MN Mongolia	☒ YU Yugoslavia
☒ FI Finland	☒ MW Malawi	☒ ZA South Africa
☒ GB United Kingdom	☒ MX Mexico	☒ ZM Zambia
☒ GD Grenada	☒ MZ Mozambique	☒ ZW Zimbabwe
☒ GE Georgia	☒ NO Norway	
☒ GH Ghana		

Check-boxes below reserved for designating States which have become party to the PCT after issuance of this sheet:

☐ ..... ☐ ..... ☐ .....

☐ ..... ☐ ..... ☐ .....

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)*

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Box No. VI PRIORITY CLAIM

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

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application:* regional Office	international application: receiving Office
item (1) (05.07.01) (05 July 2001)	09/899,794	US		
item (2) (09.01.02) (09 January 2002)	10/042,582	US		
item (3)				
item (4)				
item (5)				

☐ Further priority claims are indicated in the Supplemental Box.

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

☐ all items ☒ item (1) ☒ item (2) ☐ item (3) ☐ item (4) ☐ item (5) ☐ other, see Supplemental Box

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

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

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

ISA / US.....

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

Date *(day/month/year)* Number Country *(or regional Office)*

Box No. VIII DECLARATIONS

The following declarations are contained in Boxes Nos. VIII (i) to (v) *(mark the applicable check-boxes below and indicate in the right column the number of each type of declaration)*:		Number of declarations
☐ Box No. VIII (i)	Declaration as to the identity of the inventor	:
☐ Box No. VIII (ii)	Declaration as to the applicant's entitlement, as at the international filing date, to apply for and be granted a patent	:
☐ Box No. VIII (iii)	Declaration as to the applicant's entitlement, as at the international filing date, to claim the priority of the earlier application	:
☐ Box No. VIII (iv)	Declaration of inventorship (only for the purposes of the designation of the United States of America)	:
☐ Box No. VIII (v)	Declaration as to non-prejudicial disclosures or exceptions to lack of novelty	:

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Box No. IX CHECK LIST: LANGUAGE OF FILING

This international application contains:

(a) the following number of sheets in paper form:

request (including declaration sheets)	:	5
description (excluding sequence listing part)	:	749
claims	:	19
abstract	:	1
drawings	:	0
Sub-total number of sheets	:	774
sequence listing part of description *(actual number of sheets if filed in paper form, whether or not also filed in computer readable form; see (b) below)*	:	0
Total number of sheets	:	774

(b) sequence listing part of description filed in computer readable form

(i) ☐ only (under Section 801(a)(i))

(ii) ☐ in addition to being filed in paper form (under Section 801(a)(ii))

Type and number of carriers (diskette, CD-ROM, CD-R or other) on which the sequence listing part is contained *(additional copies to be indicated under item 9(iii), in right column)*: .....

This international application is accompanied by the following item(s) *(mark the applicable check-boxes below and indicate in right column the number of each item)*:

		Number of items
1. ☒ fee calculation sheet	:	1
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. ☐ priority document(s) identified in Box No. VI as item(s):	:	
7. ☐ translation of international application into (language):	:	
8. ☐ separate indications concerning deposited microorganism or other biological material	:	
9. ☐ sequence listing in computer readable form (indicate also type and number of carriers (diskette, CD-ROM, CD-R or other))		
(i) ☐ copy submitted for the purposes of international search under Rule 13*ter* only (and not as part of the international application)	:	
(ii) ☐ *(only where check-box (b)(i) or (b)(ii) is marked in left column)* additional copies including, where applicable, the copy for the purposes of international search under Rule 13*ter*	:	
(iii) ☐ together with relevant statement as to the identity of the copy or copies with the sequence listing part mentioned in left column	:	
10. ☒ other *(specify)*: Express Mail Certificate of Mailing dated July 3, 2002 bearing Express Mail Label No. EL398170469US	:	

Figure of the drawings which should accompany the abstract: .....

Language of filing of the international application: English

Box No. X 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 request).

SYNAPTIC PHARMACEUTICAL CORPORATION

Errol de Souza 10/10/02

NAME: Errol De Souza Date

TITLE: President and CEO

For receiving Office use only

1. Date of actual receipt of the purported international application:	2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority (if two or more are competent): ISA /	6. ☐ Transmittal of search copy delayed until search fee is paid

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

28 28

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/31068

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :Please See Extra Sheet.
US CL :514/255, 256; 544/200, 201, 208, 212

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/255, 256; 544/200, 201, 208, 212

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 practicable, search terms used)

CAS–structure
EAST/WEST–substructure image

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y, E	US 6,441,000 B1 (GIBSON et al) 27 August 2002, see entire document, especially columns 30-40 preparations 1-27.	1-2, 10-11, 19-20
Y	WO 99/59971 A1 (PFIZER INC.) 25 November 1999, see entire document, especially examples 46, 61, 69 and pages 2-3 formula I.	1-2, 10-11, 19-20, 51-61
X,P — Y,P	WO 02/02744 A2 (SYNAPTIC PHARMACEUTICAL) CORP.) 10 January 2002, see entire document, especially pages 349-358, compounds and abstract.	1-2, 10-11, 19-20, 41-42, 52-79 — 1-23, 41-79

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"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
"A"	document defining the general state of the art which is not considered to be of particular relevance	"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
"E"	earlier document published on or after the international filing date	"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
"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)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
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Date of the actual completion of the international search 11 SEPTEMBER 2002	Date of mailing of the international search report 26 SEP 2002
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer CELIA CHANG Telephone No. (703) 308-1235

Form PCT/ISA/210 (second sheet) (July 1998)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/21068

A. CLASSIFICATION OF SUBJECT MATTER:
IPC (7):

IPC7 A61K 31/445; C07D 211/80, 211/96, 401/06, 401/12, 405/06, 405/12

Form PCT/ISA/210 (extra sheet) (July 1998)*

REPORTE DE BUSQUEDA INTERNACIONAL	No. de solicitud internacional PCT/US 02/21068

A. CLASIFICACION DEL TEMA

IPC (7) : Por favor vea Hoja Extra
US CL : 514/323, 326; 546/200, 201, 209, 212
De acuerdo a la Clasificación de Patentes Internacional (IPC) o a la clasificación nacional y a la IPC.

B. CAMPOS BUSCADOS

Documentación mínima buscada (sistema de clasificación seguido por los símbolos de clasificación)
U.S. : 514/323, 326; 546/200, 201, 209, 212

Documentación buscada diferente a la documentación mínima, a la extensión que tales documentos están incluidos en los campos buscados

Base de datos electrónicos consultados durante la búsqueda internacional (nombre de la base de datos y, en donde sea práctico, términos de búsqueda utilizados)
CAS-structure
EAST/WEST-subclass image

C. DOCUMENTOS QUE SE CONSIDERA QUE SON RELEVANTES

Categoría*	Cita del documento, con indicación, en donde sea apropiado, de los pasajes relevantes	Relevante para la Reiv. No.
Y, E	US 6,441,000 B1 (GIBSON et al) 27 Agosto 2002, ver documento completo, especialmente columnas 30-40, preparaciones 1-27	1-2, 10-11, 19-20
Y	WO 99/59971 A1 (PFIZER INC.) 25 Noviembre 1999, ver documento complete, Especialmente ejemplos 46,61, 69 y páginas 2-3 fórmula I.	1-2, 10-11, 19-20, 51-61
X, P — Y, P	WO 02/02744 A2 (SYNAPTIC PHARMACEUTICAL CORP.) Enero 10, 2002, ver documento complete, especialmente páginas 349-358, compuestos y resumen.	1-2, 10-11, 19-20, 41-42, 52-79 — 1-23, 41-79

☐ Documentos adicionales se enlistan en la continuación del cuadro C. ☐ Véase familia de patentes anexa.

* Categorías especiales de los documentos citados
"A" documento que define el estado general de la técnica el cual no se considera ser de particular relevancia.
"E" documento anterior publicado en o después de la fecha de presentación internacional.
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"O" documento que se refiere a una descripción oral, uso, exhibición u otro medio
"P" documento publicado antes de la fecha de presentación internacional pero después de la fecha de prioridad reivindicada.
"T" documento posterior publicado después de la fecha de presentación internacional o fecha de prioridad y no en conflicto con la solicitud, pero citado para entender el principio o teoría fundamental de la invención.
"X" documento de relevancia particular; la invención reivindicada no puede ser considerada nueva o no se puede considerar que involucre una etapa inventiva cuando el documento es considerado de manera aislada.
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"&" documento miembro de la misma familia de patentes.

Fecha de la terminación real de la búsqueda internacional	Fecha de envío del reporte de búsqueda internacional
11 SEPTIEMBRE 2002	26 SEPTIEMBRE 2002

Nombre y dirección postal de la ISA/US	Oficial autorizado
Comisionado de Patentes y Marcas Box PCT Washington, D.C. 20231 Facsímile (705) 305-3230	CELIA CHANG Teléfono No. (708)808-1235

31

Solicitud Internacional No.
PCT/US02/21063

A. CLASIFICACION DE LA MATERIA OBJETO:
IPC (7):

IPC7 A61K 31/445; CO7D 211/30, 211/94, 401/06, 401/12, 403/06, 408/12

SUBSTITUTED ANILINIC PIPERIDINES AS MCH SELECTIVE ANTAGONISTS

BACKGROUND OF THE INVENTION

This application is a continuation-in-part of U.S. Serial No. 10/042,582, filed January 9, 2002, and of U.S. Serial No. 09/899,794, filed July 5, 2001, the contents of both of which are hereby incorporated by reference into the subject application.

Throughout this application, various publications are referenced in parentheses by author and year. Full citations for these references may be found at the end of the specification immediately preceding the sequence listings and the claims. The disclosure of these publications in their entireties are hereby incorporated by reference into this application to describe more fully the state of the art to which this invention pertains. Melanin-concentrating hormone (MCH) is a cyclic peptide originally isolated from salmonid (teleost fish) pituitaries (Kawauchi et al., 1983). In fish the 17 amino acid peptide causes aggregation of melanin within the melanophores and inhibits the release of ACTH, acting as a functional antagonist of α-MSH. Mammalian MCH (19 amino acids) is highly conserved between rat, mouse, and human, exhibiting 100% amino acid identity, but its physiological roles are less clear. MCH has been reported to participate in a variety of processes including feeding, water balance, energy metabolism, general arousal/attention state,

memory and cognitive functions, and psychiatric disorders (for reviews, see Baker, 1991; Baker, 1994; Nahon, 1994; Knigge et al., 1996). Its role in feeding or body weight regulation is supported by a recent *Nature* publication (Qu et al., 1996) demonstrating that MCH is overexpressed in the hypothalamus of *ob/ob* mice compared with *ob/+* mice, and that fasting further increased MCH mRNA in both obese and normal mice during fasting. MCH also stimulated feeding in normal rats when injected into the lateral ventricles (Rossi et al., 1997). MCH also has been reported to functionally antagonize the behavioral effects of α-MSH (Miller et al., 1993; Gonzalez et al, 1996; Sanchez et al., 1997); in addition, stress has been shown to increase POMC mRNA levels while decreasing the MCH precursor preproMCH (ppMCH) mRNA levels (Presse et al., 1992). Thus MCH may serve as an integrative neuropeptide involved in the reaction to stress, as well as in the regulation of feeding and sexual activity (Baker, 1991; Knigge et al., 1996).

Although the biological effects of MCH are believed to be mediated by specific receptors, binding sites for MCH have not been well described. A tritiated ligand ([^{3}H]-MCH) was reported to exhibit specific binding to brain membranes but was unusable for saturation analyses, so neither affinity nor B_{max} were determined (Drozdz and Eberle, 1995). Radioiodination of the tyrosine at position thirteen resulted in a ligand with dramatically reduced biological activity (see Drozdz and Eberle, 1995). In contrast, the radioiodination of the MCH analogue [Phe^{13},Tyr^{15}]-MCH was successful (Drozdz et al., 1995); the ligand retained biological activity and

exhibited specific binding to a variety of cell lines including mouse melanoma (B16-F1, G4F, and G4F-7), PC12, and COS cells.. In G4F-7 cells, the K_D = 0.118nM and the B_{max} ~1100 sites/cell. Importantly, the binding was not inhibited by α-MSH but was weakly inhibited by rat ANF (Ki = 116 nM vs. 12 nM for native MCH) (Drozdz et al., 1995). More recently specific MCH binding was reported in transformed keratinocytes (Burgaud et al., 1997) and melanoma cells (Drozdz et al., 1998), where photo-crosslinking studies suggest that the receptor is a membrane protein with an apparent molecular weight of 45-50 kDaltons, compatible with the molecular weight range of the GPCR superfamily of receptors. No radioautoradiographic studies of MCH receptor localization using this ligand have been reported as yet.

The localization and biological activities of MCH peptide suggest that the modulation of MCH receptor activity may be useful in a number of therapeutic applications. The role of MCH in feeding is the best characterized of its potential clinical uses. MCH is expressed in the lateral hypothalamus, a brain area implicated in the regulation of thirst and hunger (Grillon et al., 1997); recently orexins A and B, which are potent orexigenic agents, have been shown to have very similar localization to MCH in the lateral hypothalamus (Sakurai et al., 1998). MCH mRNA levels in this brain region are increased in rats after 24 hours of food-deprivation (Hervé and Fellman, 1997); after insulin injection, a significant increase in the abundance and staining intensity of MCH immunoreactive perikarya and fibres was observed concurrent with a

significant increase in the level of MCH mRNA (Bahjaoui-Bouhaddi et al., 1994). Consistent with the ability of MCH to stimulate feeding in rats (Rossi et al., 1997) is the observation that MCH mRNA levels are upregulated in the hypothalami of obese ob/ob mice (Qu et al., 1996), and decreased in the hypothalami of rats treated with leptin, whose food intake and body weight gains are also decreased (Sahu, 1998). MCH appears to act as a functional antagonist of the melanocortin system in its effects on food intake and on hormone secretion within the HPA (hypothalamopituitary/adrenal axis) (Ludwig et al., 1998). Together these data suggest a role for endogenous MCH in the regulation of energy balance and response to stress, and provide a rationale for the development of specific compounds acting at MCH receptors for use in the treatment of obesity and stress-related disorders.

In all species studied to date, a major portion of the neurons of the MCH cell group occupies a rather constant location in those areas of the lateral hypothalamus and subthalamus where they lie and may be a part of some of the so-called "extrapyramidal" motor circuits. These involve substantial striato- and pallidofugal pathways involving the thalamus and cerebral cortex, hypothalamic areas, and reciprocal connections to subthalamic nucleus, substantia nigra, and mid-brain centers (Bittencourt et al., 1992). In their location, the MCH cell group may offer a bridge or mechanism for expressing hypothalamic visceral activity with appropriate and coordinated motor activity. Clinically it may be of some value to consider the involvement of this MCH system in movement disorders, such as

Parkinson's disease and Huntingdon's Chorea in which extrapyramidal circuits are known to be involved.

Human genetic linkage studies have located authentic hMCH loci on chromosome 12 (12q23-24) and the variant hMCH loci on chromosome 5 (5q12-13) (Pedeutour et al., 1994). Locus 12q23-24 coincides with a locus to which autosomal dominant cerebellar ataxia type II (SCA2) has been mapped (Auburger et al., 1992; Twells et al., 1992). This disease comprises neurodegenerative disorders, including an olivopontocerebellar atrophy. Furthermore, the gene for Darier's disease, has been mapped to locus 12q23-24 (Craddock et al., 1993). Dariers' disease is characterized by abnormalities I keratinocyte adhesion and mental illnesses in some families. In view of the functional and neuroanatomical patterns of the MCH neural system in the rat and human brains, the MCH gene may represent a good candidate for SCA2 or Darier's disease. Interestingly, diseases with high social impact have been mapped to this locus. Indeed, the gene responsible for chronic or acute forms of spinal muscular atrophies has been assigned to chromosome 5q12-13 using genetic linkage analysis (Melki et al., 1990; Westbrook et al., 1992). Furthermore, independant lines of evidence support the assignment of a major schizophrenia locus to chromosome 5q11.2-13.3 (Sherrington et al., 1988; Bassett et al., 1988; Gilliam et al., 1989). The above studies suggest that MCH may play a role in neurodegenerative diseases and disorders of emotion.

Additional therapeutic applications for MCH-related compounds are suggested by the observed effects of MCH

in other biological systems. For example, MCH may regulate reproductive functions in male and female rats. MCH transcripts and MCH peptide were found within germ cells in testes of adult rats, suggesting that MCH may participate in stem cell renewal and/or differentiation of early spermatocytes (Hervieu et al., 1996). MCH injected directly into the medial preoptic area (MPOA) or ventromedial nucleus (VMN) stimulated sexual activity in female rats (Gonzalez et al., 1996). In ovariectomized rats primed with estradiol, MCH stimulated luteinizing hormone (LH) release while anti-MCH antiserum inhibited LH release (Gonzalez et al., 1997). The zona incerta, which contains a large population of MCH cell bodies, has previously been identified as a regulatory site for the pre-ovulatory LH surge (MacKenzie et al., 1984). MCH has been reported to influence release of pituitary hormones including ACTH and oxytocin. MCH analogues may also be useful in treating epilepsy. In the PTZ seizure model, injection of MCH prior to seizure induction prevented seizure activity in both rats and guinea pigs, suggesting that MCH-containing neurons may participate in the neural circuitry underlying PTZ-induced seizure (Knigge and Wagner, 1997). MCH has also been observed to affect behavioral correlates of cognitive functions. MCH treatment hastened extinction of the passive avoidance response in rats (McBride et al., 1994), raising the possibility that MCH receptor antagonists may be beneficial for memory storage and/or retention. A possible role for MCH in the modulation or perception of pain is supported by the dense innervation of the periaqueductal grey (PAG) by MCH-positive fibers. Finally, MCH may participate in the regulation of fluid

intake. ICV infusion of MCH in conscious sheep produced diuretic, natriuretic, and kaliuretic changes in response to increased plasma volume (Parkes, 1996). Together with anatomical data reporting the presence of MCH in fluid regulatory areas of the brain, the results indicate that MCH may be an important peptide involved in the central control of fluid homeostasis in mammals.

The identification of a G-protein coupled receptor for MCH has recently been published (Chambers et al., 1999; Saito et al., 1999). These groups identified MCH as the endogenous ligand for the human orphan G-protein coupled receptor SLC-1 (Lakaye et al., 1998). The rat homologue of this receptor (now called MCH-1) was reported to be localized in regions of the rat brain associated with feeding behavior (e.g. dorsomedial and ventromedial hypothalamus). The link between MCH-1 and the effects of MCH on feeding has been strengthened by recent reports on the phenotype of MCH-1 knockout mice. Two groups have shown independently (Marsh et al, 2002; Chen et al, 2002) that the targeted disruption of the MCH-1 receptor gene (MCH-1 knockout) in mice results in animals that are hyperphagic but are lean and have decreased body mass relative to wild-type littermates. The decrease in body mass is attributed to an increase in metabolism. Each group demonstrated that the MCH-1 knockout mice are resistant to diet-induced obesity, and generally exhibit weights similar to littermates maintained on regular chow.

Finally, synthetic antagonist molecules for the MCH-1 receptor have now been described in the literature. Bednarek et al. (2002) have reported on the synthesis of

high affinity peptide antagonists of MCH-1. In addition, a small molecule antagonist of MCH-1 has been described by Takekawa et al. (Takekawa et al., 2002). This compound, T-226296, exhibits high affinity for the MCH-1 receptor (~ 5-9 nM for rat and human MCH-1), and was shown to inhibit food intake induced by the intracerebroventricular application of MCH. These data validate the strategy of using an MCH-1 receptor antagonist to treat obesity.

Furthermore, in our own studies, we have tested MCH1 antagonists in several animal models that are well known as predictive for the efficacy of compounds in humans (Borowsky, et al., in press; unpublished data). These experiments indicate that MCH1 antagonists are useful to treat obesity, depression, anxiety, as well as urinary disorders.

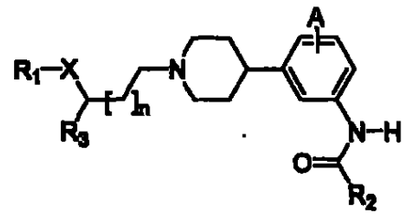
As used in this invention, the term "antagonist" refers to a compound which binds to, and decreases the activity of, a receptor in the presence of an agonist. In the case of a G-protein coupled receptor, activation may be measured using any appropriate second messenger system which is coupled to the receptor in a cell or tissue in which the receptor is expressed. Some specific, but by no means limiting, examples of well-known second messenger systems are adenylate cyclase, intracellular calcium mobilization, ion channel activation, guanylate cyclase and inositol phospholipid hydrolysis. Conversely, the term "agonist" refers to a compound which binds to, and increases activity of, a receptor as compared with the activity of the receptor in the absence of any agonist.

In one embodiment of this invention, the synthesis of novel compounds which bind selectively to the cloned human melanin-concentrating hormone-1 (MCH1) receptor, compared to other cloned G-protein coupled receptors, and inhibit the activation of the cloned receptors as measured in *in vitro* assays is disclosed. The *in vitro* receptor binding assays described hereinafter were performed using various cultured cell lines, each transfected with and expressing only a single cloned receptor.

Furthermore, the compounds of the present invention may also be used to treat abnormal conditions such as feeding disorders (obesity, bulimia and bulimia nervosa), sexual/reproductive disorders, depression, anxiety, depression and anxiety, epileptic seizure, hypertension, cerebral hemorrhage, congestive heart failure, sleep disturbances, or any condition in which antagonism of an MCH1 receptor may be beneficial. In addition, the compounds of the present invention may be used to reduce the body mass of a subject. Furthermore, the compounds of the present invention may be used to treat urinary disorders.

Summary of the Invention

This invention provides a compound having the structure:



wherein R_1 is hydrogen, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -F, -Cl, -Br, -I, -CN, $-NO_2$, $-CH_3$, $-CF_3$, $-COR_3$, $-CO_2R_3$, phenyl, phenoxy or straight chained or branched C_1-C_7 alkyl;

wherein R_2 is straight-chained or branched C_3-C_4 alkyl or cyclopropyl;

wherein R_3 is aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -F, -Cl, -Br, -I, -CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl;

wherein A is -H, -F, -Cl, -Br, -CN, $-NO_2$, $-COR_3$, $-CO_2R_3$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl;

wherein X is O or NH; and

wherein n is an integer from 0 to 5 inclusive.

In one embodiment, R_1 is aryl optionally substituted with one or more -F, -Cl, -Br, -I, -CN, $-NO_2$, $-COR_3$, $-CO_2R_3$, straight chained or branched C_1-C_7 alkyl;

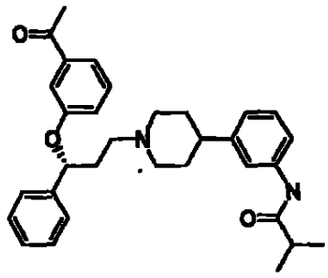
wherein R_3 is phenyl;

wherein A is H; and

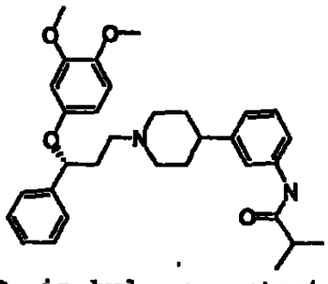
wherein X is O.

In one embodiment, R_2 is isopropyl.

In one embodiment, the compound has the structure:



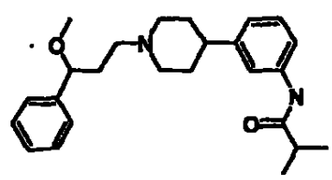
In one embodiment, compound has the structure:



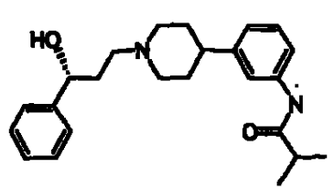
In one embodiment, R_1 is hydrogen, straight chained or branched C_1-C_7 alkyl; and wherein R_3 is aryl.

In one embodiment, R_2 is isopropyl; and A is hydrogen.

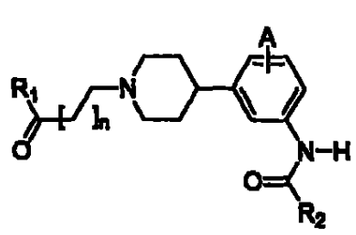
In one embodiment, the compound has the structure:



In one embodiment, the compound has the structure:



The present invention also provides a compound having the structure:



;

wherein R_1 is aryl or heteroaryl optionally substituted with one or more -F, -Cl, -Br, -I, -CN, $-NO_2$, $-OCH_3$, phenoxy, fused cyclopentanyl, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl;

wherein R_2 is straight-chained or branched C_1-C_4 alkyl or cyclopropyl;

wherein A is -H, -F, -Cl, - Br, -CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl; and

wherein n is an integer from 1 to 5 inclusive.

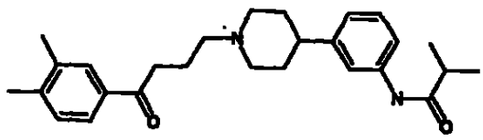
In one embodiment, R_1 is aryl optionally substituted with one or more -F, -Cl, -Br, -I or straight chained or branched C_1-C_4 alkyl; and

wherein A is H.

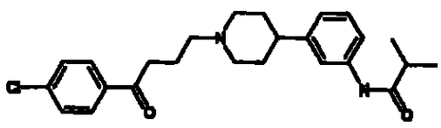
In one embodiment, R_2 is isopropyl; and

wherein n is 2.

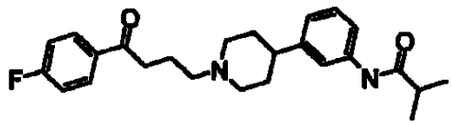
In one embodiment, the compound has the structure:



In one embodiment, the compound has the structure:



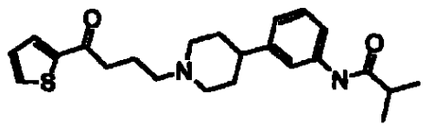
In one embodiment, the compound has the structure:



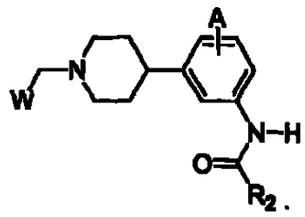
In one embodiment, R_1 is thienyl; and wherein A is H.

In one embodiment, R_2 is isopropyl.

In one embodiment, the compound has the structure:

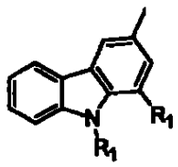


The invention provides a compound having the structure:

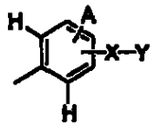


;

wherein W is



or



;

wherein each R_1 is independently hydrogen, methyl or ethyl;

wherein R_2 is straight- chained or branched C_3-C_4 alkyl or cyclopropyl;

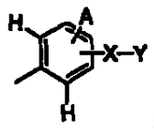
wherein R_3 is hydrogen, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -H, -F, -Cl, -Br, -I, -CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl.

wherein each A is independently -H, -F, -Cl, -Br, -CN, $-NO_2$, $-COR_3$, $-CO_2R_3$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl;

wherein X is O, NR_3, CO or may be absent; and

wherein Y is hydrogen, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -F, -Cl, -Br, -I, -CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl.

In one embodiment, W is

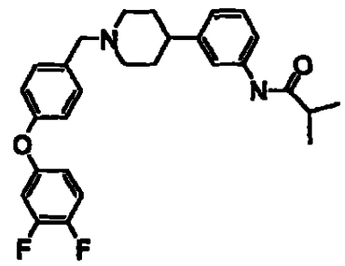


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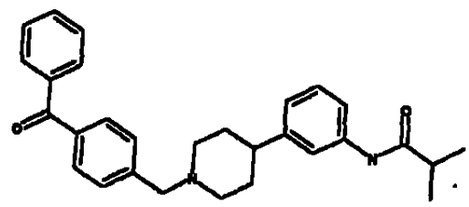
and wherein X is O or may be absent.

In one embodiment, R_2 is isopropyl.

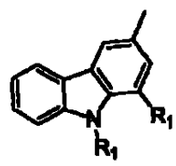
In one embodiment, the compound has the structure:



In one embodiment, the compound has the structure:



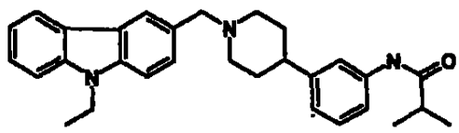
In one embodiment, W is



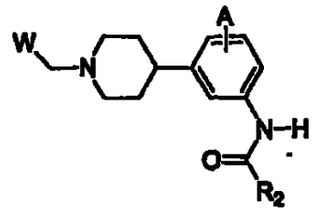
In one embodiment, A is -H, -F, -Cl, -Br.

In one embodiment, R_3 is isopropyl; and A is hydrogen.

In one embodiment, the compound has the structure:

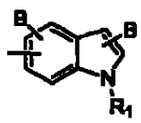
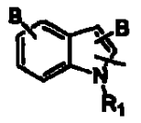


This invention provides a compound having the structure:



;

wherein W is

 or 

wherein R_1 is hydrogen, straight chained or branched C_1-C_7 alkyl, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -F, -Cl, -Br, -CN, $-NO_2$, $-OCH_3$, $-CO_2CH_3$, $-CF_3$, phenyl, straight chained or branched C_1-C_7 alkyl;

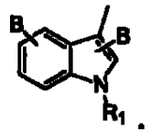
wherein R_2 is straight-chained or branched C_3-C_4 alkyl or cyclopropyl;

wherein A is -H, -F, -Cl, -Br, -CN, $-NO_2$, $-COR_1$, $-CO_2R_1$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl or phenyl.

wherein each B is independently -H, -F, -Cl, -Br, -I,

-CN, -NO_2, -COR_1, -CO_2R_1, - OCH_3, -OCF_3, -CF_3, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl or aryl, phenoxy or benzyloxy, wherein the aryl, phenoxy or benzyloxy is optionally substituted with one or more -F, -Cl, -Br, -CN, -NO_2, -COR_1, -CO_2R_1, -OCH_3, -OCF_3, -CF_3 or straight chained or branched C1 -C3 alkyl.

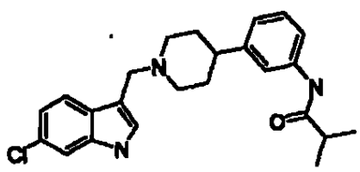
In one embodiment, W is



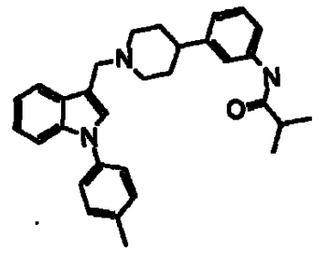
In one embodiment, R_1 is hydrogen or phenyl optionally substituted with one or more -F, -Cl, -Br, -CN, -NO_2, straight chained or branched C_1-C_7 alkyl.

In one embodiment, R_2 is isopropyl.

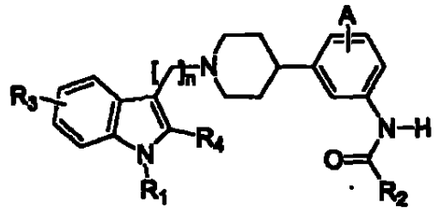
In one embodiment, the compound has the structure:



In one embodiment, the compound has the structure:



This invention provides a compound having the structure:



;

wherein R_1 is hydrogen, straight chained or branched C_1-C_7 alkyl, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -F, -Cl, -Br, -CN, -NO_2, -CF_3, -OCH_3, straight chained or branched C_1-C_3 alkyl;

wherein R_2 is straight-chained or branched C_3-C_4 alkyl or cyclopropyl;

wherein R_3 is -H, -F, -Cl, -Br, -I, -CN, -NO_2, -CF_3, -OCH_3, or straight chained or branched C_1-C_3 alkyl, monofluoroalkyl or polyfluoroalkyl, or a phenyl ring fused to C_6 and C_7 of the indole moiety;

wherein R_4 is hydrogen or aryl optionally substituted with one or more -F, -Cl, -Br, -I, -CN, -NO_2, -CF_3, straight chained or branched C_1-C_3 alkyl;

wherein A is -H, -F, -Cl, -Br, -CN, -NO_2, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl; and

wherein n is an integer from 2 to 4 inclusive.

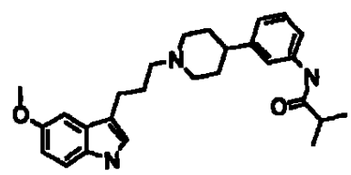
In one embodiment, R_3 is -H, -F, -Cl, -Br, -I, -CN, -NO_2, -OCF_3 or -OCH_3; and

wherein R_4 is hydrogen or phenyl optionally substituted with one or more -F, -Cl or -CF_3.

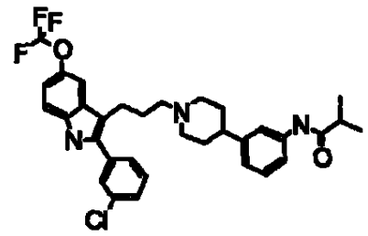
In one embodiment, R_1 is hydrogen or phenyl optionally substituted with one or more -F, -Cl, -Br, -CN, -NO_2, -CF_3, -OCH_3 or straight chained or branched C_1-C_3 alkyl;

In one embodiment, R_2 is isopropyl.

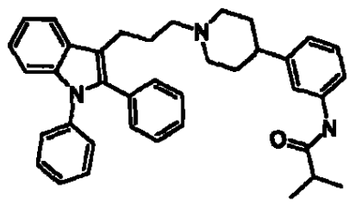
In one embodiment, the compound has the structure:



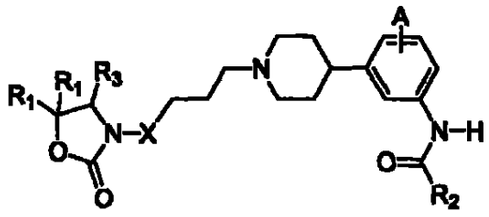
In one embodiment, the compound has the structure:



In one embodiment, the compound has the structure:



This invention provides a compound having the structure:



;

wherein each R_1 is independently hydrogen or CH_3;

wherein R_2 is straight-chained or branched C_1-C_4 alkyl or cyclopropyl;

wherein R_3 is benzyl or phenyl, wherein the benzyl or phenyl is optionally substituted with a methylenenedioxy group or one or more -F or -Cl;

wherein A is -H, -F, -Cl, - Br, -CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl;

wherein X is $(CH_2)_2$, $COCH_2$ or CONH;

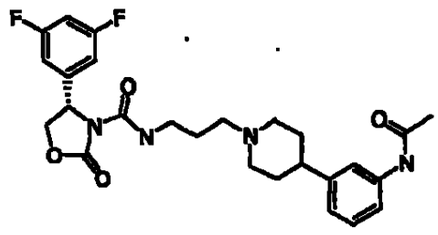
In one embodiment, R_3 is phenyl optionally substituted with one or more -F; and

wherein A is hydrogen.

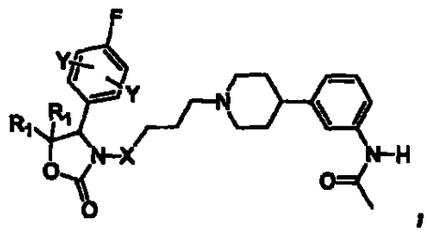
In one embodiment, X is CONH.

In one embodiment, R_2 is methyl.

In one embodiment, the compound has the structure:



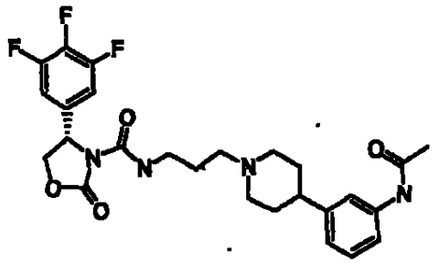
In one embodiment, the compound has the structure:



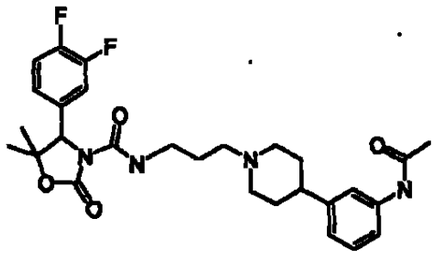
,

wherein each Y is independently hydrogen or -F.

In one embodiment, the compound has the structure:

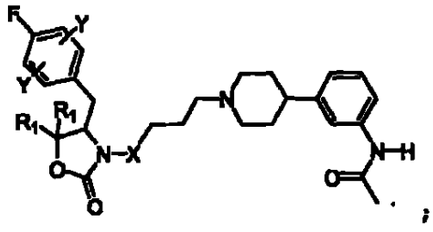


In one embodiment, the compound has the structure:



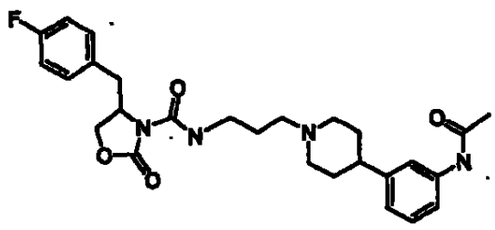
In one embodiment, R_1 is benzyl optionally substituted with a methylenedioxy group or one or more -F or -Cl.

In one embodiment, the compound has the structure:



wherein each Y is independently hydrogen or -F.

In one embodiment, the compound has the structure:



In one embodiment, the compound is enantiomerically pure.

In one embodiment, the compound is diastereomerically pure.

In one embodiment, the compound is enantiomerically and diastereomerically pure.

This invention also provides a pharmaceutical composition comprising a therapeutically amount of a compound of the invention and a pharmaceutically acceptable carrier.

In one embodiment, the amount of the compound is from about 0.01mg to about 500mg.

In one embodiment, the amount of the compound is from about 0.1mg to about 60mg.

In one embodiment, the amount of the compound is from about 1mg to about 20mg.

In one embodiment, the pharmaceutical composition consists of a carrier which is a liquid and the composition is a solution.

In one embodiment, the pharmaceutical composition consists of a carrier which is a solid and the composition is a tablet.

In one embodiment, the pharmaceutical composition consists of a carrier which is a gel and the composition is a suppository.

The invention also provides a process for making a pharmaceutical composition comprising admixing a therapeutically effective amount of the compound of any of the invention and a pharmaceutically acceptable carrier.

This invention also provides the method of treating a subject suffering from a disorder selected from the group consisting of depression, anxiety, urge incontinence, or obesity comprising administering to the subject a therapeutically effective amount of the compound of the invention.

In one embodiment, the therapeutically effective amount is between about 0.03 and about 1000 mg per day.

In one embodiment, the therapeutically effective amount is between about 0.30 and about 300 mg per day.

In one embodiment, the therapeutically effective amount is between about 1.0 and about 100 mg per day.

In one embodiment, the disorder is depression.

In one embodiment, the disorder is anxiety.

In one embodiment, the disorder is obesity.

In one embodiment, the disorder is urge incontinence.

The invention provides the method of reducing the body mass of a subject, which comprises administering to the subject an amount of a compound of the invention effective to reduce the body mass of the subject.

The invention provides the method of treating a subject suffering from depression, which comprises administering to the subject an amount of a compound of any of claims of the invention effective to treat the subject's depression.

The invention provides the method of treating a subject suffering from anxiety, which comprises administering to the subject an amount of a compound of the invention effective to treat the subject's anxiety.

The invention provides the method of alleviating urge urinary incontinence in a subject suffering from an overactive bladder, which comprises administering to the subject an amount of the compound of the invention effective to alleviate the subject's urge urinary incontinence.

The invention provides the method of managing obesity in a subject in need of weight loss, which comprises administering to the subject an amount of a compound of the invention effective to induce weight loss in the subject.

The invention provides the method of managing obesity in a subject who has experienced weight loss, which comprises administering to the subject an amount of a compound of the invention effective to maintain such weight loss in the subject.

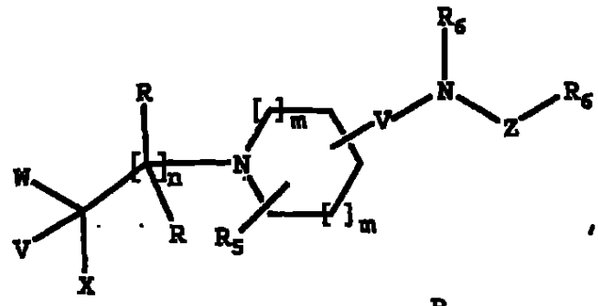
The invention provides the method of treating overactive bladder in a subject, which comprises administering to the subject an amount of a compound of any of the invention effective to treat the subject's overactive bladder.

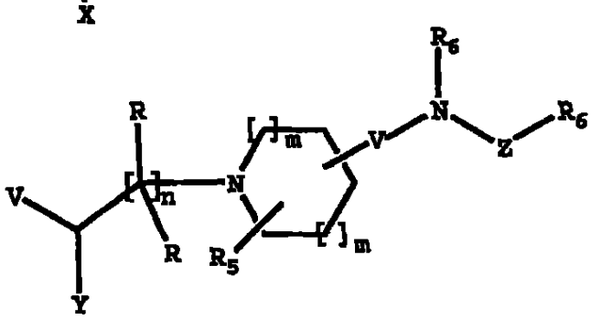
The invention provides the method of treating a disorder in a subject, wherein the symptoms of the subject can be alleviated by treatment with an MCH1 antagonist, wherein the MCH1 antagonist is the compound of the invention.

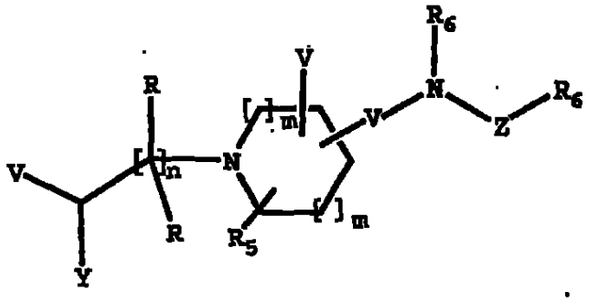
The invention provides the method of alleviating the symptoms of a disor4der in a subject, which comprises administering to the subject an amount of an MCH1 antagonist effective to alleviate the symptoms, wherein the MCH1 antagonist is the compound of the invention.

Detailed Description of the Invention

This invention provides a compound having the structure:

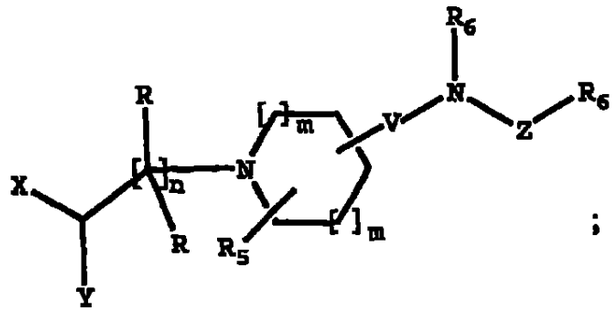






; or

10



wherein each V is independently phthalimide, aryl, phenoxy or heteroaryl, wherein the aryl, phenoxy or heteroaryl is optionally substituted with one or more F; Cl; Br; I; COR_5; CO_2R_5; $-OCOR_5$; $-CON(R_5)_2$; $-N(R_5)COR_5$; CN; $-NO_2$; $-N(R_5)_2$; $-OR_5$; $-SR_5$; $(CH_2)_qOR_5$; $(CH_2)_qR_5$; $(CH_2)_qSR_5$; straight chained or branched C_1-C_7 alkyl, monofluoroalkyl, polyfluoroalkyl, aminoalkyl, or carboxamidoalkyl; straight chained or branched C_2-C_7 alkenyl, C_2-C_7 alkynyl; aryl; phenoxy; C_3-C_7 cycloalkyl, monofluorocycloalkyl, polyfluorocycloalkyl or cycloalkenyl;

wherein each W is independently aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more F; Cl; Br; I; COR_3; $-OCOR_3$; CO_2R_3; $-CON(R_3)_2$; $-N(R_3)COR_3$; CN; $-NO_2$; $-N(R_3)_2$; $-OR_3$; $-SR_3$; $(CH_2)_qOR_3$; $(CH_2)_qSR_3$; straight chained or branched C_1-C_7 alkyl, monofluoroalkyl, polyfluoroalkyl, aminoalkyl, or carboxamidoalkyl; straight chained or branched C_2-C_7 alkenyl, C_2-C_7 alkynyl; aryl; phenoxy; C_3-C_7 cycloalkyl, monofluorocycloalkyl, polyfluorocycloalkyl or cycloalkenyl;

wherein X is hydrogen or - OR_3, provided that when X is -OR_3 the V geminal to X cannot be phthalimide;

wherein Y is hydrogen, =O (carbonyl oxygen), OR_3, OV, COV, =NNHV, =NNR_3, NER_3, NZV, NCONV (ureas), $NCONR_3$, NR_3, carbazole, indole or phthalimide;

wherein each R is independently -H; -F; straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl; straight chained or branched C_2-C_7 alkenyl or alkynyl; -$N(R_3)_2$; -NO_2; -CN; -CO_2R_3; -$OCOR_3$; -OR_3; or -$N(R_3)COR_3$; -$CON(R_3)_2$;

wherein each R_3 is independently -H; straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl; straight chained or branched C_2-C_7 alkenyl or alkynyl; C_3-C_7 cycloalkyl, monofluorocycloalkyl, polyfluorocycloalkyl or cycloalkenyl;

wherein each R_6 is -H; -NO_2; -N_3; -CN; straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl; straight chained or branched C_2-C_7 alkenyl or alkynyl; C_3-C_7 cycloalkyl, monofluorocycloalkyl, polyfluorocycloalkyl or cycloalkenyl; -$N(R_3)_2$; -OR_3; -$(CH_2)_pOR_3$; -COR_3; -CO_2R_3; -$OCOR_3$; -$CON(R_3)_2$; -$N(R_3)COR_3$; aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more F; Cl; Br; I; COR_6; CO_2R_3; -$OCOR_3$; -$CON(R_3)_2$; -$N(R_3)COR_3$; CN; -NO_2; -$N(R_3)_2$; -OR_6; -SR_6; $(CH_2)_qOR6$; $(CH_2)_qSR_6$; straight chained or branched C_1-C_7 alkyl, monofluoroalkyl, polyfluoroalkyl, aminoalkyl, or carboxamidoalkyl; straight chained or branched C_2-C_7 alkenyl, C_2-C_7 alkynyl; C_3-C_7 cycloalkyl,

monofluorocycloalkyl, polyfluorocycloalkyl or cycloalkenyl;

wherein R_6 is -H; straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl; straight chained or branched C_2-C_7 alkenyl or alkynyl; C_3-C_7 cycloalkyl, monofluorocycloalkyl, polyfluorocycloalkyl or cycloalkenyl; $-N(R_3)_2$; $-OR_3$; $-(CH_2)_pOR_3$; $-COR_3$; $-CO_2R_3$; $-OCOR_3$; $-CON(R_3)_2$; $-N(R_3)COR_3$; aryl, benzyl or heteroaryl, optionally substituted with one or more F; Cl; Br; I; COR_3; CO_2R_3; $-OCOR_3$; $-CON(R_3)_2$; $-N(R_3)COR_3$, CN; $-NO_2$; $-N(R_3)_2$; $-OR_3$; $-SR_3$; $(CH_2)_qOR_3$; $(CH_2)_qSR_3$; straight chained or branched C_1-C_7 alkyl, monofluoroalkyl, polyfluoroalkyl, aminoalkyl, or carboxamidoalkyl; aryl; benzyl; straight chained or branched C_2-C_7 alkenyl, C_2-C_7 alkynyl; C_3-C_7 cycloalkyl, monofluorocycloalkyl, polyfluorocycloalkyl or cycloalkenyl;

wherein Z is CO, SO_2 or SO_2NR_6;

wherein each m is independently an integer from 0 to 3 inclusive;

wherein each n is independently an integer from 0 to 5 inclusive;

wherein each p is independently an integer from 1 to 7 inclusive; and

wherein q is an integer from 1 to 3 inclusive;

or a pharmaceutically acceptable salt thereof.

As used in the present invention, the term "cycloalkyl" includes C_3-C_7 cycloalky moities which may be substituted with one or more of the following: F; CN; $-NO_2$; straight chained or branched C_1-C_7 alkyl, straight chained or branched C_1-C_7 monofluoroalkyl,straight chained or branched C_1-C_7 polyfluoroalkyl, straight chained or branched C_2-C_7 alkanyl, straight chained or branched C_2-C_7 alkynyl; C_3-C_7 cycloalkyl, C_3-C_7 monofluorocycloalkyl, C_3-C_7 polyfluorocycloalkyl, C_5-C_7 cycloalkenyl, $-N(R_3)_2$; $-OR_3$; $-NCOR_3$; $-COR_3$; $-CO_2R_3$; $-CON(R_3)_2$ or $(CH_2)_p$-O-$(CH_3)_m$-CH_3.

In the present invention, the term "cycloalkenyl" includes C_5-C_7 cycloalkenyl moities which may be substituted with one or more of the following: -F; -Cl; -Br, -I; CN; $-NO_2$; straight chained or branched C_1-C_7 alkyl, straight chained or branched C_1-C_7 monofluoroalkyl, straight chained or branched C_1-C_7 polyfluoroalkyl, straight chained or branched C_2-C_7 alkenyl, straight chained or branched C_2-C_7 alkynyl; C_3-C_7 cycloalkyl, C_3-C_7 monofluorocycloalkyl, C_3-C_7 polyfluorocycloalkyl, C_5-C_7 cycloalkenyl,$-N(R_3)_2$; $-OR_3$; $-NCOR_3$; $-COR_3$; $-CO_2R_3$; $-CON(R_3)_2$ or $(CH_2)_p$-O-$(CH_3)_m$-CH_3.

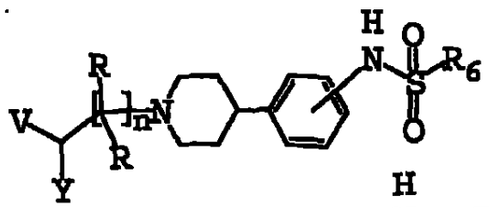
As used in the present invention, the term "heteroaryl" is used to include five and six membered unsaturated rings that may contain one or more oxygen, sulfur, or nitrogen atoms. Examples of heteroaryl groups include, but are not limited to, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazzolyl, thiadiazolyl,

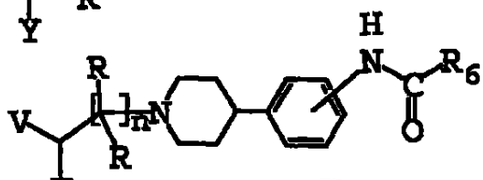
pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, and triazinyl.

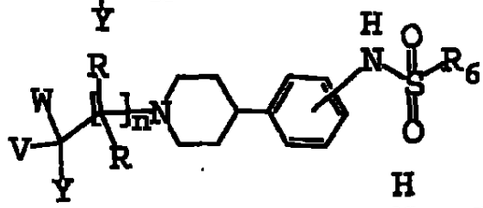
In addition, the term "heteroaryl" is used to include fused bicyclic ring systems that may contain one or more heteroatoms such as oxygen, sulfur and nitrogen. Examples of such heteroaryl groups include, but are not limited to, indolizinyl, indolyl, isoindolyl, benzo[b]furanyl, benzo[b]thiophenyl, indazolyl, benzimidazolyl, purinyl, benzoxazolyl, benzisoxazolyl, benzo[b]thiazolyl, imidazo[2,1-b]thiazolyl, cinnolinyl, quinazolinyl, quinoxalinyl, 1,8-naphthyridinyl, pteridinyl, quinolinyl, isoquinolinyl, phthalimidyl and 2,1,3-benzothiazolyl.

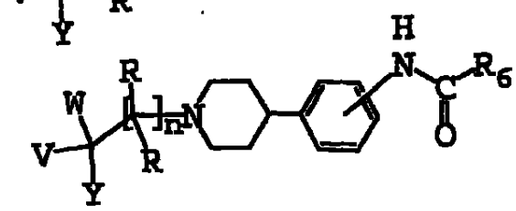
The term "heteroaryl" also includes those chemical moieties recited above which may be substituted with one or more of the following: -F; -Cl; -Br, -I; CN; $-NO_2$; straight chained or branched C_1-C_7 alkyl, straight chained or branched C_1-C_7 monofluoroalkyl, straight chained or branched C_1-C_7 polyfluoroalkyl, straight chained or branched C_2-C_7 alkenyl, straight chained or branched C_2-C_7 alkynyl; C_3-C_7 cycloalkyl, C_3-C_7 monofluorocycloalkyl, C_3-C_7 polyfluorocycloalkyl, C_3-C_7 cycloalkenyl, $-N(R_3)_2$; $-OR_3$; $-NCOR_3$; $-COR_3$; $-CO_2R_3$; $-CON(R_3)_2$ or $(CH_2)_p$-O-$(CH_3)_m$-CH_3.

In still another embodiment of the above described invention, the compound has the structure:


;

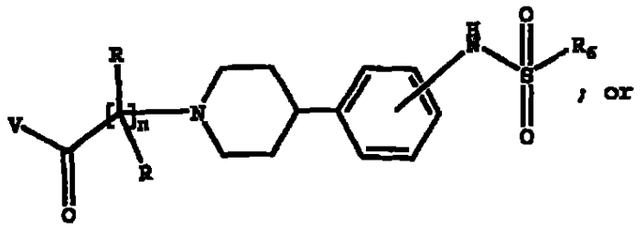

;

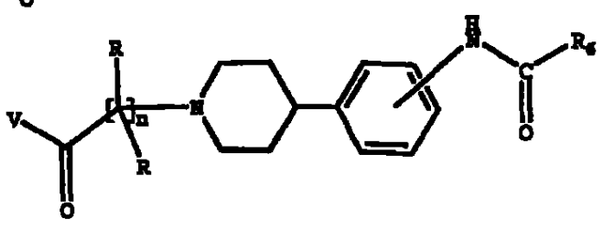

; or


.

In a further embodiment of the instant invention, R_6 is straight chained or branched C_1-C_7 alkyl; C_3-C_7 cycloalkyl; $-N(R_3)_2$; $-OR_3$; $-(CH_2)_pOR_3$; aryl, benzyl or heteroaryl, optionally substituted with one or more F; Cl; Br; I; $-OR_3$; $-(CH_2)_qOR_3$; or straight chained or branched C_1-C_7 alkyl.

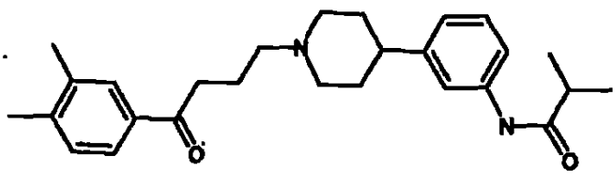
In an embodiment of the present invention, the compound has the structure:



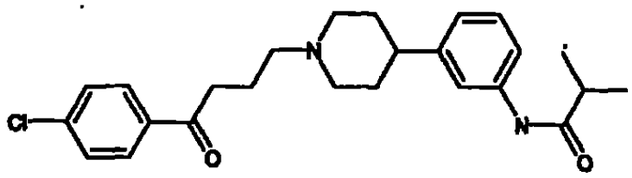


In a further embodiment of the present invention, at least one V is phenyl optionally substituted with one or more F; Cl; Br; $-OR_3$; $(CH_2)_qOR_3$; straight chained or branched C_1-C_7 alkyl; C_1-C_7 polyfluoroalkyl; or phenoxy.

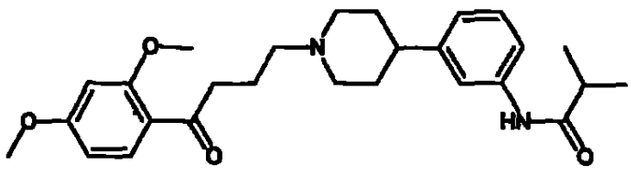
In one embodiment of the present invention, the compound is:



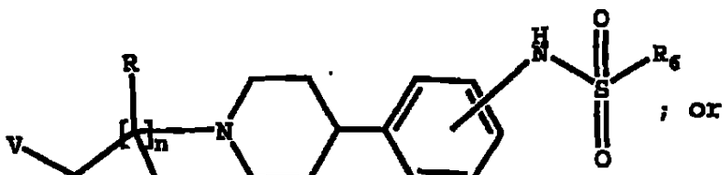
In one embodiment, the compound is:



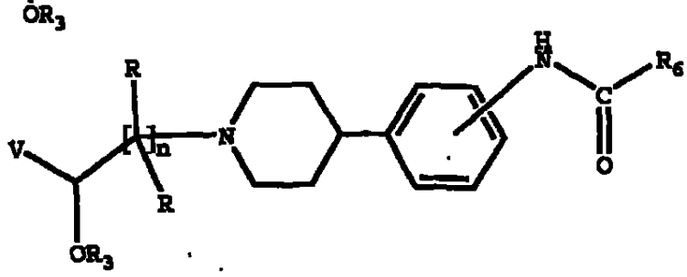
In one embodiment, the compound is:



In another embodiment of the present invention, the compound has the structure:

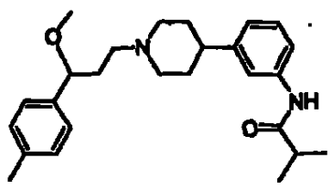


; or

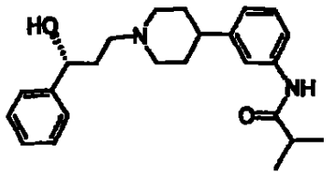


In a further embodiment of the present invention, at least one V is phenyl optionally substituted with one or more F; Cl; Br; $-OR_3$; $(CH_2)_qOR_3$; straight chained or branched C_1-C_7 alkyl; C_1-C_7 polyfluoroalkyl; or phenoxy.

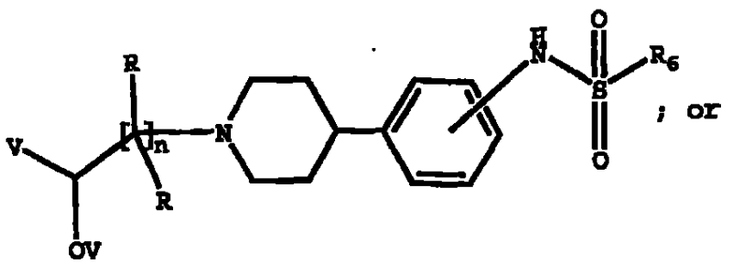
In another embodiment of the present invention, the compound is



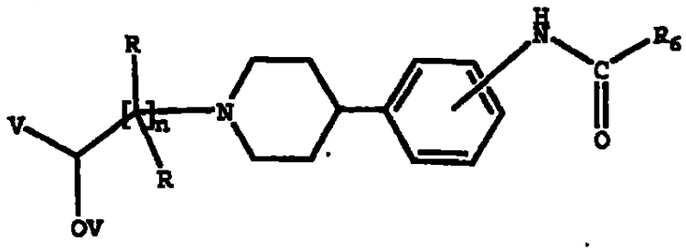
In one embodiment, the compound is



In a further embodiment of the present invention, the compound has the structure:

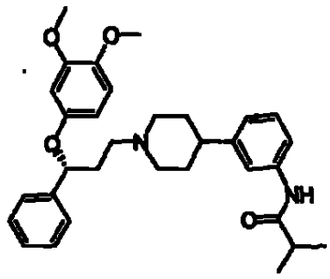


; or

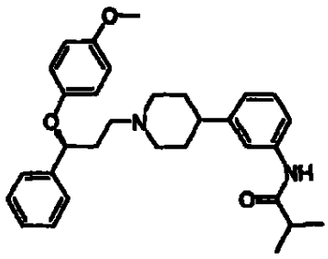


In another embodiment of the present invention, at least one V is phenyl optionally substituted with one or more F; Cl; Br; $-OR_3$; $-COR_3$; $(CH_2)_qOR_3$; straight chained or branched C_1-C_7 alkyl; C_1-C_7 polyfluoroalkyl; aryl or phenoxy.

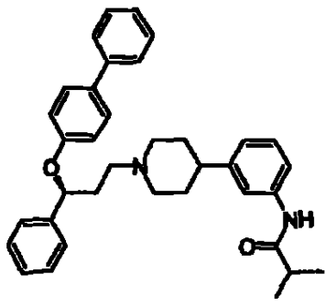
In yet another embodiment of the present invention, the compound is



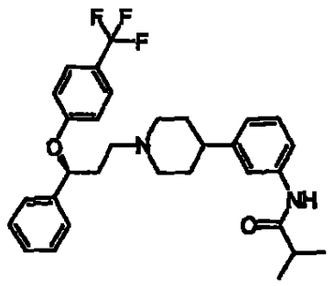
In one embodiment, the compound is



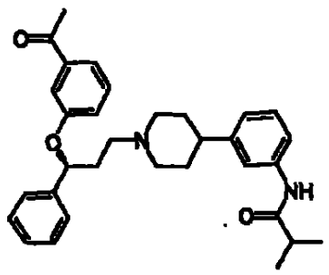
In one embodiment, the compound is



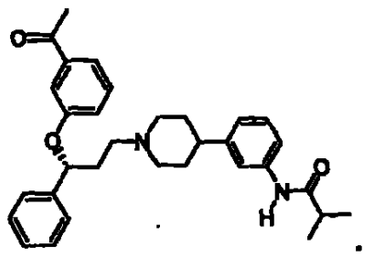
In one embodiment, the compound is



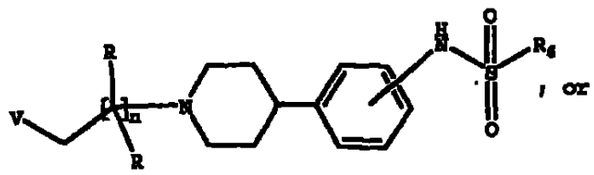
In one embodiment, the compound is



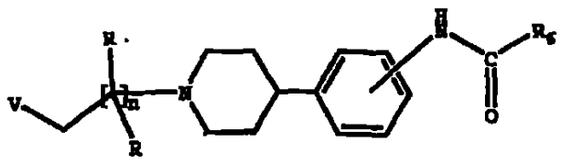
In one embodiment, the compound is



In an embodiment of the present invention, the compound has the structure:

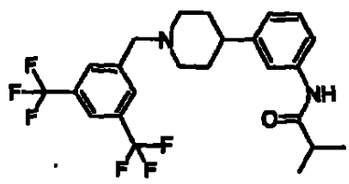


; or

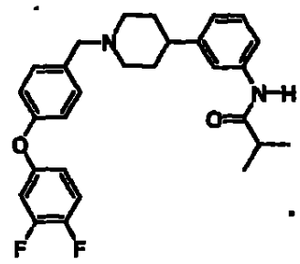


In a further embodiment of the present invention, at least one V is phenyl optionally substituted with one or more F; Cl; Br; $-OR_3$; $(CH_2)_qOR_3$; straight chained or branched C_1-C_7 alkyl; C_1-C_7 polyfluoroalkyl; or phenoxy.

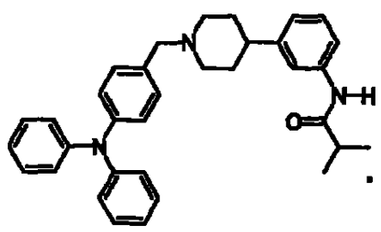
In yet another embodiment of the present invention, the compound is



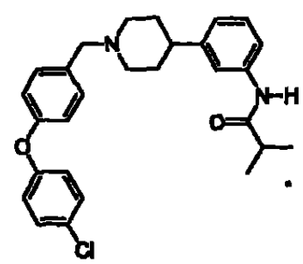
In one embodiment, the compound has the structure:



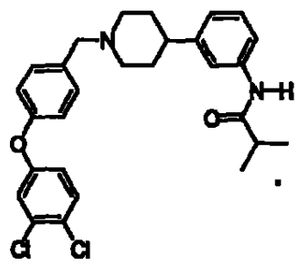
In one embodiment, the compound has the structure:



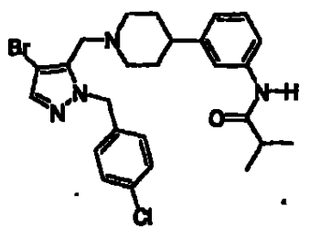
In one embodiment, the compound has the structure:



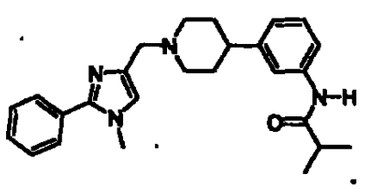
In one embodiment, the compound has the structure:



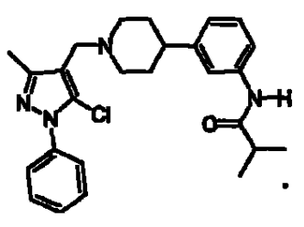
In one embodiment, the compound has the structure:



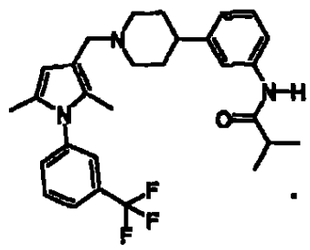
In one embodiment, the compound has the structure:



In one embodiment, the compound has the structure:



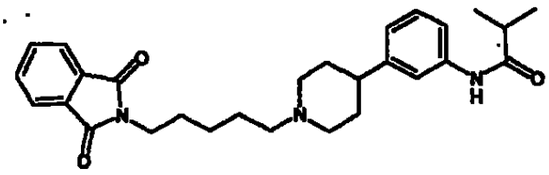
In one embodiment, the compound has the structure:



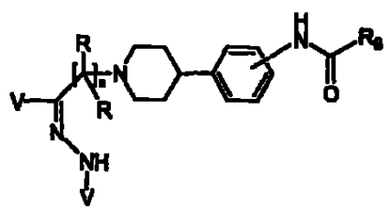
In an additional embodiment of the present invention, Y is hydrogen and V is phthalimide.

In an additional embodiment of the present invention, R_6 is straight chained or branched C_1-C_7 alkyl; C_3-C_7 cycloalkyl; $-N(R_3)_2$; $-OR_3$; $-(CH_2)_pOR_3$; aryl, benzyl or heteroaryl, optionally substituted with one or more F; Cl; Br; I; $-OR_3$; $-(CH_2)_qOR_3$; or straight chained or branched C_1-C_7 alkyl.

In a further embodiment of the present invention, the compound is

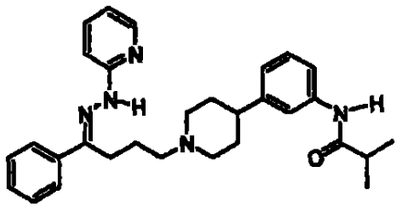


In one embodiment, the compound has the structure:

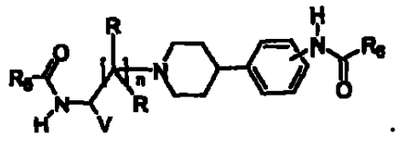


In one embodiment of the compound, at least one V is phenyl or heteroaryl optionally substituted with one or more F; Cl; Br; I; R_5; $-OR_5$; $-(CH_2)_qOR_5$; $-(CH_2)_qR_5$; straight chained or branched C_1-C_7 alkyl; C_1-C_7 monoflouroalkyl or polyflouroalkyl; or phenoxy.

In one embodiment, the compound has the structure:

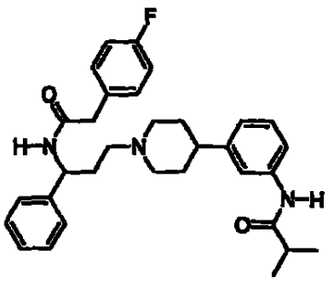


In one embodiment, the compound has the structure:

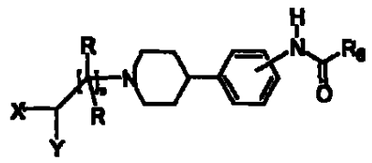


In one embodiment of the compound, V is phenyl which is optionally substituted with one or more F; Cl; Br; $-OR_5$; $-(CH_2)_qOR_5$; $-(CH_2)_qR_5$; straight chained or branched C_1-C_7 alkyl; C_1-C_7 monoflouroalkyl or polyflouroalkyl; or phenoxy.

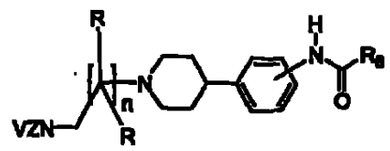
In one embodiment, the compound has the structure:



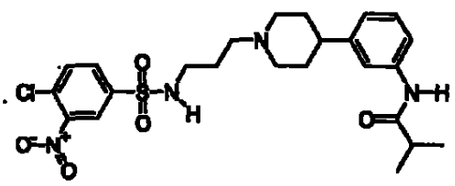
In one embodiment, the compound has the structure:



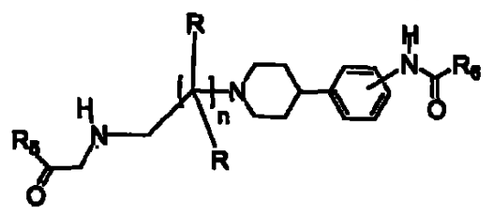
In one embodiment, the compound has the structure:



In one embodiment, the compound has the structure:

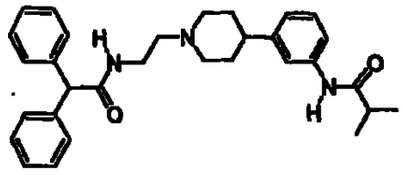


In one embodiment, the compound has the structure:

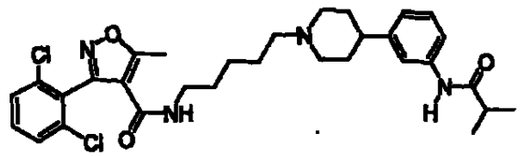


In one embodiment of the compound, R_6 is straight chained or branched C_1-C_7 alkyl; C_3-C_7 cycloalkyl; $-N(R_6)_2$; $-OR_6$; $-(CH_2)_qOR_6$; $-CH(R_6)_2$; $-(CH_2)_qR_6$; or aryl, benzyl or heteroaryl, wherein the aryl, benzyl or heteroaryl is optionally substituted with one or more F; Cl; I; R_6; $-N(R_6)_2$; $-OR_6$; $-(CH_2)_qOR_6$; $-(CH_2)_qR_6$; or straight chained or branched C_1-C_7 alkyl.

In one embodiment, the compound has the structure:

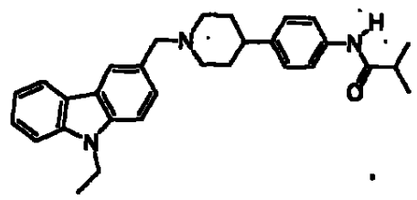


In one embodiment, the compound has the structure:

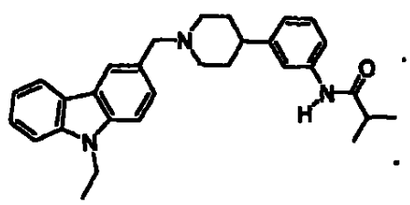


In one embodiment of the compound, X is hydrogen and Y is carbazole optionally substituted with one or more F, Cl, Br, R_5, $-OR_5$, $-(CH_2)_qOR_5$, $-(CH_2)_qR_5$; straight chained or branched C_1 - C_7 alkyl, or C_1-C_7 monoflouroalkyl or polyflouroalkyl; or phenoxy.

In one embodiment, the compound has the structure:

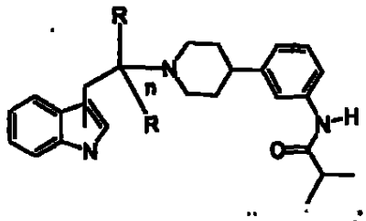


In one embodiment, the compound has the structure:

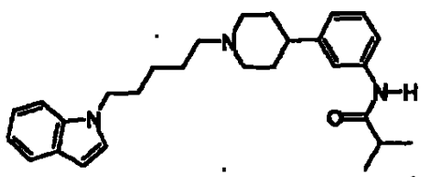


In one embodiment of the compound, Y is hydrogen and V is an indole, which can be optionally substituted with one or more F; Cl; Br; R_8; $-CO_2R_8$; $-OR_8$; $-(CH_2)_qOR_8$; $-(CH_2)_qR_8$; straight chained or branched C_1 - C_7 alkyl; C_1-C_7 monoflouroalkyl or polyflouroalkyl; or phenoxy on the 1, 2, 3, 4 , 5, 6 or 7 positions.

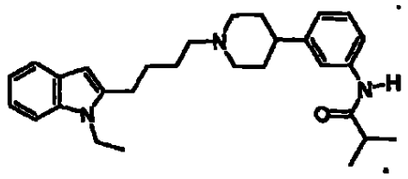
In one embodiment, the compound has the structure:



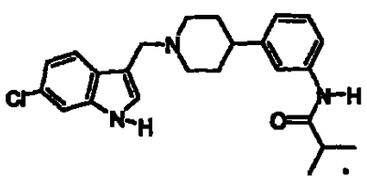
In one embodiment, the compound has the structure:



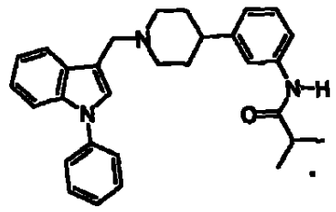
In one embodiment, the compound has the structure:



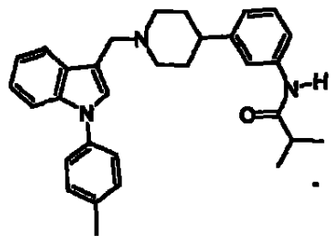
In one embodiment, the compound has the structure:



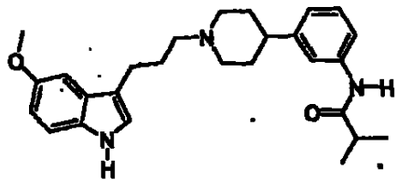
In one embodiment, the compound has the structure:



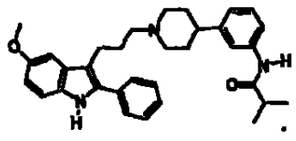
In one embodiment, the compound has the structure:



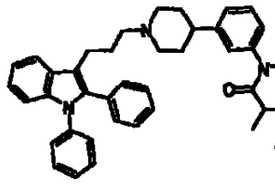
In one embodiment, the compound has the structure:



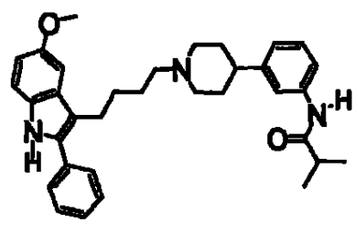
In one embodiment, the compound has the structure:



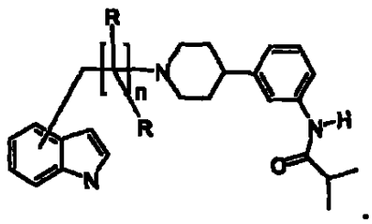
In one embodiment, the compound has the structure:



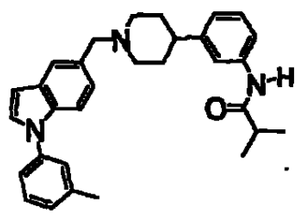
In one embodiment, the compound has the structure:



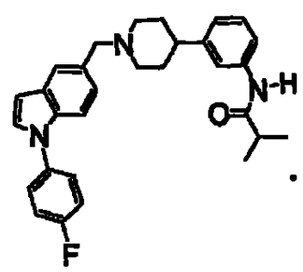
In one embodiment, the compound has the structure:



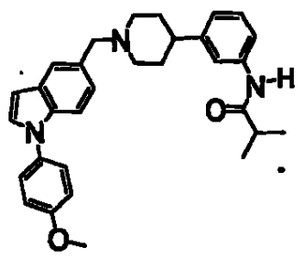
In one embodiment, the compound has the structure:



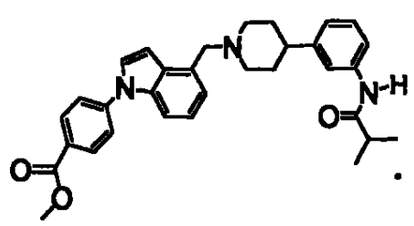
In one embodiment, the compound has the structure:



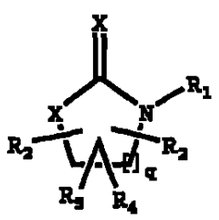
In one embodiment, the compound has the structure:



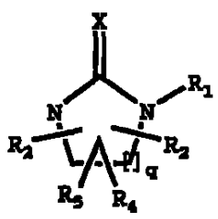
In one embodiment, the compound has the structure:



The present invention provides a compond having the srucuture:

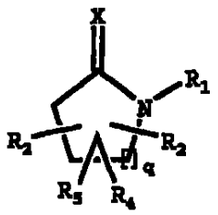


,



,

or



wherein each X is independently O or S;

wherein q is 1 or 2;

wherein each R_2 is independently H; $-(CH_2)_tXR_3$; $-(CH_2)_tC(X)N(R_3)_2$; $-(CH_2)_tCO_2R_3$; $-CO_2R_3$; straight chained or branched C_1-C_7 alkyl optionally substituted with $-N(R_3)_2$; $-CON(R_3)_2$ or $-N(R_3)C(O)R_3$; straight chained or branched C_2-C_7 alkenyl, or alkynyl; or C_3-C_7 cycloalkyl or C_5-C_7 cycloalkenyl;

wherein each t is independently an integer from 1 to 4 inclusive;

wherein each R_3 is independently H; straight chained or branched C_1-C_7 alkyl, straight chained or branched C_2-C_7 alkenyl, or alkynyl; or C_3-C_7 cycloalkyl or C_5-C_7 cycloalkenyl;

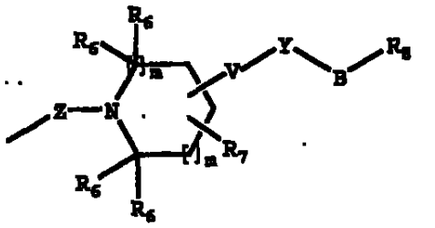
wherein R_4 is aryl, heteroaryl, C_1-C_7 alkyl substituted with one or two aryl, or C_1-C_7 alkyl substituted with one or two heteroaryl; wherein the aryl or heteroaryl may be substituted with one or more of F, Cl, Br, I, -CN, $-NO_2$, $-N(R_3)_2$, $-COR_3$, $-(CH_2)_nXR_3$, $-(CH_2)_nC(X)NR_3$, $-(CH_2)_nN(R_3)C(X)R_3$, $-(CH_2)_nCO_2R_3$, $-(CH_2)_nOCOR_3$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl OR polyfluoroalkyl or straight chained or branched C_2-C_7 aminoalkyl, alkenyl or alkynyl, or C_3-C_7 cycloalkyl or C_5-C_7 cycloalkenyl;

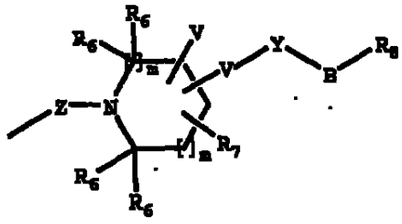
wherein each n independently is an integer from 0 to 7 inclusive;

wherein R_5 is H; aryl, C_1-C_7 alkyl substituted with aryl, heteroaryl, or C_1-C_7 alkyl substituted with heteroaryl; wherein the aryl or heteroaryl may be substituted with one or more of F, Cl, Br, I, -CN, $-NO_2$, $-N(R_3)_2$, $-COR_3$, $-(CH_2)_nXR_3$, $-(CH_2)_nC(X)NR_3$, $-(CH_2)_nCO_2R_3$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl, polyfluoroalkyl or carboxamidoalkyl, or straight chained or branched C_2-C_7 aminoalkyl, alkenyl or alkynyl, or C_3-C_7 cycloalkyl or C_5-C_7 cycloalkenyl;

where R_5 and one R_2 on adjacent carbon atoms together may form aryl, heteroaryl, indane or tetrahydronaphthyl, C_3-C_7 cycloalkyl, or heterocycloalkyl wherein one or two heteroatoms may be O, N or S;

wherein R_1 is


, or


;

wherein each V is independently aryl, phenoxy or heteroaryl, wherein the aryl, phenoxy or heteroaryl is optionally substituted with one or more F; Cl; Br; I; COR_5; CO_2R_5; -$OCOR_5$; -$CON(R_5)_2$; -$N(R_5)COR_5$; CN; -NO_2; -$N(R_5)_2$; -OR_5; -SR_5; $(CH_2)_QOR_5$; $(CH_2)_QSR_5$; straight chained or branched C_1-C_7 alkyl optionally substituted with -$CON(R_5)_2$, -$N(R_5)C(O)R_5$ or $N(R_5)_2$, straight chained or branched monofluoroalkyl or polyfluoroalkyl, straight chained or branched C_2-C_7 alkenyl, C_2-C_7 alkynyl; phenoxy; or C_3-C_7 cycloalkyl, monofluorocycloalkyl, polyfluorocycloalkyl or cycloalkenyl;

wherein each R_6 is independently H; $(CH_2)_tXR_3$; $(CH_2)_tC(X)NR_3$; $(CH_2)_tN(R_3)C(X)R_3$; $(CH_2)_tCO_2R_3$; $(CH_2)_tOCOR_3$; straight chained or branched C_1-C_7 alkyl optionally substituted with -$CON(R_3)_2$ or -$NC(O)R_3$; straight chained or branched C_2-C_7 alkyl substituted with -$N(R_3)_2$; straight

chained or branched C_2-C_7 alkenyl or alkynyl; or C_3-C_7 cycloalkyl or C_5-C_7 cycloalkenyl;

where each R_7 is independently H; F; Cl; Br; I; $-COR_3$; $-CO_2R_3$; $-(CH_2)_nXR_3$; $-(CH_2)_nN(R_3)C(O)R_3$; $-(CH_2)_nC(X)N(R_3)_2$; $-(CH_2)_nCO_2R_3$; $-CN$; $-NO_2$; $-N(R_3)_2$; straight chained or branched C_1-C_7 alkyl, hydroxyalkyl, aminoalkyl, carboxamidoalkyl, alkoxyalkyl, monofluoroalkyl or polyfluoroalkyl; straight chained or branched C_2-C_7 alkenyl or alkynyl; C_3-C_7 cycloalkyl, monofluorocycloalkyl, polyfluorocycloalkyl or C_5-C_7 cycloalkenyl, wherein the alkyl, aminoalkyl, carboxamidoalkyl, hydroxyalkyl, alkoxyalkyl, alkenyl, alkynyl, cycloalkyl or cycloalkenyl may be substituted with one or more aryl or heteroaryl, wherein the aryl or heteroaryl may be substituted with one or more of F, Cl, Br, I, $-(CH_2)_nXR_3$, $-COR_3$, $-(CH_2)_nC(X)N(R_3)_2$, $-(CH_2)_nCO_2R_3$, $-CN$, $-NO_2$, $-(CH_2)_nN(R_3)C(O)R_3$; $-N(R_3)_2$, $-SO_2R_3$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl, straight chained or branched C_2-C_7 alkenyl or alkynyl, or C_3-C_7 cycloalkyl, monofluorocycloalkyl, polyfluorocycloalkyl or C_5-C_7 cycloalkenyl; aryl or heteroaryl, wherein the aryl or heteroaryl may be substituted with one or more of F, Cl, Br, I, $-(CH_2)_nXR_3$, $-COR_3$, $-(CH_2)_nC(X)N(R_3)_2$

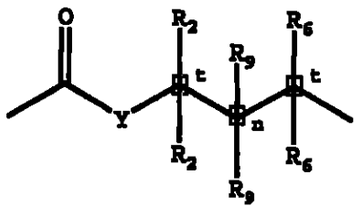
$-(CH_2)_nCO_2R_3$, $-(CH_2)_nN(R_3)C(O)R_3$; -CN, $-NO_2$, $-N(R_3)_2$, $-SO_2R_3$, straight chained or branched C_1-C_7 alkyl, straight chained or branched C_1-C_7 monofluoroalkyl or polyfluoroalkyl, straight chained or branched C_2-C_7 alkenyl or alkynyl, or C_3-C_7 cycloalkyl, monofluorocycloalkyl, polyfluorocycloalkyl or C_5-C_7 cycloalkenyl;

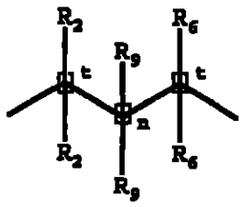
wherein B is CO, SO_2 or SO_2NR_6;

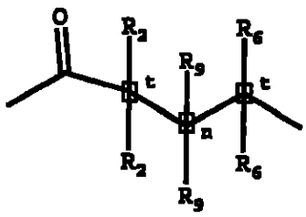
wherein R_8 is -H; straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl; straight chained or branched C_2-C_7 alkenyl or alkynyl; C_3-C_7 cycloalkyl, monofluorocycloalkyl, polyfluorocycloalkyl or cycloalkenyl; $-N(R_3)_2$; $-NR_3C(O)R_3$; $-OR_3$; $-(CH_2)_pOR_3$; $-COR_3$; $-CO_2R_3$; $-OCOR_3$;$-CON(R_3)_2$; aryl or heteroaryl, optionally substituted with one or more F; Cl; Br; I; COR_3; CO_2R_3; $-OCOR_3$; $-NR_3C(O)R_3$; $-CON(R_3)_2$; CN; $-NO_2$; $-N(R_3)_2$; $-OR_3$; $-SR_3$; $(CH_2)_qOR_3$; $(CH_2)_qSR_3$; straight chained or branched C_1-C_7 alkyl optionally substituted with $-CON(R_3)_2$, $-NR_3C(O)R_3$ or $-N(R_3)_2$; straight chained or branched monofluoroalkyl, polyfluoroalkyl; straight chained or branched C_2-C_7 alkenyl, C_2-C_7 alkynyl; C_3-C_7 cycloalkyl, monofluorocycloalkyl, polyfluorocycloalkyl or cycloalkenyl;

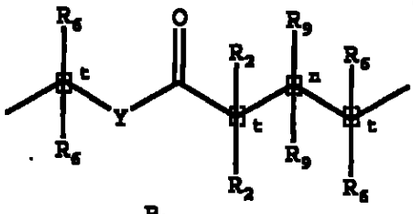
wherein each m independently is an integer from 0 to 3 inclusive;

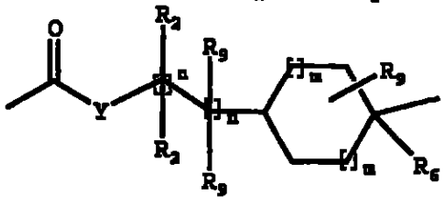
wherein Z is

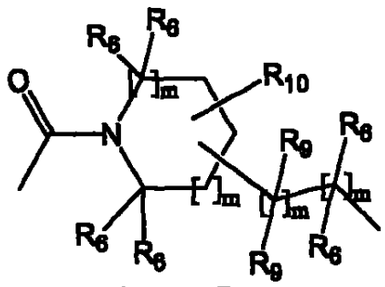


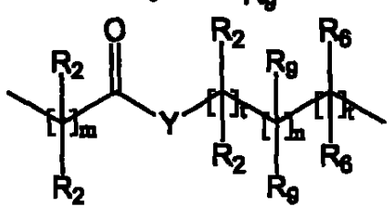




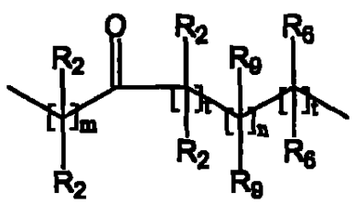








, or



;

or C_2-C_7 alkenyl, wherein the C_2-C_7 alkenyl may be unsubstituted or substituted with one or more R_9 groups;

wherein each R_9 is independently H; F; Cl; Br; I; $-(CH_2)_mXR_3$; $(CH_2)_mC(X)NR_3$; $(CH_2)_mCO_2R_3$; straight chained or branched C_1-C_7 alkyl, monofluoroalkyl, polyfluoroalkyl, aminoalkyl, or carboxamidoalkyl; straight chained or branched C_2-C_7 alkenyl, or alkynyl; or C_3-C_7 cycloalkyl or C_5-C_7 cycloalkenyl;

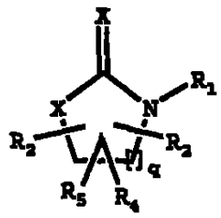
wherein R_{10} is H; $(CH_2)_tXR_3$; $(CH_2)_tC(X)NR_3$; $(CH_2)_tCO_2R_3$; straight chained or branched C_1-C_7 alkyl, carboxamidoalkyl; straight chained or branched C_2-C_7 aminoalkyl, alkenyl, or alkynyl; or C_3-C_7 cycloalkyl or C_5-C_7 cycloalkenyl;

wherein Y is S, O, or NR_{10};

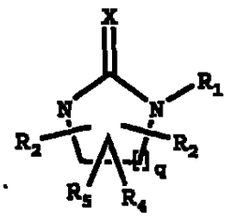
wherein each p is independently an integer from 1 to 7 inclusive;

or a pharmaceutically acceptable salt thereof.

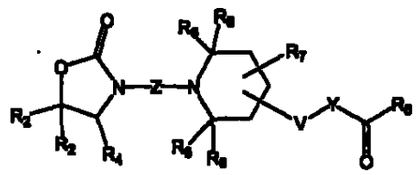
In a further embodiment of the present invention, the compound has the following structure:



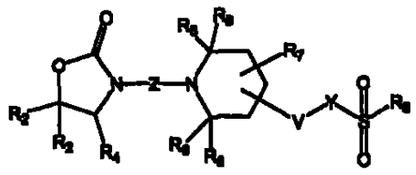
or



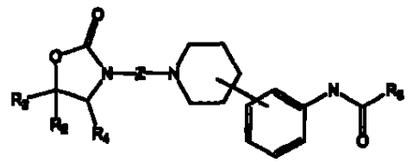
In an additional embodiment of the present invention, the compound has the structure:



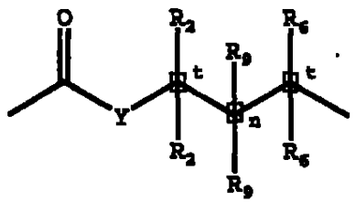
; or



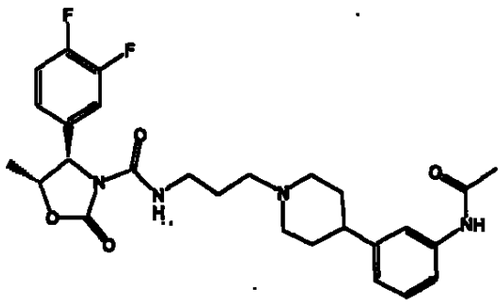
In an additional embodiment of the present invention, the compound has the structure:



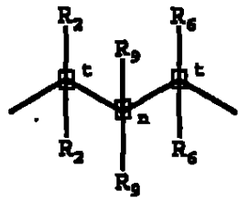
In one embodiment of the present invention, Z is:



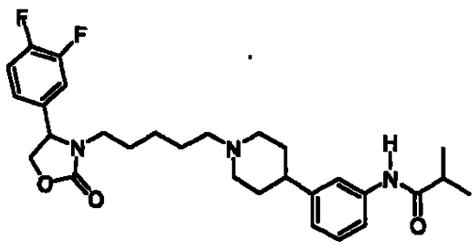
In one embodiment of the present invention, Z is:



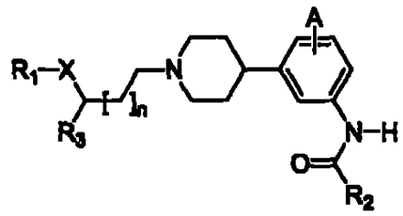
In an additional embodiment of the present invention, the compound has the structure:



In one embodiment of the present invention, the compound has the strucuture:



This invention provides a compound having the structure:



wherein R_1 is hydrogen, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -F, -Cl, -Br, -I, -CN, $-NO_2$, $-CH_3$, $-CF_3$, $-COCH_3$, $-CO_2R_2$, phenyl, phenoxy or straight chained or branched C_1-C_7 alkyl;

wherein R_2 is straight-chained or branched C_3-C_4 alkyl or cyclopropyl;

wherein R_3 is aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -F, -Cl, -Br, -I, -CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl;

wherein A is -H, -F, -Cl, -Br, -CN, $-NO_2$, $-COR_3$, $-CO_2R_3$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl;

wherein X is O or NH;

wherein n is an integer from 0 to 5 inclusive;

In one embodiment, R_1 is aryl optionally substituted with one or more -F, -Cl, -Br, -I, -CN, $-NO_2$, $-COCH_3$,

$-CO_2R_4$, straight chained or branched C_1-C_7 alkyl;

wherein R_3 is phenyl;

wherein A is H; and

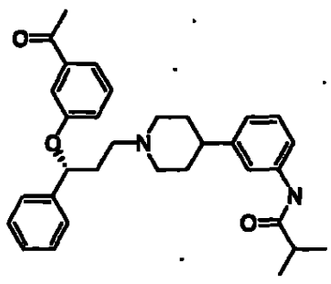
wherein X is O.

In one embodiment, R_2 is isopropyl.

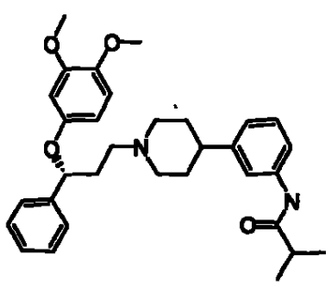
In a preferred embodiment, X is NH, R_1 is alkyl and n is 1 or 2.

In the most preferred embodiment, X is O, R_1 is 3-acetyl phenyl, R_2 is isopropyl, R_3 is phenyl and n is 1.

In one embodiment, the compound has the structure:



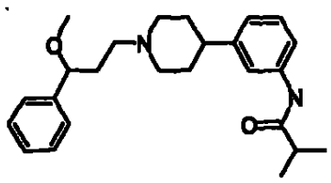
In one embodiment, compound has the structure:



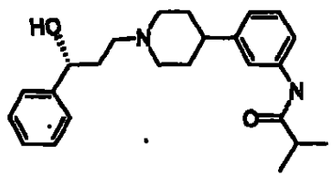
In one embodiment, R_1 is hydrogen, straight chained or branched C_1-C_7 alkyl; and wherein R_3 is aryl.

In one embodiment, R_2 is isopropyl; and A is hydrogen.

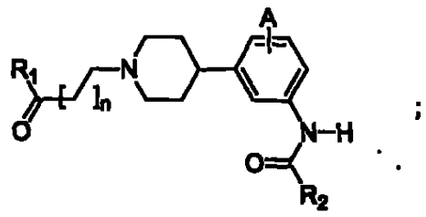
In one embodiment, the compound has the structure:



In one embodiment, the compound has the structure:



The present invention also provides a compound having the structure:



;

wherein R_1 is aryl or heteroaryl optionally substituted with one or more -F, -Cl, -Br, -I, -CN, $-NO_2$, $-OCH_3$, phenoxy, fused cyclopentanyl, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl;

wherein R_2 is straight-chained or branched C_1-C_4 alkyl or cyclopropyl;

wherein A is -H, -F, -Cl, -Br, -CN, -NO_2, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl; and

wherein n is an integer from 1 to 5 inclusive.

In one embodiment, R_1 is aryl optionally substituted with one or more -F, -Cl, -Br, -I or straight chained or branched C_1-C_4 alkyl; and

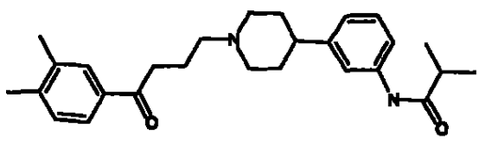
wherein A is H.

In one embodiment, R_2 is isopropyl; and

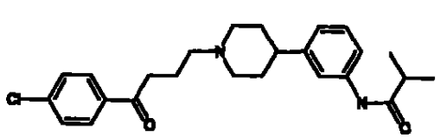
wherein n is 2.

In a preferred embodiment, n is 2 and R_2 is isopropyl.

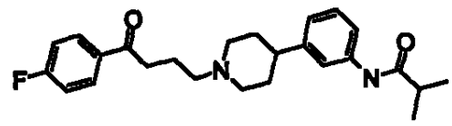
In one embodiment, the compound has the structure:



In one embodiment, the compound has the structure:



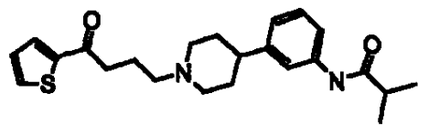
In one embodiment, the compound has the structure:



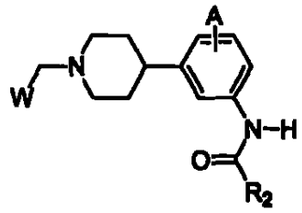
In one embodiment, R_1 is thienyl; and wherein A is H.

In one embodiment, R_2 is isopropyl.

In one embodiment, the compound has the structure:

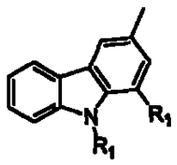


The invention provides a compound having the structure:

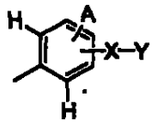


;

wherein W is



or



;

wherein each R_1 is independently hydrogen, methyl or ethyl;

wherein R_2 is straight-chained or branched C_3-C_4 alkyl or

wherein R_2 is straight- chained or branched C_3-C_4 alkyl or cyclopropyl;

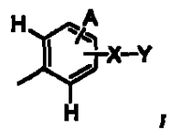
wherein R_3 is hydrogen, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -H, -F, -Cl, -Br, -I, -CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl.

wherein each A is independently -H, -F, -Cl, -Br, -CN, $-NO_2$, $-COR_3$, $-CO_2R_3$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl;

wherein X is O, NR_3, CO or may be absent; and

wherein Y is hydrogen, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -F, -Cl, -Br, -I, -CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl.

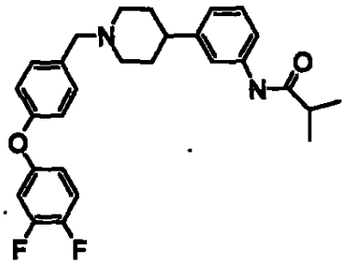
In one embodiment, W is



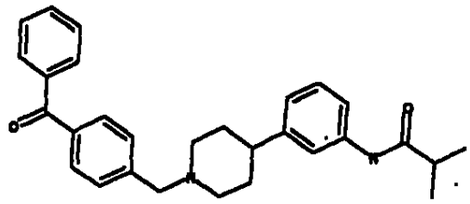
and wherein X is O or may be absent.

In one embodiment, R_2 is isopropyl.

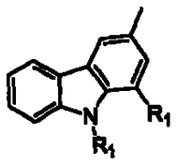
In one embodiment, the compound has the structure:



In one embodiment, the compound has the structure:



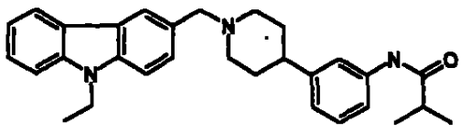
In one embodiment, W is



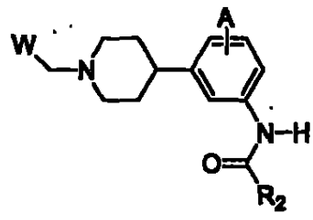
In one embodiment, A is -H, -F, -Cl, -Br.

In one embodiment, R_3 is isopropyl; and A is hydrogen.

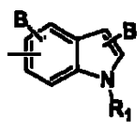
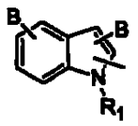
In one embodiment, the compound has the structure:



This invention provides a compound having the structure:



wherein W is

 or 

wherein R_1 is hydrogen, straight chained or branched C_1-C_7 alkyl, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -F, -Cl, -Br, -CN, $-NO_2$, $-OCH_3$, $-CO_2CH_3$, $-CF_3$, phenyl, straight chained or branched C_1-C_7 alkyl;

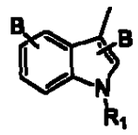
wherein R_2 is straight-chained or branched C_3-C_4 alkyl or cyclopropyl;

wherein A is -H, -F, -Cl, -Br, -CN, $-NO_2$, $-COR_1$, $-CO_2R_1$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl or phenyl.

wherein each B is independently -H, -F, -Cl, -Br, -I, -CN, $-NO_2$, $-COR_1$, $-CO_2R_1$, $-OCH_3$, $-OCF_3$, $-CF_3$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl or aryl, phenoxy or benzyloxy, wherein the aryl, phenoxy or benzyloxy is optionally substituted with one or more -F, -Cl, -Br, -CN, $-NO_2$, $-COR_1$, $-CO_2R_1$,

$-OCH_3$, $-OCF_3$, $-CF_3$ or straight chained or branched C1 -C3 alkyl.

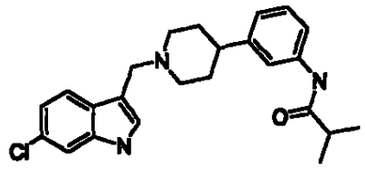
In one embodiment, W is



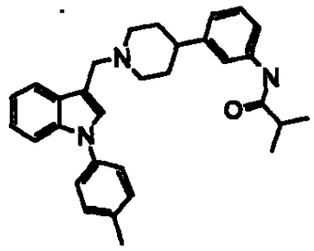
In one embodiment, R_1 is hydrogen or phenyl optionally substituted with one or more -F, -Cl, -Br, -CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl.

In one embodiment, R_2 is isopropyl.

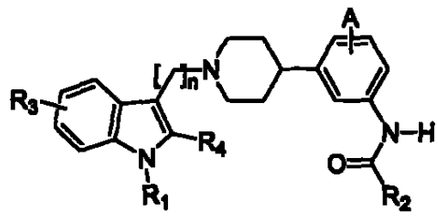
In one embodiment, the compound has the structure:



In one embodiment, the compound has the structure:



This invention provides a compound having the structure:



wherein R_1 is hydrogen, straight chained or branched C_1-C_7 alkyl, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -F, -Cl, -Br, -CN, $-NO_2$, $-CF_3$, $-OCH_3$, straight chained or branched C_1-C_3 alkyl;

wherein R_2 is straight-chained or branched C_3-C_4 alkyl or cyclopropyl;

wherein R_3 is -H, -F, -Cl, -Br, -I, -CN, $-NO_2$, $-CF_3$, $-OCH_3$, or straight chained or branched C_1-C_3 alkyl, monofluoroalkyl or polyfluoroalkyl, or a phenyl ring fused to C_5 and C_7 of the indole moiety;

wherein R_4 is hydrogen or aryl optionally substituted with one or more -F, -Cl, -Br, -I, -CN, $-NO_2$, $-CF_3$, straight chained or branched C_1-C_3 alkyl;

wherein A is -H, -F, -Cl, -Br, -CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl; and

wherein n is an integer from 2 to 4 inclusive.

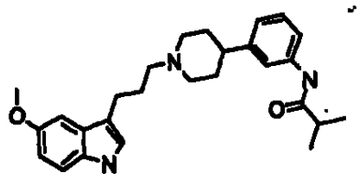
In one embodiment, R_3 is - H, -F, -Cl, -Br, -I, -CN, -NO_2, -OCF_3 or -OCH_3; and

wherein R_4 is hydrogen or phenyl optionally substituted with one or more -F, -Cl or -CF_3.

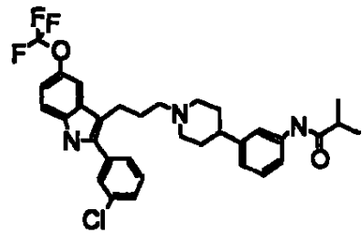
In one embodiment, R_1 is hydrogen or phenyl optionally substituted with one or more -F, -Cl, -Br, -CN, -NO_2, -CF_3, -OCH_3 or straight chained or branched C_1-C_3 alkyl;

In one embodiment, R_2 is isopropyl.

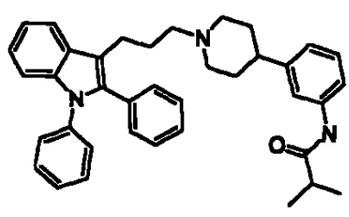
In one embodiment, the compound has the structure:



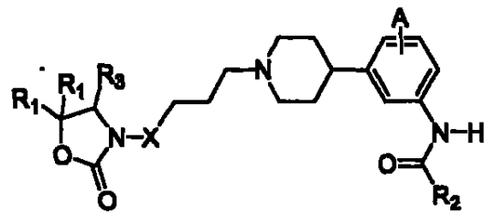
In one embodiment, the compound has the structure:



In one embodiment, the compound has the structure:



This invention provides a compound having the structure:



wherein each R_1 is independently hydrogen or CH_3;

wherein R_2 is straight-chained or branched C_1-C_4 alkyl or cyclopropyl;

wherein R_3 is benzyl or phenyl, wherein the benzyl or phenyl is optionally substituted with a methylenenedioxy group or one or more -F or -Cl;

wherein A is -H, -F, -Cl, -Br, -CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl;

wherein X is $(CH_2)_2$, $COCH_2$ or CONH;

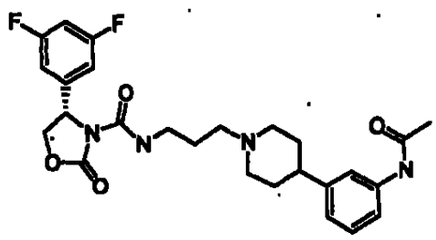
In one embodiment, R_3 is phenyl optionally substituted with one or more -F; and

wherein A is hydrogen.

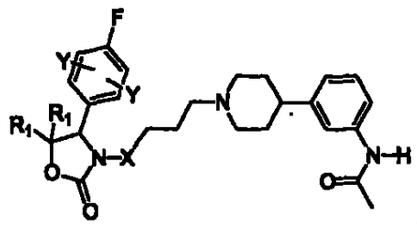
In one embodiment, X is CONH.

In one embodiment, R_2 is methyl.

In one embodiment, the compound has the structure:

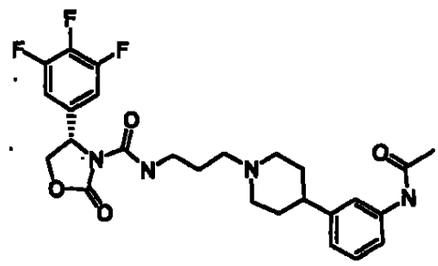


In one embodiment, the compound has the structure:

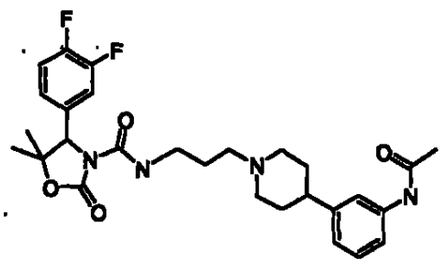


wherein each Y is independently hydrogen or -F.

In one embodiment, the compound has the structure:

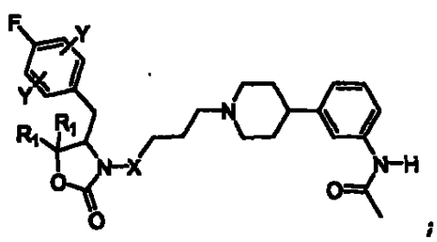


In one embodiment, the compound has the structure:



In one embodiment, R_3 is benzyl optionally substituted with a methylenedioxy group or one or more -F or -Cl.

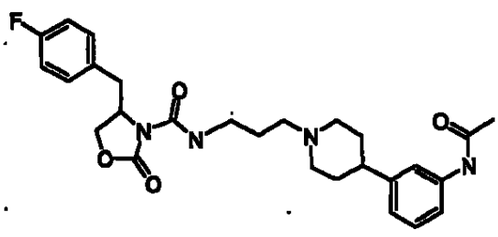
In one embodiment, the compound has the structure:



;

wherein each Y is independently hydrogen or -F.

In one embodiment, the compound has the structure:



In one embodiment, the compound is enantiomerically pure.

In one embodiment, the compound is diastereomerically pure.

In one embodiment, the compound is enantiomerically and diastereomerically pure.

This invention also provides a pharmaceutical composition comprising a therapeutically amount of a

compound of the invention and a pharmaceutically acceptable carrier.

In one embodiment, the amount of the compound is from about 0.01mg to about 500mg.

In one embodiment, the amount of the compound is from about 0.1mg to about 60mg.

In one embodiment, the amount of the compound is from about 1mg to about 20mg.

In one embodiment, the pharmaceutical composition consists of a carrier which is a liquid and the composition is a solution.

In one embodiment, the pharmaceutical composition consists of a carrier which is a solid and the composition is a tablet.

In one embodiment, the pharmaceutical composition consists of a carrier which is a gel and the composition is a suppository.

The invention also provides a process for making a pharmaceutical composition comprising admixing a therapeutically effective amount of the compound of any of the invention and a pharmaceutically acceptable carrier.

This invention also provides the method of treating a subject suffering from a disorder selected from the group consisting of depression, anxiety, urge

incontinence, or obesity comprising administering to the subject a therapeutically effective amount of the compound of the invention.

In one embodiment, the therapeutically effective amount is between about 0.03 and about 1000 mg per day.

In one embodiment, the therapeutically effective amount is between about 0.30 and about 300 mg per day.

In one embodiment, the therapeutically effective amount is between about 1.0 and about 100 mg per day.

In one embodiment, the disorder is depression.

In one embodiment, the disorder is anxiety.

In one embodiment, the disorder is obesity.

In one embodiment, the disorder is urge incontinence.

The invention provides the method of reducing the body mass of a subject, which comprises administering to the subject an amount of a compound of the invention effective to reduce the body mass of the subject.

The invention provides the method of treating a subject suffering from depression, which comprises administering to the subject an amount of a compound of any of claims of the invention effective to treat the subject's depression.

The invention provides the method of treating a subject suffering from anxiety, which comprises administering to the subject an amount of a compound of the invention effective to treat the subject's anxiety.

The invention provides the method of alleviating urge urinary incontinence in a subject suffering from an overactive bladder, which comprises administering to the subject an amount of the compound of the invention effective to alleviate the subject's urge urinary incontinence.

The invention provides the method of managing obesity in a subject in need of weight loss, which comprises administering to the subject an amount of a compound of the invention effective to induce weight loss in the subject.

The invention provides the method of managing obesity in a subject who has experienced weight loss, which comprises administering to the subject an amount of a compound of the invention effective to maintain such weight loss in the subject.

The invention provides the method of treating overactive bladder in a subject, which comprises administering to the subject an amount of a compound of any of the invention effective to treat the subject's overactive bladder.

The invention provides the method of treating a disorder in a subject, wherein the symptoms of the subject can be

alleviated by treatment with an MCH1 antagonist, wherein the MCH1 antagonist is the compound of the invention.

The invention provides the method of alleviating the symptoms of a disor4der in a subject, which comprises administering to the subject an amount of an MCH1 antagonist effective to alleviate the symptoms, wherein the MCH1 antagonist is the compound of the invention

As used in the present invention, the term "heteroaryl" is used to include five and six membered unsaturated rings that may contain one or more oxygen, sulfur, or nitrogen atoms. Examples of heteroaryl groups include, but are not limited to, carbazole, furanyl, thienyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, pyrazolyl, isoxazolyl, isothiazolyl, oxadiazolyl, triazolyl, thiadiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, and triazinyl.

In addition, the term "heteroaryl" is used to include fused bicyclic ring systems that may contain one or more heteroatoms such as oxygen, sulfur and nitrogen. Examples of such heteroaryl groups include, but are not limited to, indolizinyl, indolyl, isoindolyl, benzo[b]furanyl, benzo[b]thiophenyl, indazolyl, benzimidazolyl, purinyl, benzoxazolyl, benzisoxazolyl, benzo[b]thiazolyl, imidazo[2,1-b]thiazolyl, cinnolinyl, quinazolinyl, quinoxalinyl, 1,8-naphthyridinyl, pteridinyl, quinolinyl, isoquinolinyl, phthalimidyl and 2,1,3-benzothiazolyl.

The term "heteroaryl" also includes those chemical moieties recited above which may be substituted with one or more of the following: -F, -Cl, -Br, -I, CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl, straight chained or branched C_1-C_7 monofluoroalkyl, straight chained or branched C_1-C_7 polyfluoroalkyl, straight chained or branched C_2-C_7 alkenyl, straight chained or branched C_2-C_7 alkynyl; C_3-C_7 cycloalkyl, C_3-C_7 monofluorocycloalkyl, C_3-C_7 polyfluorocycloalkyl, C_5-C_7 cycloalkenyl,

The term "heteroaryl" further includes the N-oxides of those chemical moieties recited above which include at least one nitrogen atom.

In the present invention, the term "aryl" is phenyl or naphthyl.

The invention provides for each pure stereoisomer of any of the compounds described herein. Such stereoisomers may include enantiomers, diastereomers, or E or Z alkene or imine isomers. The invention also provides for stereoisomeric mixtures, including racemic mixtures, diastereomeric mixtures, or E/Z isomeric mixtures. Stereoisomers can be synthesized in pure form (Nógrádi, M.; Stereoselective Synthesis, (1987) VCH Editor Ebel, H. and Asymmetric Synthesis, Volumes 3 B 5, (1983) Academic Press, Editor Morrison, J.) or they can be resolved by a variety of methods such as crystallization and chromatographic techniques (Jaques, J.; Collet, A.; Wilen, S.; Enantiomer, Racemates, and Resolutions, 1981,

John Wiley and Sons and Asymmetric Synthesis, Vol. 2, 1983, Academic Press, Editor Morrison, J).

In addition the compounds of the present invention may be present as enantiomers, diasteriomers, isomers or two or more of the compounds may be present to form a racemic or diastereomeric mixture.

The compounds of the present invention are preferably 80% pure, more preferably 90% pure, and most preferably 95% pure. Included in this invention are pharmaceutically acceptable salts and complexes of all of the compounds described herein. The acids and bases from which these salts are prepared include but are not limited to the acids and bases listed herein. The acids include, but are not limited to, the following inorganic acids: hydrochloric acid, hydrobromic acid, hydroiodic acid, sulfuric acid and boric acid. The acids include, but are not limited to, the following organic acids: acetic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, maleic acid, citric acid, methanesulfonic acid, benzoic acid, glycolic acid, lactic acid and mandelic acid. The bases include, but are not limited to ammonia, methylamine, ethylamine, propylamine, dimethylamine, diethylamine, trimethylamine, triethylamine, ethylenediamine, hydroxyethylamine, morpholine, piperazine and guanidine. This invention further provides for the hydrates and polymorphs of all of the compounds described herein.

The present invention includes within its scope prodrugs of the compounds of the invention. In general, such prodrugs will be functional derivatives of the compounds

of the invention which are readily convertible in vivo into the required compound. Thus, in the present invention, the term "administering" shall encompass the treatment of the various conditions described with the compound specifically disclosed or with a compound which may not be specifically disclosed, but which converts to the specified compound in vivo after administration to the patient. Conventional procedures for the selection and preparation of suitable prodrug derivatives are described, for example, in Design of Prodrugs, ed. H. Bundgaard, Elsevier, 1985.

The present invention further includes metabolites of the compounds of the present invention. Metabolites include active species produced upon introduction of compounds of this invention into the biological milieu.

This invention further provides a pharmaceutical composition comprising a therapeutically effective amount of the compound of the invention and a pharmaceutically acceptable carrier. In one embodiment, the amount of the compound is from about 0.01 mg to about 800 mg. In another embodiment, the amount of the compound is from about 0.01 mg to about 500 mg. In yet another embodiment, the amount of the compound is from about 0.1 mg to about 250 mg. In another embodiment, the amount of the compound is from about 0.1 mg to about 60 mg. In yet another embodiment, the amount of the compound is from about 1 mg to about 20 mg. In a further embodiment, the carrier is a liquid and the composition is a solution. In another embodiment, the carrier is a solid and the composition is a tablet. In another embodiment, the carrier is a gel and the

composition is a capsule, suppository or a cream. In a further embodiment the compound may be formulated as a part of a pharmaceutically acceptable transdermal patch. In yet a further embodiment, the compound may be delivered to the subject by means of a spray or inhalant.

This invention also provides a pharmaceutical composition made by combining a therapeutically effective amount of the compound of this invention and a pharmaceutically acceptable carrier.

This invention provides a process for making a pharmaceutical composition comprising combining a therapeutically effective amount of the compound of this invention and a pharmaceutically acceptable carrier.

A solid carrier can include one or more substances which may also act as endogenous carriers (e.g. nutrient or micronutrient carriers), flavoring agents, lubricants, solubilizers, suspending agents, fillers, glidants, compression aids, binders or tablet-disintegrating agents; it can also be an encapsulating material. In powders, the carrier is a finely divided solid which is in admixture with the finely divided active ingredient. In tablets, the active ingredient is mixed with a carrier having the necessary compression properties in suitable proportions and compacted in the shape and size desired. The powders and tablets preferably contain up to 99% of the active ingredient. Suitable solid carriers include, for example, calcium phosphate, magnesium stearate, talc, sugars, lactose, dextrin, starch,

gelatin, cellulose, polyvinylpyrrolidine, low melting waxes and ion exchange resins.

Liquid carriers are used in preparing solutions, suspensions, emulsions, syrups, elixirs and pressurized compositions. The active ingredient can be dissolved or suspended in a pharmaceutically acceptable liquid carrier such as water, an organic solvent, a mixture of both or pharmaceutically acceptable oils or fats. The liquid carrier can contain other suitable pharmaceutical additives such as solubilizers, emulsifiers, buffers, preservatives, sweeteners, flavoring agents, suspending agents, thickening agents, coloring agents, viscosity regulators, stabilizers or osmoregulators. Suitable examples of liquid carriers for oral and parenteral administration include water (partially containing additives as above, e.g. cellulose derivatives, preferably sodium carboxymethyl cellulose solution), alcohols (including monohydric alcohols and polyhydric alcohols, e.g. glycols) and their derivatives, and oils (e.g. fractionated coconut oil and arachis oil). For parenteral administration, the carrier can also be an oily ester such as ethyl oleate or isopropyl myristate. Sterile liquid carriers are useful in sterile liquid form compositions for parenteral administration. The liquid carrier for pressurized compositions can be a halogenated hydrocarbon or other pharmaceutically acceptable propellent.

Liquid pharmaceutical compositions which are sterile solutions or suspensions can be utilized by for example, intramuscular, intrathecal, epidural, intraperitoneal or subcutaneous injection. Sterile solutions can also be

administered intravenously. The compounds may be prepared as a sterile solid composition which may be dissolved or suspended at the time of administration using sterile water, saline, or other appropriate sterile injectable medium. Carriers are intended to include necessary and inert binders, suspending agents, lubricants, flavorants, sweeteners, preservatives, dyes, and coatings. The compound can be administered orally in the form of a sterile solution or suspension containing other solutes or suspending agents (for example, enough saline or glucose to make the solution isotonic), bile salts, acacia, gelatin, sorbitan monoleate, polysorbate 80 (oleate esters of sorbitol and its anhydrides copolymerized with ethylene oxide) and the like.

The compound can also be administered orally either in liquid or solid composition form. Compositions suitable for oral administration include solid forms, such as pills, capsules, granules, tablets, and powders, and liquid forms, such as solutions, syrups, elixirs, and suspensions. Forms useful for parenteral administration include sterile solutions, emulsions, and suspenions.

Optimal dosages to be administered may be determined by those skilled in the art, and will vary with the particular compound in use, the strength of the preparation, the mode of administration, and the advancement of the disease condition. Additional factors depending on the particular subject being treated will result in a need to adjust dosages, including subject age, weight, gender, diet, and time of administration.

In the subject application a "therapeutically effective amount" is any amount of a compound which, when administered to a subject suffering from a disease against which the compounds are effective, causes reduction, remission, or regression of the disease. In a subject application, a "subject" is a vertebrate, a mammal or a human.

This invention provides a method of treating a subject suffering from an abnormality wherein the abnormality is alleviated by decreasing the activity of an MCH1 receptor which comprises administering to the subject an amount of a compound of the invention which is an MCH1 receptor antagonist effective to treat the subject=s abnormality.

In separate embodiments, the abnormality is a regulation of a steroid or pituitary hormone disorder, an epinephrine release disorder, a gastrointestinal disorder, a cardiovascular disorder, an electrolyte balance disorder, hypertension, diabetes, a respiratory disorder, asthma, a reproductive function disorder, an immune disorder, an endocrine disorder, a musculoskeletal disorder, a neuroendocrine disorder, a cognitive disorder, a memory disorder such as Alzheimer=s disease, a sensory modulation and transmission disorder, a motor coordination disorder, a sensory integration disorder,. a motor integration disorder, a dopaminergic function disorder such as Parkinson=s disease, a sensory transmission disorder, an olfaction disorder, a sympathetic innervation disorder, an affective disorder such as depression and anxiety, a

stress-related disorder, a fluid-balance disorder, a seizure disorder, pain, psychotic behavior such as schizophrenia, morphine tolerance, opiate addiction, migraine or a urinary disorder such as urinary incontinence.

The following description of depressive and anxiety disorders is for the purpose of illustrating the utility of the compounds of this invention. The definitions of depressive and anxiety disorders given below are those listed in Diagnostic and Statistical Manual of Mental Disorders. 4th ed. (DSM-IV; American Psychiatric Association, 1994a) or Diagnostic and Statistical Manual of Mental Disorders. 3rd ed. Revised (DSM-III-R; American Psychiatric Association, 1987). Additional information regarding these disorders can be found in this reference, as well as the others cited below, all of which are incorporated herein by reference.

Depressive disorders include major depressive disorder and dysthymic disorder (American Psychiatric Association, 1994a; American Psychiatric Association, 1994b). Major depressive disorder is characterized by the occurrence of one or more major depressive episodes without manic or hypomanic episodes. A major depressive episode is defined as a prominent and relatively persistent depressed or dysphoric mood that usually interferes with daily functioning (nearly every day for at least 2 weeks); it should include at least 4 of the following 8 symptoms: change in appetite, change in sleep, psychomotor agitation or retardation, loss of interest in usual activities or decrease in sexual drive, increased fatigue, feelings of guilt or

worthlessness, slowed thinking or impaired concentration, and a suicide attempt or suicidal ideation (Medical Economics Company, 2002). Dysthymic disorder involves a type of depression that is not severe enough to be called a major depressive episode, but that lasts much longer than major depressive disorder, without high phases.

It is contemplated that the compounds of this invention will be effective in treating depression in patients who have been diagnosed with depression by administration of any of the following tests: Hamilton Depression Rating Scale (HDRS), Hamilton depressed mood item, Clinical Global Impressions (CGI)-Severity of Illness. It is further contemplated that the compounds of the invention will be effective in inducing improvements in certain of the factors measured in these tests, such as the HDRS subfactor scores, including the depressed mood item, sleep disturbance factor and anxiety factor, and the CGI-Severity of Illness rating. It is also contemplated that the compounds of this invention will be effective in preventing relapse of major depressive episodes.

Anxiety disorders include panic disorder, agoraphobia with or without history of panic disorder, specific phobia, social phobia, obsessive-compulsive disorder, post-traumatic stress disorder, acute stress disorder and generalized anxiety disorder. It is contemplated that the compounds of this invention will be effective in treating any of all of these disorders in patients who have been diagnosed with these disorders.

Obsessive compulsive disorder is characterized by recurrent and persistent ideas, thoughts, impulses or images (obsessions) that are ego-dystonic and/or repetitive, purposeful and intentional behaviors (compulsions) that are recognized by the person as excessive or unreasonable (American Psychiatric Association, 1994a). The obsessions or compulsions cause marked distress, are time-consuming, or significantly interfere with social or occupational functioning.

It is contemplated that the compounds of this invention will be effective in treating obsessions and compulsions in patients who have been diagnosed with obsessive compulsive disorder by administration of appropriate tests, which may include, but are not limited to any of the following: Yale Brown Obsessive Compulsive Scale (YBOCS) (Goodman, 1989) (for adults), National Institute of Mental Health Global OCD Scale (NIMH GOCS), CGI-Severity of Illness scale. It is further contemplated that the compounds of the invention will be effective in inducing improvements in certain of the factors measured in these tests, such as a reduction of several points in the YBOCS total score. It is also contemplated that the compounds of this invention will be effective in preventing relapse of obsessive compulsive disorder.

Panic disorder is characterized by recurrent unexpected panic attacks and associated concern about having additional attacks, worry about the implications or consequences of the attacks, and/or a significant change in behavior related to the attacks (American Psychiatric Association, 1994a). A panic attack is defined as a

discrete period of intense fear or discomfort in which four (or more) of the following symptoms develop abruptly and reach a peak within 10 minutes: (1) palpitations, pounding heart, or accelerated heart rate; (2) sweating; (3) trembling or shaking; (4) sensations of shortness of breath or smothering; (5) feeling of choking; (6) chest pain or discomfort; (7) nausea or abdominal distress; (8) feeling dizzy, unsteady, lightheaded, or faint; (9) derealization (feelings of unreality) or depersonalization (being detached from oneself); fear of losing control; (11) fear of dying; (12) paresthesias (numbness or tingling sensations); (13) chills or hot flushes. Panic disorder may or may not be associated with agoraphobia, or an irrational and often disabling fear of being out in public.

It is contemplated that the compounds of this invention will be effective in treating panic disorder in patients who have been diagnosed with panic disorder on the basis of frequency of occurrence of panic attacks, or by means of the CGI-Severity of Illness scale. It is further contemplated that the compounds of the invention will be effective in inducing improvements in certain of the factors measured in these evaluations, such as a reduction in frequency or elimination of panic attacks, an improvement in the CGI-Severity of Illness scale or a CGI-Global Improvement score of 1 (very much improved), 2 (much improved) or 3 (minimally improved). It is also contemplated that the compounds of this invention will be effective in preventing relapse of panic disorder.

Social anxiety disorder, also known as social phobia, is characterized by a marked and persistent fear of one or

more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others (American Psychiatric Association, 1994a). Exposure to the feared situation almost invariably provokes anxiety, which may approach the intensity of a panic attack. The feared situations are avoided or endured with intense anxiety or distress. The avoidance, anxious anticipation, or distress in the feared situation(s) interferes significantly with the person's normal routine, occupational or academic functioning, or social activities or relationships, or there is marked distress about having the phobias. Lesser degrees of performance anxiety or shyness generally do not require psychopharmacological treatment.

It is contemplated that the compounds of this invention will be effective in treating social anxiety disorder in patients who have been diagnosed with social anxiety disorder by administration of any of the following tests: the Liebowitz Social Anxiety Scale (LSAS), the CGI-Severity of Illness scale, the Hamilton Rating Scale for Anxiety (HAM-A), the Hamilton Rating Scale for Depression (HAM-D), the axis V Social and Occupational Functioning Assessment Scale of DSM-IV, the axis II (ICD-10) World Health Organization Disability Assessment, Schedule 2 (DAS-2), the Sheehan Disability Scales, the Schneier Disability Profile, the World Health Organization Quality of Life-100 (WHOQOL-100), or other tests as described in Bobes, 1998, which is incorporated herein by reference. It is further contemplated that the compounds of the invention will be effective in inducing improvements as measured by these

tests, such as the a change from baseline in the Liebowitz Social Anxiety Scale (LSAS), or a CGI- Global Improvement score of 1 (very much improved), 2 (much improved) or 3 (minimally improved). It is also contemplated that the compounds of this invention will be effective in preventing relapse of social anxiety disorder.

Generalized anxiety disorder is characterized by excessive anxiety and worry (apprehensive expectation) that is persistent for at least 6 months and which the person finds difficult to control (American Psychiatric Association, 1994a). It must be associated with at least 3 of the following 6 symptoms: restlessness or feeling keyed up or on edge, being easily fatigued, difficulty concentrating or mind going blank, irritability, muscle tension, sleep disturbance. The diagnostic criteria for this disorder are described in further detail in DSM-IV, which is incorporated herein by reference (American Psychiatric Association, 1994a).

It is contemplated that the compounds of this invention will be effective in treating generalized anxiety disorder in patients who have been diagnosed with this disorder according to the diagnostic criteria described in DSM-IV. It is further contemplated that the compounds of the invention will be effective in reducing symptoms of this disorder, such as the following: excessive worry and anxiety, difficulty controlling worry, restlessness or feeling keyed up or on edge, being easily fatigued, difficulty concentrating or mind going blank, irritability, muscle tension, or sleep disturbance. It is also contemplated that the compounds

of this invention will be effective in preventing relapse of general anxiety disorder.

Post-traumatic stress disorder (PTSD), as defined by DSM-III-R/IV (American Psychiatric Association, 1987, American Psychiatric Association, 1994a), requires exposure to a traumatic event that involved actual or threatened death or serious injury, or threat to the physical integrity of self or others, and a response which involves intense fear, helplessness, or horror. Symptoms that occur as a result of exposure to the traumatic event include re-experiencing of the event in the form of intrusive thoughts, flashbacks or dreams, and intense psychological distress and physiological reactivity on exposure to cues to the event; avoidance of situations reminiscent of the traumatic event, inability to recall details of the event, and/or numbing of general responsiveness manifested as diminished interest in significant activities, estrangement from others, restricted range of affect, or sense of foreshortened future; and symptoms of autonomic arousal including hypervigilance, exaggerated startle response, sleep disturbance, impaired concentration, and irritability or outbursts of anger. A PTSD diagnosis requires that the symptoms are present for at least a month and that they cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

It is contemplated that the compounds of this invention will be effective in treating PTSD in patients who have been diagnosed with PTSD by administration of any of the following tests: Clinician-Administered PTSD Scale Part

2 (CAPS), the patient-rated Impact of Event Scale (IES) (Medical Economics Company, 2002, p. 2752). It is further contemplated that the compounds of the invention will be effective in inducing improvements in the scores of the CAPS, IES, CGI-Severity of Illness or CGI-Global Improvement tests. It is also contemplated that the compounds of this invention will be effective in preventing relapse of PTSD.

In a preferred embodiment, the subject invention provides a method of treatment or management of the following indications: depressive disorders, anxiety disorders, eating/body weight disorders, and urinary disorders. Examples of depressive disorders are major depressive disorder or dysthymic disorder. Examples of anxiety disorders are panic disorder, agoraphobia without history of panic disorder, specific phobia, social phobia, obsessive-compulsive disorder, post-traumatic stress disorder, acute stress disorder or generalized anxiety disorder. Examples of eating/body weight disorders are obesity, weight gain, bulimia, bulimia nervosa or anorexia nervosa. Examples of urinary disorders include, but are not limited to urinary incontinence overactive bladder, urge incontinence, urinary frequency, urinary urgency, nocturia or enuresis. Overactive bladder and urinary urgency may or may not be associated with benign prostatic hyperplasia.

This invention provides a method of modifying the feeding behavior of a subject, which comprises administering to the subject an amount of a compound of the invention effective to decrease the consumption of

food by the subject. This invention also provides a method of treating an eating disorder in a subject, which comprises administering to the subject an amount of a compound of the invention effective to treat the eating disorder. In an embodiment of the present invention, the eating disorder is obesity, bulimia, bulimia nervosa or anorexia nervosa.

The present invention further provides a method of reducing the body mass of a subject, which comprises administering to the subject an amount of a compound of the invention effective to reduce the body mass of the subject. This invention also provides a method of managing obesity in a subject in need of weight loss, which comprises administering to the subject an amount of a compound of the invention effective to induce weight loss in the subject. This invention also provides a method of managing obesity in a subject who has experienced weight loss, which comprises administering to the subject an amount of a compound of the invention effective to maintain such weight loss in the subject.

The present invention also provides a method of treating depression in a subject, which comprises administering to the subject an amount of a compound of the invention effective to treat the subject's depression. This invention also provides a method of treating anxiety in a subject, which comprises administering to the subject an amount of a compound of the invention effective to treat the subject's anxiety. This invention also provides a method of treating depression and anxiety in a subject, which comprises administering to the subject

an amount of a compound of the invention effective to treat the subject's depression and anxiety. This invention also provides a method of treating major depressive disorder in a subject, which comprises administering to the subject an amount of a compound of the invention effective to treat the subject's major depressive disorder. This invention also provides a method of treating dysthymic disorder in a subject, which comprises administering to the subject an amount of a compound of the invention effective to treat the subject's dysthymic disorder. This invention also provides a method of treating obsessions and compulsions in a subject with obsessive compulsive disorder, which comprises administering to the subject an amount of a compound of the invention effective to treat the subject's obsessions and compulsions. This invention also provides a method of treating panic disorder, with or without agoraphobia, in a subject, which comprises administering to the subject an amount of a compound of the invention effective to treat the subject's panic disorder. This invention also provides a method of treating social anxiety disorder in a subject, which comprises administering to the subject an amount of a compound of the invention effective to treat the subject's social anxiety disorder. This invention also provides a method of treating generalized anxiety disorder in a subject, which comprises administering to the subject an amount of a compound of the invention effective to treat the subject's generalized anxiety disorder. This invention also provides a method of treating post-traumatic stress disorder in a subject, which comprises administering to the subject an amount

of a compound of the invention effective to treat the subject's post-traumatic stress disorder.

It is contemplated that the compounds of this invention will be effective in treating obesity, including weight loss and maintenance of weight loss in patients, who have been diagnosed with obesity by the one or more of the following measurements: an increased body mass index, increased waist circumference (an indicator of intra-adominal fat), Dual Energy X-Ray Absorptiometry (DEXA) and trucal (android) fat mass. It is further contemplated that the compounds of the invention will be effective in inducing improvements in certain factors measured in these tests.

It is contemplated that the compounds of this invention will be effective in treating urinary disorders in patients who have urge or mixed (with a predominance of urge) incontinence as evidenced by the number of unnecessary episodes per week, the number of unnecessary micturitions per day and a low volume voided per micturition. It is further contemplated that the compounds of the invention will be effective in inducing improvements in certain factors measured in these tests.

The present invention also provides a method of treating a subject suffering from bipolar I or II disorder, schizoaffective disorder, a cognitive disorder with depressed mood, a personality disorder, insomnia, hypersomnia, narcolepsy, circadian rhythm sleep disorder, nightmare disorder, sleep terror disorder or sleepwalking disorder.

The present invention provides a method of treating overactive bladder with symptoms of urge urinary incontinence, urgency and/or frequency in a subject, which comprises administering to the subject an amount of a compound of the invention effective to treat the subject's overactive bladder. This invention also provides a method of alleviating urge urinary incontinence in a subject suffering from overactive bladder, which comprises administering to the subject an amount of a compound of the invention effective to alleviate the subject's urge urinary incontinence. This invention further provides a method of alleviating urinary urgency in a subject suffering from overactive bladder, which comprises administering to the subject an amount of a compound of the invention effective to alleviate the subject's urinary urgency. Additionally, this invention provides a method of alleviating urinary frequency in a subject suffering from overactive bladder, which comprises administering to the subject an amount of a compound of the invention effective to alleviate the subject's urinary frequency.

The present invention also provides a method of treating a subject suffering from a urinary disorder, which comprises administering to the subject an amount of a compound of the invention effective to treat the subject's urinary disorder. In some embodiments the urinary disorder is urinary incontinence, overactive bladder, urge incontinence, urinary frequency, urinary urgency, nocturia or enuresis.

The present invention provides a method of alleviating the symptoms of a disorder in a subject, which comprises administering to the subject an amount of an MCH1 antagonist effective to alleviate the symptoms, wherein the MCH1 antagonist is any of the compounds of the invention.

In an embodiment of the invention, the subject is a vertebrate, a mammal, a human or a canine. In another embodiment, the compound is administered orally. In yet another embodiment, the compound is administered in combination with food.

This invention will be better understood from the Experimental Details In a preferred embodiment, the subject invention provides a method of treatment for the following indications: depression, anxiety, eating/body weight disorders, and urinary disorders. Examples of eating/body weight disorders are obesity, bulimia, or bulimia nervosa. Examples of urinary disorders include, but are not limited to, urinary incontinence, overactive bladder, urge incontinence, urinary frequency, urinary urgency, nocturia, or enuresis. Overactive bladder and urinary urgency may or may not be associated with benign prostatic hyperplasia.

This invention provides a method of modifying the feeding behavior of a subject which comprises administering to the subject an amount of a compound of the invention effective to decrease the consumption of food by the subject.

This invention also provides a method of treating an eating disorder in a subject which comprises administering to the subject an amount of a compound of this invention effective to decrease the consumption of food by the subject. In an embodiment of the present invention, the eating disorder is bulimia, obesity or bulimia nervosa. In an embodiment of the present invention, the subject is a vertebrate, a mammal, a human or a canine. In a further embodiment, the compound is administered in combination with food.

The present invention further provides a method of reducing the body mass of a subject which comprises administering to the subject an amount of a compound of the invention effective to reduce the body mass of the subject.

The present invention also provides a method of treating a subject suffering from depression which comprises administering to the subject an amount of a compound of this invention effective to treat the subject's depression. The present invention further provides a method of treating a subject suffering from anxiety which comprises administering to the subject an amount of a compound of this invention effective to treat the subject's anxiety. The present invention also provides a method of treating a subject suffering from depression and anxiety which comprises administering to the subject an amount of a compound of this invention effective to treat the subject's depression and anxiety.

The present invention also provides a method of treating a subject suffering from major depressive disorder,

dysthymic disorder, bipolar I and II disorders, schizoaffective disorder, cognitive disorders with depressed mood, personality disorders, insomnia, hypersomnia, narcolepsy, circadian rhythm sleep disorder, nightmare disorder, sleep terror disorder, sleepwalking disorder, obsessive-compulsive disorder, panic disorder, with or without agoraphobia, posttraumatic stress disorder, social anxiety disorder, social phobia and generalized anxiety disorder.

The present invention also provides a method of treating a subject suffering from a urinary disorder which comprises administering to the subject an amount of a compound of this invention effective to treat the subject's a urinary disorder. In some embodiments, the urinary disorder is urinary incontinence, overactive bladder, urge incontinence, urinary frequency, urinary urgency, nocturia, or enuresis.

This invention will be better understood from the Experimental Details which follow. However, one skilled in the art will readily appreciate that the specific methods and results discussed are merely illustrative of the invention as described more fully in the claims which follow thereafter.

Experimental Section

I. Synthetic Methods for Examples

General Methods: All reactions (except for those done by parallel synthesis reaction arrays) were performed under an Argon atmosphere and the reagents, neat or in appropriate solvents, were transferred to the reaction vessel via syringe and cannula techniques. The parallel synthesis reaction arrays were performed in vials (without an inert atmosphere) using J-KEM heating shakers (Saint Louis, MO). Anhydrous solvents were purchased from Aldrich Chemical Company and used as received. The examples described in the patent were named using ACD/Name program (version 2.51, Advanced Chemistry Development Inc., Toronto, Ontario, M5H2L3, Canada). Unless otherwise noted, the ^1H spectra were recorded at 300 and 400 MHz (QE Plus and Brüker respectively) with tetramethylsilane as internal standard. s = singlet; d = doublet; t = triplet; q = quartet; p = pentet; sext; sept; br = broad; m = multiplet. Elemental analyses were performed by Robertson Microlit Laboratories, Inc. Unless otherwise noted, mass spectra were obtained using low-resolution electrospray (ESMS) and MH^+ is reported. Thin-layer chromatography (TLC) was carried out on glass plates precoated with silica gel 60 F_{254} (0.25 mm, EM Separations Tech.). Preparative thin-layer chromatography was carried out on glass sheets precoated with silica gel GF (2 mm, Analtech). Flash column chromatography was performed on Merck silica gel 60 (230 - 400 mesh). Melting points (mp) were determined in

open capillary tubes on a Mel-Temp apparatus and are uncorrected.

Piperidine Side Chain Intermediates

TERT-BUTYL 4-{[(TRIFLUOROMETHYL)SULFONYL]OXY}-1,2,3,6-TETRAHYDRO-1-PYRIDINECARBOXYLATE: *n*-Butyl lithium (17.6 mL, 44.2 mmol, 2.5 M in hexanes) was added to a solution of diisopropyl amine (96.2 mL, 44.2 mmol) in 40 mL of dry THF at 0 °C and stirred for 20 minutes. The reaction mixture was cooled to -78 °C and tert-butyl 4-oxo-1-piperidinecarboxylate (Aldrich Chemical Company, 40.0 mmol) in THF (40 mL) was added dropwise to the reaction mixture and stirred for 30 minutes. Tf_2NPh (42.0 mmol, 15.0 g) in THF (40 mL) was added dropwise to the reaction mixture and stirred at °C overnight. The reaction mixture was concentrated *in vacuo*, re-dissolved in hexanes:EtOAc (9:1), passed through a plug of alumina and the alumina plug was washed with hexanes:EtOAc (9:1). The combined extracts were concentrated to yield 16.5 g of the desired product that was contaminated with some starting Tf_2NPh.

^1H NMR (400 MHz, 400 MHz, $CDCl_3$) δ 5.77 (s, 1 H), 4.05 (dm, 2 H, J=3.0 Hz), 3.63 (t, 2 H, J=5.7 Hz), 2.45 (m, 2 H), 1.47 (s, 9 H).

TERT-BUTYL 4-[3-(AMINO)PHENYL]-1,2,3,6-TETRAHYDRO-1-PYRIDINECARBOXYLATE: A mixture of 2 M aqueous Na_2CO_3 solution (4.2 mL), tert-butyl 4-{[(trifluoromethyl)sulfonyl]oxy}-1,2,3,6-tetrahydro-1-pyridine-carboxylate (0.500 g, 1.51 mmol), 3-aminophenylboronic acid hemisulfate (0.393 g, 2.11 mmol), lithium chloride (0.191 g, 4.50 mmol) and

tetrakis- triphenylphosphine palladium (0) (0.080 g, 0.075 mmol) in dimethoxyethane (5 mL) was heated at reflux temperature for 3 hours, under an inert atmosphere (an initial degassing of the mixture is recommended to prevent the formation of triphenylphosphine oxide). The organic layer of the cooled reaction mixture was separated and the aqueous layer was washed with ethyl acetate (3X). The combined organic extracts were dried and concentrated in vacuo. The crude product was chromatographed (silica, hexanes:EtOAc:dichloromethane (6:1:1) with 1% added isopropylamine to protect the BOC group from hydrolysis) to give 0.330 g of the desired product in 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (t, 1H, J= 7.60 Hz), 6.78 (d, 1H, J= 8.4 Hz), 6.69 (t, 1H, J= 2.0 Hz), 6.59 (dd, 1H, J= 2.2, 8.0 Hz), 6.01 (m, 1H), 4.10 - 4.01 (d, 2H, J= 2.4 Hz), 3.61 (t, 2H, J= 5.6 Hz), 2.52 - 2.46 (m, 2H), 1.49 (s, 9H); ESMS m/e : 275.2 $(M + H)^+$. Anal. Calc. for $C_{16}H_{24}N_2O_2$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.78; H, 7.80; N, 9.92.

TERT-BUTYL 4-[3-(AMINO)PHENYL]-1-PIPERIDINECARBOXYLATE: A mixture of 3.10 g of tert-butyl 4-(3-aminophenyl)-1,2,3,6-tetrahydropyridine-1-carboxylate (11.3 mmol) and 1.0 g of 10% Pd/C in 200 mL of ethanol was hydrogenated at room temperature using the balloon method for 2 days. The reaction mixture was filtered and washed with ethanol. The combined ethanol extracts were concentrated *in vacuo* and the residue was chromatographed on silica (dichloromethane: methanol 95:5 with 1% isopropylamine added to protect the BOC group from hydrolysis) to give 2.63 g of the desired product (84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (t, 1H, J=

7.60 Hz), 6.62 (d, 1H, J= 8.4 Hz), 6.60 - 6.59 (m, 2H), 4.27 - 4.18 (m, 2H), 3.62 - 3.58 (m, 2H), 2.80 - 2.72 (m, 2H), 2.62 - 2.59 (m, 1H), 1.89 - 1.52 (m, 4H), 1.49 (s, 9H); ESMS m/e : 277.2 $(M + H)^+$.

TERT-BUTYL 4-[3-(ACETYLAMINO)PHENYL]-1,2,3,6-TETRAHYDRO-1-PYRIDINECARBOXYLATE: A mixture of saturated aqueous Na_2CO_3 solution (25 mL), *tert*-butyl 4-{[(trifluoromethyl)sulfonyl]oxy}-1,2,3,6-tetrahydro-1-pyridine-carboxylate (20 mmol), 3-acetamidophenylboronic acid (30 mmol) and tetrakis-triphenylphosphine palladium (0) (1.15 g) and dimethoxyethane (40 mL) was heated at reflux temperature overnight. The organic layer of the cooled reaction mixture was separated and the aqueous layer was washed with ethyl acetate (3X). The combined organic extracts were dried and concentrated *in vacuo*. The crude product was chromatograghed, giving the desired product: ^1H NMR ($CDCl_3$) δ 8.11 (br s, 1 H), 7.57 (br s, 1 H), 7.41 (br d , 1 H, J=7.8 Hz), 7.25 (apparent t, 1 H, J=7.8 Hz), 7.08 (br d, 1 H, J=7.8 Hz), 5.99 (br s, 1 H), 4.03 (br m, 2 H, J=2.7 Hz), 3.59 (t, 2 H, J=5.7 Hz), 2.46 (m, 2 H,), 2.16 (s, 3 H), 1.49 (s, 9 H).

N1-[3-(1,2,3,6-TETRAHYDRO-4-PYRIDINYL)PHENYL]ACETAMIDE: A solution of 4 M HCl in dioxane (10 mL) was added to tert-butyl 4-[3-(acetylamino)phenyl]-1,2,3,6-tetrahydro-1-pyridinecarboxylate (8.25 mmol) in dichloromethane (30 mL). The reaction mixture was stirred at room temperature overnight, concentrated *in vacuo*, giving the desired product as the hydrochloride salt (2.1 g): ^1H NMR ($CDCl_3$) δ 7.41-7.00 (m, 4 H), 6.10 (br, 1 H), 3.55 (m, 2

H), 3.16 (t, 2 H, J = 5.7 Hz), 2.44 (m, 2 H), 2.19 (s, 3 H).

TERT-BUTYL *N*-(3-BROMOPROPYL)CARBAMATE: Prepared from 3-bromopropylamine hydrobromide and BOC_2O in the presence of base in dichloromethane, 9.89 mmol: ^1H NMR ($CDCl_3$) δ 5.07 (br, 1 H), 3.31 (t, 2 H, J=6.6 Hz), 3.12 (apparent br q, 2 H, J=6.0 Hz), 1.92 (p, 2 H, J=6.6 Hz), 1.30 (s, 9H).

TERT-BUTYL *N*-(3-{4-[3-(ACETYLAMINO)PHENYL]-1,2,3,6-TETRAHYDRO-1-PYRIDINYL}PROPYL)CARBAMATE: A solution of N1-[3-(1,2,3,6-tetrahydro-4-pyridinyl)phenyl]acetamide.HCl (8.24 mmol), tert-butyl *N*-(3-bromopropyl)carbamate and potassium carbonate (33 mmol) in dry dioxane (30 mL) was heated at reflux temperature overnight. The solids were removed by filtration, the solution was concentrated *in vacuo* and the product was chromatograghed, giving the desired product (110 mg). ^1H NMR ($CDCl_3$) δ 7.65 (s, 1 H), 6.98 (s, 1 H), 7.45 (d, 1 H, J=7.8 Hz), 7.16 (apparent t, 1 H, J=7.8 Hz), 7.10 (d, 1 H, J=7.8 Hz), 6.02 (s, 1 H), 5.23 (b, 1 H), 3.40 (b, 2 H), 3.30-1.80 (m, 10 H), 2.18 (s, 3 H), 1.45 (s, 9 H).

N1-{3-[1-(3-AMINOPROPYL)-1,2,3,6-TETRAHYDRO-4-PYRIDINYL]PHENYL}ACETAMIDE: A 1:1 solution of TFA:CH_2Cl_2 (5 mL) was added to tert-butyl *N*-(3-{4-[3-(acetylamino)phenyl]-1,2,3,6-tetrahydro-1-pyridinyl}propyl)carbamate in dichloromethane (5 mL). The resulting solution was stirred at room temperature for 1-3 days, saturated $NaHCO_3$ was added until pH > 6, the organic layer was separated, and dried *in vacuo*,

giving the desired product (45 mg): ^{1}H NMR ($CDCl_3$) δ 7.68 (br, 1 H), 7.35 (dm, 1 H, J=7.8 Hz), 7.25 (apparent t, 1 H, J=7.8 Hz), 7.15 (dm, 1 H, J=7.8 Hz), 6.12 (m, 1 H), 3.22 (m, 2 H), 3.03 (t, 2 H, J=7.3 Hz), 2.78 (t, 2 H, J=5.5 Hz), 2.70-2.50 (m, 4 H), 2.10 (s, 3 H), 1.87 (p, 2 H, J=7.3 Hz).

TERT-BUTYL 4-[3-(ACETYLAMINO)PHENYL]-1-PIPERIDINECARBOXYLATE: A mixture tert-butyl 4-[3-(acetylamino)phenyl]-1,2,3,6-tetrahydro-1-pyridinecarboxylate (710 mg) and 5% Pd/C (100 mg) in EtOH (10 mL) was hydrogenated (balloon technique) at room temperature overnight. The reaction mixture was passed through a pad of Celite 545 and the pad of Celite was washed with ethanol. The combined ethanol extracts were concentrated and chromatograghed, giving the desired product (660 mg): ^{1}H NMR ($CDCl_3$) δ 7.80 (s, 1 H), 7.41-7.20 (m, 3 H), 6.94 (d, 1 H, J=7.5 Hz), 4.21 (m, 2 H), 2.75 (m, 2 H), 2.62 (m, 1 H), 2.16 (s, 3 H), 1.78 (m, 2 H), 1.56 (m, 2 H), 1.48 (s, 9 H).

N1-[3-(4-PIPERIDYL)PHENYL]ACETAMIDE: A solution of HCl in dioxane (4N, 5 mL) was added to tert-butyl 4-[3-(acetylamino)phenyl]-1-piperidinecarboxylate (660 mg) in dry dichloromethane (15 mL). The reaction mixture was stirred at room temperature overnight and concentrated *in vacuo*, giving the desired product (550 mg): mp 102-104 °C; ^{1}H NMR ($CDCl_3$) δ 2.02 (d, J=13.2 Hz, 2H), 2.11-2.45 (m, 5H), 2.67-2.77 (m, 1H), 3.00-3.10 (m, 2H), 3.51 (d, J=10.5 Hz, 2H), 6.94 (d, J=7.5 Hz, 1H), 7.20-7.46 (m, 3H), 7.60 (s, 1H); Anal. Calcd. For $C_{13}H_{19}N_2OCl+0.86\ CH_2Cl_2$: C, 50.78; H, 6.37; N, 8.55. Found: C, 50.80; H, 7.55; N, 7.01.

TERT-BUTYL N-(3-{4-[3-(ACETYLAMINO)PHENYL]PIPERIDINO}PROPYL)CARBAMATE: A solution of N1-[3-(4-piperidyl)phenyl]acetamide (550 mg, 0.210 mmol), tert-butyl N-(3-bromopropyl)carbamate (550 mg, 0.230 mmol), K_2CO_3 (1.10 g, 0.890 mmol), diisopropylethyl amine (1.50 mL) and a few crystals of KI in dioxane (20 mL) was heated at reflux temperature for 2 days. The precipitated salts were removed by filtration, concentrated *in vacuo* and the crude product was chromatographed, giving the desired product (340 mg): ^{1}H NMR ($CDCl_3$) δ 8.15 (s, 1 H), 7.47-7.44 (m, 2 H), 7.22 (t, 1 H, J=7.8 Hz), 6.94 (d, 1 H, J=7.8 Hz), 5.53 (b, 1 H), 3.23 (b, 6 H), 2.80-1.60 (m, 9 H), 2.20 (s, 3 H), 1.45 (s, 9 H).

N1-{3-[1-(3-AMINOPROPYL)-4-PIPERIDYL]PHENYL}ACETAMIDE: TFA (1.0 mL) was added to a solution of tert-butyl N-(3-{4-[3-(acetylamino)phenyl]piperidino}propyl)carbamate (340 mg) in dry dichloromethane (10 mL) and stirred at room temperature for 5 h. A 10% aqueous solution of KOH was added to the reaction mixture until pH > 6 and then the dichloromethane was removed *in vacuo*. The aqueous layer was frozen and lyophilized to give a solid, which was extracted with methanol. Removal of the solvent gave the desired product (120 mg) as an oil: ^{1}H NMR ($CDCl_3$) δ 7.23-7.16 (apparent t, 1H, J=7.5 Hz), 6.95-6.92 (m, 1H), 3.03-2.99 (m, 2H), 2.77-2.73 (t, 2H, J = 6.6 Hz), 2.50-1.60 (m, 10 H), 2.13 (s, 3 H).

TERT-BUTYL 4-(3-NITROPHENYL)-3,6-DIHYDRO-1(2H)-PYRIDINECARBOXYLATE: According to the procedure used for the synthesis of *tert*-butyl 4-[3-(amino)phenyl]-1,2,3,6-tetrahydro-1-pyridinecarboxylate, a mixture of 2 M aqueous Na_2CO_3 solution (2.2 mL), *tert*-butyl 4-{[(trifluoromethyl)sulfonyl]oxy}-1,2,3,6-tetrahydro-1-pyridine-carboxylate (0.500 g, 1.51 mmol), 3-nitrophenylboronic acid (0.353 g, 2.11 mmol), lithium chloride (0.191 g, 4.50 mmol) and tetrakis-triphenylphosphine palladium (0) (0.080 g, 0.075 mmol) in dimethoxyethane (5 mL) afforded 0.380g of the desired product.

^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H), 8.11 (d, 1H, J=8.0 Hz), 7.69 (d, 1H, J=8.0 Hz), 7.51 (t, 1H, J=8.0 Hz), 6.20 (m, 1H), 4.17-4.08 (m, 2H), 3.67 (t, 2H, J=5.6 Hz), 2.61-2.52 (m, 2H), 1.50 (s, 9H); ESMS m/e : 249.1 $(M + H - C_4H_8)^+$.

1,2,3,6-TETRAHYDRO-4-(3-NITROPHENYL)PYRIDINE: Into a stirred solution of 5.00 g (16.0 mmol) of tert-butyl 1,2,3,6-tetrahydro-4-(3-nitrophenyl)pyridine-1-carboxylate in 100 ml of 1,4-dioxane at 0°C was bubbled HCl gas for 10 minutes. The reaction mixture was allowed to warm to room temperature and the bubbling of the HCl gas was continued for an additional 1 hour. The solvent was removed *in vacuo*, the residue was dissolved in 50 mL of water and was neutralized by the addition of KOH pellets. The aqueous solution was extracted with 3 X 80 mL of dichloromethane and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by column chromatography (silica, 9 : 1 ,dichloromethane :

methanol + 1% isopropyl amine) to afford 2.85 g (87.5% yield) of the desired product: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 8.09 (d, 1H, J=8.4 Hz), 7.71 (d, 1H, J=8.0 Hz), 7.49 (t, 1H, J=8.0 Hz), 6.35-6.25 (m, 1H), 3.58 (apparent q, 2H, J=3.0 Hz), 3.14 (t, 2H, J=5.6 Hz), 2.54-2.46 (m, 2H).

TERT-BUTYL 3-(4-(3-NITROPHENYL)-3,6-DIHYDRO-1(2H)-PYRIDINYL)PROPYLCARBAMATE: A mixture of 2.80 g (14.0 mmol) of 1,2,3,6-tetrahydro-4-(3-nitrophenyl)pyridine, 3.60 g (15.0 mmol) of tert-butyl N-(3-bromopropyl)carbamate, 11.6 g (84.0 mmol) of K_2CO_3, 14.6 mL (84.0 mmol) of diisopropylethylamine and 0.78 g (2.00 mmol) of tetrabutylammonium iodide in 250 mL of 1,4-dioxane was heated at reflux temperature for 14 hours. The reaction mixture was filtered and the filtrate was dried ($MgSO_4$), concentrated *in vacuo* and the residue was purified by column chromatography (silica, 9:1, dichloromethane: methanol + 1% isopropyl amine) to afford 4.35 g (85.7% yield) of the desired product: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (t, 1H, J=1.9 Hz), 8.09 (dd, 1H, J=1.9, 8.0 Hz), 7.70 (apparent d, 1H, J=8.0 Hz), 7.49 (t, 1H, J=8.0 Hz), 6.23 (m, 1H), 3.29-3.18 (m, 4H), 2.75 (t, 2H, J=5.6 Hz), 2.64-2.54 (m, 4H), 1.82-1.70 (m, 2H), 1.44 (s, 9H); ESMS m/e : 362.2 $(M + H)^+$.

3-(4-(3-NITROPHENYL)-3,6-DIHYDRO-1(2H)-PYRIDINYL)-1-PROPANAMINE: Into a stirred solution of 4.35 (12.0 mmol) of tert-butyl 3-(4-(3-nitrophenyl)-3,6-dihydro-1(2H)-pyridinyl)propylcarbamate in 100 ml of 1,4-dioxane at 0°C was bubbled HCl gas for 10 minutes. The reaction mixture was allowed to warm to room temperature and the

bubbling was continued for an additional 1 hour. The solvent was removed *in vacuo*, the residue was dissolved in 50 mL of water and was neutralized by the addition of KOH pellets. The aqueous solution was extracted with 3 X 80 mL of dichloromethane, the combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by column chromatography (silica, 9 : 1 ,dichloromethane : methanol + 1% isopropyl amine) to afford 3.05 g (97.0% yield) of the desired product: ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (t, 1H, J=1.8 Hz), 8.09 (dd, 1H, J=1.8, 8.2 Hz), 7.69 (dd, 1H, J=1.8, 8.2 Hz), 7.48 (t, 1H, J=8.2 Hz), 6.24 (m, 1H), 3.21 (d, 2H, J=3.6 Hz), 2.84 (t, 2H, J=6.6 Hz), 2.75 (t, 2H, J=5.8 Hz), 2.64-2.54 (m, 4H), 1.76 (m, 2H); ESMS m/e : 262.2 $(M + H)^+$; *Anal. Calc.* for $C_{14}H_{19}N_3O_2$ (0.06 $CHCl_3$): C, 62.90; H, 7.16; N, 15.65. *Found:* C, 63.20; H, 7.16; N, 15.65.

METHYL (4S)-3-[({3-[4-(3-AMINOPHENYL)-1-PIPERIDINYL]PROPYL}AMINO)CARBONYL]-4-(3,4-DIFLUOROPHENYL)-6-(METHOXYMETHYL)-2-OXO-1,2,3,4-TETRAHYDRO-5-PYRIMIDINECARBOXYLATE: A mixture of 3.02 g (6.33 mmol) 5-methyl 1-(4-nitrophenyl) (6*S*)-6-(3,4-difluorophenyl)-4-(methoxymethyl)-2-oxo-3,6-dihydro-1,5(2H)-pyrimidinedicarboxylate, 1.50 g (5.80 mmol) of 3-(4-(3-nitrophenyl)-3,6-dihydro-1(2H)-pyridinyl)-1-propanamine, 7.94 g (75.5 mmol) of K_2CO_3 and 1.00 mL of methanol in 200 mL dichloromethane (under argon) was stirred at room temperature for 1 hour. The reaction mixture was filtered and concentrated *in vacuo*. The residue was dissolved in 100 mL of ethyl acetate and washed 3 X 50 mL of 5% aqueous NaOH solution, the organic layer was dried ($MgSO_4$) and concentrated *in*

vacuo. The residue was dissolved in 100 mL of anhydrous ethanol containing 0.50 g 10% Pd/C and the reaction mixture was stirred under a hydrogen balloon for 24 hours. The reaction mixture was passed through a column of Celite 545 filtering agent, washed with ethanol, the filtrate was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (silica, 9.5 : 0.5 ,dichloromethane : methanol + 1% isopropyl amine) to afford 1.65 g (52.0% yield) of the desired product: ^1H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.22-7.02 (m, 2H), 6.95 (t, J = 8.70 Hz, 1H), 6.63-6.44 (m, 4H), 4.56 (Abq, 2H), 3.62 (s, 3H), 3.33 (s, 3H), 3.32-3.20 (m, 4H), 2.96 (br s, 2H), 2.33 (t, J = 7.50 Hz, 2H), 2.11-1.94 (m, 3H), 1.81-1.64 (m, 4H); ESMS m/e : 572.3 $(M + H)^+$;

TERT-BUTYL 4-[3-(ISOBUTYRYLAMINO)PHENYL]-3,6-DIHYDRO-1(2H)-PYRIDINECARBOXYLATE: Into a solution of 4.00 g (16.0 mmol) of tert-butyl 4-(3-aminophenyl)-3,6-dihydro-1(2H)-pyridinecarboxylate and 5.60 mL (32.0 mmol) of diisopropylethylamine in 100 mL dichloromethane was slowly added 1.90 mL (19.0 mmol) of isobutyryl chloride. The reaction mixture was stirred at room temperature for 2 hours, washed with water, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by column chromatography (silica, 50 : 46 : 3 : 1, hexanes : dichloromethane : methanol : isopropyl amine) to afford 2.90 g (52.0% yield) of the desired product: ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (s, 1 H), 7.34 (d, 1 H, J=7.8 Hz), 7.27 (t, 1H, J=7.8 Hz), 7.11 (d, 1H, J=7.8 Hz), 6.04 (s, 1H), 4.05 (s, 2H), 3.62 (apparent t, 2 H, J=4.9 Hz), 2.51 (m, 3H), 1.49 (s, 9H), 1.25 (d, 6H, J=7.4 Hz); ESMS *m/e*: 345.5 $(M + H)^+$. Anal. Calc. for

$C_{20}H_{28}N_2O_3$+0.175 $CHCl_3$: C, 66.33; H, 7.77; N, 7.67. Found: C, 66.20; H, 7.41; N, 7.88

TERT-BUTYL 4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINECARBOXYLATE: A mixture of 2.90 g (8.40 mmol) of tert-butyl 4-[3-(isobutyrylamino)phenyl]-3,6-dihydro-1(2H)-pyridinecarboxylate and 0.80 g of 10% yield Pd/C in 100 mL of ethanol was stirred under a hydrogen balloon for 24 hours. The reaction mixture was passed through a column of Celite 545 filtering agent, the filtrate was dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by column chromatography (silica, 9.5 : 0.5 ,dichloromethane : methanol + 1% isopropyl amine) to afford 2.40 g (84.0% yield) of the desired product: ^1H NMR (400 MHz, $CDCl_3$) δ 7.49-7.44 (m, 2H), 7.24 (t, 1H, J=7.6 Hz), 6.93 (d, 1H, J=7.6 Hz), 4.20-4.10 (m, 2H), 2.86-2.45 (m, 4H), 1.86-1.75 (m, 4H), 1.48 (s, 9H), 1.24 (d, 6H, J=6.8 Hz); ESMS m/e : 345.2 $(M + H)^+$; Anal. Calc. for $C_{20}H_{30}N_2O_3$+0.3H_2O: C, 68.27; H, 8.77; N, 7.96. Found: C, 68.25; H, 8.54; N, 7.84.

2-METHYL-*N*-[3-(4-PIPERIDINYL)PHENYL]PROPANAMIDE: Into a stirred solution of 2.20 (6.50 mmol) of tert-butyl 4-[3-(isobutyrylamino)phenyl]-1-piperidinecarboxylate in 100 ml of 1,4-dioxane at 0 °C was bubbled HCl gas for 10 minutes. The reaction mixture was allowed to warm to room temperature and the bubbling of the HCl gas was continued for 1 hour. The solvent was removed *in vacuo*, the residue was dissolved in 50 mL of water and was neutralized by the addition of KOH pellets. The aqueous solution was extracted with 3 X 80 mL of dichloromethane, the combined organic extracts were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The

residue was purified by column chromatography (silica, 9 : 1 ,dichloromethane : methanol + 1% isopropyl amine) to afford 0.700 g (46.0% yield) of the desired product: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (s, 1H), 7.40 (d, 1H, J=7.8 Hz), 7.24 (t, 1H, J=7.8 Hz), 7.00 (d, 1H, J=7.8 Hz), 3.23-3.14 (m, 5H), 2.82-2.57 (m, 4H), 1.20 (d, 6H, J=6.8 Hz); ESMS m/e : 247.2 $(M + H)^+$; The hydrochloride salt was used for the combustion analysis: Anal. Calc. for $C_{15}H_{22}N_2O$+HCl+0.15 $CHCl_3$: C, 60.51; H, 7.76; N, 9.32. Found: C, 60.57; H, 7.83; N, 8.88.

3-(4-PIPERIDINYL)ANILINE: A solution of 4 M HCl in dioxane (25 mL) was added to *tert*-butyl 4-[3-(amino)phenyl]-1-piperidinecarboxylate (2.60 g, 9.00 mmol) in dichloromethane (250 mL). The reaction mixture was stirred at room temperature overnight, concentrated *in vacuo*, and the residue was dissolved in water (50 mL). The mixture was nuetralized using KOH pellets and extracted with methylene chloride (3 X 50 mL). The combined organic extracts were dried ($MgSO_4$), concentrated and chromatographed to give the desired product (1.03 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (t, 1H, J=7.6 Hz), 6.62-6.54 (m, 3H), 3.16 (br d, 2H, J=10.3 Hz), 2.75 (dt, 2H, J=2.7, 12.3 Hz), 2.56 (tt, 1H, J=3.6, 12.3 Hz), 1.81 (br d, 2H, J=12.3 Hz), 1.65 (dq, 2H, J=4.0, 12.3 Hz); ESMS m/e : 177.2 $(M + H)^+$.

TERT-BUTYL 4-(4-NITROPHENYL)-3,6-DIHYDRO-1(2H)-PYRIDINECARBOXYLATE: To a 25-mL RB flask, equipped with a condensor, was added tert-butyl 4-{[(trifluoromethyl)sulfonyl]oxy}-3,6-dihydro-1(2H)-pyridinecarboxylate (1.0 g), 4-nitrophenylboronic acid (0.71 g), sodium carbonate (0.430 mL of 2M solution),

lithium chloride (0.382 g), tetrakis(triphenylphosphine)- palladium (0) (0.173 g) and ethylene glycol dimethyl ether (10 mL). The reaction mixture was flushed with Argon three times, then the reaction mixture was heated to 100 °C for 3 hrs. After cooling to room temperature, the reaction mixture was diluted with methylene chloride (30 mL) and water (30 mL) and the organic layer was separated. The aqueous layer was extracted with methylene chloride (3x20 mL) and the combined organic extracts were washed with sat NH_4Cl (20 mL) and brine (20 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by chromatography (6:1=hexane:ethyl acetate with 1% NH_3) to afford the product (0.55 g, 59.9%) as a yellow oil. The compound is not stable at room temperature and should be used as promptly as practical: ^1H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, 2H, J=8.6 Hz), 7.51 (d, 2H, J=8.6 Hz), 6.24 (m, 1H), 4.13 (m, 2H), 3.67 (apparent t, 2H, J=5.5 Hz), 2.55 (m, 2H), 1.49 (s, 9H).

4-(4-NITROPHENYL)-1,2,3,6-TETRAHYDROPYRIDINE: 4-(4-Nitrophenyl)-1,2,3,6-tetrahydropyridine was prepared by a similar procedure to that used for the preparation of 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide using HCl gas and tert-Butyl 4-(4-Nitrophenyl)-3,6-dihydro-1(2*H*)-pyridinecarboxylate (130 mg) in dioxane (5.0 mL) at room temperature. The reaction mixture was concentrated *in vacuo* to give the crude product (69.8 mg) which used in the next reaction without further purification.

Oxazolidinone Intermediates:

AMINO-(3,4-DIFLUOROPHENYL)-ACETONITRILE: Through a solution of 3,4-difluorobenzaldehyde (25.0 g, 0.176 mol) in MeOH (500 mL) in a round bottom flask, was bubbled ammonia gas for two hours at room temperature. The flask was then cooled to 0 °C and trimethylsilyl cyanide was then added slowly. The reaction mixture was stirred for 2 h, at which time TLC analysis indicated that the reaction was complete (R_f = 0.35, 3:2 hexane/EtOAc). The solvent was removed *in vacuo* and the residue was subjected to flash column chromatography on silica gel to obtain the desired product, which was used in the next step without purification.

AMINO-(3,4-DIFLUOROPHENYL)-ACETIC ACID METHYL ESTER: Into a well-stirred solution of amino-(3,4-difluorophenyl)-acetonitrile (22.0 g, 0.130 mol), a solution of HCl in MeOH (200 mL) was added at room temperature. The resulting yellow solution was stirred at room temperature for 10 h and was heated at reflux temperature for 1.5 h. After cooling, the solvent was removed *in vacuo* and the resulting yellow solid was dissolved in water (200 mL). The aqueous solution was then carefully basified with 20% NaOH solution to pH 9. The aqueous layer was extracted with CH_2Cl_2 (3 x 100 mL). The organic layer was separated and dried over Na_2SO_4, filtered and the solvent was removed *in vacuo* to obtain the desired product which was used in the next step without purification.

2-AMINO-2-(3,4-DIFLUOROPHENYL)-ETHANOL: Into a well-stirred suspension of $LiAlH_4$ (4.7 g, 0.125 mol) in THF (120 mL) in a 3-necked round bottom flask fitted with a

condenser and a dropping funnel, was added a solution of amino-(3,4-difluorophenyl)-acetic acid methyl ester (10.0 g, 0.05 mol) in THF (100 mL) dropwise at 0 °C. The resulting greenish brown suspension was heated at reflux temperature for 2 h. The reaction mixture was cooled to 0 °C and then carefully quenched sequentially with 5 mL of water, 5 mL of 3N NaOH followed by 15 mL of water. The resulting suspension was filtered through a fritted glass funnel. To the filter cake was added 100 mL Et_2O and the suspension was heated at reflux temperature for 20 min. The suspension was filtered and the combined filtrates were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. 2-Amino-2-(3,4-difluorophenyl)-ethanol was obtained as a yellow glassy syrup which was used in the next step without further purification.

[1-(3,4-DIFLUOROPHENYL)-2-HYDROXY-ETHYL]-CARBAMIC ACID-TERT-BUTYL ESTER: Into a solution of 2-amino-2-(3,4-difluorophenyl)-ethanol (8.6 g, 49.7 mmol) in $CHCl_3$ (150 mL) at 0 °C was added a solution of *di*-tert-butyl dicarbonate (11.4 g, 52.0 mmol) in $CHCl_3$ (50 mL) in one portion and the resulting solution was stirred overnight at room temperature. The solvent was removed *in vacuo* and the residue was subjected to column chromatography on silica gel (2:1 hexane-EtOAc followed by EtOAc) to obtain [1-(3,4-difluorophenyl)-2-hydroxy-ethyl]-carbamic acid-tert-butyl ester as a white solid (10.0 g, 74% yield).

(+)-4-(3,4-DIFLUOROPHENYL)-OXAZOLIDIN-2-ONE: Into a well-stirred suspension of NaH (1.1 g, 45.8 mmol) in THF (40 mL) at R.T. was added a solution of [1-(3,5-

difluorophenyl)-2-hydroxy- ethyl]-carbamic acid-tert-butyl ester (5.0 g, 18.3 mmol) in THF (20 mL) via a dropping funnel at room temperature. The resulting suspension was stirred for 3 h and then quenched carefully with 10 mL of water. The biphasic mixture was extracted with 100 mL of Et_2O, washed with brine, filtered and the solvent was removed *in vacuo*. The gummy residue thus obtained was purified by column chromatography over silica gel (R_f = 0.15, 3:2 hexane-EtOAc) to obtain 4-(3,5-difluorophenyl)-oxazolidin-2-one as a white flaky solid (2.8 g, 77% yield). M.P. 81-83 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.23-7.03 (m, 3H), 6.08 (br s, 1H), 4.94 (dd, J=6.6 Hz, J=8.7 Hz, 1 H), 4.73 (t, J=8.7 Hz, 1 H), 4.13 (dd, J=6.6 Hz, J=8.7 Hz, 1 H). The enantiomers were separated by HPLC on a Chiralcel OD (20 x 250 mm) column using 80% hexane/20% isopropyl alcohol as the eluting system at 12.0 mL/min (U.V. 254 nm). The retention times for the two isomers were 16.19 min and 20.08 min respectively.

4-NITROPHENYL (4S)-4-(3,4-DIFLUOROPHENYL)-2-OXO-1,3-OXAZOLIDINE-3-CARBOXYLATE: Into a suspension of NaH (0.14 g, 5.30 mmol) in 20 mL of anhydrous THF under argon, a solution of (+)-4-(3,4-difluorophenyl)-oxazolidin-2-one (0.88 g, 4.42 mmol) in THF was added dropwise (dropping funnel). The resulting suspension was stirred at room temperature for 30 min. This suspension was then added dropwise via cannula into another round bottom flask containing a solution of 4-nitrophenylchloroformate (1.11 g, 5.30 mmol) in 25 mL of THF and cooled at -78 °C over a period of 15 min. The stirring was continued for 2 h after which the solvent was removed and the residue was purified by column

chromatography on silica gel with 1:1 hexane/CH_2Cl_2 followed by CH_2Cl_2 (R_f= 0.4, CH_2Cl_2) to obtain the desired product as a white solid (1.55 g, 86% yield).

Similarly, following the above procedure, 4-(3,5-difluorophenyl)-2-oxo-oxazolidine-3-carboxylic acid-4-nitro-phenyl ester and 4-(3,4,5-trifluorophenyl)-2-oxo-oxazolidine-3-carboxylic acid-4-nitro-phenyl ester were obtained by substituting 3,4-diflourobenzaldehyde in the first step with 3,5-diflourobenzaldehyde or 3,4,5-triflourobenzaldehyde, respectively. The oxazolidinone enantiomers were resolved by HPLC on a Chiralcel OD column (as in the previous example) and the 4-nitrophenyl carbamates were prepared using 4-nitrophenyl chloroformate.

4-NITROPHENYL (4S)-4-(3,5-DIFLUOROPHENYL)-2-OXO-1,3-OXAZOLIDINE-3-CARBOXYLATE: Following the procedure for the synthesis of 4-(3,4-difluorophenyl)-2-oxo-oxazolidine-3-carboxylic acid-4-nitro-phenyl ester, 3,5-diflourobenzaldehyde yielded the desired product.

^1H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, 2H, J= 9.3 Hz), 7.33 - 6.81 (m, 5H), 5.41 (dd, 1H, J=4.1, 8.7 Hz), 4.81 (t, 1H, J=9.3 Hz), 4.33 (dd, 1H, J=4.1, 9.3 Hz); Anal. Calc. for $C_{16}H_{10}F_2N_2O_6$+0.2EtOAc: C, 52.84; H, 3.06; N, 7.34. Found: C, 53.26; H, 2.83; N, 7.73

4-NITROPHENYL (4S)-2-OXO-4-(3,4,5-TRIFLUOROPHENYL)-1,3-OXAZOLIDINE-3-CARBOXYLATE: Following the procedure for the synthesis of 4-(3,4-difluorophenyl)-2-oxo-oxazolidine-3-carboxylic acid-4-nitro-phenyl ester, 3,4,5-triflourobenzaldehyde yielded the desired product.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, 2H, J=9.0 Hz), 7.31 (d, 2H, J=9.0 Hz), 7.11-7.02 (m, 2H), 5.37 (dd, 1H, J=4.1, 9.0 Hz), 4.81 (apparent t, 1H, J=9.0 Hz), 4.33 (dd, 1H, J=4.1, 9.0 Hz); Anal. Calc. for $C_{16}H_9F_3N_2O_5$: C, 50.27; H, 2.37; N, 7.33. Found: C, 50.56; H, 2.50; N, 7.49.

1-(3,4-DIFLUOROPHENYL)-2-METHYL-2-HYDROXYPROPYLAMINE: Into a well-stirred solution of methyl 2-amino-2-(3,4-difluorophenyl)acetate (10.5 g, 52.19 mmol) in anhydrous ether (200 mL) at 0 °C a solution of methylmagnesium bromide (3 M, 87 mL, 261 mmol) in ether was added over 10 minutes. The reaction mixture was stirred at 0 °C for 2.5 h and allowed to warm to room temperature. After 12 h, the reaction mixture was carefully poured onto a mixture of ice (300 g) and saturated aqueous ammonium chloride (50 g). The ether layer was separated and the aqueous layer was extracted with more ether (4 X 200 mL). The combined extracts were dried with magnesium sulfate and the solvent evaporated. The crude product was purified by column chromatography on silica gel using chloroform/methanol/2M ammonia in methanol (1000:20:10, 1000:40:20, 1000:80:40) as the eluent to give the product as an oil (6.5 g, 62% yield) which was used in the next step without further purification.

4-(3,4-DIFLUOROPHENYL)-5,5-DIMETHYL-2-OXO-OXAZOLIDINE: A mixture of 1-(3,4-difluorophenyl)-2-methyl-2-hydroxypropylamine (3.00 g, 14.9 mmol) and carbonyldiimidazole (2.418 g, 14.9 mmol) in dichloromethane (150 mL) was heated at reflux temperature for 36 h and the solvent evaporated. The residue was purified by column chromatography on silica

gel using chloroform/ethyl acetate (9:1) to give the product as a viscous oil which solidified on standing (1.80 g, 50% yield). The product was used in the next step without further characterization.

4-NITROPHENYL 4-(3,4-DIFLUOROPHENYL)-5,5-DIMETHYL-2-OXO-1,3-OXAZOLIDINE-3-CARBOXYLATE: Into a stirred suspension of sodium hydride (60% suspension in paraffin 203 mg, 1.4 eq.) in THF (20 mL) at 0 °C, a solution of 4-(3,4-difluorophenyl)-5,5-dimethyl-2-oxo-oxazolidine (870 mg, 3.622 mmol) in THF (5 mL) was added followed by stirring for 30 minutes. This suspension was added to a solution of 4-nitrophenyl chloroformate (950 mg, 4.71 mmol) in THF (20 mL) at -78 °C under argon and the stirring was continued for 2 h. It was slowly warmed to room temperature and after 4 h the solvent was evaporated. The residue was mixed with dichloromethane (150 mL), washed with 0.05 N sodium hydroxide (3 X 10 mL), and dried (sodium sulfate). The solvent was evaporated and the residue was purified by column chromatography on silica gel using chloroform/ethyl acetate (9:1) as the eluent to give the product as a white powder (860 mg, 59% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, 2H, J=9 Hz), 7.29 - 6.97 (m, 5H), 5.04 (s, 1H), 1.09 (s, 6H); Anal. Calc. for $C_{18}H_{14}F_2N_2O_6$+0.2% H_2O: C, 54.61; H, 3.67; N, 7.08. Found: C, 54.89; H, 3.59; N, 7.41.

(3,4-DIFLOUROPHENYL)-N(DIPHENYLMETHYLENE)METHANAMINE: Into a solution of 3,4-difluorobenzylamine (9.8 g, 69 mmol) and benzophenone (13.0 g, 71.0 mmol) in toluene (200 mL) was added a catalytic amount of $BF_3.OEt_2$ and the resulting solution was heated at reflux temperature for

12 h. The reaction mixture was concentrated in vacuo, yielding an oil (21 g, >95%), which was characterized by NMR analysis and subjected to the following reaction without any further purification. ^{1}H NMR ($CDCl_3$) δ 4.57 (s, 2H), 7.80-6.80 (m, 13H).

1-(3,4-DIFLOUROPHENYL)-1-[(DIPHENYLMETHYLENE)AMINO]PROPAN-2-OL: Into a solution of the benzhydrylindene-(3,4-difluoro-benzyl)-amine (21 g, 69 mmol) in 250 ml of dry THF was added tert-butyllithium (1.7 M, 60 ml) dropwise and the resulting solution was stirred at -78 °C for 0.5 h. To the solution was added acetaldehyde (10 ml, 180 mmol) in 100 ml of THF and the solution was stirred at -78 °C for 2 h and 25 °C for 1 h. The reaction mixture was quenched by addition of brine. The reaction mixture was diluted with 500 ml of Et_2O and washed with brine. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo* to give an oil, which was taken to the next step without any further purification. ^{1}H NMR ($CDCl_3$) δ 1.04 (d, 3H), 2.77 (broad s. 1H), 4.08(m, 1H), 4.15 (d, 1H), 7.80-6.80 (m, 13H).

1-AMINO-1-(3,4-DIFLUORO-PHENYL)-PROPAN-2-OL: A solution of crude product from the previous procedure and $MeONH_2$.HCl (10 g, 120 mmol) was diluted in 200 ml of MeOH and stirred for 12 h. The reaction mixture was concentrated *in vacuo*, yielding an oily residue, which was re-dissolved in 200 ml of EtOAc and washed with brine. The organic layer was concentrated *in vacuo* to produce an oily mixture, which was subjected to column chromatography [5% NH_3 (2.0 M in MeOH) in $CHCl_3$] to yield the desired product (8.8 g, 68% yield from 3,4-

difluorobenzylamine) as a mixture of diastereomers. ^{1}H NMR ($CDCl_3$) (~ 4:1 mixture of the diastereomers) δ 1.02 (d, J=6.0 Hz, 3 H), 1.04 (d, J=6.3 Hz, 3 H), 2.10 (br, 6 H), 3.56-3.69 (m, 2 H), 3.88-3.92 (m, 2 H), 7.02-7.17 (m, 6 H).

[1-(3,4-DIFLUOROPHENYL)-2-HYDROXY-PROPYL]-CARBAMIC ACID-TERT-BUTYL ESTER: Into a solution of 1-amino-1-(3,4-difluorophenyl)-propan-2-ol (13.1 g, 70.1 mmol) in $CHCl_3$ (150 mL) at 0 °C was added a solution of *di*-tert-butyl dicarbonate (19.3 g, 87.6 mmol) in $CHCl_3$ (50 mL) in one portion and the resulting solution was stirred overnight at room temperature. The solvent was removed *in vacuo* and the residue was subjected to column chromatography on silica gel (2:1 hexane-EtOAc followed by EtOAc) to obtain [1-(3,4-difluorophenyl)-2-hydroxy-propyl]-carbamic acid-tert-butyl ester as a viscous oil (18.4 g, 91% yield). ^{1}H NMR ($CDCl_3$) (~ 4:1 mixture of the diastereomers) δ 1.05 (d, J=6.6 Hz, 3 H), 1.25 (d, J=6.0 Hz, 3 H), 1.41 (br, 20 H), 3.92-4.19 (br, 2 H), 4.45-4.60 (m, 2 H), 5.41-5.49 (br, 2 H), 7.02-7.17 (m, 6 H).

4-(3,4-DIFLUOROPHENYL)-5-METHYL-OXAZOLIDIN-2-ONE: Into a well-stirred solution of [1-(3,4-difluorophenyl)-2-hydroxy-propyl]-carbamic acid-tert-butyl ester (0.43 g, 1.5 mmol) in THF (20 mL) was added 95% NaH (0.09 g, 3.8 mmol) at room temperature. When the reaction was carried out on a larger (> 5 g) scale, 1.0 equivalent of KH and 1.5 eq. of NaH was used as the base. The resulting suspension was stirred for 3 h at about 35 °C (warm water bath) and then quenched carefully with ice. The biphasic mixture was extracted with 100 mL of EtOAc, washed with brine, dried over Na_2SO_4, filtered and the

solvent was removed *in vacuo*. The two diastereomers were separated by column chromatography over silica gel (First isomer: 0.16 g, R_f = 0.6, 3:1 hexane-EtOAc; second isomer: 0.18 g, R_f = 0.5, 3:1 hexane-EtOAc). NOE experiments suggested that the first diastereomer had the methyl and the aryl group in trans configuration while the second diastereomer had cis relationship between the two groups. The ^{1}H NMR spectrum for the *trans* diastereomer is as follows. ^{1}H NMR ($CDCl_3$) δ 1.49 (d, J = 6.0 Hz, 3H), 4.37 (dq, J = 6.0 Hz, J = 7.2 Hz, 1H), 4.45 (d, J = 7.2 Hz, 1H), 6.63 (br s, 1H), 7.08-7.28 (m, 3H).

The ^{1}H NMR spectrum for the *cis* diastereomer is as follows. ^{1}H NMR ($CDCl_3$) δ 0.96 (d, J = 6.6 Hz, 3H), 4.91 (d, J = 8.1 Hz, 1H), 4.99 (dq, J = 6.6 Hz, J = 8.1 Hz, 1H), 6.63 (br s, 1H), 7.08-7.28 (m, 3H).

4-(3,4-DIFLUOROPHENYL)-5-METHYL-2-OXO-OXAZOLIDINE-3-CARBOXYLIC ACID-4-NITRO-PHENYL ESTER : Into a solution of one of the two diastereomers of 4-(3,4-difluorophenyl)-5-methyl-oxazolidin-2-one (0.97 g, 4.55 mmol) in 60 mL THF was added a solution of n-butyllithium in hexane (3.06 mmol, 4.9 mmol) dropwise via a syringe under argon atmosphere at -78 °C. The resulting yellow solution was stirred at -78 °C for 40 min. This solution was then added dropwise via a cannula into another round bottom flask containing a solution of 4-nitrophenylchloroformate (1.03 g, 5.1 mmol) in 60 mL of THF, cooled at -78 °C, over a period of 15 min. After five minutes, the flask was removed from the cooling bath and stirring was continued for 1 h. The reaction mixture was quenched by adding ice and it was

extracted with EtOAc. The organic extracts were washed with brine and the organic layer was dried over Na_2SO_4. The solvent was removed after filtration and the residue was purified by column chromatography on silica gel with 1:1 hexane/CH_2Cl_2 followed by CH_2Cl_2 to give the desired product.

The relative configurations of the cis and trans isomers were assigned on the basis of ^1H NMR analysis of the respective p-nitrophenyloxycarbonyl derivatives. For the trans isomer, an NOE was observed between the protons of the C-5 methyl group and the proton at C-4. No NOE was observed between the protons at the C-4 and C-5 positions of this isomer, which was thus assigned *trans* stereochemistry. For the cis isomer, no NOE was observed between the protons of the C-5 methyl group and the proton at C-4. However, a NOE was observed between the protons at the C-4 and C-5 positions, leading us to assign this isomer *cis* stereochemistry. The vicinal coupling constants of the C-4 protons of cis (J = 7.8 Hz) and trans (J = 5.1 Hz) are also consistent with the values reported for similar oxazolidinones, and were thus helpful in making the stereochemical assignments (Dondoni, A.; Perrone, D.; Semola, T. *Synthesis 1995*, 181).

Enantiomers of the diastereomers were separated by HPLC by using a Chiralcel OD column (20 x 250 mm) with 80% hexane/20% isopropyl alcohol/ 0.1 % diethylamine as the eluting system (12 mL/min) under isocratic conditions (U.V. 254 nm).

In order to assign the absolute configurations at the

stereogenic centers of the oxazolidinone rings, a new synthetic route was designed which employed an enantiomerically pure substrate derived from the chiral pool. Commercially available (*S*)-(+)-methyl lactate was converted into its pyrrolidine amide according to the method of *Martin et al* (Martin, R.; Pascual, O.; Romea, P.; Rovira, R.; Urpi, F.; Vilarrasa, J. *Tetrahedron Lett. 1997, 38,* 1633). Following the protection of the hydroxy group of (2*S*)-1-oxo-1-(1-pyrrolidinyl)-2-propanol to a TBDMS group, treatment of tert-butyl(dimethyl)silyl (1*S*)-1-methyl-2-oxo-2-(1-pyrrolidinyl)ethyl ether with 3,4-difluorophenyllithium yielded (2*S*)-2-{[tert-butyl(dimethyl)silyl]oxy}-1-(3,4-difluorophenyl)-1-propanone as the sole product, which was then converted to (2*S*)-2-{[tert-butyl(dimethyl)silyl]oxy}-1-(3,4-difluorophenyl)-1-propanone oxime. Reduction of the (2*S*)-2-{[tert-butyl(dimethyl)silyl]oxy}-1-(3,4-difluorophenyl)-1-propanone oxime with $LiAlH_4$, N-acylation, and base induced cyclization provided oxazolidinone diastereomers, which were separated by flash column chromatography. The enantiomeric purity of these isomers was confirmed by chiral HPLC analysis and their relative configurations were assigned by comparison of their ^1H NMR spectra with those of the racemic isomers. As the absolute configuration at C-5 of the lactic acid derived oxazolidinone described above is (*S*), the C-4 center in *trans* compounds also has the (*S*) configuration. Accordingly, the absolute configurations for the stereogenic centers in the *cis* compounds are assigned accordingly (4*R*,5*S*).

4-NITROPHENYL (4S,5R)-4-(3,4-DIFLUOROPHENYL)-5-METHYL-2-OXO-1,3-OXAZOLIDINE-3-CARBOXYLATE: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, 2H, J=8.8 Hz), 7.30 - 6.99 (m, 5H), 5.35 (d, 1H, J=7.7 Hz), 5.07 (apparent quintet, 1H), 1.17 (d, 3H, J=6.5 Hz); Anal. Calc. for $C_{17}H_{12}F_2N_2O_6+0.5H_2O$: C, 52.72; H, 3.38; N, 7.23. Found: C, 53.09; H, 3.19; N, 7.50.

(+)-2-AMINO-3-(3,4-DIFLUORO)-PHENYL-PROPAN-1-OL: (+)-3,4-difluorophenyl alanine (1.0 g, 5.0 mmol) was added in small portions to a stirring suspension of $LiAlH_4$ (0.480 g, 12.5 mmol) in THF (30 mL) at 0 °C. The resulting gray suspension was then heated at reflux for 2 h. The reaction mixture was cooled to 0 °C and then carefully quenched sequentially with water (0.5 mL), 3 N NaOH (0.5 mL), and water (1.50 mL). The resulting suspension was filtered through a fritted glass funnel. Ether (50 mL) was added to the filter cake and the suspension was heated at reflux temperature for 20 min. The suspension was filtered and was combined with the previous filtrate. The combined organics were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. 2-Amino-3-(3,4-difluoro)-phenyl-propan-1-ol was obtained as a white solid (0.500 g, 100%) which was used in the next step without further purification.

(+)-[1-(3,4-DIFLUOROBENZYL)-2-HYDROXY-ETHYL]-CARBAMIC ACID-TERT-BUTYL ESTER: A solution of di-tert-butyl dicarbonate (0.640 g, 2.90 mmol) in $CHCl_3$ (10 mL) was added in one portion to a solution of (+)-2-amino-3-(3,4-difluoro)-phenyl-propan-1-ol (0.500 g, 2.62 mmol) in $CHCl_3$ (20 mL) at 0 °C and the resulting solution was stirred overnight at room temperature. The solvent was

removed *in vacuo* and the residue was chromatographed (2:1 hexane-EtOAc, followed by EtOAc), giving (+)-[1-(3,4-difluorobenzyl)-2-hydroxy-ethyl]-carbamic acid-tert-butyl ester as a white solid (0.640 g, 99%).

(+)-4-(3,4-DIFLUORO-BENZYL)-OXAZOLIDIN-2-ONE: A solution of (+)-[1-(3,4-difluorobenzyl)-2-hydroxy-ethyl]-carbamic acid-tert-butyl ester (1.00 g, 4.00 mmol) in THF (10 mL) was added *via* a dropping funnel to a stirring suspension of 95% NaH (0.12 g, 5.0 mmol) in THF (20 mL) at room temperature. The resulting suspension was stirred for 3 h and then quenched carefully with water (10 mL). The biphasic mixture was extracted with Et_2O (50 mL), washed with brine, filtered and the solvent was removed *in vacuo*. The resulting gummy residue was purified by column chromatography (R_f = 0.25, 3:2 hexane-EtOAc), to give the desired product as a white solid (0.320 g, 76%).

(+)-4-(3,4-DIFLUORO-BENZYL)-OXAZOLIDIN-2-ONE-3-CARBOXYLIC ACID-4-NITRO-PHENYL ESTER: A solution of (+)-4-(3,4-difluoro-benzyl)-oxazolidin-2-one (0.210 g, 1.0 mmol) in THF (10 mL) was added dropwise *via* a dropping funnel to a stirring suspension of NaH (30.0 mg, 1.30 mmol) in anhydrous THF (10 mL) under argon. The resulting suspension was stirred at room temperature for 30 min. This suspension was then added dropwise *via* cannula to a solution of 4-nitrophenylchloroformate (0.300 g, 1.50 mmol) in THF (20 mL) at -78 °C over 15 min. Stirring was continued for 2 h after which the solvent was removed and the residue was purified by column chromatography (1:1 hexane/CH_2Cl_2, followed by

CH_2Cl_2; R_f= 0.4, CH_2Cl_2), to give the desired product as a yellow solid (0.350 g, 82%).

Similarly, following the above procedure, 4-nitrophenyl 4-(4-fluorobenzyl)-2-oxo-1,3-oxazolidine-3-carboxylate was obtained by substituting (+)-3,4-diflourophenyl alanine with *p*-fluorophenyl alanine:

4-NITROPHENYL 4-(4-FLUOROBENZYL)-2-OXO-1,3-OXAZOLIDINE-3-CARBOXYLATE: ^1H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, 2H, J=9.3 Hz), 7.42 (d, 2H, J=8.9 Hz), 7.24-6.99 (m, 4H), 4.69 - 4.59 (m, 1H), 4.35 (t, 1H, J=8.6 Hz), 4.23 (dd, 1H, J=2.7, 9.3 Hz), 3.37 (dd, 1H, J=3.8, 13.6 Hz), 2.94 (dd, 1H, J=9.3, 13.6 Hz); Anal. Calc. for $C_{17}H_{13}FN_2O_6$: C, 56.67; H, 3.64; N, 7.77. Found: C, 56.94; H, 3.76; N, 7.71.

2-[6-(4-PHENYL-1-PIPERIDINYL)HEXYL]-1H-ISOINDOLE-1,3(2H)-DIONE: To the 500 ml RB-flask was added 4-phenylpiperidine hydrochloride (5 g, 25 mmol), N-(6-bromohexyl)phthalimide (15.5 g, 50 mmol), N,N-diisopropylethylamine (21.8 ml, 125 mmol), tetrabutylammonium iodide (0.2 g), and dioxane (250 ml) at room temperature. The reaction mixture was stirred at 100 °C for 72 h. The solvent was removed *in vacuo* and the crude product was purified by flash chromatography (98:2 = Chloroform : 2N ammonia in methanol) to afford 7.67 g of the desired product (77% yield): ^1H NMR (400 MHz, $CDCl_3$) δ 7.78-7.79 (m, 2H), 7.74-7.65 (m, 2H), 7.32-7.14 (m, 5H), 3.69 (t, 2H, J=7.35 Hz), 3.06 (d, 2H, J=11.0 Hz), 2.49 (quintet, 1H, J=7.6 Hz), 2.36 (t, 2H, J=7.6 Hz), 2.02 (t, 2H, J=12.5 Hz), 1.82 (br s, 4H), 1.69 (t, 2H, J=6.3 Hz), 1.54 (br s, 2H), 1.37 (br s,

4H); ESMS m/e: 391.3 (M + H)$^+$; Anal. Calc. for $C_{25}H_{30}N_2O_2$+0.2H_2O: C, 76.19; H, 7.77; N, 7.11. Found: C, 76.14; H, 7.38; N, 7.13.

METHOD I. General procedure for the Preparation of the substituted 4-[4-(3-aminophenyl)-1-piperidinyl]-1-(phenyl)-1-butanones: A mixture of 4-(3-aminophenyl)piperidine (2.0 mmol), 2.4 mmol of the appropriate substituted phenyl butyryl chloride (e.g. 4-chloro-4'-phenoxybutyrophenone, 4-chloro-3',4'-dimethylbutyrophenone, 4-chloro-4'-chlorobutyrophenone, γ-chlorobutyrophenone, 4-chloro-3',4'-dimethoxybutyrophenone), 3.0 mmol of K_2CO_3, and 10 mg of 18-crown-6 in 5 mL of toluene were heated at 110 °C for 2.5 days. The reaction mixture was concentrated and chromatographed on silica (5% methanol in dichloromethane) to give the desired compound:

4-[4-(3-AMINOPHENYL)-1-PIPERIDINYL]-1-(4-PHENOXYPHENYL)-1-BUTANONE: Using Method I, the desired product was obtained. 305 mg; ESMS m/e : 415.4 (M + H)$^+$.

4-[4-(3-AMINOPHENYL)-1-PIPERIDINYL]-1-(3,4-DIMETHYLPHENYL)-1-BUTANONE: Using Method I, the desired product was obtained. 320 mg; ESMS m/e : 351.3 (M + H)$^+$.

4-[4-(3-AMINOPHENYL)-1-PIPERIDINYL]-1-(4-CHLOROPHENYL)-1-BUTANONE: Using Method I, the desired product was obtained. 500 mg; Anal. Calc for $C_{21}H_{25}ClN_2O$+0.3H_2O: C, 69.62; H, 7.12; N, 7.73. Found: C, 69.63; H, 7.34; N, 7.60; ESMS m/e : 357.3 (M + H)$^+$.

4-[4-(3-AMINOPHENYL)-1-PIPERIDINYL]-1-PHENYL-1-BUTANONE: Using Method I, the desired product was obtained. 250 mg; Anal. Calc for $C_{21}H_{26}N_2O+0.2H_2O$: C, 77.36; H, 8.16; N, 8.59. Found: C, 77.55; H, 8.12; N, 8.75; ESMS m/e : 323.3 $(M + H)^+$.

4-[4-(3-AMINOPHENYL)-1-PIPERIDINYL]-1-(2,4-DIMETHOXYPHENYL)-1-BUTANONE: Using Method I, the desired product was obtained. 330 mg; Anal. Calc for $C_{23}H_{30}N_2O_3+0.5H_2O$: C, 70.56; H, 7.98; N, 7.16. Found: C, 70.69; H, 7.87; N, 6.99; ESMS m/e : 383.3 $(M + H)^+$.

METHOD II. General Procedure for the Acylation or Sulfonylation of the Substituted 4-[4-(3-Aminophenyl)-1-piperidinyl]-1-(4-phenyl)-1-butanones: A mixture of 1 equivalent of a substituted 4-[4-(3-aminophenyl)-1-piperidinyl]-1-(4-phenyl)-1-butanone, 1.5 equivalent of an acid chloride or a sulfonyl chloride, and 5 equivalents of diisopropylethylamine, in dichloromethane was stirred at room temperature for two days. The reaction mixture was applied to a preparative TLC plate and eluted with dichloromethane: methanol (15:1, containing 1% isopropyl amine) to give the desired product.

METHOD III. General procedure for the Preparation of the substituted 4-N-(3-{1-[4-(phenyl)-4-oxobutyl]-4-piperidinyl}phenyl)acetamides: A mixture of N-[3-(4-piperidinyl)phenyl]acetamide (1.0 eq) and an aryl substituted chlorobutyrophenone (2.0 eq), K_2CO_3 (5.0 eq), diisopropylethylamine (3.0 eq) and tetrabutylammonium iodide (cat. 5-10%) in dioxane (0.5 to 1.0 M) were heated at reflux temperature for 16 h. The reaction

mixture was filtered and concentrated *in vacuo*. The crude product was chromatographed using silica preparative TLC (chloroform : methanol containing 0.5% isopropyl amine) to give the desired product.

Example 1

N-(3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)ACETAMIDE: Using Method III, the desired product was obtained. ^{1}H NMR ($CDCl_3$) δ 7.75 (s, 1H), 7.71 (d, 1H, J=7.6 Hz), 7.45 (d, 2H, J=7.2 Hz), 7.35 (s, 1H), 7.26-7.22 (m, 2H), 6.93 (d, 1H, J=7.6 Hz), 3.24-3.21 (m, 2H), 3.04 (t, 2H, J=7.0 Hz), 2.67-2.63 (m, 2H), 2.59-2.48 (m, 1H), 2.32 (s, 6H), 2.30-2.27 (m, 2H), 2.18 (s, 3H), 2.14-2.06 (m, 2H), 2.00-1.80 (m, 4H); ESMS m/e : 393.3 $(M + H)^+$.

Example 2

N-(3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of 0.0500 g (0.200 mmol) of 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide, 0.100 g (0.480 mmol) of 4-chloro-3',4'-dimethylbutyrophenone, 0.080 g (0.600 mmol) of K_2CO_3 and 0.090 g (0.600 mmol) of NaI in 5 mL of DMF was heated at reflux temperature for 18 hours. The reaction mixture was filtered, the filtrate was poured into 5 mL of water and washed with 3 X 5 mL of ethyl acetate. The combined organic extracts were dried ($MgSO_4$), concentrated in vacuo and purified by preparative TLC (silica; 9.5 : 0.5, dichloromethane : methanol + 1% isopropyl amine) to afford 0.067 g (80.0% yield) of the desired product: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, 1H, J=8.0 Hz), 7.44 (s, 1H), 7.38 (d, 1H, J=8.0 Hz), 7.23-7.20 (m, 2H), 7.16 (s, 1H), 6.95 (d, 1H, J=6.8

Hz), 3.13-3.11 (m, 2H), 3.02 (t, 2H, J=7.0 Hz), 2.56-2.40 (m, 4H), 2.32 (s, 6H), 2.17-2.15 (m, 2H), 2.04-1.78 (m, 6H), 1.25 (d, 6H, J=6.8 Hz); ESMS m/e : 421.3 $(M + H)^+$.

Example 3

N-(3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)CYCLOHEXANECARBOXAMIDE: Using Method II, the desired compound was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ 7.80-6.81 (m, 7H), 3.41-3.00 (m, 4H), 2.95-2.41 (m, 4H), 2.32 (s, 6H), 2.22-1.05 (m, 18H); ESMS m/e : 461.4 $(M + H)^+$.

Example 4

N-(3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-PHENYLACETAMIDE: Using Method II, the desired product was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ 7.85-7.65 (m, 2H), 7.45-6.92 (m, 10H), 3.76 (s, 2H), 3.10-2.90 (m, 4H), 2.50-2.35 (m, 3H), 2.32 (s, 6H), 2.10-1.85 (m, 4H), 1.80-1.60 (m, 4H); ESMS m/e : 469.4 $(M + H)^+$.

Example 5

N-(3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-(3-METHOXYPHENYL)ACETAMIDE: Using Method II, the desired product was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ 7.76-7.65 (m, 2H), 7.38-7.12 (m, 6H), 6.95-6.80 (m, 3H), 3.82 (s, 3H), 3.70 (s, 2H), 3.10-2.90 (m, 4H), 2.50-2.38 (m, 3H), 2.32 (s, 6H), 2.10-1.85 (m, 4H), 1.80 -1.60 (m, 4H); ESMS m/e : 499.4 $(M + H)^+$.

Example 6

N-(3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-METHOXYACETAMIDE: Using Method II, the desired product was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80-7.75 (m, 2H), 7.50-7.38 (m, 2H), 7.34-6.90 (m, 3H), 4.00 (s, 2H), 3.51 (s, 3H), 3.30-2.95 (m, 4H), 2.70-2.50 (m, 3H), 2.32 (s, 6H), 2.15 -1.80 (m, 8H); ESMS m/e : 423.3 $(M + H)^+$.

Example 7

N-(3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)METHANESULFONAMIDE: Using Method II, the desired product was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82-7.10 (m, 7H), 3.41 (s, 3H), 3.40-2.85 (m, 4H), 2.82-2.35 (m, 5H), 2.32 (s, 6H), 2.22-1.80 (m, 6H); ESMS m/e : 429.3 $(M + H)^+$.

Example 8

N-(3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)ETHANESULFONAMIDE: Using Method II, the desired product was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.71 (d, 1H, J=7.6 Hz), 7.30-7.09 (m, 4H), 7.02 (d, 1H, J=7.2 Hz), 3.36-3.05 (m, 6H), 2.77-2.52 (m, 3H), 2.32 (s, 6H), 2.15-1.82 (m, 8H), 1.37 (t, 3H, J=7.4 Hz); ESMS m/e : 443.3 $(M + H)^+$

Example 9

N-(3-{1-[4-(4-CHLOROPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)ACETAMIDE: Using Method III, the desired product was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, 2H, J=8.8 Hz), 7.55-7.40 (m, 3H), 7.35 (s, 1H), 7.22 (t, 1H, J=8.0 Hz), 6.92 (d, 1H, J=8.0 Hz), 3.30-3.27 (m, 2H), 3.09 (t, 2H, J=7.0 Hz), 2.76-2.39 (m, 5H),

2.20 (s, 3H), 2.17-1.85 (m, 6H); ESMS m/e : 399.3 $(M + H)^+$.

Example 10

N-(3-{1-[4-(4-CHLOROPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Using Method II, the desired product was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, 2H, J=8.6 Hz), 7.45 (d, 2H, J=8.6 Hz), 7.39 (d, 1H, J=7.2 Hz), 7.32 (s, 1H), 7.24 (t, 1H, J=7.8 Hz), 6.94 (d, 1H, J=8.4 Hz), 3.21-3.18 (m, 2H), 3.05 (t, 2H, J=7.0 Hz), 2.64-2.51 (m, 4H), 2.28-1.86 (m, 8H), 1.26 (d, 6H, J=6.8 Hz); ESMS m/e : 427.3 $(M + H)^+$.

Example 11

N-(3-{1-[4-(4-CHLOROPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)CYCLOHEXANECARBOXAMIDE: Using Method II, the desired product was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, 2H, J=8.4 Hz), 7.55-7.19 (m, 5H), 6.93 (d, 1H, J=7.6 Hz), 3.25-3.00 (m, 4H), 2.65-2.45 (m, 4H), 2.30-1.50 (m, 18H); ESMS m/e : 467.3 $(M + H)^+$.

Example 12

N-(3-{1-[4-(4-CHLOROPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-PHENYLACETAMIDE: Using Method II, the desired product was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, 2H, J=8.4 Hz), 7.46-7.26 (m, 9H), 7.20 (t, 1H, J=7.6 Hz), 6.92 (d, 1H, J=7.6 Hz), 3.75 (s, 2H), 3.15-3.13 (m, 2H), 3.03 (t, 2H, J=7.0 Hz), 2.64-2.46 (m, 3H), 2.22-1.60 (m, 8H); ESMS m/e : 475.3 $(M + H)^+$.

Example 13

N-(3-{1-[4-(4-CHLOROPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-(3-METHOXYPHENYL)ACETAMIDE: Using

Method II, the desired product was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, 2H, J=8.4 Hz), 7.44 (d, 2H, J=8.4 Hz) 7.38 (s, 1H), 7.35-7.25 (m, 3H), 7.19 (t, 1H, J=7.8 Hz), 6.94-6.86 (m, 3H), 3.81 (s, 3H), 3.72 (s, 2H), 3.12-3.09 (m, 2H), 3.02 (t, 2H, J=6.8 Hz), 2.57-2.44 (m, 3H), 2.20-1.60 (m, 8H); ESMS m/e : 505.3 $(M + H)^+$.

Example 14

N-(3-{1-[4-(4-CHLOROPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-METHOXYACETAMIDE: Using Method II, the desired product was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, 2H, J=8.4 Hz), 7.50-7.25 (m, 5H), 6.98 (d, 1H, J=7.8 Hz), 4.01 (s, 2H), 3.57 (s, 3H), 3.30-3.15 (m, 2H), 3.06 (t, 2H, J=6.8 Hz), 2.70-2.50 (m, 3H), 2.35-1.80 (m, 8H); ESMS m/e : 429.3 $(M + H)^+$.

Example 15

N-(3-{1-[4-(4-CHLOROPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)METHANESULFONAMIDE: Using Method II, the desired product was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-6.96 (m, 8H), 3.48 (s, 3H), 3.28-2.90 (m, 6H), 2.80-2.57 (m, 3H), 2.38-1.86 (m, 6H); ESMS m/e : 435.2 $(M + H)^+$.

Example 16

N-(3-{1-[4-(4-CHLOROPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)ETHANESULFONAMIDE: Using Method II, the desired product was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, 2H, J=8.2 Hz), 7.45 (d, 2H, J=8.2 Hz), 7.30-7.08 (m, 3H), 6.99 (d, 1H, J=7.6 Hz), 3.26-3.02 (m, 6H), 2.69-2.45 (m, 3H), 2.32-1.75 (m, 8H), 1.36 (t, 3H, J=7.4 Hz); ESMS m/e : 449.3 $(M + H)^+$.

Example 17

N-{3-[1-(4-OXO-4-PHENYLBUTYL)-4-PIPERIDINYL]PHENYL}ACETAMIDE: Using Method III, the desired product was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10-6.80 (m, 9H), 3.40-2.95 (m, 4H), 2.85-2.20 (m, 3H), 2.19 (s, 3H), 2.15-1.70 (m, 8H); ESMS m/e : 365.3 $(M + H)^+$.

Example 18

2-METHYL-N-{3-[1-(4-OXO-4-PHENYLBUTYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Using Method II, the desired product was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, 2H, J=7.4 Hz), 7.57 (t, 1H, J=7.4 Hz), 7.48 (t, 2H, J=7.4 Hz), 7.45-7.20 (m, 2H), 7.24 (t, 1H, J=8.0 Hz), 6.94 (d, 1H, 8.0 Hz), 3.24-3.21 (m, 2H), 3.09 (t, 2H, J=7.0 Hz), 2.57-2.25 (m, 4H), 2.31-1.84 (m, 8H), 1.26 (d, 6H, J=7.2 Hz); ESMS m/e : 393.3 $(M + H)^+$.

Example 19

N-{3-[1-(4-OXO-4-PHENYLBUTYL)-4-PIPERIDINYL]PHENYL}-2-PHENYLACETAMIDE: Using Method II, the desired product was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, 2H, J=7.6 Hz), 7.65-7.15 (m, 11H), 6.92 (d, 2H, J=7.2 Hz), 3.74 (s, 2H), 3.20-2.95 (m, 4H), 2.65-2.40 (m, 3H), 2.25-1.70 (m, 8H); ESMS m/e : 441.3 $(M + H)^+$.

Example 20

2-(3-METHOXYPHENYL)-N-{3-[1-(4-OXO-4-PHENYLBUTYL)-4-PIPERIDINYL]PHENYL}ACETAMIDE: Using Method II, the desired product was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, 2H, J=7.6 Hz), 7.56 (t, 1H, J=7.62 Hz), 7.46 (t, 2H, J=7.6 Hz), 7.40 (s, 1H), 7.37-7.26 (m, 2H), 7.19

(t, 1H, J=7.8 Hz), 6.94-6.86 (m, 3H), 3.81 (s, 3H), 3.71 (s, 3H), 3.12-3.03 (m, 4H), 2.57-2.44 (m, 3H), 2.16-1.77 (m, 8H); ESMS m/e : 471.3 $(M + H)^+$.

Example 21

N-(3-{1-[4-(2,4-DIMETHOXYPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)ACETAMIDE: Using Method III, the desired product was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, 1H, J=8.8 Hz), 7.54 (d, 1H, J=7.6 Hz), 7.33 (s, 1H), 7.22 (t, 1H, J=7.6 Hz), 6.93 (d, 1H, J=7.6 Hz), 6.53 (d, 1H, J=8.8 Hz), 6.46 (s, 1H), 3.90 (s, 3H), 3.86 (s, 3H), 3.48-3.27 (m, 2H), 3.05 (t, 2H, J=6.8 Hz), 2.90-2.68 (m, 2H), 2.65-2.38 (m, 3H), 2.25 (s, 3H), 2.18-1.80 (m, 6H); ESMS m/e : 425.3 $(M + H)^+$.

Example 22

N-(3-{1-[4-(2,4-DIMETHOXYPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Using Method II, the desired product was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, 1H, J=8.6 Hz), 7.41-7.37 (m, 2H), 7.24 (t, 1H, J=7.8 Hz), 6.96 (d, 1H, J=7.8 Hz), 6.54 (d, 1H, J=8.6 Hz), 6.46 (s, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.11-3.08 (m, 2H), 2.98 (t, 2H, J=7.2 Hz), 2.53-2.46 (m, 4H), 2.13-1.79 (m, 8H), 1.25 (d, 6H, J=6.8 Hz); ESMS m/e : 453.3 $(M + H)^+$.

Example 23

N-(3-{1-[4-(2,4-DIMETHOXYPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-PHENYLACETAMIDE: Using Method II, the desired product was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (m, 12H), 3.89 (s, 3H), 3.86 (s, 3H), 3.74 (s, 2H), 3.22-2.90 (m, 4H), 2.64-2.40 (m, 3H), 2.25-1.70 (m, 8H); ESMS m/e : 501.3 $(M + H)^+$.

Example 24

N-(3-{1-[4-(2,4-DIMETHOXYPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-(3-METHOXYPHENYL)ACETAMIDE: Using Method II, the desired product was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, 1H, J=8.8 Hz), 7.48-7.15 (m, 5H), 6.95-6.80 (m, 3H), 6.58-6.45 (m, 2H), 3.89 (s, 3H), 3.86 (s, 3H), 3.81 (s, 3H), 3.72 (s, 2H), 3.25-2.95 (m, 4H), 2.65-2.40 (m, 3H), 2.30-1.95 (m, 4H), 1.93-1.72 (m, 4H); ESMS m/e : 531.3 $(M + H)^+$.

Example 25

N-(3-{1-[4-OXO-4-(4-PHENOXYPHENYL)BUTYL]-4-PIPERIDINYL}PHENYL)ACETAMIDE: Using Method III, the desired product was obtained.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15-6.75 (m, 13H), 3.30-2.80 (m, 4H), 2.75-2.10 (m, 5H), 2.03 (s, 3H), 2.00-1.60 (m, 6H); ESMS m/e : 457.3 $(M + H)^+$.

Example 26

2-METHYL-N-(3-{1-[4-OXO-4-(4-PHENOXYPHENYL)BUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Using Method II, the desired product was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, 2H, J=8.8 Hz), 7.43-7.15 (m, 6H), 7.10-6.93 (m, 5H), 3.42-2.95 (m, 4H), 2.80-2.45 (m, 4H), 2.20-1.80 (m, 8H), 1.14 (d, 6H, J=6.8 Hz); ESMS m/e : 485.4 $(M + H)^+$.

Example 27

2-(3-METHOXYPHENYL)-N-(3-{1-[4-OXO-4-(4-PHENOXYPHENYL)BUTYL]-4-PIPERIDINYL}PHENYL)ACETAMIDE: Using Method II, the desired product was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, 2H, J=8.8 Hz), 7.41-7.18 (m, 7H), 7.08-6.99 (m, 5H), 6.94-6.87 (m, 3H), 3.82 (s, 3H), 3.70 (s, 2H), 3.10-2.95 (m, 4H), 2.55-2.40 (m, 3H),

2.15-1.95 (m, 4H), 1.81- 1.70 (m, 4H); ESMS m/e : 563.4 $(M + H)^+$.

Example 28

N'-(3-{1-[4-(4-CHLOROPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-N,N-DIMETHYLSULFAMIDE: Using Method II, the desired product was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, 2H, J=8.8 Hz), 7.44 (d, 2H, J=8.8 Hz), 7.27 (s, 1H), 7.25-7.10 (m, 2H), 6.94 (d, 1H, J=7.6 Hz), 3.30-3.10 (m, 2H), 3.04 (t, 2H, J=6.8 Hz), 2.83 (s, 6H), 2.68-2.45 (m, 3H), 2.30-1.75 (m, 8H); ESMS m/e : 464.3 $(M + H)^+$.

Example 29

N-(3-{1-[4-OXO-4-(2-THIENYL)BUTYL]-4-PIPERIDINYL}PHENYL)ACETAMIDE: Using Method III, the desired product was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ 7.90-6.78 (m, 7H), 3.22-2.88 (m, 4H), 2.69-2.25 (m, 5H), 2.02 (s, 3H), 2.00-1.64 (m, 6H); ESMS m/e : 371.2 $(M + H)^+$.

Example 30

N-(3-{1-[4-(4-ISOPROPYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)ACETAMIDE: Using Method III, the desired product was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ 8.00-6.78 (m, 8H), 3.15-2.98 (m, 4H), 2.77-2.15 (m, 4H), 2.03 (s, 3H), 2.00-1.62 (m, 8H), 0.927 (d, 6H, J=6.0 Hz); ESMS m/e : 407.3 $(M + H)^+$.

Example 31

N-(3-{1-[4-(4-METHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)ACETAMIDE: Using Method III, the desired product was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ

7.90-6.80 (m, 8H), 3.10- 2.45 (m, 7H), 2.32 (S, 3H), 2.02 (s, 3H), 2.01-1.68 (m, 8H); ESMS m/e : 379.3 $(M + H)^+$.

Example 32

N-(3-{1-[4-(4-BROMOPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)ACETAMIDE: Using Method III, the desired product was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ 7.90-6.80 (m, 8H), 3.30-3.05 (m, 4H), 2.70-2.45 (m, 3H), 2.05 (s, 3H), 1.98-1.65 (m, 8H); ESMS m/e : 444.0 $(M + H)^+$.

EXAMPLE 33

N-(3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-PROPANESULFONAMIDE: Using Method II, the desired product was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.71 (d, 1H, J=7.6 Hz), 7.27-7.00 (m, 5H), 3.32-3.24 (m, 3H), 3.10-3.02 (m, 2H), 2.78-2.50 (m, 3H), 2.32 (s, 6H), 2.19-1.84 (m, 8H), 1.39 (d, 6H, J=6.8 Hz); ESMS m/e : 458.4 $(M + H)^+$.

Example 34

N-(3-{1-[4-OXO-4-(4-PHENOXYPHENYL)BUTYL]-4-PIPERIDINYL}PHENYL)-2-PROPANESULFONAMIDE: Using Method II, the desired product was obtained. ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, 2H, J=7.6 Hz), 7.44 (t, 2H, J=7.6 Hz), 7.27-7.00 (m, 9H), 3.35-2.96 (m, 5H), 2.69-2.45 (m, 3H), 2.14-1.79 (m, 8H), 1.39 (d, 6H, J=6.8 Hz); ESMS m/e : 521.4 $(M + H)^+$.

Example 35

N-(3-{1-[3-(4-CHLOROPHENYL)-3-METHOXYPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of 3-

methoxy-3-(p-chlorophenyl)-1-chloropropane (27.4 mg, 0.125 mmol), 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide (28.3 mg, 0.125 mmol), diisopropylethylamine (0.50 mL) and catalytic amount of tetrabutylammonium iodide in dioxane (2.0 mL) was stirred at 90 °C for 72 hrs. The reaction mixture was concentrated to a small volume and chromatographed using preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave N-(3-{1-[3-(4-chlorophenyl)-3-methoxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (39.5 mg, 73.8% yield) as a thick oil: ^1H NMR δ 7.48 (S, 1 H), 7.34-7.3 (m, 2H), 7.25 (m, 4H), 6.96 (d, 1H, J=7.4 Hz), 4.20 (apparent dd, 1H, J=5.9, 7.6 Hz), 3.2 (s, 3H), 3.04 (d, 1H, J=10.1 Hz), 2.99 (d, 1H, J=10.1 Hz), 2.49 (h, 4H, J=6.6 Hz), 2.20-2.10 (m, 4H), 1.82 (m, 4H), 1.25 (d, 6H, J=7.1 Hz); ESMS *m/e*: 429.4 $(M + H)^+$.

Example 36

N-(3-{1-[6-(1,3-DIOXO-1,3-DIHYDRO-2H-ISOINDOL-2-YL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: The synthetic method is the same as described for 2-[6-(4-phenyl-1-piperidinyl)hexyl]-1H-isoindole-1,3(2H)-dione. N-(3-{1-[6-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)hexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: 506 mg (56% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 7.86-7.80 (m, 2H), 7.73-7.68 (m, 2H), 7.44 (s, 1H), 7.37 (d, 1H, J=8.3 Hz), 7.22 (t, 1H, J=7.7 Hz), 6.96 (d, 1H, J=7.7 Hz), 3.69 (t, 2H, J=7.2 Hz), 3.01 (apparent d, 2H, J=11.3 Hz), 2.58-2.40 (m, 2H), 2.33 (m, 2H) 1.98 (dt, 2H, J=3.2, 11.3 Hz), 1.84-1.64 (m, 4H), 1.51 (q, 2H, J=7.1 Hz), 1.43-1.30 (m, 6H), 1.24 (d, 6H, J=6.8 Hz); ESMS m/e: 476.4 $(M + H)^+$.

Example 37

N-{3-[1-(3-METHOXY-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: A mixture of 3-methoxy-3-phenyl-1-chloropropane (23.1 mg, 0.126 mmol), 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide (28.3 mg, 0.126 mmol), diisopropylethylamine (0.50 mL) and catalytic amount of tetrabutylammonium iodide in dioxane (2.0 mL) was stirred at 90 °C for 72 hrs. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave N-{3-[1-(3-methoxy-3-phenylpropyl)-4-piperidinyl]phenyl}-2-methylpropanamide (45.4 mg, 91.2% yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (S, 1 H), 7.34-7.25 (m, 5H), 7.25 (m, 2H), 6.96 (d, 1H, J=7.4 Hz), 4.20 (apparent dd, 1H, J=5.9, 7.6 Hz), 3.2 (s, 3H), 3.04 (d, 1H, J=10.1 Hz), 2.99 (d, 1H, J=10.1Hz), 2.49 (apparent sept, partially hidden, 4H, J=6.6 Hz), 2.3-2.1(m, 4H), 1.82 (m, 4H), 1.25 (d, 6H, J=7.1 Hz); ESMS m/e: 395.4 $(M + H)^+$.

Example 38

N-(3-{1-[4-(1,3-DIOXO-1,3-DIHYDRO-2H-ISOINDOL-2-YL)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: The synthetic method is the same as described for 2-[6-(4-phenyl-1-piperidinyl)hexyl]-1H-isoindole-1,3(2H)-dione.

N-(3-{1-[4-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)butyl]-4-piperidinyl}phenyl)-2-methylpropanamide: 664 mg (74% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 7.87-7.78 (m, 2H), 7.76-7.64 (m, 2H), 7.47 (s, 1H), 7.39 (d, 1H, J=7.6 Hz), 7.21 (t, 1H, J=8.1 Hz), 6.94 (d, 1H, J=7.6 Hz), 3.72 (t, 2H, J=6.8 Hz), 3.37-3.22 (m, 2H), 3.0 (apparent d, 2H, J=10.7 Hz), 2.75 (q, 2H, J=7.0 Hz), 2.64-2.33 (m, 4H), 1.99 (dt, 2H, J=2.6, 11.7 Hz), 1.86-1.65 (m, 2H), 1.63-1.50 (m, 2H), 1.23 and 1,21 (two d, 6H, J=5.5 Hz);

ESMS m/e: 448.4 $(M + H)^+$; Anal. Calc. for $C_{27}H_{34}N_3ClO_3+0.4H_2O$: C, 66.02; H, 7.14; N, 8.55. Found: C, 66.07; H,.6.78; N, 8.65.

Example 39

N-(3-{1-[4-(1,3-DIOXO-1,3-DIHYDRO-2H-ISOINDOL-2-YL)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: The synthetic method is the same as described for 2-[6-(4-phenyl-1-piperidinyl)hexyl]-1H-isoindole-1,3(2H)-dione. N-(3-{1-[5-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)pentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: 614 mg (64% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 7.87-7.8 (m, 2H), 7.76-7.68 (m, 2H), 7.48 (s, 1H), 7.41 (d, 1H, J=7.6 Hz), 7.21 (t, 1H, J=7.6 Hz), 6.95 (d, 1H, J=7.6 Hz), 3.69 (t, 2H, J=7.2 Hz), 3.39-3.28 (m, 2H), 3.02 (apparent d, 2H, J=11.6 Hz), 2.78 (q, 2H, J=7.2 Hz), 2.64-2.52 (m, 1H), 2.52-2.40 (m, 1H), 2.40-2.31 (m, 2H), 2.01 (dt, 2H, J=3.7, 11.1 Hz), 1.85-1.64 (m, 2H), 1.58 (q, 2H, J=7.6 Hz), 1.45-1.32 (m, 2H), 1.23 (d, 6H, J=6.9 Hz); ESMS m/e: 462.4 $(M + H)^+$; Anal. Calc. for $C_{28}H_{39}N_3ClO_3$: C, 67.52; H, 7.29; N, 8.44. Found: C, 67.04; H, 7.06; N, 8.38.

Example 40

2-METHYL-N-{3-[1-(4-PHENYLBUTYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: A mixture of 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide (28.3 mg, 0.100 mmol), 4-phenyl-1-chlorobutane (21.1 mg, 0.125 mmol), diisopropylethylamine (0.50 mL), catalytic amount of tetrabutylammonium iodide and dioxane (2.0 mL) was heated at reflux temperature for 3 days. The reaction mixture was concentrated and chromatographed using preparative TLC plates [2.5% of NH_3 (2.0 M in methanol)

in $CHCl_3$] afforded the product, 2-methyl-N-{3-[1-(4-phenylbutyl)-4-piperidinyl]phenyl}propanamide (9.50 mg, 25.1% yield) as a thick oil: ^1H NMR δ 7.37 (s, 1H), 7.29 (apparent d, 1H, J=7.9 Hz), 7.18 (m, 3H), 7.11 (m, 3H), 6.90 (apparent d, 1H, J=7.9 Hz), 3.02 (d, 2H, J=6.8 Hz), 2.41 (m, 4H, partially hidden), 2.01 (m, 2H), 1.78 (m, 4H), 1.57 (m, 4H), 1.18 (d, 6H, J=7.7 Hz); ESMS *m/e*: 379.4 $(M + H)^+$.

Example 41

N-(3-{1-[3-(1,3-DIOXO-1,3-DIHYDRO-2H-ISOINDOL-2-YL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:

The synthetic method is the same as described for 2-[6-(4-phenyl-1-piperidinyl)hexyl]-1H-isoindole-1,3(2H)-dione. N-(3-{1-[3-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide: 810 mg (93% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 7.87-7.82 (m, 2H), 7.73-7.68 (m, 2H), 7.57 (s, 1H), 7.36 (d, 1H, J=8.5 Hz), 7.18 (t, 1H, J=7.7 Hz), 6.79 (d, 1H, J=7.1 Hz), 3.78 (t, 2H, J=6.8 Hz), 3.06 (quintet, 2H, J=6 Hz), 2.95 (apparent d, 2H, J=12.2 Hz), 2.58-2.31 (m, 4H), 1.96-1.83 (m, 2H), 1.70 (apparent d, 2H, J=12.1 Hz), 1.52 (dt, 2H, J=3.5, 12.5 Hz), 1.03 (d, 6H, J=6.5 Hz); ESMS m/e: 434.4 $(M + H)^+$.

Example 42

N-(3-{1-[(3S)-3-HYDROXY-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of (S)-(-)-3-chloro-1-phenyl-1-propanol (0.426 g, 2.50 mmol, 99%ee), 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide (0.565 g, 2.00 mmol), diisopropylethylamine (1.29 g, 10.0 mmol), dioxane (5.0 mL) and catalytic amount of tetrabutylammonium iodide

was stirred at 90 °C for 72 hrs. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (306 mg, 39.3 % yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (s, 1 H), 7.42 (d, 4H, J=8.1 Hz), 7.35 (m, 1 H), 7.30 (d, 1 H, J=8.0 Hz), 7.23 (t, 1H, J=8.1 Hz), 7.12 (s, 1H), 6.96 (apparent dd, 1H, J=8.0 Hz), 5.0 (apparent dd, 1H, J=4.4, 8.3 Hz), 3.18 (apparent dd, 2H, J=2.5, 12.5 Hz), 2.74 (m, 2 H), 2.50 (m, 2H), 2.3-2.1 (m, 6H), 1.8 (m, 2H), 1.25 (d, 6H, J=7.1 Hz); ESMS m/e: 389.2 $(M + H)^+$.

Example 43

N-(3-{1-[3-METHOXY-3-(4-METHYLPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of 3-methoxy-3-(p-tolyl)-1-chloropropane (24.9 mg, 0.126 mmol), 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide (28.3 mg, 0.126 mmol), diisopropylethylamine (0.50 mL) and catalytic amount of tetrabutylammonium iodide in dioxane (2.0 mL) was stirred at 90 °C for 72 hrs. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (10.9 mg, 21.2 % yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (s, 1 H), 7.38 (m, 1H), 7.3-7.1 (m, 5 H), 6.96 (d, 1H, J=7.4 Hz), 4.18 (apparent dd, 1H, J=5.6, 7.9 Hz), 3.24 (d, 1H, J=8.2 Hz), 3.2 (s, 3H), 3.11 (m, 2H, J=10.1Hz), 2.49 (m, 4H), 2.35 (s, 3H), 2.3-2.1(m, 3H), 1.92 (d, 4H), 1.25 (d, 6H, J=7.1 Hz); ESMS m/e: 409.4 $(M + H)^+$.

Example 44

N-{3-[1-(3-ISOPROPOXY-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: A mixture of 3-

isopropyl-3'-phenyl-1-chloropropane (26.6 mg, 0.126 mmol), 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide (28.3 mg, 0.126 mmol), diisopropylethylamine (0.50 mL) and catalytic amount of tetrabutylammonium iodide in dioxane (2.0 mL) was stirred at 90 °C for 72 hrs. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (14.1 mg, 26.5% yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.43-7.37 (m, 2H), 7.33 (m, 3H), 7.23 (m, 2H), 6.95 (d, 1H, J=8.4 Hz), 4.46 (apparent dd, 1H, J=5.0, 8.3 Hz), 3.49 (apparent sept, 1H, J=7.1 Hz), 3.10 (s, 2H), 2.70 (m, 2H), 2.52 (apparent sept, partially hidden, 4H, J=6.6 Hz), 2.30-2.10 (m, 2H), 1.90-1.80 (d, 4H), 1.25 (d, 6H, J=7.1 Hz), 1.15 (d, 3H, J=6.4 Hz), 1.08 (d, 3H, J=6.4 Hz); ESMS *m/e*: 423.4 $(M + H)^+$.

Example 45

N-(3-{1-[4,4-BIS(4-FLUOROPHENYL)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of 4,4-bis(4-fluoro-phenyl)-1-chloro-butane (39.0 mg, 0.126 mmol), 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide (28.3 mg, 0.126 mmol), diisopropylethylamine (0.50 mL) and catalytic amount of tetrabutylammonium iodide in dioxane (2.0 mL) was stirred at 90 °C for 72 hrs. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (15.9 mg, 25.2 % yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.41 (s, 1H), 7.3-7.15 (m, 4H), 7.10 (m, 3H), 6.89 (apparent t, 5H), 3.81 (t, 1H, J=7.8 Hz), 3.30 (s, 1H), 2.91 (d, 1H, J=12,5 Hz), 2.80 (m, 1H), 2.40 (m, 2H), 2.31 (t, 1H, J=8.0 Hz), 1.93 (apparent q, 3H, J=8.0 Hz), 1.72 (m, 3H), 1.40 (m, 2H),

1.20 (m, 2H), 1.15 (d, 6H, J=8.1 Hz); ESMS *m/e*: 491.4 $(M + H)^+$

EXAMPLE 46

N-{3-[1-(3-METHOXYBENZYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: A mixture of 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide (28.3 mg, 0.100 mmol), 3-methoxybenzyl chloride (19.6 mg, 0.125 mmol), diisopropylethylamine (0.50 mL), catalytic amount of tetrabutylammonium iodide and dioxane (2.0 mL). Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] afforded the desired product (10.2 mg, 27.9% yield) as a yellow solid: ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.35 (apparent d, 1H, J=8.3 Hz), 7.27-7.21 (m, 2H), 6.95 (apparent t, 3H, J=6.9 Hz), 6.82 (apparent dd, 1H, J=2.4, 8.3 Hz), 3.84 (m, 3H), 3.56 (s, 2H), 3.05 (d, 2H, J=10.5 Hz), 2.51 (apparent sept, partially hidden, 4H, J=7.2 Hz), 2.13 (apparent t, 2H, J=9.7 Hz), 1.88 (m, 2H), 1.25 (d, 6H, J=6.7 Hz); ESMS *m/e*: 367.3 $(M + H)^+$.

Example 47

N-(3-{1-[3,5-BIS(TRIFLUOROMETHYL)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (28.3 mg, 0.100 mmol), 3,5-bis(trifluoromethyl)benzyl bromide (38.4 mg, 0.125 mmol), diisopropylethylamine (0.50 mL), catalytic amount of tetrabutylammonium iodide and dioxane (2.0 mL). Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (12.2 mg, 25.8% yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 2H), 7.77 (s, 1H), 7.53 (s, 1H), 7.30-7.21 (m, 2H), 7.16 (s,

1H), 6.98 (apparent d, 1H, J=7.6 Hz), 3.62 (s, 2H), 2.94 (d, 2H, J=9.4 Hz), 2.51 (apparent sept, partially hidden, 2H, J=6.6 Hz), 2.14 (m, 2H), 1.82 (m, 4H), 1.25 (d, 6H, J=6.6 Hz); ESMS *m/e*: 473.2 $(M + H)^+$.

Example 48

N-(3-{1-[(3R)-3-(3,4-DIMETHOXYPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE

Method A

4-{[(1R)-3-chloro-1-phenylpropyl]oxy}-1,2-dimethoxybenzene: A mixture of 3,4-dimethoxyphenol (4.07 g, 26.4 mmol), (S)-(-)-3-chloro-phenyl-1-propanol (4.50 g, 26.4 mmol, 99%ee, Aldrich Chemical Co.), triphenylphosphine (6.92 g, 26.4 mmol) and diethyl azodicarboxylate (4.59 g, 26.4 mmol) in THF (110 mL) was stirred at room temperature for 24 h. The reaction mixture was concentrated *in vacuo*. At this point, the residue can either be washed with pentane (x3) and the combined pentane extracts were concentrated and chromatographed (silica with hexanes-EtOAc 8:1 as the eluent) to give the desired product (as described as a general procedure by: Srebnik, M.; Ramachandran, P.V.; Brown, H.C. *J. Org. Chem. 1988, 53,* 2916-2920). This procedure was performed on a smaller scale reaction and only a 40% yield of the product was realized.

Alternatively, on a larger scale (26.4 mmol), the crude product was triturated with a small amount of dichloromethane and the precipitated triphenylphosphine oxide was filtered. The filtrate was concentrated and the crude product was chromatographed to give the desired product as a thick yellow oil (7.30 g, 88.9%

yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.32 (m, 4H), 7.20 (m, 1H), 6.64 (d, 1H, J=8.7 Hz), 6.51 (d, 1H, J=2.7 Hz), 6.30 (dd, 1H, J=2.7, 8.7 Hz), 5.27 (apparent dd, 1H, J=4.5, 8.7 Hz), 3.79 (s, 3H), 3.77 (s, 3H), 3.61 (m, 1H), 2.45 (m, 1 H), 2.20 (m, 1H), 1.80 (s, 1H); ESMS *m/e*: 307.11 $(M+H)^+$.

N-(3-{1-[(3R)-3-(3,4-DIMETHOXYPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of potassium carbonate (321 mg, 2.32 mmol), sodium iodide (522 mg, 3.48 mmol), 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (570 mg, 2.32 mmol) and 4-{[(1R)-3-chloro-1-phenylpropyl]oxy}-1,2-dimethoxybenzene (712 mg, 2.32 mmol) in DMF (5.0 mL) was stirred at 100 °C for 3 hrs, at which time TLC indicated that the reaction was complete. The reaction mixture was poured into water (50 mL) and the aqueous layer was extracted with methylene chloride (3x30 mL). The combined organic extracts were washed with brine (30 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by Prep-TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] to afford the product (970 mg, 90.1%) as a thick oil.

Method B

Into a 25-mL RB-flask was added triphenylphosphine (9.80 mg, 0.0375 mmol), diethyl azodicarboxylate (5.22 mg, 0.0300 mmol), N-(3-{1-[(3S)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (9.53 mg, 0.0250 mmol), 3,4-dimethoxyphenol (7.70 mg, 0.050 mmol) and THF (1.0 mL) at room temperature. The reaction mixture was stirred at room temperature overnight (16 hrs). The solvent was removed under reduced pressure and the

residue was purified by preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] to afford the desired product (4.4 mg, 34.1 % yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (s, 1 H), 7.40-7.30 (m, 4H), 7.25 (m, 3H), 6.97 (d, 1H, J=7.8 Hz), 6.64 (d, 1H, J=9.1 Hz), 6.51 (d, 1H, J=2.6 Hz), 6.29 (d, 1H, J=2.6, 9.1 Hz), 5.20 (apparent dd, 1H, J=4.4, 8.5 Hz), 3.80 (s, 3H), 3.77 (s, 3H), 3.23 (m, 2H), 2.77 (m, 2 H), 2.5 (m, 2H), 2.3-2.1(m, 6H), 1.80 (m, 2H), 1.25 (d, 6H, J=7.9 Hz); ESMS *m/e*: 517.4 $(M + H)^+$.

Example 49

2-METHYL-N-(3-{1-[(3S)-3-PHENOXY-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (9.53 mg, 0.0250 mmol), phenol (4.70 mg, 0.050 mmol), triphenylphosphine (9.80 mg, 0.0375 mmol) and diethyl azodicarboxylate (5.22 mg, 0.0300 mmol) in THF (1.0 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (2.7 mg, 23.6 % yield) as a thick oil: ^1H NMR δ 7.46 (s, 2H), 7.40-7.30 (m, 4H), 7.25 (m, 3 H), 7.20 (m, 2H), 6.97 (apparent d, 1H, J=7.4 Hz), 6.89 (apparent tt, 1H, J=0.8, 7.6 Hz), 6.84 (apparent dt, 1H, J=0.8, 8.0 Hz), 5.20 (apparent dd, 1H, J=4.4, 8.5 Hz), 3.35 (m, 2H), 2.91 (m, 2H), 2.60 (m, 2H), 2.30-2.10 (m, 6H), 1.90 (m, 2H), 1.25 (d, 6H, J=7.9 Hz); ESMS *m/e*: 457.4 $(M + H)^+$;

Example 50

N-(3-{1-[(3S)-3-(4-METHOXYPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of N-

(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (9.53 mg, 0.0250 mmol), 4-methoxyphenol (6.20 mg, 0.050 mmol), triphenylphosphine (9.80 mg, 0.0375 mmol) and diethyl azodicarboxylate (5.2 mg, 0.0300 mmol) in THF (1.0 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (4.6 mg, 37.9 % yield) as a thick oil. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38-7.14 (m, 8H), 6.90 (apparent d, 1H, J=7.7 Hz), 6.72-6.46 (m, 4H), 5.09 (apparent dd, 1H, J=4.8, 8.1 Hz), 3.64 (s, 3H), 3.18 (m, 2H), 2.73 (m, 2H), 2.50 (m, 2H), 2.37-1.72 (m, 8H), 1.25 (d, 6H, J=7.4 Hz); ESMS *m/e*: 487.4 $(M + H)^+$.

Example 51

N-(3-{1-[(3S)-3-(3-CHLOROPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (9.53 mg, 0.0250 mmol), 3-chlorophenol (6.40 mg, 0.050 mmol), triphenylphosphine (9.80 mg, 0.0375 mmol) and diethyl azodicarboxylate (5.22 mg, 0.0300 mmol) in THF (1.0 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (4.9 mg, 40.0 % yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (s, 1H), 7.35-7.10 (m, 7H), 7.02 (t, 1H, J=8.0 Hz), 6.90 (d, 1H, J=7.6 Hz), 6.84-6.75 (m, 2H), 6.65 (m, 1H), 5.09 (apparent dd, 1H, J=4.99, 8.1 Hz), 3.10 (m, 2H), 2.60 (m, 2H), 2.50 (m, 2H), 2.30-1.70 (m, 8H), 1.18 (d, 6H, J=6.8 Hz); ESMS *m/e*: 491.4 $(M + H)^+$.

Example 52

N-(3-{1-[(3S)-3-(4-CHLOROPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (9.53 mg, 0.0250 mmol), 4-chlorophenol (6.40 mg, 0.050 mmol), triphenylphosphine (9.80 mg, 0.0375 mmol) and diethyl azodicarboxylate (5.22 mg, 0.0300 mmol) in THF (1.0 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (3.3 mg, 26.9 % yield) as a thick oil: ^1H NMR δ 7.36 (s, 1H), 7.35-7.22 (m, 7H), 7.12 (m, 2H), 6.97 (apparent d, 1H, J=7.2 Hz), 6.77 (m, 2H), 5.23 (m, 1H), 3.18 (m, 2H), 2.70 (m, 2H), 2.50 (m, 2H), 2.40-1.80 (m, 8H), 1.25 (d, 6H, J=6.8 Hz); ESMS *m/e*: 491.4 $(M + H)^+$.

Example 53

2-METHYL-N-[3-(1-{(3S)-3-PHENYL-3-[4-(TRIFLUOROMETHYL)PHENOXY]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (9.53 mg, 0.0250 mmol), 4-trifluoromethylphenol (8.100 mg, 0.050 mmol), triphenylphosphine (9.8 mg, 0.0375 mmol) and diethyl azodicarboxylate (5.22 mg, 0.0300 mmol) in THF (1.0 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (5.10 mg, 38.9 % yield) as a thick oil: ^1H NMR δ 8.06 (s, 1H), 7.49 (s, 1H), 7.44 (apparent d, 2H, J=.6 Hz), 7.38-7.30 (m, 4H), 7.30-7.20 (m, 3H), 6.96

(apparent d, 1H, J=7.6 Hz), 6.91 (apparent d, 2H, J=8.6 Hz), 5.34 (m, 1H), 3.19 (m, 2H), 2.72 (m, 2H), 2.53 (m, 2H), 2.40-1.80 (m, 8H), 1.25 (d, 6H, J=6.8 Hz); ESMS *m/e*: 525.4 $(M + H)^+$.

Example 54

N-(3-{1-[(3R)-3-(2,5-DIFLUOROPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (9.53 mg, 0.0250 mmol), 2,5-difluorophenol (6.50 mg, 0.050 mmol), triphenylphosphine (9.80 mg, 0.0375 mmol) and diethyl azodicarboxylate (5.22 mg, 0.0300 mmol) in THF (1.0 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (3.60 mg, 29.3 % yield) as a thick oil: ^1H NMR δ 7.46 (s, 1H), 7.40-7.32 (m, 4H), 7.31-7.20 (m, 2H), 7.17 (s, 1H), 7.01-6.92 (m, 2H), 6.65-6.42 (m, 2H), 5.27 (m, 1H), 3.13 (m, 2H), 2.64 (m, 2H), 2.51 (m, 2H), 2.28-1.80 (m, 8 H), 1.25 (d, 6H, J=7.1 Hz); ESMS *m/e*: 493.4 $(M + H)^+$.

Example 55

N-(3-{1-[(3S)-3-(3,4-DICHLOROPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of N-(3-{1-[(3S)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (9.53 mg, 0.0250 mmol), 3,4-dichlorophenol (8.20 mg, 0.050 mmol), triphenylphosphine (9.80 mg, 0.0375 mmol) and diethyl azodicarboxylate (5.22 mg, 0.0300 mmol) in THF (1.0 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5%

of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (5.20 mg, 39.7 % yield) as a thick oil: ^1H NMR ($CDCl_3$) δ 7.70-7.63 (m, 2H), 7.55 (m, 1H), 7.47-7.43 (m, 3H), 7.40-7.19 (m, 3H), 7.00-6.50 (m, 2H), 6.69 (dd, 1H, J=2.2, 8.8 Hz), 5.25 (m, 1H), 3.20 (m, 2H), 2.70 (m, 2H), 2.53 (m, 2H), 2.40-2.20 (m, 4H), 2.10-1.80 (m, 4H), 1.25 (d, 6H, J=7.1 Hz); ESMS *m/e*: 525.4 $(M+H)^+$.

Example 56

2-METHYL-N-(3-{1-[(3R)-3-PHENOXY-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: A mixture of N-(3-{1-[(3S)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (9.53 mg, 0.0250 mmol), phenol (4.70 mg, 0.050 mmol), triphenylphosphine (9.80 mg, 0.0375 mmol) and diethyl azodicarboxylate (5.22 mg, 0.0300 mmol) in THF (1.0 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (4.1 mg, 36.0 % yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.40-7.15 (m, 10H), 6.97 (d, 1H, J=7.6 Hz), 6.88-6.82 (m, 2H), 5.26 (m, 1H), 3.18 (m, 2H), 2.75 (m, 2H), 2.53 (m, 2H), 2.40-2.10 (m, 4H), 2.10-1.80 (m, 4H), 1.25 (d, 6H, J=6.9 Hz); ESMS *m/e*: 457.4 $(M+H)^+$.

Example 57

N-(3-{1-[(3R)-3-HYDROXY-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE

Method A

Into a 25-mL RB-flask was added (R)-(+)-3-chloro-1-phenyl-1-propanol (0.545 g, 3.19 mmol, 99%ee, Aldrich Chemical Co.), 2-methyl-*N*-[3-(4-

piperidinyl)phenyl]propanamide (0.748 g, 3.04 mmol), potassium carbonate (0.420 g, 3.04 mmol) and sodium iodide (0.684 g, 4.56 mmol) and DMF (6.0 mL) at room temperature. After stirring at 100 °C for 3 hrs, the TLC showed the reaction was complete. The reaction mixture was poured into water (50 mL) and the aqueous layer was extracted with methylene chloride (3x20 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography (1:1= hexane: ethyl acetate with 1% isopropylamine) to afford the desired product (1.09 g, 94.3 % yield) as light-yellow solid: ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (s, 1H), 7.46-7.35 (m, 6H), 7.27 (m, 2H), 6.98 (apparent d, 1H, J=7.6 Hz), 5.02 (apparent dd, 1H, J=4.4, 8.1 Hz), 3.18 (apparent dd, 2H, J=2.5, 12.5 Hz), 2.74 (m, 2 H), 2.50 (m, 2H), 2.30-2.10 (m, 6H), 1.80 (m, 2H), 1.25 (d, 6H, J=7.1 Hz); ESMS *m/e*: 381.2 $(M + H)^+$.

The hydrochloric salt was prepared by addition of a slight excess of 1 N HCl in ether (1.2 eq.) to a solution of the free base in dichloromethane. The solvent was removed under reduced pressure, the residue was washed with ether and dried under reduced pressure: Anal. Calc. for $C_{24}H_{32}N_2O_2$+HCl+0.8H_2O: C, 66.82; H, 8.08; N, 6.49; Cl, 8.22. Found: C, 66.90; H, 7.78; N, 6.63; Cl, 8.52.

Method B

Into a 25-mL RB-flask was added (R)-(+)-3-chloro-1-phenyl-1-propanol (0.426 g, 2.50 mmol), 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (0.565 g, 2.00 mmol),

diisopropylethylamine (1.29 g, 10.0 mmol), dioxane (5.0 mL) and catalytic amount of tetrabutylammonium iodide at room temperature. After stirring at 90 °C for 72 hrs, the reaction mixture was poured into water (50 mL) and the aqueous layer was extracted with methylene chloride (3x20 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by preparative TLC plates (1:5:100=isopropylamine:methanol:ethyl acetate) to afford the desired product (0.260 g, 34.2 % yield) as light-yellow solid.

Example 58

N-(3-{1-[(3S)-3-(4-CYANO-PHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: N-(3-{1-[(3S)-3-(4-cyanophenoxy)-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide

A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 4-cyanophenol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (4.70 mg, 71.3 % yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (m, 2H), 7.48 (d, 2H, J=8.4 Hz), 7.30-7.20 (m, 3H), 7.20 (m, 3H), 6.97 (apparent d, 1H, J=8.4 Hz), 6.92 (apparent d, 2H, J=8.4 Hz), 5.36 (apparent dd, 1H, J=3.9, 7.6 Hz), 3.12 (m, 2H), 2.61 (m, 2H), 2.53 (apparent sept, partially hidden, 2H, J=7.6 Hz), 2.30-2.10 (m, 6H), 1.82

(m, 2H), 1.25 (d, 6H, J=6.8 Hz); ESMS *m/e*: 482.2 $(M + H)^+$.

Example 59

N-(3-{1-[(3S)-3-(4-FLUOROPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 4-fluorophenol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (4.20 mg, 64.7% yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (m, 2H), 7.30-7.20 (m, 5H), 7.20 (m, 3H), 6.97 (apparent d, 1H, J=7.7 Hz), 6.87 (m, 1H), 6.76 (m, 1H), 5.26 (apparent dd, 1H, J=4.0, 8.1 Hz), 3.09 (m, 2H), 2.66 (m, 2H), 2.51 (m, 2H), 2.3-2.1 (m, 6H), 1.82 (m, 2H), 1.25 (d, 6H, overlapped); ESMS *m/e*: 475.2 $(M + H)^+$.

Example 60

N-(3-{1-[(3S)-3-(4-BROMOPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 4-bromophenol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] the desired product (0.70 mg, 9.6% yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.48

(m, 2H), 7.30-7.20 (m, 5H), 7.20 (m, 3H), 6.97 (apparent d, 1H, J=8.5 Hz), 6.73 (apparent d, 2H, J=8.5 Hz), 5.22 (apparent dd, 1H, J=4.9, 7.8 Hz), 3.15 (m, 2H), 2.65 (m, 2H), 2.51 (apparent sept, partially hidden, 2H, J=7.6 Hz), 2.30-2.10 (m, 6H), 1.82 (m, 2H), 1.25 (d, 6H, J=6.8 Hz); ESMS *m/e*: 535.1 $(M + H)^+$.

Example 61

N-(3-{1-[(3S)-3-(3-METHOXYPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 3-methoxyphenol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (3.1 mg, 46.6 % yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, 1H, J=6.7 Hz), 7.42 (s, 1H), 7.3-7.20 (m, 3H), 7.20 (m, 3H), 7.07 (t, 1H, J=8.4 Hz), 6.97 (apparent d, 1H, J=6.7 Hz), 6.40 (m, 3H), 5.27 (apparent dd, 1H, J=5.3, 8.0 Hz), 3.74 (s, 3H), 3.38 (m, 2H), 2.93 (m, 2H), 2.61 (s, 1H), 2.53 (apparent sept, partially hidden, 1H, J=6.5 Hz), 2.30-2.10 (m, 6H), 1.82 (m, 2H), 1.25 (d, 6H, J=6.9 Hz); ESMS *m/e*: 487.3 $(M + H)^+$.

Example 62

N-(3-{1-[(3S)-3-(4-CYANO-2-METHOXYPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 2-methoxy-4-cyanophenol (100 mg),

triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (5.50 mg, 76.5 % yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.38 (s, 1H), 7.37 (d, 2H, J=2.4 Hz), 7.20 (m, 4H), 7.10 (d, 1H, J=2.4 Hz), 7.08 (s, 1H), 6.99 (apparent d, 1H, J=8.3 Hz), 6.76 (apparent d, 1H, J=8.3 Hz), 5.43 (apparent dd, 1H, J=5.1, 8.0 Hz), 3.91 (s, 3H), 3.34 (m, 2H), 2.63 (m, 2H), 2.63 (s, 1H), 2.53 (apparent sept, partially hidden, 1H, J=7.7 Hz), 2.30-2.10 (m, 6H), 1.82 (m, 2H), 1.28 (d, 6H, J=6.8 Hz); ESMS *m/e*: 512.2 $(M + H)^+$.

Example 63

N-(3-{1-[(3R)-3-(5-ACETYL-2-METHOXYPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:

A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 2-methoxy-5-acetylphenol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (1.60 mg, 22.2 % yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, 2H, J=2.4 Hz), 7.3-7.2 (m, 5H), 7.20 (m, 3H), 6.97 (apparent d, 1H, J=6.7 Hz), 6.69 (apparent d, 1H, J=8.0 Hz), 5.47 (apparent dd, 1H, J=4.3, 7.8 Hz), 3.95 (s, 3H), 3.38 (m, 2H), 2.93 (m, 2H), 2.61 (s, 1H), 2.53 (apparent sept, partially hidden, 1H, J=7.6 Hz), 2.50 (s, 3H), 2.30-2.10 (m, 6H),

1.82 (m, 2H), 1.25 (d, 6H, J=6.8 Hz); ESMS m/e: 529.6 $(M + H)^+$.

Example 64

N-(3-{1-[(3R)-3-(2-ACETYLPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of N-(3-{1-[(3S)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.2 mg, 0.0137 mmol), 2-acetylphenol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (1.70 mg, 24.9 % yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (m, 1H), 7.55 (s, 1H), 7.30-7.20 (m, 5H), 7.20 (m, 3H), 6.97 (m, 2H), 6.76 (apparent d, 1H), 5.49 (apparent dd, 1H, J=4.3, 8.0 Hz), 3.38 (m, 2H), 2.93 (m, 2H), 2.71 (s, 3H), 2.60 (s, 1H), 2.53 (apparent sept, partially hidden, 1H, J=7.6 Hz), 2.30-2.10 (m, 6H), 1.82 (m, 2H), 1.25 (d, 6H, J=6.9 Hz); ESMS *m/e*: 498.8 (M^+).

Example 65

N-[3-(1-{(3R)-3-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]-3-PHENYLPROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: A mixture of N-(3-{1-[(3S)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 2-fluoro-5-trifluoromethylphenol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired

product (2.50 mg, 33.7 % yield) as a thick oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.67 (m, 1H), 7.54 (m, 1H), 7.45 (m, 2H), 7.30-7.10 (m, 6H), 7.14 (d, 1H, J=7.4 Hz), 6.97 (apparent d, 1H, J=7.7 Hz), 5.37 (apparent dd, 1H, J=5.0, 8.5 Hz), 3.4 (m, 2H), 2.8 (m, 2H), 2.6 (s, 1H), 2.53 (apparent sept, partially hidden, 1H, J=7.4 Hz), 2.30-2.10 (m, 6H), 1.80 (m, 2H), 1.25 (d, 6H, J=7.1 Hz, overlapped); ESMS *m/e*: 542.6 (M^+), 543.54 $(M + H)^+$.

Example 66

N-[3-(1-{(3S)-3-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]-3-PHENYLPROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 2-fluoro-5-trifluoromethylphenol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (3.00 mg, 40.4% yield) as a thick oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.67 (m, 2H), 7.55 (m, 2H), 7.50-7.40 (m, 3H), 7.30-7.10 (m, 3H), 7.17 (d, 1H, J=8.9 Hz), 7.07 (apparent d, 1H, J=6.7 Hz), 6.97 (apparent d, 1H, J=7.8 Hz), 5.37 (apparent dd, 1H, J=4.2, 8.1 Hz), 3.37 (m, 2H), 2.93 (m, 2H), 2.63 (s, 1H), 2.50 (apparent sept, partially hidden, 1H, J=7.9 Hz), 2.30-2.10 (m, 6H), 1.85 (m, 2H), 1.25 (d, 6H, J=6.9 Hz); ESMS *m/e*: 542.7 $(M + H)^+$.

Example 67

N-(3-{1-[(3S)-3-(2,5-DIFLUOROPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 2,5-difluorophenol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (2.70 mg, 40.1 % yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.40-7.30 (m, 4H), 7.20 (m, 2H), 7.17 (s, 1H), 6.97 (m, 2H), 6.58 (m, 1H), 6.51 (m, 1H), 5.27 (apparent dd, 1H, J=5.1, 8.2 Hz), 3.13 (apparent d, J=9.7 Hz, 2H), 2.64 (m, 2H), 2.51 (m, 2H), 2.34 (apparent sept, partially hidden, J=7.1 Hz, 1H), 2.17 (m, 3H), 1.90-1.80 (m, 4H), 1.25 (d, 6H, J=7.1 Hz); ESMS m/e: 493.1 $(M + H)^+$.

Example 68

N-(3-{1-[(3R)-3-(3-CHLOROPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of N-(3-{1-[(3S)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 3-chlorophenol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (2.4 mg, 35.8% yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (m, 2H), 7.30-7.20 (m, 3H), 7.20 (m, 3H), 6.90 (apparent d, 1H, J=7.7 Hz), 6.71 (apparent d, 1H, J=2.9 Hz), 6.69

(apparent t, 1H, J=2.9 Hz), 6.67 (apparent t, 1H, J=2.9 Hz), 6.65 (apparent d, 1H, J=2.9 Hz), 5.09 (apparent dd, 1H, J=4.8, 8.1 Hz), 3.18 (m, 2H), 2.73 (m, 2H), 2.50 (apparent sept, partially hidden, 2H, J=7.1 Hz), 2.30-2.10 (m, 6H), 1.89 (m, 2H), 1.25 (d, 6H, overlapped); ESMS *m/e*: 491.1 $(M + H)^+$.

Example 69

(1S)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL 1-NAPHTHOATE: Into a 25-mL RB-flask was added N-(3-{1-[(3S)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 1-naphthalenecarbonyl chloride (100 mg), diisopropylethylamine (0.30 mL) in THF (0.50 mL) at room temperature. After stirring for 16 hrs at room temperature, the reaction mixture was concentrated under reduced pressure. The residue was purified using preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (4.70 mg, 71.3 % yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 8.90 (d, 1H, J=8.9 Hz), 8.28 (apparent dd, 1H, J=1.5, 7.2 Hz), 8.03 (d, 1H, J=8.7 Hz), 7.88 (dm, 2H, J=8.7 Hz), 7.60-7.48 (m, 7H), 7.40-7.32 (m, 3H), 7.25 (m, 1H), 6.90 (apparent d, 1H, J=7.4 Hz), 6.18 (apparent dd, 1H, J=5.7, 7.8 Hz), 3.42 (m, 2H), 2.84 (m, 2H), 2.53 (m, 2H), 2.44 (apparent sept, partially hidden, 4H, J=7.5 Hz), 2.30-2.10 (m, 2H), 1.82 (m, 2H), 1.25 (d, 6H, J=6.8 Hz); ESMS *m/e*: 535.6 $(M + H)^+$.

Example 70

N-(3-{1-[(3S)-3-(3-ACETYLPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-

piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 2-acetylphenol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (1.50 mg, 22.0% yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (m, 1H), 7.55 (s, 1H), 7.30-7.20 (m, 5H), 7.20 (m, 3H), 6.97 (m, 2H), 6.76 (apparent d, 1H), 5.49 (apparent dd, 1H, J=4.3, 8.0 Hz), 3.38 (m, 2H), 2.93 (m, 2H), 2.75 (s, 3H), 2.53 (apparent sept, partially hidden, 2H, J=7.6 Hz), 2.30-2.10 (m, 6H), 1.92 (m, 2H), 1.25 (d, 6H, J=6.9 Hz); ESMS *m/e*: 498.81 (M^+), 499.6 $(M + H)^+$.

Example 71

N-(3-{1-[(3S)-3-(2-FLUOROPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 2-fluorophenol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (3.5 mg, 53.9% yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.65 (m, 1H), 7.41 (s, 1H), 7.40-7.10 (m, 5H), 7.05 (m, 2H), 6.97 (apparent d, 1H, J=8.7 Hz), 6.86 (m, 2H), 6.79 (apparent dt, 1H, J=2.4, 7.9 Hz), 5.31 (apparent dd, 1H, J=4.5, 8.0 Hz), 3.39 (m, 2H), 2.97 (m, 2H), 2.53 (apparent sept, partially hidden, 2H, J=7.5 Hz), 2.3-2.1

(m, 6H), 1.92 (m, 2H), 1.25 (d, 6H, J=6.7 Hz); ESMS m/e: 475.7 $(M + H)^+$.

Example 72

(4S)-N-(3-{4-[3-(ACETYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-4-(3,5-DIFLUOROPHENYL)-2-OXO-1,3-OXAZOLIDINE-3-CARBOXAMIDE

Method: Into a 20 ml vial was added N1-{3-[1-(3-aminopropyl)-4-piperidyl]phenyl}acetamide (15 mg, 0.054 mmol), (4*S*)-4-(3,5-difluorophenyl)-2-oxo-oxazolidine-3-carboxylic acid-4-nitro-phenyl ester (39.3 mg, 1.08 mmol, 2 eq) and dichloromethane with 0.6% of methanol (3 ml) at room temperature. After stirring at room temperature for 3 hrs, the reaction mixture was filtered, and purified by preparative silica TLC (19:1 = chloroform : methanol) to afford the desired product (18.3 mg, 68% yield); ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (br s, 1H), 7.40 (d, 1H, J=8.0 Hz), 7.36-7.28 (m, 2H), 7.24 (t, 1H, J=8.0 Hz), 6.99 (d, 1H, J=8.0 Hz), 6.86-6.82 (m, 2H), 5.41 (dd, 1H, J=4.1, 9.0 Hz), 4.72 (t, 1H, J=9.0 Hz), 4.22 (dd, 1H, J=3.9, 9.1 Hz), 3.42-3.29 (m, 2H); 3.02 (d, 2H J=11.1 Hz), 2.52-2.38 (m, 3H), 2.16 (s, 3H), 2.08-1.98 (m, 2H), 1.86-1.70 (m, 6H); ESMS m/e: 501.2 $(M + H)^+$; Anal. Calc. for $C_{26}H_{30}F_2N_4O_4+0.5H_2O$: C, 60.64; H, 6.18; N, 10.88. Found: C, 60.67; H, 5.79; N, 10.86.

Example 73

The synthetic method is the same as described for the synthesis of (4S)-*N*-(3-{4-[3-(acetylamino)phenyl]-1-piperidinyl}propyl)-4-(3,5-difluorophenyl)-2-oxo-1,3-oxazolidine-3-carboxamide.

(4S)-N-(3-{4-[3-(ACETYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-2-OXO-4-(3,4,5-TRIFLUOROPHENYL)-1,3-OXAZOLIDINE-3-CARBOXAMIDE: 18.8 mg (67% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (br s, 1H), 7.41-7.20 (m, 3H), 7.02-6.91 (m, 3H), 5.37 (dd, 1H, J=3.8, 8.9 Hz), 4.71 (t, 1H, J=9 Hz), 4.21 (dd, 1H, J=4, 9.3 Hz), 3.43-3.27 (m, 2H), 3.02 (d, 2H, J=11.0 Hz), 2.53-2.37 (m, 3H), 2.16 (s, 3H), 2.08-1.97 (m, 2H), 1.85-1.69 (m, 6H); ESMS m/e: 519.2 $(M + H)^+$; Anal. Calc. for $C_{26}H_{29}F_3N_4O_4+0.5H_2O$: C, 59.20; H, 5.73; N, 10.62. Found: C, 59.40; H, 5.35; N, 10.65.

Example 74

The synthetic method is the same as described for the synthesis of (4S)-*N*-(3-{4-[3-(acetylamino)phenyl]-1-piperidinyl}propyl)-4-(3,5-difluorophenyl)-2-oxo-1,3-oxazolidine-3-carboxamide.

N-(3-{4-[3-(ACETYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-4-(3,4-DIFLUOROPHENYL)-5,5-DIMETHYL-2-OXO-1,3-OXAZOLIDINE-3-CARBOXAMIDE: 19.6 mg (68% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (t, 1H, J=5.9 Hz), 7.41 (d, 1H, J=8.8 Hz), 7.33 (s, 1H), 7.27-7.14 (m, 2H), 7.02-6.88 (m, 3H), 5.04 (s, 1H), 3.34 (qm, 2H, J=6.3 Hz), 3.02 (dm, 2H, J=10.9 Hz), 2.53-2.38 (m, 3H), 2.16 (s, 3H), 2.07-1.96 (m, 2H), 1.87-1.69 (m, 6H), 1.62 (s, 3H), 1.02 (s, 3H); ESMS m/e: 529.3 $(M + H)^+$; Anal. Calc. for $C_{28}H_{34}F_2N_4O_4$: C, 63.62; H, 6.48; N, 10.60. Found: C, 63.15; H, 6.27; N, 10.48.

Example 75

The synthetic method is the same as described for the synthesis of (4S)-*N*-(3-{4-[3-(acetylamino)phenyl]-1-

piperidinyl}propyl)-4- (3,5-difluorophenyl)-2-oxo-1,3-oxazolidine-3-carboxamide.

(4S,5R)-N-(3-{4-[3-(ACETYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-4-(3,4-DIFLUOROPHENYL)-5-METHYL-2-OXO-1,3-OXAZOLIDINE-3-CARBOXAMIDE: 20.5 mg (74% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (t, 1H, J=5.5 Hz), 7.40 (d, 1H, J=7.8 Hz), 7.37-6.89 (m, 6H), 5.35 (d, 1H, J=7.5 Hz), 5.02-4.93 (m, 1H), 3.41-3.25 (m, 2H), 3.02 (d, 2H, J=10.8 Hz), 2.53-2.37 (m, 3H), 2.16 (s, 3H), 2.07 (m, 2H), 1.89-1.68 (m, 6H), 1.04 (d, 3H, J=6.4 Hz); ESMS m/e: 515.3 $(M + H)^+$; Anal. Calc. for $C_{27}H_{32}F_2N_4O_4+0.5H_2O$: C, 61.94; H, 6.35; N, 10.70. Found: C, 61.90; H, 6.13; N, 10.64.

Example 76

The synthetic method is the same as described for the synthesis of (4S)-*N*-(3-{4-[3-(acetylamino)phenyl]-1-piperidinyl}propyl)-4-(3,5-difluorophenyl)-2-oxo-1,3-oxazolidine-3-carboxamide.

N-(3-{4-[3-(ACETYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-4-(4-FLUOROBENZYL)-2-OXO-1,3-OXAZOLIDINE-3-CARBOXAMIDE: 17.4 mg (65% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (t, 1H, J=5.6 Hz), 7.4 (d, 1H, J=7.2 Hz), 7.34 (s, 1H), 7.28-7.14 (m, 3H), 7.05-6.95 (m, 3H), 4.69-4.60 (m, 1H), 4.26 (t, 1H, J=8.8 Hz), 4.15 (dd, 1H, J=3.2, 9 Hz), 3.43 (q, 2H, J=6.2 Hz), 3.3 (dm 1H, J=13.6 Hz), 3.04 (dm, 2H, J=11 Hz), 2.87 (dd, 1H, J=9.3, 14.4 Hz), 2.53-2.42 (m, 3H), 2.16 (s, 3H), 2.09-1.99 (m, 2H), 1.87-1.65 (m, 6H); ESMS m/e: 497.3 $(M + H)^+$; Anal. Calc. for $C_{27}H_{33}FN_4O_4+0.5H_2O$: C, 64.14; H, 6.78; N, 11.08. Found: C, 64.26; H, 6.39; N, 11.12.

Example 77

2-METHYL-N-(3-{1-[(3R)-3-(2-NITROPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: A mixture of N-(3-{1-[(3S)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 2-nitrophenol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (2.37 mg, 34.5% yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, 1H), 7.90 (m, 1H), 7.45 (m 1H), 7.30-7.20 (m, 5H), 7.20 (m, 2H), 6.98 (m, 2H), 6.89 (apparent d, 1H, J=7.7 Hz), 5.62 (apparent dd, 1H, J=4.1, 8.9 Hz), 3.10 (m, 2H), 2.60 (m, 2H), 2.53 (m, 2H), 2.30-2.10 (m, 6H), 1.90 (m, 2H), 1.25 (d, 6H, overlapped); ESMS *m/e*: 502.3 $(M + H)^+$.

Example 78

N-(3-{1-[(3S)-3-([1,1'-BIPHENYL]-4-YLOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 4-phenylphenol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (3.00 mg, 41.2% yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.48 (m, 2H), 7.40-7.30 (m, 8H), 7.30-7.25 (m, 4H), 6.97 (apparent d, 1H, J=7.6 Hz), 6.91 (apparent d, 2H, J=8.7

Hz), 5.34 (apparent dd, 1H, J=4.4, 8.0 Hz), 3.40 (m, 2H), 2.98 (m, 2H), 2.53 (apparent sept, partially hidden, 1H, J=8.1 Hz), 2.44 (m, 1H), 2.30-2.10 (m, 6H), 1.93 (d, 2H), 1.26 (d, 6H, J=6.9 Hz); ESMS *m/e*: 533.4 (M + H)$^+$.

Example 79

2-METHYL-N-(3-{1-[(3R)-3-(3-NITROPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: A mixture of N-(3-{1-[(3S)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 3-nitrophenol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (2.80 mg, 40.8 % yield) as a thick oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (dm, 1H), 7.71 (t, 1H, J=1.8 Hz), 7.50-7.40 (m, 2H), 7.40-7.25 (m, 7H), 7.17 (apparent dd, 1H, J=2.4, 8.2), 6.97 (apparent d, 1H, J=7.7 Hz), 5.45 (apparent dd, 1H, J=5.0, 8.1 Hz), 3.45 (m, 2H), 2.89 (m, 2H), 2.53 (apparent sept, partially hidden, 2H, J=8.3 Hz), 2.30-2.10 (m, 6H), 1.92 (m, 2H), 1.25 (d, 6H, J=6.8 Hz); ESMS *m/e*: 502.3 (M + H)$^+$.

Example 80

N-(3-{1-[(3S)-3-(2-ETHOXYPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 2-ethoxyphenol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg,

0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (1.16 mg, 15.5% yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.52 (s, 1H), 7.40-7.33 (m, 4H), 7.30-7.20 (m, 3H), 6.97 (apparent d, 1H, J=7.7 Hz), 6.88 (m, 2H), 6.68 (m, 2H), 5.21 (m, 1H), 4.11 (q, 2H, J=7.3 Hz), 3.37 (m, 2H), 2.71 (m, 2H), 2.53 (apparent sept, partially hidden, 2H, J=7.6 Hz), 2.30-2.10 (m, 6H), 1.89 (m, 2H), 1.49 (t, 3H, J=7.3 Hz), 1.25 (d, 6H, J=6.8 Hz); ESMS *m/e*: 501.4 $(M + H)^+$.

Example 81

2-METHYL-N-(3-{1-[(3S)-3-(1-NAPHTHYLOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: A mixture of N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.20 mg, 0.0137 mmol), 1-naphthol (100 mg), triphenylphosphine (30.0 mg, 0.115 mmol) and diethyl azodicarboxylate (7.42 mg, 0.0426 mmol) in THF (0.50 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (4.30 mg, 66.2% yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.72 (d, 1H, J=8.5 Hz), 7.59 (d, 1H, J=8.5 Hz), 7.5 (m, 2H), 7.45-7.30 (m, 6H), 7.25 (m, 3H), 7.17 (apparent dd, 1H, J=2.6, 9.0 Hz), 7.01 (apparent d, 1H, J=2.6 Hz), 6.97 (apparent d, 1H, J=7.9 Hz), 5.46 (apparent dd, 1H, J=4.5, 8.1 Hz), 3.12 (m, 2H), 2.61 (m, 2H), 2.53 (apparent sept, partially hidden, 2H, J=7.9 Hz), 2.30-2.10 (m, 6H), 1.90 (m, 2H), 1.25 (d, 6H, J=7.3 Hz, overlapped); ESMS *m/e*: 507.2 $(M + H)^+$.

Example 82

N-(3-{1-[(3S)-3-(1,3-DIOXO-1,3-DIHYDRO-2H-ISOINDOL-2-YL)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE

Step 1:

2-[(1*S*)-3-CHLORO-1-PHENYLPROPYL]-1H-ISOINDOLE-1,3(2H)-DIONE: According to the general procedure described in Srebnik, M.; Ramachandran, P.V.; Brown, H.C. *J. Org. Chem.* 1988, *53*, 2916-2920, a mixture of phthalimide (0.147 g, 1.0 mmol), (R)-(+)-3-chloro-phenyl-1-propanol (0.171 g, 1.0 mmol), triphenylphosphine (0.262 g, 1.0 mmol) and diethyl azodicarboxylate (0.174 g, 1.0 mmol) in 5.0 mL of THF was stirred at room temperature for 24 h. The reaction mixture was concentrated *in vacuo*. The residue was washed with pentane (x3) and the combined pentane extracts were concentrated and chromatographed (silica with hexanes-EtOAc 8:1 as the eluent) to give the desired product (0.121 g, 50.2 %) as a yellow solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (apparent dd, 2H, J=2.9 Hz), 7.70 (apparent dd, 2H, J=2.9 Hz), 7.56 (m, 2H), 7.39-7.27 (m, 3H), 5.64 (apparent dd, 1H, J=7.0, 9.2 Hz), 3.57 (m, 2H), 3.05 (m, 1H), 2.82 (apparent sept, 1H, J=7.0 Hz); ESMS *m/e*: 300.13 $(M+H)^+$.

Step 2:

N-(3-{1-[(3S)-3-(1,3-DIOXO-1,3-DIHYDRO-2H-ISOINDOL-2-YL)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of potassium carbonate

(29.2 mg, 0.211 mmol), sodium iodide (47.5 mg, 0.317 mmol), 2-methyl-N-[3-(4-piperidinyl)phenyl]propanamide (51.8 mg, 0.211 mmol) 2-[(1*S*)-3-chloro-1-phenylpropyl]-1*H*-isoindole-1,3(2*H*)-dione (63.1 mg, 0.211 mmol) in DMF (5.0 mL) was stirred at 100 °C for 3 hrs, at which time TLC indicated that the reaction was complete. The reaction mixture was poured into water (50 mL) and the aqueous layer was extracted with methylene chloride (3x30 mL). The combined organic extracts were washed with brine (30 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by Prep-TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] to give the desired product (74.1 mg, 77.1 %) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (apparent dd, 2H, J=2.9 Hz), 7.69 (apparent dd, 2H, J=2.9 Hz), 7.56 (apparent dt, 3H, J=2.9, 7.3 Hz), 7.33 (m, 4H), 7.21 (t, 1H, J=7.8 Hz), 7.09 (s, 1H), 6.81 (apparent d, 1H, J=7.8 Hz), 5.49 (apparent dd, 1H, J=5.5, 9.5 Hz), 2.98 (d, 1H, J=9.5 Hz), 2.87 (m, 2H), 2.50 (apparent sept, 1H, J=6.7 Hz), 2.40-2.35 (m, 4H), 1.94 (m, 2H), 1.70-1.50 (m, 4H), 1.25 (d, 6H, J=7.9 Hz); ESMS *m/e*: 510.37 $(M+H)^+$.

Example 83

2-METHYL-N-(3-{1-[(3*S*)-3-(4-PHENOXYPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE

STEP 1:

4-{[(1*S*)-3-CHLORO-1-PHENYLPROPYL]OXY}-(4-PHENOXY)BENZENE: A mixture of 4-phenoxyphenol (1.86 g, 10.0 mmol), (R)-(-)-3-chloro-phenyl-1-propanol (1.70 g, 10.0 mmol), triphenylphosphine (2.62 g, 10.0 mmol),

diethyl azodicarboxylate (1.57 mL, 10.0 mmol) in 5.0 mL of THF was stirred at room temperature for 24 h. The reaction mixture was concentrated *in vacuo*. The residue was washed with pentane (x3) and the combined pentane extracts were concentrated and chromatographed (silica with hexanes-EtOAc 97:3 as the eluent) to give the desired product as a thick oil which solidified on standing (2.51 g, 75.7 %): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.4-7.23 (m, 7H), 7.03 (apparent t, 1H, J=7.3 Hz), 6.91 (apparent dm, 2H, J=7.8 Hz), 6.93 (apparent q, 4H, J=7.8 Hz), 5.31 (apparent dd, 1H, J=4.5, 8.6 Hz), 3.82 (m, 1H), 3.62 (apparent quintet, 1H, J=5.6 Hz), 2.47 (m, 1H), 2.20 (m, 1H).

Step 2:

2-METHYL-N-(3-{1-[(3*S*)-3-(4-PHENOXYPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: A mixture of 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (65.5 mg, 0.266 mmol), 4-{[(1*S*)-3-chloro-1-phenylpropyl]oxy}-(4-phenoxy)benzene (0.100 mg, 0.296 mmol), potassium carbonate (40.9 mg, 0.296 mmol) and sodium iodide (67.0 mg, 0.444 mmol) in DMF (1.0 mL) at 100 °C for 3 hours. The reaction mixture was poured into water (50 mL) and the aqueous layer was extracted with methylene chloride (3x30 mL). The combined organic extracts were washed with brine (30 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by Prep-TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] to give the desired product (0.109 g, 74.6 %) as a thick oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.40-7.30 (m, 4H), 7.20-7.10 (m, 6 H), 7.09 (s, 1H), 6.99 (apparent d, 1H,

J=7.8 Hz), 6.98 (apparent t, 1H, J=7.8 Hz), 6.93 (apparent d, 2H, J=8.4 Hz), 6.84 (m, 2H), 5.20 (apparent dd, 1H, J=4.4, 8.5 Hz), 3.03 (m, 2H), 2.51 (m, 4H), 2.24 (apparent sept, 1H, J=7.8 Hz), 2.20-2.10 (m, 3H), 1.90 (m, 4H), 1.25 (d, 6H, J=7.9 Hz); ESMS m/e: 549.41 $(M+H)^+$; Anal. Calc. for $C_{36}H_{40}N_2O_3$: C, 78.80; H, 7.35; N, 5.11. Found: C, 78.58; H, 7.48; N, 5.09.

Example 84

***N*-(4-{1-[(3*R*)-3-(3,4-DIMETHOXYPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE**

Step 1:

1-[(3*R*)-3-(3,4-DIMETHOXYPHENOXY)-3-PHENYLPROPYL]-4-(4-NITROPHENYL)-1,2,3,6-TETRAHYDROPYRIDINE: A mixture of potassium carbonate (24.0 mg, 0.174 mmol), sodium iodide (39.0 mg, 0.260 mmol), 4-(4-nitrophenyl)-1,2,3,6-tetrahydropyridine (35.4 mg, 0.174 mmol) and 4-{[(1*R*)-3-chloro-1-phenylpropyl]oxy}-1,2-dimethoxybenzene (53.4 mg, 0.174 mmol) in DMF (0.5 mL) was stirred at 100 °C for 3 hrs, at which time TLC indicated that the reaction was complete. The reaction mixture was poured into water (5.0 mL) and the aqueous layer was extracted with methylene chloride (3x30 mL). The combined organic extracts were washed with brine (30 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by Prep-TLC plates [1:1=hexane:ethyl acetate with 1% NH_3] afforded the product (63.1 mg, 76.6 %) as a yellow oil. The product was used in next reaction without further purification.

Step 2:

4-{1-[(3R)-3-(3,4-DIMETHOXYPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}ANILINE: A 25-mL RB flask, equipped with a hydrogen-filled balloon, was charged with 1-[(3R)-3-(3,4-dimethoxyphenoxy)-3-phenylpropyl]-4-(4-nitrophenyl)-1,2,3,6-tetrahydropyridine (63.0 mg, 0.133 mmol), palladium on carbon (5.0 mol-eq%, 0.00665 mmol, 7.04 mg) and ethanol (2.0 mL) at room temperature. After 1 hr the reaction mixture was filtered through a plug of Celite 545 and concentrated under reduced pressure. The crude product (54.1 mg, 89.4%) was used in next reaction without further purification.

STEP 3:

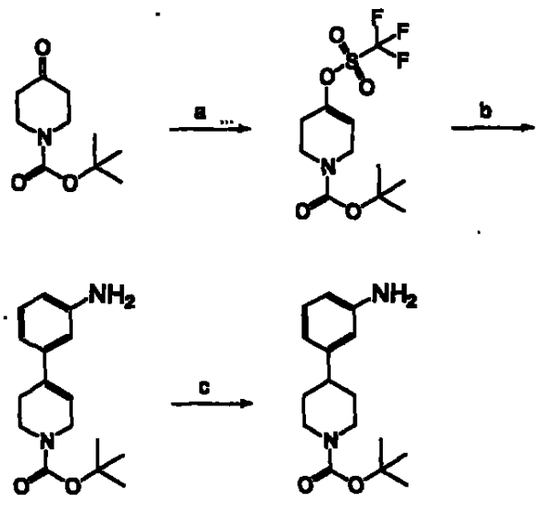
N-(4-{1-[(3R)-3-(3,4-DIMETHOXYPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of 4-{1-[(3R)-3-(3,4-dimethoxyphenoxy)-3-phenylpropyl]-4-piperidinyl}aniline (5.31 mg, 0.0119 mmol), isobutyryl chloride (2.08 mg, 0.019 mmol), N,N-diisopropylethylamine (8.40 mg, 0.0650 mmol) in methylene chloride (1.0 mL) was stirred at room temperature for 24 hours. The reaction mixture was concentrated and chromatographed using a preparative TLC plate [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] to give the product (3.5 mg, 56.5 %) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, 1H, J=8.6 Hz), 7.30-7.20 (m, 4H), 7.20(m, 1H), 7.11 (d, 2H, J=8.6 Hz), 7.04 (s, 1H), 6.57 (d, 1H, J=8.3 Hz), 6.44 (d, 1H, J=2.6 Hz), 6.22 (dd, 1H, J=2.6, 8.3 Hz), 5.09 (apparent dd, 1H, J=4.4, 8.1 Hz), 3.72 (s, 3H), 3.70 (s, 3H), 3.08 (m, 2H), 2.57 (m, 2 H), 2.43 (apparent sept, partially hidden, 2H, J=6.8 Hz),

2.30-2.10 (m, 6H), 1.80 (m, 2H), 1.25 (d, 6H, J=7.9 Hz); ESMS *m/e*: 517.3 $(M+H)^+$.

Example 85

N-(3-{1-[(3S)-3-(3-ACETYLPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Into a 25-mL RB-flask was added triphenylphosphine (9.80 mg, 0.0375 mmol), diethyl azodicarboxylate (5.22 mg, 0.0300 mmol), N-(3-{1-[(3R)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (9.53 mg, 0.0250 mmol), 3-hydroxyacetophenone (100 mg) and THF (1.0 mL) at room temperature. The reaction mixture was stirred at room temperature overnight (16 hrs). The solvent was removed under reduced pressure and the residue was purified by preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] to afford the desired product (2.73 mg, 39.9%) as a thick oil: ^1H NMR ($CDCl_3$) δ 7.70-7.64 (m, 2H), 7.54 (m, 2H), 7.49-7.44 (m, 6H), 7.25 (m, 1H), 7.05 (d, 1H, J=8.3 Hz), 6.96 (apparent d, 1H, J=7.7 Hz), 5.34 (apparent dd, 1H, J=4.8, 8.2 Hz), 3.15 (m, 2H), 2.67 (m, 2H), 2.52 (s, 3H), 2.53 (apparent sept, partially hidden, 2H, J=7.6 Hz), 2.30-2.10 (m, 6H), 1.89 (m, 2H), 1.25 (d, 6H, J=6.9 Hz); ESMS *m/e*: 499.4 $(M + H)^+$.

Scheme A. Synthesis of tert-Butyl 4-(3-aminophenyl)-1-piperidinecarboxylate

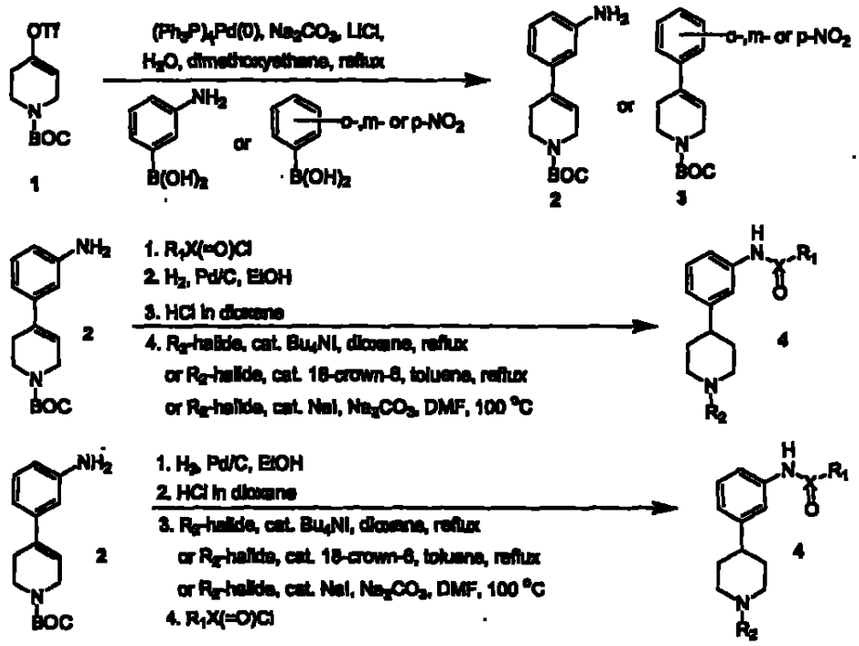


a. n-BuLi, diisopropylamine, THF, $PhN(Tf)_2$, -78 °C to room temperature, 81%

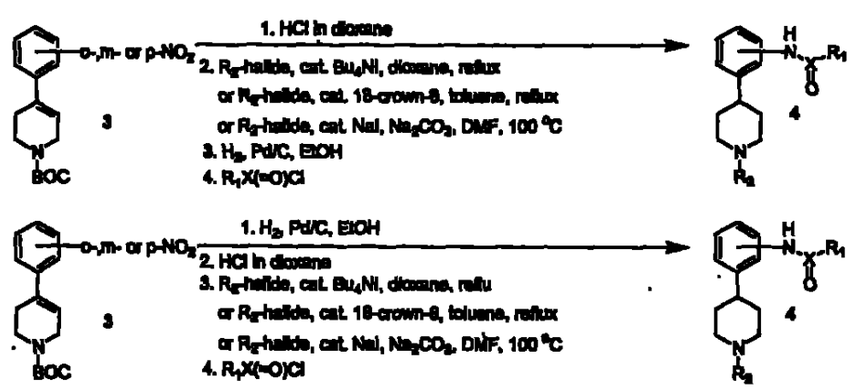
b. 3-aminophenylboronic acid hemisulfate, LiCl, tetrakis-triphenylphosphine -palladium (0), Na_2CO_3, DME-H_2O, reflux, 81%

c. 10% Pd/C, ethanol, H_2, room temperature, balloon method, 84%

Scheme B1. A General Synthesis of the MCH Antagonists



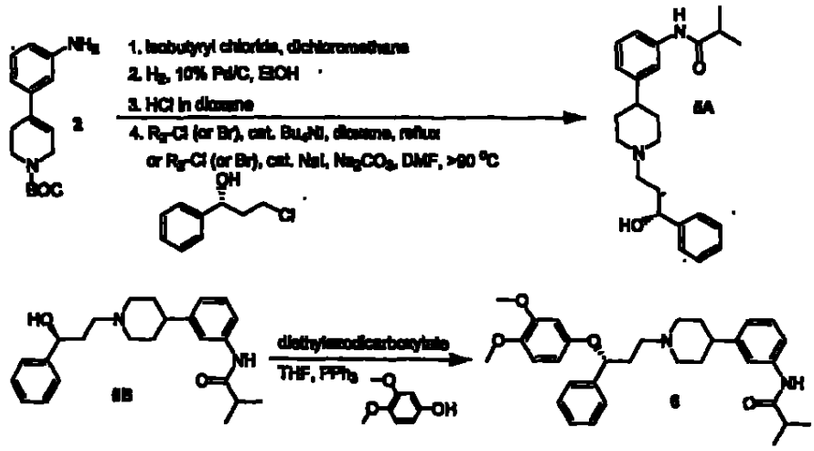
Scheme B2. A General Synthesis of the MCH Antagonists



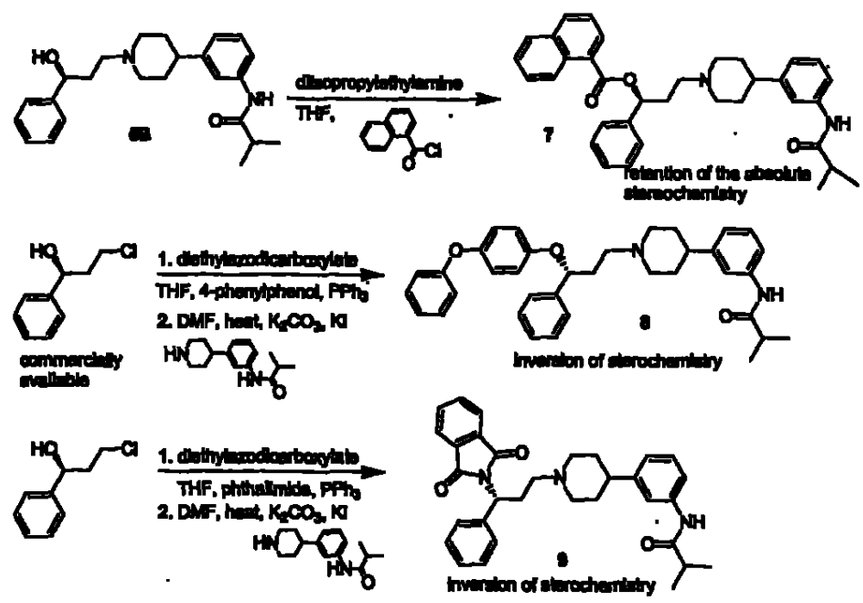
X = C, S(=O) halide = Cl, Br

5

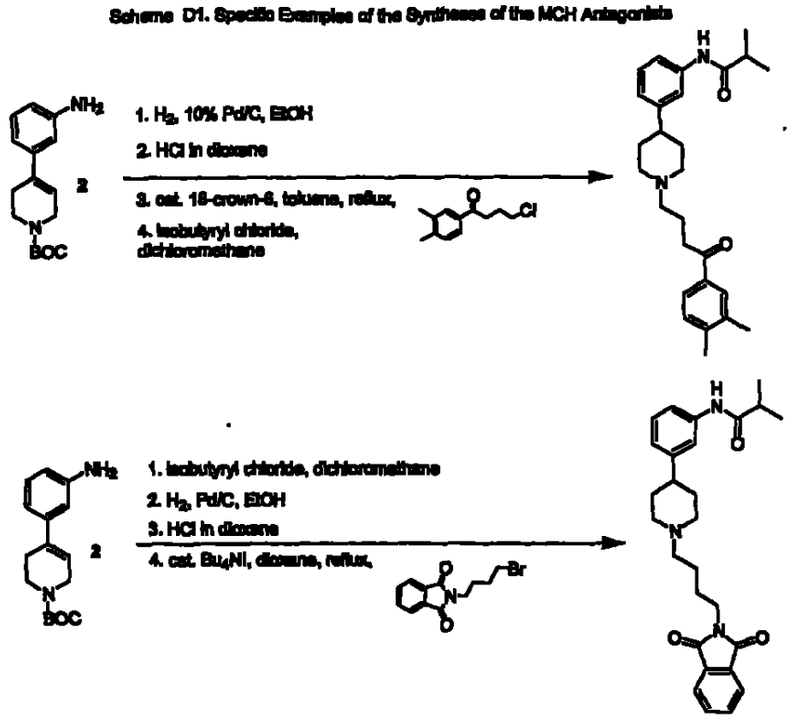
Scheme C1. Specific Examples of the Syntheses of the MCH Antagonists



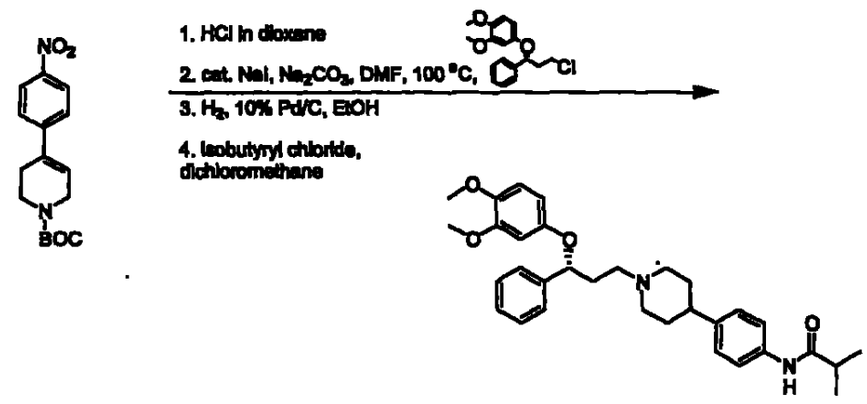
Scheme C2. Specific Examples of the Syntheses of the MCH Antagonists



Scheme D1. Specific Examples of the Syntheses of the MCH Antagonists

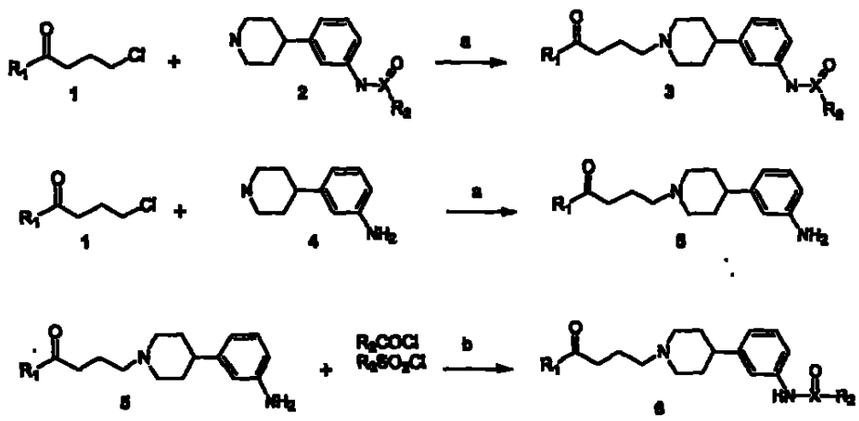


Scheme D2. Specific Examples of the Syntheses of the MCH Antagonists



5

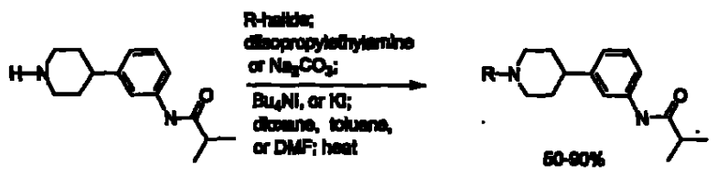
Scheme E: General Synthesis of the MCH Antagonists



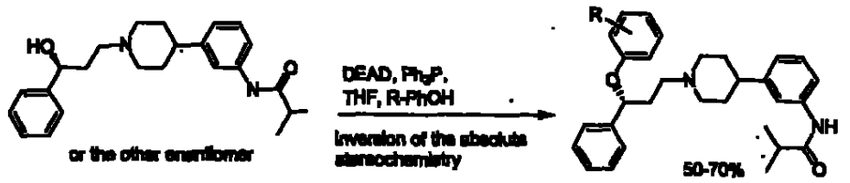
a. dioxane, diisopropylethylamine, Bu_4NI, reflux
or DMF, KI, Na_2CO_3, 90-100 °C
or toluene, 110 °C, 18-crown-6
b. diisopyropylethylamine, dichloromethane

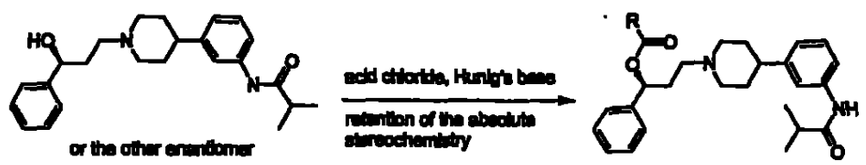
X = S(=O), C
R_1 = Aromatic, substituted aromatic or heterocyclic
R_2 = aliphatic oraromatic

Scheme F. General Synthesis of the MCH Antagonists



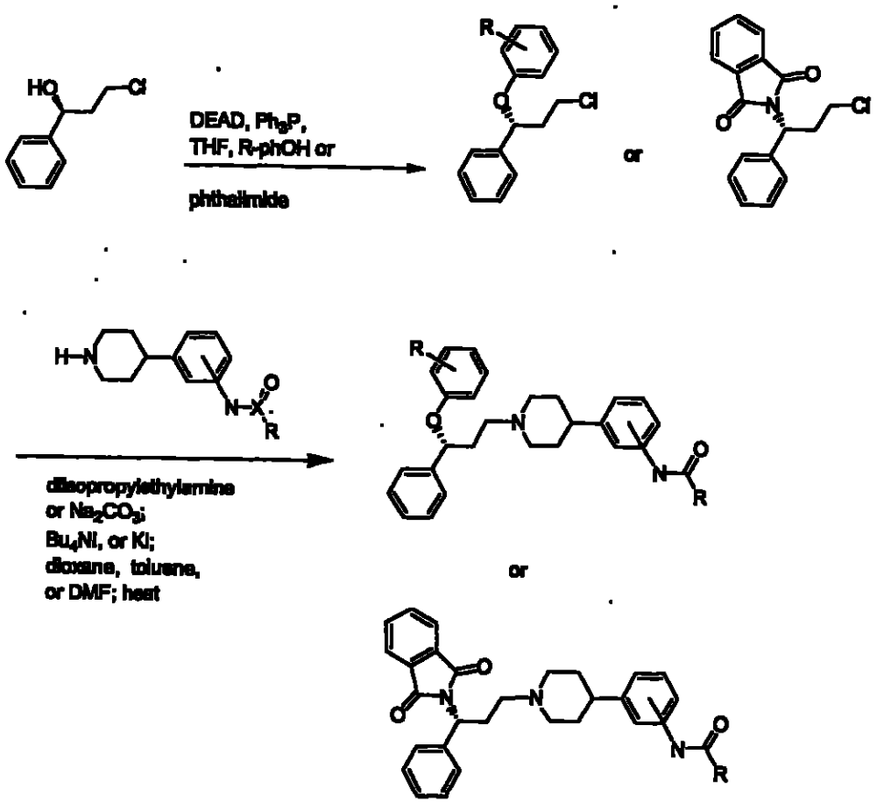
If R = $(CH_2)_nCHOH$-Ar, then,





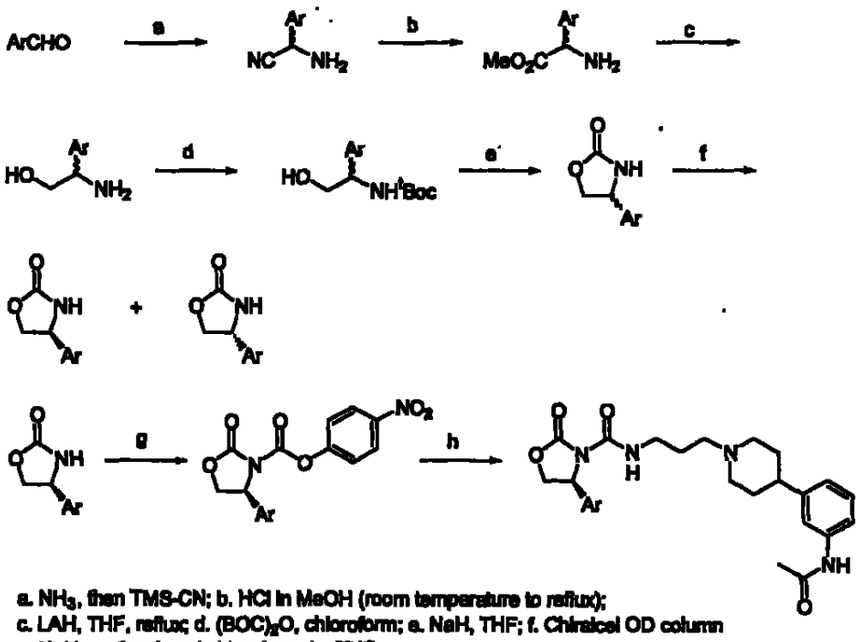
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Scheme G. General Synthesis of the MCH Antagonists



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Scheme H: Synthesis of Oxazolidinones

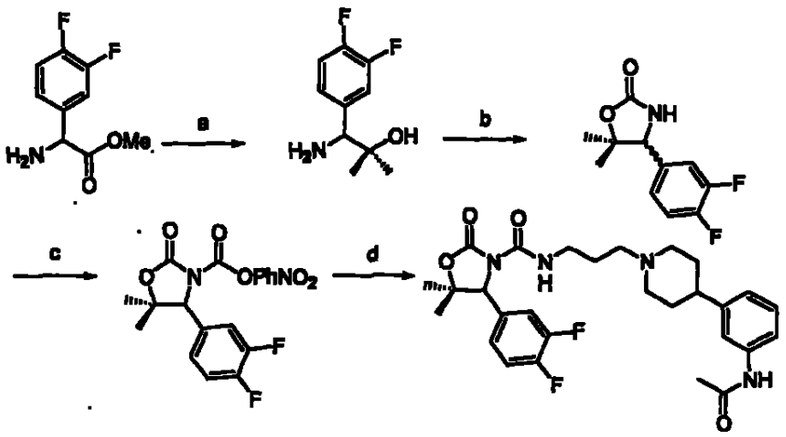


a. NH_3, then TMS-CN; b. HCl in MeOH (room temperature to reflux);
c. LAH, THF, reflux; d. $(BOC)_2O$, chloroform; e. NaH, THF; f. Chiralcel OD column
g. NaH, p-nitrophenyl chloroformate, THF;
h. an amine such as N-[3-[1-(3-aminopropyl)-4-piperidinyl]phenyl]acetamide

Ar = 3,4-difluorophenyl, 3,5-difluorophenyl or 3,4,5-trifluorophenyl

5

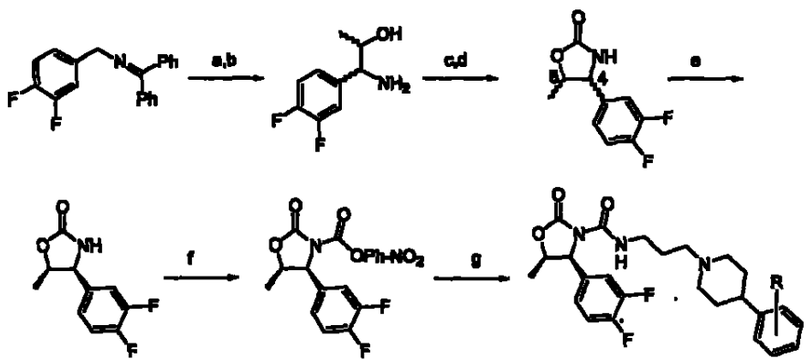
Scheme I: Synthesis of gem-Dialkyl Substituted Oxazolidinones



a. methyl magnesium bromide, THF; b. N,N-carbonyldiimidazole, DCM; c. NaH, THF, p-nitrophenylchloroformate; d. an amine such as N-[3-[1-(3-aminopropyl)-4-piperidinyl]phenyl]acetamide

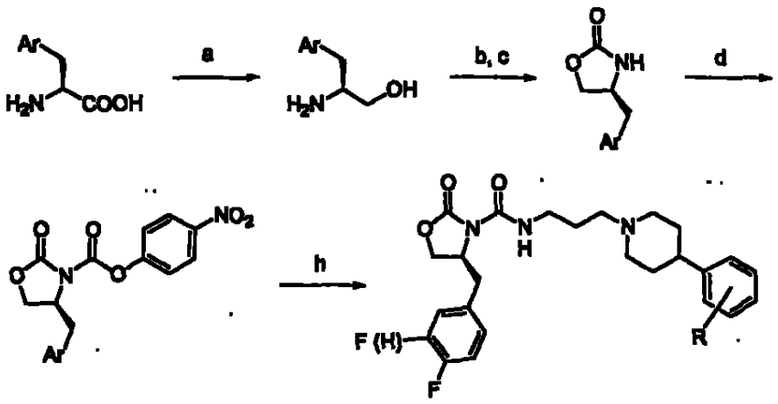
5

Scheme J: Synthesis and Chiral Resolution of Oxazolidinones



[a] (a) t-BuLi, THF, RCHO (b) $CH_3ONH_2.HCl$, MsOH, 60-68% over 2 steps (c) Boc_2O, $CHCl_3$, >90% (d) NaH,THF, 76-82% (e) separate diastereomers by column chromatography and separate enantiomers by chiral phase HPLC, 10-16% (f) n-BuLi, THF, 4-nitrophenylchloroformate, ~75%
(g) THF, >80%, an amine such as N-[3-[1-(3-aminopropyl)-4-piperidinyl]phenyl]acetamide

Scheme K: Synthesis Oxazolidinones from Amino Acids

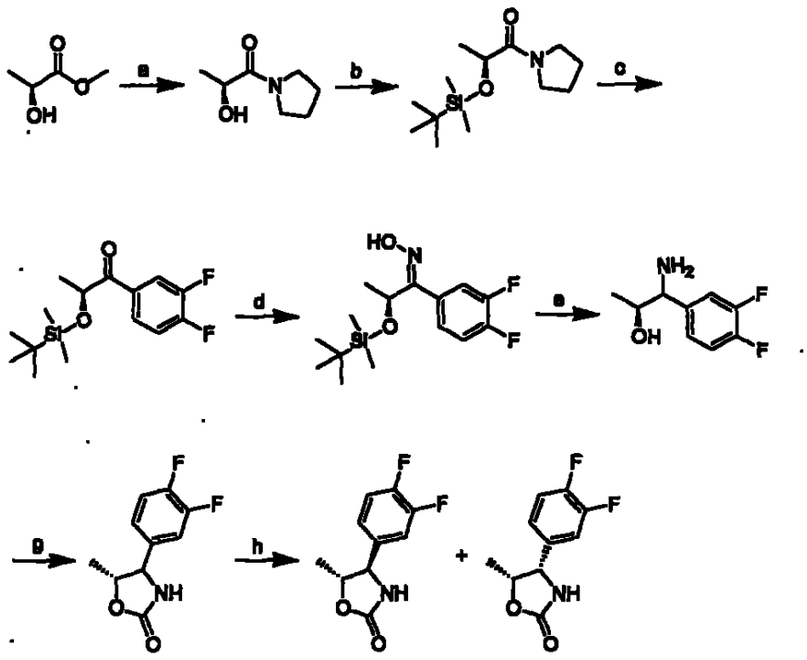


a. LAH, THF; b. $(BOC)_2O$, $CHCl_3$; c. NaH, THF; d. p-nitrophenylchloroformate, NaH, THF; h. an amine such as N-(3-[1-(3-aminopropyl)-4-piperidinyl]phenyl)acetamide

Ar = aromatic such as 4-fluorophenyl or 3,4-difluorophenyl

5

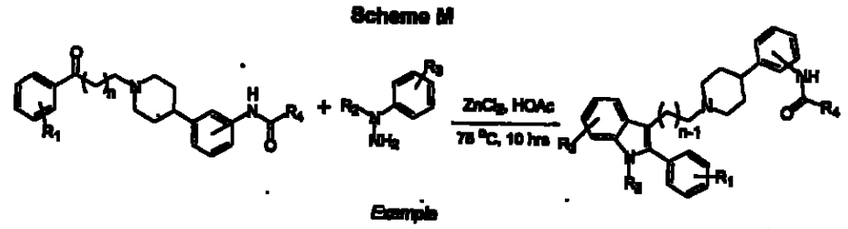
Scheme L: Determination of the Absolute Stereochemistry of the Di-Substituted Oxazolidinones Using Lactic Acid Derivatives



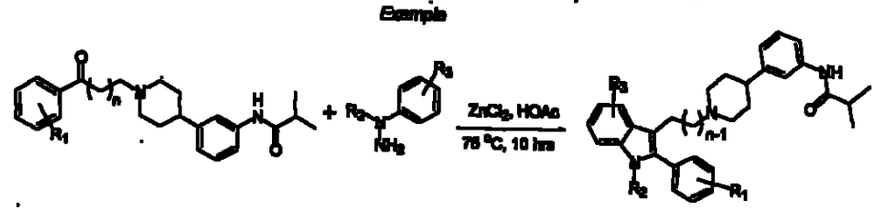
a. pyrrolidine, methanol, heat; b. t-butyldimethylsilyl chloride; c. LAH, ether, reflux
d. $(BOC)_2O$, chloroform; e. NaH, THF; h. silica gel chromatography

For more details, See: Lagu, B.; Wetzel, J. M.; Forray, C.; Patane, M. A.; Bock, M. G. "Determination of the Relative and Absolute Stereochemistry of a Potent α1A Selective Adrenoceptor Antagonist" Bioorg. Med. Chem. Lett. 2000, 10, 2705.

Scheme M

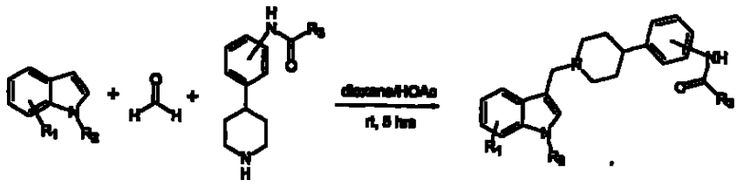


Example

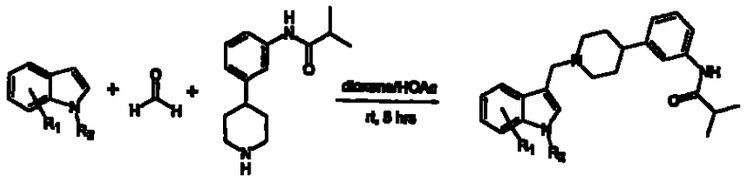


n=2, R1=H, R2=Ph, R3=H
n=5, R1=H, R2=H, R3=6-OMe
n=1, R1=H, R2=Ph, R3=H
n=4, R1=H, R2=H, R3=6-OMe

Scheme N

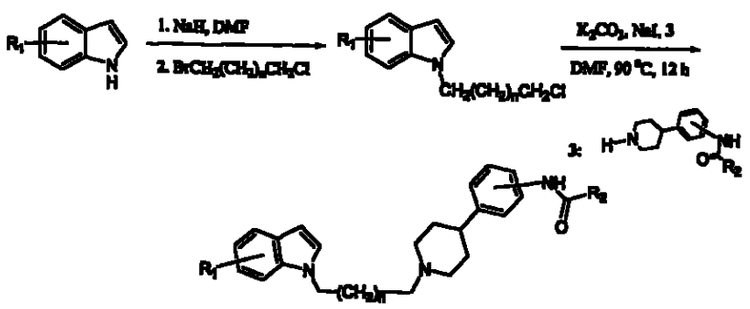


Example

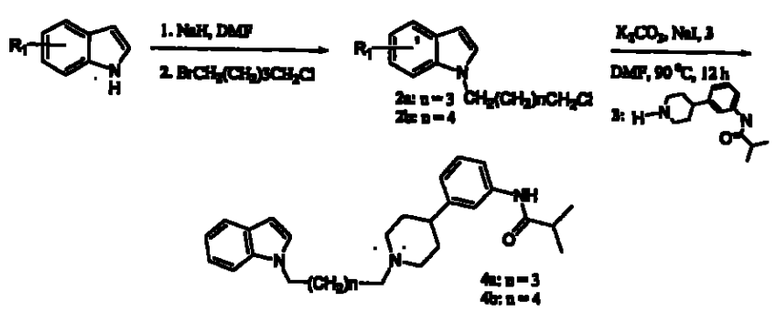


R1=6-Cl, R2=H
R1=H, R2=4'-tolyl

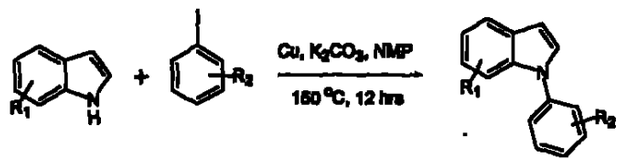
Scheme P



Example

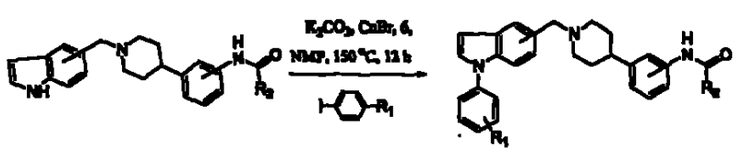


Scheme O

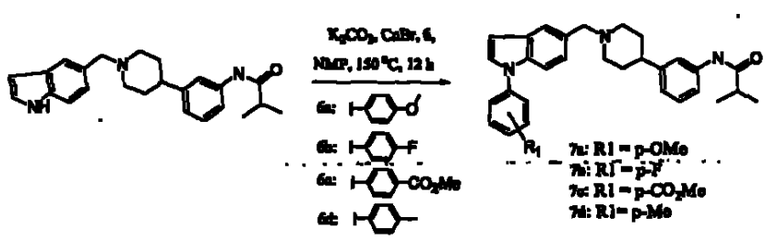


R1=H, R2=4'-Me

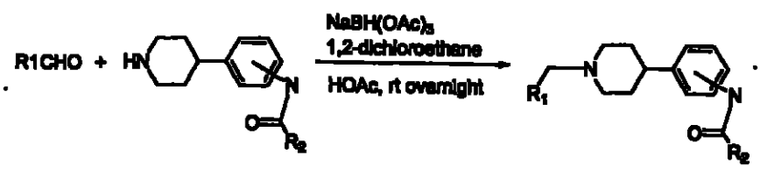
Scheme Q



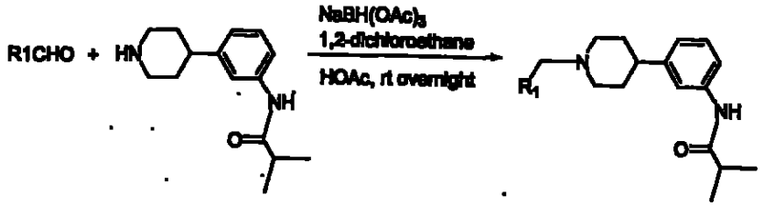
Example



Scheme R



Example



EXPERIMENTAL SECTION

The following additional abbreviations are used: HOAc, acetic acid; DMF, *N*,*N*-dimethylformamide; EtOAc, ethyl acetate; MeOH, methanol; NMP, 1-methyl-2-pyrrolidinone; TEA, triethylamine; THF, tetrahydrofuran; All solvent ratios are volume/volume unless stated otherwise.

1-(4-METHYLPHENYL)1H-INDOLE: A mixture of 1-*H*-indole (58.5 mg, 0.500 mmol), 1-(iodo)-4-methylbenzene (0.218 g, 1.00 mmol), copper powder (32.0 mg, 0.500 mmol), and K_2CO_3 (0.138 g, 1.00 mmol) in 1-methyl-2-pyrrolidinone (1 mL) was heated at 150 °C for 12 h under argon. The resulting mixture was diluted with H_2O (6 mL). The aqueous layer was extracted with CH_2Cl_2 (3 X 10 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, and concentrated in vacuo. The residue was purified by preparative TLC using EtOAc/hexane (1:4) to give the desired product (82 mg, 79%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, 1H, *J* = 7.7 Hz), 7.52 (d, 1H, *J* = 7.4 Hz), 7.38 (d, 2H, *J* = 8.4 Hz), 7.34-7.29 (m, 3H), 7.21 (t, 1H, *J* = 7.0 Hz), 7.15 (t, 1H, *J* = 7.0 Hz), 6.66 (d, 1H, 3.3 Hz), 2.43 (s, 3H); ESMS *m/e*: 208.0 $(M + H)^+$.

Example 86

N-(3-{1-[(6-CHLORO-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A solution of 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (0.369 g, 1.50 mmol) and 37 wt % aqueous formaldehyde (30.0 mg, 1.50 mmol) in 1 mL of HOAc:dioxane (1:4) was added to 6-chloro-1-*H*-indole (0.152 g, 1.00 mmol) and the reaction mixture was stirred for 12 h at room

temperature. The resulting mixture was diluted with H_2O (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 X 100 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by preparative TLC on silica using 5% of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product (79 mg, 42%). ^1H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.04 (s, 1H), 7.52 (t, 2H, *J* = 8.1 Hz), 7.35 (d, 2H, *J* = 13.3 Hz), 7.18 (t, 1H, *J* = 7.9 Hz), 7.09 (dd, 1H, *J* = 1.9, 8.5 Hz), 6.85 (d, 1H, *J* = 7.4 Hz), 5.18 (s, 1H), 4.01 (s, 2H), 2.55 (septet, 1H, *J* = 6.8 Hz), 2.48-2.34 (m, 3H), 2.08-1.95 (m, 4H), 1.78 (d, 2H, *J* = 12.8 Hz), 1.22 (d, 6H, *J* = 6.8 Hz); ESMS *m/e*: 410.1 $(M + H)^+$.

Example 87

2-METHYL-N-[3-(1-{[1-(4-METHYLPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: According to the procedure used for the synthesis of *N*-(3-{1-[(6-chloro-1*H*-indol-3-yl)methyl]-4-piperidinyl}phenyl)-2-methylpropanamide, 1-(4-methylphenyl)-1*H*-indole (0.207 g, 1.00 mmol) provided 2-methyl-*N*-[3-(1-{[1-(4-methylphenyl)-1*H*-indol-3-yl]methyl}-4-piperidinyl)phenyl]propanamide (0.441 g, 78%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.73 (d, 1H, *J* = 7.2 Hz), 7.58-7.51 (m, 2H), 7.43-7.36 (m, 3H), 7.35-7.29 (m, 3H), 7.26-7.15 (m, 3H), 6.89 (d, 1H, *J* = 7.7 Hz), 4.07 (s, 2H), 3.36 (d, 2H, *J* = 11.6 Hz), 2.59-2.39 (m, 6H), 2.55 (sept, 1H, *J* = 6.7 Hz), 2.10-1.98 (m, 2H), 1.83 (d, 2H, *J* = 12.9 Hz), 1.23 (d, 6H, *J* = 6.9 Hz); ESMS *m/e*: 466.2 $(M + H)^+$.

2-[(1*S*)-3-CHLORO-1-PHENYLPROPYL]-1*H*-ISOINDOLE-1,3(2*H*)-DIONE: Triphenylphosphine (5.25 g, 20.0 mmol) and diethyl azodicarboxylate (3.58 g, 20.0 mmol) were added to a solution of (1*R*)-3-chloro-1-phenyl-1-propanol (3.42 g, 20.0 mmol) and phthalimide (2.94 g, 20.0 mmol) in THF (100 mL). The reaction mixture was stirred for 4 h at room temperature. The solvent was removed under reduced pressure and the residue was triturated with pentane (3 X 50 mL). The combined pentane fractions were concentrated *in vacuo* and the crude product was purified by chromatography on silica using EtOAc/hexane (3:97) to give the desired product (4.40 g, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, 1H, J = 5.7 Hz), 7.81 (d, 1H, J = 5.5 Hz), 7.70 (d, 1H, J = 5.4 Hz), 7.69 (d, 1H, J = 5.8 Hz), 7.55 (d, 2H, J = 7.2 Hz), 7.38-7.28 (m, 3H), 5.64 (dd, 1H, J = 6.8, 9.2 Hz), 3.56 (t, 2H, J = 6.4 Hz), 3.11-3.02 (m, 1H), 2.85-2.75 (m, 1H); ESMS *m/e*: 300.1 $(M + H)^+$.

***N*-(3-{1-[(3*S*)-3-(1,3-DIOXO-1,3-DIHYDRO-2*H*-ISOINDOL-2-YL)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** A mixture of 2-[(1*S*)-3-chloro-1-phenylpropyl]-1*H*-isoindole-1,3(2*H*)-dione (4.50 g, 15.0 mmol), 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (4.26 g, 15.0 mmol), K_2CO_3 (4.16 g, 30.0 mmol), and NaI (3.40 g, 20.0 mmol) in DMF (40 mL) was stirred at 90 °C for 12 hrs. The reaction mixture was diluted with water (50 mL), extracted with CH_2Cl_2 (3 X 50 mL), and the combined organic extracts were washed with brine (50 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by chromatography on silica using 5% of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product (5:10 g, 74%). ^{1}H NMR (400 MHz,

$CDCl_3$) δ 7.83 (d, 1H, J = 5.5 Hz), 7.82 (d, 1H, J = 5.5 Hz), 7.71 (d, 1H, J = 5.5 Hz), 7.70 (d, 1H, J = 5.4 Hz), 7.56 (d, 2H, J = 7.1 Hz), 7.35-7.27 (m, 5H), 7.22 (t, 1H, J = 7.5 Hz), 7.09 (s, 1H), 6.81 (d, 1H, J = 7.8 Hz), 5.49 (dd, 1H, J = 5.5, 9.6 Hz), 2.97 (d, 1H, J = 10.1 Hz), 2.92-2.82 (m, 2H), 2.44 (sept, 1H, J = 6.7 Hz), 2.40-2.29 (m, 3H), 2.00-1.83 (m, 2H), 1.79-1.39 (m, 5H), 1.26 (d, 6H, J = 6.9 Hz); ESMS m/e: 510.4 $(M + H)^+$.

N-(3-{1-[(3*S*)-3-AMINO-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of *N*-(3-{1-[(3*S*)-3-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (4.60 g, 9.06 mmol) and hydrazine (3.62 g, 72.4 mmol) in ethanol (150 mL) was refluxed for 12 h. The resulting white precipitate was filtered out and the filtrate was concentrated under vacuum. The residue was washed with CH_2Cl_2/EtOAc (1:1, 3 X 50 mL) and the combined organic fractions were concentrated *in vacuo* to give the desired product (2.90 g, 95%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.39-7.30 (m, 6H), 7.29-7.19 (m, 2H), 6.95 (d, 1H, J = 7.2), 4.01 (t, 1H, J = 6.8 Hz), 3.04 (t, 2H, J = 10.6 Hz), 2.62-2.30 (m, 6H), 2.05-1.70 (m, 8H), 1.24 (d, 6H, J = 6.8 Hz); ESMS m/e: 380.4 $(M + H)^+$.

Example 88

2-METHYL-N-(3-{1-[(3S)-3-PHENYL-3-(PROPIONYLAMINO)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: According to the procedure used for the synthesis of *N*-(3-{1-[(3*S*)-3-(acetylamino)-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide, *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (11.0 mg, 0.0280 mmol) and propionyl chloride (3.80 mg, 0.0420 mmol) provided 2-methyl-*N*-(3-{1-[(3*S*)-3-phenyl-3-(propionylamino)propyl]-4-piperidinyl}phenyl)propanamide (12 mg, 97% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.59 (s, 1H), 7.40-7.20 (m, 7H), 6.96 (s, 1H), 5.19-5.12 (m, 1H), 3.18 (d, 1 H, *J* = 12.0 Hz), 2.99 (d, 1H, *J* = 10.4 Hz), 2.93-2.86 (m, 1H), 2.61-2.40 (m, 3H), 2.38-2.23 (m, 3H), 2.19-1.75 (m, 8H), 1.25 (d, 6H, *J* = 6.9 Hz), 1.22-1.08 (m, 3H); ESMS *m/e*: 436.4 $(M + H)^+$.

Example 89

***N*-{3-[1-((3*S*)-3-{[(4-FLUOROPHENYL)ACETYL]AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** A mixture of N-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (11.0 mg, 0.0280 mmol) and (4-fluorophenyl)acetyl chloride (7.20 mg, 0.0420 mmol) in THF (5 mL) was stirred at room temperature for 4 h. The solvent was removed under reduced pressure and the residue was purified by preparative TLC using Hexane:EtOAc (2:1) to give the desired product (13 mg, 90% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, 1H, *J* = 8.4 Hz), 7.59 (s, 1H), 7.31-6.93 (m, 13H), 5.13 (q, 1H, *J* = 6.0 Hz), 3.56 (s, 2H), 3.07 (d, 1H, *J* = 11.7 Hz), 2.91 (d, 1H, *J* = 11.0 Hz), 2.62-2.42 (m, 2H), 2.40-2.30 (m, 1H), 2.12-1.54 (m, 9H), 1.24 (d, 6H, *J* = 6.7 Hz); ESMS *m/e*: 515.3 $(M + H)^+$.

Example 90

N-(3-{1-[3-(1,2-DIPHENYL-1H-INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of 1,1-diphenylhydrazine hydrochloride (10.3 mg, 0.0470 mmol), 2-methyl-*N*-{3-[1-(5-oxo-5-phenylpentyl)-4-piperidinyl]phenyl}propanamide (14.7 mg, 0.0362 mmol), $ZnCl_2$ (14.85 mg, 0.109 mmol), and HOAc (0.5 mL) was heated for 4 h at 80 °C. The resulting crude mixture was diluted with water (10 mL), the aqueous layer was neutralized with saturated K_2CO_3 and extracted with CH_2Cl_2 (3 X 20 mL). The combined organic layers were concentrated *in vacuo* and the residue was purified by preparative TLC using 5% of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product *N*-(3-{1-[3-(1,2-diphenyl-1*H*-indol-3-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide (4.1 mg, 37%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.71-7.65 (m, 1H), 7.42 (d, 1H, *J* = 7.4 Hz), 7.39 (s, 1H), 7.36-7.15 (m, 15H), 6.94 (d, 1H, *J* = 7.8 Hz), 3.12 (d, 2H, *J* = 11.2 Hz), 2.90 (t, 2H, *J* = 7.8 Hz), 2.59-2.45 (m, 3H), 2.19-1.91 (m, 7H), 1.82 (d, 2H, *J* = 13.5 Hz), 1.24 (d, 6H, *J* = 6.9 Hz); ESMS *m/e*: 555.3 $(M + H)^+$.

Example 91

***N*-(3-{1-[3-(5-METHOXY-2-PHENYL-1*H*-INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** According to the procedure used for the synthesis of *N*-(3-{1-[3-(1,2-diphenyl-1*H*-indol-3-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide, 2-methyl-*N*-{3-[1-(5-oxo-5-phenylpentyl)-4-piperidinyl]phenyl}propanamide (15.6 mg, 38.2 mmol), and 1-(4-methoxyphenyl)hydrazine hydrochloride (8.00 mg,

0.0458 mmol) provided *N*-(3-{1-[3-(5-methoxy-2-phenyl-1*H*-indol-3-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide (3.9 mg, 20%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.55 (d, 2H, *J* = 7.4 Hz), 7.43-7.39 (m, 3H), 7.38-7.35 (m, 2H), 7.27-7.19 (m, 3H), 7.08 (d, 1H, *J* = 7.4 Hz), 6.94 (d, 1H, *J* = 7.6 Hz), 6.87 (dd, 1H, *J* = 4.0, 6.6 Hz), 3.88 (s, 3H), 3.80-3.69 (m, 1H), 2.99 (d, 2H, *J* = 11.7 Hz), 2.89 (t, 2H, *J* = 7.3), 2.55-2.39 (m, 4H), 2.02-1.88 (m, 3H), 1.82-1.68 (m, 4H), 1.24 (d, 6H, *J* = 6.9 Hz); ESMS *m/e*: 510.3 $(M + H)^+$.

Example 92

***N*-(3-{1-[4-(5-METHOXY-2-PHENYL-1*H*-INDOL-3-YL)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** According to the procedure used for the synthesis of *N*-(3-{1-[3-(1,2-diphenyl-1*H*-indol-3-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide, 2-methyl-*N*-{3-[1-(6-oxo-6-phenylhexyl)-4-piperidinyl]phenyl}propanamide (14.3 mg, 0.0339 mmol) and 1-(4-methoxyphenyl)hydrazine hydrochloride (7.10 mg, 0.0407 mmol) provided *N*-(3-{1-[4-(5-methoxy-2-phenyl-1*H*-indol-3-yl)butyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.8 mg, 33%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, 2H, *J* = 7.8 Hz), 7.61-7.15 (m, 11H), 6.97 (d, 1H, *J* = 7.0 Hz), 3.88 (s, 3H), 3.09 (d, 2H, *J* = 11.3 Hz), 2.99 (t, 2H, *J* = 7.0 Hz), 2.55-2.35 (m, 4H), 2.12-1.70 (m, 6H), 1.68-1.52 (m, 2H), 1.48-1.34 (m, 2H), 1.25 (d, 6H, *J* = 6.7 Hz); ESMS *m/e*: 524.3 $(M + H)^+$.

Example 93

2-METHYL-*N*-(3-{1-[(1-PHENYL-1*H*-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: According to the procedure used for the synthesis of *N*-(3-{1-[3-(1,2-

diphenyl-1*H*-indol-3-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide, *N*-{3-[1-(3,3-dimethoxypropyl)-4-piperidinyl]phenyl}-2-methylpropanamide (15.2 mg, 0.0436 mmol) and 1,1-diphenylhydrazine hydrochloride (11.6 mg, 0.0524 mmol) provided 2-methyl-*N*-(3-{1-[(1-phenyl-1*H*-indol-3-yl)methyl]-4-piperidinyl}phenyl)propanamide (11 mg, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, 1H, *J* = 7.8 Hz), 7.57 (d, 1H, *J* = 7.7 Hz), 7.54-7.47 (m, 4H), 7.43-7.32 (m, 4H), 7.25-7.16 (m, 4H), 6.95 (d, 1H, *J* = 7.8 Hz), 3.87 (s, 2H), 2.53-2.47 (m, 2H), 2.21 (dt, 2H, *J* = 3.0, 10.5 Hz), 2.12-1.77 (m, 6H), 1.24 (d, 6H, *J* = 6.9 Hz); ESMS *m/e*: 451.3 $(M + H)^+$.

Example 94

2-METHYL-*N*-(3-{1-[(4*E*)-4-PHENYL-4-(2-PYRIDINYLHYDRAZONO)BUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: According to the procedure used for the synthesis of *N*-(3-{1-[3-(1,2-diphenyl-1*H*-indol-3-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide, 2-methyl-*N*-{3-[1-(4-oxo-4-phenylbutyl)-4-piperidinyl]phenyl}propanamide (8.70 mg, 0.0223 mmol) and 2-hydrazinopyridine (2.92 mg, 0.0268 mmol) provided 2-methyl-*N*-(3-{1-[(4*E*)-4-phenyl-4-(2-pyridinylhydrazono)butyl]-4-piperidinyl}phenyl)propanamide (2.5 mg, 24%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, 1H, *J* = 8.6 Hz), 7.85 (d, 1H, *J* = 7.3 Hz), 7.64-7.27 (m, 9H), 7.09 (d, 1H, *J* = 8.0 Hz), 6.97 (d, 1H, *J* = 8.4 Hz), 6.73 (q, 1H, *J* = 6.6 Hz), 3.52-3.48 (m, 2H), 3.20-3.10 (m, 2H), 2.85-1.75 (m, 13H), 1.26 (d, 6H, *J* = 6.8 Hz); ESMS *m/e*: 484.4 $(M + H)^+$.

Example 95

***N*-(3-{1-[3-(5-METHOXY-1*H*-INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** According to the procedure used for the synthesis of *N*-(3-{1-[3-(1,2-diphenyl-1*H*-indol-3-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide, *N*-(3-{1-[4-(1,3-dioxolan-2-yl)butyl]-4-piperidinyl}phenyl)-2-methylpropanamide (23.5 mg, 0.0628 mmol) and 1-(4-methoxyphenyl)hydrazine hydrochloride (13.2 mg, 0.0774 mmol) provided *N*-(3-{1-[3-(5-methoxy-1*H*-indol-3-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide (11 mg, 42%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.45 (s, 1H), 7.32 (d, 1H, *J* = 8.4 Hz), 7.28-7.21 (m, 2H), 7.10 (s, 1H), 7.05 (d, 1H, *J* = 2.3 Hz), 7.00-6.91 (m, 2H), 6.85 (dd, 1H, *J* = 2.7, 9.0 Hz), 3.87 (s, 3H), 3.06 (d, 2H, *J* = 11.6 Hz), 2.75 (t, 2H, *J* = 7.2 Hz), 2.55-2.42 (m, 4H), 2.08-1.90 (m, 4H), 1.88-1.74 (m, 4H), 1.25 (d, 6H, *J* = 6.9 Hz); ESMS *m/e*: 434.2 $(M + H)^+$.

TERT-BUTYL 4-[3-(PROPIONYLAMINO)PHENYL]-1-PIPERIDINECARBOXYLATE: Propionyl chloride (5.53 g, 0.0597 mol) was added dropwise to a solution of tert-butyl 4-(3-aminophenyl)-1-piperidinecarboxylate (15.0 g, 0.0543 mol) and TEA (16.5 g, 0.163 mol) in THF (200 mL) and the mixture was stirred at room temperature for 3 h. Water (50 mL) was added to the reaction mixture, the aqueous layer was extracted with CH_2Cl_2 (3 X 100 mL), and the combined organic extracts were washed with brine (50 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by chromatography on silica using hexane/EtOAc (10:1) to afford the product (18.8 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (s, 1H),

7.34-7.21 (m, 3H), 6.93 (d, 1H, *J* = 7.4 Hz), 2.77 (t, 2H, *J* = 11.5 Hz), 2.68-2.58 (m, 1H), 2.38 (q, 2H, *J* = 7.6 Hz), 1.87-1.67 (m, 4H), 1.67-1.54 (m, 2H), 1.48 (s, 9H), 1.25 (t, 3H, *J* = 7.5 Hz); ESMS *m/e*: 333.4 (M + H)$^+$.

N-[3-(4-PIPERIDINYL)PHENYL]PROPANAMIDE: Into a stirred solution of tert-butyl 4-[3-(propionylamino)phenyl]-1-piperidinecarboxylate (18.8 g, 0.0543 mmol) in dioxane (100 mL) at 5 °C was bubbled HCl gas for 2 h. The solvent was removed in vacuo, the residue was dissolved in water (100 mL) and neutralized by adding 10% KOH aqueous solution. The aqueous layer was extracted (3 X 200 mL) with a mixture of $CHCl_3$/isopropyl alcohol (3:1), and the combined organic layers were washed with brine (100 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by column chromatography on silica using 5% of NH_3 (2.0 M in methanol) in CH_2Cl_2 to afford the desired product (12.6 g, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (s, 1H), 7.32 (d, 1H, *J* = 7.2 Hz), 7.28-7.21 (m, 1H), 7.09 (s, 1H), 6.97 (d, 1H, *J* = 7.6 Hz), 3.18 (d, 2H, *J* = 12.6 Hz), 2.73 (dt, 2H, *J* = 2.2, 11.2 Hz), 2.65-2.57 (m, 1H), 2.38 (q, 2H, *J* = 7.4 Hz), 1.83 (d, 2H, *J* = 12.1 Hz), 1.70-1.61 (m, 3H), 1.25 (t, 3H, *J* = 7.5 Hz); ESMS *m/e*: 233.1 (M + H)$^+$.

TERT-BUTYL 4-{3-[(CYCLOPROPYLCARBONYL)AMINO]PHENYL}-1-PIPERIDINECARBOXYLATE: According to the procedure used for the synthesis of tert-butyl 4-[3-(propionylamino)phenyl]-1-piperidinecarboxylate, tert-butyl 4-(3-aminophenyl)-1-piperidinecarboxylate (16.47 g 0.0596 mol) and cyclopropanecarbonyl chloride (6.27 g,

0.0597 mol) provided the tert-butyl 4-{3-[(cyclopropylcarbonyl)amino]phenyl}-1-piperidinecarboxylate (18.1 g, 100%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55-7.46 (m, 2H), 7.29-7.21 (m, 2H), 6.96-6.89 (m, 1H), 2.79 (t, 2H, *J* = 12.1 Hz), 2.68-2.58(m, 1H), 1.84 (d, 2H, *J* = 12.6 Hz), 1.83-1.76 (m, 4H), 1.48 (s, 9H), 1.19-1.12 (m, 1H), 1.09-1.05 (m, 2H), 0.89-0.75 (m, 2H); ESMS *m/e*: 345.5 $(M + H)^+$.

N-[3-(4-PIPERIDINYL)PHENYL]CYCLOPROPANECARBOXAMIDE: According to the procedure used for the synthesis of *N*-[3-(4-piperidinyl)phenyl]propanamide, tert-butyl 4-{3-[(cyclopropylcarbonyl)amino]phenyl}-1-piperidinecarboxylate (18.9 g, 0.0543 mol) provided *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide (13.2 g, 100 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.36-7.22 (m, 3H), 7.23 (d, 1H, *J* = 6.9 Hz), 3.17 (d, 2H, *J* = 11.9 Hz), 2.72 (dt, 2H, *J* = 2.6, 12.2 Hz), 2.65-2.55 (m, 1H), 1.82 (d, 2H, *J* = 13.9 Hz), 1.63 (dt, 3H, *J* = 4.1, 12.5 Hz), 1.53-1.45 (m, 1H), 1.11-1.06 (m, 2H), 0.87-0.81 (m, 2H); ESMS *m/e*: 245.03 $(M + H)^+$.

1-(6-CHLOROHEXYL)-1H-INDOLE: To a mixture of NaH (0.249 g, 10.0 mmol) in DMF (5 mL) at 0 °C was added a solution of 1-*H*-indole (0.585 g, 5.00 mmol) in DMF (2 mL). The reaction mixture was stirred for 30 minutes and warmed up to room temperature. Then 1-bromo-6-chlorohexane (0.998 g, 5.00 mmol) was added dropwise by syringe and the reaction mixture was stirred overnight. The reaction mixture was diluted with EtOAc (30 mL), washed with water (3 X 10 mL), dried over $MgSO_4$, concentrated *in vacuo* and purified by chromatography using hexane/EtOAc (97.5:2.5) to give the desired product (0.900 g, 76 %).

^{1}H NMR ($CDCl_3$) δ 7.76-7.54 (m, 1H), 7.47-6.96 (m, 4H), 6.60-6.34 (m, 1H), 4.13 (t, 2H, *J* = 6.8 Hz), 3.50 (t, 2H, *J* = 5.6 Hz), 1.98-1.79 (m, 2H), 1.79-1.64 (m, 2H), 1.54-1.17 (m, 4H).

1-(5-CHLOROPENTYL)-1H-INDOLE: According to the procedure used for the synthesis of 1-(6-chlorohexyl)-1*H*-indole, 1-*H*-indole (0.585 g, 5.00 mmol) and 1-bromo-5-chloropentane (0.928 g, 5.00 mmol) gave the desired product (0.890 g, 80%). ^{1}H NMR ($CDCl_3$) δ 7.76-7.51 (m, 1H), 7.44-6.96 (m, 4H), 6.60-6.38 (m, 1H), 4.11 (t, 2H, *J* = 6.8 Hz), 3.47 (t, 2H, *J* = 6.4 Hz), 1.97-1.79 (m, 2H), 1.79-1.61 (m, 2H), 1.58-1.32 (m, 2H).

Example 96

***N*-(3-{1-[6-(1H-INDOL-1-YL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** 1-(6-Chlorohexyl)-1*H*-indole (23.6 mg, 0.100 mmol), 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (24.6 mg, 0.100 mmol), K_2CO_3 (27.6 mg, 0.200 mmol), NaI (22.5 mg, 0.150 mmol) and DMF (1.00 mL) were combined and stirred overnight at 100 °C. The reaction mixture was cooled to room temperature and the crude material was purified by preparative TLC using 5 % of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product as a yellow solid (40 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08-6.52 (m, 11H), 4.17 (t, 2H, *J* = 7.2 Hz), 3.26 (d, 2H, *J* = 11.6 Hz), 2.74-2.52 (m, 4H), 2.44-2.28 (m, 2H), 2.20-2.02 (m, 2H), 1.98-1.82 (m,4H), 1.78-1.62 (m, 2H), 1.43-1.28 (m, 4H), 1.28 (d, 6H, *J* = 6.8 Hz); ESMS *m/e*: 446.5 $(M + H)^+$.

Example 97

***N*-(3-{1-[5-(1*H*-INDOL-1-YL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared as above, using 1-(5-chloropentyl)-1*H*-indole (22.2 mg, 0.100 mmol), 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (24.6 mg, 0.100 mmol), K_2CO_3 (27.6 mg, 0.200 mmol), NaI (23.0 mg, 0.150 mmol) and DMF (1.00 mL), giving the desired product as a yellow oil (36 mg, 81%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.08-6.52 (m, 11H), 4.19 (t, 2H, *J* = 7.2 Hz), 3.26-3.10 (m, 2H), 2.71-2.55 (m, 2H), 2.55-2.42 (m, 2H), 2.35-2.12 (m, 2H), 2.12-1.80 (m, 6H), 1.80-1.57 (m, 2H), 1.51-1.34 (m, 2H), 1.31 (d, 6H, *J* = 6.8 Hz); ESMS *m/e*: 432.2 $(M + H)^+$.

Example 98

***N*-(4-{1-[(9-ETHYL-9*H*-CARBAZOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** According to the procedure used for the synthesis of *N*-(3-{1-[4-(4-CHLOROPHENOXY)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE (Example 108) *N*-(3-{1-[3-(1,2-diphenyl-1*H*-indol-3-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide, 9-ethyl-9*H*-carbazole-3-carbaldehyde (22.3 mg, 0.100 mmol) and 2-methyl-*N*-[4-(4-piperidinyl)phenyl]propanamide (24.6 mg, 0.100 mmol) provided *N*-(4-{1-[(9-ethyl-9*H*-carbazol-3-yl)methyl]-4-piperidinyl}phenyl)-2-methylpropanamide. The product was obtained as a white crystalline solid (20 mg, 44%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.21-7.09 (m, 12H), 4.38 (q, 2H, *J* = 7.2 Hz), 3.81 (s, 2H), 3.25-3.03 (m, 2H), 2.60-2.38 (m, 2H), 2.31-2.09 (m, 2H), 1.98-1.69 (m, 4H), 1.44 (t, 3H, *J* = 7.2 Hz), 1.23 (d, 6H, *J* = 6.8 Hz); ESMS *m/e*: 454.3 $(M + H)^+$.

Example 99

***N*-(3-{1-[(9-ETHYL-9*H*-CARBAZOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** According to the procedure used for the synthesis of *N*-(3-{1-[4-(4-CHLOROPHENOXY)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE (Example 108) *N*-(4-{1-[(9-ethyl-9*H*-carbazol-3-yl)methyl]-4-piperidinyl}phenyl)-2-methylpropanamide, 9-ethyl-9*H*-carbazole-3-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide afforded *N*-(3-{1-[(9-ethyl-9*H*-carbazol-3-yl)methyl]-4-piperidinyl}phenyl)-2-methylpropanamide (37 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24-6.29 (m, 12H), 4.37 (q, 2H, *J* = 7.2 Hz), 3.82 (s, 2H), 3.23-3.06 (m, 2H), 2.65-2.38 (m, 2H), 2.31-2.11 (m, 2H), 2.01-1.73 (m, 4H), 1.43 (t, 3H, *J* = 7.2 Hz), 1.25 (d, 6H, *J* = 4.0 Hz); ESMS m/e: 454.3 $(M + H)^+$.

Example 100

***N*-[3-(1-{[1-(4-METHOXYPHENYL)-1H-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** According to the procedure used for the synthesis of 1-(4-methylphenyl)1*H* -indole, *N*-{3-[1-(1H-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide (37.5 mg, 0.100 mmol) and 1-iodo-4-methoxybenzene (46.8 mg, 0.200 mmol) gave the desired product (27 mg, 56%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-6.58 (m, 14H), 3.88 (s, 3H), 3.67 (s, 2H), 3.14-3.01 (m, 2H), 2.57-2.41 (m, 2H), 2.25-2.01 (m, 2H), 1.93-1.69 (m, 4H), 1.24 (d, 6H, *J* = 7.2 Hz); ESMS m/e: 482.2 $(M + H)^+$.

Example 101

***N*-[3-(1-{[1-(4-FLUOROPHENYL)-1H-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** According to

the procedure used for the synthesis of 1-(4-methylphenyl)1*H*-indole, *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide (37.5 mg, 0.100 mmol) and 1-fluoro-4-iodobenzene (44.4 mg, 0.200 mmol) gave the desired product (21 mg, 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71-6.60 (m, 14H), 3.69 (s, 2H), 3.19-2.99 (m, 2H), 2.62-2.41 (m, 2H), 2.22-2.07 (m, 2H), 1.94-1.70 (m, 4H), 1.24 (d, 6H, *J* = 6.8 Hz); ESMS *m/e*: 470.2 $(M + H)^+$.

Example 102

METHYL-4-[5-({4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-IPERIDINYL}METHYL)-1H-INDOL-1-YL]BENZOATE: According to the procedure used for the synthesis of 1-(4-methylphenyl)1*H*-indole, *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide (37.5 mg, 0.100 mmol) and methyl 4-iodobenzoate (52.4 mg, 0.200 mmol) gave the desired product (11 mg, 22%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31-6.64 (m, 14H), 3.96 (s, 3H), 3.67 (s, 2H), 3.16-2.96 (m, 2H), 2.57-2.41 (m, 2H), 2.18-2.02 (m, 2H), 1.91-1.73 (m, 4H), 1.24 (d, 6H, *J* = 6.8 Hz); ESMS *m/e*: 510.2 $(M + H)^+$.

Example 103

2-METHYL-N-[3-(1-{[1-(3-METHYLPHENYL)-1H-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: According to the procedure used for the synthesis of 1-(4-methylphenyl)1*H*-indole, *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide (37.5 mg, 0.100 mmol) and 1-iodo-3-methylbenzene (43.6 mg, 0.200 mmol) gave the desired product (28 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-6.60 (m, 14H), 3.66 (s, 2H), 3.16-2.96 (m, 2H), 2.59-2.44 (m, 2H), 2.44 (s, 3H), 2.18-2.01 (m, 2H),

1.91-1.68 (m, 4H), 1.24 (d, 6H, J = 6.8 Hz); ESMS m/e: 466.2 $(M + H)^+$.

Example 104

***N*-{3-[1-(3-{[(4-CHLORO-3-NITROPHENYL)SULFONYL]AMINO}PROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** A mixture of *N*-{3[1-(2-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide (10.0 mg, 0.0350 mmol), 4-chloro-3-nitrobenzenesulfonyl chloride (9.90 mg, 0.0380 mmol), and TEA (7.00 mg, 0.0700 mmol) in THF (2 mL) was stirred for 12 h at room temperature. The crude product was purified by preparative TLC (CH_2Cl_2/MeOH/isopropyl amine = 19:1:0.2) to give the desired product (16 mg, 86%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.45-8.38 (m, 1H), 8.02 (d, 1H, J = 8.4 Hz), 7.72 (d, 1H, J = 8.8 Hz), 7.48-7.40 (m, 3H), 7.29-7.24 (m, 2H), 6.96 (d, 1H, J = 7.5 Hz), 3.17-3.09 (m, 4H), 2.63-2.48 (m, 4H), 2.15 (t, 2H, J = 11.8 Hz), 1.96-1.72 (m, 6H), 1.25 (d, 6H, J = 6.9 Hz); ESMS m/e: 523.2 $(M + H)^+$.

Example 105

***N*-[3-(1-{5-[4-(3,4-DIFLUOROPHENYL)-2-OXO-1,3-OXAZOLIDIN-3-YL]PENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** A mixture of 3-(5-bromopentyl)-4-(3,4-difluorophenyl)-1,3-oxazolidin-2-one (38.0 mg, 0.110 mmol), 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (26.0 mg, 0.100 mmol), NaI (23.0 mg, 0.150 mmol), and K_2CO_3 (14.0 mg, 0.100 mmol) in DMF (2 mL) was heated for 1 h at 50°C. The crude product was purified by preparative TLC using CH_2Cl_2/MeOH/isopropyl amine (19:1:0.2) to give the desired product (21 mg, 41%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.39-7.32 (m, 2H), 7.26-7.20 (m, 2H),

7.18-7.11 (m, 1H), 7.10- 7.03 (m, 1H), 6.96 (d, 1H, J = 7.6 Hz), 4.80-4.73 (m, 1H), 4.62 (t, 1H, J = 7.9 Hz), 4.09-4.04 (m, 1H), 3.51-3.42 (m, 1H), 3.03 (d, 2H, J = 11.7 Hz), 2.82-2.72 (m, 1H), 2.51-2.42 (m, 2H), 2.32 (t, 2H, J = 7.9 Hz), 2.11 (s, 1H), 2.03-1.97 (m, 2H), 1.85-1.70 (m, 4H), 1.49 (m, 4H), 1.31-1.27 (m, 1H), 1.24 (d, 6H, J = 6.9 Hz); ESMS m/e: 514.4 $(M + H)^+$.

Example 106

3-(2,6-DICHLOROPHENYL)-*N*-(5-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PENTYL)-5-METHYL-4-ISOXAZOLECARBOXAMIDE: A mixture of 3-(2,6-dichlorophenyl)-4-formyl-5-isoxazolecarbonyl chloride (69.0 mg, 0.250 mmol), *N*-{3-[1-(5-aminopentyl)-4-piperidinyl]phenyl}-2-ethylpropanamide (44.0 mg, 0.150 mmol), TEA (30.0 mg, 0.300 mmol) in THF (2 mL) was stirred for 12 h at room temperature. The crude product was purified by preparative TLC using CH_2Cl_2/MeOH/isopropyl amine (19:1:0.2) to give the desired product (52 mg, 67%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.52-7.49 (m, 2H), 7.49-7.41 (m, 2H), 7.39-7.31 (m, 2H), 7.29-7.21 (m, 2H), 6.92 (d, 1H, J = 7.6 Hz), 3.25-3.11 (m, 5H), 2.81-2.74 (m, 4H), 2.58-2.44 (m, 4H), 2.30-2.19 (m, 2H), 1.93- 1.78 (m, 4H), 1.56-1.44 (m, 2H), 1.31-1.28 (m, 2H), 1.24 (d, 6H, J = 6.6 Hz); ESMS m/e: 585.2 $(M + H)^+$.

Example 107

***N*-[3-(1-{2-[(DIPHENYLACETYL)AMINO]ETHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** A mixture of *N*-{3[1-(2-aminoethyl)-4-piperidinyl]phenyl}-2-methylpropanamide (20.0 mg, 0.0700 mmol), diphenylacetyl chloride (23.0 mg, 0.110 mmol), and TEA (20.0 mg, 0.140 mmol) in THF (2 mL) was stirred overnight at 23 °C. The

crude product was purified by preparative TLC using CH_2Cl_2/MeOH/isopropyl amine (19:1:0.2) to give the desired product (8.0 mg, 47%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.37-7.20 (m, 13H), 6.97-6.92 (m, 1H), 6.67 (s, 1H), 4.98 (s, 1H), 3.43 (q, 2H, *J* = 5.9 Hz), 2.90 (d, 2H, *J* = 11.6 Hz), 2.57-2.42 (m, 4H), 2.11 (t, 2H, *J* = 10.4 Hz), 1.75 (d, 2H, *J* = 12.4 Hz), 1.70-1.58 (m, 2H), 1.25 (d, 6H, *J* = 6.7 Hz); ESMS *m/e*: 484.2 $(M + H)^+$.

Example 108

***N*-(3-{1-[4-(4-CHLOROPHENOXY)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** 4-(4-chlorophenoxy)benzaldehyde (0.119 g, 0.510 mmol) and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (0.126 g, 0.510 mmol) were mixed in 1,2-dichloroethane (5 mL) and then treated with sodium triacetoxyborohydride (0.424 g, 2.00 mmol) and HOAc (0.03 mL, 0.5 mmol). The mixture was stirred overnight at room temperature. The reaction mixture was neutralized with saturated $NaHCO_3$ aqueous solution and the aqueous layer was extracted with CH_2Cl_2 (3 X 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, concentrated *in vacuo*, and purified by preparative TLC using 5% of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product (53 mg, 23%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.34-7.19 (m, 7H), 6.98-6.87 (m, 5H), 3.50 (s, 2H), 2.98 (d, 2H, *J* = 11.8 Hz), 2.58-2.44 (m, 2H), 2.10-1.98 (m, 2H), 1.83-1.76 (m, 4H), 1.24 (d, 6H, *J* = 6.8 Hz); ESMS *m/e*: 463.2 $(M + H)^+$.

Example 109

N-{3-[1-({2,5-DIMETHYL-1-[3-(TRIFLUOROMETHYL)PHENYL]-1*H*-PYRROL-3-YL}METHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by the procedure described in example 108, substituting 2,5-dimethyl-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrrole-3-carbaldehyde (0.136 g, 0.510 mmol) for 4-(4-chlorophenoxy)benzaldehyde. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69-7.56 (m, 2H), 7.53-7.32 (m, 4H), 7.28-7.18 (m, 2H), 6.99 (s, 1H), 5.98 (s, 1H), 3.43 (s, 2H), 3.16-3.06 (m, 2H), 2.57-2.42 (m, 2H), 2.07-1.95 (m, 8H), 1.89-1.76 (m, 4H), 1.24 (d, 6H, J = 6.8 Hz); ESMS *m/e*: 498.2 $(M + H)^+$.

Example 110

N-(3-{1-[4-(3,4-DIFLUOROPHENOXY)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by the procedure described in example 108, substituting 4-(3,4-difluorophenoxy)benzaldehyde (0.119 g, 0.510 mmol) for 4-(4-chlorophenoxy)benzaldehyde. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.32 (d, 2H, J = 8.4 Hz), 7.28-7.21 (m, 2H), 7.14-7.06 (m, 2H), 6.98-6.94 (m, 3H), 6.86-6.79 (m, 1H), 6.76-6.69 (m, 1H); 3.51 (s, 2H), 2.99 (d, 2H, J = 11.7 Hz), 2.55-2.44 (m, 2H), 2.12-2.02 (m, 2H), 1.86-1.74 (m, 4H), 1.25 (d, 6H, J = 7.0 Hz); ESMS *m/e*: 465.2 $(M + H)^+$.

Example 111

N-(3-{1-[(5-CHLORO-3-METHYL-1-PHENYL-1*H*-PYRAZOL-4-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by the procedure described in example 108, substituting 5-chloro-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde (0.113 g, 0.510 mmol) for 4-(4-chlorophenoxy)benzaldehyde. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62-7.19 (m, 9H), 6.97 (s, 1H), 3.43 (s, 2H), 3.08-2.98

(m, 2H), 2.58-2.43 (m, 2H), 2.39-2.32 (m, 3H), 2.18-1.71 (m, 6H), 1.24 (d, 6H, J = 6.9 Hz); ESMS m/e: 451.2 $(M + H)^+$.

Example 112

N-(3-{1-[4-(3,4-DICHLOROPHENOXY)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by the procedure described in example 108, substituting 4-(3,4-dichlorophenoxy)benzaldehyde (0.136 g, 0.510 mmol) for 4-(4-chlorophenoxy)benzaldehyde. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.36-7.18 (m, 6H), 7.08 (d, 1H, J = 1.8 Hz), 6.96 (d, 3H, J = 6.8 Hz), 6.84 (dd, 1H, J = 2.8, 8.9 Hz), 3.51 (s, 2H), 2.99 (d, 2H, J = 11.5 Hz), 2.55-2.42 (m, 2H), 2.12-2.02 (m, 2H), 1.84-1.73 (m, 4H), 1.24 (d, 6H, J = 7.0 Hz); ESMS m/e: 497.1 $(M + H)^+$.

Example 113

2-METHYL-*N*-(3-{1-[(2-PHENYL-1*H*-IMIDAZOL-4-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by the procedure described in example 108, substituting 2-phenyl-1*H*-imidazole-4-carbaldehyde (88.0 mg, 0.510 mmol) for 4-(4-chlorophenoxy)benzaldehyde. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, 2H, J = 7.4 Hz), 7.65-7.31 (m, 6H), 7.28-7.18 (m, 2H), 7.12-7.05 (m, 1H), 6.95-6.88 (m, 1H), 3.69 (s, 2H), 3.17-3.05 (m, 2H), 2.62-2.45 (m, 2H), 2.28-2.18 (m, 2H), 1.88-1.70 (m, 4H), 1.25 (d, 6H, J = 6.8 Hz); ESMS m/e: 403.2 $(M + H)^+$.

Example 114

N-(3-{1-[4-(DIPHENYLAMINO)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by the procedure described in example 108, substituting 4-(diphenylamino)benzaldehyde (0.139 g, 0.510 mmol) for 4-

(4-chlorophenoxy)benzaldehyde. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.39-6.92 (m, 18H), 3.49 (s, 2H), 3.02-2.99 (m, 2H), 2.59-2.43 (m, 2H), 2.15-2.03 (m, 2H), 1.92-1.76 (m, 4H), 1.23 (d, 6H, *J* = 6.8 Hz); ESMS *m/e*: 504.2 $(M + H)^+$.

Example 115

N-[3-(1-{[4-BROMO-1-(4-CHLOROBENZYL)-1*H*-PYRAZOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by the procedure described in example 108, substituting 4-bromo-1-(4-chlorobenzyl)-1*H*-pyrazole-5-carbaldehyde (0.153 g, 0.510 mmol) for 4-(4-chlorophenoxy)benzaldehyde. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (s, 1H), 7.36 (d, 1H, *J* = 8.8 Hz), 7.34-7.30 (m, 3H), 7.29-7.26 (m, 1H), 7.22 (t, 1H, *J* = 7.8 Hz), 7.16 (d, 2H, *J* = 8.6 Hz), 6.95 (d, 1H, *J* = 7.5 Hz), 5.24 (s, 2H), 3.61 (s, 2H), 3.09 (d, 2H, *J* = 11.9 Hz), 2.55-2.42 (m, 2H), 2.19 (dt, 2H, *J* = 4.4, 11.4 Hz), 1.89-1.76 (m, 4H), 1.24 (d, 6H, *J* = 6.7 Hz); ESMS *m/e*: 529.1 $(M + H)^+$.

1-(3-[{(1*R*)-3-CHLORO-PHENYLPROPYL]OXY}PHENYL)ETHANONE:

Azodicarboxylate (5.37 g, 0.0310 mol) was added to a solution of triphenylphosphine (8.09 g, 0.0308 mol), 1*S*-3-chloro-1-phenyl-1-propanol (4.20 g, 0.031 mol) and, 1-(3-hydroxyphenyl)ethanone in THF (150 mL). The reaction mixture was stirred for 4 days at 23 °C. The solvent was removed under reduced pressure and the residue was triturated with ether/hexane (1:2, (3 X 100 mL). The combined organic fractions were concentrated *in vacuo* and the crude product was purified by chromatography using EtOAc/hexane (1:14) to give the desired product (6.55 g, 74%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48-7.31 (m,

6H), 7.26 (t, 2H, J = 8.2 Hz), 7.04 (d, 1H, J = 8.1 Hz), 5.44 (dd, 1H, J = 4.4, 8.1 Hz), 3.83-3.74 (m, 1H), 3.63-3.56 (m, 1H), 2.51 (s, 3H), 2.51-2.45 (m, 1H), 2.29-2.17 (m, 1H); ESMS m/e: 289.0 $(M + H)^+$.

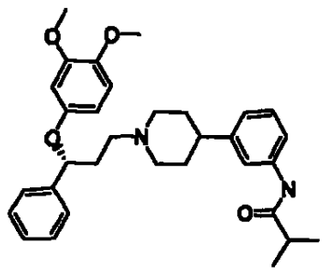
Example 116

***N*-(3-{1-[(3R)-3-(3-ACETYLPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** A mixture of 1-(3-{[(1R)-3-chloro-1-phenylpropyl]oxy}phenyl)ethanone (58.5 mg, 0.200 mmol), 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (56.8 mg, 0.200 mmol), NaI (34.0 mg, 0.200 mmol) and K_2CO_3 (55.5 mg, 0.400 mmol) in DMF (1 mL) was stirred at 100 °C for 3 h. The solvent was removed under reduced pressure and the residue was purified by chromatography on silica using 5 % of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product (98 mg, 98%). ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.49-7.21 (m, 11H), 7.09-7.03 (m, 1H), 6.96 (d, 1H, J = 7.9 Hz), 5.32 (dd, 1H, J = 5.0, 7.9 Hz), 3.08-2.98 (m, 2H), 2.57-2.43 (m, 6H), 2.11-1.72 (m, 9H), 1.25 (d, 6H, J = 6.8 Hz); ESMS m/e: 499.4 $(M + H)^+$.

Procedures:

Procedure A (see also example 48)

***N*-(3-{1-[(3R)-3-(3,4-DIMETHOXYPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:**



Method A

4-{[(1R)-3-CHLORO-1-PHENYLPROPYL]OXY}-1,2-DIMETHOXYBENZENE: A mixture of 3,4-dimethoxyphenol (4.07 g, 26.4 mmol), (*S*)-(-)-3-chloro-phenyl-1-propanol (4.50 g, 26.4 mmol, 99% ee, Aldrich Chemical Co.), triphenylphosphine (6.92 g, 26.4 mmol) and diethyl azodicarboxylate (4.59 g, 26.4 mmol) in THF (110 mL) was stirred at room temperature for 24 h. The reaction mixture was concentrated *in vacuo*. At this point, the residue can either be washed with pentane and the combined pentane extracts were concentrated and chromatographed with hexane:EtOAc (8:1) as the eluent to give the desired product (as described as a general procedure by: Srebnik, M.; Ramachandran, P.V.; Brown, H.C. *J. Org. Chem.* 1988, *53*, 2916-2920). This procedure was performed on a smaller scale reaction and only a 40% yield of the product was realized.

Alternatively, on a larger scale (26.4 mmol), the crude product was triturated with a small amount of dichloromethane and the precipitated triphenylphosphine oxide was filtered. The filtrate was concentrated and the crude product was chromatographed to give the desired product as a thick yellow oil (7.30 g, 88.9% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.32 (m, 4H), 7.20 (m, 1H), 6.64 (d, 1H, J = 8.7 Hz), 6.51 (d, 1H, J = 2.7 Hz), 6.30 (dd, 1H, J = 2.7, 8.7 Hz), 5.27 (apparent dd, 1H, J = 4.5, 8.7 Hz), 3.79 (s, 3H), 3.77 (s, 3H), 3.61 (m, 1H), 2.45 (m, 1 H), 2.20 (m, 1H), 1.80 (s, 1H); ESMS m/e: 307.1 $(M + H)^+$.

N-(3-{1-[(3*R*)-3-(3,4-DIMETHOXYPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:

A mixture of potassium carbonate (321 mg, 2.32 mmol), sodium iodide (522 mg, 3.48 mmol), 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (570 mg, 2.32 mmol) and 4-{[(1*R*)-3-chloro-1-phenylpropyl]oxy}-1,2-dimethoxybenzene (712 mg, 2.32 mmol) in DMF (5.00 mL) was stirred at 100 °C for 3 h, at which time TLC indicated that the reaction was complete. The reaction mixture was poured into water (50 mL) and the aqueous layer was extracted with methylene chloride (3 x 30 mL). The combined organic extracts were washed with brine (30 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by Preparatory TLC [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] to afford the product (970 mg, 90.1%) as a thick oil.

Method B

Into a 25-mL RB-flask was added triphenylphosphine (9.80 mg, 0.0375 mmol), diethyl azodicarboxylate (5.22 mg, 0.0300 mmol), *N*-(3-{1-[(3*S*)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (9.53 mg, 0.0250 mmol), 3,4-dimethoxyphenol (7.70 mg, 0.0500 mmol) and THF (1.00 mL) at room temperature. The reaction mixture was stirred at room temperature overnight (16 h). The solvent was removed under reduced pressure and the residue was purified by preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] to afford the desired product (4.40 mg, 34.1 % yield) as a thick oil: ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (s, 1 H), 7.40-7.30 (m, 4H), 7.25 (m, 3H), 6.97 (d, 1H, J = 7.8 Hz), 6.64 (d, 1H, J = 9.1 Hz), 6.51 (d, 1H, J = 2.6 Hz), 6.29 (d, 1H, J = 2.6, 9.1 Hz), 5.20 (apparent dd, 1H, J = 4.4, 8.5 Hz), 3.80

(s, 3H), 3.77 (s, 3H), 3.23 (m, 2H), 2.77 (m, 2H), 2.5 (m, 2H), 2.3-2.1 (m, 6H), 1.80 (m, 2H), 1.25 (d, 6H, J = 7.9 Hz); ESMS *m/e*: 517.4 $(M + H)^+$.

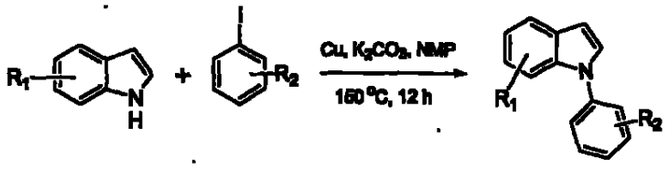
Procedure B (see also example 49)

2-METHYL-*N*-(3-{1-[(3*S*)-3-PHENOXY-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: A mixture of *N*-(3-{1-[(3*R*)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide (9.53 mg, 0.0250 mmol), phenol (4.70 mg, 0.050 mmol), triphenylphosphine (9.80 mg, 0.0375 mmol) and diethyl azodicarboxylate (5.22 mg, 0.0300 mmol) in THF (1.00 mL) was stirred at room temperature for 3 days. Chromatography using silica preparative TLC plates [2.5% of NH_3 (2.0 M in methanol) in $CHCl_3$] gave the desired product (2.70 mg, 23.6 % yield) as a thick oil: ^1H NMR δ 7.46 (s, 2H), 7.40-7.30 (m, 4H), 7.25 (m, 3H), 7.20 (m, 2H), 6.97 (apparent d, 1H, J = 7.4 Hz), 6.89 (apparent tt, 1H, J = 0.8, 7.6 Hz), 6.84 (apparent dt, 1H, J = 0.8, 8.0 Hz), 5.20 (apparent dd, 1H, J = 4.4, 8.5 Hz), 3.35 (m, 2H), 2.91 (m, 2H), 2.60 (m, 2H), 2.30-2.10 (m, 6H), 1.90 (m, 2H), 1.25 (d, 6H, J = 7.9 Hz); ESMS *m/e*: 457.4 $(M + H)^+$;

Procedure C

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Scheme O

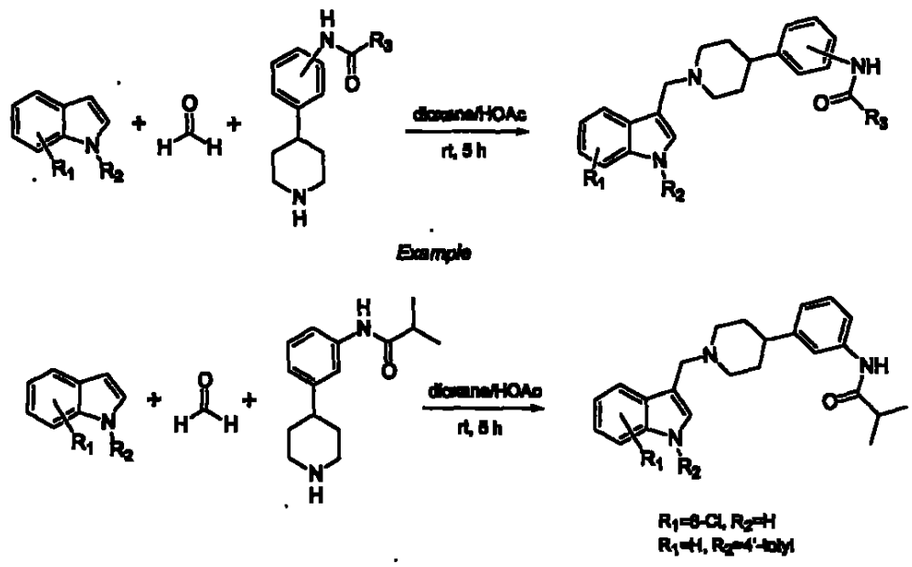


R_1=H, R_2=4'-Me

1-(4-METHYLPHENYL)1H-INDOLE: A mixture of 1-H-indole (58.5 mg, 0.500 mmol), 1-iodo-4-methylbenzene (0.218 g, 1.00 mmol), copper powder (32.0 mg, 0.500 mmol), and K_2CO_3 (0.138 g, 1.00 mmol) in 1-methyl-2-pyrrolidinone (1.00 mL) was heated at 150 °C for 12 h under argon. The resulting mixture was diluted with H_2O (6 mL). The aqueous layer was extracted with CH_2Cl_2 (3 X 10 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by preparative TLC using EtOAc:hexane (1:4) to give the desired product (82.0 mg, 79.0 %): ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, 1H, J = 7.7 Hz), 7.52 (d, 1H, J = 7.4 Hz), 7.38 (d, 2H, J = 8.4 Hz), 7.34-7.29 (m, 3H), 7.21 (t, 1H, J = 7.0 Hz), 7.15 (t, 1H, J = 7.0 Hz), 6.66 (d, 1H, J = 3.3 Hz), 2.43 (s, 3H); ESMS *m/e*: 208.0 $(M + H)^+$.

Procedure D (see also example 86)

218
Scheme N

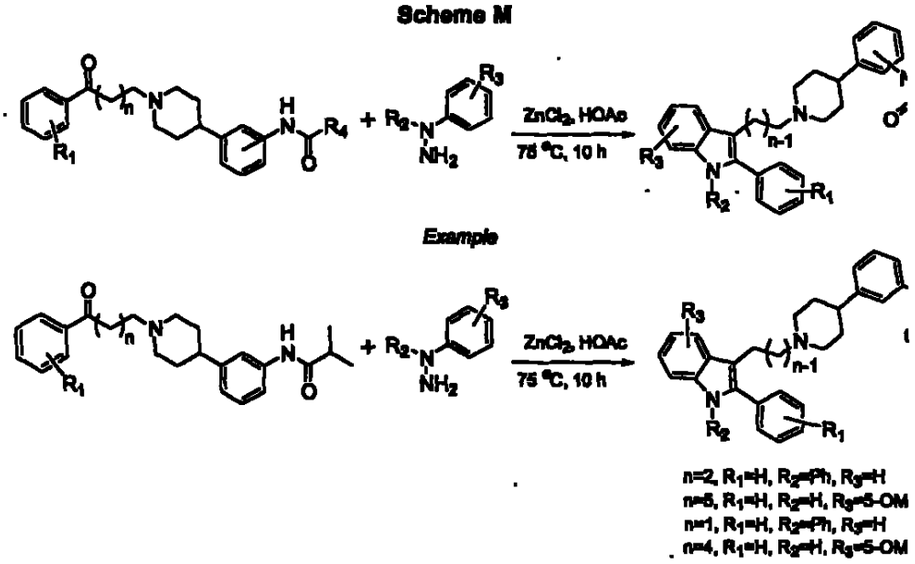


N-(3-{1-[(6-CHLORO-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A solution of 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (0.369 g, 1.50 mmol) and 37 wt % aqueous formaldehyde (30.0 mg, 1.50 mmol) in 1.00 mL of HOAc:dioxane (1:4) was added to 6-chloro-1-H-indole (0.152 g, 1.00 mmol) and the reaction mixture was stirred for 12 h at room temperature. The resulting mixture was diluted with H_2O (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 X 100 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by preparative TLC plates using 5% of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product (79.0 mg, 42.0 %): ^1H NMR (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.04 (s, 1H), 7.52 (t, 2H, J = 8.1 Hz), 7.35 (d, 2H, J = 13.3 Hz), 7.18 (t, 1H, J = 7.9 Hz), 7.09 (dd, 1H, J = 1.9, 8.5 Hz), 6.85 (d, 1H, J

= 7.4 Hz), 5.18 (s, 1H), 4.01 (s, 2H), 2.55 (septet, 1H, J = 6.8 Hz), 2.48-2.34 (m, 3H), 2.08-1.95 (m, 4H), 1.78 (d, 2H, J = 12.8 Hz), 1.22 (d, 6H, J = 6.8 Hz); ESMS m/e: 410.1 $(M + H)^+$.

Procedure E (see also example 90)

Scheme M

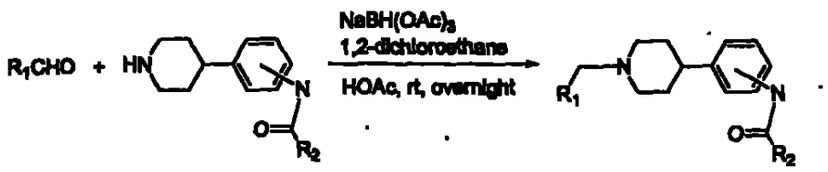


N-(3-{1-[3-(1,2-DIPHENYL-1H-INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of 1,1-diphenylhydrazine hydrochloride (10.3 mg, 0.0470 mmol), 2-methyl-N-{3-[1-(5-oxo-5-phenylpentyl)-4-piperidinyl]phenyl}propanamide (14.7 mg, 0.0362 mmol), $ZnCl_2$ (14.8 mg, 0.109 mmol), and HOAc (0.500 mL) was heated for 4 h at 80 °C. The resulting crude mixture was diluted with water (10 mL), the aqueous layer was neutralized with saturated K_2CO_3 (10 mL) and extracted with CH_2Cl_2 (3 X 20 mL). The combined organic layers were concentrated *in vacuo* and the residue was purified

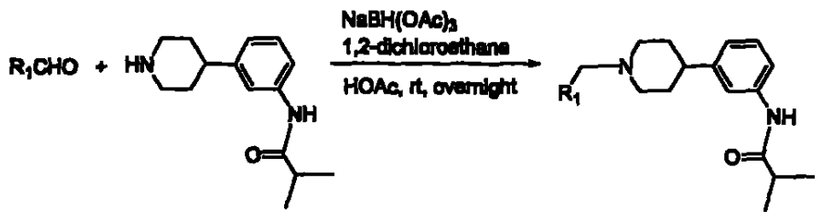
by preparative TLC plates using 5% of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product *N*-(3-{1-[3-(1,2-diphenyl-1H-indol-3-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide (4.10 mg, 37.0 %): ^1H NMR (400 MHz, $CDCl_3$) δ 7.71-7.65 (m, 1H), 7.42 (d, 1H, J = 7.4 Hz), 7.39 (s, 1H), 7.36-7.15 (m, 15H), 6.94 (d, 1H, J = 7.8 Hz), 3.12 (d, 2H, J = 11.2 Hz), 2.90 (t, 2H, J = 7.8 Hz), 2.59-2.45 (m, 3H), 2.19-1.91 (m, 7H), 1.82 (d, 2H, J = 13.5 Hz), 1.24 (d, 6H, J = 6.9 Hz); ESMS *m/e*: 555.3 $(M + H)^+$.

Procedure F (see also example 108)

Scheme R



Example

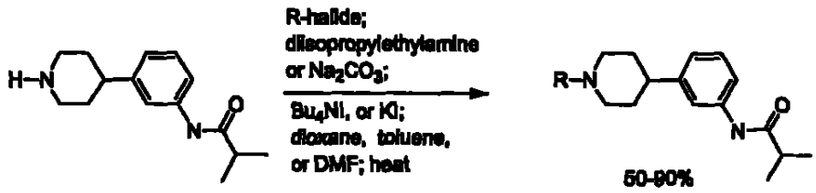


***N*-(3-{1-[4-(4-CHLOROPHENOXY)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** A solution of 4-(4-chlorophenoxy)benzaldehyde (0.119 g, 0.510 mmol) and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (0.126 g, 0.510 mmol) in 1,2-dichloroethane (5.00 mL)

was treated with sodium triacetoxyborohydride (0.424 g, 2.00 mmol) and HOAc (0.0300 mL, 0.500 mmol) at room temperature. The mixture was stirred overnight at room temperature. The reaction mixture was neutralized with saturated $NaHCO_3$ aqueous solution (10 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, concentrated *in vacuo* and purified by preparative TLC plates using 5% of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product (53.0 mg, 23.0 %): ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.34-7.19 (m, 7H), 6.98-6.87 (m, 5H), 3.50 (s, 2H), 2.98 (d, 2H, J = 11.8 Hz), 2.58-2.44 (m, 2H), 2.10-1.98 (m, 2H), 1.83-1.76 (m, 4H), 1.24 (d, 6H, J = 6.8 Hz); ESMS m/e: 463.2 $(M + H)^+$.

Procedure G (see also example 116)

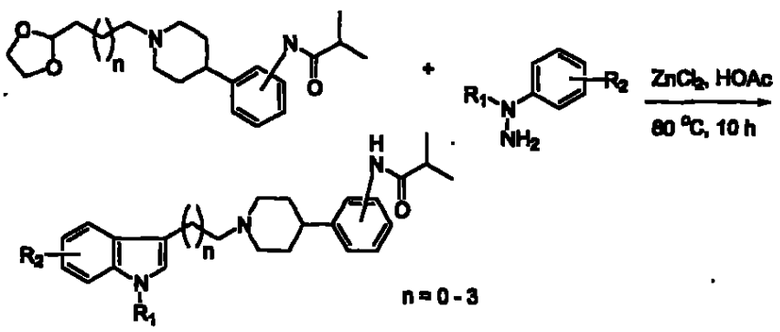
Scheme F



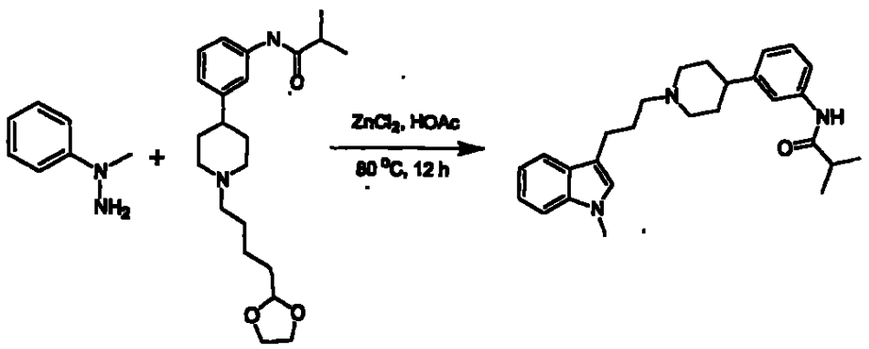
N-(3-{1-[(3R)-3-(3-ACETYLPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A mixture of 1-(3-{[(1R)-3-chloro-1-phenylpropyl]oxy}phenyl)ethanone (58.5 mg, 0.200 mmol), 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (56.8 mg, 0.200 mmol), NaI (34.0 mg, 0.200 mmol) and K_2CO_3 (55.5 mg, 0.400 mmol) in DMF (1.00 mL) was stirred at 100 °C for 3 h. The

solvent was removed under reduced pressure and the residue was purified by chromatography on silica using 5 % of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product (98.0 mg, 98.0 %): ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.49-7.21 (m, 11H), 7.09-7.03 (m, 1H), 6.96 (d, 1H, J = 7.9 Hz), 5.32 (dd, 1H, J = 5.0, 7.9 Hz), 3.08-2.98 (m, 2H), 2.57-2.43 (m, 6H), 2.11-1.72 (m, 9H), 1.25 (d, 6H, J = 6.8 Hz); ESMS m/e: 499.4 $(M + H)^+$.

Scheme S



Procedure E

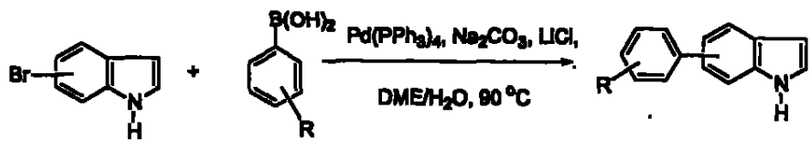


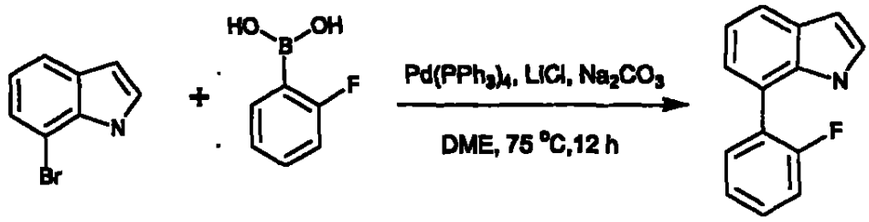
2-METHYL-N-(3-{1-[3-(1-METHYL-1H-INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: A mixture of *N*-(3-{1-(4-

(1,3-dioxolan-2-yl)butyl]-4-piperidinyl}phenyl)-2-methylpropanamide (100 mg, 0.270 mmol), 1-methyl-1-phenylhydrazine (106 mg, 0.870 mmol), $ZnCl_2$ (119 mg, 0.870 mmol), and HOAc (1.00 mL) was heated for 12 h at 80 °C. The resulting crude mixture was diluted with water (20 mL), the aqueous layer was neutralized with saturated K_2CO_3 solotion (10 mL) and extracted with CH_2Cl_2 (3 X 20 mL). The combined organic layers were concentrated *in vacuo* and the residue was purified by preparative TLC using 3 % of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product 2-methyl-*N*-(3-{1-[3-(1-methyl-1H-indol-3-yl)propyl]-4-piperidinyl}phenyl)propanamide (20.7 mg, 18.7 %):
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, 1H, J = 8.1 Hz), 7.45 (s, 1H), 7.35 (d, 1H, J = 7.4 Hz), 7.26-7.24 (m, 4H), 7.09 (t, 1H, J = 7.3 Hz), 6.97 (d, 1H, J = 7.3 Hz), 6.86 (s, 1H), 3.75 (s, 3H), 3.11 (d, 2H, J = 11.6 Hz), 2.79 (t, 2H, J = 7.3 Hz), 2.51-2.50 (m, 4H), 2.12-1.81 (m, 8H), 1.25 (d, 6H, J = 7.1 Hz); Anal. Calcd for $C_{27}H_{35}N_3O$+0.225$CHCl_3$: C, 73.57; H, 7.99; N, 9.45. Found: C, 73.93; H, 7.90; N, 9.23; ESMS *m/e*: 418.2 $(M + H)^+$.

Procedure I

Scheme T

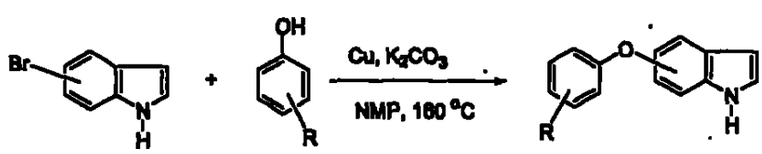


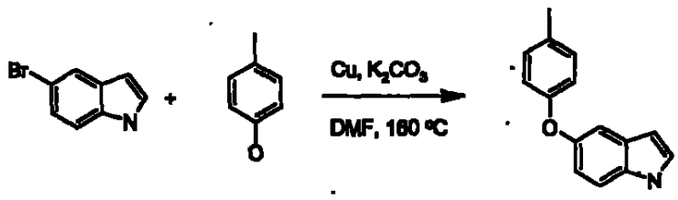


7-(2-FLUOROPHENYL)-1H-INDOLE: A mixture of 2-fluorophenylboronic acid (83.4 mg, 0.600 mmol), 7-bromo-1H-indole (98.0 mg, 0.500 mmol), LiCl (42.0 mg, 1.00 mmol), Na_2CO_3 (2.0 M, 0.100 mL), $Pd(PPh_3)_4$ (115 mg, 0.100 mmol) and DME (2.00 mL) was heated at 75 °C for 12 h under Argon. The resulting crude mixture was diluted with water (40 mL), the aqueous layer was extracted with CH_2Cl_2 (3 X 20 mL). The combined organic layers were washed with brine (30 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by preparative TLC using hexane:EtOAc (8:1) to give the desired product 7-(2-fluorophenyl)-1H-indole (108 mg, 100 %): ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (br s, 1H), 7.71 (dm, 1H, *J* = 7.3), 7.55 (dt, 1H, *J* = 7.3, 1.6 Hz), 7.39 (m, 1 H), 7.30-7.19 (m, 5H), 6.62 (dd, 1H, *J* = 2.1-3.3 Hz); ESMS *m/e*: 211.9 $(M + H)^+$.

Procedure J

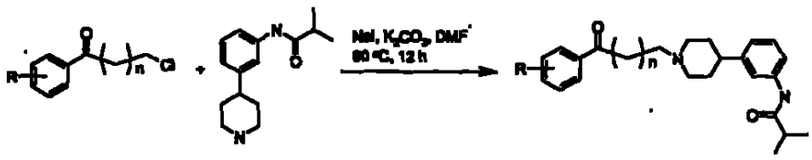
Scheme U



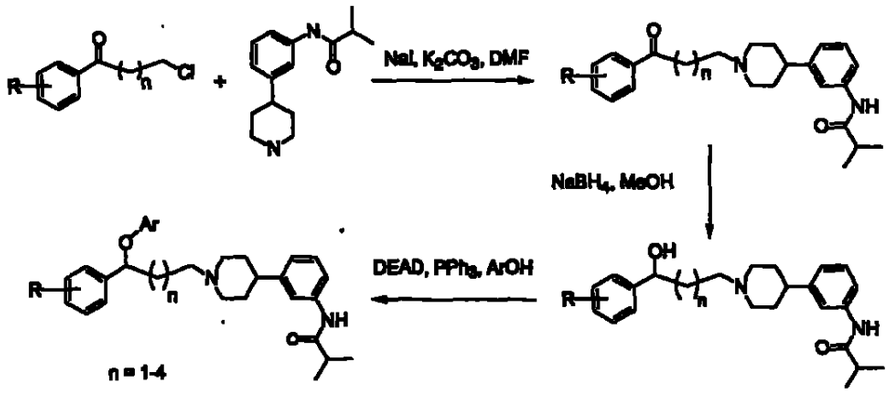


5-(4-METHYLPHENOXY)-1H-INDOLE: A mixture of 5-bromo-1*H*-indole (98.0 mg, 0.500 mmol), p-cresol (108 mg, 1.00 mmol); Cu (32.0 mg, 0.500 mmol), K_2CO_3 (138 mg, 1.00 mL) and DMF (1.00 mL) was heated at 160 °C for 12 h. The resulting crude mixture was diluted with water (40 mL), the aqueous layer was extracted with CH_2Cl_2 (3 X 20 mL). The combined organic layers were washed with brine (30 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by preparative TLC using hexane:EtOAc (4:1) to give the desired product 5-(4-methylphenoxy)-1*H*-indole (57.5 mg, 51.5 %): ESMS *m/e*: 224.0 $(M + H)^+$.

Procedure K

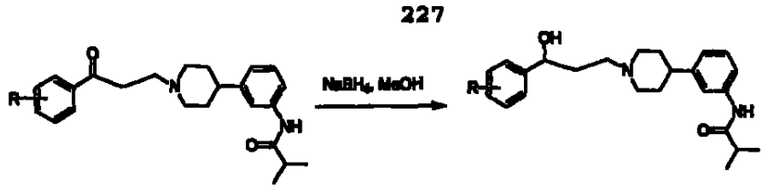


Scheme AN

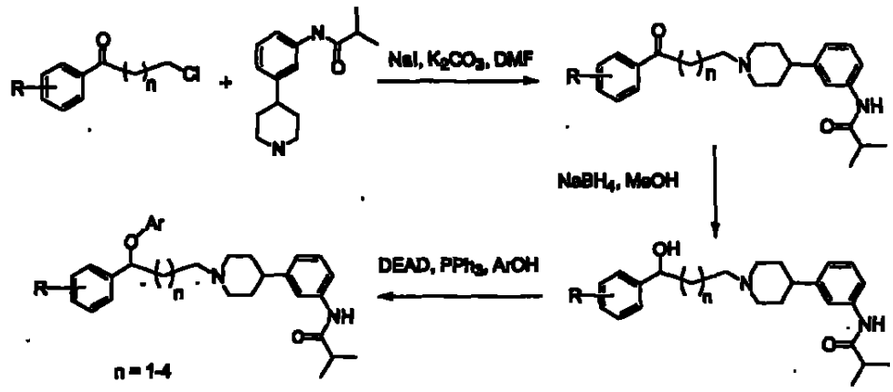


N-(3-{1-[7-(2-FLUOROPHENYL)-7-OXOHEPTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: A 50-mL round-bottom flask was charged with a solution of 7-chloro-1-oxo-1(2-fluorophenyl)heptane (2.42 g, 10.0 mmol), 2-methyl-*N*-[3-(4-piperidyl)phenyl] propanamide (2.46 g, 10.0 mmol), K_2CO_3 (2.76 g, 20.0 mmol) and NaI (2.25 g, 15.0 mmol) in DMF (25.0 mL). The mixture was stirred for 10 min at 25 °C and then heated at 100 °C for 12 h, cooled to 25 °C and diluted with EtOAc (100 mL). The reaction mixture was washed with water (4 X 50 mL) and the aqueous layer was extracted with EtOAc (100 mL). The organic layers were washed with brine (50 mL), dried over $MgSO_4$, concentrated *in vacuo* and the crude product was purified by chromatography (EtOAc:MeOH 97:3) to give the desired product (3.70 g, 82.0 %).

Procedure L



Scheme AN

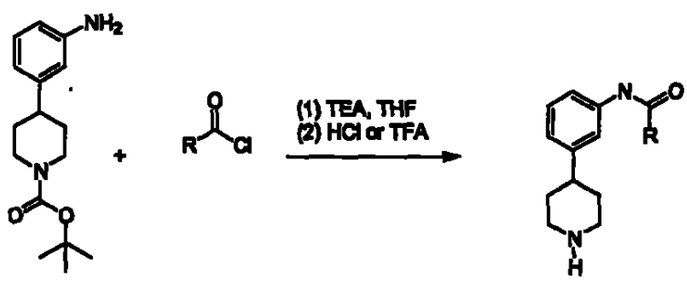


N-(3-{1-[7-(2-FLUOROPHENYL)-7-HYDROXYHEPTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: To a 50-mL round-bottomed flask charged with *N*-(3-{1-[7-(2-fluorophenyl)-7-oxoheptyl]-4-piperidinyl}phenyl)-2-methylpropanamide (5.0 mmol) and methanol (20 mL) was added $NaBH_4$ (7.5 mmol) at 0 °C in an ice-bath. The reaction mixture was warmed to 25 °C and stirred for 2 h. The reaction was monitored by TLC (EtOAc:MeOH 95:5). If necessary, another 5.0 mmol of $NaBH_4$ was added to the reaction mixture and the reaction mixture was refluxed for 1 h. The reaction was quenched with water (5.0 mL) and diluted with EtOAc (10 mL). The organic layer was separated, washed with saturated $NaHCO_3$ solution (10 mL), dried over $MgSO_4$ and concentrated *in vacuo*. The crude

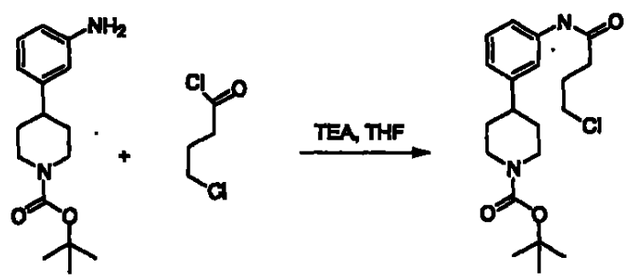
product was purified by chromatography (EtOAc:MeOH 97:3) to give the desired product (90%).

Procedure M

Scheme A

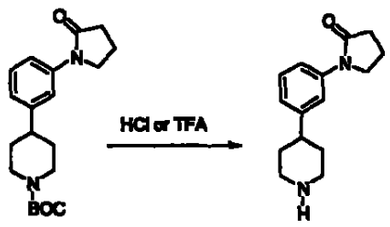


Step 1: If reacted individually, a solution of the amine or aniline (1.00 eq), diisopropylethylamine or TEA (2.00 eq) and an electrophile (1.50 eq) in CH_2Cl_2 was stirred for 24 h at 23 °C. The solvent was removed *in vacuo* and the crude product was chromatographed (silica) to give the final product.



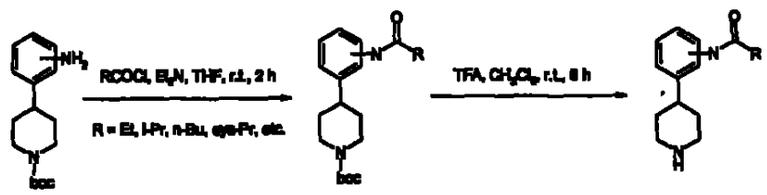
TERT-BUTYL 4-{3-[(4-CHLOROBUTANOYL)AMINO]PHENYL}-1-PIPERIDINECARBOXYLATE (3.32 g, 87.4 %) was synthesized according to Scheme A and Procedure M: ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.47 (s, 1H), 7.37 (m, 1H), 7.28 (m, 1H), 6.97 (d, 1H, J = 7.6 Hz), 3.89 (t, 1H, J = 6.4

Hz), 3.74 (m, 2H), 2.79- 2.75 (m, 4H), 2.64 (m, 2H), 1.88-1.77 (m, 4H), 1.60-1.59 (m, 4H), 1.48 (s, 9H).



Step B:

***TERT*-BUTYL 4-[3-(2-OXO-1-PYRROLIDINYL)PHENYL]-1-PIPERIDINECARBOXYLATE:** To a solution of *tert*-butyl 4-[3-(2-oxo-1-pyrrolidinyl)phenyl]-1-piperidinecarboxylate (0.429 g, 16.9 mmol) in dioxane (100 mL) was bubbled HCl gas for 1 h at 25 °C. The resulting crude mixture was basified with 10% KOH solution (100 mL), the aqueous layer was extracted with 3:1 $CHCl_3$:iso-propyl alcohol (3 X 150 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by preparative TLC using 20% NH_3 (2.0 M in MeOH) in CH_2Cl_2 solution to give the desired product tert-butyl 4-[3-(2-oxo-1-pyrrolidinyl)phenyl]-1-piperidinecarboxylate (245 mg, 78.7 %): ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 (t, 1H, J = 1.8 Hz), 7.41 (ddd, 1H, J = 8.1, 2.3, 0.9 Hz), 7.30 (t, 1H, J = 7.9 Hz), 7.02 (d, 1H, J = 7.9 Hz), 3.86 (t, 2H, J = 7.3 Hz), 3.21 (dt, 2H, J = 11.9, 2.9 Hz), 2.76 (dt, 2H, J = 12.1, 2.4 Hz), 2.65 (tt, 1H, J = 11.9, 3.5 Hz), 2.61 (t, 2H, J = 8.3 Hz), 2.22 (br s, 1H), 2.16 (qt, 2H, J = 7.5 Hz), 1.85 (d, 2H, J = 12.4 Hz), 1.67 (dq, 2H, J = 12.5, 4.0 Hz).



TERT-BUTYL 4-(4-AMINOPHENYL)-1-PIPERIDINECARBOXYLATE: Available from Arch Chemical Company, NJ.

2-METHYL-N-[4-(4-PIPERIDINYL)PHENYL]PROPANAMIDE: To a solution of *tert*-butyl 4-(4-aminophenyl)-1-piperidinecarboxylate (8.20 g, 29.7 mmol) and triethylamine (8.4 mL, 60 mmol) in dry THF (100 mL) at 0 °C was slowly added a solution of 2-methylpropanoyl chloride (3.84 g, 36.0 mmol) in THF (50 mL). The reaction mixture was then warmed up to room temperature and stirred for 2 h. After removing the solvent *in vacuo*, the crude product was purified by recrystallization (hexane/THF), affording the desired amide, *tert*-butyl 4-[4-(isobutyrylamino)phenyl]-1-piperidinecarboxylate, as a white solid (8.60 g, 84%). The tert-butyl 4-[4-(isobutyrylamino)phenyl]-1-piperidinecarboxylate was dissolved in CH_2Cl_2 (50 mL) at room temperature, TFA (13.68 g, 120 mmol, 5 equiv.) was added by syringe. The reaction mixture was stirred for 3 or 4 h and another 5 equivalents of TFA was added and the mixture was stirred for 2 or 3 more hours. The reaction solution was then basified to pH > 14 by KOH

(aq, 2 M). The solution was extracted with CH_2Cl_2 (8 x 200 mL). The combined organic layer was dried over K_2CO_3. Removal of solvent under reduced pressure gave the free amine, 2-methyl-*N*-[4-(4-piperidinyl)phenyl]propanamide, as a brownish solid (5.99 g, 98%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.55-7.35 (m, 2H), 7.35-6.9 (m, 3H), 3.26-2.98 (m, 2H), 2.84-2.64 (m, 2H), 2.64-2.53 (m, 1H), 2.53-2.32 (m, 1H), 1.90-1.68 (m, 2H), 1.68-1.36 (m, 3H), 1.22 (d, 6H, J = 6.0 Hz); ESMS *m/e*: 247.1 $(M + H)^+$.

***N*-[4-(4-PIPERIDINYL)PHENYL]PROPANAMIDE:** Prepared by the procedure for 2-methyl-*N*-[4-(4-piperidinyl)phenyl]propanamide using tert-butyl 4-(4-aminophenyl)-1-piperidinecarboxylate and propanoyl chloride: ESMS *m/e*: 233.1 $(M + H)^+$.

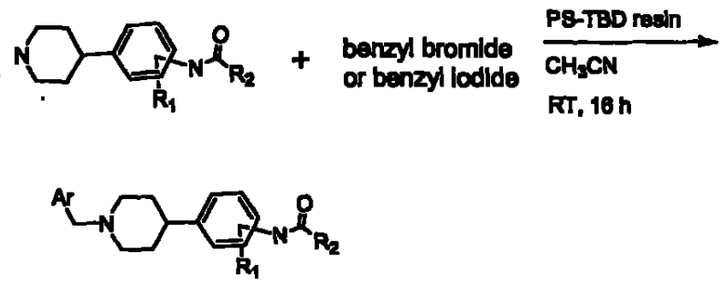
***N*-[4-(4-PIPERIDINYL)PHENYL]BUTANAMIDE:** Prepared by the procedure for 2-methyl-*N*-[4-(4-piperidinyl)phenyl]propanamide using tert-butyl 4-(4-aminophenyl)-1-piperidinecarboxylate and butanoyl chloride: ESMS *m/e*: 247.2 $(M + H)^+$.

***N*-[3-(4-PIPERIDINYL)PHENYL]CYCLOPROPANECARBOXAMIDE:** Prepared by the procedure for 2-methyl-*N*-[4-(4-piperidinyl)phenyl]propanamide using tert-butyl 4-(3-aminophenyl)-1-piperidinecarboxylate and cyclopropanecarbonyl chloride: Anal. Calcd for $C_{15}H_{20}N_2O+0.15CH_2Cl_2$: C, 70.8; H, 7.87; N, 10.9. found: C, 70.9; H, 7.68; N, 11.1; ESMS *m/e*: 245.0 $(M + H)^+$.

N-[3-(4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by the procedure for 2-methyl-*N*-[4-(4-piperidinyl)phenyl]propanamide using *tert*-butyl 4-(3-aminophenyl)-1-piperidinecarboxylate and propanoyl chloride: Anal. Calcd for $C_{14}H_{20}N_2O$: C, 72.2; H, 8.63; N, 12.1. found: C, 72.4; H, 8.68; N, 12.1; ESMS *m/e*: 233.1.

Procedure N

Scheme AV



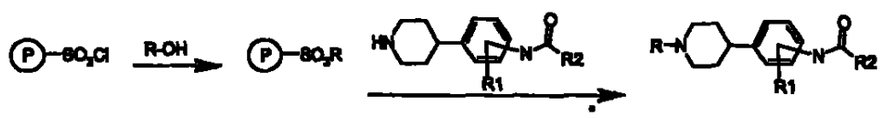
The library was constructed in polypropylene Robbins 46 well plates Reactor Blocks. In the initial incubation period, each well was charged with PS-TBD resin (from Argonaut Technologies, 0.280 mmol, 2.50 eq, 200 mg) and piperidine (0.120 mmol, 1.10 eq) in acetonitrile (0.500 mL) and agitated for 1 h. A solution of benzyl iodide or bromide (0.110 mmol, 1.00 eq) in acetonitrile (0.500 mL) was added to each well followed by additional acetonitrile (1.00 mL) to make a total volume of 2.00 mL and the mixture was rotated in a Robbins rotating oven at room temperature for 16 h. Then AP-Isocyanate resin (Argonaut Technologies, 250 mg, 0.430 mmol, 4.00 eq) was added to each well and reacted further at room temperature for another 12 h. The mixture was filtered

and the filtrate was concentrated *in vacuo* to obtain the desired product that was characterized via LC-MS.

Procedure O

Alkylation of Piperidines Using Alcohols and PS-TSCl Resin in Robbins 48 well "Reactor Blocks"

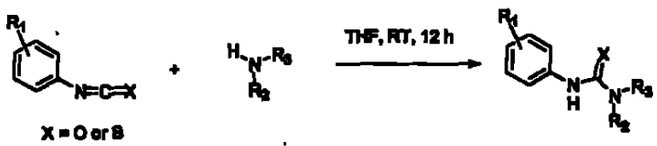
Scheme W

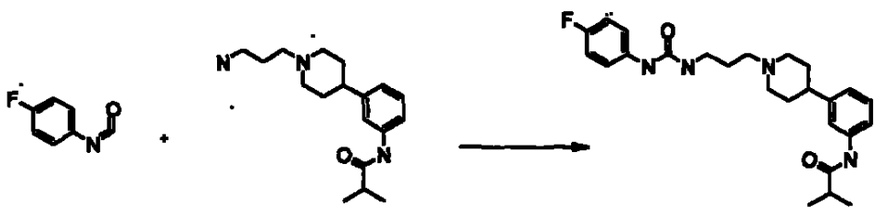


The library was constructed in polypropylene Robbins "Reactor Blocks", 46 well plates. PS-TSCl resin (100 mg, 1.00 eq, purchased from Argonaut Technologies) was placed in each well of the "Reactor Blocks" 46 well plates. To each well was added an alcohol (1.50 mmol) in 3.00 mL of CH_2Cl_2 and pyridine (1:1). The mixture was stirred for 5 h and the resin was washed with CH_2Cl_2 (3 x 4mL), DMF (5 x 4.0 mL), DMF/H_2O (3:1, 5 x 4.0 mL), THF (3 x 4.0 mL), CH_2Cl_2 (3 x 4.0 mL), acetonitrile (2 x 4.0 mL) and dried under reduced pressure. A solution of an amine (0.0750 mmol, 0.500 eq) and N,N-diisopropylethyl amine (19.0 mg, 0.150 mmol, 1.00 eq) in acetonitrile (3.00 mL) was added to the well containing the derivatized resin and the mixture was reacted at 70 °C for 16 h. Finally, AP-Isocyanate resin (120 mg, 0.150 mmol, 1.00 eq) and THF (2.00 mL) was added to the reaction vessel and reacted at room temperature for another 3 h. The solution was filtered into the Robbins receiving plates and concentrated *in vacuo* to give the desired tertiary amine, which was analyzed via LC-MS.

Procedure P

Scheme AB



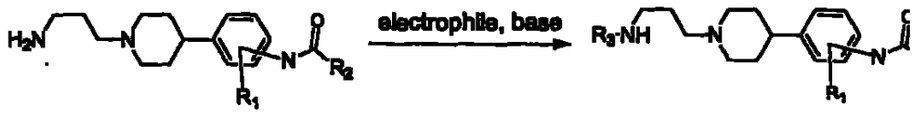


N-{3-[1-(3-{[(4-FLUOROANILINO)CARBONYL]AMINO}PROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: A solution of *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide (26.4 mg, 0.0870 mol), 1-fluoro-4-isocyanatobenzene (11.9 mg, 0.0870 mmol), in THF (1.00 mL) was stirred for 12 h at 25 °C. The resulting crude mixture was diluted with water (10 mL), the aqueous layer was extracted with CH_2Cl_2 (3 X 20 mL). The combined organic layers were concentrated *in vacuo* and the residue was purified by preparative TLC using 2.5 % of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product *N*-{3-[1-(3-{[(4-fluoroanilino)carbonyl]amino}propyl)-4-piperidinyl]phenyl}-2-methylpropanamide (4.18 mg, 10.9 %): ^1H NMR (400 MHz, $CDCl_3$) 7.45 (q, 2H, J = 4.7 Hz), 7.23-7.21 (m, 4H), 7.05 (t, 4H, J = 7.8 Hz), 6.75 (m, 1H), 4.05 (m, 1H), 3.19 (s, 1H), 2.71 (m, 1H),

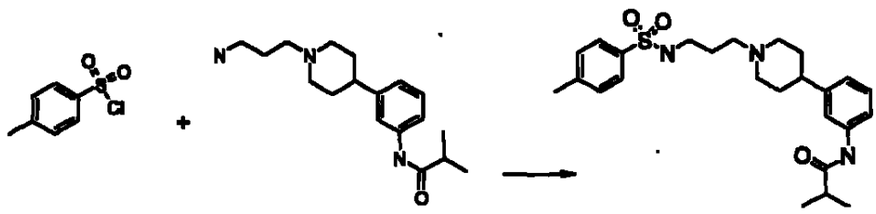
2.53 (m, 1H), 2.26-2.21 (m, 3H), 1.80-1.60 (m, 9H), 1.25 (d, 6H, J = 6.4 Hz); ESMS *m/e*: 439.4 $(M + H)^+$.

Procedure Q1

Scheme AT



If reacted individually, a solution of the amine (1.0 eq), an electrophile (1.5 eq), diisopropylethylamine (2.0 eq) in CH_2Cl_2 was stirred for 1 day. The solvent was removed *in vacuo* and the crude product was chromatographed to give the final product.



2-METHYL-*N*-{3-[1-(3-{[(4-METHYLPHENYL)SULFONYL]AMINO}PROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: A solution of 4-methylbenzenesulfonyl chloride (16.6 mg, 0.0870 mmol), *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide (26.4 mg, 0.0870 mmol), TEA (10.0 mg, 0.174 mmol) in THF (1.00 mL) was stirred for 12 h at 25 °C. The resulting crude mixture was diluted with water (20 mL), the aqueous layer was extracted with CH_2Cl_2 (2 X 20 mL). The combined organic layers were concentrated

in vacuo and the residue was purified by preparative TLC using 2.5 % of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product 2-methyl-*N*-{3-[1-(3-{[(4-methylphenyl)sulfonyl]amino}propyl)-4-piperidinyl]phenyl}propanamide (17.3 mg, 43.6 %): ^1H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.53 (s, 1H), 7.41 (s, 1H), 7.32-7.21 (m, 4H), 7.16 (s, 1H), 6.97 (d, 1H, J = 7.9 Hz), 3.44 (t, 2H, J = 6.3 Hz), 3.15 (d, 2H, J = 9.8 Hz), 2.62-2.45 (m, 4H), 2.15 (m, 3H), 2.05 (s, 3H), 1.95-1.71 (m, 5H), 1.26 (d, 6H, J = 6.6 Hz); ESMS *m/e*: 458.2 $(M + H)^+$.

Procedure Q_2

The Capture and Release Method for the Synthesis and Purification of the Piperidine Library

The commercially obtained Amberlyst 15 exchange resin (Aldrich) was activated using the following procedure:

1. The resin was shaken in methanol for 24 hr.
2. The resin was filtered and washed with methanol on a fritted funnel.
3. The resin was neutralized with 2N NH_3 in MeOH (pH checked) - shaken for 1 hr.
4. The neutralized resin was acidified with 3M HCl in MeOH (pH checked) - shaken for 1 hr.
5. The resin was captured on a fritted funnel and washed with MeOH.
6. The resin was dried *in vacuo* and stored.

Synthesis (Acylation of the Amines):

The library was constructed in polypropylene Robbins "Reactor Blocks", 46 well plates. In each plate an array of 5 amines (0.10 mmol) and 8 electrophiles (acid

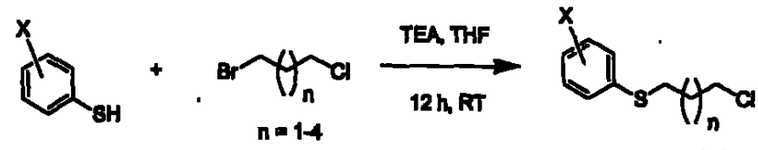
chlorides, sulfonyl chlorides, 1.5 eq.) in the presence of triethylamine (2.0 eq) in THF/DCM 3:1 (2.0 mL) were reacted overnight to give 40 compounds/plate. The reactions were rigorously monitored via TLC to the depletion of the starting amine due to the ensuing purification methodology via the acidic Amberlyst 15 resin. Following the disappearance of the starting amine, the desired products were captured and then released using the process outlined below.

Purification of the Piperidine Products: Activated Amberlyst 15 ion-exchange resin (0.90 g, Aldrich) was added to each well, and the plates were rotated for 2 hours in a Robbins rotating oven to capture the desired final product from the reaction mixture. The solvent was filtered and the resin was washed with CH_3OH and CH_2Cl_2 (x 3) alternately with each of the solvents (for 10 minutes each time). After the last filtration, 2 N ammonia in methanol was added to the resin (2 mL to each well) and the reaction blocks were rotated for 2 hours to release the desired compounds from the resin. The final compounds were filtered into Robbins' "Receiving Blocks", the solvent was removed and the compounds were analyzed via LC-MS.

Procedure R

238

Scheme Z



X = F, Cl, Br, I

[(3-CHLOROPROPYL)SULFANYL]BENZENE: A mixture of benzenethiol (0.550 g, 5.00 mmol), 1-bromo-3-chloropropane (106 mg, 5.50 mmol), TEA (1.01 g, 10.0 mmol) and THF (10.0 mL) was stirred for 12 h at 25 °C. The resulting crude mixture was diluted with water (40 mL), the aqueous layer was extracted with CH_2Cl_2 (3 X 30 mL). The combined organic layers were concentrated *in vacuo* and the residue was purified by preparative TLC using hexane:EtOAc (10:1) to give the desired product [(3-chloropropyl)sulfanyl]benzene (1.05 g, 100 %).

Scheme AA



X = F, Cl, Br, I

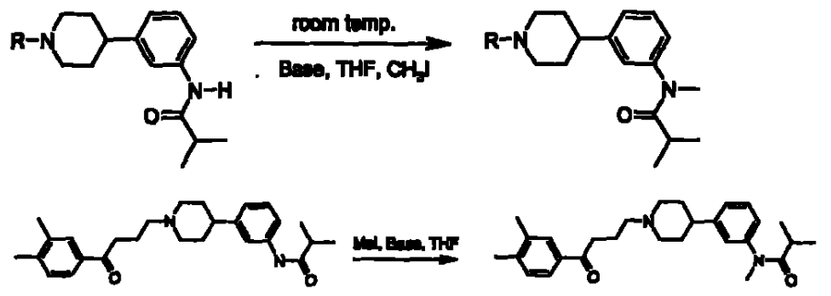
Procedure B

3-CHLOROPROPYL 4-FLUOROPHENYL SULFOXIDE: A solution of 3-chloropropyl 4-fluorophenyl sulfide (77.5 mg, 0.380 mmol) in CH_2Cl_2 (2.00 mL) was cooled to 0 °C. To this solution *m*-CPBA (78.7 mg, 0.460 mmol) was added. The reaction mixture was stirred at 0 °C for 30 min, then at

23 °C for 4 h. The resulting crude mixture was diluted with 10% aqueous Na_2SO_3 (10 mL), the aqueous layer was extracted with CH_2Cl_2 (2 X 15 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by preparative TLC using 2.5 % of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product 3-chloropropyl 4-fluorophenyl sulfoxide (47.8 mg, 57.0 %).

Procedure T

Scheme AD

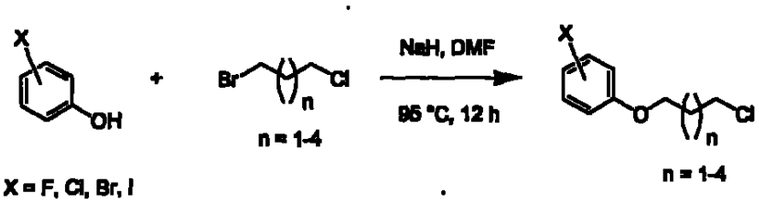


N-(3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-*N*,2-DIMETHYLPROPANAMIDE: A mixture of *N*-(3-{1-[4-(3,4-dimethylphenyl)-4-oxobutyl]-4-piperidinyl}phenyl)-2-methylpropanamide (15.0 mg, 0.0357 mmol), MeI (5.07 mg, 0.0357 mmol), NaOtBu (6.86 mg, 0.0714 mmol) and THF (1.00 mL) was stirred for 5 h at 25 °C. The resulting crude mixture was diluted with water (10 mL), the aqueous layer was extracted with CH_2Cl_2 (3 X 20 mL). The combined organic layers were concentrated *in vacuo* and the residue was purified by preparative TLC using 4.0 % of NH_3 (2.0 M in methanol) in CH_2Cl_2 to afford the desired product *N*-(3-{1-[4-(3,4-

dimethylphenyl)-4- oxobutyl]-4-piperidinyl}phenyl)-*N*,2-dimethylpropanamide (13.8 mg, 89.1 %): ^{1}H NMR (400 MHz, $CDCl_3$) 7.76 (s, 1H), 7.72 (dd, 1H, J = 1.8, 7.7 Hz), 7.33(t, 1H, J = 8.8 Hz), 7.22 (d, 1H, J = 7.8 Hz), 7.18(d, 1H, J = 8.8 Hz), 7.01 (m, 2H), 3.24 (s, 3H), 3.10 (d, 1H, J = 10.6 Hz), 3.00 (t, 1H, J = 7.6 Hz), 2.49-2.44 (m, 4H), 2.33 (s, 6H), 2.112.10 (m, 2H), 1.99 (m, 1H), 1.79-1.77 (m, 4H), 1.26 (t, 2H, J = 7.6 Hz), 1.02 (d, 6H, J = 7.6 Hz); ESMS m/e: 435.2 $(M + H)^+$.

Procedure U

Scheme AX



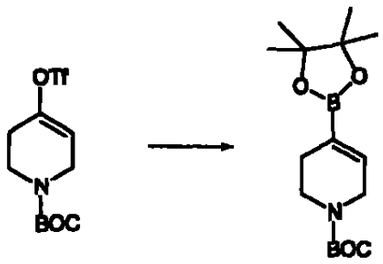


1-[3-(3-CHLOROPROPOXY)PHENYL]ETHANONE: To a suspension of NaH (50.5 mg, 2.00 mmol) in DMF (1.00 mL) was added 1-(3-hydroxyphenyl)ethanone (136 mg, 1.00 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 1 h. To this mixture was added a solution of 1-bromo-3-chloropropane (188 mg, 1.20 mmol) in DMF (0.500 mL). The reaction mixture was stirred at room temperature for 5 h. The resulting crude mixture was diluted with water (20 mL), the aqueous layer was extracted with CH_2Cl_2 (3 x

20 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by preparative TLC using hexane:EtOAc (4:1) to afford the desired product 1-[3-(3-chloropropoxy)phenyl]ethanone (235 mg, 55.2 %): ^1H NMR (400 MHz, $CDCl_3$) δ 7.7 (d, 1H, J = 6.6 Hz), 7.52(s, 1H), 7.25 (t, 1H, J = 6.6 Hz), 7.01 (m, 1H), 4.11 (t, 2H, J = 7.9 Hz), 3.69 (t, 2H, J = 7.9 Hz), 2.61 (s, 3H), 1.95-1.92 (m, 2H).

Procedure V

Scheme AE



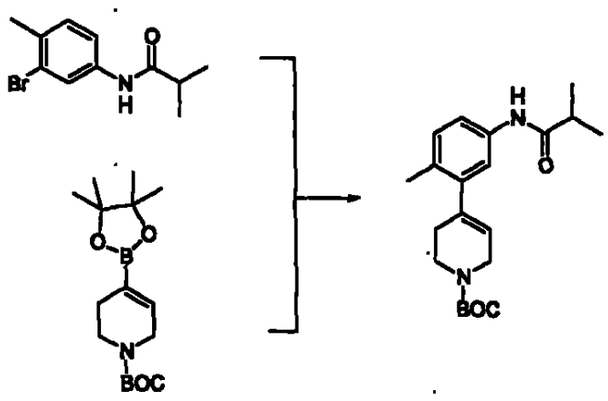
1-[(2,2-DIMETHYLPROPANOYL)OXY]-4-(4,4,5,5-TETRAMETHYL-1,3,2-DIOXABOROLAN-2-YL)-1,2,3,6-TETRAHYDROPYRIDINE:

To a 50-mL RB-flask, charged with bis(pinacolato)diboron (422 mg, 1.66 mmol), KOAc (444 mg, 4.53 mmol) and $PdCl_2dppf$ (37.0 mg, 3.00 mol%), dppf (25.0 mg, 3.00 mol%), was added a solution of 1-[(2,2-dimethylpropanoyl)oxy]-1,2,3,6-tetrahydro-4-pyridinyl trifluoromethanesulfonate (500 mg, 1.51 mmol) in 1,4-dioxane (10.0 mL) at room temperature under argon. The mixture was heated at 80 °C overnight. After cooled to room temperature, the mixture was filtered through celite and the celite was washed with EtOAc (3 x 20 mL). The filtrates were concentrated *in vacuo*. The resulting residue was dissolved in EtOAc and washed with H_2O and

brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude material was purified by flash chromatography (1:9 EtOAc:hexane) to give 1-[(2,2-dimethylpropanoyl)oxy]-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,2,3,6-tetrahydropyridine (355 mg, 76.0 %).

Procedure W

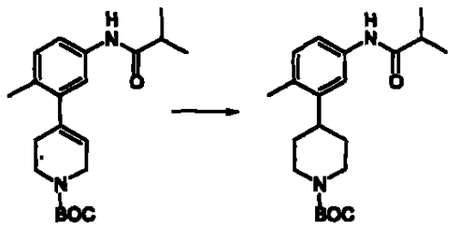
Scheme AF



TERT-BUTYL 4-[5-(ISOBUTYRYLAMINO)-2-METHYLPHENYL]-3,6-DIHYDRO-1(2H)-PYRIDINECARBOXYLATE: To a 50-mL RB flask containing 1-[(2,2-dimethylpropanoyl)oxy]-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,2,3,6-tetrahydropyridine (500 mg, 1.62 mmol), K_2CO_3 (670 mg, 4.86 mmol) and $PdCl_2dppf$ (155 mg) was added a solution of N-(3-bromo-4-methylphenyl)-2-methylpropanamide (415mg, 1.62 mmol) in DMF (10.0 mL) at room temperature under argon. The mixture was heated to 80 °C under argon overnight. After cooled to room temperature, the mixture was filtered through celite and the celite was

washed with EtOAc (3 x 20 mL). The filtrates were washed with H_2O (20 mL), brine (20 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude material was purified flash chromatography (20% EtOAc/ hexane) to give tert-butyl 4-[5-(isobutyrylamino)-2-methylphenyl]-3,6-dihydro-1(2H)-pyridinecarboxylate (360 mg, 62.0 %).

Scheme AG

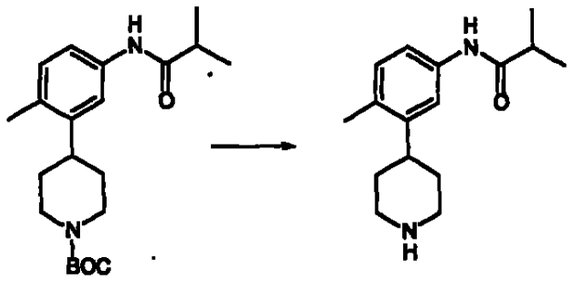


Procedure X

TERT-BUTYL 4-[5-(ISOBUTYRYLAMINO)-2-METHYLPHENYL]-1-PIPERIDINECARBOXYLATE: A solution of tert-butyl 4-[5-(isobutyrylamino)-2-methylphenyl]-3,6-dihydro-1(2H)-pyridinecarboxylate (335 mg, 0.93 mmol) and 10% Pd/C (35.0 mg) in EtOH (20.0 mL) was hydrogenated at room temperature overnight using the hydrogen balloon method. The reaction mixture was filtered through celite and washed with ethanol (3 x 10 mL). The combined extracts were concentrated *in vacuo* to afford tert-butyl 4-[5-(isobutyrylamino)-2-methylphenyl]-1-piperidinecarboxylate (335 mg, 100 %).

Procedure Y

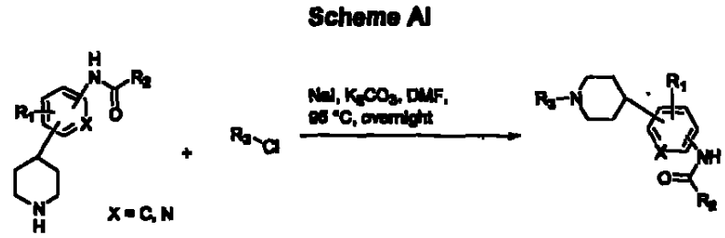
Scheme AH

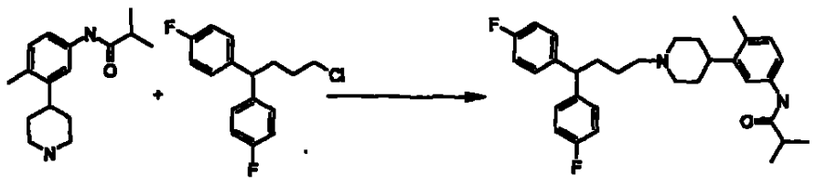


2-METHYL-*N*-[4-METHYL-3-(4-PIPERIDINYL)PHENYL] PROPANAMIDE: Into a solution of tert-butyl 4-[5-(isobutyrylamino)-2-methylphenyl]-1-piperidinecarboxylate (335 mg, 0.930 mmol) in CH_2Cl_2 (10.0 mL) was added TFA (10.0 mL) at room temperature. The reaction mixture was stirred for 2 h and concentrated *in vacuo*. The residue was dissolved in 20 mL of $CHCl_3$/i-PrOH (3:1) and was basified with 5% KOH solution (10 mL). The aqueous layer was extracted with $CHCl_3$/i-PrOH (3:1, 3 x 10 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give 2-methyl-*N*-[4-methyl-3-(4-piperidinyl)phenyl]propanamide (190 mg, 78.0 %).

Procedure Z

Scheme AI



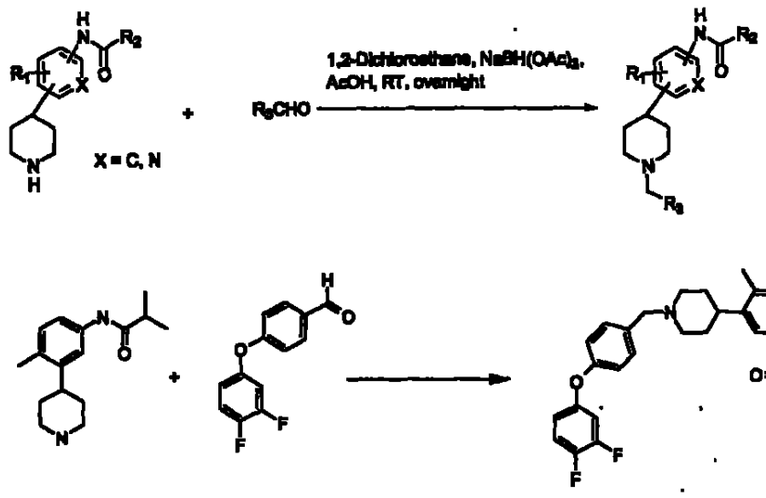


N-(3-{1-[4,4-BIS(4-FLUOROPHENYL)BUTYL]-4-PIPERIDINYL}-4-METHYLPHENYL)-2-METHYLPROPANAMIDE: A solution of 2-methyl-*N*-[4-methyl-3-(4-piperidinyl)phenyl]propanamide (49.0 mg, 0.190 mmol), 1-[4-chloro-1-(4-fluorophenyl)butyl]-4-fluorobenzene (58.0 mg, 0.210 mmol), NaI (42.0 mg, 0.280 mmol) and K_2CO_3 (52.0 mg, 0.380 mmol) in DMF (10.0 mL) was heated at 95 °C overnight. The mixture was diluted with water (20 mL) and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated in *vacuo*. The crude product was purified by flash chromatography [5% NH_3 (2.0 M in MeOH) in CH_2Cl_2] to afford *N*-(3-{1-[4,4-bis(4-fluorophenyl)butyl]-4-piperidinyl}-4-methylphenyl)-2-methylpropanamide (37.0 mg, 38.0 %).

Procedure AA

246

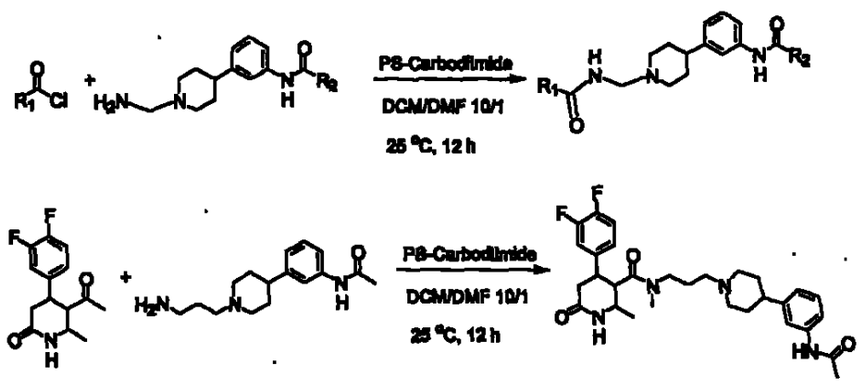
Scheme AJ



***N*-(3-{1-[4-(3,4-DIFLUOROPHENOXY)BENZYL]-4-PIPERIDINYL}-4-METHYLPHENYL)-2-METHYLPROPANAMIDE:** To a solution of 4-(3,4-Difluorophenoxy)benzaldehyde (41.0 mg, 0.170 mmol) and 2-methyl-*N*-[4-methyl-3-(4-piperidinyl)phenyl]propanamide (45.0 mg, 0.170 mmol) in 1,2-dichloroethane (5.00 mL) was added sodium triacetoxyborohydride (110 mg, 0.520 mmol) and AcOH (10.0 µL, 0.170 mmol) at room temperature. The mixture was stirred overnight. The reaction mixture was quenched by saturated $NaHCO_3$ solution (10 mL) and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, concentrated *in vacuo*. The crude product was purified by preparative TLC using 5% NH_3 (2.0 M in MeOH) in CH_2Cl_2 to give the desired product *N*-(3-{1-[4-(3,4-difluorophenoxy)benzyl]-4-piperidinyl}-4-methylphenyl)-2-methylpropanamide (44.0 mg, 54.0 %).

Procedure AC

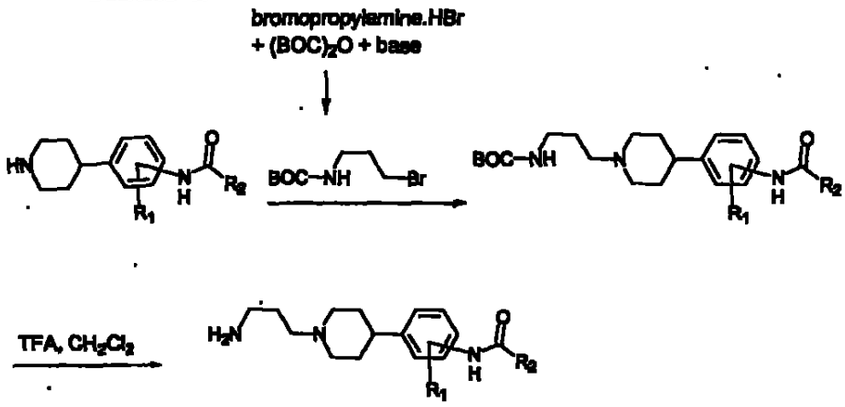
Scheme AT: Synthesis of Amides using PS-Carbodiimide Resin



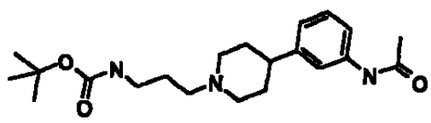
A mixture of a carboxylic acid (0.0800 mmol) and PS-Carbodiimide Resin (2.00 eq, 80.0 mg, 1.34 mmol/g) in DCM:DMF (10:1, 3.00 mL) was shaken for 30 min. To the reaction mixture was added amine (0.0540 mmol) and the resulting mixture was shaken for 12 h at room temperature. The reaction mixture was filtered and the resin was washed with CH_2Cl_2. The combined organic extracts were concentrated to a small volume, applied to a preparative TLC plate and eluted with 6 % NH_3 (2.0 M in MeOH) in CH_2Cl_2 to give the desired product.

Procedure AD

Scheme X



TERT-BUTYL N-(3-BROMOPROPYL)CARBAMATE: Prepared from 3-bromopropylamine hydrobromide and BOC_2O in the presence of base in CH_2Cl_2: ^1H NMR (300 MHz) δ 5.07 (br, 1 H), 3.31 (t, 2 H, J = 6.6 Hz), 3.12 (apparent br q, 2 H, J = 6.0 Hz), 1.92 (p, 2 H, J = 6.6 Hz), 1.30 (s, 9H).



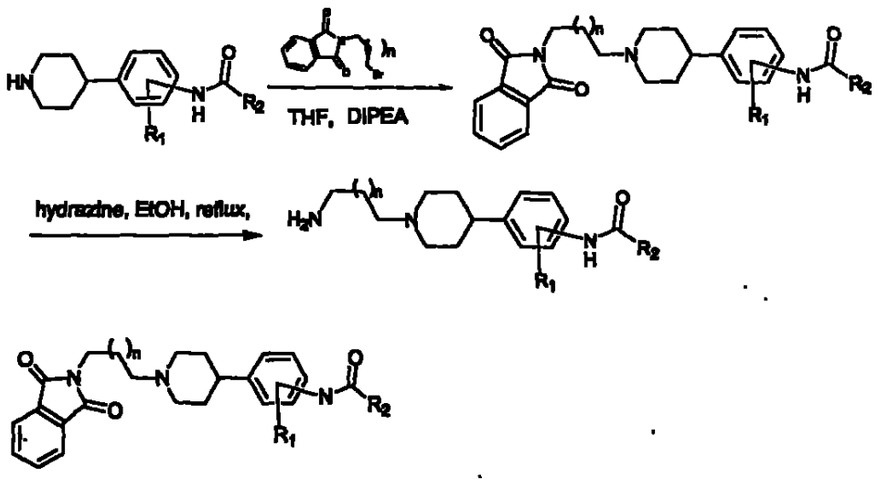
Step 1. To a solution of piperidine (19.3 mmol) in dioxane (20.0 mL) was *N*-(tert-butoxycarbonyl)-3-bromopropylamine (21.2 mmol) and potassium carbonate (38.7 mmol) at room temperature and the mixture was heated at reflux temperature for 24 h. The reaction mixture was cooled to room temperature, concentrated *in vacuo* and partitioned between $CHCl_3$ (40 mL) and water (5 mL). The organic layer was washed with brine, dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (ethyl acetate: methanol 9:1) to yield the required product tert-butyl 3-{4-[3-(acetylamino)phenyl]-1-

piperidinyl}propylcarbamate as a colorless oil: ESMS *m/e*: 376.2 $[M+H]^+$.

Step 2. HCl gas was bubbled into a solution of the boc-protected amine (12.1 mmol) in dioxane (5.00 mL) for 10-20 minutes at 0-5 °C. The resulting solution was stirred at 0-5 °C for 1 h, concentrated, neutralized with 10 % KOH solution (10 mL) and extracted into CH_2Cl_2 (25 mL). The organic extract was washed with brine, dried over sodium sulfate and concentrated *in vacuo*. The crude product was chromatographed to give the desired product *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}acetamide: ESMS *m/e*: 276.1 $[M+H]^+$.

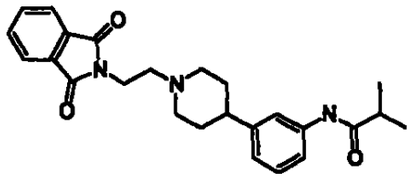
Procedure AE

Scheme Y

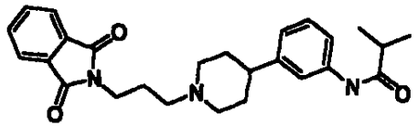


Step 1: A mixture of piperidine (1.00 eq, 0.0226 mmol), *N*-(bromoalkyl)phthalimide (1.50 eq, 0.0338 mmol), Bu_4NI (200 mg) and diisopropylethylamine (5.00 eq, 0.113 mmol)

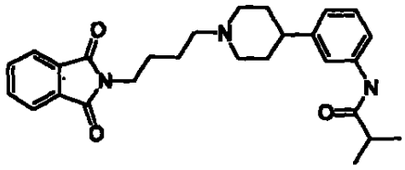
in dioxane (200 mL) was heated at 99 °C for 24 h. The reaction was followed by TLC analysis (95:5 CH_2Cl_2:methanol). If necessary additional 0.0113 mmol of the appropriate bromoalkylphthalimides was added to each reaction mixture and the heating was continued for additional 48 h. The reaction mixture was cooled to room temperature, the ammonium salts were filtered out and the solvent was removed under reduced pressure. The crude product was chromatographed to give the desired product.



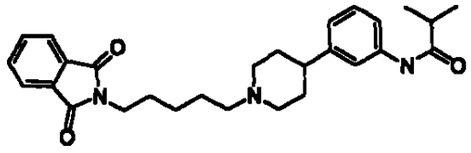
ESMS m/e: 420.2
$[M+H]^+$



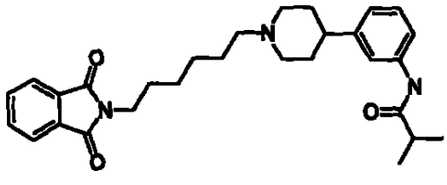
ESMS m/e: 434.4
$[M+H]^+$



ESMS m/e: 448.4
$[M+H]^+$

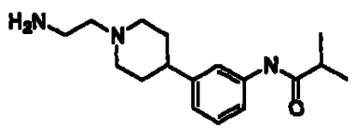


ESMS m/e: 462.4
$[M+H]^+$

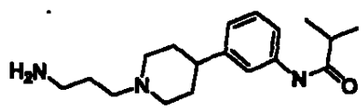


ESMS m/e: 476.4
$[M+H]^+$

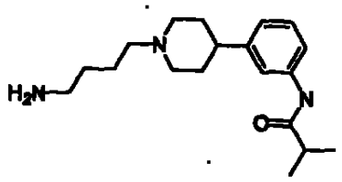
Step 2: Deprotection of the resulting phthalimides was conducted by heating a solution of phthaliamide-protected amines with excess hydrazine hydrate (10 eq) in ethanol (0.5-1.0 M) at 90 °C for 4 h. The reaction mixture was monitored by TLC to completion. Upon the reaction was completed, the mixture was cooled to room temperature, the insoluble by-products were filtered out through celite and the solvent was removed *in vacuo*. The crude product was chromatographed (dichloromethane-methanol-isoprpylamine) to give the desired products.



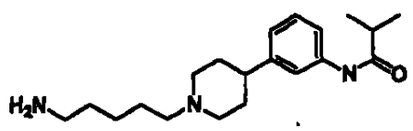
ESMS m/e: 290.2 $[M+H]^+$



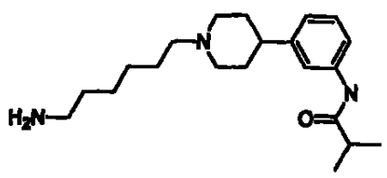
ESMS m/e: 304.1 $[M+H]^+$



ESMS m/e: 318.2 $[M+H]^+$

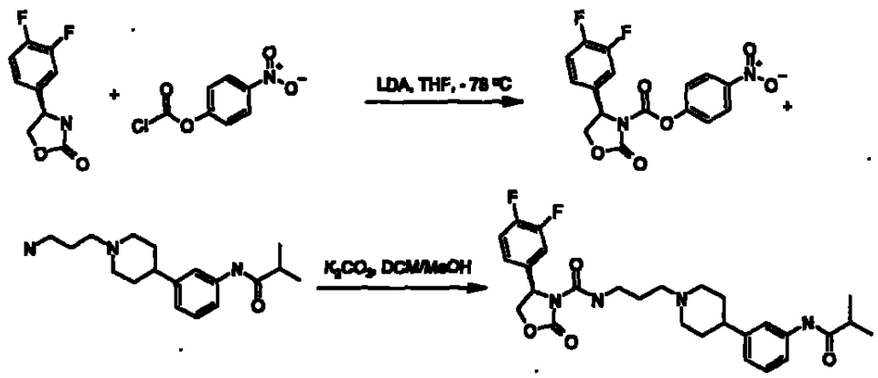


ESMS m/e: 332.2 $[M+H]^+$

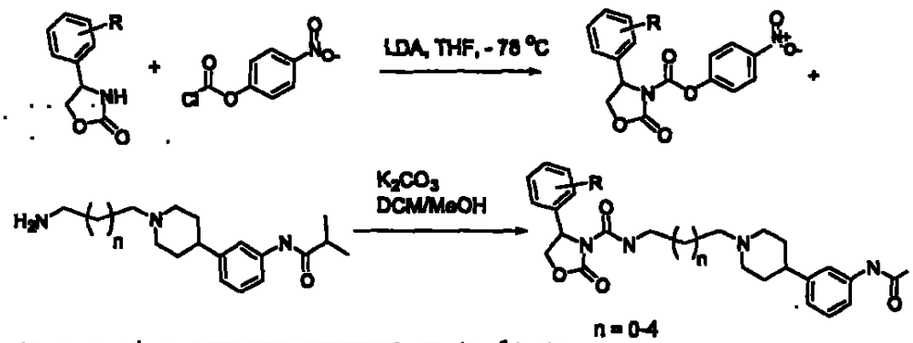


ESMS m/e: 346.3 $[M+H]^+$

Procedure AF



Scheme H



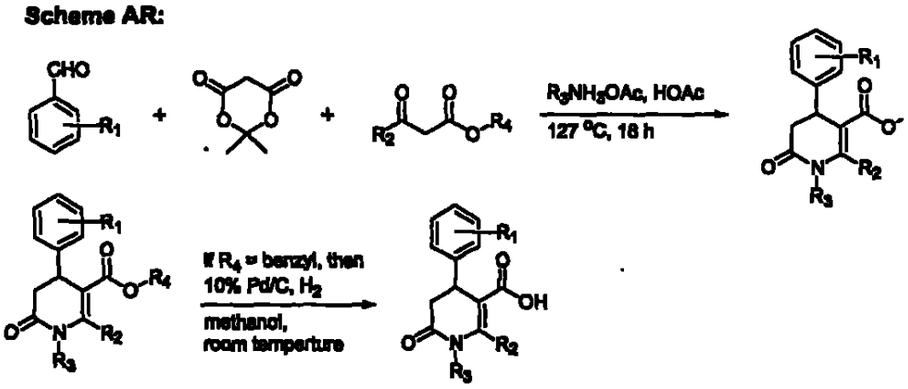
(4R)-4-(3,4-DIFLUOROPHENYL)-N-(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-2-OXO-1,3-OXAZOLIDINE-3-CARBOXAMIDE was synthesized according to Scheme H and Procedure AF: To a solution of (4*R*)-4-(3,4-difluorophenyl)-1,3-oxazolidin-2-one (this compound and analogs were prepared according to *J. Med. Chem* 2000, 43, 2775) (0.300 mol, 60.0 mg) in THF (5.00 mL) was added LDA (2.0 M in THF, 0.390 mmol, 0.200 mL) at -78 °C under argon. After 30 min at -78 °C, to the mixture was added a solution of 4-nitrophenyl chloroformate (0.330 mmol, 51.2 mg) in THF (0.500 mL) at -78 °C. After stirring for 30 min at -78 °C the reaction

mixture was diluted with a saturated Na_2CO_3 solution (5.0 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by preparative TLC plates (10:1 hexane:ethyl acetate) to afford 4-nitrophenyl (4*R*)-4-(3,4-difluorophenyl)-2-oxo-1,3-oxazolidine-3-carboxylate (51.5 mg, 54.0 %).

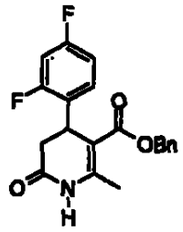
4-Nitrophenyl (4R)-4-(3,4-difluorophenyl)-2-oxo-1,3-oxazolidine-3-carboxylate (169 mg, 0.465 mmol), N-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide (141 mg, 0.465 mmol), K_2CO_3 (0.193 g, 1.39 mmol), CH_2Cl_2 (10 mL), and methanol (0.1 mL) were combined in a flask. The mixture was stirred overnight at room temperature, the solvent was removed *in vacuo*, and the residue was purified by chromatography [2.5% of NH_3 (2.0 M in methanol) in CH_2Cl_2] to afford the desired product (26.1 mg, 10.6 %): ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (t, 1H, J = 5.5 Hz), 7.45 (s, 2H), 7.38 (d, 1H, J = 8.6 Hz), 7.24-7.12 (m, 3H), 7.06 (m, 1H), 6.97 (d, 1H, J = 8.6 Hz), 5.40 (dd, 1H, J = 3.9-8.8 Hz), 4.71 (t, 1H, J = 8.8 Hz), 4.23 (dd, 1H, J = 4.4, 9.1 Hz), 3.32 (qt, 2H, J = 6.1 Hz), 2.99 (d, 2H, J = 11.0 Hz), 2.49 (qt, 2H, J = 7.0 Hz), 2.41(t, 2H, J = 7.0 Hz), 1.99-1.97 (m, 2H), 1.82-1.68 (m, 6H), 1.23 (d, 6H, J = 7.3 Hz); Anal. Calcd. for $C_{28}H_{34}F_2N_4O_4$+HCl+0.185$CHCl_3$: C, 57.6; H, 6.04; N, 9.54. Found: C, 58.5; H, 6.08; N, 9.47; ESMS *m/e*: 529.1 $(M + H)^+$.

Procedure AG

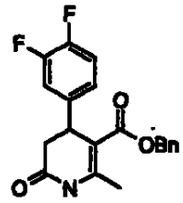
Scheme AR:



Step 1: A solution of ketoester (10 mmol), Meldrum's acid (10 mmol), aldehyde (10 mmol) and an ammonium acetate (11 mmol) in HOAc (10 mL) was heated at reflux temperature for 18 h.[1] The cooled reaction mixture was poured over ice (100 g). The precipitated oils were collected and dried under reduced pressure. The benzyl ester protected analogs solidified upon trituration with a mixture of ether/hexane.



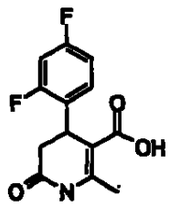
1.05 g, 29.0 %



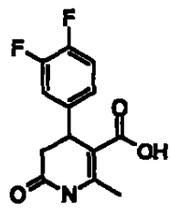
523 mg, 15.0%

[1] MORALES, A.; OCHOA, E.; SUAREZ, M.; VERDECIA, Y.; GONZALEZ, L.; MARTIN, N.; QUINTEIRO, M.; SEOANE, C.; SOTO, J. L.; *J. Heterocycl. Chem.* [JHTCAD] **1996**, *33 (1)*, 103-107.

Step 2: A mixture of a benzyl ester and 10% Pd/C in methanol was hydrogenated using the balloon method at room temperature. The reaction mixture was monitored (TLC) to completion, filtered through Celite 545 and the Celite filter cake was washed with methanol (3 x 10 mL). The combined methanol extracts were concentrated *in vacuo* to give the desired carboxylic acid that was used in the next step without any further purification.

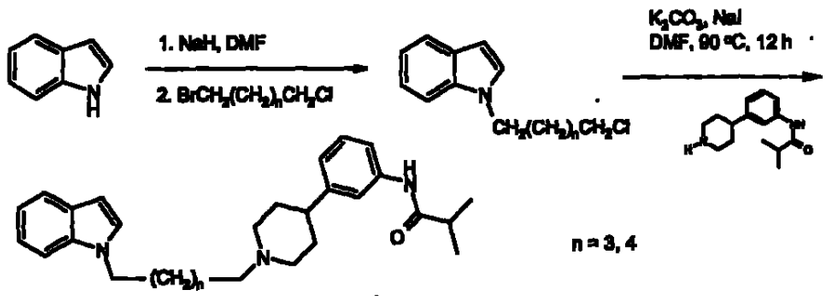


4-(2,4-DIFLUOROPHENYL)-2-METHYL-6-OXO-1,4,5,6-TETRAHYDRO-3-PYRIDINECARBOXYLIC ACID was synthesized according to Procedure AG and Scheme AR: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.82 (s, 1H), 7.00-6.72 (m, 3H), 4.51 (d, 1H, J = 8.4 Hz), 2.90 (dd, 1H, J = 8.4, 16.3 Hz), 2.68 (d, 1H, J = 16.3 Hz), 2.46 (s, 3H).



4-(3,4-DIFLUOROPHENYL)-2-METHYL-6-OXO-1,4,5,6-TETRAHYDRO-3-PYRIDINECARBOXYLIC ACID was synthesized according to Procedure AG and Scheme AR: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.40-6.80 (m, 4 H), 4.23 (d, 1 H, J = 7.5 avg. Hz), 2.93 (dd, 1 H, J = 16.8, 7.5 avg. Hz), 2.68 (d, 1 H, J = 16.5 avg. Hz), 2.45 (s, 3 H).

Procedure AH



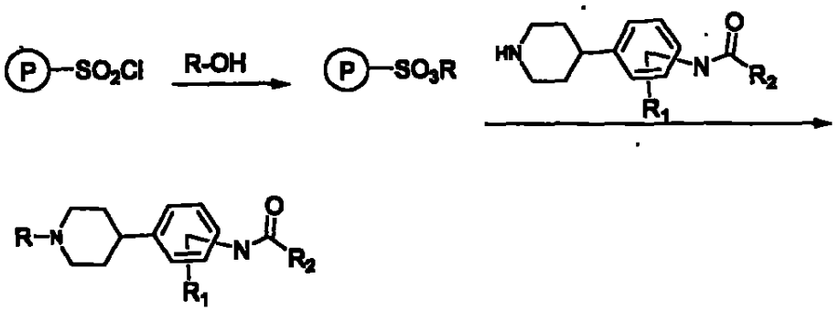
1-(6-CHLOROHEXYL)-1H-INDOLE: To a mixture of NaH (0.249 g, 10.0 mmol) in DMF (5.00 mL) was added a solution of 1-*H*-indole (0.585 g, 5.00 mmol) in DMF (2.00 mL) at 0 °C. The reaction mixture was stirred for 30 minutes at 0 °C and warmed up to room temperature. To the reaction mixture 1-bromo-6-chlorohexane (0.998 g, 5.00 mmol) was added dropwise via syringe and the reaction mixture was stirred overnight. The reaction mixture was diluted with EtOAc (30 mL), washed with water (3 X 10 mL), brine (10 mL), dried over $MgSO_4$, concentrated *in vacuo* and purified by chromatography using hexane:EtOAc (97.5:2.5) to give the desired product (0.900 g, 76.0 %): ^1H NMR (400 MHz, $CDCl_3$) δ 7.76-7.54 (m, 1H), 7.47-6.96 (m, 4H), 6.60-6.34 (m, 1H), 4.13 (t, 2H, J = 6.8 Hz), 3.50 (t, 2H, J = 5.6 Hz), 1.98-1.79 (m, 2H), 1.79-1.64 (m, 2H), 1.54-1.17 (m, 4H).

***N*-(3-{1-[6-(1H-INDOL-1-YL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** A mixture of 1-(6-Chlorohexyl)-1*H*-indole (23.6 mg, 0.100 mmol), 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (24.6 mg, 0.100 mmol), K_2CO_3 (27.6 mg, 0.200 mmol), NaI (22.5 mg, 0.150 mmol) and DMF (1.00 mL) was heated at 100 °C for 12 h. The reaction mixture was cooled to room temperature and the crude material was purified by preparative TLC using 5 %

of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product as a yellow solid (40 mg, 90 %): ^1H NMR (400 MHz, $CDCl_3$) δ 8.08-6.52 (m, 11H), 4.17 (t, 2H, J = 7.2 Hz), 3.26 (d, 2H, J = 11.6 Hz), 2.74-2.52 (m, 4H), 2.44-2.28 (m, 2H), 2.20-2.02 (m, 2H), 1.98-1.82 (m, 4H), 1.78-1.62 (m, 2H), 1.43-1.28 (m, 4H), 1.28 (d, 6H, J = 6.8 Hz); ESMS m/e: 446.5 $(M + H)^+$.

Procedure AI:

Scheme AU: Preparation of tert-Piperdines Usingd PS-SO2Cl Resin

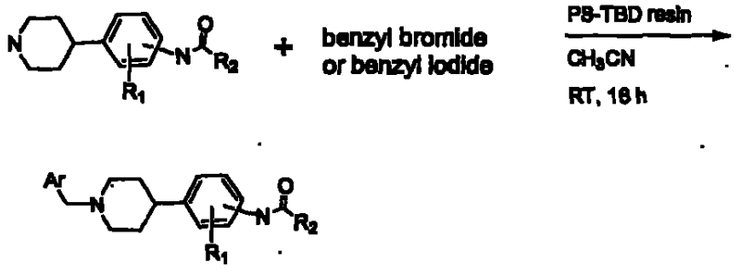


The library was constructed in polypropylene Robbins "Reactor Blocks", 48 well plates. PS-TSCl resin (100 mg, 1.00 eq, purchased from Argonaut Technologies) was placed in each well of the "Reactor Blocks" 48 well plates. To each well was added 2-10 eq of an alcohol in dichloromethane:pyridine (1:1, 3.00 mL). The mixture was stirred at room temperature for 5 h and the resin was washed with dichloromethane (3 x 4.00 mL), DMF (5 x 4.00 mL), DMF/H_2O (3:1, 5 x 4.00 mL), THF (3 x 4.00 mL), dichloromethane (3 x 4.00 mL), acetonitrile (2 x 4.00 mL) and dried under reduced pressure. A solution of an amine (0.0750 mmol, 0.500 eq) and N,N-diisopropylethyl amine (19.0 mg, 0.150 mmol, 1.00 eq) in acetonitrile

(3.00 mL) was added to the well containing the derivatized resin and the mixture was reacted at 70 °C for 16 h in the Robbins rotating oven. After cooling, AP-isocyanate resin (120 mg, 0.150 mmol, 1.00 eq) and THF (2.00 mL) was added to the each reaction vessel and reacted at room temperature for additional 3 h. The solution was filtered into the Robbins® receiving plates and concentrated *in vacuo* to give the desired tertiary amines which were analyzed via LC-MS.

Procedure AJ:

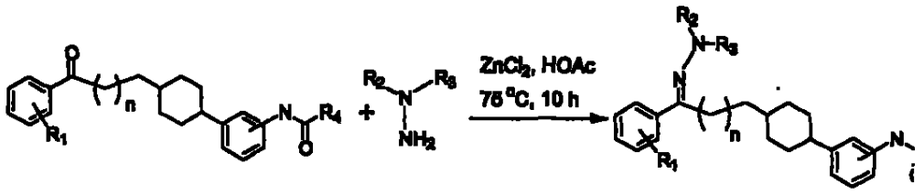
Scheme AV: Preparation of tert-Piperidines Using Piperdines,



The library was constructed in polypropylene Robbins® 48 well plates Reactor Blocks. In the initial incubation period, each well was charged with PS-TBD resin (from Argonaut Technologies, 200 mg, 0.280 mmol, 2.50 eq) and piperidine (0.120 mmol, 1.10 eq) in acetonitrile (0.500 mL) and agitated for 1 h. A solution of benzyl iodide or bromide (0.110 mmol, 1.00 eq) in acetonitrile (0.500 mL) was added to each well followed by additional acetonitrile (1.00 mL) to make a total volume of 2 mL and the mixture was rotated in a Robbins rotating oven at room temperature for 16 h. Then AP-Isocyanate resin (Argonaut Technologies, 250 mg (0.430 mmol, 4.00 eq) was

added to each well and reacted further at room temperature for another 12 h. The mixture was filtered and the filtrate was concentrated *in vacuo* to obtain the desired product that was characterized via LC-MS.

Scheme AX



Example 117

N-(3-{1-[3-(4-BROMOPHENYL)-3-OXOPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Procedure K (KI) and Scheme E (K_2CO_3) using 1-(4-bromophenyl)-3-chloro-1-propanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 457.1 (M + H)$^+$.

Example 118

***N*-(3-{1-[3-(4-CHLOROPHENYL)-3-OXOPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Procedure K (KI) and Scheme E (K_2CO_3) using 3-chloro-1-(4-chlorophenyl)-1-propanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 413.1 (M + H)$^+$.

Example 119

***N*-(3-{1-[3-(4-METHOXYPHENYL)-3-OXOPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Procedure K (KI) and Scheme E (K_2CO_3) using 3-chloro-1-(4-

methoxyphenyl)-1-propanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 409.2 (M + H)$^+$.

Example 120

***N*-(3-{1-[3-(2,3-DIHYDRO-1*H*-INDEN-5-YL)-3-OXOPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Procedure K (KI) and Scheme E (K_2CO_3) using 3-chloro-1-(2,3-dihydro-1*H*-inden-5-yl)-1-propanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 419.2 (M + H)$^+$.

Example 121

2-METHYL-*N*-{3-[1-(3-OXO-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Procedure K (KI) and Scheme E (K_2CO_3) using 3-chloro-1-phenyl-1-propanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 379.2 (M + H)$^+$.

Example 122

2-METHYL-*N*-(3-{1-[3-(4-METHYLPHENYL)-3-OXOPROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Procedure K (KI) and Scheme E (K_2CO_3) using 3-chloro-1-(4-methylphenyl)-1-propanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 393.2 (M + H)$^+$.

Example 123

***N*-(3-{1-[3-(4-FLUOROPHENYL)-3-OXOPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Procedure K (KI) and Scheme E (K_2CO_3) using 3-chloro-1-(4-fluorophenyl)-1-propanone and 2-methyl-*N*-[3-(4-

piperidinyl)phenyl]propanamide: ESMS *m/e*: 397.2 (M + H)$^+$.

Example 124

***N*-(3-{1-[3-(4-CHLOROPHENYL)-3-HYDROXYPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure L and Scheme AN using *N*-(3-{1-[3-(4-chlorophenyl)-3-oxopropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 415.1 (M + H)$^+$.

Example 125

***N*-(3-{1-[3-(4-CHLOROPHENYL)-3-(3,4-DIFLUOROPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-chlorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 3,4-difluorophenol: ESMS *m/e*: 526.8 (M + H)$^+$.

Example 126

***N*-(3-{1-[3-(4-CHLOROPHENYL)-3-(2-METHYLPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-chlorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and *o*-cresol: ESMS *m/e*: 505.4 (M + H)$^+$.

Example 127

***N*-(3-{1-[3-(4-FLUOROPHENYL)-3-HYDROXYPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure L and Scheme AN using *N*-(3-{1-[3-(4-fluorophenyl)-3-oxopropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 399.2 (M + H)$^+$.

Example 128

N-(3-{1-[3-HYDROXY-3-(4-METHOXYPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure L and Scheme AN using *N*-(3-{1-[3-(4-methoxyphenyl)-3-oxopropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 411.2 $(M + H)^+$.

Example 129

N-(3-{1-[3-(4-BROMOPHENYL)-3-HYDROXYPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure L and Scheme AN using *N*-(3-{1-[3-(4-bromophenyl)-3-oxopropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 459.1 $(M + H)^+$.

Example 130

N-(3-{1-[3-(4-CHLOROPHENYL)-3-(4-METHOXYPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-chlorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methoxyphenol: ESMS *m/e*: 520.8 $(M + H)^+$.

Example 131

N-(3-{1-[3-(4-CHLOROPHENOXY)-3-(4-FLUOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-chlorophenol: ESMS *m/e*: 509.1 $(M + H)^+$.

Example 132

N-(3-{1-[3-(4-FLUOROPHENYL)-3-(2,3,4,5,6-PENTAFLUOROPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN

using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 2,3,4,5,6-pentafluorophenol: ESMS *m/e*: 564.7 (M + H)$^+$.

Example 133

***N*-(3-{1-[3-(4-BROMOPHENYL)-3-(2-METHYLPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-bromophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 2-methylphenol: ESMS *m/e*: 548.8 (M + H)$^+$.

Example 134

***N*-(3-{1-[3-(3,4-DIFLUOROPHENOXY)-3-(4-FLUOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 3,4-difluorophenol: ESMS *m/e*: 511.1 (M + H)$^+$.

Example 135

***N*-(3-{1-[3-(4-BROMOPHENOXY)-3-(4-FLUOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-bromophenol: ESMS *m/e*: 553.0 (M + H)$^+$.

Example 136

***N*-(3-{1-[3-(3,4-DICHLOROPHENOXY)-3-(4-FLUOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN

using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 3,4-dichlorophenol: ESMS *m/e*: 542.7 $(M + H)^+$.

Example 137

***N*-[3-(1-{3-(4-FLUOROPHENYL)-3-[4-(TRIFLUOROMETHYL)PHENOXY]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethyl)phenol: ESMS *m/e*: 543.1 $(M + H)^+$.

Example 138

***N*-(3-{1-[3-(3-BROMOPHENOXY)-3-(4-FLUOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 3-bromophenol: ESMS *m/e*: 552.7 $(M + H)^+$.

Example 139

***N*-(3-{1-[3-(4-FLUOROPHENOXY)-3-(4-FLUOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-fluorophenol: ESMS *m/e*: 493.2 $(M + H)^+$.

Example 140

***N*-(3-{1-[3-(3-FLUOROPHENOXY)-3-(4-FLUOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-

methylpropanamide and 3- fluorophenol: ESMS *m/e*: 492.9 $(M + H)^+$.

Example 141

***N*-(3-{1-[3-(2,6-DICHLOROPHENOXY)-3-(4-FLUOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 2,6-dichlorophenol: ESMS *m/e*: 543.0 $(M + H)^+$.

Example 142

***N*-(3-{1-[3-(2,5-DIFLUOROPHENOXY)-3-(4-FLUOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 2,5-difluorophenol: ESMS *m/e*: 511.5 $(M + H)^+$.

Example 143

***N*-(3-{1-[3-(3-CHLOROPHENOXY)-3-(4-FLUOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 3-chlorophenol: ESMS *m/e*: 509.1 $(M + H)^+$.

Example 144

***N*-(3-{1-[3-(4-BROMOPHENYL)-3-(3-METHYLPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-bromophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-

methylpropanamide and 3- methylphenol: ESMS *m/e*: 549.1 $(M + H)^+$.

Example 145

***N*-(3-{1-[3-([1,1'-BIPHENYL]-4-YLOXY)-3-(4-BROMOPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-bromophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-phenylphenol: ESMS *m/e*: 611.2 $(M + H)^+$.

Example 146

***N*-(3-{1-[3-(2,4-DIFLUOROPHENOXY)-3-(4-FLUOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 2,4-difluorophenol: ESMS *m/e*: 511.1 $(M + H)^+$.

Example 147

***N*-(3-{1-[3-(4-BROMOPHENYL)-3-(3-METHOXYPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-bromophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 3-methoxyphenol: ESMS *m/e*: 564.6 $(M + H)^+$.

Example 148

METHYL 4-(1-(4-BROMOPHENYL)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPOXY)BENZOATE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-bromophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-

2-methylpropanamide and methyl 4-hydroxybenzoate: ESMS *m/e*: 593.0 $(M + H)^+$.

Example 149

***N*-(3-{1-[3-(4-BROMOPHENYL)-3-(4-PHENOXYPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-bromophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-phenoxyphenol: ESMS *m/e*: 626.6 $(M + H)^+$.

Example 150

***N*-(3-{1-[3-(4-BROMOPHENYL)-3-(2-CHLORO-4-METHYLPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-bromophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 2-chloro-4-methylphenol: ESMS *m/e*: 583.0 $(M + H)^+$.

Example 151

***N*-(3-{1-[3-(4-BROMOPHENYL)-3-PHENOXYPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-bromophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenol: ESMS *m/e*: 535.0 $(M + H)^+$.

Example 152

***N*-[3-(1-{3-(4-BROMOPHENYL)-3-[4-(TRIFLUOROMETHYL)PHENOXY]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-bromophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethyl)phenol: ESMS *m/e*: 603.1 $(M + H)^+$.

Example 153

***N*-(3-{1-[3-(2-ACETYLPHENOXY)-3-(4-BROMOPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-bromophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 2-acetylphenol: ESMS *m/e*: 576.6 $(M + H)^+$.

Example 154

***N*-(3-{1-[3-(3-ACETYLPHENOXY)-3-(4-BROMOPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-bromophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 3-acetylphenol: ESMS *m/e*: 576.9 $(M + H)^+$.

Example 155

***N*-(3-{1-[3-(3-ACETYLPHENOXY)-3-(2,3-DIHYDRO-1H-INDEN-5-YL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(2,3-dihydro-1*H*-inden-5-yl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 3-acetylphenol: ESMS *m/e*: 539.2 $(M + H)^+$.

Example 156

***N*-(3-{1-[3-(2,3-DIHYDRO-1H-INDEN-5-YL)-3-PHENOXYPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(2,3-dihydro-1*H*-inden-5-yl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenol: ESMS *m/e*: 497.2 $(M + H)^+$.

Example 157

N-(3-{1-[3-(2-ACETYLPHENOXY)-3-(2,3-DIHYDRO-1H-INDEN-5-YL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:

Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(2,3-dihydro-1H-inden-5-yl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide 2-acetylphenol: ESMS *m/e*: 539.1 $(M + H)^+$.

Example 158

N-(3-{1-[3-(4-BROMOPHENOXY)-3-(4-BROMOPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-bromophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-bromophenol: ESMS *m/e*: 612.7 $(M + H)^+$.

Example 159

N-(3-{1-[3-(4-BROMOPHENYL)-3-(4-CHLOROPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-bromophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-chlorophenol: ESMS *m/e*: 568.7 $(M + H)^+$.

Example 160

N-(3-{1-[3-(4-BROMOPHENYL)-3-(4-FLUOROPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-bromophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-fluorophenol: ESMS *m/e*: 552.8 $(M + H)^+$.

Example 161

N-(3-{1-[3-(2,3-DIHYDRO-1*H*-INDEN-5-YL)-3-(4-METHOXYPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(2,3-dihydro-1*H*-inden-5-yl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methoxyphenol: ESMS *m/e*: 527.3 $(M + H)^+$.

Example 162

N-(3-{1-[3-(2,3-DIHYDRO-1*H*-INDEN-5-YL)-3-(4-FLUOROPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(2,3-dihydro-1*H*-inden-5-yl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-fluorophenol: ESMS *m/e*: 515.2 $(M + H)^+$.

Example 163

N-(3-{1-[3-(2,3-DIHYDRO-1*H*-INDEN-5-YL)-3-HYDROXYPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE

Prepared by Procedure L and Scheme AN using *N*-(3-{1-[3-(2,3-dihydro-1*H*-inden-5-yl)-3-oxopropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 421.2 $(M + H)^+$.

Example 164

N-[3-(1-{3-(2,3-DIHYDRO-1*H*-INDEN-5-YL)-3-[4-(TRIFLUOROMETHYL)PHENOXY]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(2,3-dihydro-1*H*-inden-5-yl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-trifluoromethylphenol: ESMS *m/e*: 565.0 $(M + H)^+$.

Example 165

N-(3-{1-[3-(4-BROMOPHENOXY)-3-(2,3-DIHYDRO-1*H*-INDEN-5-YL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:

Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(2,3-dihydro-1*H*-inden-5-yl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-bromophenol:

ESMS *m/e*: 577.4 $(M + H)^+$.

Example 166

N-(3-{1-[3-(3-ACETYLPHENOXY)-3-(4-CHLOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-chlorophanyl)-3-hydroxypropyl]-4-piperidinyl}phanyl)-2-methylpropanamide and 3-acetylphenol: SMS *m/e*: 533.1 $(M + H)^+$.

Example 167

N-(3-{1-[3-(4-METHOXYPHENOXY)-3-(4-METHOXYPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-hydroxy-3-(4-methoxyphenyl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methoxyphenol: ESMS *m/e*: 517.4 $(M + H)^+$.

Example 168

N-(3-{1-[3-(4-CHLOROPHENOXY)-3-(2,3-DIHYDRO-1*H*-INDEN-5-YL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:

Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(2,3-dihydro-1*H*-inden-5-yl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-chlorophenol: ESMS *m/e*: 531.1 $(M + H)^+$.

Example 169

N-(3-{1-[3-(2-ACETYLPHENOXY)-3-(4-CHLOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-chlorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 2-acetylphenol: ESMS *m/e*: 533.4 $(M + H)^+$.

Example 170

N-(3-{1-[3-(4-BROMOPHENYL)-3-(4-METHOXYPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-bromophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methoxyphenol: ESMS *m/e*: 565.0 $(M + H)^+$.

Example 171

N-(3-{1-[3-(4-BROMOPHENOXY)-3-(4-CHLOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-chlorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-bromophenol: ESMS m/e: 568.8 $(M + H)^+$.

Example 172

N-(3-{1-[3-(4-CHLOROPHENOXY)-3-(4-CHLOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-chlorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-chlorophenol: ESMS *m/e*: 525.0 $(M + H)^+$.

Example 173

N-(3-{1-[3-(4-METHOXYPHENYL)-3-PHENOXYPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-hydroxy-3-(4-methoxyphenyl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenol: ESMS *m/e*: 487.4 $(M + H)^+$.

Example 174

N-(3-{1-[3-(4-FLUOROPHENYL)-3-PHENOXYPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenol: ESMS *m/e*: 475.6 $(M + H)^+$.

Example 175

N-(3-{1-[3-(2-ACETYLPHENOXY)-3-(4-FLUOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 2-acetylphenol: ESMS *m/e*: 517.1 $(M + H)^+$.

Example 176

N-(3-{1-[3-(3-ACETYLPHENOXY)-3-(4-FLUOROPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 3-acetylphenol: ESMS *m/e*: 516.9 $(M + H)^+$.

Example 177

N-(3-{1-[3-(4-FLUOROPHENYL)-3-(4-METHOXYPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by

Procedure A and Scheme AN using *N*-(3-{1-[3-(4-fluorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methoxyphenol: ESMS *m/e*: 505.2 $(M + H)^+$.

Example 178

N-(3-{1-[3-(4-CHLOROPHENOXY)-3-(4-METHOXYPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-hydroxy-3-(4-methoxyphenyl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-cholorophenol: ESMS *m/e*: 521.5 $(M + H)^+$.

Example 179

N-(3-{1-[3-(3-ACETYLPHENOXY)-3-(4-METHOXYPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-hydroxy-3-(4-methoxyphenyl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 3-acetylphenol: ESMS *m/e*: 529.0 $(M + H)^+$.

Example 180

N-(3-{1-[3-(4-CHLOROPHENYL)-3-PHENOXYPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-chlorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenol. ESMS *m/e*: 490.9 $(M + H)^+$.

Example 181

N-(3-{1-[3-(4-BROMOPHENOXY)-3-(4-METHOXYPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-hydroxy-3-(4-methoxyphenyl)propyl]-4-piperidinyl}phenyl)-2-

methylpropanamide and 4- bromophenol: ESMS m/e: 564.9 $(M + H)^+$.

Example 182

***N*-[3-(1-{3-(4-METHOXYPHENYL)-3-[4-(TRIFLUOROMETHYL)PHENOXY]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-hydroxy-3-(4-methoxyphenyl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-trifluoromethyphenol: ESMS m/e: 555.1 $(M + H)^+$.

Example 183

***N*-(3-{1-[3-(4-CHLOROPHENYL)-3-(4-FLUOROPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-chlorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-fluorophenol: ESMS m/e: 509.1 $(M + H)^+$.

Example 184

***N*-(3-{1-[3-(4-FLUOROPHENOXY)-3-(4-METHOXYPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-hydroxy-3-(4-methoxyphenyl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-fluorophenol: ESMS m/e: 505.5 $(M + H)^+$.

Example 185

***N*-(3-{1-[3-(2-ACETYLPHENOXY)-3-(4-METHOXYPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-hydroxy-3-(4-methoxyphenyl)propyl]-4-piperidinyl}phenyl)-2-

methylpropanamide and 2- acetylphenol: ESMS *m/e*: 529.2 $(M + H)^+$.

Example 186

***N*-[3-(1-{3-(4-CHLOROPHENYL)-3-[4-(TRIFLUOROMETHYL)PHENOXY]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using *N*-(3-{1-[3-(4-chlorophenyl)-3-hydroxypropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-trifluoromethylphenol: SMS *m/e*: 559.1 $(M + H)^+$.

Example 187

***N*-(3-{1-[(3*S*)-3-(3-ACETYLPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}-4-METHYLPHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme AI using 1-(3-{[(1*S*)-3-chloro-1-phenylpropyl]oxy}phenyl)ethanone and 2-methyl-*N*-[4-methyl-3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 513.0 $(M + H)^+$.

2-(ISOPENTYLOXY)-1-NAPHTHALDEHYDE: 2-Hydroxy-1-naphthaldehyde (1.72 g, 10.0 mmol) and THF (50 ml) were combined in a flask. NaH (312 mg, 13 mmol) was added, followed by 1-bromo-3-methylbutane (1.20 mL, 10.0 mmol). The solution was stirred at room temperature overnight, the solvent was removed *in vacuo*, and the residue was purified by chromatography (5-10 % ethyl acetate / hexane): ^1H NMR (400 MHz, $CDCl_3$) δ 10.9 (s, 1H), 9.28 (dd, 1H, *J* = 0.7 Hz, 8.6 Hz), 8.02 (d, 1H, *J* = 9.1 Hz), 7.75 (d, 1H, *J* = 8.1 Hz), 7.63-7.59 (m, 1H), 7.43-7.39 (m, 1H), 7.27 (d, 1H, *J* = 9.2 Hz), 4.25 (t, 2H, *J* = 6.5 Hz), 1.98-1.84 (m, 1H), 1.80-1.75 (m, 2H), 0.99 (d, 6H, *J* = 6.6 Hz); ESMS *m/e*: 242.8 $(M + H)^+$.

Example 188

N-[3-(1-{[2-(ISOPENTYLOXY)-1-NAPHTHYL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 2-(isopentyloxy)-1-naphthaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 473.3 $(M + H)^+$.

2-PROPOXY-1-NAPHTHALDEHYDE: Prepared according to the Procedure for 2-(isopentyloxy)-1-naphthaldehyde using 2-hydroxy-1-naphthaldehyde and 1-bromopropane.

Example 189

2-METHYL-*N*-(3-{1-[(2-PROPOXY-1-NAPHTHYL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 2-propoxy-1-naphthaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 445.2 $(M + H)^+$.

4-{[(1-FORMYL-2-NAPHTHYL)OXY]METHYL}BENZONITRILE: Prepared according to the Procedure for 2-(isopentyloxy)-1-naphthaldehyde using 2-hydroxy-1-naphthaldehyde and 4-(bromomethyl)benzonitrile.

Example 190

N-{3-[1-({2-[(4-CYANOBENZYL)OXY]-1-NAPHTHYL}METHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 4-{[(1-formyl-2-naphthyl)oxy]methyl}benzonitrile and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 518.2 $(M + H)^+$.

[(1-FORMYL-2-NAPHTHYL)OXY]ACETONITRILE: Prepared according to the Procedure for 2-(isopentyloxy)-1-

naphthaldehyde using 2-hydroxy-1-naphthaldehyde and bromoacetonitrile.

Example 191

N-[3-(1-{[2-(CYANOMETHOXY)-1-NAPHTHYL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using [(1-formyl-2-naphthyl)oxy]acetonitrile and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 442.2 $(M + H)^+$.

2-[(3-CHLOROBENZYL)OXY]-1-NAPHTHALDEHYDE: Prepared according to the Procedure for 2-(isopentyloxy)-1-naphthaldehyde using 2-hydroxy-1-naphthaldehyde and 1-(bromomethyl)-3-chlorobenzene.

Example 192

N-{3-[1-({2-[(3-CHLOROBENZYL)OXY]-1-NAPHTHYL}METHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 2-[(3-chlorobenzyl)oxy]-1-naphthaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 527.2 $(M + H)^+$.

Example 193

N-(3-{1-[4-(4-CHLOROPHENOXY)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 4-(4-chlorophenoxy)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.34-7.19 (m, 7H), 6.98-6.87 (m, 5H), 3.50 (s, 2H), 2.98 (d, 2H, J = 11.8 Hz), 2.58-2.44 (m, 2H), 2.10-1.98 (m, 2H), 1.83-1.76 (m, 4H), 1.24 (d, 6H, J = 6.8 Hz); ESMS *m/e*: 463.2 $(M + H)^+$.

Example 194

N-(3-{1-[4-(3,4-DIFLUOROPHENOXY)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 4-(3,4-difluorophenoxy)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 465.2 (M + H)$^+$.

4-(ISOPENTYLOXY)-1-NAPHTHALDEHYDE: Prepared according to the Procedure for 2-(isopentyloxy)-1-naphthaldehyde using 4-hydroxy-1-naphthaldehyde and 1-bromo-3-methylbutane.

Example 195

N-[3-(1-{[4-(ISOPENTYLOXY)-1-NAPHTHYL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 4-(isopentyloxy)-1-naphthaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 473.3 (M + H)$^+$.

Example 196

N-(3-{1-[4-(4-METHOXYPHENOXY)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 4-(4-methoxyphenoxy)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 459.2 (M + H)$^+$.

4-PROPOXY-1-NAPHTHALDEHYDE: Prepared according to the Procedure for 2-(isopentyloxy)-1-naphthaldehyde using 4-hydroxy-1-naphthaldehyde and 1-bromopropane.

Example 197

2-METHYL-*N*-(3-{1-[(4-PROPOXY-1-NAPHTHYL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F

and Scheme R using 4- propoxy-1-naphthaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 445.2 $(M + H)^+$.

Example 198

***N*-(3-{1-[4-(3,4-DICHLOROPHENOXY)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R using 4-(3,4-dichlorophenoxy)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*:497.1 $(M + H)^+$.

Example 199

***N*-(3-{1-[4-(DIPHENYLAMINO)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R using 4-(diphenylamino)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 504.2 $(M + H)^+$.

Example 200

***N*-{3-[1-({2,5-DIMETHYL-1-[3-(TRIFLUOROMETHYL)PHENYL]-1*H*-PYRROL-3-YL}METHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R using 2,5-dimethyl-1-[3-(trifluoromethyl)phenyl]-1*H*-pyrrole-3-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 498.2 $(M + H)^+$.

Example 201

2-METHYL-*N*-(3-{1-[1-(2-PHENYL-1,3-THIAZOL-4-YL)ETHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 1-(2-phenyl-1,3-thiazol-4-yl)ethanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 434.2 $(M + H)^+$.

Example 202

N-(3-{1-[(5-CHLORO-3-METHYL-1-PHENYL-1*H*-PYRAZOL-4-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 5-chloro-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 451.2 $(M + H)^+$.

Example 203

2-METHYL-*N*-(3-{1-[(2-PHENYL-1*H*-IMIDAZOL-4-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 2-phenyl-1*H*-imidazole-4-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 403.2 $(M + H)^+$.

Example 204

N-[3-(1-{[4-BROMO-1-(4-CHLOROBENZYL)-1*H*-PYRAZOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 4-bromo-1-(4-chlorobenzyl)-1*H*-pyrazole-5-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 529.1 $(M + H)^+$.

Example 205

2-METHYL-*N*-{3-[1-(3-PHENOXYBENZYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure F and Scheme R using 3-phenoxybenzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 429.2 $(M + H)^+$.

Example 206

N-(3-{1-[3-(3,4-DICHLOROPHENOXY)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by

Procedure F and Scheme R using 3-(3,4-dichlorophenoxy)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 497.15 (M + H)$^+$.

Example 207

N-(3-{1-[3-(3,5-dichlorophenoxy)benzyl]-4-piperidinyl}phenyl)-2-methylpropanamide: Prepared by Procedure F and Scheme R using 3-(3,5-dichlorophenoxy)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 497.2 (M + H)$^+$.

Example 208

2-METHYL-*N*-(3-{1-[3-(4-METHYLPHENOXY)BENZYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 3-(4-methylphenoxy)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 443.2 (M + H)$^+$.

Example 209

2-METHYL-*N*-[3-(1-{3-[3-(TRIFLUOROMETHYL)PHENOXY]BENZYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure F and Scheme R using 3-[3-(trifluoromethyl)phenoxy]benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 497.2 (M + H)$^+$.

Example 210

N-(3-{1-[3-(4-CHLOROPHENOXY)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 3-(4-chlorophenoxy)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 463.2 (M + H)$^+$.

Example 211

***N*-(3-{1-[3-(DIMETHYLAMINO)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R using 3-(dimethylamino)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 380.2 (M + H)$^+$.

Example 212

***N*-(3-{1-[3-(4-METHOXYPHENOXY)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R using 3-(4-methoxyphenoxy)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 459.2 (M + H)$^+$.

Example 213

***N*-(3-{1-[3-(4-TERT-BUTYLPHENOXY)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R using 3-(4-tert-butylphenoxy)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 485.3 (M + H)$^+$.

Example 214

2-METHYL-*N*-(3-{1-[3-NITRO-4-(1-PIPERIDINYL)BENZYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 3-nitro-4-(1-piperidinyl)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 465.2 (M + H)$^+$.

Example 215

N-(3-{1-[(3,4-DIMETHYLTHIENO[2,3-B]THIEN-2-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 3,4-dimethylthieno[2,3-*b*]thiophene-2-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 427.1 $(M + H)^+$.

Example 216

2-METHYL-*N*-{3-[1-({3-[4-(TRIFLUOROMETHYL)PHENYL]-1*H*-PYRAZOL-4-YL}METHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure F and Scheme R using 3-[4-(trifluoromethyl)phenyl]-1*H*-pyrazole-4-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 471.1 $(M + H)^+$.

Example 217

2-METHYL-*N*-(3-{1-[4-(1*H*-1,2,4-TRIAZOL-1-YL)BENZYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 4-(1*H*-1,2,4-triazol-1-yl)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 404.1 $(M + H)^+$.

Example 218

2-METHYL-*N*-(3-{1-[(5-METHYL-1-PHENYL-1*H*-PYRAZOL-4-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 5-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 417.1 $(M + H)^+$.

Example 219

2-METHYL-*N*-(3-{1-[4-(4-MORPHOLINYL)-3-NITROBENZYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 4-(4-morpholinyl)-3-nitrobenzaldehyde

and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 467.1 $(M + H)^+$.

Example 220

***N*-{3-[1-({5-[2-CHLORO-4-(TRIFLUOROMETHYL)PHENYL]-2-FURYL}METHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R using 5-[2-chloro-4-(trifluoromethyl)phenyl]-2-furaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 505.0 $(M + H)^+$.

Example 221

ETHYL 4-({4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}METHYL)-2,5-DIMETHYL-1-PHENYL-1*H*-PYRROLE-3-CARBOXYLATE: Prepared by Procedure F and Scheme R using ethyl 4-formyl-2,5-dimethyl-1-phenyl-1*H*-pyrrole-3-carboxylate and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 502.2 $(M + H)^+$.

Example 222

ETHYL 5-(4-CHLOROPHENYL)-2-({4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}METHYL)-3-FUROATE: Prepared by Procedure F and Scheme R using ethyl 5-(4-chlorophenyl)-2-formyl-3-furoate and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 509.0 $(M + H)^+$.

Example 223

***N*-{3-[1-(2,3-DIHYDRO-1,4-BENZODIOXIN-6-YLMETHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R using 2,3-dihydro-1,4-benzodioxine-6-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 395.1 $(M + H)^+$.

Example 224

2-METHYL-*N*-(3-{1-[(6-PHENOXY-3-PYRIDINYL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 6-phenoxynicotinaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 430.1 $(M + H)^+$.

Example 225

2-METHYL-*N*-[3-(1-{[5-(2-PYRIDINYL)-2-THIENYL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure F and Scheme R using 5-(2-pyridinyl)-2-thiophenecarbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 420.1 $(M + H)^+$.

Example 226

2-METHYL-*N*-{3-[1-({5-[1-METHYL-3-(TRIFLUOROMETHYL)-1H-PYRAZOL-5-YL]-2-THIENYL}METHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure F and Scheme R using 5-[1-methyl-3-(trifluoromethyl)-1*H*-pyrazol-5-yl]-2-thiophenecarbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 491.0 $(M + H)^+$.

Example 227

2-METHYL-*N*-[3-(1-{[1-(PHENYLSULFONYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure F and Scheme R using 1-(phenylsulfonyl)-1*H*-indole-3-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 516.1 $(M + H)^+$.

Example 228

N-(3-{1-[(1,5-DIMETHYL-3-OXO-2-PHENYL-2,3-DIHYDRO-1*H*-PYRAZOL-4-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1*H*-pyrazole-4-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 447.2 $(M + H)^+$.

Example 229

N-(3-{1-[4-(4-TERT-BUTYL-1,3-THIAZOL-2-YL)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 4-(4-tert-butyl-1,3-thiazol-2-yl)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide.

Example 230

N-{3-[1-(2,3-DIHYDRO-1-BENZOFURAN-5-YLMETHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 2,3-dihydro-1-benzofuran-5-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 379.1 $(M + H)^+$.

Example 231

2-METHYL-*N*-(3-{1-[(4-METHYL-2-PHENYL-5-PYRIMIDINYL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 4-methyl-2-phenyl-5-pyrimidinecarbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 429.2 $(M + H)^+$.

Example 232

N-{3-[1-(2,1,3-BENZOTHIADIAZOL-5-YLMETHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 2,1,3-benzothiadiazole-5-

carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 395.1 $(M + H)^+$.

Example 233

2-METHYL-*N*-(3-{1-[(5-PHENYL-2-THIENYL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 5-phenyl-2-thiophenecarbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 419.1 $(M + H)^+$.

Example 234

***N*-{3-[1-(3,4-DIHYDRO-2*H*-1,5-BENZODIOXEPIN-7-YLMETHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R using 3,4-dihydro-2*H*-1,5-benzodioxepine-7-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 409.2 $(M + H)^+$.

Example 235

2-METHYL-*N*-[3-(1-{[3-(2-THIENYL)-1*H*-PYRAZOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure F and Scheme R using 3-(2-thienyl)-1*H*-pyrazole-4-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 409.1 $(M + H)^+$.

Example 236

***N*-{3-[1-([1,1'-BITHIENYL]-4-YLMETHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R using 2,2'-Bithiophene-5-carboxaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 425.0 $(M + H)^+$.

Example 237

N-{3-{1-[(2,2-DIMETHYL-3,4-DIHYDRO-2H-CHROMEN-6-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 2,2-dimethyl-6-chromanecarbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 421.2 $(M + H)^+$.

Example 238

2-METHYL-*N*-{3-[1-({5-[1-METHYL-5-(TRIFLUOROMETHYL)-1H-PYRAZOL-3-YL]-2-THIENYL}METHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure F and Scheme R using 5-[1-methyl-5-(trifluoromethyl)-1*H*-pyrazol-3-yl]-2-thiophenecarbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 491.1 $(M + H)^+$.

Example 239

2-METHYL-*N*-(3-{1-[(2-PHENYL-1,3-THIAZOL-4-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 2-phenyl-1,3-thiazole-4-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 420.0 $(M + H)^+$.

Example 240

2-METHYL-*N*-(3-{1-[(3-PHENOXY-2-THIENYL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 3-phenoxy-2-thiophenecarbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 435.0 $(M + H)^+$.

Example 241

N-{3-[1-({2-[(4-CHLOROPHENYL)SULFANYL]-3-THIENYL}METHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R

using 2-[(4-chlorophenyl)sulfanyl]-3-thiophenecarbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 485.0 $(M + H)^+$.

Example 242

***N*-[3-(1-{[1-(4-CHLOROPHENYL)-1*H*-PYRROL-2-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R using 1-(4-chlorophenyl)-1*H*-pyrrole-2-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 436.0 $(M + H)^+$.

Example 243

2-METHYL-*N*-{3-[1-({5-[2-(TRIFLUOROMETHOXY)PHENYL]-2-FURYL}METHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure F and Scheme R using 5-[2-(trifluoromethoxy)phenyl]-2-furaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 487.1 $(M + H)^+$.

Example 244

2-METHYL-*N*-(3-{1-[2-(4-MORPHOLINYL)BENZYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 2-(4-morpholinyl)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e:* 422.2 $(M + H)^+$.

Example 245

***N*-[3-(1-{[3-(4-METHOXYPHENYL)-1H-PYRAZOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R using 3-(4-methoxyphenyl)-1*H*-pyrazole-4-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e:* 433.1 $(M + H)^+$.

Example 246

2-METHYL-*N*-(3-{1-[4-(1*H*-PYRAZOL-1-YL)BENZYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 4-(1*H*-pyrazol-1-yl)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e:* 402.8 $(M + H)^+$.

Example 247

2-METHYL-*N*-{3-[1-(4-QUINOLINYLMETHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure F and Scheme R using 4-quinolinecarbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e:* 388.1 $(M + H)^+$.

Example 248

2-METHYL-*N*-(3-{1-[4-(4-MORPHOLINYL)BENZYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 4-(4-morpholinyl)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e:* 422.5 $(M + H)^+$.

Example 249

2-METHYL-*N*-(3-{1-[4-(2-THIENYL)BENZYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 4-(2-thienyl)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e:* 419.1 $(M + H)^+$.

Example 250

2-METHYL-*N*-(3-{1-[(2-METHYL-5-PHENYL-3-FURYL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 2-methyl-5-phenyl-3-furaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e:* 417.2 $(M + H)^+$.

Example 251

N-{3-{1-[3-(CYCLOPENTYLOXY)-4-METHOXYBENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 3-(cyclopentyloxy)-4-methoxybenzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 451.1 (M + H)$^+$.

Example 252

2-METHYL-*N*-{3-[1-({5-[4-(TRIFLUOROMETHOXY)PHENYL]-2-FURYL}METHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE:
Prepared by Procedure F and Scheme R using 5-[4-(trifluoromethoxy)phenyl]-2-furaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 487.1 (M + H)$^+$.

Example 253

N-{3-[1-(1-BENZOTHIEN-2-YLMETHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 1-benzothiophene-2-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 393.2 (M + H)$^+$.

Example 254

2-METHYL-*N*-{3-[1-({5-[3-(TRIFLUOROMETHOXY)PHENYL]-2-FURYL}METHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE:
Prepared by Procedure F and Scheme R using 5-[3-(trifluoromethoxy)phenyl]-2-furaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 487.2 (M + H)$^+$.

Example 255

2-METHYL-*N*-{3-[1-(2-QUINOLINYLMETHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure F and Scheme R using 2-quinolinecarbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e:* 388.1 $(M + H)^+$.

Example 256

N-(3-{1-[4-(1*H*-IMIDAZOL-1-YL)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 4-(1*H*-imidazol-1-yl)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e:* 403.2 $(M + H)^+$.

Example 257

N-{3-[1-(9*H*-FLUOREN-2-YLMETHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 9*H*-fluorene-2-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e:* 425.1 $(M + H)^+$.

Example 258

METHYL 3-[5-({4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}METHYL)-2-FURYL]-2-THIOPHENECARBOXYLATE: Prepared by Procedure F and Scheme R using methyl 3-(5-formyl-2-furyl)-2-thiophenecarboxylate and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e:* 467.1 $(M + H)^+$.

Example 259

2-METHYL-*N*-{3-[1-(4-PHENOXYBENZYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure F and Scheme R using 4-phenoxybenzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e:* 429.2 $(M + H)^+$.

Example 260

N-{3-[1-([1,1'-BIPHENYL]-4-YLMETHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using [1,1'-biphenyl]-4-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 413.2 (M + H)$^+$.

Example 261

N-(3-{1-[4-(DIBUTYLAMINO)BENZYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure F and Scheme R using 4-(dibutylamino)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 464.6 (M + H)$^+$.

Example 262

2-METHYL-*N*-[3-(1-{4-[(4-METHYLPHENYL)SULFANYL]-3-NITROBENZYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure F and Scheme R using 4-[(4-methylphenyl)sulfanyl]-3-nitrobenzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e* 504.2 (M + H)$^+$.

Example 263

2-METHYL-*N*-(3-{1-[4-(1,2,3-THIADIAZOL-4-YL)BENZYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R using 4-(1,2,3-thiadiazol-4-yl)benzaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 421.1 (M + H)$^+$.

1-(3-{[(1*S*)-3-CHLORO-1-PHENYLPROPYL]OXY}PHENYL)ETHANONE: (1*R*)-3-Chloro-1-phenyl-1-propanol (1.000 g, 5.86 mmol), 1-(3-hydroxyphenyl)ethanone (0.797 g, 5.86 mmol), triphenylphosphine (1.54 g, 5.86 mmol) and

diethylazodicarboxylate (1.53 g, 8.79 mmol) were combined in a flask, which was immediately flushed with argon. THF (20 mL) was added and the mixture was stirred overnight under argon. THF was removed *in vacuo*, the crude product was dissolved in 50 mL of CH_2Cl_2/H_2O (1:1) and the organic layer was separated and dried over $MgSO_4$. After removing the solvent *in vacuo*, the residue was purified by flash chromatography using 10 % ethyl acetate/hexane to yield the desired product (900 mg, 76.0 %): ^1H NMR (400 MHz, $CDCl_3$) δ 7.49-7.46 (m, 2H), 7.40-7.26 (m, 6H), 7.07-7.04 (m, 1H), 5.46-5.43 (dd, 1H, *J* = 4.4 Hz, 8.8 Hz), 3.84-3.78 (m, 1H), 3.64-3.59 (m, 1H), 2.52 (s, 3H), 2.51-2.46 (m, 1H), 2.29-2.22 (m, 1H).

4-(3,4-DIFLUOROPHENOXY)BENZALDEHYDE: 4-Fluorobenzaldehyde (5.32 mL, 49.6 mmol), 3,4-difluorophenol (7.10 g, 54.6 mmol) and K_2CO_3 (8.31 g, 60.1 mmol) were combined in a flask, which was immediately flushed with argon. DMF (50.0 mL) was added and the mixture was heated at reflux under argon for 6 h. Upon cooling to room temperature, EtOAc (100 mL) and H_2O (100 mL) were added; the ethyl acetate layer was separated and washed with H_2O (2 X 100 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and the solvent was removed *in vacuo*. The desired product was obtained (11.4 g, 98.0 %): ^1H NMR (400 MHz, $CDCl_3$) δ 9.95 (s, 1H), 7.88 (dd, 2H, *J* = 0.8 Hz, 8.8 Hz), 7.24-7.17 (m, 1H), 7.07 (d, 2H, *J* = 8.8 Hz), 6.97-6.92 (m, 1H), 6.86-6.82 (m, 1H); ESMS *m/e*: 235.0 $(M + H)^+$.

TERT-BUTYL 4-(4,4,5,5-TETRAMETHYL-1,3,2-DIOXABOROLAN-2-YL)-3,6-DIHYDRO-1(2H)-PYRIDINECARBOXYLATE: To a flask

were added bis(pinacolato)diboron (422 mg, 1.66 mmol), KOAc (444 mg, 4.53 mmol), $PdCl_2$dppf (37.0 mg, 3.00 mol%), dppf (25.0 mg, 3.00 mol%) and the flask was flushed with argon. A solution of *tert*-butyl 4-{[(trifluoromethyl)sulfonyl]oxy}-1,2,3,6-tetrahydro-1-pyridinecarboxylate (500 mg, 1.51 mmol) in 1,4-dioxane (10.0 ml) was added and the mixture was stirred at 80 °C overnight. The mixture was filtered through Celite and the filtrate was evaporated *in vacuo*. The resulting residue was dissolved in EtOAc and washed with H_2O, followed by brine. The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude material was purified by flash chromatography (10% EtOAC/hexane) to give *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-1(2*H*)-pyridinecarboxylate (355 mg, 76.0%): ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.44 (br s, 1H), 3.93 (br s, 2H), 3.42 (br s, 2H), 2.21 (br s, 2H), 1.45 (s, 9H), 1.25 (s, 12H); ESMS *m/e*: 310.4 $(M + H)^+$.

N-(6-BROMO-2-PYRIDINYL)-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 using 2-methylpropanoyl chloride and 6-bromo-2-pyridinamine: ESMS *m/e*: 242.8 $(M + H)^+$.

TERT-BUTYL 4-[6-(ISOBUTYRYLAMINO)-2-PYRIDINYL]-3,6-DIHYDRO-1(2H)-PYRIDINECARBOXYLATE: Prepared by Procedure W and Scheme AF using *N*-(6-bromo-2-pyridinyl)-2-methylpropanamide and *tert*-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-1(2*H*)-pyridinecarboxylate: ESMS *m/e*: 245.8 $(M - 100)^+$.

2-METHYL-N-[6-(4-PIPERIDINYL)-2-PYRIDINYL]PROPANAMIDE: Prepared by Procedures X and Y, Schemes AG and AH,

respectively using tert- butyl 4-[6-(isobutyrylamino)-2-pyridinyl]-3,6-dihydro-1(2*H*)-pyridinecarboxylate: ESMS *m/e*: 248.1 $(M + H)^+$.

Example 264

***N*-(6-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}-2-PYRIDINYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme AI using 4-chloro-1-(3,4-dimethylphenyl)-1-butanone and 2-methyl-*N*-[6-(4-piperidinyl)-2-pyridinyl]propanamide: ESMS *m/e*: 422.1 $(M + H)^+$.

Example 265

***N*-(6-{1-[4,4-BIS(4-FLUOROPHENYL)BUTYL]-4-PIPERIDINYL}-2-PYRIDINYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme AI using 1-[4-chloro-1-(4-fluorophenyl)butyl]-4-fluorobenzene and 2-methyl-*N*-[6-(4-piperidinyl)-2-pyridinyl]propanamide: ESMS *m/e*: 492.2 $(M + H)^+$.

Example 266

***N*-(6-{1-[4-(3,4-DIFLUOROPHENOXY)BENZYL]-4-PIPERIDINYL}-2-PYRIDINYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure AA and Scheme AJ using 4-(3,4-difluorophenoxy)benzaldehyde and 2-methyl-*N*-[6-(4-piperidinyl)-2-pyridinyl]propanamide: ESMS *m/e*: 466.0 $(M + H)^+$.

***N*-(3-BROMO-4-METHYLPHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure Q1 using 2-methylpropanoyl chloride and 3-bromo-4-methylaniline: ESMS *m/e*: 255.9 $(M + H)^+$.

TERT-BUTYL 4-[5-(ISOBUTYRYLAMINO)-2-METHYLPHENYL]-3,6-DIHYDRO-1(2H)-PYRIDINECARBOXYLATE: Prepared by Procedure W and Scheme AF using *N*-(3-bromo-4-methylphenyl)-2-methylpropanamide and tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-1(2*H*)-pyridinecarboxylate: ESMS *m/e*: 259.1 (M - 100)$^+$.

2-METHYL-*N*-[4-METHYL-3-(4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedures X and Y, Schemes AG and AH, respectively using tert-butyl 4-[5-(isobutyrylamino)-2-methylphenyl]-3,6-dihydro-1(2*H*)-pyridinecarboxylate: ESMS *m/e*: 261.0 (M + H)$^+$.

Example 267

N-(3-{1-[4-(3,4-DIFLUOROPHENOXY)BENZYL]-4-PIPERIDINYL}-4-METHYLPHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure AA and Scheme AJ using 4-(3,4-difluorophenoxy)benzaldehyde and using 2-methyl-*N*-[4-methyl-3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 479.1 (M + H)$^+$.

N-(5-BROMO-2-METHYLPHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 using 2-methylpropanoyl chloride and 5-bromo-2-methylaniline: ESMS *m/e*: 255.9 (M + H)$^+$.

TERT-BUTYL 4-[3-(ISOBUTYRYLAMINO)-4-METHYLPHENYL]-3,6-DIHYDRO-1(2H)-PYRIDINECARBOXYLATE: Prepared by Procedure W and Scheme AF using *N*-(5-bromo-2-methylphenyl)-2-methylpropanamide and tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-

dihydro-1(2*H*)-pyridinecarboxylate: ESMS m/e: 259.1 (M - 100)$^+$.

2-METHYL-*N*-[2-METHYL-5-(4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedures X and Y, Schemes AG and AH, respectively using tert-butyl 4-[3-(isobutyrylamino)-4-methylphenyl]-3,6-dihydro-1(2*H*)-pyridinecarboxylate: ESMS *m/e*: 261.0 (M + H)$^+$.

Example 268

***N*-(5-{1-[(9-ETHYL-9*H*-CARBAZOL-3-YL)METHYL]-4-PIPERIDINYL}-2-METHYLPHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure AA and Scheme AJ using 9-ethyl-9*H*-carbazole-3-carbaldehyde and 2-methyl-*N*-[2-methyl-5-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 468.1 (M + H)$^+$.

Example 269

***N*-(5-{1-[4-(3,4-DIFLUOROPHENOXY)BENZYL]-4-PIPERIDINYL}-2-METHYLPHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure AA and Scheme AJ using 4-(3,4-difluorophenoxy)benzaldehyde and 2-methyl-*N*-[2-methyl-5-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 479.2 (M + H)$^+$.

Example 270

***N*-(3-{1-[(9-ETHYL-9*H*-CARBAZOL-3-YL)METHYL]-4-PIPERIDINYL}-4-METHYLPHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure AA and Scheme AJ using 9-ethyl-9*H*-carbazole-3-carbaldehyde and 2-methyl-*N*-[4-methyl-3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 468.1 (M + H)$^+$.

Example 271

2-METHYL-*N*-[2-METHYL-5-(4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure G and Scheme AI using 1-[4-chloro-1-(4-fluorophenyl)butyl]-4-fluorobenzene and 2-methyl-*N*-[2-methyl-5-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 505.1 $(M + H)^+$.

Example 272

N-(3-{1-[(3*S*)-3-(3-ACETYLPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}-4-METHYLPHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme AI using 1-(3-{[(1*S*)-3-chloro-1-phenylpropyl]oxy}phenyl)ethanone and 2-methyl-*N*-[4-methyl-3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 513.0 $(M + H)^+$.

Example 273

N-(5-{1-[(3*S*)-3-(3-ACETYLPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}-2-METHYLPHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme AI using 1-(3-{[(1*S*)-3-chloro-1-phenylpropyl]oxy}phenyl)ethanone and 2-methyl-*N*-[2-methyl-5-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 512.9 $(M + H)^+$.

N-(2-IODOPHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 using 2-methylpropanoyl chloride and 2-iodoaniline: ESMS *m/e*: 289.9 $(M + H)^+$.

TERT-BUTYL 4-[2-(ISOBUTYRYLAMINO)PHENYL]-3,6-DIHYDRO-1(2*H*)-PYRIDINECARBOXYLATE: Prepared by Procedure W and Scheme AF using *N*-(2-iodophenyl)-2-methylpropanamide and tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-

yl)-3,6-dihydro-1(2*H*)-pyridinecarboxylate: ESMS *m/e*: 245.1 $(M - 100)^+$.

2-METHYL-*N*-[2-(4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedures X and Y, Schemes AG and AH, respectively using tert-butyl 4-[2-(isobutyrylamino)phenyl]-3,6-dihydro-1(2*H*)-pyridinecarboxylate: ESMS *m/e*: 247.1 $(M + H)^+$.

Example 274

***N*-(2-{1-[(9-ETHYL-9*H*-CARBAZOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure AA and Scheme AJ using 9-ethyl-9*H*-carbazole-3-carbaldehyde and 2-methyl-*N*-[2-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 454.1 $(M + H)^+$.

Example 275

***N*-(3-{1-[4,4-BIS(4-FLUOROPHENYL)BUTYL]-4-PIPERIDINYL}-4-METHYLPHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme AI using 1-[4-chloro-1-(4-fluorophenyl)butyl]-4-fluorobenzene and 2-methyl-*N*-[4-methyl-3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 505.0 $(M + H)^+$.

Example 276

***N*-(2-{1-[4,4-BIS(4-FLUOROPHENYL)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme AI using 1-[4-chloro-1-(4-fluorophenyl)butyl]-4-fluorobenzene and 2-methyl-*N*-[2-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 490.9 $(M + H)^+$.

N-[2-BROMO-4-(TRIFLUOROMETHOXY)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 using 2-methylpropanoyl chloride and 2-bromo-4-(trifluoromethoxy)aniline: ESMS *m/e*: 325.9 $(M + H)^+$.

TERT-BUTYL 4-[2-(ISOBUTYRYLAMINO)-5-(TRIFLUOROMETHOXY)PHENYL]-3,6-DIHYDRO-1(2*H*)-PYRIDINECARBOXYLATE: Prepared by Procedure W and Scheme AF using *N*-[2-bromo-4-(trifluoromethoxy)phenyl]-2-methylpropanamide and tert-butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydro-1(2*H*)-pyridinecarboxylate: ESMS *m/e*: 329.0 $(M - 100)^+$.

2-METHYL-*N*-[2-(4-PIPERIDINYL)-4-(TRIFLUOROMETHOXY)PHENYL]PROPANAMIDE: Prepared by Procedures X and Y, Schemes AG and AH, respectively using tert-butyl 4-[2-(isobutyrylamino)-5-(trifluoromethoxy)phenyl]-3,6-dihydro-1(2*H*)-pyridinecarboxylate: ESMS *m/e*: 330.9 $(M + H)^+$.

Example 277

N-[2-{1-[4,4-BIS(4-FLUOROPHENYL)BUTYL]-4-PIPERIDINYL}-4-(TRIFLUOROMETHOXY)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme AI using 1-[4-chloro-1-(4-fluorophenyl)butyl]-4-fluorobenzene and 2-methyl-*N*-[2-(4-piperidinyl)-4-(trifluoromethoxy)phenyl]propanamide: ESMS *m/e*: 574.8 $(M + H)^+$.

N-{3-[1-(4-HYDROXYBUTYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 4-chloro-1-butanol and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 319.3 $(M + H)^+$.

N-{3-[1-(5-HYDROXYPENTYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 5-chloro-1-pentanol and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 333.3 $(M + H)^+$.

N-{3-[1-(6-HYDROXYHEXYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 6-chloro-1-hexanol and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 347.3 $(M + H)^+$.

N-{3-[1-(3-HYDROXYPROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 3-chloro-1-propanol and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 305.3 $(M + H)^+$.

N-(3-{1-[(2*S*)-2-HYDROXY-2-PHENYLETHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using (1*S*)-2-chloro-1-phenylethanol and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 367.2 $(M + H)^+$.

N-(3-{1-[(2*R*)-2-HYDROXY-2-PHENYLETHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using (1*R*)-2-chloro-1-phenylethanol and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 367.2 $(M + H)^+$.

N-(3-{1-[(2*S*)-3-HYDROXY-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by

Procedure G and Scheme B1 using (2*R*)-3-chloro-2-methyl-1-propanol and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 319.2 $(M + H)^+$.

***N*-(3-{1-[(2*R*)-3-HYDROXY-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using (2*S*)-3-chloro-2-methyl-1-propanol and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 319.2 .$(M + H)^+$.

Example 278

***N*-(3-{1-[(3*R*)-3-HYDROXY-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure G and Scheme B1 using (1*R*)-3-chloro-1-phenyl-1-propanol and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 379.2 $(M + H)^+$.

Example 279

***N*-{3-[1-(4-HYDROXY-4-PHENYLBUTYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure L and Scheme AN, Step 1 using 2-methyl-*N*-{3-[1-(4-oxo-4-phenylbutyl)-4-piperidinyl]phenyl}propanamide: Anal. Calcd for $C_{25}H_{34}N_2O_2 + 0.08CHCl_3$: C, 74.5; H, 8.50; N, 6.93. Found: C, 74.5; H, 8.63; N, 6.81; ESMS *m/e*: 395.2 $(M + H)^+$.

Example 280

***N*-{3-[1-(5-HYDROXY-5-PHENYLPENTYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure L and Scheme AN, Step 1 using 2-methyl-*N*-{3-[1-(5-oxo-5-phenylpentyl)-4-piperidinyl]phenyl}propanamide: Anal. Calcd for

$C_{26}H_{36}N_2O_2+0.25CHCl_3$: C, 71.9; H, 8.33; N, 6.39. Found: C, 71.3; H, 8.96; N, 6.86; ESMS *m/e*: 409.2 $(M + H)^+$.

Example 281

***N*-{3-[1-(6-HYDROXY-6-PHENYLHEXYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE**: Prepared by Procedure L and Scheme AN, Step 1 using 2-methyl-*N*-{3-[1-(6-oxo-6-phenylhexyl)-4-piperidinyl]phenyl}propanamide: Anal. Calcd for $C_{27}H_{38}N_2O_2+0.1CHCl_3$: C, 75.5; H, 8.93; N, 6.50. Found: C, 75.3; H, 8.52; N, 6.00; ESMS *m/e*: 423.2 $(M + H)^+$.

Example 282

***N*-{3-[1-(7-HYDROXY-7-PHENYLHEPTYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE**: Prepared by Procedure L and Scheme AN, Step 1 using 2-methyl-*N*-{3-[1-(7-oxo-7-phenylheptyl)-4-piperidinyl]phenyl}propanamide: Anal. Calcd for $C_{28}H_{40}N_2O_2+0.1CHCl_3$: C, 75.8; H, 9.10; N, 6.29. Found: C, 75.1; H, 9.24; N, 6.51; ESMS *m/e*: 437.1 $(M + H)^+$.

Example 283

***N*-(3-{1-[4-(4-FLUOROPHENYL)-4-HYDROXYBUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE**: Prepared by Procedure L and Scheme AN, Step 1 using *N*-(3-{1-[4-(4-fluorophenyl)-4-oxobutyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 413.1 $(M + H)^+$.

Example 284

4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLBUTYL 3-(2,6-DICHLOROPHENYL)-5-METHYL-4-ISOXAZOLECARBOXYLATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(4-hydroxy-4-phenylbutyl)-

4-piperidinyl]phenyl}-2- methylpropanamide and 3-(2,6-dichlorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (m, 1H), 7.47 (m, 2H), 7.44-7.39 (m, 3H), 7.25 (m, 2H), 7.09 (s, 1H), 7.03 (m, 2H), 6.95 (m, 1H), 6.83 (m, 1H), 5.75 (t, 1H, J = 7.1 Hz), 3.03 (t, 2H, J = 7.2 Hz), 2.93 (m, 2H), 2.78 (s, 3H), 2.48 (m, 3H), 2.25 (m, 2H), 1.48 (m, 3H), 1.77 (m, 2H), 1.54 (m, 2H), 1.25 (d, 6H, J = 7.3 Hz); ESMS *m/e*: 647.7 $(M + H)^+$.

Example 285

4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLBUTYL (4-FLUOROPHENYL)ACETATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(4-hydroxy-4-phenylbutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and (4-fluorophenyl)acetyl chloride: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.34-7.19 (m, 8H), 7.11 (m, 1H), 6.98 (m, 3H), 5.75 (t, 1H, J = 6.8 Hz), 3.61 (s, 2H), 2.92 (d, 2H, J = 8.1 Hz), 2.48 (m, 2H), 2.31 (m, 2H), 1.99-1.84 (m, 4H), 1.84-1.67 (m, 5H), 1.55-1.35 (m, 2H), 1.25 (d, 6H, J = 6.9 Hz); ESMS *m/e*: 531.1 $(M + H)^+$.

Example 286

3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL (4-FLUOROPHENYL)ACETATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(3-hydroxypropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and (4-fluorophenyl)acetyl chloride: ESMS *m/e*: 441.3 $(M + H)^+$.

Example 287

3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL 3-(2-CHLORO-6-FLUOROPHENYL)-5-METHYL-4-

ISOXAZOLECARBOXYLATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(3-hydroxypropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2-chloro-6-fluorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 542.2 $(M + H)^+$.

Example 288

3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL 3-(2,6-DICHLOROPHENYL)-5-METHYL-4-ISOXAZOLECARBOXYLATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(3-hydroxypropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2,6-dichlorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 558.2 $(M + H)^+$.

Example 289

3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL 3-(2-CHLOROPHENYL)-5-METHYL-4-ISOXAZOLECARBOXYLATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(3-hydroxypropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2-chlorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 524.2 $(M + H)^+$.

Example 290

(1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL 3-(2,6-DICHLOROPHENYL)-5-METHYL-4-ISOXAZOLECARBOXYLATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-(3-{1-[(3*S*)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 3-(2,6-dichlorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 633.6 $(M + H)^+$.

Example 291

4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}BUTYL 3-(2-CHLORO-6-FLUOROPHENYL)-5-METHYL-4-ISOXAZOLECARBOXYLATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(4-hydroxybutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2-chloro-6-fluorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: Anal. Calcd for $C_{30}H_{35}ClFN_3O_4+CH_2Cl_2$: C, 63.3; H, 6.23; N, 7.33. Found: C, 63.0; H, 6.39; N, 7.03; ESMS *m/e*: 556.2 $(M + H)^+$.

Example 292

4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}BUTYL 3-(2-CHLOROPHENYL)-5-METHYL-4-ISOXAZOLECARBOXYLATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(4-hydroxybutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2-chlorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 538.2 $(M + H)^+$.

Example 293

3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL 5-METHYL-3-PHENYL-4-ISOXAZOLECARBOXYLATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(3-hydroxypropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 5-methyl-3-phenyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 490.3 $(M + H)^+$.

Example 294

4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}BUTYL 3-(2,6-DICHLOROPHENYL)-5-METHYL-4-ISOXAZOLECARBOXYLATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(4-hydroxybutyl)-4-piperidinyl]phenyl}-2-

methylpropanamide and 3-(2,6-dichlorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 572.2 $(M + H)^+$.

Example 295

4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLBUTYL 3-(2-CHLORO-6-FLUOROPHENYL)-5-METHYL-4-ISOXAZOLECARBOXYLATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(4-hydroxy-4-phenylbutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2-chloro-6-fluorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: Anal. Calcd for $C_{36}H_{39}ClFN_3O_4 + 0.54CHCl_3$: C, 63.0; H, 5.72; N, 6.03. Found: C, 63.0; H, 5.54; N, 6.05; ESMS *m/e*: 632.2 $(M + H)^+$.

Example 296

4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}BUTYL 5-METHYL-3-PHENYL-4-ISOXAZOLECARBOXYLATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(4-hydroxybutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 5-methyl-3-phenyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 504.3 $(M + H)^+$.

Example 297

6-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}HEXYL 3-(2,6-DICHLOROPHENYL)-5-METHYL-4-ISOXAZOLECARBOXYLATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(6-hydroxyhexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2,6-dichlorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 600.0 $(M + H)^+$.

Example 298

6-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}HEXYL 5-METHYL-3-PHENYL-4-ISOXAZOLECARBOXYLATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(6-hydroxyhexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 5-methyl-3-phenyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 532.1 $(M + H)^+$.

Example 299

4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}BUTYL (4-FLUOROPHENYL)ACETATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(4-hydroxybutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and (4-fluorophenyl)acetyl chloride: ESMS *m/e*: 455.3 $(M + H)^+$.

Example 300

4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLBUTYL 3-(2-CHLOROPHENYL)-5-METHYL-4-ISOXAZOLECARBOXYLATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(4-hydroxy-4-phenylbutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2-chlorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 614.2 $(M + H)^+$.

Example 301

4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLBUTYL 5-METHYL-3-PHENYL-4-ISOXAZOLECARBOXYLATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-{3-[1-(4-hydroxy-4-phenylbutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 5-methyl-3-phenyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 580.0 $(M + H)^+$.

Example 302

(1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL (4-FLUOROPHENYL)ACETATE: Prepared by Procedure Q1 and Scheme C2 (TEA) using *N*-(3-{1-[(3*S*)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and (4-fluorophenyl)acetyl chloride: Anal. Calcd for $C_{32}H_{37}FN_2O_3+0.07CHCl_3$: C, 73.4; H, 7.12; N, 5.34. Found: C, 73.4; H, 6.96; N, 5.14; ESMS *m/e*: 517.1 $(M + H)^+$.

Example 303

***N*-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)BENZAMIDE:** Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and benzoyl chloride: Anal. Calcd for $C_{31}H_{37}N_3O_2+0.55CHCl_3$: C, 69.0; H, 6.89; N, 7.65. Found: C, 69.7; H, 6.73; N, 6.03; ESMS m/e: 484.4 $(M + H)^+$.

Example 304

***N*-[3-(1-{(3*S*)-3-[(DIPHENYLACETYL)AMINO]-3-PHENYLPROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and diphenylacetyl chloride: ESMS *m/e*: 574.3 $(M + H)^+$.

Example 305

3-CHLORO-*N*-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)BENZAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-

methylpropanamide and 3- chlorobenzoyl chloride: ESMS m/e: 518.3 $(M + H)^+$.

Example 306

3,5-DICHLORO-*N*-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)BENZAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 3,5-dichlorobenzoyl chloride: ESMS m/e: 552.3 $(M + H)^+$.

Example 307

2-(ETHYLSULFANYL)-*N*-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)NICOTINAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 2-(ethylsulfanyl)nicotinoyl chloride: ESMS m/e: 545.3 $(M + H)^+$.

Example 308

N-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)[1,1'-BIPHENYL]-4-CARBOXAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and [1,1'-biphenyl]-4-carbonyl chloride: ESMS m/e: 560.3 $(M + H)^+$.

Example 309

N-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)-2-PYRIDINECARBOXAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-

methylpropanamide and 2- pyridinecarbonyl chloride: ESMS *m/e*: 484.6 $(M + H)^+$.

Example 310

N-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)-2-METHOXYBENZAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 2-methoxybenzoyl chloride: ESMS *m/e*: 514.1 $(M + H)^+$.

Example 311

N-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)-1-NAPHTHAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthoyl chloride: ESMS *m/e*: 533.7 $(M + H)^+$.

Example 312

2,4-DIFLUORO-*N*-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)BENZAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 2,4-difluorobenzoyl chloride: ESMS *m/e*: 520.2 $(M + H)^+$.

Example 313

3-(2-CHLORO-6-FLUOROPHENYL)-*N*-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)-5-METHYL-4-ISOXAZOLECARBOXAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide

and 3-(2-chloro-6-fluorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: ESMS m/e: 617.2 $(M + H)^+$.

Example 314

3-CHLORO-*N*-*(*(1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)-2-THIOPHENECARBOXAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 3-chloro-2-thiophanecarbonyl chloride: ESMS *m/e*: 524.2 $(M + H)^+$.

Example 315

***N*-*(*(1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)-2-PHENOXYNICOTINAMIDE:** Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 2-phenoxynicotinoyl chloride: ESMS *m/e*: 577.3 $(M + H)^+$.

Example 316

1-(4-CHLOROPHENYL)-*N*-*(*(1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)-3-PROPYL-1H-PYRAZOLE-4-CARBOXAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(4-chlorophenyl)-3-propyl-1*H*-pyrazole-4-carbonyl chloride: ESMS *m/e*: 626.3 $(M + H)^+$.

Example 317

4-CHLORO-*N*-*(*(1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)-1,3-DIMETHYL-1H-PYRAZOLO[3,4-*B*]PYRIDINE-5-CARBOXAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-

3-phenylpropyl]-4- piperidinyl}phenyl)-2-methylpropanamide and 4-chloro-1,3-dimethyl-1*H*-pyrazolo[3,4-*b*]pyridine-5-carbonyl chloride: ESMS *m/e*: 587.3 $(M + H)^+$.

Example 318

5-(3,5-DICHLOROPHENOXY)-*N*-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)-1H-PYRROLE-2-CARBOXAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 5-(3,5-dichlorophenoxy)-1*H*-pyrrole-2-carbonyl chloride: ESMS *m/e*: 634.2 $(M + H)^+$.

Example 319

***N*-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)NICOTINAMIDE:** Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and nicotinoyl chloride: ESMS *m/e*: 485.3 $(M + H)^+$.

Example 320

3,4-DIFLUORO-*N*-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)BENZAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 3,4-difluorobenzoyl chloride: ESMS *m/e*: 520.3 $(M + H)^+$.

Example 321

***N*-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)-1-PHENYL-3-PROPYL-1H-PYRAZOLE-4-CARBOXAMIDE:** Prepared by Procedure Q1 and Scheme AC

using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-phenyl-3-propyl-1*H*-pyrazole-4-carbonyl chloride: ESMS *m/e*: 592.2 $(M + H)^+$.

Example 322

4-(DIMETHYLAMINO)-*N*-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)BENZAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(dimethylamino)benzoyl chloride: ESMS *m/e*: 527.3 $(M + H)^+$.

Example 323

***N*-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)-2-THIOPHENECARBOXAMIDE:** Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 2-thiophenecarbonyl chloride: ESMS *m/e*: 490.2 $(M + H)^+$.

Example 324

***N*-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)-5-NITRO-2-FURAMIDE:** Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 5-nitro-2-furoyl chloride: ESMS *m/e*: 519.2 $(M + H)^+$.

Example 325

***N*-(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-5-METHYL-3-PHENYL-4-**

ISOXAZOLECARBOXAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 5-methyl-3-phenyl-4-isoxazolecarbonyl chloride: ESMS m/e: 489.1 (M + H)$^+$.

Example 326

N-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)-2-FURAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 2-furoyl chloride: ESMS *m/e*: 474.2 (M + H)$^+$.

Example 327

N-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)-1-(4-NITROPHENYL)-5-(TRIFLUOROMETHYL)-1*H*-PYRAZOLE-4-CARBOXAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(4-nitrophenyl)-5-(trifluoromethyl)-1*H*-pyrazole-4-carbonyl chloride: ESMS *m/e*: 663.2 (M + H)$^+$.

Example 328

3-(2-CHLORO-6-FLUOROPHENYL)-*N*-(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-5-METHYL-4-ISOXAZOLECARBOXAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2-chloro-6-fluorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 541.2 (M + H)$^+$.

Example 329

N-[3-(1-{3-[(DIPHENYLACETYL)AMINO]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by

Procedure Q1 and Scheme AC using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and diphenylacetyl chloride: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.33-7.21 (m, 13H), 6.94 (m, 2H), 4.88 (s, 1H), 3.39 (t, 2H, J = 5.6 Hz), 2.93 (d, 2H, J = 11.3 Hz), 2.52-2.36 (m, 4H), 1.97 (t, 2H, J = 11.3 Hz), 1.83-1.58 (m, 6H), 1.24 (d, 6H, J = 7.6 Hz); Anal. Calcd for $C_{32}H_{39}N_3O_2$+HCl+0.19$CHCl_3$: C, 69.44; H, 7.27; N, 7.55. Found: C, 69.44; H, 7.43; N, 7.43; ESMS *m/e*: 498.4 $(M + H)^+$.

Example 330

***N*-(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-1-BENZOTHIOPHENE-3-CARBOXAMIDE:** Prepared by Procedure Q1 and Scheme AC using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 1-benzothiophene-3-carbonyl chloride: ESMS *m/e*: 464.2 $(M + H)^+$.

Example 331

3-(2-CHLOROPHENYL)-*N*-(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-5-METHYL-4-ISOXAZOLECARBOXAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2-chlorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 523.1 $(M + H)^+$.

Example 332

3-(2,6-DICHLOROPHENYL)-*N*-(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-5-METHYL-4-ISOXAZOLECARBOXAMIDE: Prepared by Procedure Q1 and Scheme AC using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2,6-

dichlorophenyl)-5-methyl- 4-isoxazolecarbonyl chloride: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, 1H, J = 2.3 Hz), 7.48 (s, 1H), 7.4 (m, 1H), 7.39 (s, 1H), 7.37 (m, 2H), 7.24 (t, 1H, J = 7.2 Hz), 6.92 (d, 1H, J = 7.9 Hz), 6.06 (s, 1H), 3.31 (q, 2H, J = 6.4 Hz), 2.94 (d, 2H, J = 10.8 Hz), 2.79 (s, 3H), 2.53 (q, 1H, J = 6.1), 2.47 (tt, 1H, J = 4.2, 11.4 Hz), 2.29 (t, 2H, J = 7.2 Hz), 1.99 (t, 2H, J = 11.4 Hz), 1.81 (m, 2H), 1.69 (dt, 2H, J = 2.4, 11.6), 1.59 (q, 2H, J = 6.6 Hz), 1.24 (d, 6H, J = 6.5 Hz); ESMS *m/e*: 557.0 $(M + H)^+$.

1-[3-(3-CHLOROPROPOXY)PHENYL]ETHANONE: Prepared by Procedure U and Scheme AK using 1-(3-hydroxyphenyl)ethanone and 1-bromo-3-chloropropane.

1-(3-CHLOROPROPOXY)-2-FLUOROBENZENE: Prepared by Procedure U and Scheme AK using 2-fluorophenol and 1-bromo-3-chloropropane.

1-CHLORO-3-(3-CHLOROPROPOXY)BENZENE: Prepared by Procedure U and Scheme AK using 3-chlorophenol and 1-bromo-3-chloropropane.

1-CHLORO-4-(3-CHLOROPROPOXY)BENZENE: Prepared by Procedure U and Scheme AK using 4-chlorophenol and 1-bromo-3-chloropropane.

1-(3-CHLOROPROPOXY)-3-FLUOROBENZENE: Prepared by Procedure U and Scheme AK using 3-fluorophenol and 1-bromo-3-chloropropane.

1-(3-CHLOROPROPOXY)-4-FLUOROBENZENE: Prepared by Procedure U and Scheme AK using 4-fluorophenol and 1-bromo-3-chloropropane.

1-CHLORO-2-(3-CHLOROPROPOXY)BENZENE: Prepared by Procedure U and Scheme AK using 2-chlorophenol and 1-bromo-3-chloropropane.

4-(3-CHLOROPROPOXY)-1,2-DIMETHYLBENZENE: Prepared by Procedure U and Scheme AK using 3,4-dimethylphenol and 1-bromo-3-chloropropane.

1-BROMO-2-(3-CHLOROPROPOXY)BENZENE: Prepared by Procedure U and Scheme AK using 2-bromophenol and 1-bromo-3-chloropropane.

1-BROMO-3-(3-CHLOROPROPOXY)BENZENE: Prepared by Procedure U and Scheme AK using 3-bromophenol and 1-bromo-3-chloropropane.

1-BROMO-4-(3-CHLOROPROPOXY)BENZENE: Prepared by Procedure U and Scheme AK using 4-bromophenol and 1-bromo-3-chloropropane.

1-(3-CHLOROPROPOXY)-4-METHYLBENZENE: Prepared by Procedure U and Scheme AK using *p*-cresol and 1-bromo-3-chloropropane.

4-BROMOPHENYL (2R)-3-CHLORO-2-METHYLPROPYL ETHER: Prepared by Procedure U and Scheme AK using 4-bromophenol and (2*S*)-1-bromo-3-chloro-2-methylpropane.

1-{[(2R)-3-CHLORO-2-METHYLPROPYL]OXY}-2,4,5-TRIFLUOROBENZENE: Prepared by Procedure U and Scheme AK

using 2,4,5- trifluorophenol and (2*S*)-1-bromo-3-chloro-2-methylpropane.

1-CHLORO-3-{[(2R)-3-CHLORO-2-METHYLPROPYL]OXY}BENZENE: Prepared by Procedure U and Scheme AK using 3-chlorophenol and (2*S*)-1-bromo-3-chloro-2-methylpropane.

1-{[(2R)-3-CHLORO-2-METHYLPROPYL]OXY}-4-FLUOROBENZENE: Prepared by Procedure U and Scheme AK using 4-fluorophenol and (2*S*)-1-bromo-3-chloro-2-methylpropane.

1-{[(2R)-3-CHLORO-2-METHYLPROPYL]OXY}-3-FLUOROBENZENE: Prepared by Procedure U and Scheme AK using 3-fluorophenol and (2*S*)-1-bromo-3-chloro-2-methylpropane.

1-CHLORO-2-{[(2R)-3-CHLORO-2-METHYLPROPYL]OXY}BENZENE: Prepared by Procedure U and Scheme AK using 2-chlorophenol and (2*S*)-1-bromo-3-chloro-2-methylpropane.

1-{[(2R)-3-CHLORO-2-METHYLPROPYL]OXY}-2-FLUOROBENZENE: Prepared by Procedure U and Scheme AK using 2-fluorophenol and (2*S*)-1-bromo-3-chloro-2-methylpropane.

1-CHLORO-4-{[(2R)-3-CHLORO-2-METHYLPROPYL]OXY}BENZENE: Prepared by Procedure U and Scheme AK using 4-chlorophenol and (2*S*)-1-bromo-3-chloro-2-methylpropane.

3-BROMOPHENYL (2R)-3-CHLORO-2-METHYLPROPYL ETHER: Prepared by Procedure U and Scheme AK using 3-bromophenol and (2*S*)-1-bromo-3-chloro-2-methylpropane.

2-BROMOPHENYL (2R)-3-CHLORO-2-METHYLPROPYL ETHER: Prepared by Procedure U and Scheme AK using 2-bromophenol and (2*S*)-1-bromo-3-chloro-2-methylpropane.

1-{[(2*S*)-3-CHLORO-2-METHYLPROPYL]OXY}-3-FLUOROBENZENE: Prepared by Procedure U and Scheme AK using 3-fluorophenol and (2*R*)-1-bromo-3-chloro-2-methylpropane.

1-{[(2*S*)-3-CHLORO-2-METHYLPROPYL]OXY}-4-FLUOROBENZENE: Prepared by Procedure U and Scheme AK using 4-fluorophenol and (2*R*)-1-bromo-3-chloro-2-methylpropane.

1-{[(2*S*)-3-CHLORO-2-METHYLPROPYL]OXY}-2-FLUOROBENZENE: Prepared by Procedure U and Scheme AK using 2-fluorophenol and (2*R*)-1-bromo-3-chloro-2-methylpropane.

1-CHLORO-2-{[(2*S*)-3-CHLORO-2-METHYLPROPYL]OXY}BENZENE: Prepared by Procedure U and Scheme AK using 2-chlorophenol and (2*R*)-1-bromo-3-chloro-2-methylpropane.

1-CHLORO-4-{[(2*S*)-3-CHLORO-2-METHYLPROPYL]OXY}BENZENE: Prepared by Procedure U and Scheme AK using 4-chlorophenol and (2*R*)-1-bromo-3-chloro-2-methylpropane.

4-BROMOPHENYL (2*S*)-3-CHLORO-2-METHYLPROPYL ETHER: Prepared by Procedure U and Scheme AK using 4-bromophenol and (2*R*)-1-bromo-3-chloro-2-methylpropane.

3-BROMOPHENYL (2*S*)-3-CHLORO-2-METHYLPROPYL ETHER: Prepared by Procedure U and Scheme AK using 3-bromophenol and (2*R*)-1-bromo-3-chloro-2-methylpropane.

2-BROMOPHENYL (2*S*)-3-CHLORO-2-METHYLPROPYL ETHER: Prepared by Procedure U and Scheme AK using 2-bromophenol and (2*R*)-1-bromo-3-chloro-2-methylpropane.

1-CHLORO-3-{[(2*S*)-3-CHLORO-2-METHYLPROPYL]OXY}BENZENE: Prepared by Procedure U and Scheme AK using 3-chlorophenol and (2*R*)-1-bromo-3-chloro-2-methylpropane.

1-[3-(4-CHLOROBUTOXY)PHENYL]ETHANONE: Prepared by Procedure U and Scheme AK using 1-(3-hydroxyphenyl)ethanone and 1-bromo-4-chlorobutane.

1-[3-(4-CHLOROBUTOXY)PHENYL]ETHANONE: Prepared by Procedure U and Scheme AK using 1-(3-hydroxyphenyl)ethanone and 1-bromo-4-chlorobutane.

1-(4-CHLOROBUTOXY)-3-METHOXYBENZENE: Prepared by Procedure U and Scheme AK using 3-methoxyphenol and 1-bromo-4-chlorobutane.

1-(4-CHLOROBUTOXY)-4-METHOXYBENZENE: Prepared by Procedure U and Scheme AK using 4-methoxyphenol and 1-bromo-4-chlorobutane.

1-(4-CHLOROBUTOXY)-2-METHOXYBENZENE: Prepared by Procedure U and Scheme AK using 2-methoxyphenol and 1-bromo-4-chlorobutane.

4-(4-CHLOROBUTOXY)-1,2-DIMETHYLBENZENE: Prepared by Procedure U and Scheme AK using 3,4-dimethylphenol and 1-bromo-4-chlorobutane.

1-{3-[(5-CHLOROPENTYL)OXY]PHENYL}ETHANONE: Prepared by Procedure U and Scheme AK using 1-(3-hydroxyphenyl)ethanone and 1-bromo-5-chloropentane.

1-{3-[(5-CHLOROPENTYL)OXY]PHENYL}ETHANONE: Prepared by Procedure U and Scheme AK using 1-(3-hydroxyphenyl)ethanone and 1-bromo-5-chloropentane.

1-{3-[(6-CHLOROHEXYL)OXY]PHENYL}ETHANONE: Prepared by Procedure U and Scheme AK using 1-(3-hydroxyphenyl)ethanone and 1-bromo-6-chlorohexane.

1-{3-[(6-CHLOROHEXYL)OXY]PHENYL}ETHANONE: Prepared by Procedure U and Scheme AK using 1-(3-hydroxyphenyl)ethanone and 1-bromo-6-chlorohexane.

Example 333

N-(3-{1-[(2*S*)-2-(3-ACETYLPHENOXY)-2-PHENYLETHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure B and Scheme B1 using 1-(3-hydroxyphenyl)ethanone and *N*-(3-{1-[(2*R*)-2-hydroxy-2-phenylethyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 485.0 $(M + H)^+$.

Example 334

N-(3-{1-[(2*S*)-2-(2-ACETYLPHENOXY)-2-PHENYLETHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure B and Scheme B1 using 1-(2-hydroxyphenyl)ethanone and *N*-(3-{1-[(2*R*)-2-hydroxy-2-phenylethyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 485.2 $(M + H)^+$.

Example 335

N-(3-{1-[(2*S*)-2-(3-CHLOROPHENOXY)-2-PHENYLETHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure B and Scheme B1 using 3-chlorophenol and *N*-(3-

{1-[(2*R*)-2-hydroxy-2-phenylethyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 477.1 $(M + H)^+$.

Example 336

***N*-(3-{1-[(2*S*)-2-(3,4-DIMETHOXYPHENOXY)-2-PHENYLETHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure B and Scheme B1 using 3,4-dimethoxyphenol and *N*-(3-{1-[(2*R*)-2-hydroxy-2-phenylethyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 503.2 $(M + H)^+$.

Example 337

***N*-(3-{1-[(2*R*)-2-(4-FLUOROPHENOXY)-2-PHENYLETHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure B and Scheme B1 using 4-fluorophenol and *N*-(3-{1-[(2*S*)-2-hydroxy-2-phenylethyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 461.2 $(M + H)^+$.

Example 338

***N*-(3-{1-[(2*R*)-2-(3-METHOXYPHENOXY)-2-PHENYLETHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure B and Scheme B1 using 3-methoxyphenol and *N*-(3-{1-[(2*S*)-2-hydroxy-2-phenylethyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 472.9 $(M + H)^+$.

Example 339

***N*-(3-{1-[(2*R*)-2-(3-CHLOROPHENOXY)-2-PHENYLETHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure B and Scheme B1 using 3-chlorophenol and *N*-(3-{1-[(2*S*)-2-hydroxy-2-phenylethyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 478.5 $(M + H)^+$.

N-{3-[1-(3,3-DIMETHOXYPROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 3-bromo-1,1-dimethoxypropane and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 349.2 $(M + H)^+$.

Example 340

N-(3-{1-[(3*S*)-3-(3-ACETYLPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE: Prepared by Procedure B and Scheme B1 using 1-(3-hydroxyphenyl)ethanone and *N*-(3-{1-[(3*R*)-3-hydroxy-3-phenylpropyl]-4-piperidinyl}phenyl)cyclopropanecarboxamide: ESMS *m/e*: 497.1 $(M + H)^+$.

Example 341

N-(3-{1-[3-(3-ACETYLPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-[3-(3-chloropropoxy)phenyl]ethanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 423.2 $(M + H)^+$.

Example 342

N-(3-{1-[3-(3-ACETYLPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-[3-(3-chloropropoxy)phenyl]ethanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 421.2 $(M + H)^+$.

Example 343

N-(3-{1-[3-(2-FLUOROPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by

Procedure G and Scheme B1 using 1-(3-chloropropoxy)-2-fluorobenzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 399.2 $(M + H)^+$.

Example 344

***N*-(3-{1-[3-(3-CHLOROPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 1-chloro-3-(3-chloropropoxy)benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 415.2 $(M + H)^+$.

Example 345

***N*-(3-{1-[3-(4-CHLOROPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 1-chloro-4-(3-chloropropoxy)benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, 1H, J = 3.2, 5.7 Hz), 7.53 (dd, 1H, J = 3.2, 5.7 Hz), 7.50 (m, 1H), 7.31 (m, 1H), 7.24-7.20 (m, 2H), 6.94 (d, 1H, J = 7.9 Hz), 6.85-6.82 (m, 2H), 4.00 (t, 2H, J = 6.1 Hz), 3.07 (d, 2H, J = 10.9 Hz), 2.55 (m, 3H), 2.50 (sept, 1H, J = 6.2 Hz), 2.08 (dt, 2H, J = 3.1, 10.9 Hz), 2.00 (m, 2H), 1.83 (m, 3H), 1.69 (qt, 1H, J = 6.2 Hz), 1.24 (d, 6H, J = 6.8 Hz); Anal. Calcd for $C_{24}H_{31}ClN_2O_2$+HCl: C, 63.8; H, 7.09; N, 6.21. Found: C, 63.3; H, 7.04; N, 6.27; ESMS *m/e*: 415.2 $(M + H)^+$.

Example 346

***N*-(3-{1-[3-(3-FLUOROPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 1-(3-chloropropoxy)-3-fluorobenzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 399.2 $(M + H)^+$.

Example 347

N-(3-{1-[3-(4-FLUOROPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-(3-chloropropoxy)-4-fluorobenzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 399.2 $(M + H)^+$.

Example 348

N-(3-{1-[3-(2-CHLOROPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-chloro-2-(3-chloropropoxy)benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 415.2 $(M + H)^+$.

Example 349

N-(3-{1-[3-(3,4-DIMETHYLPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 4-(3-chloropropoxy)-1,2-dimethylbenzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 409.2 $(M + H)^+$.

Example 350

N-(3-{1-[3-(2-BROMOPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-bromo-2-(3-chloropropoxy)benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (dd, 1H, J = 1.6, 7.9 Hz), 7.48 (s, 1H), 7.32 (m, 1H), 7.28-7.22 (m, 3H), 7.17 (s, 1H), 6.98 (d, 1H, J = 7.7 Hz), 6.93 (dd, 1H, J = 1.4, 8.4 Hz), 6.82 (dt, 1H, J = 7.6, 1.4 Hz), 4.11 (t, 2H, J = 6.3 Hz), 3.07 (d, 2H, J = 11.3 Hz), 2.61 (t, 2H, J = 6.9 Hz), 2.50 (m, 3H), 2.07

(m, 1H), 1.8-1.75 (m, 5H), 1.25 (d, 6H, J = 6.7 Hz); Anal. Calcd for $C_{24}H_{31}BrN_2O_2.HCl+0.2\ CHCl_3$: C, 55.9; H, 6.24; N, 5.39. Found: C, 55.8; H, 6.23; N, 5.47; ESMS *m/e*: 459.1 $(M + H)^+$.

Example 351

***N*-(3-{1-[3-(3-BROMOPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 1-bromo-3-(3-chloropropoxy)benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 459.1 $(M + H)^+$.

Example 352

***N*-(3-{1-[3-(4-BROMOPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 1-bromo-4-(3-chloropropoxy)benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.37 (d, 2H, J = 7.6 Hz), 7.26 (m, 3H), 6.97 (d, 1H, J = 7.7 Hz), 6.79 (d, 2H, J = 7.7 Hz), 4.01 (t, 2H, J = 5.6 Hz), 3.08 (d, 2H, J = 9.4 Hz), 2.53 (m, 4H), 2.05 (m, 4H), 1.84 (m, 4H), 1.24 (d, 6H, J = 5.9 Hz); Anal. Calcd for $C_{24}H_{31}BrN_2O_2.HCl+0.34CHCl_3$: C, 54.5; H, 6.08; N, 5.22. Found: C, 54.5; H, 6.22; N, 5.22; ESMS *m/e*: 459.1 $(M + H)^+$.

Example 353

***N*-(3-{1-[(3*R*)-3-(3,4-DIMETHOXYPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-*N*,2-DIMETHYLPROPANAMIDE:** Prepared by Procedure T and Scheme AD using *N*-(3-{1-[(3*R*)-3-(3,4-dimethoxyphenoxy)-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and methyl iodide: ESMS *m/e*: 531.2 $(M + H)^+$.

Example 354

***N*-(3-{1-[(3*R*)-3-(3-ACETYLPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-*N*,2-DIMETHYLPROPANAMIDE:** Prepared by Procedure T and Scheme AD using *N*-(3-{1-[(3*R*)-3-(3-acetylphenoxy)-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and methyl iodide: ESMS *m/e*: 513.2 (M + H)$^+$.

Example 355

***N*-(3-{1-[(3*S*)-3-(3-ACETYLPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-*N*,2-DIMETHYLPROPANAMIDE:** Prepared by Procedure T and Scheme AD using *N*-(3-{1-[(3*S*)-3-(3-acetylphenoxy)-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide and methyl iodide: ESMS *m/e*: 513.2 (M + H)$^+$.

Example 356

***N*-(3-{1-[(2*S*)-3-(4-BROMOPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 4-bromophenyl (2*R*)-3-chloro-2-methylpropyl ether and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 473.0 (M + H)$^+$.

Example 357

2-METHYL-*N*-(3-{1-[(2*S*)-2-METHYL-3-(2,4,5-TRIFLUOROPHENOXY)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-{[(2*R*)-3-chloro-2-methylpropyl]oxy}-2,4,5-trifluorobenzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 449.2 (M + H)$^+$.

Example 358

N-(3-{1-[(2*S*)-3-(3-CHLOROPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-chloro-3-{[(2*R*)-3-chloro-2-methylpropyl]oxy}benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 429.2 $(M + H)^+$.

Example 359

N-(3-{1-[(2*S*)-3-(4-FLUOROPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-{[(2*R*)-3-chloro-2-methylpropyl]oxy}-4-fluorobenzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 413.2 $(M + H)^+$.

Example 360

N-(3-{1-[(2*S*)-3-(3-FLUOROPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-{[(2*R*)-3-chloro-2-methylpropyl]oxy}-3-fluorobenzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 413.2 $(M + H)^+$.

Example 361

N-(3-{1-[(2*S*)-3-(2-CHLOROPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-chloro-2-{[(2*R*)-3-chloro-2-methylpropyl]oxy}benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 429.1 $(M + H)^+$.

Example 362

N-(3-{1-[(2*S*)-3-(2-FLUOROPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-{[(2*R*)-3-chloro-2-methylpropyl]oxy}-2-fluorobenzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 413.2 $(M + H)^+$.

Example 363

N-(3-{1-[(2*S*)-3-(4-CHLOROPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-chloro-4-{[(2*R*)-3-chloro-2-methylpropyl]oxy}benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 429.2 $(M + H)^+$.

Example 364

N-(3-{1-[(2*S*)-3-(3-BROMOPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 3-bromophenyl (2*R*)-3-chloro-2-methylpropyl ether and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 474.0 $(M + H)^+$.

Example 365

N-(3-{1-[(2*S*)-3-(2-BROMOPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 2-bromophenyl (2*R*)-3-chloro-2-methylpropyl ether and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 473.0 $(M + H)^+$.

Example 366

N-(3-{1-[(2*R*)-3-(3-FLUOROPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-{[(2*S*)-3-chloro-2-methylpropyl]oxy}-3-fluorobenzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 413.2 $(M + H)^+$.

Example 367

N-(3-{1-[(2*R*)-3-(4-FLUOROPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-{[(2*S*)-3-chloro-2-

methylpropyl]oxy}-4- fluorobenzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 413.8 $(M + H)^+$.

Example 368

***N*-(3-{1-[(2*R*)-3-(2-CHLOROPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 1-chloro-2-{[(2*S*)-3-chloro-2-methylpropyl]oxy}benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 429.1 $(M + H)^+$.

Example 369

***N*-(3-{1-[(2*R*)-3-(4-CHLOROPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 1-chloro-4-{[(2*S*)-3-chloro-2-methylpropyl]oxy}benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 429.1 $(M + H)^+$.

Example 370

***N*-(3-{1-[(2*R*)-3-(4-BROMOPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 4-bromophenyl (2*S*)-3-chloro-2-methylpropyl ether and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 473.0 $(M + H)^+$.

Example 371

***N*-(3-{1-[(2*R*)-3-(3-BROMOPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 3-bromophenyl (2*S*)-3-chloro-2-methylpropyl ether and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 473.0 $(M + H)^+$.

Example 372

***N*-(3-{1-[(2*R*)-3-(2-BROMOPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 2-bromophenyl (2*S*)-3-chloro-2-methylpropyl ether and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 473.0 $(M + H)^+$.

Example 373

***N*-(3-{1-[(2*R*)-3-(3-CHLOROPHENOXY)-2-METHYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 1-chloro-3-{[(2*S*)-3-chloro-2-methylpropyl]oxy}benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 429.1 $(M + H)^+$.

Example 374

***N*-(3-{1-[3-(5,5-DIMETHYL-1,3-DIOXAN-2-YL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 2-(3-bromopropyl)-5,5-dimethyl-1,3-dioxane and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 403.2 $(M + H)^+$

Example 375

***N*-(3-{1-[4-(3-ACETYLPHENOXY)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 1-[3-(4-chlorobutoxy)phenyl]ethanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 437.2 $(M + H)^+$.

Example 376

***N*-(3-{1-[4-(3-METHOXYPHENOXY)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 1-(4-chlorobutoxy)-3-methoxybenzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 425.2 $(M + H)^+$.

Example 377

N-(3-{1-[4-(4-METHOXYPHENOXY)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-(4-chlorobutoxy)-4-methoxybenzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 425.2 $(M + H)^+$.

Example 378

N-(3-{1-[4-(2-METHOXYPHENOXY)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-(4-chlorobutoxy)-2-methoxybenzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 425.2 $(M + H)^+$.

Example 379

N-(3-{1-[4-(3,4-DIMETHYLPHENOXY)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 4-(4-chlorobutoxy)-1,2-dimethylbenzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 423.2 $(M + H)^+$.

Example 380

N-(3-{1-[4-(1,3-DIOXOLAN-2-YL)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 2-(4-chlorobutyl)-1,3-dioxolane and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 375.2 $(M + H)^+$

Example 381

N-(3-{1-[5-(3-ACETYLPHENOXY)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 1-{3-[(5-

chloropentyl)oxy]phenyl}ethanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 451.3 $(M + H)^+$.

Example 382

***N*-(3-{1-[5-(3-ACETYLPHENOXY)PENTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure G and Scheme B1 using 1-{3-[(5-chloropentyl)oxy]phenyl}ethanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 449.2 $(M + H)^+$.

Example 383

***N*-(3-{1-[6-(3-ACETYLPHENOXY)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 1-{3-[(6-chlorohexyl)oxy]phenyl}ethanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 465.3 $(M + H)^+$.

Example 384

***N*-(3-{1-[6-(3-ACETYLPHENOXY)HEXYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure G and Scheme B1 using 1-{3-[(6-chlorohexyl)oxy]phenyl}ethanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 463.3 $(M + H)^+$.

Example 385

***N*-(3-{1-[4-(4-CHLOROPHENOXY)-4-(4-CHLOROPHENYL)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure B and Scheme AN using 4-chlorophenol and *N*-(3-{1-[4-(4-chlorophenyl)-4-hydroxybutyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 562.9 $(M + 23)^+$.

Example 386

2-METHYL-N-(3-{1-[2-(1-METHYL-2-PHENYL-1H-INDOL-3-YL)ETHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(4-oxo-4-phenylbutyl)-4-piperidinyl]phenyl}propanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 480.3 $(M + H)^+$.

Example 387

2-METHYL-N-(3-{1-[2-(2-PHENYL-1H-BENZO[G]INDOL-3-YL)ETHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(4-oxo-4-phenylbutyl)-4-piperidinyl]phenyl}propanamide and 1-(1-naphthyl)hydrazine hydrochloride: ESMS *m/e*: 516.4 $(M + H)^+$.

Example 388

2-METHYL-N-(3-{1-[3-(2-PHENYL-1H-BENZO[G]INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(5-oxo-5-phenylpentyl)-4-piperidinyl]phenyl}propanamide and 1-(1-naphthyl)hydrazine hydrochloride: ESMS *m/e*: 530.2 $(M + H)^+$.

Example 389

2-METHYL-N-[3-(1-{3-[2-PHENYL-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(5-oxo-5-phenylpentyl)-4-piperidinyl]phenyl}propanamide and 1-[4-(trifluoromethoxy)phenyl]hydrazine hydrochloride: ESMS *m/e* : 564.2 $(M + H)^+$.

Example 390

2-METHYL-N-[3-(1-{4-[2-PHENYL-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL]BUTYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(6-oxo-6-phenylhexyl)-4-piperidinyl]phenyl}propanamide and 1-[4-(trifluoromethoxy)phenyl]hydrazine hydrochloride: ESMS *m/e*: 578.2 $(M + H)^+$.

Example 391

2-METHYL-N-(3-{1-[3-(1-METHYL-2-PHENYL-1H-INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(5-oxo-5-phenylpentyl)-4-piperidinyl]phenyl}propanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 495.3 $(M + H)^+$.

Example 392

N-(3-{1-[4-(1,2-DIPHENYL-1H-INDOL-3-YL)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(6-oxo-6-phenylhexyl)-4-piperidinyl]phenyl}propanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: $(M + H)^+$. 570.3

Example 393

2-METHYL-N-[3-(1-{5-[2-PHENYL-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL]PENTYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(7-oxo-7-phenylheptyl)-4-piperidinyl]phenyl}propanamide and 1-[4-(trifluoromethoxy)phenyl]hydrazine hydrochloride: ESMS *m/e*: 592.3 $(M + H)^+$.

Example 394

N-(3-{1-[5-(1,2-DIPHENYL-1H-INDOL-3-YL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(7-oxo-7-phenylheptyl)-4-piperidinyl]phenyl}propanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 584.3 $(M + H)^+$.

Example 395

2-METHYL-N-(3-{1-[5-(1-METHYL-2-PHENYL-1H-INDOL-3-YL)PENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(7-oxo-7-phenylheptyl)-4-piperidinyl]phenyl}propanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 522.3 $(M + H)^+$.

Example 396

2-METHYL-N-(3-{1-[4-(2-PHENYL-1H-BENZO[G]INDOL-3-YL)BUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(6-oxo-6-phenylhexyl)-4-piperidinyl]phenyl}propanamide and 1-(1-naphthyl)hydrazine hydrochloride: ESMS *m/e*: 544.3 $(M + H)^+$.

Example 397

2-METHYL-N-(3-{1-[4-(1-METHYL-2-PHENYL-1H-INDOL-3-YL)BUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(6-oxo-6-phenylhexyl)-4-piperidinyl]phenyl}propanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 508.3 $(M + H)^+$.

Example 398

2-METHYL-N-(3-{1-[5-(2-PHENYL-1H-BENZO[G]INDOL-3-YL)PENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(7-

oxo-7-phenylheptyl)-4-piperidinyl]phenyl}propanamide and 1-(1-naphthyl)hydrazine hydrochloride: ESMS m/e: 558.2 (M + H)$^+$.

Example 399

2-METHYL-N-(3-{1-[2-(5-METHYL-2-PHENYL-1H-INDOL-3-YL)ETHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(4-oxo-4-phenylbutyl)-4-piperidinyl]phenyl}propanamide and 1-(4-methylphenyl)hydrazine hydrochloride: ESMS m/e: 480.2 (M + H)$^+$.

Example 400

N-(3-{1-[2-(7-METHOXY-2-PHENYL-1H-INDOL-3-YL)ETHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(4-oxo-4-phenylbutyl)-4-piperidinyl]phenyl}propanamide and 1-(2-methoxyphenyl)hydrazine hydrochloride: ESMS m/e: 496.2 (M + H)$^+$.

Example 401

2-METHYL-N-(3-{1-[2-(7-METHYL-2-PHENYL-1H-INDOL-3-YL)ETHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(4-oxo-4-phenylbutyl)-4-piperidinyl]phenyl}propanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS m/e: 480.2 (M + H)$^+$.

Example 402

N-(3-{1-[3-(7-METHOXY-2-PHENYL-1H-INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(5-oxo-5-phenylpentyl)-4-piperidinyl]phenyl}propanamide and 1-

5-phenylpentyl)-4-piperidinyl]phenyl}propanamide and 1-(2-methoxyphenyl)hydrazine hydrochloride: ESMS *m/e*: 510.2 $(M + H)^+$.

Example 403

2-METHYL-N-(3-{1-[4-(7-METHYL-2-PHENYL-1H-INDOL-3-YL)BUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(6-oxo-6-phenylhexyl)-4-piperidinyl]phenyl}propanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 508.3 $(M + H)^+$.

Example 404

N-(3-{1-[2-(5-METHOXY-2-PHENYL-1H-INDOL-3-YL)ETHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(4-oxo-4-phenylbutyl)-4-piperidinyl]phenyl}propanamide and 1-(4-methoxyphenyl)hydrazine hydrochloride: ESMS *m/e*: 496.2 $(M + H)^+$.

Example 405

2-METHYL-N-(3-{1-[3-(5-METHYL-2-PHENYL-1H-INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(5-oxo-5-phenylpentyl)-4-piperidinyl]phenyl}propanamide and 1-(4-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 494.3 $(M + H)^+$.

Example 406

N-(3-{1-[4-(7-METHOXY-2-PHENYL-1H-INDOL-3-YL)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE

Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(6-oxo-6-phenylhexyl)-4-piperidinyl]phenyl}propanamide and 1-(2-methoxyphenyl)hydrazine hydrochloride: ESMS *m/e*: 524.3 $(M + H)^+$.

Example 407

2-METHYL-N-(3-{1-[3-(1-PHENYL-1H-INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure H and Scheme S using *N*-(3-{1-[4-(1,3-dioxolan-2-yl)butyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 480.2 $(M + H)^+$.

Example 408

2-METHYL-N-(3-{1-[2-(1-PHENYL-1H-INDOL-3-YL)ETHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure H and Scheme S using *N*-(3-{1-[3-(1,3-dioxolan-2-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 466.2 $(M + H)^+$.

Example 409

2-METHYL-N-(3-{1-[2-(7-METHYL-1H-INDOL-3-YL)ETHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure H and Scheme S using *N*-(3-{1-[3-(1,3-dioxolan-2-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride:. ESMS *m/e*: 404.2 $(M + H)^+$.

Example 410

2-METHYL-N-(3-{1-[2-(1-METHYL-1H-INDOL-3-YL)ETHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure

H and Scheme S using *N*-(3-{1-[3-(1,3-dioxolan-2-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 404.2 $(M + H)^+$.

Example 411

2-METHYL-N-(3-{1-[2-(5-METHYL-1H-INDOL-3-YL)ETHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure H and Scheme S using *N*-(3-{1-[3-(1,3-dioxolan-2-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(4-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 404.2 $(M + H)^+$.

Example 412

2-METHYL-N-[3-(1-{2-[5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL]ETHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure H and Scheme S using *N*-(3-{1-[3-(1,3-dioxolan-2-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-[4-(trifluoromethoxy)phenyl]hydrazine hydrochloride: ESMS *m/e*: 474.2 $(M + H)^+$.

Example 413

N-(3-{1-[3-(1H-BENZO[G]INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure H and Scheme S using *N*-(3-{1-[4-(1,3-dioxolan-2-yl)butyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(1-naphthyl)hydrazine hydrochloride: ESMS 454.2 *m/e*: $(M + H)^+$.

Example 414

2-METHYL-N-(3-{1-[3-(1-METHYL-1H-INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure H and Scheme S. A mixture of *N*-(3-{1-[4-(1,3-dioxolan-2-yl)butyl]-4-piperidinyl}phenyl)-2-methylpropanamide (100

mg, 0.270 mmol), 1-methyl- 1-phenylhydrazine (106 mg, 0.870 mmol), $ZnCl_2$ (119 mg, 0.870 mmol) and HOAc (1.00 mL) was heated for 12 h at 80 °C. The resulting crude mixture was diluted with water (20 mL), the aqueous layer was neutralized with a saturated K_2CO_3 solution (10 mL) and extracted with CH_2Cl_2 (3 X 20 mL). The combined organic layers were concentrated *in vacuo* and the residue was purified by preparative TLC using 3 % of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product 2-methyl-*N*-(3-{1-[3-(1-methyl-1*H*-indol-3-yl)propyl]-4-piperidinyl}phenyl)propanamide (20.7 mg, 18.7 %): ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, 1H, J = 8.1 Hz), 7.45 (s, 1H), 7.35 (d, 1H, J = 7.4 Hz), 7.25 (m, 4H), 7.09 (t, 1H, J = 7.3 Hz), 6.97 (d, 1H, J = 7.3 Hz), 6.86 (s, 1H), 3.75 (s, 3H), 3.11 (d, 2H, J = 11.6 Hz), 2.79 (t, 2H, J = 7.3 Hz), 2.51 (m, 4H), 2.12-1.81 (m, 8H), 1.25 (d, 6H, J = 7.1 Hz); Anal. Calcd for $C_{27}H_{33}N_3O+0.225$ $CHCl_3$: C, 73.57; H, 7.99; N, 9.45. Found: C, 73.93; H, 7.90; N, 9.23; ESMS m/e: 418.2 $(M + H)^+$.

Example 415

2-METHYL-N-(3-{1-[3-(5-METHYL-1H-INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure H and Scheme 8 using *N*-(3-{1-[4-(1,3-dioxolan-2-yl)butyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(4-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 418.2 $(M + H)^+$.

Example 416

2-METHYL-N-[3-(1-{3-[5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure H and Scheme 8 using *N*-(3-{1-[4-(1,3-dioxolan-2-yl)butyl]-4-piperidinyl}phenyl)-2-methylpropanamide

and 1-[4-(trifluoromethoxy)phenyl]hydrazine hydrochloride: ESMS *m/e*: 488.2 $(M + H)^+$.

Example 417

2-METHYL-N-(3-{1-[3-(7-METHYL-1H-INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure H and Scheme S using *N*-(3-{1-[4-(1,3-dioxolan-2-yl)butyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 418.2 $(M + H)^+$.

Example 418

N-(3-{1-[3-(7-METHOXY-1H-INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure H and Scheme S using *N*-(3-{1-[4-(1,3-dioxolan-2-yl)butyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methoxyphenyl)hydrazine hydrochloride: ESMS *m/e*: 434.0 $(M + H)^+$.

Example 419

N-(3-{1-[2-(7-METHOXY-1H-INDOL-3-YL)ETHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure H and Scheme S using *N*-(3-{1-[3-(1,3-dioxolan-2-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methoxyphenyl)hydrazine hydrochloride: ESMS *m/e*: 420.2 $(M + H)^+$.

Example 420

N-(3-{1-[2-(5-METHOXY-1H-INDOL-3-YL)ETHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure H and Scheme S using *N*-(3-{1-[3-(1,3-dioxolan-2-yl)propyl]-4-piperidinyl}phenyl)-2-methylpropanamide

and 1-(4-methoxyphenyl)hydrazine hydrochloride: ESMS m/e: 420.2 $(M + H)^+$.

Example 421

2-METHYL-N-(3-{1-[4-(5-METHYL-2-PHENYL-1H-INDOL-3-YL)BUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-{3-[1-(6-oxo-6-phenylhexyl)-4-piperidinyl]phenyl}propanamide and 1-(4-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 508.3 $(M + H)^+$.

Example 422

2-METHYL-N-[4-(1-{[1-(4-METHYLPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[4-(4-piperidinyl)phenyl]propanamide and 1-(4-methylphenyl)-1*H*-indole: ESMS *m/e*: 466.2 $(M + H)^+$.

Example 423

N-[4-(1-{[1-(4-METHYLPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]BUTANAMIDE: Prepared by Procedure D and Scheme N using *N*-[4-(4-piperidinyl)phenyl]butanamide and 1-(4-methylphenyl)-1*H*-indole: ESMS *m/e*: 466.2 $(M + H)^+$.

Example 424

N-[3-(1-{[2-(2-AMINOPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 2-(1*H*-indol-2-yl)aniline: ESMS *m/e*: 467.2 $(M + H)^+$.

Example 425

ETHYL 3-({4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}METHYL)-1H-INDOLE-2-CARBOXYLATE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and ethyl 1*H*-indole-2-carboxylate: ESMS *m/e*: 448.2 $(M + H)^+$.

Example 426

2-METHYL-N-(3-{1-[(1-METHYL-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 1-methyl-1*H*-indole: ESMS *m/e*: 390.2 $(M + H)^+$.

Example 427

N-(3-{1-[(5-METHOXY-2-METHYL-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 5-methoxy-2-methyl-1*H*-indole: ESMS *m/e*: 420.2 $(M + H)^+$.

Example 428

2-METHYL-N-(3-{1-[(1-METHYL-2-PHENYL-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 1-methyl-2-phenyl-1*H*-indole: ESMS *m/e*: 466.2 $(M + H)^+$.

Example 429

2-METHYL-N-(3-{1-[(5-NITRO-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 5-nitro-1*H*-indole: ESMS *m/e*: 421.1 $(M + H)^+$.

Example 430

2-METHYL-N-(3-{1-[(2-METHYL-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 2-methyl-1H-indole: ESMS *m/e*: 390.2 $(M + H)^+$.

Example 431

N-(3-{1-[(4-BROMO-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 4-bromo-1*H*-indole: ESMS *m/e*: 455.0 $(M + H)^+$.

Example 432

N-[3-(1-{[2-(4-FLUOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 2-(4-fluorophenyl)-1H-indole: ESMS *m/e*: 470.0 $(M + H)^+$.

Example 433

N-(3-{1-[(1,2-DIPHENYL-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 1,2-diphenyl-1H-indole: ESMS *m/e*: 528.2 $(M + H)^+$.

Example 434

N-[3-(1-{[2-(4-CHLOROPHENYL)-1-ETHYL-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-

[3-(4-piperidinyl)phenyl]propanamide and 2-(4-chlorophenyl)-1-ethyl-1*H*-indole: ESMS *m/e*: 514.1 $(M + H)^+$.

Example 435

N-(3-{1-[(5-CHLORO-2-METHYL-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 5-chloro-2-methyl-1*H*-indole: ESMS *m/e*: 424.1 $(M + H)^+$.

Example 436

N-(3-{1-[(5-CYANO-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 1*H*-indole-5-carbonitrile: ESMS *m/e*: 401.1 $(M + H)^+$.

Example 437

2-METHYL-N-(3-{1-[(5-METHYL-2-PHENYL-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 5-methyl-2-phenyl-1*H*-indole: ESMS *m/e*: 466.2 $(M + H)^+$.

Example 438

2-METHYL-N-[3-(1-{[1-(4-NITROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 1-(4-nitrophenyl)-1*H*-indole: ESMS *m/e*: 497.2 $(M + H)^+$.

Example 439

N-[3-(1-{[1-(2-FLUOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 1-(2-fluorophenyl)-1*H*-indole: ESMS *m/e*: 470.1 $(M + H)^+$.

Example 440

N-(3-{1-[(5,6-DIMETHOXY-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 5,6-dimethoxy-1*H*-indole: ESMS *m/e*: 436.2 $(M + H)^+$.

Example 441

2-METHYL-N-[3-(1-{[1-(3-METHYLPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 1-(3-methylphenyl)-1*H*-indole: ESMS *m/e*: 466.2 $(M + H)^+$.

Example 442

2-METHYL-N-{3-[1-({1-[3-(TRIFLUOROMETHYL)PHENYL]-1H-INDOL-3-YL}METHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 1-[3-(trifluoromethyl)phenyl]-1*H*-indole: ESMS *m/e*: 520.2 $(M + H)^+$.

Example 443

N-[3-(1-{[1-(4-METHOXYPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-

piperidinyl)phenyl]propanamide and 5-methoxy-2-phenyl-1H-indole: ESMS *m/e*: 482.2 $(M + H)^+$.

Example 445

2-METHYL-N-(3-{1-[(5-METHYL-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure D and Scheme N using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 5-methyl-1H-indole: ESMS *m/e*: 390.2 $(M + H)^+$.

Example 446

N-[3-(1-{[1-(2-NITROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 1-(2-nitrophenyl)-1H-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 497.2 $(M + H)^+$.

Example 447

N-[3-(1-{[1-(2-METHOXYPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 1-(2-methoxyphenyl)-1H-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 482.2 $(M + H)^+$.

Example 448

2-METHYL-*N*-{3-[1-({1-[2-(TRIFLUOROMETHYL)PHENYL]-1H-INDOL-3-YL}METHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure D and Scheme N using 1-[2-(trifluoromethyl)phenyl]-1H-indole, and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 520.2 $(M + H)^+$.

Example 449

N-(3-{1-[(5-METHOXY-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 1*H*-indol-5-yl methyl ether and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 406.2 $(M + H)^+$.

Example 450

N-[3-(1-{[1-(4-FLUOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 1-(4-fluorophenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 470.2 $(M + H)^+$.

Example 451

N-[3-(1-{[1-(3-METHOXYPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 1-(3-methoxyphenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 482.2 $(M + H)^+$.

Example 452

2-METHYL-*N*-[3-(1-{[1-(2-METHYLPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 1-(2-methylphenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 466.2 $(M + H)^+$.

Example 453

ETHYL 3-({4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}METHYL)-5-METHOXY-1H-INDOLE-2-CARBOXYLATE: Prepared by Procedure D and Scheme N using ethyl 5-methoxy-1*H*-indole-2-carboxylate and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 478.2 $(M + H)^+$.

Example 454

***N*-(3-{1-[(5-FLUORO-1*H*-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure D and Scheme N using 5-fluoro-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 394.2 $(M + H)^+$.

1-PHENYL-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 1*H*-indole and iodobenzene: ESMS *m/e*: 193.9 $(M + H)^+$.

1-(4-CHLOROPHENYL)-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 1*H*-indole and 1-chloro-4-iodobenzene: ESMS *m/e*: 227.9 $(M + H)^+$.

1-(3-CHLOROPHENYL)-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 1*H*-indole and 1-chloro-3-iodobenzene: ESMS *m/e*: 227.9 $(M + H)^+$.

1-(2-CHLOROPHENYL)-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 1*H*-indole and 1-chloro-2-iodobenzene: ESMS *m/e*: 227.9 $(M + H)^+$.

1-[2-(TRIFLUOROMETHYL)PHENYL]-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 1*H*-indole and 1-iodo-2-(trifluoromethyl)benzene: ESMS *m/e*: 262.0 $(M + H)^+$.

4-(1*H*-INDOL-1-YL)BENZONITRILE: Prepared by Procedure C and Scheme O using 1*H*-indole and 4-iodobenzonitrile: ESMS *m/e*: 219.0 $(M + H)^+$.

1-(4-NITROPHENYL)-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 1*H*-indole and 1-iodo-4-nitrobenzene: ESMS *m/e*: 238.2 $(M + H)^+$.

1-(2-NITROPHENYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 1H-indole and 1-iodo-2-nitrobenzene: ESMS *m/e*: 238.2 $(M + H)^+$.

Example 455

N-[3-(1-{[1-(4-CHLOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 1-(4-chlorophenyl)-1H-indole and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 472.1 $(M + H)^+$.

Example 456

N-[3-(1-{[1-(3-CHLOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 1-(3-chlorophenyl)-1H-indole and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 472.1 $(M + H)^+$.

Example 457

N-[3-(1-{[1-(2-CHLOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]CYCLOPROPANECARBOXAMIDE: Prepared by Procedure D and Scheme N using 1-(2-chlorophenyl)-1H-indole and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 484.1 $(M + H)^+$.

Example 458

N-[3-(1-{[1-(3-CHLOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 1-(3-chlorophenyl)-1H-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 486.1 $(M + H)^+$.

Example 459

N-[3-(1-{[1-(4-CHLOROPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 1-(4-chlorophenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 486.2 $(M + H)^+$.

Example 460

N-[3-(1-{[1-(2-CHLOROPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 1-(2-chlorophenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 486.2 $(M + H)^+$.

Example 461

N-[3-(1-{[1-(2-CHLOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 1-(2-chlorophenyl)-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 472.1 $(M + H)^+$.

Example 462

N-[3-(1-{[1-(4-CHLOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]CYCLOPROPANECARBOXAMIDE: Prepared by Procedure D and Scheme N using 1-(4-chlorophenyl)-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 484.1 $(M + H)^+$.

Example 463

N-[3-(1-{[1-(3-CHLOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]CYCLOPROPANECARBOXAMIDE: Prepared by

Procedure D and Scheme N using 1-(3-chlorophenyl)-1H-indole and N-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS m/e: 484.1 $(M + H)^+$.

Example 464

N-(3-{1-[(1-PHENYL-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure D and Scheme N using 1-phenyl-1H-indole and N-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 438.2 $(M + H)^+$.

Example 465

N-(3-{1-[(1-PHENYL-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE: Prepared by Procedure D and Scheme N using 1-phenyl-1H-indole and N-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS m/e: 450.2 $(M + H)^+$.

6-CHLORO-1-(4-NITROPHENYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 6-chloro-1H-indole and 1-iodo-4-nitrobenzene: ESMS m/e: 272.6 $(M + H)^+$.

6-CHLORO-1-(2,3-DICHLOROPHENYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 6-chloro-1H-indole and 1,2-dichloro-3-iodobenzene: ESMS m/e: 296.5 $(M + H)^+$.

6-CHLORO-1-(3-METHYLPHENYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 6-chloro-1H-indole and 1-iodo-3-methylbenzene: ESMS m/e: 241.9 $(M + H)^+$.

6-CHLORO-1-(2-METHYLPHENYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 6-chloro-1H-indole and 1-iodo-2-methylbenzene: ESMS m/e: 241.9 $(M + H)^+$.

2-(6-CHLORO-1H-INDOL-1-YL)PHENYL METHYL ETHER: Prepared by Procedure C and Scheme O using 6-chloro-1*H*-indole and 1-iodo-2-methoxybenzene: ESMS *m/e*: 257.9 $(M + H)^+$.

6-CHLORO-1-[3-(TRIFLUOROMETHYL)PHENYL]-1H-INDOLE: Prepared by Procedure C and Scheme O using 6-chloro-1*H*-indole and 1-iodo-3-(trifluoromethyl)benzene: ESMS *m/e*: 295.6 $(M + H)^+$.

6-CHLORO-1-(2-FLUOROPHENYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 6-chloro-1*H*-indole and 1-fluoro-2-iodobenzene: ESMS *m/e*: 245.9 $(M + H)^+$.

6-CHLORO-1-(3-CHLOROPHENYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 6-chloro-1*H*-indole and 1-chloro-3-iodobenzene: ESMS *m/e*: 261.9 $(M + H)^+$.

6-CHLORO-1-(4-CHLOROPHENYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 6-chloro-1*H*-indole and 1-chloro-4-iodobenzene: ESMS *m/e*: 262.9 $(M + H)^+$.

6-CHLORO-1-(2-CHLOROPHENYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 6-chloro-1*H*-indole and 1-chloro-2-iodobenzene: ESMS *m/e*: 262.9 $(M + H)^+$.

3-(6-CHLORO-1H-INDOL-1-YL)PHENYL METHYL ETHER: Prepared by Procedure C and Scheme O using 6-chloro-1H-indole and 1-iodo-3-methoxybenzene: ESMS *m/e*: 257.9 $(M + H)^+$.

6-CHLORO-1-[4-(TRIFLUOROMETHYL)PHENYL]-1H-INDOLE: Prepared by Procedure C and Scheme O using 6-chloro-1H-

indole and 1-iodo-4-(trifluoromethyl)benzene ESMS *m/e*: 295.6 $(M + H)^+$.

6-CHLORO-1-(4-METHYLPHENYL)-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 6-chloro-1*H*-indole and 1-iodo-4-methylbenzene: ESMS *m/e*: 241.9 $(M + H)^+$.

6-CHLORO-1-(4-FLUOROPHENYL)-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 6-chloro-1*H*-indole and 1-fluoro-4-iodobenzene: ESMS *m/e*: 245.9 $(M + H)^+$.

Example 466

N-[3-(1-{[6-CHLORO-1-(4-FLUOROPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]CYCLOPROPANECARBOXAMIDE: Prepared by Procedure D and Scheme N using 6-chloro-1-(4-fluorophenyl)-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 502.1 $(M + H)^+$.

Example 467

N-[3-(1-{[6-CHLORO-1-(4-FLUOROPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 6-chloro-1-(4-fluorophenyl)-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 490.1 $(M + H)^+$.

Example 468

N-(3-{1-[(6-FLUORO-1*H*-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure D and Scheme N using 6-fluoro-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 380.1 $(M + H)^+$.

Example 469

N-{3-{1-[(6-FLUORO-1*H*-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE: Prepared by Procedure D and Scheme N using 6-fluoro-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 392.1 $(M + H)^+$.

Example 470

N-{3-{1-[(6-FLUORO-1*H*-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 6-fluoro-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 394.1 $(M + H)^+$.

Example 471

N-[3-(1-{[6-CHLORO-1-(4-FLUOROPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 6-chloro-1-(4-fluorophenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 504.1 $(M + H)^+$.

Example 472

N-[3-(1-{[6-CHLORO-1-(2-FLUOROPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 6-chloro-1-(2-fluorophenyl)-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 490.1 $(M + H)^+$.

Example 473

N-[3-(1-{[6-CHLORO-1-(2-FLUOROPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]CYCLOPROPANECARBOXAMIDE: Prepared by Procedure D and Scheme N using 6-chloro-1-(2-fluorophenyl)-1*H*-indole and *N*-[3-(4-

piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 502.1 $(M + H)^+$.

Example 474

***N*-[3-(1-{[6-CHLORO-1-(2-FLUOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure D and Scheme N using 6-chloro-1-(2-fluorophenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide ESMS *m/e*: 504.1 $(M + H)^+$.

Example 475

***N*-[3-(1-{[6-CHLORO-1-(4-CHLOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:** Prepared by Procedure D and Scheme N using 6-chloro-1-(4-chlorophenyl)-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]propanamide ESMS *m/e*: 506.1 $(M + H)^+$.

Example 476

***N*-[3-(1-{[6-CHLORO-1-(4-CHLOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure D and Scheme N using 6-chloro-1-(4-chlorophenyl)-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide ESMS *m/e*: 518.1 $(M + H)^+$.

Example 477

***N*-[3-(1-{[6-CHLORO-1-(4-CHLOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure D and Scheme N using 6-chloro-1-(4-chlorophenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide ESMS *m/e*: 520.1 $(M + H)^+$.

Example 478

***N*-[3-(1-{[6-CHLORO-1-(3-CHLOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:** Prepared by Procedure D and Scheme N using 6-chloro-1-(3-chlorophenyl)-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 506.1 $(M + H)^+$.

Example 479

***N*-[3-(1-{[6-CHLORO-1-(3-CHLOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure D and Scheme N using 6-chloro-1-(3-chlorophenyl)-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, 1H, J = 8.4 Hz), 7.68 (s, 1H), 7.49 (m, 2H), 7.44 (d, 2H, J = 7.9 Hz), 7.49-7.25 (m, 4H), 7.21 (d, 1H, J = 7.9 Hz), 7.17 (d, 1H, J = 7.9 Hz), 6.93 (d, 1H, J = 7.9 Hz), 3.79 (s, 2H), 3.13 (d, 2H, J = 9.4 Hz), 2.48 (sept, 1H, J = 7.5 Hz), 2.16 (m, 2H), 1.80 (m, 4H), 1.51 (s, 1H), 1.06 (m, 2H), 0.806 (m, 2H); Anal. Calcd for $C_{30}H_{29}Cl_2N_3O+HCl+1.4H_2O$: C, 62.11; H, 5.70; N, 7.24. Found: C, 62.19; H, 6.21; N, 7.06; ESMS *m/e*: 519.2 $(M + H)^+$.

Example 480

***N*-[3-(1-{[6-CHLORO-1-(3-CHLOROPHENYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure D and Scheme N using 6-chloro-1-(3-chlorophenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 520.1 $(M + H)^+$.

Example 481

***N*-(3-{1-[(5-FLUORO-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by

Procedure D and Scheme N using 5-fluoro-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 392.1 $(M + H)^+$.

Example 482

***N*-[3-(1-{[6-CHLORO-1-(2-CHLOROPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure D and Scheme N using 6-chloro-1-(2-chlorophenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 520.2 $(M + H)^+$.

Example 483

***N*-[3-(1-{[6-CHLORO-1-(3-METHOXYPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure D and Scheme N using 3-(6-chloro-1*H*-indol-1-yl)phenyl methyl ether and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 516.2 $(M + H)^+$.

Example 484

***N*-[3-(1-{[6-CHLORO-1-(2-METHOXYPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure D and Scheme N using 2-(6-chloro-1*H*-indol-1-yl)phenyl methyl ether and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 516.2 $(M + H)^+$.

Example 485

***N*-[3-(1-{[6-CHLORO-1-(2,3-DICHLOROPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure D and Scheme N using 6-chloro-1-(2,3-dichlorophenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 555.1 $(M + H)^+$.

Example 486

N-[3-(1-{[6-CHLORO-1-(4-METHYLPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 6-chloro-1-(4-methylphenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 500.2 $(M + H)^+$.

Example 487

N-{3-[1-({6-CHLORO-1-[3-(TRIFLUOROMETHYL)PHENYL]-1*H*-INDOL-3-YL}METHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 6-chloro-1-[3-(trifluoromethyl)phenyl]-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 554.2 $(M + H)^+$.

Example 488

N-{3-[1-({6-CHLORO-1-[4-(TRIFLUOROMETHYL)PHENYL]-1*H*-INDOL-3-YL}METHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 6-chloro-1-[4-(trifluoromethyl)phenyl]-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 554.2 $(M + H)^+$.

Example 489

N-[3-(1-{[6-CHLORO-1-(2-METHYLPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 6-chloro-1-(2-methylphenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 500.2 $(M + H)^+$.

Example 490

N-[3-(1-{[6-CHLORO-1-(3-METHYLPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 6-chloro-1-

(3-methylphenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 500.2 $(M + H)^+$.

Example 491

***N*-(3-{1-[(7-CHLORO-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE**: Prepared by Procedure D and Scheme N using 7-chloro-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 408.1 $(M + H)^+$.

Example 492

***N*-(3-{1-[(7-CHLORO-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE**: Prepared by Procedure D and Scheme N using 7-chloro-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 410.1 $(M + H)^+$.

Example 493

***N*-(3-{1-[(4-FLUORO-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE**: Prepared by Procedure D and Scheme N using 4-fluoro-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 380.2 $(M + H)^+$.

Example 494

***N*-(3-{1-[(7-CHLORO-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE**: Prepared by Procedure D and Scheme N using 7-chloro-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 396.1 $(M + H)^+$.

Example 495

2-METHYL-*N*-(3-{1-[(6-METHYL-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure D and Scheme N using 6-methyl-1*H*-indole and 2-methyl-*N*-[3-

(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 390.2 $(M + H)^+$.

Example 496

***N*-[3-(1-{[6-(BENZYLOXY)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure D and Scheme N using 6-(benzyloxy)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 482.2 $(M + H)^+$.

Example 497

***N*-(3-{1-[(6-METHOXY-1*H*-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure D and Scheme N using 1*H*-indol-6-yl methyl ether and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 406.2 $(M + H)^+$.

Example 498

METHYL 3-({4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}METHYL)-1*H*-INDOLE-6-CARBOXYLATE: Prepared by Procedure D and Scheme N using methyl 1*H*-indole-6-carboxylate and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 434.2 $(M + H)^+$.

Example 499

2-METHYL-*N*-[3-(1-{[6-(TRIFLUOROMETHYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 6-(trifluoromethyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.66 (s, 1H), 7.63 (s, 2H), 7.44 (d, 1H, J = 8.4 Hz), 7.39 (s, 2H), 7.32 (d, 1H, J = 8.4 Hz), 7.16 (t, 1H, J = 8.4 Hz), 6.84 (d, 1H, J = 8.4 Hz), 4.06 (s,

2H), 3.27 (d, 2H, J = 11.6 Hz), 2.56 (sept, 1H, J = 6.8 Hz), 2.37 (m, 3H), 1.93 (m, 2H), 1.75 (m, 2H), 1.22 (d, 6H, J = 6.8 Hz); Anal. Calcd for $C_{25}H_{28}F_3N_3O+2HCl+0.5EtOAc$: C, 57.8; H, 6.11; N, 7.50. Found: C, 56.5; H, 6.46; N, 7.77; ESMS *m/e*: 444.2 $(M + H)^+$.

1-(2-PYRIDINYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 2-iodopyridine and 1*H*-indole: ESMS *m/e*: 195.0 $(M + H)^+$.

1-(3-PYRIDINYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 3-iodopyridine and 1*H*-indole: ESMS *m/e*: 195.0 $(M + H)^+$.

Example 500

2-METHYL-*N*-[3-(1-{[1-(3-PYRIDINYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 1-(3-pyridinyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 453.2 $(M + H)^+$.

Example 501

2-METHYL-*N*-[3-(1-{[1-(2-PYRIDINYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 1-(2-pyridinyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 453.2 $(M + H)^+$.

Example 502

***N*-(3-{1-[(6-FLUORO-1-PHENYL-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE**: Prepared by Procedure D and Scheme N using 6-fluoro-1-phenyl-1*H*-

indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 470.2 $(M + H)^+$.

Example 503

***N*-(3-{1-[(6-CHLORO-1-PHENYL-1*H*-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure D and Scheme N using 6-chloro-1-phenyl-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 486.2 $(M + H)^+$.

7-METHYL-1-PHENYL-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 7-methyl-1*H*-indole and iodobenzene: ESMS *m/e*: 208.1 $(M + H)^+$.

METHYL 1-PHENYL-1*H*-INDOLE-6-CARBOXYLATE: Prepared by Procedure C and Scheme O using methyl 1*H*-indole-6-carboxylate and iodobenzene: ESMS *m/e*: 252.0 $(M + H)^+$.

6-METHYL-1-PHENYL-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 6-methyl-1*H*-indole and iodobenzene: ESMS *m/e*: 208.0 $(M + H)^+$.

7-CHLORO-1-PHENYL-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 7-chloro-1*H*-indole and iodobenzene: ESMS *m/e*: 228.0 $(M + H)^+$.

6-NITRO-1-PHENYL-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 6-nitro-1*H*-indole and iodobenzene: ESMS *m/e*: 238.2 $(M + H)^+$.

6-METHOXY-1-PHENYL-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 1*H*-indol-6-yl methyl ether and iodobenzene: ESMS *m/e*: 224.0 $(M + H)^+$.

BENZYL 1-PHENYL-1H-INDOL-6-YL ETHER: Prepared by Procedure C and Scheme O using 6-(benzyloxy)-1*H*-indole and iodobenzene: ESMS *m/e*: 300.0 $(M + H)^+$.

1-PHENYL-1H-INDOL-6-YL TRIFLUOROMETHYL ETHER: Prepared by Procedure C and Scheme O using 6-(trifluoromethoxy)-1*H*-indole and iodobenzene: ESMS *m/e*: 278.0 $(M + H)^+$.

7-METHOXY-1-PHENYL-1H-INDOLE: Prepared by Procedure C and Scheme O using 1*H*-indol-7-yl methyl ether and iodobenzene: ESMS *m/e*: 224.0 $(M + H)^+$.

1-PHENYL-6-(TRIFLUOROMETHYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 6-(trifluoromethyl)-1*H*-indole and iodobenzene: ESMS *m/e*: 262.0 $(M + H)^+$.

1-(4-PYRIDINYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 1*H*-indole and 4-iodopyridine: ESMS *m/e*: 195 $(M + H)^+$.

Example 504

N-[3-(1-{[6-(BENZYLOXY)-1-PHENYL-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using benzyl 1-phenyl-1*H*-indol-6-yl ether and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 558.0 $(M + H)^+$.

Example 505

2-METHYL-*N*-(3-{1-[(6-METHYL-1-PHENYL-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure D and Scheme N using 6-methyl-1-phenyl-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ^1H NMR (400 MHz, $CDCl_3$) δ

7.66 (s, 1H), 7.64 (d, 1H, J = 7.8 Hz), 7.51 (d, 1H, J = 3.9 Hz), 7.50 (m, 3H), 7.4 (m, 2H), 7.36-7.32 (m, 2H), 7.31 (s, 1H), 7.19 (t, 1H, J= 7.8 Hz), 7.04 (d, 1H, J = 7.8 Hz), 6.91 (d, 1H, J = 7.8 Hz), 3.94 (s, 2H), 3.25 (d, 2H, J = 9.2 Hz), 2.52 (sept, 1H, J = 6.4 Hz), 2.46 (s, 3H), 2.28 (dt, 2H, J = 11.8, 2.6 Hz), 1.89 (dq, 2H, J = 2.9 Hz), 1.80 (m, 3H), 1.22 (d, 6H, J = 6.9 Hz); Anal. Calcd for $C_{31}H_{35}N_3O$+HCl+0.6EtOAc: C, 72.2; H, 7.41; N, 7.57. Found: C, 71.0; H, 7.40; N, 7.66; ESMS *m/e*: 466 $(M + H)^+$.

Example 506

METHYL 3-({4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}METHYL)-1-PHENYL-1H-INDOLE-6-CARBOXYLATE: Prepared by Procedure D and Scheme N using methyl 1-phenyl-1*H*-indole-6-carboxylate and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 510.0 $(M + H)^+$.

Example 507

2-METHYL-*N*-(3-{1-[(6-NITRO-1H-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure D and Scheme N using 6-nitro-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 421.0 $(M + H)^+$.

Example 508

2-METHYL-*N*-[3-(1-{[1-PHENYL-6-(TRIFLUOROMETHYL)-1H-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 1-phenyl-6-(trifluoromethyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 520.0 $(M + H)^+$.

Example 509

2-METHYL-*N*-(3-{1-[(7-METHYL-1-PHENYL-1*H*-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure D and Scheme N using 7-methyl-1-phenyl-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 466.0 $(M + H)^+$.

Example 510

***N*-(3-{1-[(7-METHOXY-1*H*-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure D and Scheme N using 1*H*-indol-7-yl methyl ether and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 406.0 $(M + H)^+$.

Example 511

***N*-(3-{1-[(7-METHOXY-1-PHENYL-1*H*-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure D and Scheme N using 7-methoxy-1-phenyl-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 482.0 $(M + H)^+$.

Example 512

***N*-(3-{1-[(7-CHLORO-1-PHENYL-1*H*-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure D and Scheme N using 7-chloro-1-phenyl-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 488.6 $(M + H)^+$.

Example 513

2-METHYL-*N*-(3-{1-[(7-NITRO-1*H*-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure D and Scheme N using 7-nitro-1*H*-indole and 2-methyl-*N*-[3-

(4-piperidinyl)phenyl]propanamide: ESMS m/e: 421.1 $(M + H)^+$.

Example 514

N-(3-{1-[(7-NITRO-1*H*-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE: Prepared by Procedure D and Scheme N using 7-nitro-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS m/e: 419.5 $(M + H)^+$.

Example 515

N-(3-{1-[(7-NITRO-1*H*-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure D and Scheme N using 7-nitro-1*H*-indole and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 407.3 $(M + H)^+$.

7-(2-FLUOROPHENYL)-1*H*-INDOLE: Prepared by Procedure I and Scheme T using 7-bromo-1*H*-indole and 2-fluorophenylboronic acid: ESMS m/e: 211.9 $(M + H)^+$.

Example 516

N-[3-(1-{[7-(2-FLUOROPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N. A solution of 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide (23.3 mg, 0.0948 mmol) and 37 wt % aqueous formaldehyde (11.4 mg, 0.142 mmol) in 1.00 mL of HOAc:dioxane (1:4) was added to 7-(2-fluorophenyl)-1*H*-indole (20.0 mg, 0.0948 mmol) and the reaction mixture was stirred for 12 h at room temperature. The resulting mixture was diluted with H_2O (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 X 10 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, and concentrated *in*

vacuo. The residue was purified by preparative TLC on silica using 4 % of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product (56.1 mg, 100%): ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 7.73 (dd, 1H, *J* = 2.8, 6.3 Hz), 7.69 (s, 1H), 7.53 (dt, 1H, *J* = 1.8, 7.6 Hz), 7.44 (d, 1H, *J* = 8.1 Hz), 7.38 (m, 2H), 7.32 (s, 1H), 7.27-7.21 (m, 4H), 7.17 (t, 1H, *J* = 7.6 Hz), 6.88 (d, 1H, *J* = 7.6 Hz), 3.92 (s, 2H); 3.20 (d, 1H, *J* = 11.6 Hz), 2.51 (qt, 1H, *J* = 6.7 Hz), 2.42 (m, 1H), 2.25 (dt, 2H, *J* = 2.2, 11.6 Hz), 1.89-1.72 (m, 5H), 1.22 (d, 6H, *J* = 7.3 Hz); ESMS *m/e*: 470.1 $(M + H)^+$.

7-(4-ETHYLPHENYL)-1H-INDOLE: Prepared by Procedure I and Scheme T using 7-bromo-1*H*-indole and 4-ethylphenylboronic acid: ESMS *m/e*: 222.0 $(M + H)^+$.

7-(2-NAPHTHYL)-1H-INDOLE: Prepared by Procedure I and Scheme T using 7-bromo-1*H*-indole and 2-naphthylboronic acid: ESMS *m/e*: 244.0 $(M + H)^+$.

7-(3-CHLOROPHENYL)-1H-INDOLE: Prepared by Procedure I and Scheme T using 7-bromo-1*H*-indole and 3-chlorophenylboronic acid: ESMS *m/e*: 227.9 $(M + H)^+$.

6-(2-FLUOROPHENYL)-1H-INDOLE: Prepared by Procedure I and Scheme T using 6-bromo-1*H*-indole and 2-fluorophenylboronic acid: ESMS *m/e*: 211.9 $(M + H)^+$.

7-(3-NITROPHENYL)-1H-INDOLE: Prepared by Procedure I and Scheme T using 7-bromo-1*H*-indole and 3-nitrophenylboronic acid: ESMS *m/e*: 238.9 $(M + H)^+$.

1-[4-(1*H*-INDOL-7-YL)PHENYL]ETHANONE: Prepared by Procedure I and Scheme T using 7-bromo-1*H*-indole and 4-acetylphenylboronic acid: ESMS *m/e*: 235.2 $(M + H)^+$.

6-(2-METHYLPHENYL)-1*H*-INDOLE: Prepared by Procedure I and Scheme T using 6-bromo-1*H*-indole and 2-methylphenylboronic acid: ESMS *m/e*: 207.9 $(M + H)^+$.

6-(3-CHLOROPHENYL)-1*H*-INDOLE: Prepared by Procedure I and Scheme T using 6-bromo-1*H*-indole and 3-chlorophenylboronic acid: ESMS *m/e*: 227.9 $(M + H)^+$.

1-[4-(1*H*-INDOL-6-YL)PHENYL]ETHANONE: Prepared by Procedure I and Scheme T using 6-bromo-1*H*-indole and 4-acetylphenylboronic acid: ESMS *m/e*: 235.8 $(M + H)^+$.

7-(2-METHYLPHENYL)-1*H*-INDOLE: Prepared by Procedure I and Scheme T using 7-bromo-1H-indole and 2-methylphenylboronic acid: ESMS *m/e*: 208 $(M + H)^+$.

6-(4-ETHYLPHENYL)-1*H*-INDOLE: Prepared by Procedure I and Scheme T using 6-bromo-1*H*-indole and 4-ethylphenylboronic acid: ESMS *m/e*: 221.9 $(M + H)^+$.

Example 517

2-METHYL-*N*-[3-(1-{[7-(2-NAPHTHYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 7-(2-naphthyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 502.2 $(M + H)^+$.

Example 518

N-[3-(1-{[7-(4-ETHYLPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 7-(4-ethylphenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 480.2 $(M + H)^+$.

Example 519

2-METHYL-*N*-[3-(1-{[6-(2-METHYLPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 6-(2-methylphenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ^1H NMR (400 MHz, $CDCl_3$) δ 8.2 (s, 1H), 7.53 (m, 4H), 7.41 (d, 1H, J = 8.4 Hz), 7.34 (m, 2H), 7.27-7.12 (m, 5H), 6.81 (d, 1H, J = 8.4 Hz), 4.09 (s, 2H), 3.32 (d, 2H, J = 11.4 Hz), 2.57 (q, 2H, J = 7.6 Hz), 2.43 (m, 3H), 2.08 (s, 3H), 1.98 (m, 1H), 1.75 (m, 2H), 1.22 (d, 6H, J = 6.3 Hz); Anal. Calcd for $C_{31}H_{35}N_3O+CHCl_3+DMF$: C, 57.0; H, 6.09; N, 8.06. Found: C, 56.5; H, 5.94; N, 7.76; ESMS *m/e*: 466.2 $(M + H)^+$.

Example 520

N-[3-(1-{[7-(3-CHLOROPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 7-(3-chlorophenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 486.1 $(M + H)^+$.

Example 521

2-METHYL-*N*-[3-(1-{[7-(3-NITROPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 7-(3-nitrophenyl)-1*H*-

indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 497.0 $(M + H)^+$.

Example 522

***N*-[3-(1-{[7-(4-ACETYLPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure D and Scheme N using 1-[4-(1*H*-indol-7-yl)phenyl]ethanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 493.6 $(M + H)^+$.

Example 523

***N*-[3-(1-{[6-(4-ETHYLPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure D and Scheme N using 6-(4-ethylphenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 480.1 $(M + H)^+$.

Example 524

2-METHYL-*N*-[3-(1-{[7-(2-METHYLPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 7-(2-methylphenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 466.1 $(M + H)^+$.

Example 525

***N*-[3-(1-{[6-(2-FLUOROPHENYL)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure D and Scheme N using 6-(2-fluorophenyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 470.2 $(M + H)^+$.

5-(4-METHYLPHENOXY)-1*H*-INDOLE: Prepared by Procedure J and Scheme U using 5-bromo-1*H*-indole and *p*-cresol: ESMS *m/e*: 224.0 $(M + H)^+$.

Example 526

N-(3-{1-[(5-BROMO-1*H*-INDOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure D and Scheme N using 5-bromo-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 454.0 $(M + H)^+$.

1-(4-PYRIDINYL)-6-(TRIFLUOROMETHYL)-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 6-(trifluoromethyl)-1*H*-indole and 4-iodopyridine: ESMS *m/e*: 262.9 $(M + H)^+$.

Example 527

2-METHYL-*N*-[3-(1-{[5-(4-METHYLPHENOXY)-1*H*-INDOL-3-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure D and Scheme N using 5-(4-methylphenoxy)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 481.9 $(M + H)^+$.

1-(4-METHYLPHENYL)-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 1*H*-indole and 1-iodo-4-methylbenzene: ESMS *m/e*: 208.0 $(M + H)^+$.

1-(3-METHYLPHENYL)-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 1*H*-indole and 1-iodo-3-methylbenzene: ESMS *m/e*: 208.0 $(M + H)^+$.

1-[3-(TRIFLUOROMETHYL)PHENYL]-1*H*-INDOLE: Prepared by Procedure C and Scheme O using 1*H*-indole and 1-iodo-3-(trifluoromethyl)benzene: ESMS *m/e*: 262.0 $(M + H)^+$.

1-(4-METHOXYPHENYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 1H-indole and 1-iodo-4-methoxybenzene: ESMS *m/e*: 224.0 $(M + H)^+$.

1-(2-METHOXYPHENYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 1H-indole and 1-iodo-2-methoxybenzene: ESMS *m/e*: 224.0 $(M + H)^+$.

1-(3-METHOXYPHENYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 1H-indole and 1-iodo-3-methoxybenzene: ESMS *m/e*: 224.0 $(M + H)^+$.

1-(2-METHYLPHENYL)-1H-INDOLE: Prepared by Procedure C and Scheme O using 1H-indole and 1-iodo-2-methylbenzene: ESMS *m/e*: 208.0 $(M + H)^+$.

6-FLUORO-1-PHENYL-1H-INDOLE: Prepared by Procedure C and Scheme O using 6-fluoro-1H-indole and iodobenzene: ESMS *m/e*: 212.0 $(M + H)^+$.

6-CHLORO-1-PHENYL-1H-INDOLE: Prepared by Procedure C and Scheme O using 6-chloro-1H-indole and iodobenzene: ESMS *m/e*: 228.0 $(M + H)^+$.

7-CHLORO-1-PHENYL-1H-INDOLE: Prepared by Procedure C and Scheme O using 7-chloro-1H-indole and iodobenzene: ESMS *m/e*: 228.0 $(M + H)^+$.

6-(2-FLUOROPHENYL)-1H-INDOLE: Prepared by Procedure I and Scheme T using 6-bromo-1H-indole and 2-fluorophenylboronic acid: ESMS *m/e*: 211.9 $(M + H)^+$.

Example 528

2-METHYL-*N*-{3-[1-(7-OXO-7-PHENYLHEPTYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure K and Scheme B1 using 7-chloro-1-phenyl-1-heptanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 435.1 $(M + H)^+$.

Example 529

2-METHYL-*N*-{3-[1-(6-OXO-6-PHENYLHEXYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure K and Scheme B1 using 6-chloro-1-phenyl-1-hexanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: Anal. Calcd for $C_{27}H_{36}N_2O_2+0.1CHCl_3$: C, 75.3; H, 8.39; N, 6.46. Found: C, 75.4; H, 7.89; N, 6.18; ESMS *m/e*: 421.1 $(M + H)^+$.

Example 530

2-METHYL-*N*-{3-[1-(5-OXO-5-PHENYLPENTYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure K and Scheme B1 using 5-chloro-1-phenyl-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 407.1 $(M + H)^+$.

Example 531

***N*-(3-{1-[4-(4-METHOXYPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-methoxyphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 409.2 $(M + H)^+$.

Example 532

***N*-(3-{1-[4-(4-CHLOROPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-chlorophenyl)-1-

butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 413.1 $(M + H)^+$.

Example 533

***N*-(3-{1-[4-(4-BROMOPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 1-(4-bromophenyl)-4-chloro-1-butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 457.1 $(M + H)^+$.

Example 534

***N*-(3-{1-[4-(4-TERT-BUTYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 1-(4-tert-butylphenyl)-4-chloro-1-butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 435.2 $(M + H)^+$.

Example 535

***N*-(3-{1-[4-(4-FLUOROPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-fluorophenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 397.2 $(M + H)^+$.

Example 536

***N*-(3-{1-[4-OXO-4-(4-PHENOXYPHENYL)BUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-phenoxyphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 471.2 $(M + H)^+$.

Example 537

***N*-(3-{1-[4-(4-ISOPROPYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-isopropylphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 433.2 $(M + H)^+$.

Example 538

***N*-(3-{1-[4-(4-METHOXYPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-methoxyphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 421.2 $(M + H)^+$.

Example 539

***N*-(3-{1-[4-OXO-4-(4-PHENOXYPHENYL)BUTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-phenoxyphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 483.2 $(M + H)^+$.

Example 540

***N*-(3-{1-[4-(4-ISOPROPYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-isopropylphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 421.3 $(M + H)^+$.

Example 541

***N*-(3-{1-[4-(4-TERT-BUTYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure K and Scheme B1 using 1-(4-tert-butylphenyl)-4-chloro-1-butanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 447.2 $(M + H)^+$.

Example 542

***N*-(3-{1-[4-(4-METHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-methylphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 393.2 $(M + H)^+$.

Example 543

***N*-(3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 4-chloro-1-(3,4-dimethylphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 407.2 $(M + H)^+$.

Example 544

***N*-(3-{1-[4-(4-BROMOPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure K and Scheme B1 using 1-(4-bromophenyl)-4-chloro-1-butanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 469.1 $(M + H)^+$.

Example 545

***N*-(3-{1-[5-(4-FLUOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-(4-fluorophenyl)-1-

pentanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 411.2 $(M + H)^+$.

Example 546

N-(3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE: Prepared by Procedure K and Scheme B1 using 4-chloro-1-(3,4-dimethylphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 419.2 $(M + H)^+$.

Example 547

N-(3-{1-[4-(4-METHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE: Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-methylphenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 405.2 $(M + H)^+$.

Example 548

N-(3-{1-[4-(4-FLUOROPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE: Prepared by Procedure K and Scheme B1 using 4-chloro-1-(4-fluorophenyl)-1-butanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 409.2 $(M + H)^+$.

Example 549

N-(3-{1-[5-(3-FLUOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE: Prepared by Procedure K and Scheme B1 using 5-chloro-1-(3-fluorophenyl)-1-pentanone and *N*-[3-(4-

piperidinyl)phenyl]cyclopropanecarboxamide: ESMS m/e: 423.2 $(M + H)^+$.

Example 550

N-[3-(1-{5-OXO-5-[4-(TRIFLUOROMETHYL)PHENYL]PENTYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure K and Scheme B1 using 5-chloro-1-[4-(trifluoromethyl)phenyl]-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 461.2 $(M + H)^+$.

Example 551

N-(3-{1-[5-(4-FLUOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE: Prepared by Procedure K and Scheme B1 using 5-chloro-1-(4-fluorophenyl)-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS m/e: 423.2 $(M + H)^+$.

Example 552

N-(3-{1-[5-(3-NITROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure K and Scheme B1 using 5-chloro-1-(3-nitrophenyl)-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 438.2 $(M + H)^+$.

Example 553

N-(3-{1-[5-(3-NITROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE: Prepared by Procedure K and Scheme B1 using 5-chloro-1-(3-nitrophenyl)-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS m/e: 450.2 $(M + H)^+$.

Example 554

N-(3-{1-[5-(2-FLUOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure K and Scheme B1 using 5-chloro-1-(2-fluorophenyl)-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 411.2 $(M + H)^+$.

Example 555

N-(3-{1-[5-(3-FLUOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure K and Scheme B1 using 5-chloro-1-(3-fluorophenyl)-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 411.2 $(M + H)^+$.

Example 556

N-(3-{1-[5-(4-NITROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure K and Scheme B1 using 5-chloro-1-(4-nitrophenyl)-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 438.1 $(M + H)^+$.

Example 557

N-(3-{1-[5-(4-NITROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE: Prepared by Procedure K and Scheme B1 using 5-chloro-1-(4-nitrophenyl)-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 450.1 $(M + H)^+$.

Example 558

N-(3-{1-[5-(4-CHLOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE: Prepared by Procedure K and Scheme B1 using 5-chloro-1-(4-

chlorophenyl)-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 439.1 $(M + H)^+$.

Example 559

***N*-[3-(1-{5-OXO-5-[2-(TRIFLUOROMETHYL)PHENYL]PENTYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-[2-(trifluoromethyl)phenyl]-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 461.2 $(M + H)^+$.

Example 560

***N*-[3-(1-{5-OXO-5-[2-(TRIFLUOROMETHYL)PHENYL]PENTYL}-4-PIPERIDINYL)PHENYL]CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-[2-(trifluoromethyl)phenyl]-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 473.2 $(M + H)^+$.

Example 561

***N*-(3-{1-[5-(4-CHLOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-(4-chlorophenyl)-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 427.1 $(M + H)^+$.

Example 562

***N*-(3-{1-[5-(3-CHLOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-(3-chlorophenyl)-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 427.1 $(M + H)^+$.

Example 563

***N*-(3-{1-[5-(2-FLUOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-(2-fluorophenyl)-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 423.1 $(M + H)^+$.

Example 564

***N*-(3-{1-[5-(3-CHLOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-(3-chlorophenyl)-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 439.1 $(M + H)^+$.

Example 565

***N*-[3-(1-{5-OXO-5-[4-(TRIFLUOROMETHYL)PHENYL]PENTYL}-4-PIPERIDINYL)PHENYL]CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-[4-(trifluoromethyl)phenyl]-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 473.2 $(M + H)^+$.

Example 566

***N*-(3-{1-[5-(2-CHLOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-(2-chlorophenyl)-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 427.1 $(M + H)^+$.

Example 567

***N*-(3-{1-[5-(2-CHLOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-(2-chlorophenyl)-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 439.1 $(M + H)^+$.

Example 568

***N*-[3-(1-{5-OXO-5-[3-(TRIFLUOROMETHYL)PHENYL]PENTYL}-4-PIPERIDINYL)PHENYL]CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-[3-(trifluoromethyl)phenyl]-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 473.2 $(M + H)^+$.

Example 569

***N*-(3-{1-[4-(3,4-DIMETHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-*N*,2-DIMETHYLPROPANAMIDE:** Prepared by Procedure T and Scheme AD using *N*-(3-{1-[4-(3,4-dimethylphenyl)-4-oxobutyl]-4-piperidinyl}phenyl)-2-methylpropanamide and methyl iodide: ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.72 (dd, 1H, J = 1.8, 7.7 Hz), 7.33 (t, 1H, J = 8.8 Hz), 7.22 (d, 1H, J = 7.8 Hz), 7.18 (d, 1H, J = 8.8 Hz), 7.01 (m, 2H), 3.24 (s, 3H), 3.10 (d, 1H, J = 10.6 Hz), 3.00 (t, 1H, J = 7.6 Hz), 2.49 (m, 4H), 2.33 (s, 6H), 2.11 (m, 3H), 1.99 (m, 1H), 1.79 (m, 4H), 1.26 (t, 2H, J = 7.6 Hz), 1.02 (d, 6H, J = 7.6 Hz); ESMS *m/e*: 435.2 $(M + H)^+$.

Example 570

2-METHYL-*N*-{3-[1-(1-METHYL-4-OXO-4-PHENYLBUTYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure K

and Scheme B1 using 4-chloro-1-phenyl-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 407.2 $(M + H)^+$.

Example 571

***N*-[3-(1-{5-OXO-5-[3-(TRIFLUOROMETHYL)PHENYL]PENTYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:** Prepared by Procedure K and Scheme B1 using 5-chloro-1-[3-(trifluoromethyl)phenyl]-1-pentanone and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 461.2 $(M + H)^+$.

3-(5-CHLOROPENTANOYL)-4-(3,4-DIFLUOROPHENYL)-1,3-OXAZOLIDIN-2-ONE: Prepared by Procedure AF and Scheme H using 4-(3,4-difluorophenyl)-1,3-oxazolidin-2-one and 5-chloropentanoyl chloride.

3-(5-CHLOROPENTYL)-4-(3,4-DIFLUOROPHENYL)-1,3-OXAZOLIDIN-2-ONE: Prepared by Procedure G and Scheme C1 using 4-(3,4-difluorophenyl)-1,3-oxazolidin-2-one and 1-bromo-5-chloropentane.

Example 572

***N*-[3-(1-{5-[(4R)-4-(3,4-DIFLUOROPHENYL)-2-OXO-1,3-OXAZOLIDIN-3-YL]-5-OXOPENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using (4R)-3-(5-chloropentanoyl)-4-(3,4-difluorophenyl)-1,3-oxazolidin-2-one and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 528.2 $(M + H)^+$.

Example 573

(4R)-4-(3,4-DIFLUOROPHENYL)-*N*-(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-2-OXO-

1,3-OXAZOLIDINE-3-CARBOXAMIDE: Prepared by Procedure AF and Scheme H using 4-nitrophenyl (4R)-4-(3,4-difluorophenyl)-2-oxo-1,3-oxazolidine-3-carboxylate and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (t, 1H, J = 5.5 Hz), 7.45 (s, 2H), 7.38 (d, 1H, J = 8.6 Hz), 7.24-7.12 (m, 3H), 7.06 (m, 1H), 6.97 (d, 1H, J = 8.6 Hz), 5.40 (dd, 1H, J = 3.9,8.8 Hz), 4.71 (t, 1H, J = 8.8 Hz), 4.23 (dd, 1H, J = 4.4, 9.1 Hz), 3.32 (qt, 2H, J = 6.1 Hz), 2.99 (d, 2H, J = 11.0 Hz), 2.49 (qt, 2H, J = 7.0 Hz), 2.41 (t, 2H, J = 7.0 Hz), 1.99 (m, 2H), 1.82-1.68 (m, 6H), 1.23 (d, 6H, J = 7.3 Hz); ESMS *m/e*: 529.1 $(M + H)^+$.

(4*S*)-3-(5-CHLOROPENTYL)-4-(3,4-DIFLUOROPHENYL)-1,3-OXAZOLIDIN-2-ONE: Prepared by Procedure G and Scheme C1 using (4*S*)-4-(3,4-difluorophenyl)-1,3-oxazolidin-2-one and 1-bromo-5-chloropentane.

Example 574

N-[3-(1-{5-[(4*S*)-4-(3,4-DIFLUOROPHENYL)-2-OXO-1,3-OXAZOLIDIN-3-YL]PENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: . Prepared by Procedure G and Scheme B1 using (4*S*)-3-(5-chloropentyl)-4-(3,4-difluorophenyl)-1,3-oxazolidin-2-one and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.32 (d, 1H, J = 8.6 Hz), 7.26-7.21 (m, 2H), 7.20-7.12 (m, 2H), 7.06 (m, 1H), 6.97 (d, 1H, J = 6.96 Hz), 4.76 (dd, 1H, J = 6.3, 8.3 Hz), 4.62 (t, 1H, J = 9.0 Hz), 4.06 (dd, 1H, J = 6.4, 8.7 Hz), 3.46 (m, 1H), 3.0 (d, 2H, J = 9.0 Hz), 2.77 (q, 1H, J = 6.8 Hz), 2.50 (q, 2H, J = 6.8 Hz), 2.31 (t, 2H, J = 6.8 Hz), 2.01 (m, 4H), 1.81 (m, 4H), 1.48 (m, 4H), 1.26 (d, 6H, J = 7.3

Hz); Anal. Calcd for $C_{28}H_{37}F_2N_3O_3$+HCl+0.25$CHCl_3$: C, 60.6; H, 6.65; N, 7.25. Found: C, 60.7; H, 6.91; N, 7.05; ESMS *m/e*: 514.2 $(M + H)^+$.

Example 575

***N*-[3-(1-{5-[(4*S*)-4-(3,4-DIFLUOROPHENYL)-2-OXO-1,3-OXAZOLIDIN-3-YL]-5-OXOPENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using (4*S*)-3-(5-chloropentanoyl)-4-(3,4-difluorophenyl)-1,3-oxazolidin-2-one and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 528.1 $(M + H)^+$.

Example 576

(4*S*)-4-(3,4-DIFLUOROPHENYL)-*N*-(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-2-OXO-1,3-OXAZOLIDINE-3-CARBOXAMIDE: Prepared by Procedure AF and Scheme H using 4-nitrophenyl (4*S*)-4-(3,4-difluorophenyl)-2-oxo-1,3-oxazolidine-3-carboxylate and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 529.1 $(M + H)^+$.

Example 577

(4*S*)-*N*-(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-2-OXO-4-(3,4,5-TRIFLUOROPHENYL)-1,3-OXAZOLIDINE-3-CARBOXAMIDE: Prepared by Procedure AF and Scheme H using 4-nitrophenyl (4*S*)-4-(3,4-difluorophenyl)-2-oxo-1,3-oxazolidine-3-carboxylate and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 547.1 $(M + H)^+$.

Example 578

(4*S*)-4-(3,5-DIFLUOROPHENYL)-*N*-(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-2-OXO-

1,3-OXAZOLIDINE-3-CARBOXAMIDE: Prepared by Procedure AF and Scheme H using 4-nitrophenyl (4*S*)-4-(3,4-difluorophenyl)-2-oxo-1,3-oxazolidine-3-carboxylate and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 529.2 $(M + H)^+$.

Example 579

N-(3-{1-[3-(PHENYLSULFANYL)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure G and Scheme B1 using [(3-chloropropyl)sulfanyl]benzene and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 382.9 $(M + H)^+$.

Example 580

N-(3-{1-[3-(PHENYLSULFANYL)PROPYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE: Prepared by Procedure G and Scheme B1 using [(3-chloropropyl)sulfanyl]benzene and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 395.1 $(M + H)^+$.

Example 581

2-METHYL-*N*-(3-{1-[3-(PHENYLSULFANYL)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure G and Scheme B1 using [(3-chloropropyl)sulfanyl]benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ^1H NMR (400 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.48 (s, 1H), 7.33 (m, 3H), 7.27 (t, 2H, J = 7.5 Hz), 7.20 (t, 1H, J = 7.9 Hz), 7.15 (tt, 1H, J = 7.2, 1.4 Hz), 6.95 (d, 1H, J = 7.6 Hz), 2.97 (t, 4H, J = 7.3 Hz), 2.46 (m, 4H), 1.99 (dt, 2H, J = 11.4, 3.0 Hz), 1.84 (qt, 2H, J = 7.3 Hz), 1.77 (m, 4H), 1.21 (d, 6H, J = 6.8 Hz); ESMS *m/e*: 396.8 $(M + H)^+$.

Example 582

N-(3-{1-[6-(PHENYLSULFANYL)HEXYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE: Prepared by Procedure G and Scheme B1 using [(6-chlorohexyl)sulfanyl]benzene and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 437.4 $(M + H)^+$.

Example 583

N-(3-{1-[4-(PHENYLSULFANYL)BUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure G and Scheme B1 using [(4-chlorobutyl)sulfanyl]benzene and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 396.8 $(M + H)^+$.

Example 584

N-(3-{1-[4-(PHENYLSULFANYL)BUTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE: Prepared by Procedure G and Scheme B1 using [(4-chlorobutyl)sulfanyl]benzene and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 409.5 $(M + H)^+$.

Example 585

2-METHYL-*N*-(3-{1-[4-(PHENYLSULFANYL)BUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure G and Scheme B1 using [(4-chlorobutyl)sulfanyl]benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 410.6 $(M + H)^+$.

Example 586

2-METHYL-*N*-(3-{1-[5-(PHENYLSULFANYL)PENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure G

and Scheme B1 using [(5-chloropentyl)sulfanyl]benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 425.1 $(M + H)^+$.

Example 587

***N*-(3-{1-[5-(PHENYLSULFANYL)PENTYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure G and Scheme B1 using [(5-chloropentyl)sulfanyl]benzene and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 423.1 $(M + H)^+$.

[(6-CHLOROHEXYL)SULFANYL]BENZENE: Prepared by Procedure R and Scheme Z using benzenethiol and 1-bromo-6-chlorohexane.

[(4-CHLOROBUTYL)SULFANYL]BENZENE: Prepared by Procedure R and Scheme Z using benzenethiol and 1-bromo-4-chlorobutane.

Example 588

***N*-(3-{1-[6-(PHENYLSULFANYL)HEXYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure G and Scheme B1 using [(6-chlorohexyl)sulfanyl]benzene and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 425.4 $(M + H)^+$.

[(5-CHLOROPENTYL)SULFANYL]BENZENE: Prepared by Procedure R and Scheme Z using benzenethiol and 1-bromo-5-chloropentane.

[(3-CHLOROPROPYL)SULFANYL]BENZENE: Prepared by Procedure R and Scheme Z using benzenethiol and 1-bromo-

3-chloropropane: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.34 (m, 2H), 7.32-7.26 (m, 2H), 7.19 (tt, 1H, J = 1.4, 7.3 Hz), 3.67 (t, 2H, J = 6.6 Hz), 3.08 (t, 2H, J = 6.6 Hz), 2.06 (qt, 2H, J = 6.6 Hz).

Example 589

***N*-(3-{1-[5-(PHENYLSULFANYL)PENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure G and Scheme B1 using [(5-chloropentyl)sulfanyl]benzene and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 411.1 $(M + H)^+$.

3-CHLOROPROPYL 4-FLUOROPHENYL SULFIDE: Prepared by Procedure R and Scheme Z using 4-fluorobenzenethiol and 1-bromo-3-chloropropane.

1-BROMO-2-[(3-CHLOROPROPYL)SULFANYL]BENZENE: Prepared by Procedure R and Scheme Z using 2-bromobenzenethiol and 1-bromo-3-chloropropane.

3-CHLOROPROPYL 4-FLUOROPHENYL SULFOXIDE: Prepared by Procedure S and Scheme AA using 3-chloropropyl 4-fluorophenyl sulfide and 1 eq *m*-CPBA: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.62 (m, 2H), 7.28-7.21 (m, 2H), 3.65 (m, 2H), 2.94 (m, 2H), 2.28 (m, 1H), 2.06 (m, 1H); ESMS *m/e*: 220.9 $(M + H)^+$.

3-CHLOROPROPYL 3-FLUOROPHENYL SULFIDE: Prepared by Procedure R and Scheme Z using 3-fluorobenzenethiol and 1-bromo-3-chloropropane.

3-CHLOROPROPYL 2-FLUOROPHENYL SULFIDE: Prepared by Procedure R and Scheme Z using 2-fluorobenzenethiol and 1-bromo-3-chloropropane.

1-BROMO-2-[(3-CHLOROPROPYL)SULFINYL]BENZENE: Prepared by Procedure S and Scheme AA using 1-bromo-2-[(3-chloropropyl)sulfanyl]benzene and 1 eq *m*-CPBA: ESMS *m/e*: 282.8 $(M + H)^+$.

1-CHLORO-2-[(3-CHLOROPROPYL)SULFANYL]BENZENE: Prepared by Procedure R and Scheme Z using 2-chlorobenzenethiol and 1-bromo-3-chloropropane.

1-CHLORO-3-[(3-CHLOROPROPYL)SULFANYL]BENZENE: Prepared by Procedure R and Scheme Z using 3-chlorobenzenethiol and 1-bromo-3-chloropropane.

1-CHLORO-4-[(3-CHLOROPROPYL)SULFANYL]BENZENE: Prepared by Procedure R and Scheme Z using 4-chlorobenzenethiol and 1-bromo-3-chloropropane.

1-BROMO-3-[(3-CHLOROPROPYL)SULFANYL]BENZENE: Prepared by Procedure R and Scheme Z using 3-bromobenzenethiol and 1-bromo-3-chloropropane.

1-BROMO-4-[(3-CHLOROPROPYL)SULFANYL]BENZENE: Prepared by Procedure R and Scheme Z using 4-bromobenzenethiol and 1-bromo-3-chloropropane.

3-CHLOROPROPYL 3,4-DIMETHYLPHENYL SULFIDE: Prepared by Procedure R and Scheme Z using 3,4-dimethylbenzenethiol and 1-bromo-3-chloropropane.

Example 590

N-[3-(1-{3-[(4-FLUOROPHENYL)SULFINYL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure G and Scheme B1 using 3-chloropropyl 4-

fluorophenyl sulfoxide and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (m, 2H), 7.53 (s, 1H), 7.24 (m, 5H), 6.94 (d, 1H, J = 7.7 Hz), 2.89 (m, 4H), 2.45 (m, 4H), 1.99 (m, 3H), 1.77 (m, 5H), 1.24 (d, 6H, J = 6.8 Hz); Anal. Calcd for $C_{24}H_{31}FN_2O_2S$+0.6EtOAc: C, 65.5; H, 7.45; N, 5.79. Found: C, 65.4; H, 7.30; N, 5.73; ESMS *m/e*: 431.1 $(M + H)^+$.

Example 591

***N*-[3-(1-{3-[(2-BROMOPHENYL)SULFINYL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure G and Scheme B1 using 1-bromo-2-[(3-chloropropyl)sulfinyl]benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: Anal. Calcd for $C_{24}H_{31}BrN_2O_2S$+0.3$CHCl_3$: ESMS *m/e*: 491.0 $(M + H)^+$.

Example 592

***N*-{3-[1-((3*S*)-3-{[(3,4-DIFLUOROPHENYL)SULFONYL]AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure Q1 and Scheme AC using 3,4-difluorobenzenesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 556.2 $(M + H)^+$.

Example 593

3-CHLORO-*N*-((1*S*)-3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}-1-PHENYLPROPYL)-2-THIOPHENECARBOXAMIDE: Prepared by Procedure Q1 and Scheme AC using 3-chloro-2-thiophenecarbonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 524.2 $(M + H)^+$.

Example 594

N-(3-{1-[(3*S*)-3-({[5-(DIMETHYLAMINO)-1-NAPHTHYL]SULFONYL}AMINO)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 and Scheme AC using 5-(dimethylamino)-1-naphthalenesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 613.3 $(M + H)^+$.

Example 595

2-METHYL-*N*-{3-[1-((3*S*)-3-{[(4-METHYLPHENYL)SULFONYL]AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure Q1 and Scheme AC using 4-methylbenzenesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 534.2 $(M + H)^+$.

Example 596

N-{3-[1-((3*S*)-3-{[(3,5-DICHLORO-2-HYDROXYPHENYL)SULFONYL]AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared Procedure Q1 and Scheme AC using 3,5-dichloro-2-hydroxybenzenesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 605.4 $(M + H)^+$.

Example 597

2-METHYL-*N*-[3-(1-{(3*S*)-3-[(METHYLSULFONYL)AMINO]-3-PHENYLPROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure Q1 and Scheme AC using methanesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 458.6 $(M + H)^+$.

Example 598

***N*-{3-[1-((3*S*)-3-{[(4-FLUOROPHENYL)SULFONYL]AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure Q1 and Scheme AC using 4-fluorobenzenesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 538.1 $(M + H)^+$.

Example 599

***N*-{3-[1-((3*S*)-3-{[(4-TERT-BUTYLPHENYL)SULFONYL]AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure Q1 and Scheme AC using 4-tert-butylbenzenesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 576.2 $(M + H)^+$.

Example 600

***N*-{3-[1-((3*S*)-3-{[(2,5-DICHLOROPHENYL)SULFONYL]AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure Q1 and Scheme AC using 2,5-dichlorobenzenesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 588.0 $(M + H)^+$.

Example 601

2-METHYL-*N*-[3-(1-{(3*S*)-3-PHENYL-3-[(PROPYLSULFONYL)AMINO]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure Q1 and Scheme AC using 1-propanesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 486.2 $(M + H)^+$.

Example 602

N-{3-[1-((3*S*)-3-{[(3,5-DIMETHYL-4-ISOXAZOLYL)SULFONYL]AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 and Scheme AC using 3,5-dimethyl-4-isoxazolesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 2H), 7.3-7.1 (m, 5H), 7.05 (t, 2H, J = 6.5 Hz), 6.81 (d, 1H, J = 7.1 Hz), 4.65 (dd, 1H, J = 6.3, 2.2 Hz), 3.11 (t, 2H, J = 7.2 Hz), 2.4 (m, 4H), 2.2 (s, 3H), 2.05 (m, 2H), 2.01 (s, 3H), 2.0-1.8 (m, 7H), 1.21 (d, 6H, J = 7.1 Hz); ESMS *m/e*: 539.5 $(M + H)^+$.

Example 603

METHYL 3-{[(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)AMINO]SULFONYL}-2-THIOPHENECARBOXYLATE: Prepared Procedure Q1 and Scheme AC using methyl 3-(chlorosulfonyl)-2-thiophenecarboxylate and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: Anal. Calcd for $C_{24}H_{33}N_3O_5S_2.HCl$: C, 6.00; H, 5.30; N, 7.72. Found: C, 52.9; H, 6.04; N, 7.59; ESMS *m/e*: 508.2 $(M + H)^+$.

Example 604

2-METHYL-*N*-{3-[1-((3*S*)-3-{[(4-PHENOXYANILINO)CARBONYL]AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure P and Scheme AB using 1-isocyanato-4-phenoxybenzene and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 591.3 $(M + H)^+$.

PIPERIDINYL]PHENYL}-2- METHYLPROPANAMIDE: Prepared by Procedure Q1 and Scheme AC using 3,5-dimethyl-4-isoxazolesulfonyl chloride and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 2H), 7.3-7.1 (m, 5H), 7.05 (t, 2H, J = 6.5 Hz), 6.81 (d, 1H, J = 7.1 Hz), 4.65 (dd, 1H, J = 6.3, 2.2 Hz), 3.11 (t, 2H, J = 7.2 Hz), 2.4 (m, 4H), 2.2 (s, 3H), 2.05 (m, 2H), 2.01 (s, 3H), 2.0-1.8 (m, 7H), 1.21 (d, 6H, J = 7.1 Hz); ESMS *m/e*: 539.5 $(M + H)^+$.

Example 603

METHYL 3-{[(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)AMINO]SULFONYL}-2-THIOPHENECARBOXYLATE: Prepared Procedure Q1 and Scheme AC using methyl 3-(chlorosulfonyl)-2-thiophenecarboxylate and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: Anal. Calcd for $C_{24}H_{33}N_3O_5S.HCl$: C, 6.00; H, 5.30; N, 7.72. Found: C, 52.9; H, 6.04; N, 7.59; ESMS *m/e*: 508.2 $(M + H)^+$.

Example 604

2-METHYL-*N*-{3-[1-((3*S*)-3-{[(4-PHENOXYANILINO)CARBONYL]AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure P and Scheme AB using 1-isocyanato-4-phenoxybenzene and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 591.3 $(M + H)^+$.

Example 605

N-[3-(1-{(3*S*)-3-[(ANILINOCARBONYL)AMINO]-3-PHENYLPROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure P and Scheme AB using isocyanatobenzene and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 499.2 $(M + H)^+$.

Example 606

***N*-{3-[1-((3*S*)-3-{[(TERT-BUTYLAMINO)CARBOTHIOYL]AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure P and Scheme AB using 2-isothiocyanato-2-methylpropane and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 495.1 $(M + H)^+$.

Example 607

***N*-{3-[1-((3*S*)-3-{[(2-FLUOROANILINO)CARBONYL]AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure P and Scheme AB using 1-fluoro-2-isocyanatobenzene and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 517.0 $(M + H)^+$.

Example 608

2-METHYL-*N*-[3-(1-{(3*S*)-3-PHENYL-3-[(2-TOLUIDINOCARBOTHIOYL)AMINO]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure P and Scheme AB using 1-isothiocyanato-2-methylbenzene and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 529.1 $(M + H)^+$.

Example 609

***N*-{3-[1-((3*S*)-3-{[(BENZYLAMINO)CARBONYL]AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:**

phenylpropyl]-4- piperidinyl}phenyl)-2-methylpropanamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 7.67 (d, 1H, J = 7.9 Hz), 7.31-7.13 (m, 13H), 6.38 (s, 1H), 6.80 (d, 1H, J = 7.9 Hz), 5.54 (m, 1H), 4.81 (m, 1H), 4.41 (dd, 1H, J = 14.8, 6.2 Hz), 4.29 (dd, 1H, J = 14.9, 5.4 Hz), 2.99 (d, 1H, J = 11.2 Hz), 2.87 (d, 1H, J = 11.2 Hz), 2.67 (q, 1H, J = 6.2 Hz), 2.3 (m, 3H), 2.0-1.5 (m, 7H), 1.23 (d, 6H, J = 6.7 Hz); ESMS *m/e*: 513.2 $(M + H)^+$.

Example 610

2-METHYL-*N*-{3-[1-((3*S*)-3-{[(2-NITROANILINO)CARBONYL]AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure P and Scheme AB using 1-isocyanato-2-nitrobenzene and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 543.6 $(M + H)^+$.

Example 611

***N*-{3-[1-((3*S*)-3-{[(3,4-DICHLOROANILINO)CARBONYL]AMINO}-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure P and Scheme AB using 1,2-dichloro-4-isocyanatobenzene and *N*-(3-{1-[(3*S*)-3-amino-3-phenylpropyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 567.1 $(M + H)^+$.

Example 612

2-METHYL-*N*-(3-{1-[(3*S*)-3-({[2-(METHYLSULFANYL)ANILINO]CARBONYL}AMINO)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure P and Scheme AB using 1-isocyanato-2-(methylsulfanyl)benzene and *N*-(3-{1-[(3*S*)-3-amino-3-

phenylpropyl]-4- piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 545.0 $(M + H)^+$.

Example 613

***N*-{3-[1-(3-{[(4-FLUOROANILINO)CARBONYL]AMINO}PROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure P and Scheme AB using 1-fluoro-4-isocyanatobenzene and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$) δ 7.45 (q, 2H, J = 4.7 Hz), 7.23 (m, 4H), 7.05 (t, 4H, J = 7.8 Hz), 6.75 (m, 1H), 4.05 (m, 1H), 3.19 (s, 1H), 2.71 (m, 1H), 2.53 (m, 1H), 2.25 (m, 3H), 1.8 (m, 9H), 1.25 (d, 6H, J = 6.4 Hz); ESMS *m/e*: 441.1 $(M + H)^+$.

Example 614

***N*-{3-[1-(3-{[(3,4-DICHLOROANILINO)CARBONYL]AMINO}PROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure P and Scheme AB using 1,2-dichloro-4-isocyanatobenzene and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 493.2 $(M + H)^+$.

Example 615

2-METHYL-*N*-[3-(1-{3-[(2-TOLUIDINOCARBOTHIOYL)AMINO]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure P and Scheme AB using 1-isothiocyanato-2-methylbenzene and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 453.2 $(M + H)^+$.

Example 616

N-{3-[1-(3-{[(BENZYLAMINO)CARBONYL]AMINO}PROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure P and Scheme AB using (isocyanatomethyl)benzene and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 437.2 $(M + H)^+$.

Example 617

N-{3-[1-(3-{[(4-ETHOXYANILINO)CARBONYL]AMINO}PROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure P and Scheme AB using 1-ethoxy-4-isocyanatobenzene and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 467.2 $(M + H)^+$.

Example 618

N-[3-(1-{3-[(ANILINOCARBONYL)AMINO]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure P and Scheme AB using isocyanatobenzene and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 422.9 $(M + H)^+$.

Example 619

2-METHYL-*N*-(3-{1-[3-({[2-(METHYLSULFANYL)ANILINO]CARBONYL}AMINO)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure P and Scheme AB using 1-isocyanato-2-(methylsulfanyl)benzene and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 469.1 $(M + H)^+$.

Example 620

N-{3-[1-(3-{[(TERT-BUTYLAMINO)CARBOTHIOYL]AMINO}PROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure P and Scheme AB using 2-isothiocyanato-2-methylpropane and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 419.0 $(M + H)^+$.

Example 621

2-METHYL-*N*-{3-[1-(3-{[(4-PHENOXYANILINO)CARBONYL]AMINO}PROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure P and Scheme AB using 1-isocyanato-4-phenoxybenzene and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 515.5 $(M + H)^+$.

Example 622

N-(3-{4-[3-(ACETYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-4-(2,4-DIFLUOROPHENYL)-2-METHYL-6-OXO-1,4,5,6-TETRAHYDRO-3-PYRIDINECARBOXAMIDE: Prepared by Procedure AC and Scheme AM using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}acetamide and 4-(2,4-difluorophenyl)-2-methyl-6-oxo-1,4,5,6-tetrahydro-3-pyridinecarboxylic acid: ESMS *m/e*: 525.2 $(M + H)^+$.

Example 623

N-(3-{4-[3-(ACETYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-4-(3,4-DIFLUOROPHENYL)-2-METHYL-6-OXO-1,4,5,6-TETRAHYDRO-3-PYRIDINECARBOXAMIDE: Prepared by Procedure AC and Scheme AM using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}acetamide and 4-(3,4-difluorophenyl)-2-methyl-6-oxo-1,4,5,6-tetrahydro-3-pyridinecarboxylic acid: ESMS *m/e*: 525.2 $(M + H)^+$.

Example 624

***N*-(6-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}HEXYL)-1-(4-NITROPHENYL)-5-(TRIFLUOROMETHYL)-1H-PYRAZOLE-4-CARBOXAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 1-(4-nitrophenyl)-5-(trifluoromethyl)-1H-pyrazole-4-carbonyl chloride: ESMS *m/e*: 629.2 $(M + H)^+$.

Example 625

***N*-[3-(1-{6-[(DIPHENYLACETYL)AMINO]HEXYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and diphenylacetyl chloride: ESMS *m/e*: 540.3 $(M + H)^+$.

Example 626

5-(3,5-DICHLOROPHENOXY)-*N*-(6-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}HEXYL)-2-FURAMIDE:
Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 5-(3,5-dichlorophenoxy)-2-furoyl chloride: ESMS *m/e*: 600.2 $(M + H)^+$.

Example 627

***N*-(6-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}HEXYL)-2-PHENOXYNICOTINAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 2-phenoxynicotinoyl chloride: ESMS *m/e*: 543.3 $(M + H)^+$.

Example 628

N-(6-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}HEXYL)-2-NAPHTHAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 2-naphthoyl chloride: ESMS *m/e*: 500.3 $(M + H)^+$.

Example 629

1-BENZYL-3-TERT-BUTYL-*N*-(6-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}HEXYL)-1*H*-PYRAZOLE-5-CARBOXAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 1-benzyl-3-*tert*-butyl-1*H*-pyrazole-5-carbonyl chloride: ESMS *m/e*: 586.3 $(M + H)^+$.

Example 630

3-CHLORO-*N*-(6-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}HEXYL)-4-(ISOPROPYLSULFONYL)-2-THIOPHENECARBOXAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-chloro-4-(isopropylsulfonyl)-2-thiophenecarbonyl chloride: ESMS *m/e*: 596.2 $(M + H)^+$.

Example 631

N-[3-(1-{6-[(ANILINOCARBONYL)AMINO]HEXYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and phenyl isocyanate : ESMS *m/e*: 465.2 $(M + H)^+$.

Example 632

***N*-{3-[1-(6-{[(2,4-DICHLOROANILINO)CARBONYL]AMINO}HEXYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 2,4-dichlorophenyl isocyanate: ESMS *m/e*: 533.2 (M + H)$^+$.

Example 633

***N*-(6-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}HEXYL)-1-PHENYL-5-PROPYL-1*H*-PYRAZOLE-4-CARBOXAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 1-phenyl-5-propyl-1*H*-pyrazole-4-carbonyl chloride: ESMS *m/e*: 558.3 (M + H)$^+$.

Example 634

2-METHYL-*N*-{3-[1-(6-{[(1-NAPHTHYLAMINO)CARBONYL]AMINO}HEXYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 1-naphthyl isocyanate: ESMS *m/e*: 515.3 (M + H)$^+$.

Example 635

***N*-{3-[1-(6-{[([1,1'-BIPHENYL]-4-YLAMINO)CARBONYL]AMINO}HEXYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 4-biphenyl isocyanate: ESMS *m/e*: 541.3 (M + H)$^+$.

Example 636

2-METHYL-*N*-{3-[1-(6-{[(2-NAPHTHYLAMINO)CARBONYL]AMINO}HEXYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(6-aminohexyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 2-naphthyl isocyanate: ESMS *m/e*: 515.3 $(M + H)^+$.

Example 637

N-{3-[1-(3-{[(3,4-DIMETHOXYPHENYL)SULFONYL]AMINO}PROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3,4-dimethoxybenzenesulfonyl chloride: ESMS *m/e*: 504.2 $(M + H)^+$.

Example 638

N-(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-5-METHYL-3-PHENYL-4-ISOXAZOLECARBOXAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 5-methyl-3-phenyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 489.3 $(M + H)^+$.

Example 639

N-{3-[1-(3-{[(4-FLUOROPHENYL)ACETYL]AMINO}PROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and (4-fluorophenyl)acetyl chloride: ESMS *m/e*: 440.3 $(M + H)^+$.

Example 640

N-{3-[1-(3-{[(4-CHLORO-3-NITROPHENYL)SULFONYL]AMINO}PROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 4-chloro-3-nitrobenzenesulfonyl chloride: ESMS *m/e*: 523.1 $(M + H)^+$.

Example 641

2-(4-CHLOROPHENOXY)-*N*-(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)NICOTINAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 2-(4-chlorophenoxy)nicotinoyl chloride: ESMS *m/e*: 535.2 $(M + H)^+$.

Example 642

5-(3,5-DICHLOROPHENOXY)-*N*-(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-2-FURAMIDE:

Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 5-(3,5-dichlorophenoxy)-2-furoyl chloride: ESMS *m/e*: 558.2 $(M + H)^+$.

Example 643

N-{3-[1-(3-{[(2-FLUOROPHENYL)SULFONYL]AMINO}PROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 2-fluorobenzenesulfonyl chloride: ESMS m/e: 462.2 $(M + H)^+$.

Example 644

N-{3-[1-(3-{[(3,5-DIMETHYL-4-ISOXAZOLYL)SULFONYL]AMINO}PROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3,5-dimethyl-4-isoxazolesulfonyl chloride:. ESMS *m/e*: 463.2 $(M + H)^+$.

Example 644

N-{3-[1-(3-{[(4-TERT-BUTYLPHENYL)SULFONYL]AMINO}PROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 4-tert-butylbenzenesulfonyl chloride: ESMS *m/e*: 500.3 $(M + H)^+$.

Example 646

N-{3-[1-(6-AMINOHEXYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure AE and Scheme Y using *N*-(3-{1-[6-(1,3-dioxo-1,3-dihydro-2*H*-isoindol-2-yl)hexyl]-4-piperidinyl}phenyl)-2-methylpropanamide and hydrazine hydrate: ESMS *m/e*: 346.2 $(M + H)^+$.

Example 647

N-{3-[1-(2-{[([1,1'-BIPHENYL]-4-YLAMINO)CARBONYL]AMINO}ETHYL)-4-PIPERIDINYL}PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(2-aminoethyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 4-biphenyl isocyanate: ESMS *m/e*: 485.2 $(M + H)^+$.

Example 648

5-(3,5-DICHLOROPHENOXY)-*N*-(2-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}ETHYL)-3-FURAMIDE:

Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(2-aminoethyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 5-(3,5-dichlorophenoxy)-3-furoyl chloride: ESMS *m/e*: 544.1 $(M + H)^+$.

Example 649

N-[3-(1-{2-[(DIPHENYLACETYL)AMINO]ETHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(2-aminoethyl)-4-piperidinyl]phenyl}-2-methylpropanamide and diphenylacetyl chloride: ESMS *m/e*: 484.2 $(M + H)^+$.

Example 650

***N*-(2-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}ETHYL)-2-NAPHTHAMIDE:** Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(2-aminoethyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 2-naphthoyl chloride: ESMS *m/e*: 444. 2 $(M + H)^+$.

Example 651

3-(2,6-DICHLOROPHENYL)-*N*-(4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}BUTYL)-5-METHYL-4-ISOXAZOLECARBOXAMIDE:

Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2,6-dichlorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 571.2 $(M + H)^+$.

Example 652

3-(2,6-DICHLOROPHENYL)-N-(5-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PENTYL)-5-METHYL-4-ISOXAZOLECARBOXAMIDE: Prepared by Procedure Q1 (THF) and Scheme AT using *N*-{3-[1-(5-aminopentyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2,6-dichlorophenyl)-5-methyl-4-isoxazolecarbonyl chloride. ESMS m/e: 585.2 $(M + H)^+$.

Example 653

N-[3-(1-{4-[(DIPHENYLACETYL)AMINO]BUTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure Q2(THF/DCM, 1:3)) and Scheme AT using *N*-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and diphenylacetyl chloride: ESMS *m/e*: 512.0 $(M + H)^+$.

Example 654

N-[3-(1-{5-[(DIPHENYLACETYL)AMINO]PENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure Q2(THF/DCM, 1:3)) and Scheme AT using *N*-{3-[1-(5-aminopentyl)-4-piperidinyl]phenyl}-2-methylpropanamide and diphenylacetyl chloride: ESMS *m/e*: 526.0 $(M + H)^+$.

Example 655

3,5-DICHLORO-*N*-(4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}BUTYL)BENZAMIDE: Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using *N*-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3,5-dichlorobenzoyl chloride: ESMS *m/e*: 490.0 $(M + H)^+$.

Example 656

5-(3,5-DICHLOROPHENOXY)-*N*-(4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}BUTYL)-2-FURAMIDE:

Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using *N*-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 5-(3,5-dichlorophenoxy)-2-furoyl chloride: ESMS *m/e*: 572.0 $(M + H)^+$.

Example 657

3-CHLORO-*N*-(4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}BUTYL)BENZAMIDE: Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using *N*-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-chlorobenzoyl chloride: ESMS *m/e*: 456.0 $(M + H)^+$.

Example 658

3,4-DIFLUORO-*N*-(4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}BUTYL)BENZAMIDE: Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using *N*-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3,4-difluorobenzoyl chloride: ESMS *m/e*: 458.0 $(M + H)^+$.

Example 659

N-{3-[1-(4-{[(3,5-DICHLOROANILINO)CARBONYL]AMINO}BUTYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using *N*-(3-{1-[4-(formylamino)butyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 3,5-dichlorophenyl isocyanate: ESMS *m/e*: 505.0 $(M + H)^+$.

Example 660

N-{3-[1-(4-{[([1,1'-BIPHENYL]-4-YLAMINO)CARBONYL]AMINO}BUTYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using *N*-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 4-biphenyl isocyanate: ESMS *m/e*: 513.0 $(M + H)^+$.

Example 661

2-METHYL-*N*-(3-{1-[5-(4-NITROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure K and Scheme B1 (K_2CO_3) using 5-chloro-1-(4-nitrophenyl)-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 452.2 $(M + H)^+$.

Example 662

N-(3-{1-[5-(4-FLUOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure K and Scheme B1 (K_2CO_3) using 5-chloro-1-(4-fluorophenyl)-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 425.2 $(M + H)^+$.

Example 663

2-METHYL-*N*-[3-(1-{5-OXO-5-[2-(TRIFLUOROMETHYL)PHENYL]PENTYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure K and Scheme B1 (K_2CO_3) using 5-chloro-1-[2-(trifluoromethyl)phenyl]-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 475.2 $(M + H)^+$.

Example 664

N-(3-{1-[5-(3-BROMOPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by

Procedure K and Scheme B1 (K_2CO_3) using 1-(3-bromophenyl)-5-chloro-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 485.1 $(M + H)^+$.

Example 665

2-METHYL-*N*-(3-{1-[5-(3-NITROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure K and Scheme B1 (K_2CO_3) using 5-chloro-1-(3-nitrophenyl)-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 452.2 $(M + H)^+$.

Example 666

***N*-(3-{1-[5-(3-CHLOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme B1 (K_2CO_3) using 1-(3-chlorophenyl)-5-chloro-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 441.1 $(M + H)^+$.

Example 667

***N*-(3-{1-[5-(4-BROMOPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme B1 (K_2CO_3) using 1-(4-bromophenyl)-5-chloro-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 485.1 $(M + H)^+$.

Example 668

***N*-(3-{1-[5-(2-IODOPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme B1 (K_2CO_3) using 1-(2-iodophenyl)-5-chloro-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 533.0 $(M + H)^+$.

Example 669

N-(3-{1-[5-(3-FLUOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure K and Scheme B1 (K_2CO_3) using 1-(3-fluorophenyl)-5-chloro-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 425.2 $(M + H)^+$.

Example 670

2-METHYL-*N*-[3-(1-{5-OXO-5-[3-(TRIFLUOROMETHYL)PHENYL]PENTYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure K and Scheme B1 (K_2CO_3) using 1-[3-(trifluoromethyl)phenyl]-5-chloro-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 475.2 $(M + H)^+$.

Example 671

N-(3-{1-[5-(2-FLUOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure K and Scheme B1 (K_2CO_3) using 1-(2-fluorophenyl)-5-chloro-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 425.2 $(M + H)^+$.

Example 672

N-(3-{1-[5-(3-IODOPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure K and Scheme B1 (K_2CO_3) using 1-(3-iodophenyl)-5-chloro-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 533.0 $(M + H)^+$.

Example 673

N-(3-{1-[5-(2-CHLOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by

Procedure K and Scheme B1 (K_2CO_3) using 1-(2-chlorophenyl)-5-chloro-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 441.1 $(M + H)^+$.

Example 674

2-METHYL-*N*-[3-(1-{5-OXO-5-[4-(TRIFLUOROMETHYL)PHENYL]PENTYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure K and Scheme B1 (K_2CO_3) using 1-[4-(trifluoromethyl)phenyl]-5-chloro-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 475.2 $(M + H)^+$.

Example 675

***N*-(3-{1-[5-(4-CHLOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme B1 (K_2CO_3) using 1-(4-chlorophenyl)-5-chloro-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 441.1 $(M + H)^+$.

Example 676

***N*-(3-{1-[5-(4-IODOPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme B1 (K_2CO_3) using 1-(4-iodophenyl)-5-chloro-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 533 $(M + H)^+$.

Example 677

***N*-(3-{1-[5-(2-BROMOPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme B1 (K_2CO_3) using 1-(2-bromophenyl)-5-chloro-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 485.1 $(M + H)^+$.

Example 678

2-(4-CHLOROPHENOXY)-*N*-(4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}BUTYL)NICOTINAMIDE: Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using *N*-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 2-(4-chlorophenoxy)nicotinoyl chloride: ESMS *m/e*: 549.0 $(M + H)^+$.

Example 679

***N*-(4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}BUTYL)-3,4-DIMETHOXYBENZAMIDE:** Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using *N*-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3,4-dimethoxybenzoyl chloride: ESMS *m/e*: 482.0 $(M + H)^+$.

Example 680

3-(2-CHLOROPHENYL)-*N*-(4-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}BUTYL)-5-METHYL-4-ISOXAZOLECARBOXAMIDE: Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using *N*-{3-[1-(4-aminobutyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2-chlorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 537.0 $(M + H)^+$.

Example 681

3-(2-CHLOROPHENYL)-*N*-(5-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PENTYL)-5-METHYL-4-ISOXAZOLECARBOXAMIDE: Prepared by Procedure Q2 (THF/DCM, 1:3) and Scheme AT using *N*-{3-[1-(5-aminopentyl)-4-piperidinyl]phenyl}-2-methylpropanamide and 3-(2-chlorophenyl)-5-methyl-4-isoxazolecarbonyl chloride: ESMS *m/e*: 551.0 $(M + H)^+$.

Example 682

2-METHYL-*N*-{3-[1-(3-{1-METHYL-2-[4-(TRIFLUOROMETHYL)PHENYL]-1*H*-INDOL-3-YL}PROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 562.2 $(M + H)^+$.

Example 683

2-METHYL-*N*-{3-[1-(3-{1-METHYL-2-[4-(TRIFLUOROMETHYL)PHENYL]-1*H*-INDOL-3-YL}PROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS *m/e*: 632.2 $(M + H)^+$.

Example 684

2-METHYL-*N*-{3-[1-(3-{2-[4-(TRIFLUOROMETHYL)PHENYL]-1*H*-INDOL-3-YL}PROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide and phenylhydrazine: ESMS *m/e*: 548.2 $(M + H)^+$.

Example 685

2-METHYL-*N*-{3-[1-(3-{1-PHENYL-2-[4-(TRIFLUOROMETHYL)PHENYL]-1*H*-INDOL-3-YL}PROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-

piperidinyl)phenyl]propanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 624.2 $(M + H)^+$.

Example 686

2-METHYL-*N*-{3-[1-(3-{2-[4-(TRIFLUOROMETHYL)PHENYL]-1H-BENZO[*G*]INDOL-3-YL}PROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide and 1-naphthylhydrazine hydrochloride: ESMS *m/e*: 598.2 $(M + H)^+$.

Example 687

2-METHYL-*N*-{3-[1-(3-{7-METHYL-2-[4-(TRIFLUOROMETHYL)PHENYL]-1H-INDOL-3-YL}PROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 562.2 $(M + H)^+$.

Example 688

2-METHYL-*N*-{3-[1-(3-{5-METHYL-2-[4-(TRIFLUOROMETHYL)PHENYL]-1H-INDOL-3-YL}PROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide and 4-methylphenylhydrazine hydrochloride: ESMS *m/e*: 562.2 $(M + H)^+$.

Example 689

N-{3-[1-(3-{5-METHOXY-2-[4-(TRIFLUOROMETHYL)PHENYL]-1*H*-INDOL-3-YL}PROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide and 4-methoxyphenylhydrazine hydrochloride: ESMS *m/e*: 578.2 (M + H)$^+$.

Example 690

N-[3-(1-{3-[2-(3-FLUOROPHENYL)-7-METHYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 512.2 (M + H)$^+$.

Example 691

N-[3-(1-{3-[2-(4-CHLOROPHENYL)-1-METHYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 528.2 (M + H)$^+$.

Example 692

N-[3-(1-{3-[2-(4-FLUOROPHENYL)-5-METHOXY-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methoxyphenylhydrazine hydrochloride: ESMS *m/e*: 528.2(M + H)$^+$.

Example 693

N-[3-(1-{3-[2-(2-FLUOROPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS *m/e*: 498.2 $(M + H)^+$.

Example 694

N-[3-(1-{3-[2-(3-FLUOROPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS *m/e*: 582.2 $(M + H)^+$.

Example 695

N-[3-(1-{3-[2-(2-FLUOROPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS *m/e*: 582.2 $(M + H)^+$.

Example 696

N-[3-(1-{3-[2-(4-FLUOROPHENYL)-1-PHENYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 548.2 $(M + H)^+$.

Example 697

***N*-[3-(1-{3-[2-(2-FLUOROPHENYL)-1*H*-BENZO[*g*]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS *m/e*: 547.7 $(M + H)^+$.

Example 698

***N*-[3-(1-{3-[2-(2-FLUOROPHENYL)-5-METHYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS *m/e*: 512.2($M + H)^+$.

Example 699

***N*-[3-(1-{3-[2-(3-FLUOROPHENYL)-1*H*-BENZO[*g*]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS *m/e*: 548.2 $(M + H)^+$.

Example 700

***N*-[3-(1-{3-[2-(4-FLUOROPHENYL)-1-METHYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 512.2 $(M + H)^+$.

Example 701

N-[3-(1-{3-[2-(3-FLUOROPHENYL)-5-METHOXY-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methoxyphenylhydrazine hydrochloride: ESMS *m/e*: 528.2 $(M + H)^+$.

Example 702

N-[3-(1-{3-[2-(3-FLUOROPHENYL)-1-PHENYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 574.2 $(M + H)^+$.

Example 703

N-[3-(1-{3-[2-(4-CHLOROPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS *m/e*: 598.2 $(M + H)^+$.

Example 704

N-[3-(1-{3-[2-(3-FLUOROPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS *m/e*: 498.2 $(M + H)^+$.

Example 705

N-[3-(1-{3-[2-(3-FLUOROPHENYL)-1-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 512.2 $(M + H)^+$.

Example 706

N-[3-(1-{3-[2-(3-FLUOROPHENYL)-5-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS *m/e*: 512.2 $(M + H)^+$.

Example 707

N-[3-(1-{3-[2-(4-CHLOROPHENYL)-1H-BENZO[G]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS *m/e*: 564.2 $(M + H)^+$.

Example 708

N-[3-(1-{3-[2-(4-CHLOROPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-phenylhydrazine hydrochloride: ESMS *m/e*: 514.2 $(M + H)^+$.

Example 709

N-[3-(1-{3-[2-(2-FLUOROPHENYL)-1-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 512.2 $(M + H)^+$.

Example 710

N-[3-(1-{3-[2-(2-FLUOROPHENYL)-7-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 512.2 $(M + H)^+$.

Example 711

N-[3-(1-{3-[2-(2-FLUOROPHENYL)-1-PHENYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 574.2 $(M + H)^+$.

Example 712

N-[3-(1-{3-[2-(2-FLUOROPHENYL)-5-METHOXY-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methoxyphenylhydrazine hydrochloride: ESMS *m/e*: 528.2 $(M + H)^+$.

Example 713

N-[3-(1-{3-[2-(4-CHLOROPHENYL)-5-METHOXY-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methoxyphenylhydrazine hydrochloride: ESMS *m/e*: 544.2 $(M + H)^+$.

Example 714

N-[3-(1-{3-[2-(4-FLUOROPHENYL)-1*H*-BENZO[*G*]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS *m/e*: 548.2 $(M + H)^+$.

Example 715

N-[3-(1-{3-[2-(4-FLUOROPHENYL)-5-(TRIFLUOROMETHOXY)-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS *m/e*: 582.9 $(M + H)^+$.

Example 716

N-[3-(1-{3-[2-(4-FLUOROPHENYL)-7-METHYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 512.2 $(M + H)^+$.

Example 717

N-[3-(1-{3-[2-(4-FLUOROPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS *m/e*: 498.2 $(M + H)^+$.

Example 718

N-[3-(1-{3-[2-(4-FLUOROPHENYL)-5-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS *m/e*: 512.2 $(M + H)^+$.

Example 719

N-[3-(1-{3-[2-(4-CHLOROPHENYL)-7-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS m/e: 528.2 $(M + H)^+$.

Example 720

N-[3-(1-{3-[2-(4-CHLOROPHENYL)-5-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS *m/e*: 528.2 $(M + H)^+$.

Example 721

***N*-[3-(1-{3-[2-(4-CHLOROPHENYL)-1-PHENYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 590.2 $(M + H)^+$.

Example 722

***N*-[3-(1-{3-[2-(3-CHLOROPHENYL)-7-METHYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 528.1 $(M + H)^+$.

Example 723

***N*-[3-(1-{3-[2-(3-CHLOROPHENYL)-5-(TRIFLUOROMETHOXY)-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS *m/e*: 598.2 $(M + H)^+$.

Example 724

***N*-[3-(1-{3-[2-(3-CHLOROPHENYL)-1-METHYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 528.2 $(M + H)^+$.

Example 725

N-[3-(1-{3-[2-(3-CHLOROPHENYL)-1-PHENYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 590.3 $(M + H)^+$.

Example 726

N-[3-(1-{3-[2-(3-CHLOROPHENYL)-5-METHOXY-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methoxyphenylhydrazine hydrochloride: ESMS *m/e*: 544.3 $(M + H)^+$.

Example 727

N-[3-(1-{3-[2-(3-CHLOROPHENYL)-5-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS *m/e*: 528.2 $(M + H)^+$.

Example 728

N-[3-(1-{3-[2-(3-CHLOROPHENYL)-1H-BENZO[*G*]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS *m/e*: 564.2 $(M + H)^+$.

Example 729

N-[3-(1-{3-[2-(3-CHLOROPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS *m/e*: 514.2 $(M + H)^+$.

Example 730

N-[3-(1-{3-[2-(2-CHLOROPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS *m/e*: 514.2 $(M + H)^+$.

Example 731

N-[3-(1-{3-[2-(2-CHLOROPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS *m/e*: 598.2 $(M + H)^+$.

Example 732

N-[3-(1-{3-[2-(2-CHLOROPHENYL)-1H-BENZO[*G*]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS *m/e*: 564.2 $(M + H)^+$.

Example 733

***N*-[3-(1-{3-[2-(2-CHLOROPHENYL)-7-METHYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 528.2 $(M + H)^+$.

Example 734

***N*-[3-(1-{3-[2-(2-CHLOROPHENYL)-1-PHENYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 590.2 $(M + H)^+$.

Example 735

***N*-[3-(1-{3-[2-(2-CHLOROPHENYL)-1-METHYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 528.2 $(M + H)^+$.

Example 736

***N*-[3-(1-{3-[2-(2-CHLOROPHENYL)-5-METHYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS *m/e*: 528.2 $(M + H)^+$.

Example 737

N-[3-(1-{3-[2-(3-IODOPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS *m/e*: 606.2 $(M + H)^+$.

Example 738

N-[3-(1-{3-[2-(3-IODOPHENYL)-1-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 620.2 $(M + H)^+$.

Example 739

N-[3-(1-{3-[2-(3-IODOPHENYL)-1-PHENYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 682.2 $(M + H)^+$.

Example 740

N-[3-(1-{3-[2-(3-IODOPHENYL)-1H-BENZO[G]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS *m/e*: 656.2 $(M + H)^+$.

Example 741

N-[3-(1-{3-[2-(3-IODOPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS *m/e*: 690.2 $(M + H)^+$.

Example 742

N-[3-(1-{3-[2-(3-IODOPHENYL)-5-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS *m/e*: 620.2 $(M + H)^+$.

Example 743

N-[3-(1-{3-[2-(3-IODOPHENYL)-7-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 620.2 $(M + H)^+$.

Example 744

N-[3-(1-{3-[2-(4-IODOPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-

(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS *m/e*: 690.1 $(M + H)^+$.

Example 745

***N*-[3-(1-{3-[2-(4-IODOPHENYL)-5-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS *m/e*: 620.1 $(M + H)^+$.

Example 746

***N*-[3-(1-{3-[2-(4-IODOPHENYL)-7-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 620.1 $(M + H)^+$.

Example 747

***N*-[3-(1-{3-[2-(4-IODOPHENYL)-1-PHENYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 682.1 $(M + H)^+$.

Example 748

***N*-[3-(1-{3-[2-(4-IODOPHENYL)-1-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-

methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 620.1 $(M + H)^+$.

Example 749

***N*-[3-(1-{3-[2-(4-IODOPHENYL)-1H-BENZO[*G*]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS *m/e*: 656.1 $(M + H)^+$.

Example 750

***N*-[3-(1-{3-[2-(4-IODOPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS *m/e*: 606.1 $(M + H)^+$.

Example 751

***N*-[3-(1-{3-[2-(3-BROMOPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS *m/e*: 642.0 $(M + H)^+$.

Example 752

***N*-[3-(1-{3-[2-(4-BROMOPHENYL)-1H-BENZO[*G*]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-

methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS m/e: 608.0 $(M + H)^+$.

Example 753

***N*-[3-(1-{3-[2-(4-BROMOPHENYL)-7-METHYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 572 $(M + H)^+$.

Example 754

***N*-[3-(1-{3-[2-(4-BROMOPHENYL)-5-(TRIFLUOROMETHOXY)-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS *m/e*: 642 $(M + H)^+$.

Example 755

***N*-[3-(1-{3-[2-(3-BROMOPHENYL)-1*H*-BENZO[*G*]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS *m/e*: 608.0 $(M + H)^+$.

Example 756

***N*-[3-(1-{3-[2-(4-BROMOPHENYL)-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-

methylpropanamide and phenylhydrazine: ESMS *m/e*: 558.1 $(M + H)^+$.

Example 757

***N*-[3-(1-{3-[2-(3-BROMOPHENYL)-1-PHENYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 634.0 $(M + H)^+$.

Example 758

***N*-[3-(1-{3-[2-(3-BROMOPHENYL)-1-METHYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 572.0 $(M + H)^+$.

Example 759

***N*-[3-(1-{3-[2-(4-BROMOPHENYL)-1-METHYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 572.0 $(M + H)^+$.

Example 760

***N*-[3-(1-{3-[2-(4-BROMOPHENYL)-1-PHENYL-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-

methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 634.0 $(M + H)^+$.

Example 761

N-[3-(1-{3-[2-(4-BROMOPHENYL)-5-METHOXY-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methoxyphenylhydrazine hydrochloride: ESMS *m/e*: 588.1 $(M + H)^+$.

Example 762

N-[3-(1-{3-[2-(3-BROMOPHENYL)-7-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 572 $(M + H)^+$.

Example 763

N-[3-(1-{3-[2-(3-BROMOPHENYL)-5-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS *m/e*: 572 $(M + H)^+$.

Example 764

N-[3-(1-{3-[2-(4-BROMOPHENYL)-5-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(4-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-

methylpropanamide and 4- methylphenylhydrazine hydrochloride: ESMS m/e: 572.0 $(M + H)^+$.

Example 765

N-[3-(1-{3-[2-(3-BROMOPHENYL)-5-METHOXY-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(3-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methoxyphenylhydrazine hydrochloride: ESMS *m/e*: 588.0 $(M + H)^+$.

Example 766

2-METHYL-*N*-[3-(1-{3-[2-(3-NITROPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-(3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and phenylhydrazine: ESMS *m/e*: 525.2 $(M + H)^+$.

Example 767

2-METHYL-*N*-[3-(1-{3-[2-(3-NITROPHENYL)-1H-BENZO[*G*]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-(3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 1-naphthylhydrazine hydrochloride: ESMS *m/e*: 575.1 $(M + H)^+$.

Example 768

2-METHYL-*N*-[3-(1-{3-[2-(3-NITROPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-(3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 4-

(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS *m/e*: 609.1 $(M + H)^+$.

Example 769

2-METHYL-*N*-[3-(1-{3-[5-METHYL-2-(3-NITROPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:

Prepared by Procedure E and Scheme M using 2-methyl-*N*-(3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 4-methylphenylhydrazine hydrochloride: ESMS *m/e*: 539.2 $(M + H)^+$.

Example 770

***N*-[3-(1-{3-[5-METHOXY-2-(3-NITROPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:**

Prepared by Procedure E and Scheme M using 2-methyl-*N*-(3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 4-methoxyphenylhydrazine hydrochloride: ESMS *m/e*: 555.2 $(M + H)^+$.

Example 771

2-METHYL-*N*-[3-(1-{3-[2-(3-NITROPHENYL)-1-PHENYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:

Prepared by Procedure E and Scheme M using 2-methyl-*N*-(3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 601.1 $(M + H)^+$.

Example 772

2-METHYL-*N*-[3-(1-{3-[1-METHYL-2-(3-NITROPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:

Prepared by Procedure E and Scheme M using 2-methyl-N-

(3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 539.2 $(M + H)^+$.

Example 773

2-METHYL-*N*-[3-(1-{3-[7-METHYL-2-(3-NITROPHENYL)-1*H*-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-(3-{1-[5-(3-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 539.2 $(M + H)^+$.

Example 774

N-[3-(1-{3-[5-METHOXY-2-(4-NITROPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-(3-{1-[5-(4-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 4-methoxyphenylhydrazine hydrochloride: ESMS *m/e*: 555.6 $(M + H)^+$.

Example 775

N-[3-(1-{3-[2-(2-BROMOPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS *m/e*: 557.9 $(M + H)^+$.

Example 776

2-METHYL-N-[3-(1-{3-[5-METHYL-2-(4-NITROPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:

Prepared by Procedure E and Scheme M using 2-methyl-*N*-(3-{1-[5-(4-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 4-methylphenylhydrazine hydrochloride: ESMS *m/e*: 539.1 (M + H)$^+$.

Example 777

2-METHYL-N-[3-(1-{3-[2-(4-NITROPHENYL)-1H-BENZO[G]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-(3-{1-[5-(4-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 1-naphthylhydrazine hydrochloride: ESMS *m/e*: 574.7 (M + H)$^+$.

Example 778

2-METHYL-N-(3-{1-[(5E)-5-(4-NITROPHENYL)-5-(PHENYLHYDRAZONO)PENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:
Prepared by Procedure E and Scheme AX using 2-methyl-*N*-(3-{1-[5-(4-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and phenylhydrazine: ESMS *m/e*: 542.4 (M + H)$^+$.

Example 779

2-METHYL-N-[3-(1-{3-[7-METHYL-2-(4-NITROPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:
Prepared by Procedure E and Scheme M using 2-methyl-*N*-(3-{1-[5-(4-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 538.8 (M + H)$^+$.

Example 780

2-METHYL-N-{3-[1-((5E)-5-(4-NITROPHENYL)-5-{[4-(TRIFLUOROMETHOXY)PHENYL]HYDRAZONO}PENTYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure E and Scheme M using 2-methyl-*N*-(3-{1-[5-(4-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS *m/e*: 626.2 $(M + H)^+$.

Example 781

N-[3-(1-{3-[2-(2-BROMOPHENYL)-1H-BENZO[G]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS *m/e*: 608.0 $(M + H)^+$.

Example 782

N-[3-(1-{3-[2-(2-BROMOPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS *m/e*: 641.9 $(M + H)^+$.

Example 783

N-[3-(1-{3-[2-(2-BROMOPHENYL)-7-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 572.0 $(M + H)^+$.

Example 784

N-[3-(1-{3-[2-(2-BROMOPHENYL)-1-PHENYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 634 $(M + H)^+$.

Example 785

N-[3-(1-{3-[2-(2-BROMOPHENYL)-5-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS *m/e*: 572.0 $(M + H)^+$.

Example 786

N-[3-(1-{3-[2-(2-IODOPHENYL)-5-(TRIFLUOROMETHOXY)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-(trifluoromethoxy)phenylhydrazine hydrochloride: ESMS *m/e*: 690.0 $(M + H)^+$.

Example 787

N-[3-(1-{3-[2-(2-IODOPHENYL)-5-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 4-methylphenylhydrazine hydrochloride: ESMS *m/e*: 620.2 $(M + H)^+$.

Example 788

2-METHYL-N-[3-(1-{3-[1-METHYL-2-(4-NITROPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:

Prepared by Procedure E and Scheme M using 2-methyl-*N*-(3-{1-[5-(4-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 539.6 $(M + H)^+$.

Example 789

2-METHYL-N-[3-(1-{3-[2-(4-NITROPHENYL)-1-PHENYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE:

Prepared by Procedure E and Scheme M using 2-methyl-*N*-(3-{1-[5-(4-nitrophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)propanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 601.6 $(M + H)^+$.

Example 790

N-[3-(1-{3-[2-(2-IODOPHENYL)-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and phenylhydrazine: ESMS *m/e*: 606.1 $(M + H)^+$.

Example 791

N-[3-(1-{3-[2-(2-IODOPHENYL)-1H-BENZO[G]INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:

Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-naphthylhydrazine hydrochloride: ESMS *m/e*: 656.1 $(M + H)^+$.

Example 792

N-[3-(1-{3-[2-(2-IODOPHENYL)-1-PHENYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1,1-diphenylhydrazine hydrochloride: ESMS *m/e*: 682.1 $(M + H)^+$.

Example 793

N-[3-(1-{3-[2-(2-IODOPHENYL)-7-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-iodophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-(2-methylphenyl)hydrazine hydrochloride: ESMS *m/e*: 619.6 $(M + H)^+$.

Example 794

N-[3-(1-{3-[2-(2-BROMOPHENYL)-1-METHYL-1H-INDOL-3-YL]PROPYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure E and Scheme M using *N*-(3-{1-[5-(2-bromophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide and 1-methyl-1-phenylhydrazine: ESMS *m/e*: 572 $(M + H)^+$.

Example 795

4-(3,4-DIFLUOROPHENYL)-N-(3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-2-METHYL-6-OXO-1,4,5,6-TETRAHYDRO-3-PYRIDINECARBOXAMIDE: Prepared by Procedure AC and Scheme AM using 4-(3,4-difluorophenyl)-2-methyl-6-oxo-1,4,5,6-tetrahydro-3-pyridinecarboxylic acid and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 553.0 $(M + H)^+$.

Example 796

4-(2,4-DIFLUOROPHENYL)-*N*-{3-{4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)-2-METHYL-6-OXO-1,4,5,6-TETRAHYDRO-3-PYRIDINECARBOXAMIDE: Prepared by Procedure AC and Scheme AN using 4-(2,4-difluorophenyl)-2-methyl-6-oxo-1,4,5,6-tetrahydro-3-pyridinecarboxylic acid and *N*-{3-[1-(3-aminopropyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 553.0 $(M + H)^+$.

Example 797

N-{3-{1-[4-(4-METHOXYPHENYL)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure O and Scheme W using 4-(4-methoxyphenyl)-1-butanol and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 409 $(M + H)^+$.

Example 798

N-(4-{1-[3-(1,2-DIPHENYL-1*H*-INDOL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure O and Scheme W using 3-(1,2-diphenyl-1*H*-indol-3-yl)-1-propanol and *N*-[4-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 542.0 $(M + H)^+$.

Example 799

N-{4-[1-(3,3-DIPHENYLPROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure O and Scheme W using 3,3-diphenyl-1-propanol and *N*-[4-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 427.0 $(M + H)^+$.

Example 800

2-METHYL-*N*-(3-{1-[4-(4-NITROPHENYL)BUTYL]-4-PIPERIDINYL}PHENYL): Prepared by Procedure O and Scheme W using 4-(4-nitrophenyl)-1-butanol and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 424.2 $(M + H)^+$.

Example 801

2-METHYL-*N*-(3-{1-[2-(1-NAPHTHYL)ETHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE Prepared by Procedure O and Scheme W using 2-(1-naphthyl)ethanol and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 401.2 $(M + H)^+$.

Example 802

N-{3-[1-(3,3-DIPHENYLPROPYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE: Prepared by Procedure O and Scheme W using 3,3-diphenyl-1-propanol and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 441.2 $(M + H)^+$.

Example 803

N-(3-{1-[3-(3,4-DIMETHOXYPHENYL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure O and Scheme W using 3-(3,4-dimethoxyphenyl)-1-propanol and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 425.2 $(M + H)^+$.

Example 804

2-METHYL-*N*-{3-[1-(3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure O and Scheme W using 3-phenyl-1-propanol and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 365.2 $(M + H)^+$.

Example 805

2-METHYL-*N*-(3-{1-[3-(4-PYRIDINYL)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure O and Scheme W using 3-(4-pyridinyl)-1-propanol and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 366.2 $(M + H)^+$.

Example 806

***N*-{3-[1-(4-TERT-BUTYLBENZYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure AJ and Scheme AV using 1-bromomethyl)-4-tert-butylbenzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 393.0 $(M + H)^+$.

Example 807

***N*-{3-[1-(4-BENZOYLBENZYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure AJ and Scheme AV using [4-(bromomethyl)phenyl](phenyl)methanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS m/e: 441.0 $(M + H)^+$.

1,2-DICHLORO-4-{[(1*S*)-3-CHLORO-1-PHENYLPROPYL]OXY}BENZENE: Prepared by Procedure A using 3,4-dichlorophenol and (1*R*)-3-chloro-1-phenyl-1-propanol.

Example 808

***N*-(3-{1-[(3*S*)-3-(3,4-DICHLOROPHENOXY)-3-PHENYLPROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A using 1,2-dichloro-4-{[(1*S*)-3-chloro-1-phenylpropyl]oxy}benzene and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 525.3 $(M + H)^+$.

Example 809

N-(3-{1-[6-(2-FLUOROPHENYL)-6-HYDROXYHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure L and Scheme AN using *N*-(3-{1-[6-(2-fluorophenyl)-6-oxohexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 441.3 $(M + H)^+$.

Example 810

N-[3-(1-{5-HYDROXY-5-[4-(TRIFLUOROMETHYL)PHENYL]PENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure L and Scheme AN using 2-methyl-*N*-[3-(1-{5-oxo-5-[4-(trifluoromethyl)phenyl]pentyl}-4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 477.2 $(M + H)^+$.

Example 811

N-(3-{1-[5-(4-FLUOROPHENYL)-5-HYDROXYPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure L and Scheme AN using *N*-(3-{1-[5-(4-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 427.2 $(M + H)^+$.

Example 812

N-(3-{1-[7-(2-FLUOROPHENYL)-7-HYDROXYHEPTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure L and Scheme AN using *N*-(3-{1-[7-(2-fluorophenyl)-7-oxoheptyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 455.2 $(M + H)^+$.

Example 813

N-(3-{1-[6-(3-FLUOROPHENYL)-6-HYDROXYHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure L and Scheme AN using *N*-(3-{1-[6-(3-

fluorophenyl)-6-oxohexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 441.2 $(M + H)^+$.

Example 814

***N*-(3-{1-[5-(2-FLUOROPHENYL)-5-HYDROXYPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure L and Scheme AN using *N*-(3-{1-[5-(2-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 427.2 $(M + H)^+$.

Example 815

***N*-(3-{1-[5-(3-FLUOROPHENYL)-5-HYDROXYPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure L and Scheme AN using *N*-(3-{1-[5-(3-fluorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 427.2 $(M + H)^+$.

Example 816

***N*-(3-{1-[5-(3-CHLOROPHENYL)-5-HYDROXYPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure L and Scheme AN using *N*-(3-{1-[5-(3-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 443.1 $(M + H)^+$.

Example 817

***N*-(3-{1-[6-(4-FLUOROPHENYL)-6-HYDROXYHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure L and Scheme AN using *N*-(3-{1-[6-(4-fluorophenyl)-6-oxohexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 441.2 $(M + H)^+$.

Example 818

***N*-(3-{1-[6-(4-CHLOROPHENYL)-6-HYDROXYHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure L and Scheme AN using *N*-(3-{1-[6-(4-chlorophenyl)-6-oxohexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 456.9 $(M + H)^+$.

Example 819

***N*-(3-{1-[5-(4-CHLOROPHENYL)-5-HYDROXYPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure L and Scheme AN using *N*-(3-{1-[5-(4-chlorophenyl)-5-oxopentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 443.0 $(M + H)^+$.

Example 820

***N*-(4-{1-[(9-ETHYL-9*H*-CARBAZOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)BUTANAMIDE:** Prepared by Procedure F and Scheme R, without HOAc, using 9-ethyl-9*H*-carbazole-3-carbaldehyde and *N*-[4-(4-piperidinyl)phenyl]butanamide: ESMS *m/e*: 454.2 $(M + H)^+$.

Example 821

***N*-(3-{1-[(9-ETHYL-9H-CARBAZOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure F and Scheme R, without HOAc, using 9-ethyl-9*H*-carbazole-3-carbaldehyde and *N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 440.5 $(M + H)^+$.

Example 822

***N*-(3-{1-[(1,9-DIMETHYL-9*H*-CARBAZOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R, without HOAc, using 1,9-dimethyl-9*H*-carbazole-3-carbaldehyde and 2-methyl-*N*-[3-

(4-piperidinyl)phenyl]propanamide: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05-6.77 (m, 10H), 5.20-5.12 (m, 1H), 4.04 (s, 3H), 3.93 (s, 2H), 3.34-3.24 (m, 2H), 2.79 (s, 3H), 2.56-2.38 (m, 2H), 2.38-2.26 (m, 2H), 2.08-1.88 (m, 2H), 1.82-1.70 (m, 2H), 1.16 (d, 6H, J = 6.8 Hz); ESMS *m/e*: 454.2 $(M + H)^+$.

Example 823

***N*-(3-{1-[(9-ETHYL-9*H*-CARBAZOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)CYCLOPROPANECARBOXAMIDE:** Prepared by Procedure F and Scheme R, without HOAc, using 9-ethyl-9*H*-carbazole-3-carbaldehyde and *N*-[3-(4-piperidinyl)phenyl]cyclopropanecarboxamide: ESMS *m/e*: 452.6 $(M + H)^+$.

Example 824

1-(3-{1-[(9-ETHYL-9*H*-CARBAZOL-3-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-PYRROLIDINONE: Prepared by Scheme R and Procedure F. A solution of 1-(9-ethyl-9*H*-carbazol-3-yl)ethanone (22.3 mg, 0.100 mmol) and 1-[3-(4-piperidinyl)phenyl]-2-pyrrolidinone (27.2 mg, 0.100 mmol) in 1,2-dichloroethane (1.00 mL) was treated with sodium triacetoxyborohydride (63.6 mg, 0.300 mmol) and HOAc (5.70 uL, 0.100 mmol). The mixture was stirred overnight at room temperature. The reaction mixture was treated with a saturated aqueous $NaHCO_3$ solution (10 mL). The aqueous layer was extracted with CH_2Cl_2 (3 X 10 mL) and the combined organic layers were washed with brine (10 mL), dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by preparative TLC using 5% of NH_3 (2.0 M in methanol) in CH_2Cl_2 to give the desired product 1-(3-{1-[(9-ethyl-9*H*-carbazol-3-yl)methyl]-4-

piperidinyl}phenyl)-2- pyrrolidinone (4.60 mg, 9.43 %): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, 1H, J = 7.4 Hz), 7.99 (s, 1H), 7.43-7.28 (m, 5H), 6.96 (d, 1H, J = 7.4 Hz), 4.31 (q, 2H, J = 6.8 Hz), 3.77 (t, 2H, J = 7.3 Hz), 3.70 (s, 2H), 3.06 (d, 2H, J = 10.6 Hz), 2.56-2.42 (m, 3H) , 2.07 (m, 4H) , 1.77 (m, 4H) , 1.36 (m, 3H); ESMS *m/e*: 452.5 $(M + H)^+$.

***N*-{3-[1-(1*H*-INDOL-5-YLMETHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R, without HOAc, using 1*H*-indole-5-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 376.2 $(M + H)^+$.

1-(4-CHLOROBUTYL)-1*H*-INDOLE: Prepared by Procedure AH, and Scheme P using 1*H*-indole and 1-bromo-4-chlorobutane: ^{1}NMR (400 MHz, $CDCl_3$) δ 7.72-7.02 (m, 5H), 6.49 (d, 1H, J = 2.8 Hz), 4.13 (t, 2H, J = 6.8 Hz), 3.48 (t, 2H, J = 6.8 Hz), 2.06-1.92 (m, 2H), 1.80-1.70 (m, 2H).

1-(3-CHLOROPROPYL)-1*H*-INDOLE: Prepared by Procedure AH, and Scheme P using 1H-indole and 1-bromo-3-chloropropane: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.04 (m, 5H), 6.50 (d, 1H, J = 2.8 Hz), 4.31 (t, 2H, J = 6.8 Hz), 3.42 (t, 2H, J = 6.4 Hz), 2.28-2.20 (m, 2H).

Example 825

***N*-(4-{1-[5-(1*H*-INDOL-1-YL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure AH and Scheme P using 1-(5-chloropentyl)-1*H*-indole and 2-methyl-*N*-[4-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 432.3 $(M + H)^+$.

Example 826

***N*-(4-{1-[5-(1*H*-INDOL-1-YL)PENTYL]-4-PIPERIDINYL}PHENYL)BUTANAMIDE:** Prepared by Procedure AH and Scheme P using 1-(5-chloropentyl)-1*H*-indole and *N*-[4-(4-piperidinyl)phenyl]butanamide: ESMS *m/e*: 432.3 $(M + H)^+$.

Example 827

***N*-(4-{1-[5-(1*H*-INDOL-1-YL)PENTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure AH and Scheme P using 1-(5-chloropentyl)-1*H*-indole and *N*-[4-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 418.2 $(M + H)^+$.

Example 828

***N*-(4-{1-[6-(1*H*-INDOL-1-YL)HEXYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE:** Prepared by Procedure AH and Scheme P using 1-(6-chlorohexyl)-1*H*-indole and *N*-[4-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 432.3 $(M + H)^+$.

Example 829

2-METHYL-*N*-(3-{1-[(1-METHYL-1*H*-INDOL-2-YL)METHYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure F and Scheme R, without HOAc, using 1-methyl-1*H*-indole-2-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 390.3 $(M + H)^+$.

Example 830

***N*-{3-[1-(1*H*-INDOL-4-YLMETHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R, without HOAc, using 1*H*-indole-4-carbaldehyde and 2-

methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 376.2 $(M + H)^+$.

Example 831

***N*-{4-{1-[6-(1*H*-INDOL-1-YL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure AH and Scheme P using 1-(6-chlorohexyl)-1*H*-indole and 2-methyl-*N*-[4-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 446.3 $(M + H)^+$.

Example 832

***N*-{3-[1-(1*H*-INDOL-7-YLMETHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R, without HOAc, using 1*H*-indole-7-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 376.2 $(M + H)^+$.

Example 833

***N*-[3-(1-{[1-(4-METHOXYPHENYL)-1*H*-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-4-methoxybenzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 482.0 $(M + H)^+$.

Example 834

METHYL 4-[4-({4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}METHYL)-1*H*-INDOL-1-YL]BENZOATE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using methyl 4-iodobenzoate and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 510.3 $(M + H)^+$.

Example 835

2-METHYL-*N*-[3-(1-{[1-(3-METHYLPHENYL)-1H-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-3-methylbenzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 466.3 $(M + H)^+$.

Example 836

***N*-[3-(1-{[1-(4-FLUOROPHENYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-fluoro-4-iodobenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$) δ 7.66-6.92 (m, 12H), 6.65 (d, 1H, J = 3.2 Hz), 3.69 (s, 2H), 3.15-3.02 (m, 2H), 2.58-2.40 (m, 2H), 2.20-2.04 (m, 2H), 1.94-1.76 (m, 4H), 1.25 (d, 6H, J = 6.8 Hz); ESMS *m/e*: 470.6 $(M + H)^+$.

Example 837

***N*-(3-{1-[4-(1H-INDOL-1-YL)BUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure AH and Scheme P using 1-(4-chlorobutyl)-1H-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 418.3 $(M + H)^+$.

Example 838

***N*-[3-(1-{[1-(4-CHLOROPHENYL)-1H-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-chloro-4-iodobenzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 486.2 $(M + H)^+$.

Example 839

***N*-[3-(1-{[1-(3-METHOXYPHENYL)-1*H*-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-3-methoxybenzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 482.2 $(M + H)^+$.

Example 840

***N*-(4-{1-[4-(1*H*-INDOL-1-YL)BUTYL]-4-PIPERIDINYL}PHENYL)BUTANAMIDE:** Prepared by Procedure AH and Scheme P using 1-(4-chlorobutyl)-1*H*-indole and *N*-[4-(4-piperidinyl)phenyl]butanamide: ESMS *m/e*: 418.2 $(M + H)^+$.

Example 841

***N*-[3-(1-{[1-(2-METHOXYPHENYL)-1*H*-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-2-methoxybenzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 482.2 $(M + H)^+$.

Example 842

***N*-[3-(1-{[1-(3-CHLOROPHENYL)-1*H*-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-chloro-3-iodobenzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 486.2 $(M + H)^+$.

Example 843

METHYL 2-[5-({4-[3-(ISOBUTYRYLAMINO)PHENYL]-1-PIPERIDINYL}METHYL)-1H-INDOL-1-YL]BENZOATE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using methyl 2-iodobenzoate and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 510.2 $(M + H)^+$.

Example 844

***N*-(3-{1-[3-(1H-INDOL-1-YL)PROPYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure AH and Scheme P using 1-(3-chloropropyl)-1*H*-indole and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 404.2 $(M + H)^+$.

Example 845

2-METHYL-*N*-{3-[1-({1-[4-(TRIFLUOROMETHYL)PHENYL]-1H-INDOL-5-YL}METHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-4-(trifluoromethyl)benzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 520.2 $(M + H)^+$.

Example 846

***N*-(3-{1-[(1-[1,1'-BIPHENYL]-2-YL-1H-INDOL-5-YL)METHYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 2-iodo-1,1'-biphenyl and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 528.3 $(M + H)^+$.

Example 847

2-METHYL-*N*-[3-(1-{[1-(2-METHYLPHENYL)-1*H*-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-2-methylbenzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 466.2 $(M + H)^+$.

Example 848

2-METHYL-*N*-[3-(1-{[1-(4-METHYLPHENYL)-1*H*-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-4-methylbenzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 466.3 $(M + H)^+$.

Example 849

***N*-[3-(1-{[1-(2-CHLOROPHENYL)-1*H*-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-chloro-2-iodobenzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 486.2 $(M + H)^+$.

Example 850

2-METHYL-*N*-{3-[1-({1-[3-(TRIFLUOROMETHYL)PHENYL]-1*H*-INDOL-5-YL}METHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-3-(trifluoromethyl)benzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$) δ 7.80-6.94 (m, 12H), 6.69 (d, 1H, J = 3.6 Hz), 3.36 (s, 2H), 3.10-3.00 (m, 2H), 2.58-2.42 (m, 2H), 2.16-2.02 (m, 2H),

1.85-1.75 (m, 4H), 1.25 (d, 6H, J = 7.2 Hz); ESMS *m/e*: 520.2 $(M + H)^+$.

Example 851

2-METHYL-*N*-[3-(1-{[1-(2-NITROPHENYL)-1*H*-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-2-nitrobenzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 497.2 $(M + H)^+$.

Example 852

***N*-[3-(1-{[1-(2-FLUOROPHENYL)-1*H*-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-fluoro-2-iodobenzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 470.2 $(M + H)^+$.

Example 853

2-METHYL-*N*-[3-(1-{[1-(1-NAPHTHYL)-1*H*-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodonaphthalene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 502.2 $(M + H)^+$.

Example 854

***N*-[3-(1-{[1-(2,3-DICHLOROPHENYL)-1*H*-INDOL-5-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1,2-dichloro-3-iodobenzene and *N*-{3-[1-(1*H*-indol-5-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ^1H

NMR (400 MHz, $CDCl_3$) δ 7.68-6.94 (m, 12H), 6.68 (d, 1H, J = 2.8 Hz), 3.69 (s, 2H), 3.15-3.02 (m, 2H), 2.54-2.42 (m, 2H), 2.18-2.02 (m, 2H), 1.88-1.76 (m, 4H), 1.25 (d, 6H, J = 6.8 Hz); ESMS *m/e*: 520.1 $(M + H)^+$.

Example 855

***N*-[3-(1-{[1-(2,3-DICHLOROPHENYL)-1*H*-INDOL-7-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1,2-dichloro-3-iodobenzene and *N*-{3-[1-(1*H*-indol-7-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 520.2 $(M + H)^+$.

Example 856

***N*-[3-(1-{[1-(3-METHOXYPHENYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-3-methoxybenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 482.3 $(M + H)^+$.

Example 857

***N*-[3-(1-{[1-(2,3-DICHLOROPHENYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1,2-dichloro-3-iodobenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 520.2 $(M + H)^+$.

Example 858

***N*-[3-(1-{[1-(3-CHLOROPHENYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu,

using 1-chloro-3- iodobenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 486.2 $(M + H)^+$.

Example 859

2-METHYL-*N*-[3-(1-{[1-(3-METHYLPHENYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-3-methylbenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 466.3 $(M + H)^+$.

Example 860

***N*-[3-(1-{[1-(3-METHOXYPHENYL)-1H-INDOL-7-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-3-methoxybenzene and *N*-{3-[1-(1*H*-indol-7-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 482.3 $(M + H)^+$.

Example 861

2-METHYL-*N*-{3-[1-({1-[3-(TRIFLUOROMETHYL)PHENYL]-1H-INDOL-4-YL}METHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-3-(trifluoromethyl)benzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 520.2 $(M + H)^+$.

Example 862

***N*-[3-(1-{[1-(3,4-DIMETHYLPHENYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-

piperidinyl]phenyl}-2- methylpropanamide and 4-iodo-1,2-dimethylbenzene: ESMS *m/e*: 480.0 (M + H)$^+$.

Example 863

***N*-[3-(1-{[1-(3,4-DIFLUOROPHENYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1,3-dichloro-5-iodobenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 520.0 (M + H)$^+$.

Example 864

***N*-[3-(1-{[1-(3,4-DICHLOROPHENYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1,2-dichloro-4-iodobenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 520.0 (M + H)$^+$.

Example 865

***N*-[3-(1-{[1-(2-CHLORO-4-FLUOROPHENYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 2-chloro-4-fluoro-1-iodobenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 504.0 (M + H)$^+$.

Example 866

***N*-[3-(1-{[1-(2,4-DIFLUOROPHENYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 2,4-difluoro-1-iodobenzene and *N*-{3-[1-(1*H*-indol-

4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 488.0 $(M + H)^+$.

Example 867

2-METHYL-*N*-[3-(1-{[1-(3-PYRIDINYL)-1H-INDOL-7-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 3-iodopyridine and *N*-{3-[1-(1*H*-indol-7-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 453.1 $(M + H)^+$.

Example 868

***N*-{3-[1-(1H-INDOL-6-YLMETHYL)-4-PIPERIDINYL]PHENYL}-2-METHYLPROPANAMIDE:** Prepared by Procedure F and Scheme R using 1*H*-indole-6-carbaldehyde and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 376.2 $(M + H)^+$.

Example 869

2-METHYL-*N*-[3-(1-{[1-(4-PYRIDINYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 4-iodopyridine and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 453.2 $(M + H)^+$.

Example 870

2-METHYL-*N*-[3-(1-{[1-(2-PYRIDINYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 2-iodopyridine and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 453.2 $(M + H)^+$.

Example 871

N-[3-(1-{[1-(2-FLUOROPHENYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-fluoro-2-iodobenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 470.1 $(M + H)^+$.

Example 872

N-[3-(1-{[1-(4-CHLOROPHENYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-chloro-4-iodobenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 486.1 $(M + H)^+$.

Example 873

2-METHYL-*N*-[3-(1-{[1-(3-PYRIDINYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 3-iodopyridine and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 453.2 $(M + H)^+$.

Example 874

N-[3-(1-{[1-(2,3-DIMETHYLPHENYL)-1*H*-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-2,3-dimethylbenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 480.1 $(M + H)^+$.

Example 875

N-[3-(1-{[1-(3-FLUOROPHENYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-fluoro-3-iodobenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 470.1 $(M + H)^+$.

Example 876

2-METHYL-*N*-{3-[1-({1-[2-(TRIFLUOROMETHYL)PHENYL]-1H-INDOL-4-YL}METHYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-2-(trifluoromethyl)benzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 520.1 $(M + H)^+$.

Example 877

N-[3-(1-{[1-(2-CHLOROPHENYL)-1H-INDOL-4-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-chloro-2-iodobenzene and *N*-{3-[1-(1*H*-indol-4-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 486.1 $(M + H)^+$.

Example 878

N-[3-(1-{[1-(2,3-DIMETHYLPHENYL)-1H-INDOL-7-YL]METHYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure C and Scheme Q1, with CuBr in place of Cu, using 1-iodo-2,3-dimethylbenzene and *N*-{3-[1-(1H-indol-7-ylmethyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 480.0 $(M + H)^+$.

2-METHYL-*N*-[3-(1-{5-OXO-5-[4-(TRIFLUOROMETHYL)PHENYL]PENTYL}-4-PIPERIDINYL)PHENYL]PROPANAMIDE: Prepared by Procedure K and Scheme E using 5-chloro-1-[4-(trifluoromethyl)phenyl]-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 475.1 (M + H)$^+$.

N-(3-{1-[5-(4-FLUOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure K and Scheme E using 5-chloro-1-(4-fluorophenyl)-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 425.2 (M + H)$^+$.

N-(3-{1-[5-(3-FLUOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure K and Scheme E using 5-chloro-1-(3-fluorophenyl)-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 425.2 (M + H)$^+$.

N-(3-{1-[5-(3-CHLOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure K and Scheme E using 5-chloro-1-(3-chlorophenyl)-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 441.1 (M + H)$^+$.

N-(3-{1-[5-(4-CHLOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure K and Scheme E using 5-chloro-1-(4-chlorophenyl)-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 441.1 (M + H)$^+$.

Example 879

2-METHYL-*N*-{3-[1-(3-OXO-3-PHENYLPROPYL)-4-PIPERIDINYL]PHENYL}PROPANAMIDE: Prepared by Procedure K and Scheme E using K_2CO_3 instead of Na_2CO_3 and NaI instead of KI and 3-chloro-1-phenyl-1-propanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 379.3 $(M + H)^+$.

Example 880

***N*-(3-{1-[7-(2-FLUOROPHENYL)-7-OXOHEPTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme E using K_2CO_3 instead of Na_2CO_3 and NaI instead of KI and 7-chloro-1-(2-fluorophenyl)-1-heptanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ^1H NMR (400 MHz, $CDCl_3$), δ 8.17 (s, br, 1H), 8.06-6.88 (m, 8H), 3.08-2.94 (m, 4H), 2.62-2.48 (m, 1H), 2.48-2.38 (m, 1H), 2.38-2.15 (m, 2H), 2.02-1.92 (m, 2H), 1.84-1.77 (m, 4H), 1.77-1.66 (m, 2H), 1.62-1.46 (m, 2H), 1.46-1.29 (M, 4H), 1.21 (d, 6H, J = 6.8 Hz); ESMS *m/e*: 453.2 $(M + H)^+$.

Example 881

***N*-(3-{1-[5-(2-FLUOROPHENYL)-5-OXOPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme E using K_2CO_3 instead of Na_2CO_3 and NaI instead of KI and 5-chloro-1-(2-fluorophenyl)-1-pentanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 425.2 $(M + H)^+$.

Example 882

***N*-(3-{1-[6-(3-FLUOROPHENYL)-6-OXOHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme E using K_2CO_3 instead of Na_2CO_3 and

NaI instead of KI and 6-chloro-1-(3-fluorophenyl)-1-hexanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 439.2 $(M + H)^+$.

Example 883

***N*-(3-{1-[6-(2-FLUOROPHENYL)-6-OXOHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme E using K_2CO_3 instead of Na_2CO_3 and NaI instead of KI and 6-chloro-1-(2-fluorophenyl)-1-hexanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 439.2 $(M + H)^+$.

Example 884

***N*-(3-{1-[7-(4-FLUOROPHENYL)-7-OXOHEPTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme E using K_2CO_3 instead of Na_2CO_3 and NaI instead of KI and 7-chloro-1-(4-fluorophenyl)-1-heptanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 453.2 $(M + H)^+$.

Example 885

***N*-(3-{1-[6-(4-CHLOROPHENYL)-6-OXOHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme E using K_2CO_3 instead of Na_2CO_3 and NaI instead of KI and 6-chloro-1-(4-chlorophenyl)-1-hexanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 455.1 $(M + H)^+$.

Example 886

***N*-(3-{1-[7-(4-CHLOROPHENYL)-7-OXOHEPTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme E using K_2CO_3 instead of Na_2CO_3 and NaI instead of KI and 7-chloro-1-(4-chlorophenyl)-1-

heptanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 469.1 $(M + H)^+$.

Example 887

***N*-(3-{1-[6-(4-FLUOROPHENYL)-6-OXOHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K and Scheme E using K_2CO_3 instead of Na_2CO_3 and NaI instead of KI and 6-chloro-1-(4-fluorophenyl)-1-hexanone and 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide: ESMS *m/e*: 439.1 $(M + H)^+$.

Example 888

***N*-(3-{1-[6-(3-ACETYLPHENOXY)-6-(2-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 1-(3-hydroxyphenyl)ethanone and *N*-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 559.5 $(M + H)^+$.

Example 889

***N*-(3-{1-[6-(2-FLUOROPHENOXY)-6-(2-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluorophenol and *N*-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 535.1 $(M + H)^+$.

Example 890

***N*-(3-{1-[6-(4-FLUOROPHENOXY)-6-(2-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-fluorophenol and *N*-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^1H NMR (400 MHz,

$CDCl_3$), HCl salt δ 7.72- 6.72 (m, 12H), 5.42-5.34 (m, 1H), 3.68-3.58 (m, br, 2H), 3.02-2.92 (m, 2H), 2.80-2.46 (m, 6H), 2.05-1.78 (m, 6H), 1.68-1.56 (m, 1H), 1.56-1.38 (m, 3H), 1.25 (d, 6H, J = 6.8 Hz); ESMS *m/e*: 535.1 $(M + H)^+$.

Example 891

***N*-(3-{1-[6-(2-FLUOROPHENYL)-6-(2-METHOXYPHENOXY)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-methoxyphenol and *N*-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 547.0 $(M + H)^+$.

Example 892

***N*-(3-{1-[6-(2-FLUOROPHENYL)-6-(4-METHOXYPHENOXY)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-methoxyphenol and *N*-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 547.1 $(M + H)^+$.

Example 893

***N*-(3-{1-[6-(4-ACETYLPHENOXY)-6-(2-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 1-(4-hydroxyphenyl)ethanone and *N*-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 559.2 $(M + H)^+$.

Example 894

***N*-(3-{1-[6-(3,4-DIMETHOXYPHENOXY)-6-(2-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-**

METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 3,4-dimethoxyphenol and *N*-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 577.6 $(M + H)^+$.

Example 895

N-(3-{1-[6-(2-ETHOXYPHENOXY)-6-(2-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 2-ethoxyphenol and *N*-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 561.1 $(M + H)^+$.

Example 896

N-(3-{1-[6-(4-BROMOPHENOXY)-6-PHENYLHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 4-bromophenol and *N*-{3-[1-(6-hydroxy-6-phenylhexyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 577.0 $(M + H)^+$.

Example 897

N-(3-{1-[6-(4-FLUOROPHENOXY)-6-(4-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 4-fluorophenol and *N*-(3-{1-[6-(4-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$), HCl salt δ 8.22 (s, br, 1H), 7.74-6.70 (m, 12H), 5.05-4.94 (m, 1H), 3.66-3.52 (m, br, 2H), 3.02-2.83 (m, br, 2H), 2.81-2.58 (m, br, 4H), 2.58-2.36 (m, br, 2H), 2.02-1.66 (m, br, 6H), 1.66-1.46 (m, br, 1H), 1.46-1.35 (m, br, 3H), 1.26 (d, 6H, J = 6.0 Hz); ESMS *m/e*: 535.1 $(M + H)^+$.

Example 898

N-(3-{1-[6-(4-METHOXYPHENOXY)-6-PHENYLHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 4-methoxyphenol and *N*-{3-[1-(6-hydroxy-6-phenylhexyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 529.6 $(M + H)^+$.

Example 899

N-(3-{1-[6-(4-CHLOROPHENOXY)-6-(4-CHLOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 4-chlorophenol and *N*-(3-{1-[6-(4-chlorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 566.9 $(M + H)^+$.

Example 900

N-(3-{1-[6-(4-BROMOPHENOXY)-6-(4-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 4-bromophenol and *N*-(3-{1-[6-(4-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 595.0 $(M + H)^+$.

Example 901

N-(3-{1-[6-(4-CHLOROPHENOXY)-6-(4-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 4-chlorophenol and *N*-(3-{1-[6-(4-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$), HCl salt δ 7.93 (s, 1H), 7.72-6.68 (m, 12H), 5.06-4.98 (m, 1H), 3.66-3.50 (m, br, 2H), 3.02-2.82 (m, br, 2H), 2.80-2.57 (m, br, 4H), 2.57-2.38 (m, br, 2H), 2.02-1.76 (m, br, 6H), 1.64-1.48 (m, br, 1H), 1.48-1.36

(m, br, 3H), 1.25 (d, 6H, J = 6.8 Hz); Anal. Calc. for $C_{32}H_{41}Cl_2FN_2O_2 \cdot 0.5EtOAc$: C, 66.55; H, 7.18; N, 4.43; Found: C, 66.35; H, 6.86; N, 4.46. ESMS m/e: 550.8 $(M + H)^+$.

Example 902

***N*-(3-{1-[6-(4-CHLOROPHENYL)-6-(4-FLUOROPHENOXY)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-fluorophenol and *N*-(3-{1-[6-(4-chlorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$), HCl salt δ 8.22 (s, br, 1H), 7.74-6.68 (m, 12H), 5.04-4.92 (m, 1H), 3.66-3.50 (m, br, 2H), 3.00-2.82 (br, 2H), 2.80-2.58 (m, br, 4H), 2.58-2.40 (m, br, 2H), 2.00-1.68 (m, br, 6H), 1.66-1.46 (m, br, 1H), 1.46-1.36 (br, 3H), 1.25 (d, 6H, J = 7.2 Hz); ESMS m/e: 551.1 $(M + H)^+$.

Example 903

***N*-(3-{1-[6-(3-ACETYLPHENOXY)-6-PHENYLHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 1-(3-hydroxyphenyl)ethanone and *N*-{3-[1-(6-hydroxy-6-phenylhexyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS m/e: 541.2 $(M + H)^+$.

Example 904

***N*-(3-{1-[6-(4-CHLOROPHENOXY)-6-PHENYLHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-chlorophenol and *N*-{3-[1-(6-hydroxy-6-phenylhexyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$), HCl salt δ 8.28 (s, 1H), 7.78-6.70 (m, 13H), 5.08-4.98 (m, 1H), 3.64-3.46 (m, br, 2H), 3.02-2.82 (br, 2H), 2.82-2.56 (m,

br, 4H), 2.56-2.34 (m, br, 2H), 2.05-1.75 (m, br, 6H), 1.64-1.48 (m, br, 1H), 1.48-1.34 (br, 3H), 1.25 (d, 6H, J = 6.8 Hz); ESMS *m/e*: 533.1 $(M + H)^+$.

Example 905

***N*-(3-{1-[6-(4-BROMOPHENOXY)-6-(4-CHLOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-bromophenol and *N*-(3-{1-[6-(4-chlorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 611.0 $(M + H)^+$.

Example 906

***N*-(3-{1-[6-(4-CHLOROPHENYL)-6-(4-METHOXYPHENOXY)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-methoxyphenol and *N*-(3-{1-[6-(4-chlorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 563.1 $(M + H)^+$.

Example 907

***N*-(3-{1-[6-(4-FLUOROPHENYL)-6-(4-METHOXYPHENOXY)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-methoxyphenol and *N*-(3-{1-[6-(4-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$), HCl salt δ 8.11 (s, 1H), 7.65-6.84 (m, 12H), 5.21-5.10 (m, 1H), 3.66-3.56 (m, br, 2H), 3.02-2.82 (br, 2H), 2.82-2.56 (m, br, 4H), 2.54 (s, 3H), 2.53-2.32 (m, br, 2H), 2.02-1.70 (m, br, 6H), 1.64-1.48 (m, br, 1H), 1.48-1.34 (br, 3H), 1.25 (d, 6H, J = 6.8 Hz); ESMS *m/e*: 547.1 $(M + H)^+$.

Example 908

N-(3-{1-[6-(3-ACETYLPHENOXY)-6-(4-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 1-(3-hydroxyphenyl)ethanone and *N*-(3-{1-[6-(4-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 559.1 $(M + H)^+$.

Example 909

N-(3-{1-[6-(4-FLUOROPHENOXY)-6-PHENYLHEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 4-fluorophenol and *N*-{3-[1-(6-hydroxy-6-phenylhexyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$), HCl salt δ 8.05 (s, br, 1H), 7.72-6.70 (m, 13H), 5.06-4.96 (m, 1H), 3.66-3.51 (m, 2H), 3.01-2.82 (m, br, 2H), 2.82-2.57 (m, br, 4H), 2.57-2.34 (m, br, 2H), 2.05-1.78 (m, br, 6H), 1.64-1.52 (m, br, 1H), 1.52-1.16 (m, br, 3H), 1.25 (d, 6H, J = 7.2 Hz); ESMS *m/e*: 517.0 $(M + H)^+$.

Example 910

N-(3-{1-[6-(2-ACETYLPHENOXY)-6-(2-FLUOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 1-(2-hydroxyphenyl)ethanone and *N*-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 559.0 $(M + H)^+$.

Example 911

N-[3-(1-{6-(4-FLUOROPHENYL)-6-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]HEXYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and *N*-(3-{1-

[6-(4-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^{1}H NMR (400 MHz, $CDCl_3$), HCl salt δ 8.23 (s, br, 1H), 7.74-6.88 (m, 11H), 5.20-5.12 (m, 1H), 3.68-3.52 (m, br, 2H), 3.02-2.82 (m, br, 2H), 2.82-2.60 (m, 4H), 2.58-2.38 (m, br, 2H), 2.12-2.02 (m, br, 1H), 2.02-1.80 (m, br, 5H), 1.68-1.52 (m, br, 1H), 1.52-1.36 (br, 3H), 1.25 (d, 6H, J = 7.2 Hz) ; ESMS *m/e*: 603.3 $(M + H)^+$.

Example 912

***N*-(3-{1-[6-(3-ACETYLPHENOXY)-6-(4-CHLOROPHENYL)HEXYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 1-(3-hydroxyphenyl)ethanone and *N*-(3-{1-[6-(4-chlorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^{1}H NMR (400 MHz, $CDCl_3$), HCl salt δ 8.41 (s, 1H), 7.72-6.84 (m, 12H), 5.18-5.10 (m, 1H), 3.62-3.50 (m, br, 2H), 3.00-2.92 (m, 2H), 2.90-2.58 (m, 4H), 2.54 (s, 3H), 2.50-2.12 (m, 2H), 2.02-1.70 (m, br, 6H), 1.64-1.50 (m, br, 1H), 1.50-1.14 (m, br, 3H), 1.25 (d, 6H, J = 6.8 Hz); ESMS *m/e*: 575.3 $(M + H)^+$.

Example 913

***N*-[3-(1-{6-(2-FLUOROPHENYL)-6-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]HEXYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and *N*-(3-{1-[6-(2-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^{1}H NMR (400 MHz, $CDCl_3$), HCl salt δ 8.35 (s, 1H), 7.68-6.82 (m, 11H), 5.58-5.48 (m, 1H), 3.64-3.50 (m, 2H), 3.01-2.94 (m, br, 2H), 2.92-2.54 (m, 4H), 2.48-2.32 (m, br, 2H), 2.20-2.04 (m, 1H), 2.01-1.80 (m, 5H), 1.70-1.54 (m, 1H), 1.54-1.36

(m, 3H), 1.25 (d, 6H, J = 7.2 Hz). Anal. Calc. for $C_{34}H_{40}ClF_3N_2O_2 \cdot 0.6MeOH$: C, 63.12; H, 6.49; N, 4.25; Found: C, 63.38; H, 6.61; N, 3.95. ESMS *m/e*: 603.3 $(M + H)^+$.

Example 914

***N*-[3-(1-{6-(4-CHLOROPHENYL)-6-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]HEXYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and *N*-(3-{1-[6-(4-chlorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 619.2 $(M + H)^+$.

Example 915

***N*-[3-(1-{6-(3-FLUOROPHENYL)-6-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]HEXYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and *N*-(3-{1-[6-(3-fluorophenyl)-6-hydroxyhexyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 603.3 $(M + H)^+$.

Example 916

***N*-[3-(1-{6-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]-6-PHENYLHEXYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and *N*-{3-[1-(6-hydroxy-6-phenylhexyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 585.3 $(M + H)^+$.

Example 917

***N*-[3-(1-{7-(2-FLUOROPHENYL)-7-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]HEPTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme

AN using 2-fluoro-5-(trifluoromethyl)phenol and *N*-(3-{1-[7-(2-fluorophenyl)-7-hydroxyheptyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 617.3 $(M + H)^+$.

Example 918

***N*-(3-{1-[5-(4-FLUOROPHENYL)-5-(4-METHOXYPHENOXY)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-methoxyphenol and *N*-(3-{1-[5-(4-fluorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 533.1 $(M + H)^+$.

Example 919

***N*-(3-{1-[5-(4-BROMOPHENOXY)-5-(4-FLUOROPHENYL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-bromophenol and *N*-(3-{1-[5-(4-fluorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$), HCl salt δ 7.94 (s, br, 1H), 7.68-6.64 (m, 12H), 5.12-5.04 (m, 1H), 3.68-3.52 (m, br, 2H), 3.01-2.82 (br, 2H), 2.78-2.58 (m, br, 4H), 2.57-2.38 (m, br, 2H), 2.05-1.80 (m, br, 6H), 1.64-1.38 (m, br, 2H), 1.25 (d, 6H, J = 7.2 Hz); ESMS *m/e*: 581.0 $(M + H)^+$.

Example 920

***N*-(3-{1-[5-(4-CHLOROPHENOXY)-5-(4-CHLOROPHENYL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-chlorophenol and *N*-(3-{1-[5-(4-chlorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$), HCl salt δ 7.86 (s, br, 1H), 7.62-6.72 (m, 12H), 5.12-5.02 (m, 1H), 3.68-3.52 (m, br, 2H), 3.02-2.82 (br, 2H), 2.82-2.56 (m, br, 4H), 2.56-2.40 (m, br, 2H), 2.06-

1.80 (m, br, 6H), 1.64- 1.40 (m, br, 2H), 1.25 (d, 6H, J = 6.8 Hz). Anal. Calc. for $C_{32}H_{39}Cl_3N_2O_2 \cdot 1.3MeOH$: C, 63.25; H, 7.07; N, 4.42; Found: C, 63.41; H, 6.99; N, 4.17. ESMS *m/e*: 553.0 $(M + H)^+$.

Example 921

***N*-(3-{1-[5-(4-CHLOROPHENOXY)-5-PHENYLPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-chlorophenol and *N*-{3-[1-(5-hydroxy-5-phenylpentyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$), HCl salt δ 7.72-6.72 (m, 13H), 5.12-5.04 (m, 1H), 3.66-3.52 (m, br, 2H), 3.01-2.83 (br, 2H), 2.68-2.62 (m, br, 2H), 2.62-2.48 (m, br, 4H), 2.04-1.82 (m, br, 6H), 1.62-1.40 (m, br, 2H), 1.25 (d, 6H, J = 7.2 Hz); ESMS *m/e*: 519.1 $(M + H)^+$.

Example 922

***N*-(3-{1-[5-(3-ACETYLPHENOXY)-5-(4-FLUOROPHENYL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 1-(3-hydroxyphenyl)ethanone and *N*-(3-{1-[5-(4-fluorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 545.1 $(M + H)^+$.

Example 923

***N*-(3-{1-[5-(4-CHLOROPHENYL)-5-(4-FLUOROPHENOXY)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-fluorophenol and *N*-(3-{1-[5-(4-chlorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$), HCl salt δ 8.05 (s, br, 1H), 7.74-6.68 (m, 12H), 5.08-4.99 (m, 1H), 3.67-3.56 (m, br, 2H), 3.02-2.82 (br, 2H), 2.80-2.57 (m, br, 4H), 2.57-2.38 (m, br, 2H), 2.05-

1.80 (m, br, 6H), 1.64- 1.40 (m, br, 2H), 1.25 (d, 6H, J = 7.2 Hz). Anal. Calc. for $C_{32}H_{39}Cl_2FN_2O_2 \cdot 1.3EtOAc$: C, 64.93; H, 7.24; N, 4.07. Found: C, 65.01; H, 6.97; N, 3.85. ESMS *m/e*: 537.1 $(M + H)^+$.

Example 924

***N*-(3-{1-[5-(4-BROMOPHENOXY)-5-PHENYLPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-bromophenol and *N*-{3-[1-(5-hydroxy-5-phenylpentyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$), HCl salt δ 7.74-6.66 (m, 13H), 5.13-5.02 (m, 1H), 3.73-3.51 (m, br, 2H), 3.05-2.83 (br, 2H), 2.83-2.62 (br, 4H), 2.62-2.42 (m, br, 2H), 2.10-1.80 (m, br, 6H), 1.65-1.37 (m, br, 2H), 1.25 (d, 6H, J = 6.8 Hz); ESMS *m/e*: 562.9 $(M + H)^+$.

Example 925

***N*-(3-{1-[5-(4-CHLOROPHENYL)-5-(4-METHOXYPHENOXY)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-methoxyphenol and *N*-(3-{1-[5-(4-chlorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$), HCl salt δ 8.13 (s, br, 1H), 7.72-6.70 (m, 12H), 5.08-4.97 (m, 1H), 3.72 (s, 3H), 3.66-3.50 (m, br, 2H), 3.03-2.82 (br, 2H), 2.80-2.54 (m, br, 4H), 2.53-2.17 (m, br, 2H), 2.08-1.78 (m, br, 6H), 1.65-1.38 (m, br, 2H), 1.25 (d, 6H, J = 6.8 Hz). Anal. Calc. for $C_{32}H_{42}Cl_2N_2O_2 \cdot 0.54CH_2Cl_2$: C, 63.80; H, 6.88; N, 4.44. Found: C, 63.84; H, 7.18; N, 4.00. ESMS *m/e*: 549.1 $(M + H)^+$.

Example 926

***N*-(3-{1-[5-(4-FLUOROPHENOXY)-5-(4-FLUOROPHENYL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-fluorophenol and *N*-(3-{1-[5-(4-fluorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^{1}H NMR (400 MHz, $CDCl_3$), HCl salt δ 7.62-6.70 (m, 12H), 5.10-5.00 (m, 1H), 3.71-3.56 (m, br, 2H), 3.04-2.82 (br, 2H), 2.78-2.64 (m, br, 3H), 2.64-2.48 (m, br, 3H), 2.05-1.82 (m, br, 6H), 1.62-1.42 (m, br, 2H), 1.25 (d, 6H, J = 6.0 Hz); ESMS *m/e*: 521.2 $(M + H)^+$.

Example 927

***N*-(3-{1-[5-(3-ACETYLPHENOXY)-5-PHENYLPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 1-(3-hydroxyphenyl)ethanone and *N*-{3-[1-(5-hydroxy-5-phenylpentyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 526.9 $(M + H)^+$.

Example 928

***N*-(3-{1-[5-(4-METHOXYPHENOXY)-5-PHENYLPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-methoxyphenol and *N*-{3-[1-(5-hydroxy-5-phenylpentyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 515.6 $(M + H)^+$.

Example 929

***N*-[3-(1-{5-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]-5-[4-(TRIFLUOROMETHYL)PHENYL]PENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and *N*-[3-(1-{5-hydroxy-5-[4-(trifluoromethyl)phenyl]pentyl}-4-

piperidinyl)phenyl]-2-methylpropanamide: ESMS *m/e*: 639.2 $(M + H)^+$.

Example 930

***N*-[3-(1-{5-(3-CHLOROPHENYL)-5-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]PENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and *N*-(3-{1-[5-(3-chlorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$), HCl salt δ 8.17 (s, br, 1H), 7.75-6.88 (m, 11H), 5.26-5.14 (m, 1H), 3.68-3.56 (m, br, 2H), 3.05-2.90 (br, 2H), 2.90-2.60 (m, br, 4H), 2.56-2.36 (m, br, 2H), 2.18-1.84 (m, br, 6H), 1.70-1.44 (m, br, 2H), 1.25 (d, 6H, J = 7.2 Hz). Anal. Calc. for $C_{33}H_{38}Cl_2F_4N_2O_2 \cdot 0.9EtOAc$: C, 60.98; H, 6.32; N, 3.89; Found: C, 60.99; H, 6.17; N, 3.81. ESMS *m/e*: 605.2 $(M + H)^+$.

Example 931

***N*-[3-(1-{5-(2-FLUOROPHENYL)-5-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]PENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and *N*-(3-{1-[5-(2-fluorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^1H NMR (400 MHz, $CDCl_3$), HCl salt δ 7.89 (s, br, 1H), 7.72-6.88 (m, 11H), 5.59-5.48 (m, 1H), 3.70-3.48 (br, 2H), 3.05-2.84 (br, 2H), 2.82-2.58 (m, br, 4H), 2.58-2.40 (m, br, 2H), 2.22-1.82 (m, br, 6H), 1.71-1.42 (m, br, 2H), 1.25 (d, 6H, J = 6.4 Hz); ESMS *m/e*: 589.3 $(M + H)^+$.

Example 932

***N*-[3-(1-{5-(3-FLUOROPHENYL)-5-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]PENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and *N*-(3-{1-[5-(3-fluorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^{1}H NMR (400 MHz, $CDCl_3$), HCl salt δ 7.79 (s, br, 1H), 7.63-6.82 (m, 11H), 5.24-5.15 (m, 1H), 3.70-3.56 (br, 2H), 3.04-2.84 (br, 2H), 2.82-2.60 (m, br, 4H), 2.60-2.42 (m, br, 2H), 2.20-1.83 (m, br, 6H), 1.70-1.44 (m, br, 2H), 1.25 (d, 6H, J = 6.4 Hz); ESMS *m/e*: 589.3 $(M + H)^+$.

Example 933

***N*-(3-{1-[5-(3-ACETYLPHENOXY)-5-(4-CHLOROPHENYL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 1-(3-hydroxyphenyl)ethanone and *N*-(3-{1-[5-(4-chlorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^{1}H NMR (400 MHz, $CDCl_3$), HCl salt δ 8.05 (s, br, 1H), 7.74-6.88 (m, 12H), 5.27-5.16 (m, 1H), 3.69-3.52 (m, br, 2H), 3.10-2.81 (br, 2H), 2.81-2.57 (m, br, 4H), 2.54 (s, 3H), 2.52-2.40 (m, br, 2H), 2.05-1.80 (m, br, 6H), 1.66-1.42 (m, br, 2H), 1.25 (d, 6H, J = 6.8 Hz); Anal. Calc. for $C_{34}H_{42}Cl_2N_2O_3 \cdot 0.5CH_2Cl_2 \cdot 1.0H_2O$: C, 63.46; H, 6.91; N, 4.30. Found: C, 63.46; H, 7.09; N, 4.00. ESMS *m/e*: 561.1 $(M + H)^+$.

Example 934

***N*-[3-(1-{5-(4-CHLOROPHENYL)-5-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]PENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol and *N*-(3-{1-

[5-(4-chlorophenyl)-5- hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ^{1}H NMR (400 MHz, $CDCl_3$), HCl salt δ 7.61-6.92 (m, 11H), 5.24-5.16 (m, 1H), 3.70-3.58 (m, 2H), 3.02-2.91 (br, 2H), 2.80-2.64 (m, br, 3H), 2.64-2.50 (m, 3H), 2.18-1.94 (m, br, 6H), 1.62-1.44 (m, br, 2H), 1.25 (d, 6H, J = 7.2 Hz); ESMS *m/e*: 605.3 $(M + H)^+$.

Example 935

***N*-[3-(1-{5-(4-FLUOROPHENYL)-5-[2-FLUORO-5-(TRIFLUOROMETHYL)PHENOXY]PENTYL}-4-PIPERIDINYL)PHENYL]-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 2-fluoro-5-(trifluoromethyl)phenol *N*-(3-{1-[5-(4-fluorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 589.3 $(M + H)^+$.

Example 936

***N*-(3-{1-[5-(4-BROMOPHENOXY)-5-(4-CHLOROPHENYL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-bromophenol and *N*-(3-{1-[5-(4-chlorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 597.2 $(M + H)^+$.

Example 937

***N*-(3-{1-[5-(4-CHLOROPHENOXY)-5-(4-FLUOROPHENYL)PENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure A and Scheme AN using 4-chlorophenol and *N*-(3-{1-[5-(4-fluorophenyl)-5-hydroxypentyl]-4-piperidinyl}phenyl)-2-methylpropanamide: ESMS *m/e*: 537.3 $(M + H)^+$.

Example 938

N-(3-{1-[5-(2-ACETYLPHENOXY)-5-PHENYLPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 1-(2-hydroxyphenyl)ethanone and *N*-{3-[1-(5-hydroxy-5-phenylpentyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 527.0 $(M + H)^+$.

Example 939

N-(3-{1-[5-(2-ETHOXYPHENOXY)-5-PHENYLPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 2-ethoxyphenol and *N*-{3-[1-(5-hydroxy-5-phenylpentyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 529.2 $(M + H)^+$.

Example 940

N-(3-{1-[5-(4-FLUOROPHENOXY)-5-PHENYLPENTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure A and Scheme AN using 4-fluorophenol and *N*-{3-[1-(5-hydroxy-5-phenylpentyl)-4-piperidinyl]phenyl}-2-methylpropanamide: ESMS *m/e*: 503.2 $(M + H)^+$.

Example 941

N-(3-{1-[4-(4-FLUOROPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure K (KI) and Scheme E (K_2CO_3) using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 4-chloro-1-(4-fluorophenyl)-1-butanone: ESMS *m/e*: 411.2 $(M + H)^+$.

Example 942

2-METHYL-*N*-(3-{1-[3-(1H-PYRROL-3-YL)PROPYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure K (KI) and Scheme E (K_2CO_3) using 2-methyl-*N*-[3-(4-

piperidinyl)phenyl]propanamide and 3-(3-bromopropyl)-1*H*-pyrrole: ESMS *m/e*: 354.2 $(M + H)^+$.

Example 943

***N*-(3-{1-[4-(4-ISOPROPYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K (KI) and Scheme E (K_2CO_3) using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 4-chloro-1-(4-isopropylphenyl)-1-butanone: ESMS *m/e*: 435.2 $(M + H)^+$.

Example 944

***N*-(3-{1-[4-(4-METHOXYPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K (KI) and Scheme E (K_2CO_3) using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 4-chloro-1-(4-methoxyphenyl)-1-butanone: ESMS *m/e*:423.2 $(M + H)^+$.

Example 945

2-METHYL-*N*-(3-{1-[4-(4-METHYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure K (KI) and Scheme E (K_2CO_3) using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 4-chloro-1-(4-methylphenyl)-1-butanone: ESMS *m/e*: 407.2 $(M + H)^+$.

Example 946

***N*-(3-{1-[4-(4-TERT-BUTYLPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE:** Prepared by Procedure K (KI) and Scheme E (K_2CO_3) using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 1-(4-tert-butylphenyl)-4-chloro-1-butanone: ESMS *m/e*: 449.2 $(M + H)^+$.

Example 947

N-(3-{1-[4-(4-BROMOPHENYL)-4-OXOBUTYL]-4-PIPERIDINYL}PHENYL)-2-METHYLPROPANAMIDE: Prepared by Procedure K (KI) and Scheme E (K_2CO_3) using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 1-(4-bromophenyl)-4-chloro-1-butanone: ESMS *m/e*: 471.3 $(M + H)^+$.

Example 948

2-METHYL-*N*-(3-{1-[4-OXO-4-(2-THIENYL)BUTYL]-4-PIPERIDINYL}PHENYL)PROPANAMIDE: Prepared by Procedure K (KI) and Scheme E (K_2CO_3) using 2-methyl-*N*-[3-(4-piperidinyl)phenyl]propanamide and 4-chloro-1-(2-thienyl)-1-butanone: ESMS *m/e*: 399.1 $(M + H)^+$.

II. Synthetic Methods for General Structures

The examples described in Section I are merely illustrative of the methods used to synthesize MCH1 antagonists. Further derivatives may be obtained utilizing generalized methods based on the synthetic methods used to synthesize the examples.

It may be necessary to incorporate protection and deprotection strategies for substituents such as amino, amido, carboxylic acid, and hydroxyl groups in the generalized synthetic methods to form further derivatives. Methods for protection and deprotection of such groups are well-known in the art, and may be found, for example in Green, T.W. and Wuts, P.G.M. (1991) Protection Groups in Organic Synthesis, 2nd Edition John Wiley & Sons, New York.

III. Oral Compositions

As a specific embodiment of an oral composition of a compound of this invention, 100 mg of one of the compounds described herein is formulated with sufficient finely divided lactose to provide a total amount of 580 to 590 mg to fill a size O hard gel capsule.

IV. Pharmacological Evaluation of Compounds at Cloned rat MCH1 Receptor

The pharmacological properties of the compounds of the present invention were evaluated at the cloned rat MCH1 receptor using protocols described below.

Host Cells

A broad variety of host cells can be used to study heterologously expressed proteins. These cells include but are not restricted to assorted mammalian lines such as: Cos-7, CHO, LM(tk-), HEK293, Peak rapid 293, etc.; insect cell lines such as: Sf9, Sf21, etc.; amphibian cells such as xenopus oocytes; and others.

COS 7 cells are grown on 150 mm plates in DMEM with supplements (Dulbecco's Modified Eagle Medium with 10% bovine calf serum, 4 mM glutamine, 100 units/ml penicillin/100 Fg/ml streptomycin) at 37°C, 5% CO_2. Stock plates of COS-7 cells are trypsinized and split 1:6 every 3-4 days.

Human embryonic kidney 293 cells are grown on 150 mm plates in DMEM with supplements (10% bovine calf serum, 4 mM glutamine, 100 units/ml penicillin/100 Fg/ml streptomycin) at 37°C, 5% CO_2. Stock plates of 293 cells are trypsinized and split 1:6 every 3-4 days.

Human embryonic kidney Peak rapid 293 (Peakr293) cells are grown on 150 mm plates in DMEM with supplements (10% fetal bovine serum, 10% L-glutamine, 50 Fg/ml gentamycin) at 37°C, 5% CO_2. Stock plates of Peak rapid 293 cells are trypsinized and split 1:12 every 3-4 days.

Mouse fibroblast LM(tk-) cells are grown on 150 mm plates in DMEM with supplements (Dulbecco's Modified Eagle Medium with 10% bovine calf serum, 4 mM glutamine, 100 units/ml penicillin/100 Fg/ml streptomycin) at 37°C, 5% CO_2. Stock plates of LM(tk-) cells are trypsinized and split 1:10 every 3-4 days.

Chinese hamster ovary (CHO) cells were grown on 150 mm plates in HAM-s F-12 medium with supplements (10% bovine calf serum, 4 mM L-glutamine and 100 units/ml penicillin/ 100 Fg/ml streptomycin) at 37°C, 5% CO_2. Stock plates of CHO cells are trypsinized and split 1:8 every 3-4 days.

Mouse embryonic fibroblast NIH-3T3 cells are grown on 150 mm plates in Dulbecco-s Modified Eagle Medium (DMEM) with supplements (10% bovine calf serum, 4 mM glutamine, 100 units/ml penicillin/100 Fg/ml streptomycin) at 37°C, 5% CO_2. Stock plates of NIH-3T3 cells are trypsinized and split 1:15 every 3-4 days.

Sf9 and Sf21 cells are grown in monolayers on 150 mm tissue culture dishes in TMN-FH media supplemented with 10% fetal calf serum, at 27°C, no CO_2. High Five insect cells are grown on 150 mm tissue culture dishes in Ex-Cell 400™ medium supplemented with L-Glutamine, also at 27°C, no CO_2.

In some cases, cell lines that grow as adherent monolayers can be converted to suspension culture to increase cell yield and provide large batches of uniform assay material for routine receptor screening projects.

Transient expression

DNA encoding proteins to be studied can be transiently expressed in a variety of mammalian, insect, amphibian and other cell lines by several methods including but not restricted to; calcium phosphate-mediated, DEAE-dextran mediated, Liposomal-mediated, viral-mediated, electroporation-mediated and microinjection delivery.

Each of these methods may require optimization of assorted experimental parameters depending on the DNA, cell line, and the type of assay to be subsequently employed.

A typical protocol for the calcium phosphate method as applied to Peak rapid 293 cells is described as follows:

Adherent cells are harvested approximately twenty-four hours before transfection and replated at a density of 3.5×10^6 cells/dish in a 150 mm tissue culture dish and allowed to incubate over night at 37°C at 5% CO_2. 250 Fl of a mixture of $CaCl_2$ and DNA (15 Fg DNA in 250 mM $CaCl_2$) is added to a 5 ml plastic tube and 500 Fl of 2X HBS (280 mM NaCl, 10 mM KCl, 1.5 mM Na_2HPO_4, 12 mM dextrose, 50 mM HEPES) is slowly added with gentle mixing. The mixture is allowed to incubate for 20 minutes at room temperature to allow a DNA precipitate to form. The DNA precipitate mixture is then added to the culture medium in each plate and incubated for 5 hours at 37°C, 5% CO_2. After the incubation, 5ml of culture medium (DMEM, 10% FBS, 10% L-glut and 50 µg/ml gentamycin) is added to each plate. The cells are then incubated for 24 to 48 hours at 37°C, 5% CO_2.

A typical protocol for the DEAE-dextran method as applied to Cos-7 cells is described as follows; Cells to be used for transfection are split 24 hours prior to the transfection to provide flasks which are 70-80% confluent at the time of transfection. Briefly, 8 Fg of receptor DNA plus 8 Fg of any additional DNA needed (e.g. G_w protein expression vector, reporter construct, antibiotic resistance marker, mock vector, etc.) are

added to 9 ml of complete DMEM plus DEAE-dextran mixture (10 mg/ml in PBS). Cos-7 cells plated into a T225 flask (sub-confluent) are washed once with PBS and the DNA mixture is added to each flask. The cells are allowed to incubate for 30 minutes at 37°C, 5% CO_2. Following the incubation, 36 ml of complete DMEM with 80 FM chloroquine is added to each flask and allowed to incubate an additional 3 hours. The medium is then aspirated and 24 ml of complete medium containing 10% DMSO for exactly 2 minutes and then aspirated. The cells are then washed 2 times with PBS and 30 ml of complete DMEM added to each flask. The cells are then allowed to incubate over night. The next day the cells are harvested by trypsinization and reseeded as needed depending upon the type of assay to be performed.

A typical protocol for liposomal-mediated transfection as applied to CHO cells is described as follows; Cells to be used for transfection are split 24 hours prior to the transfection to provide flasks which are 70-80% confluent at the time of transfection. A total of 10Fg of DNA which may include varying ratios of receptor DNA plus any additional DNA needed (e.g. G_α protein expression vector, reporter construct, antibiotic resistance marker, mock vector, etc.) is used to transfect each 75 cm^2 flask of cells. Liposomal mediated transfection is carried out according to the manufacturer=s recommendations (LipofectAMINE, GibcoBRL, Bethesda, MD). Transfected cells are harvested 24 hours post transfection and used or reseeded according the requirements of the assay to be employed.

A typical protocol for the electroporation method as applied to Cos-7 cells is described as follows; Cells to be used for transfection are split 24 hours prior to the transfection to provide flasks which are subconfluent at the time of transfection. The cells are harvested by trypsinization resuspended in their growth media and counted. 4 x 10^6 cells are suspended in 300 Fl of DMEM and placed into an electroporation cuvette. 8 Fg of receptor DNA plus 8 Fg of any additional DNA needed (e.g. G_α protein expression vector, reporter construct, antibiotic resistance marker, mock vector, etc.) is added to the cell suspension, the cuvette is placed into a BioRad Gene Pulser and subjected to an electrical pulse (Gene Pulser settings: 0.25 kV voltage, 950 FF capacitance). Following the pulse, 800 Fl of complete DMEM is added to each cuvette and the suspension transferred to a sterile tube. Complete medium is added to each tube to bring the final cell concentration to 1 x 10^5 cells/100 Fl. The cells are then plated as needed depending upon the type of assay to be performed.

A typical protocol for viral mediated expression of heterologous proteins is described as follows for baculovirus infection of insect Sf9 cells. The coding region of DNA encoding the receptor disclosed herein may be subcloned into pBlueBacIII into existing restriction sites or sites engineered into sequences 5' and 3' to the coding region of the polypeptides.. To generate baculovirus, 0.5 Fg of viral DNA (BaculoGold) and 3 Fg of DNA construct encoding a polypeptide may be co-transfected into 2 x 10^6 *Spodoptera frugiperda* insect Sf9 cells by the calcium phosphate co-precipitation method, as outlined in by Pharmingen (in "Baculovirus Expression

Vector System: Procedures and Methods Manual"). The cells then are incubated for 5 days at 27°C. The supernatant of the co-transfection plate may be collected by centrifugation and the recombinant virus plaque purified. The procedure to infect cells with virus, to prepare stocks of virus and to titer the virus stocks are as described in Pharmingen-s manual. Similar principals would in general apply to mammalian cell expression via retro-viruses, Simliki forest virus and double stranded DNA viruses such as adeno-, herpes-, and vacinia-viruses, and the like.

Stable expression

Heterologous DNA can be stably incorporated into host cells, causing the cell to perpetually express a foreign protein. Methods for the delivery of the DNA into the cell are similar to those described above for transient expression but require the co-transfection of an ancillary gene to confer drug resistance on the targeted host cell. The ensuing drug resistance can be exploited to select and maintain cells that have taken up the heterologous DNA. An assortment of resistance genes are available including but not restricted to Neomycin, Kanamycin, and Hygromycin. For the purposes of receptor studies, stable expression of a heterologous receptor protein is carried out in, but not necessarily restricted to, mammalian cells including, CHO, HEK293, LM(tk-), etc.

Cell membrane preparation

For binding assays, pellets of transfected cells are suspended in ice-cold buffer (20 mM Tris.HCl, 5 mM EDTA, pH 7.4) and homogenized by sonication for 7 sec. The

cell lysates are centrifuged at 200 x g for 5 min at 4°C. The supernatants are then centrifuged at 40,000 x g for 20 min at 4°C. The resulting pellets are washed once in the homogenization buffer and suspended in binding buffer (see methods for radioligand binding). Protein concentrations are determined by the method of Bradford (1976) using bovine serum albumin as the standard. Binding assays are usually performed immediately, however it is possible to prepare membranes in batch and store frozen in liquid nitrogen for future use.

Radioligand binding assays

Radioligand binding assays for the rat MCH1 receptor were carried out using plasmid pcDNA3.1-rMCH1-f (ATCC Patent Deposit Designation No. PTA-3505). Plasmid pcDNA3.1-rMCH1-f comprises the regulatory elements necessary for expression of DNA in a mammalian cell operatively linked to DNA encoding the rat MCH1 receptor so as to permit expression thereof. Plasmid pcDNA3.1-rMCH1-f was deposited on July 05, 2001, with the American Type Culture Collection (ATCC), 12301 Parklawn Drive, Rockville, Maryland 20852, U.S.A. under the provisions of the Budapest Treaty for the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure and was accorded ATCC Patent Deposit Designation No. PTA-3505.

Binding assays can also be performed as described hereinafter using plasmid pEKJ.HR-TL231 (ATCC Accession No. 203197) Plasmid pEKJ.HR-TL231 encodes the human MCH1 receptor and was deposited on September 17, 1998, with the American Type Culture Collection (ATCC), 12301

Parklawn Drive, Rockville, Maryland 20852, U.S.A. under the provisions of the Budapest Treaty for the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure and was accorded ATCC Accession No. 203197.

Human embryonic kidney Peak rapid 293 cells (Peakr293 cells) were transiently transfected with DNA encoding the MCH1 receptor utilizing the calcium phosphate method and cell membranes were prepared as described above. Binding experiments with membranes from Peakr293 cells transfected with the rat MCH1 receptor were performed with 0.08 nM [^{3}H]Compound A (the synthesis of Compound A is described in detail below) using an incubation buffer consisting of 50 mM Tris pH 7.4, 10 mM $MgCl_2$, 0.16 mM PMSF, 1 mM 1,10 phenantroline and 0.2% BSA. Binding was performed at 25°C for 90 minutes. Incubations were terminated by rapid vacuum filtration over GF/C glass fiber filters, presoaked in 5% PEI using 50 nM Tris pH 7.4 as wash buffer. In all experiments, nonspecific binding is defined using 10 pM Compound A.

Functional assays

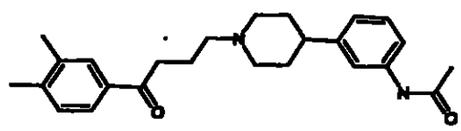
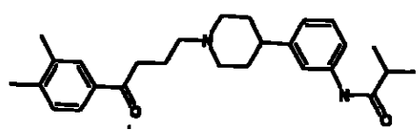
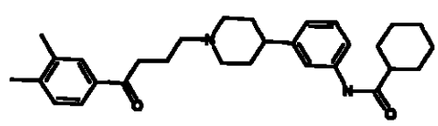
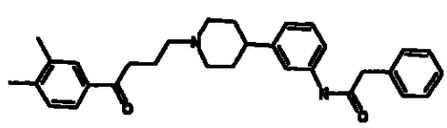
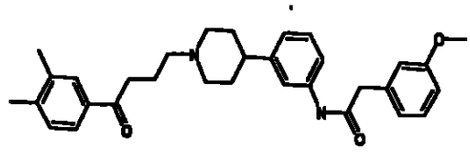
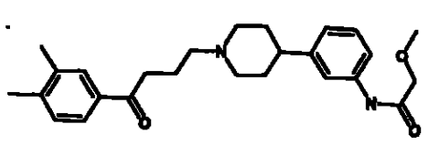
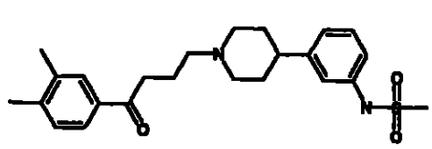
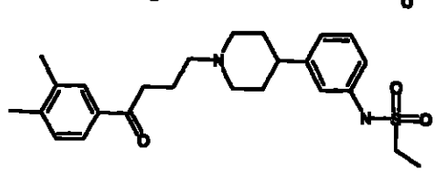
Cells may be screened for the presence of endogenous mammalian receptor using functional assays. Cells with no or a low level of endogenous receptor present may be transfected with the exogenous receptor for use in functional assays.

A wide spectrum of assays can be employed to screen for receptor activation. These range from traditional measurements of phosphatidyl inositol, cAMP, Ca^{++}, and

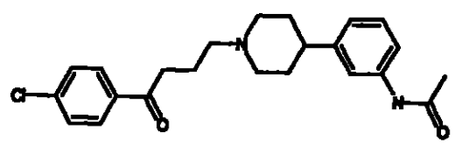
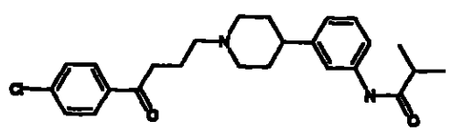
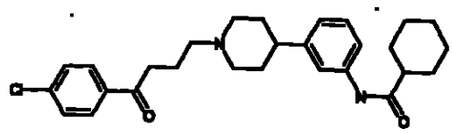
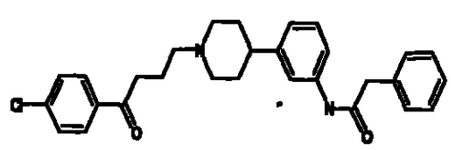
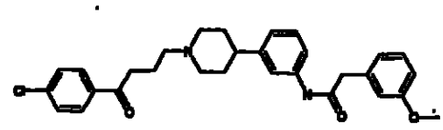
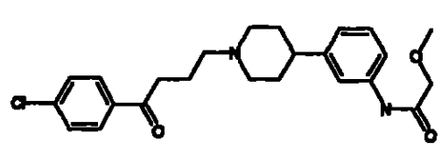
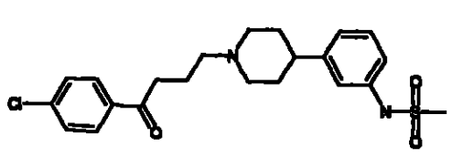
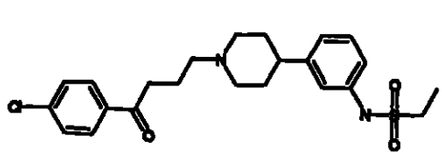
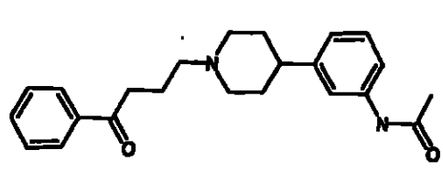
K^+, for example; to systems measuring these same second messengers but which have been modified or adapted to be higher throughput, more generic, and more sensitive; to cell based platforms reporting more general cellular events resulting from receptor activation such as metabolic changes, differentiation, and cell division/proliferation, for example; to high level organism assays which monitor complex physiological or behavioral changes thought to be involved with receptor activation including cardiovascular, analgesic, orexigenic, anxiolytic, and sedation effects, for example.

Radioligand Binding Assay Results

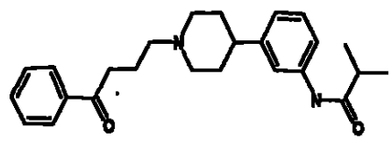
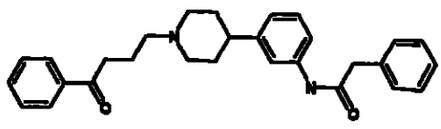
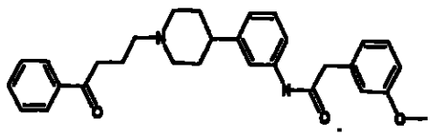
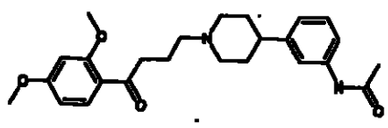
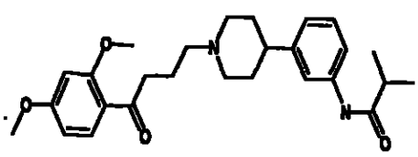
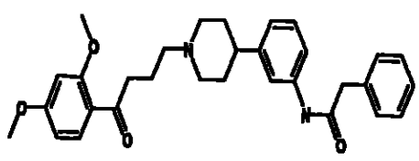
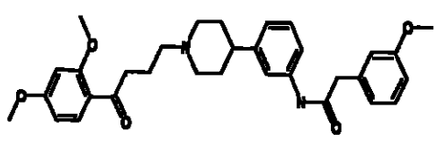
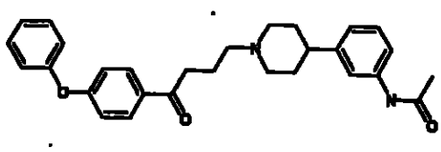
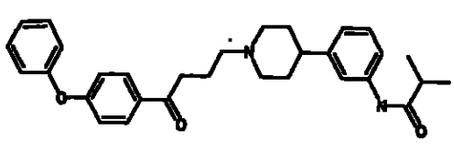
The compounds described above were assayed using cloned rat MCH1. The binding affinities of the compounds are shown in Table I.

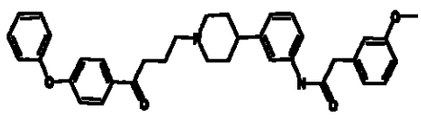
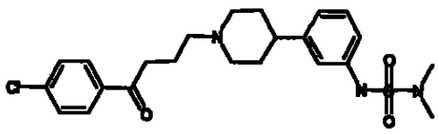
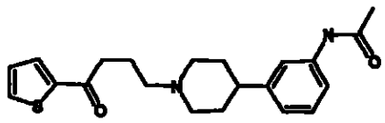
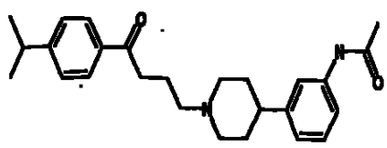
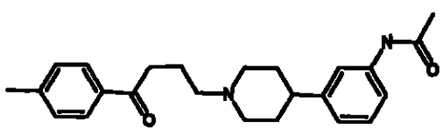
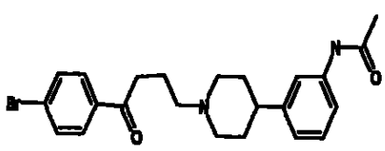
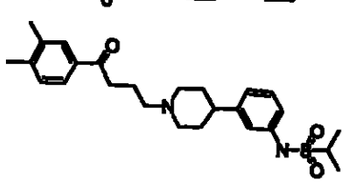
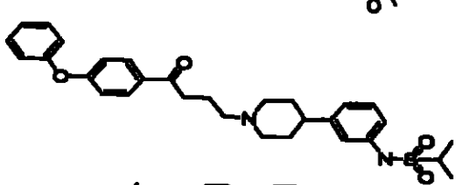
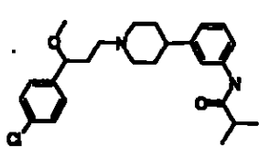
EXAMPLE No.	STRUCTURE	Ki (nM) rMCH1
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2		3.9
3		768
4		357
5		14.2
6		274
7		1000
8		627

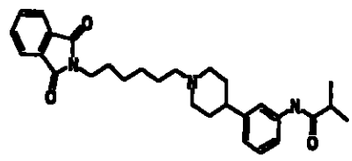
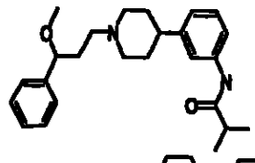
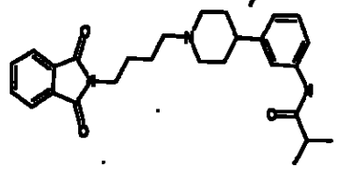
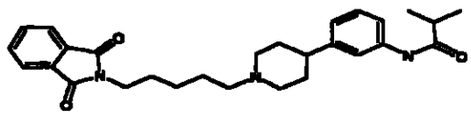
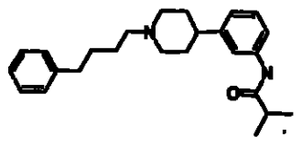
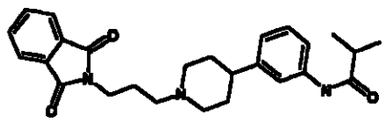
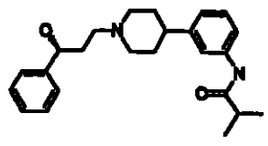
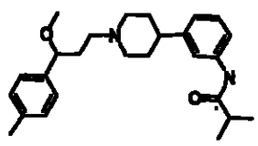
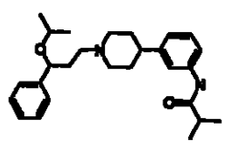
503

9		69
10		2.8
11		197
12		84
13		11.9
14		167
15		720
16		272
17		342

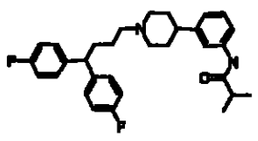
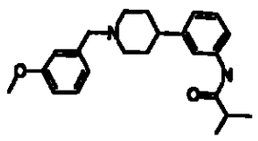
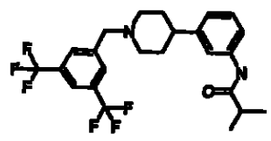
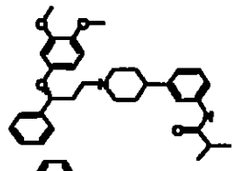
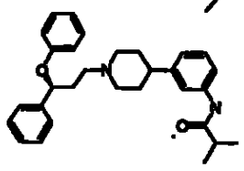
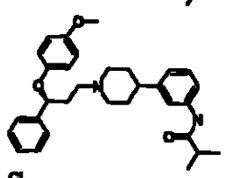
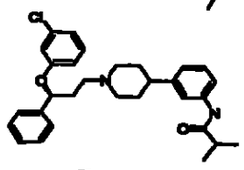
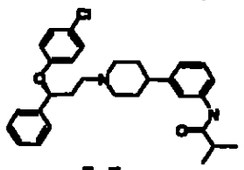
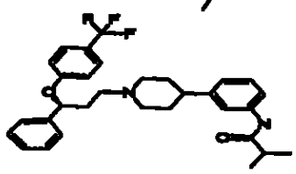
504

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19		506
20		21
21		630
22		.52
23		1036
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25		483
26		192

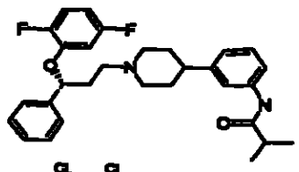
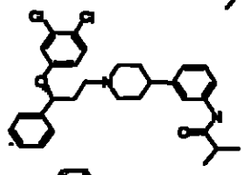
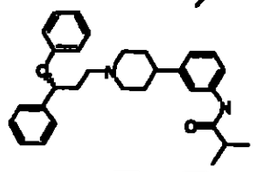
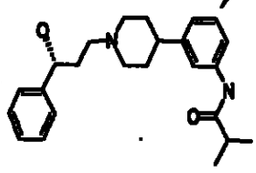
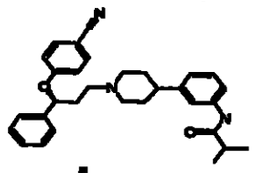
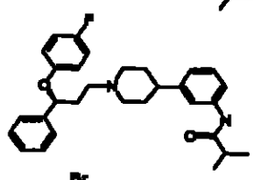
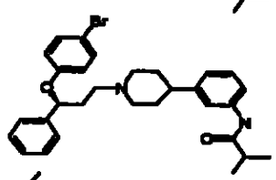
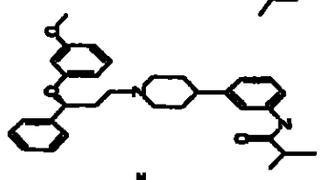
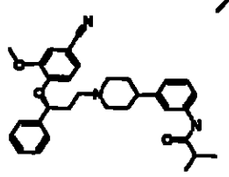
27		91
28		511
29		654
30		382
31		382
32		160
33		615
34		651
35		11.5

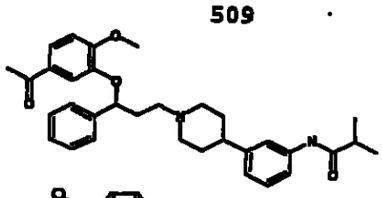
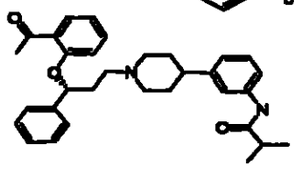
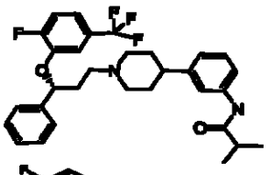
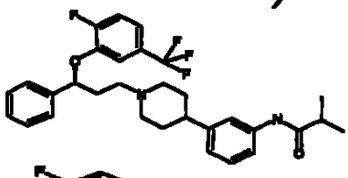
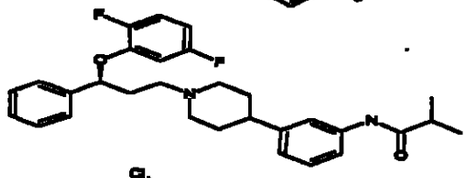
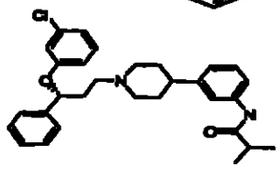
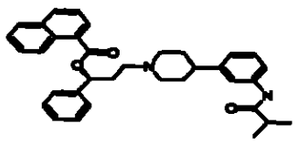
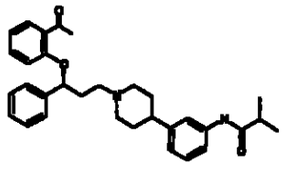
36		62
37		29.1
38		18.2
39		11.8
40		.50
41		946
42		118
43		12
44		11.5

507

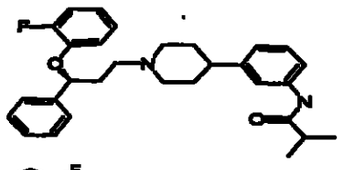
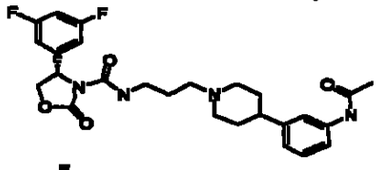
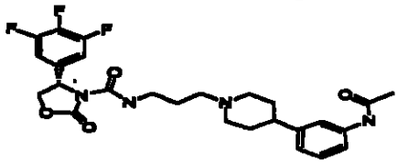
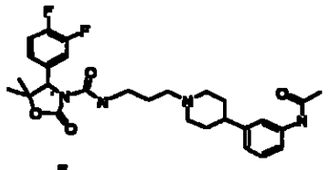
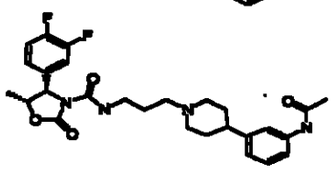
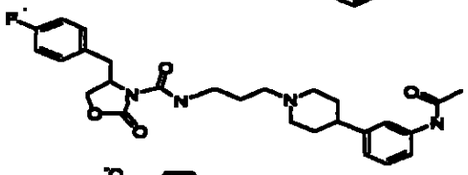
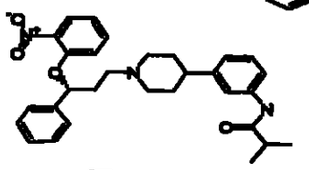
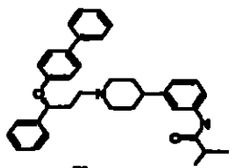
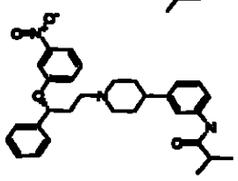
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46		187
47		52
48		6.7
49		7.1
50		3.9
51		3.1
52		3.8
53		7.1

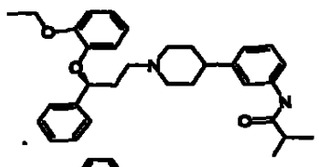
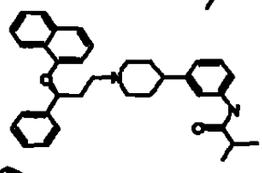
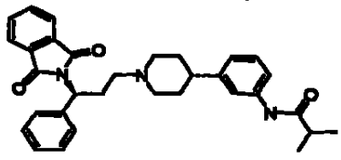
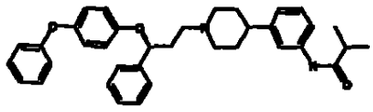
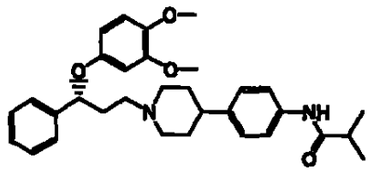
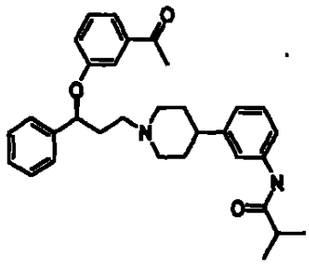
508

54		4.9
55		5
56		22.3
57		16.6
58		2.01
59		12.9
60		0.923
61		13.8
62		12.8

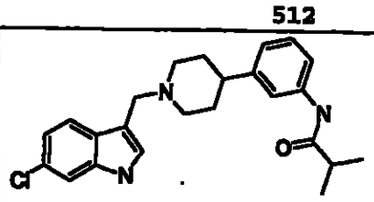
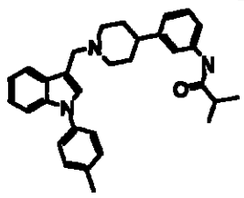
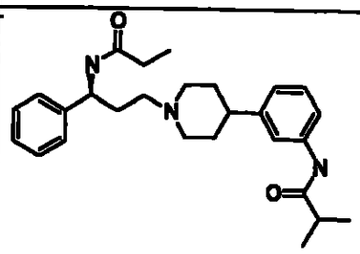
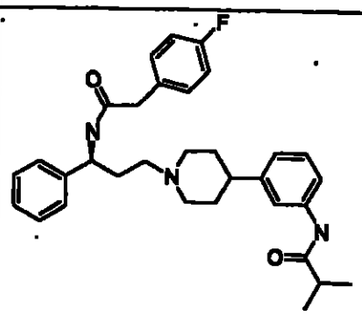
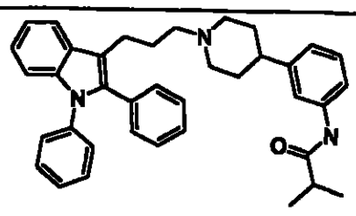
63		22.4
64		14.8
65		17
66		3.3
67		.5.9
68		9.3
69		32.5
70		60

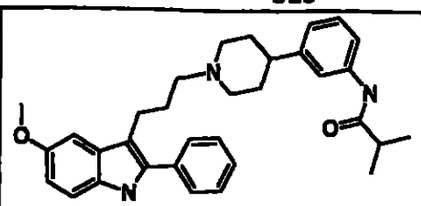
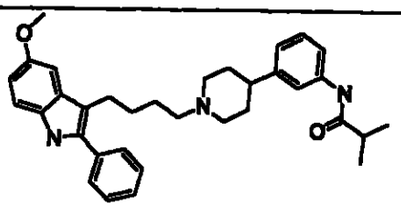
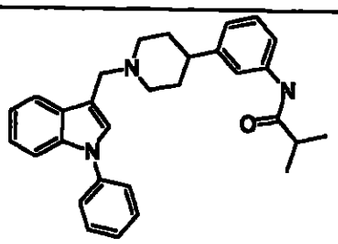
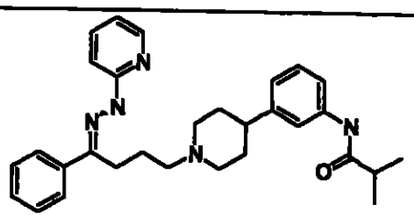
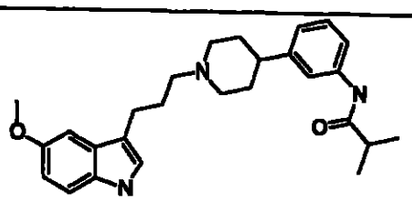
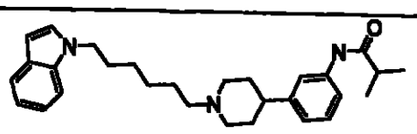
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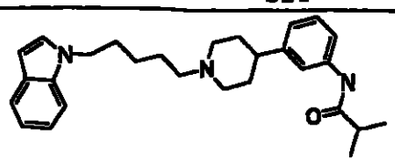
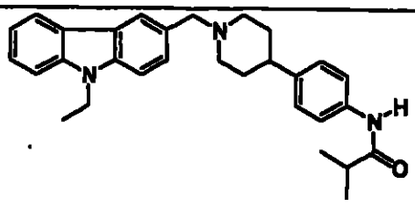
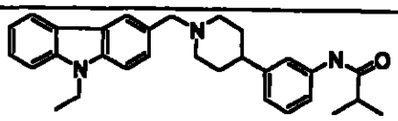
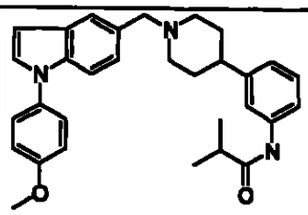
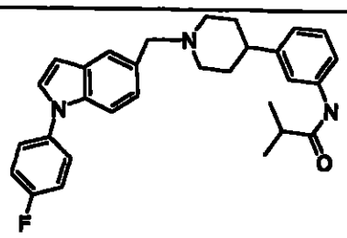
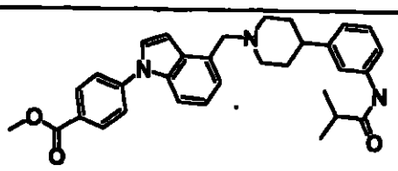
71		6.6
72		31.4
73		22.3
74		48.6
75		11.8
76		44.6
77		25.7
78		22.2
79		19.4

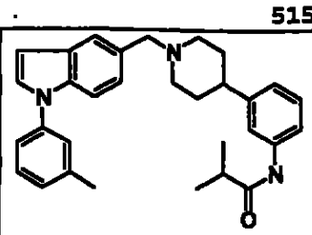
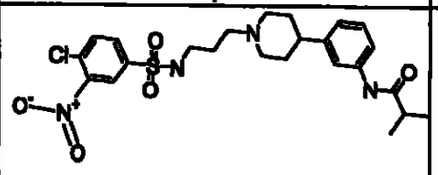
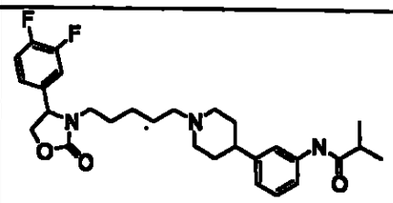
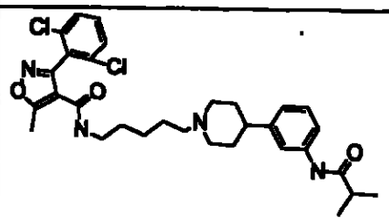
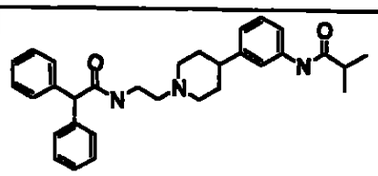
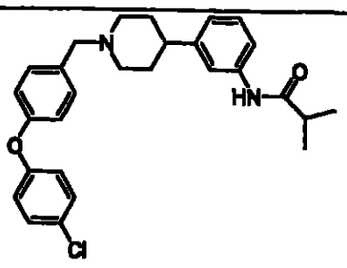
80		14.3
81		377
82		11.2
83		48.1
84		121
85		3.2

EXAMPLE	STRUCTURE	Ki (nM) rMCH1

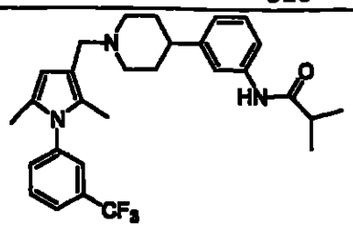
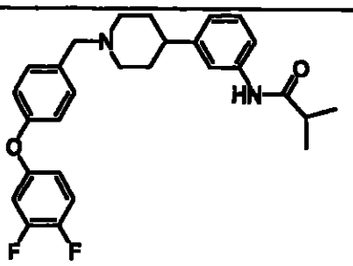
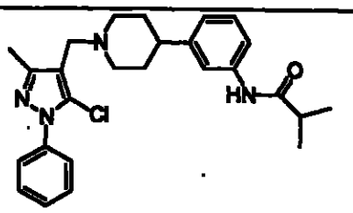
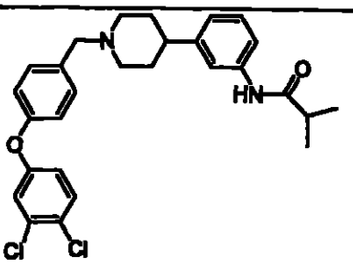
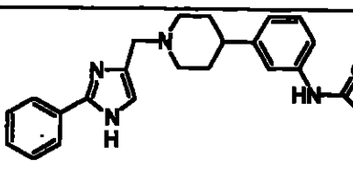
86		20.6
87		14.9
88		16.0
89		3.0
90		3.0

91		2.3
92		8.0
93		4.2
94		2.3
95		5.4
96		15.9

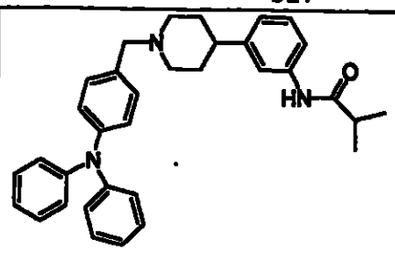
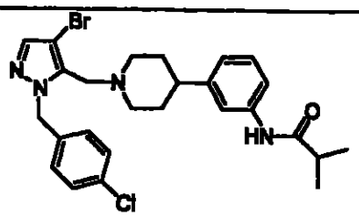
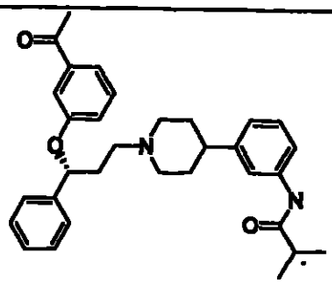
97		27.3
98		37.9
99		1.7
100		27.5
101		7.8
102		38.4

103		21.3
104		11.2
105		4.6
106		7.1
107		1.7
108		5.2

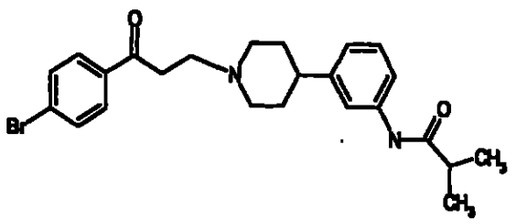
516

109		20.9
110		1.8
111		ND
112		6.1
113		ND

517

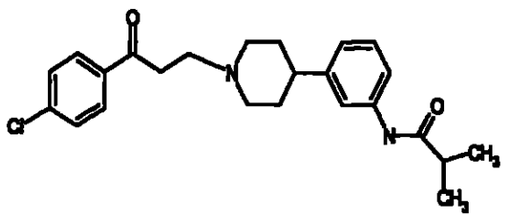
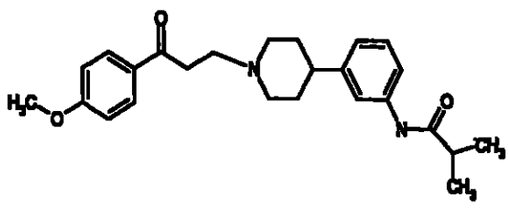
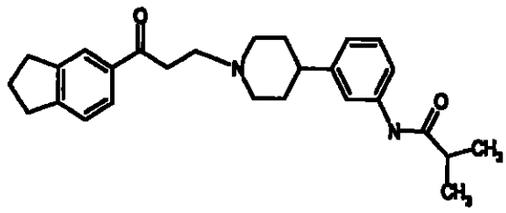
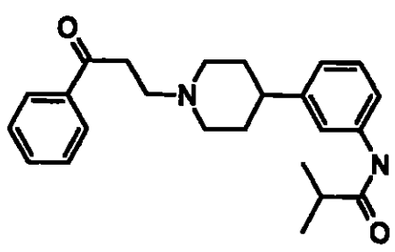
114		3.6
115		ND
116		3.8

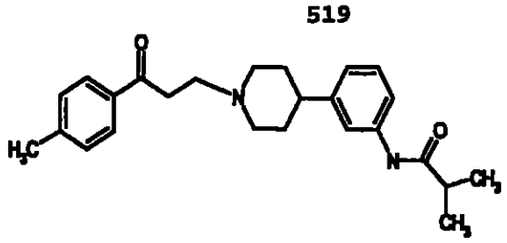
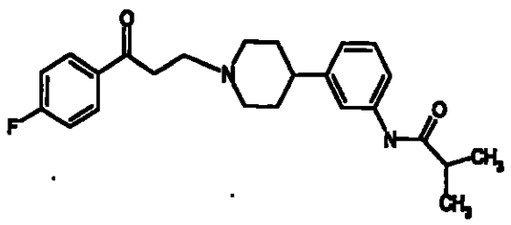
117

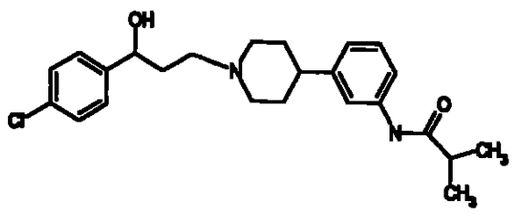
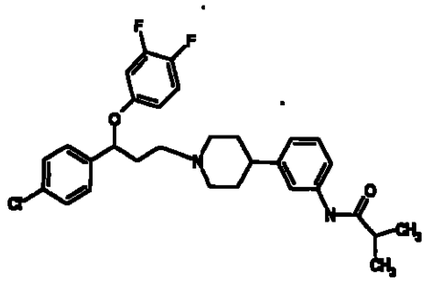


19.0

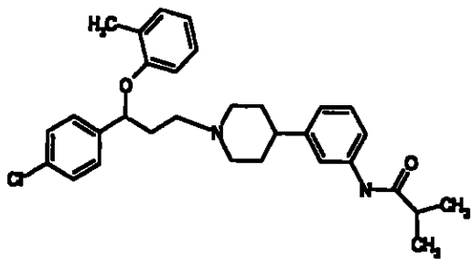
518

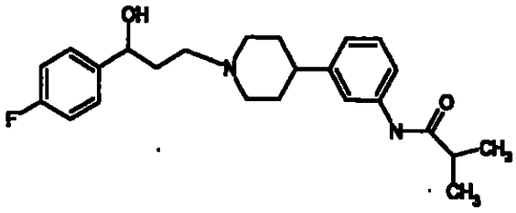
118		43.6
119		75.7
120		31.1
121		183.7

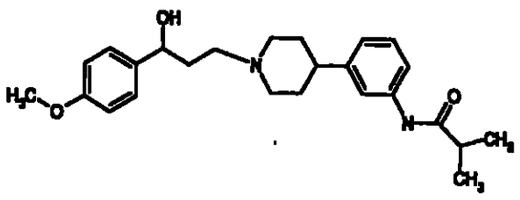
122		85.1
123		449.8

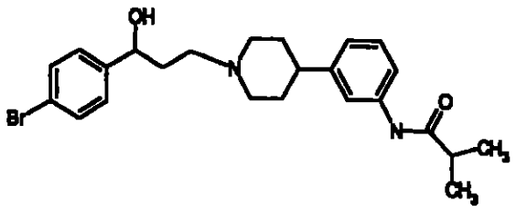
Example	Structure	rMCH1 Ki (nM)
124		33.0
125		5.4

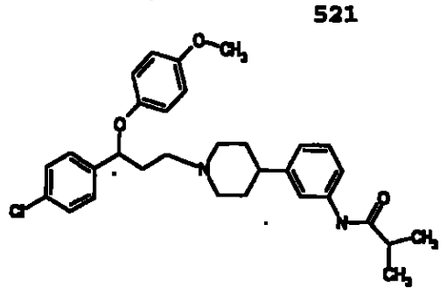
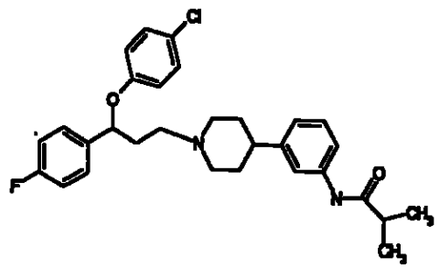
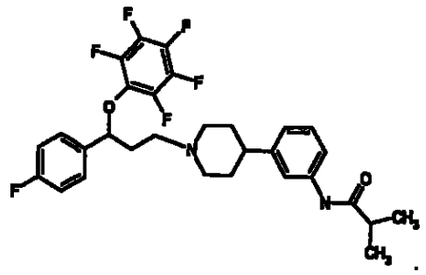
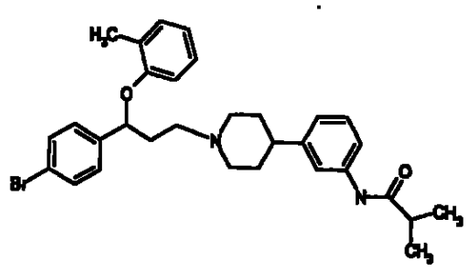
520

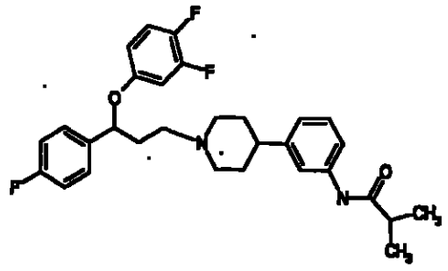
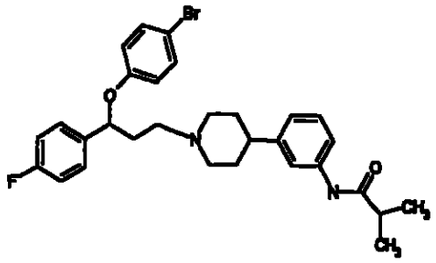
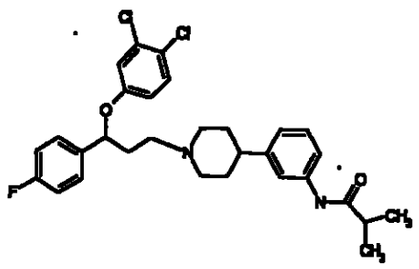
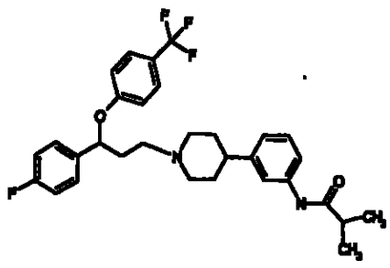
126  13.8

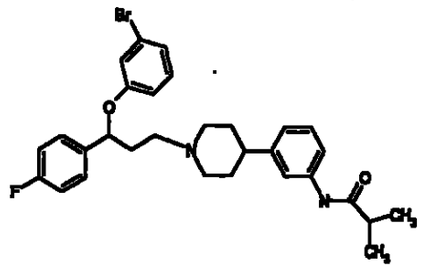
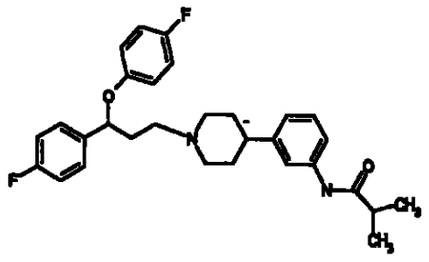
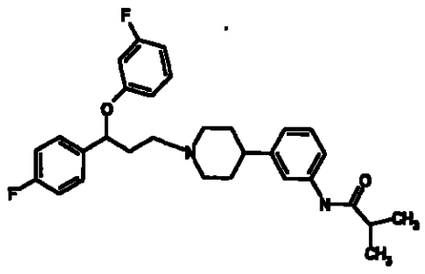
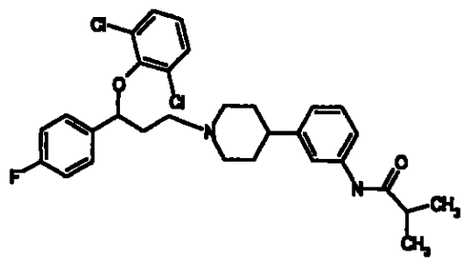
127  168.5

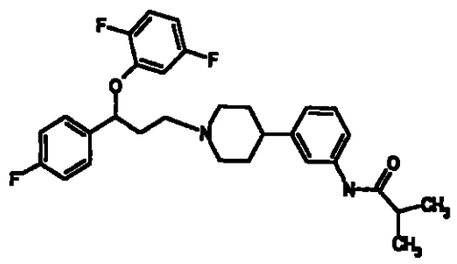
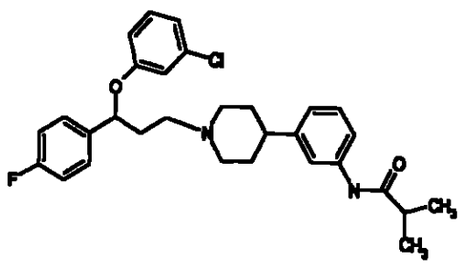
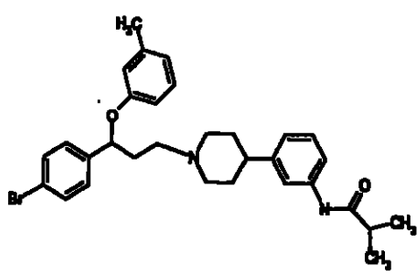
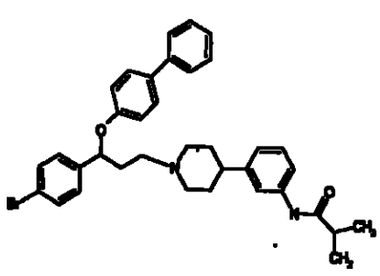
128  328.8

129  38.8

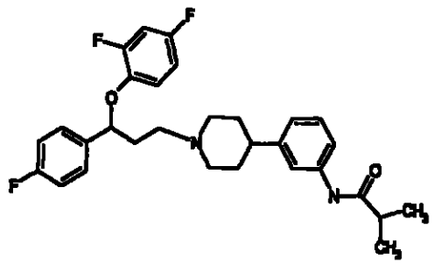
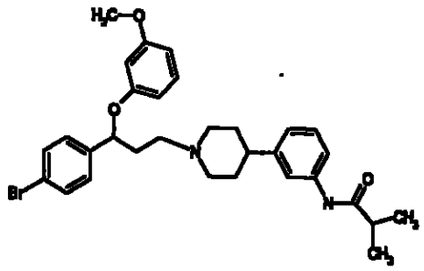
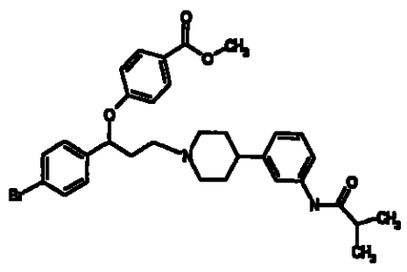
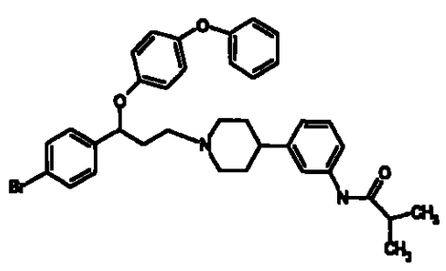
130		6.0
131		11.9
132		41.7
133		14.1

134		38.6
135		10.9
136		15.9
137		25.2

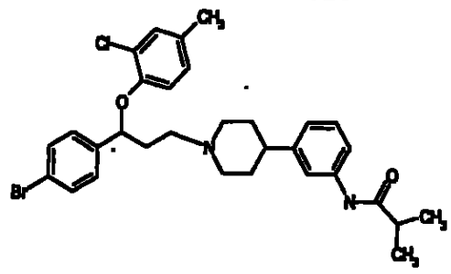
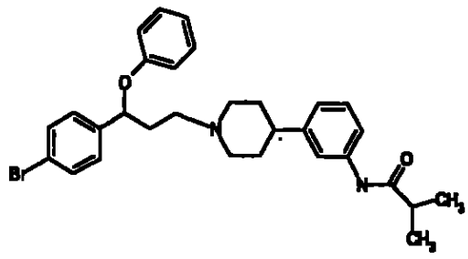
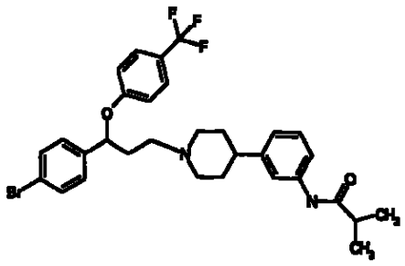
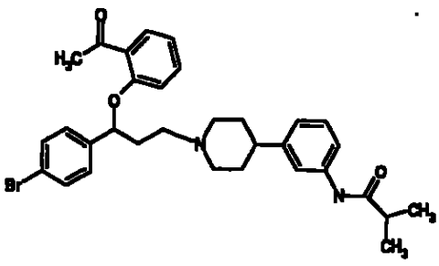
138		9.3
139		38.7
140		27.4
141		61.0

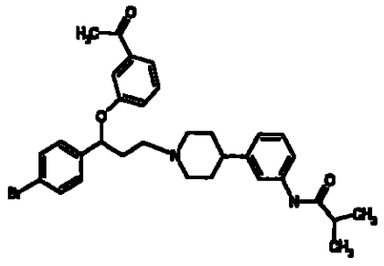
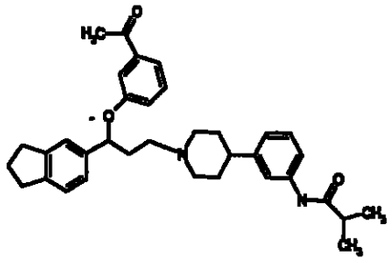
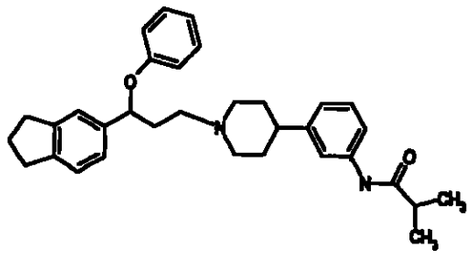
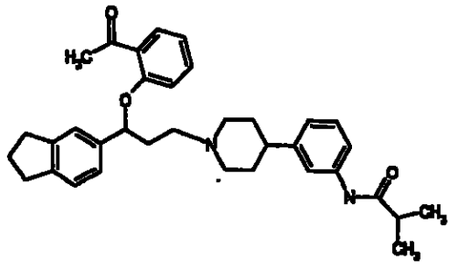
142		18.3
143		8.7
144		13.4
145		196.8

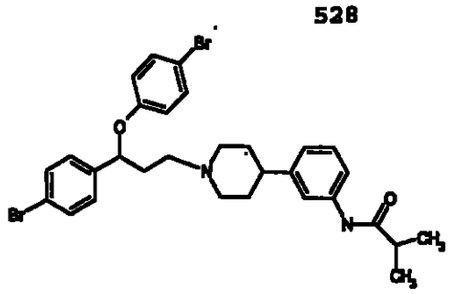
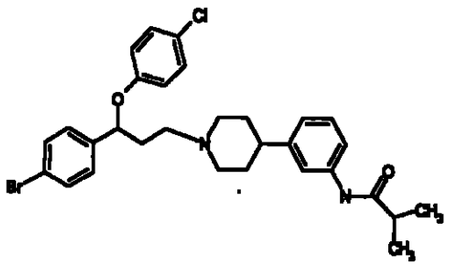
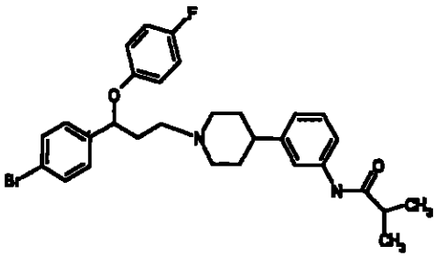
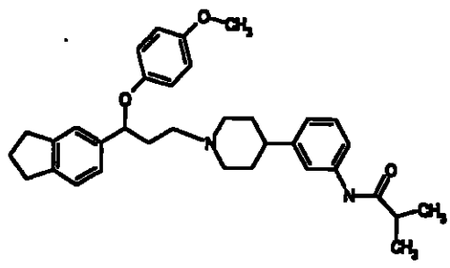
525

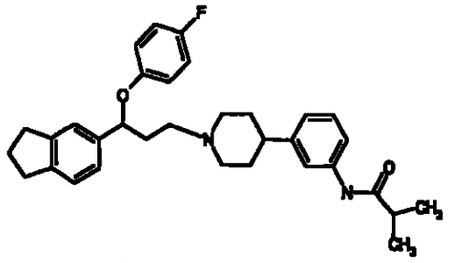
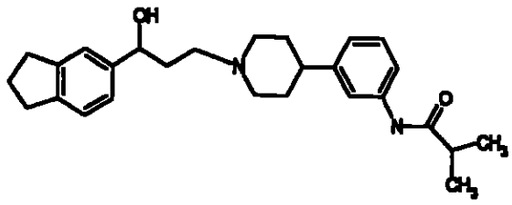
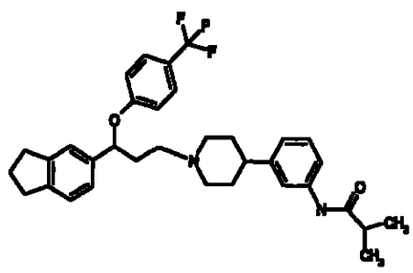
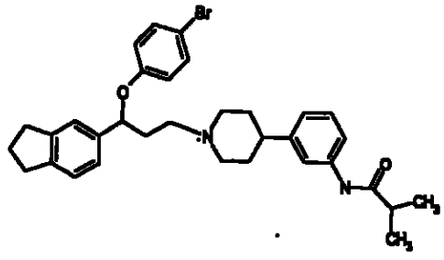
146		19.2
147		8.7
148		24.7
149		148.9

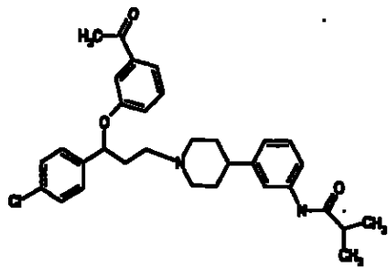
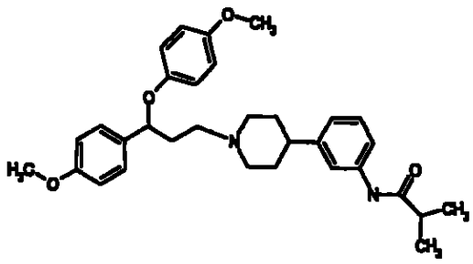
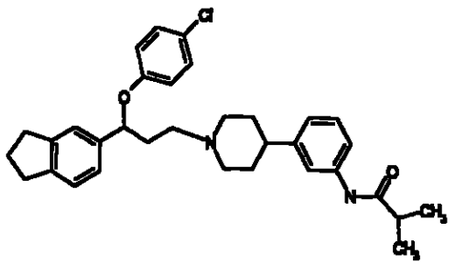
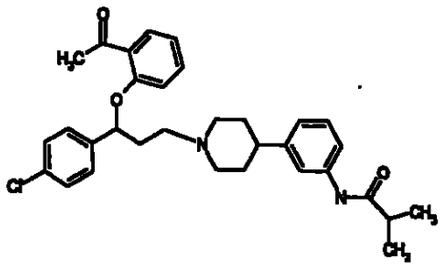
526

150		8.0
151		14.2
152		13.3
153		8.1

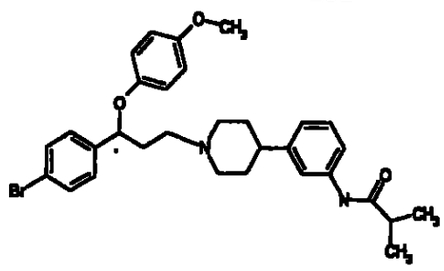
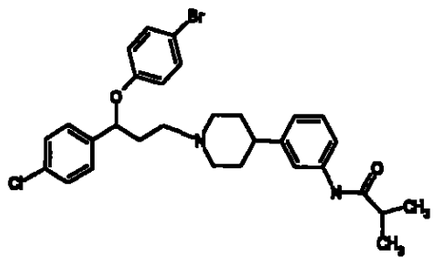
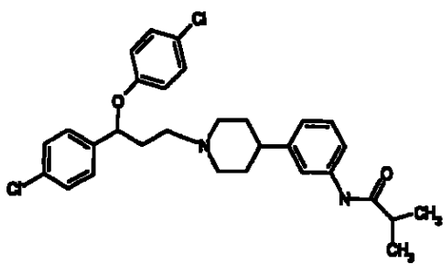
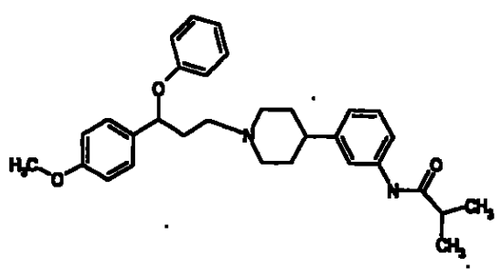
154		9.3
155		7.4
156		8.8
157		15.4

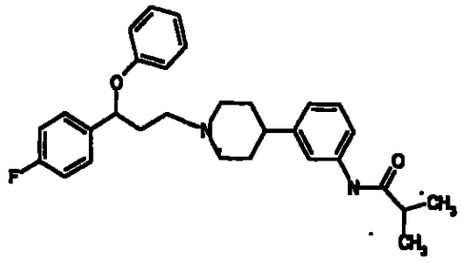
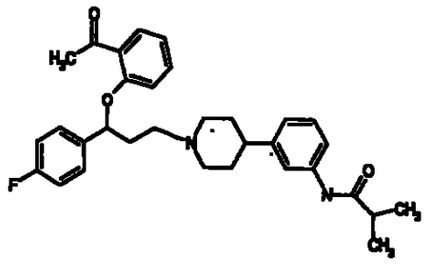
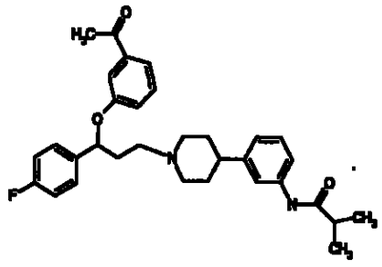
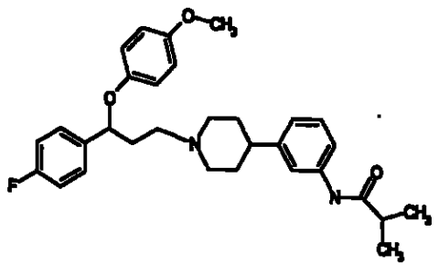
158		7.8
159		4.5
160		6.2
161		7.9

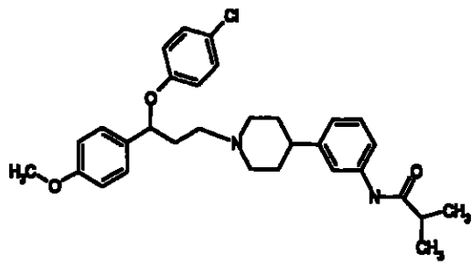
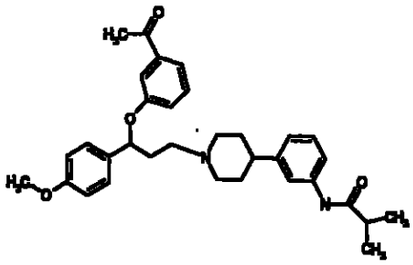
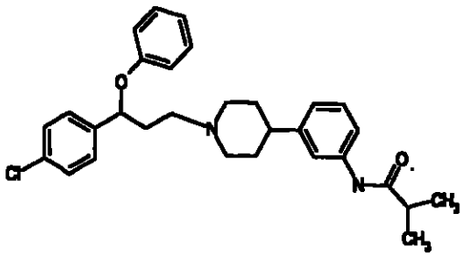
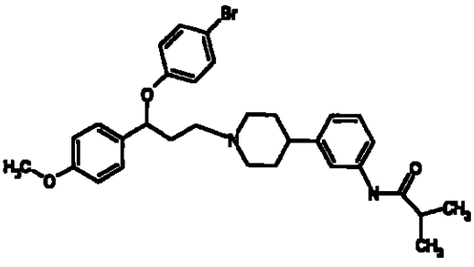
162		7.2
163		58.3
164		16.3
165		6.2

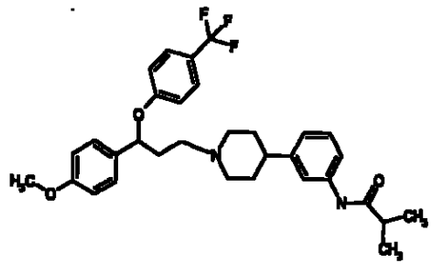
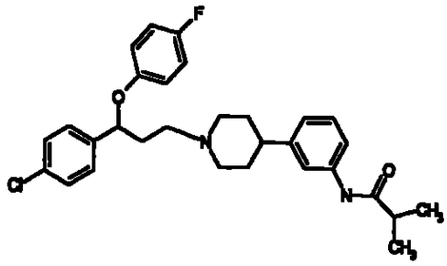
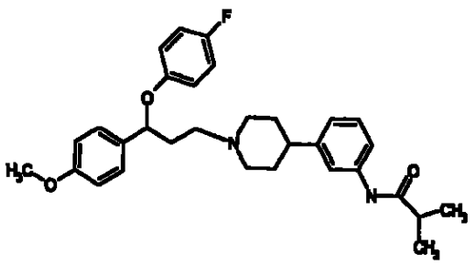
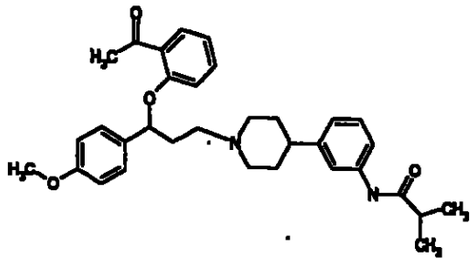
166		7.7
167		80.4
168		7.0
169		7.7

531

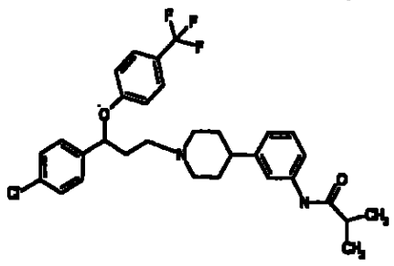
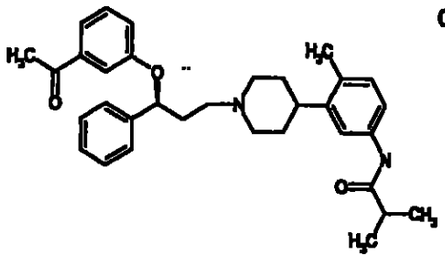
170		3.0
171		3.7
172		3.0
173		112.3

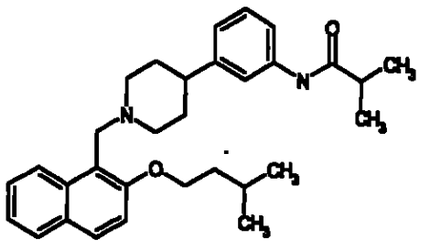
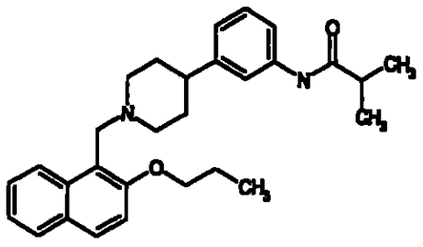
174		17.0
175		16.2
176		11.8
177		6.8

178		119.2
179		82.3
180		9.7
181		91.9

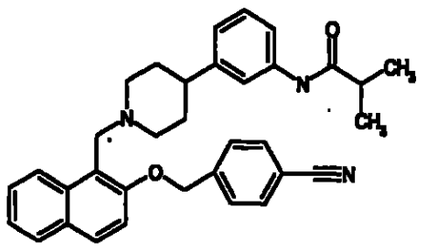
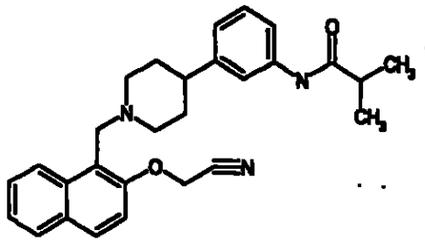
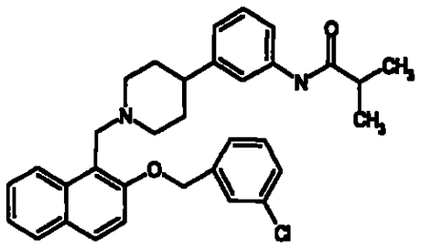
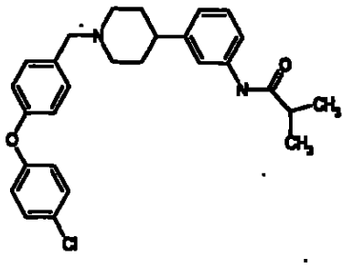
182		101.3
183		4.0
184		105.2
185		20.6

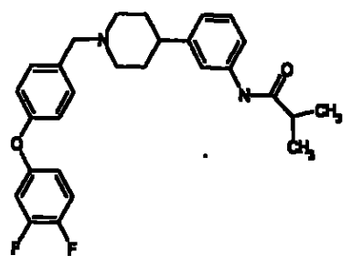
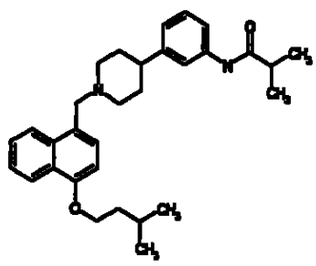
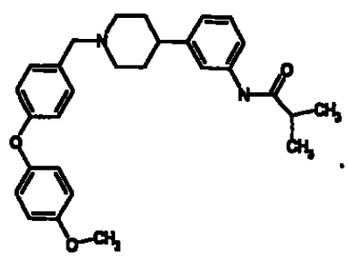
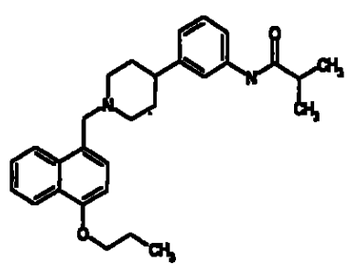
535

186			4.9
187		Chiral	15.6

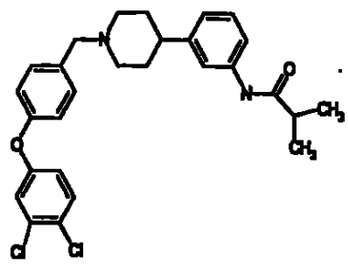
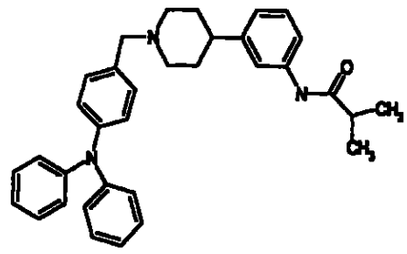
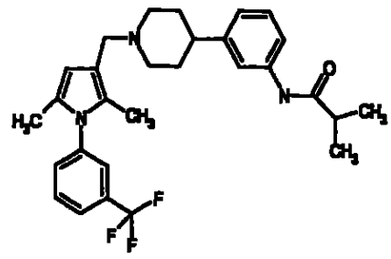
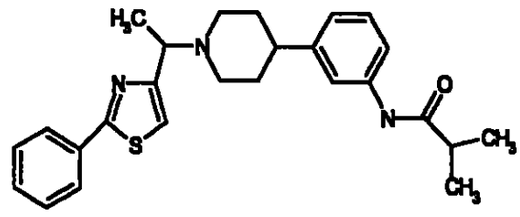
Example	Structure	rMCH1 Ki (nM)
188		531.5
189		436.3

536

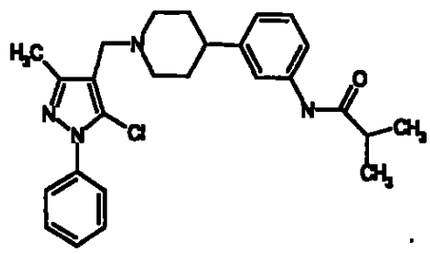
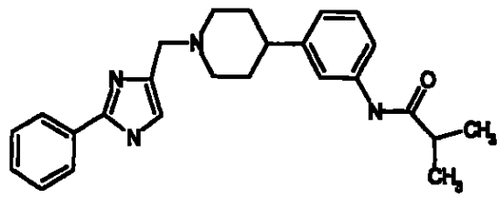
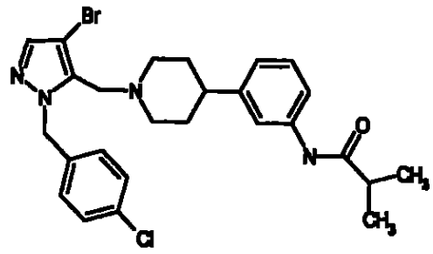
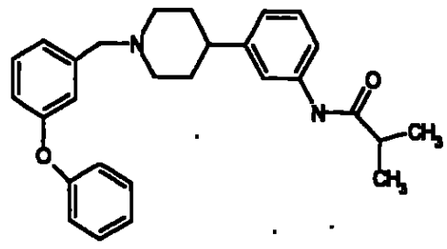
190		435.6
191		648.7
192		60.5
193		5.2

194		537	1.8
195			106.0
196			35.2
197			63.1

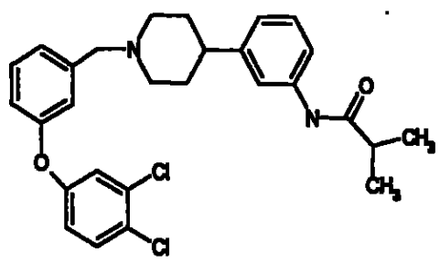
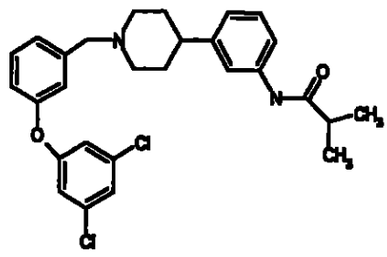
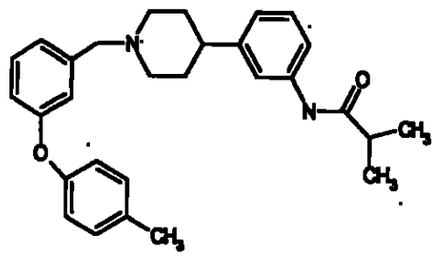
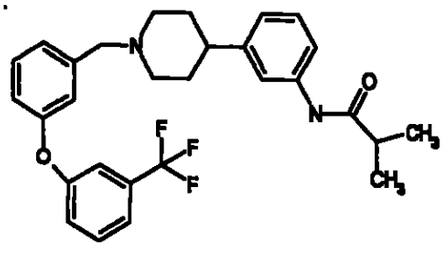
538

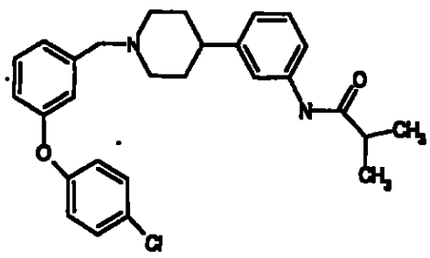
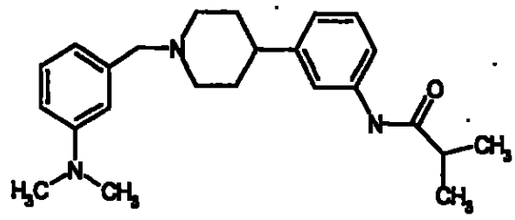
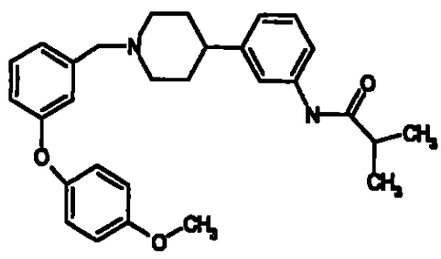
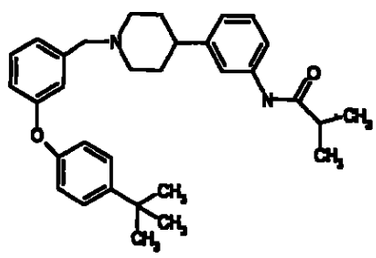
198		6.1
199		3.6
200		20.9
201		996.1

539

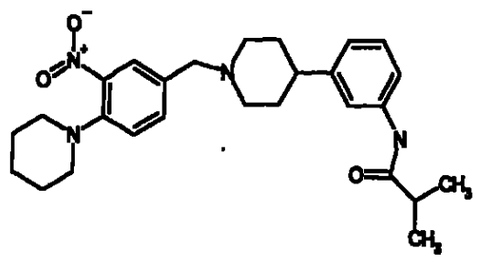
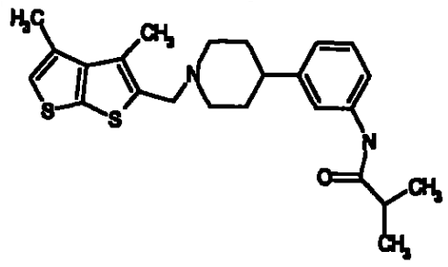
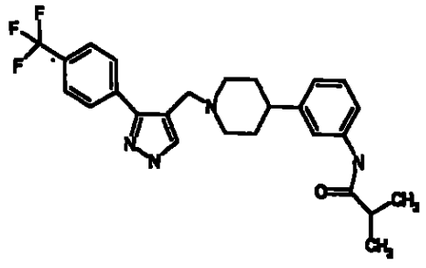
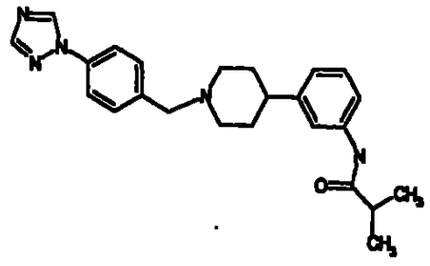
202		154.7
203		79.6
204		39.8
205		28.0

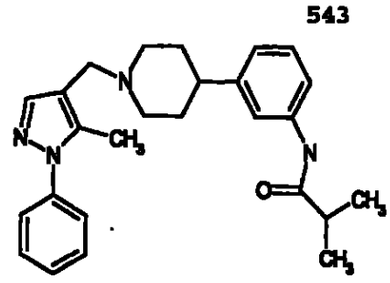
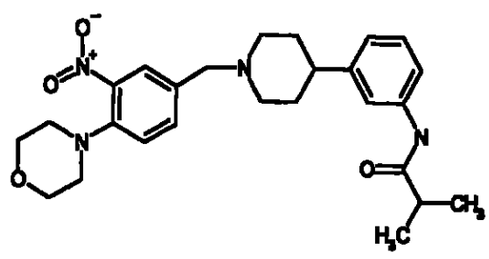
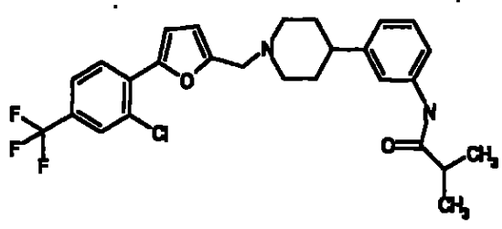
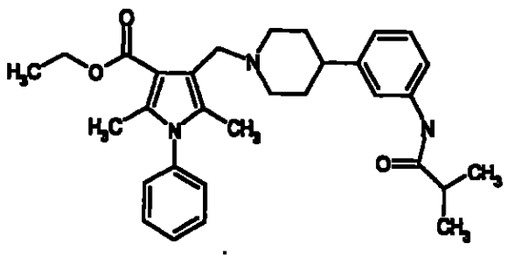
540

206		17.7
207		136.8
208		30.8
209		64.8

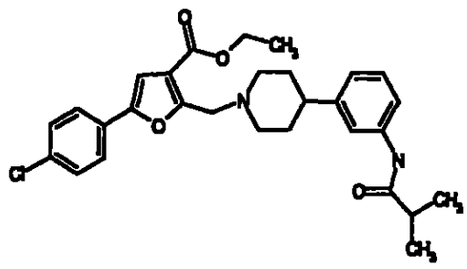
210		541 23.3
211		111.3
212		43.0
213		519.1

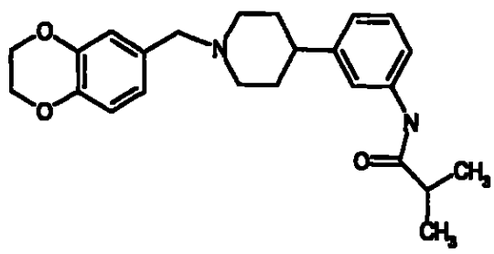
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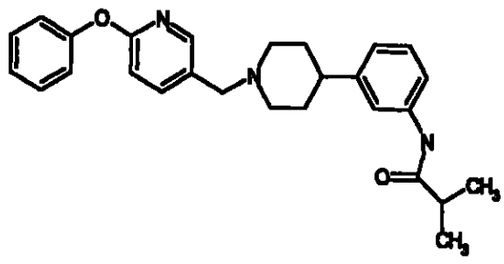
214		56.3
215		283.1
216		817.9
217		300.1

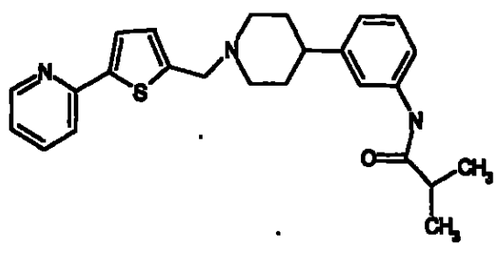
218		543	125.6
219			68.8
220			158.6
221			545.7

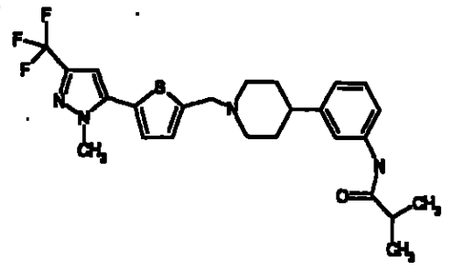
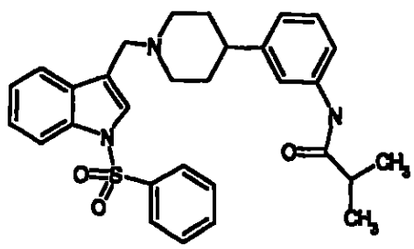
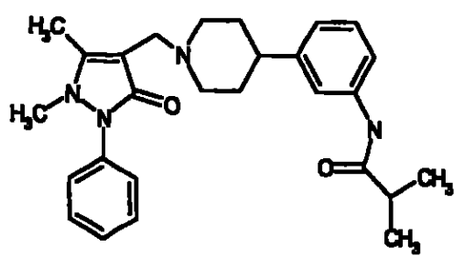
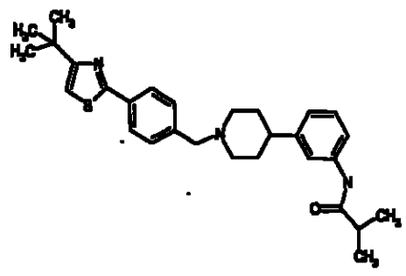
544

222  152.4

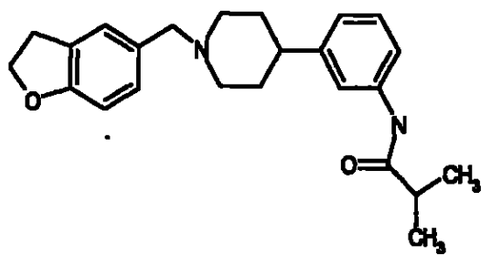
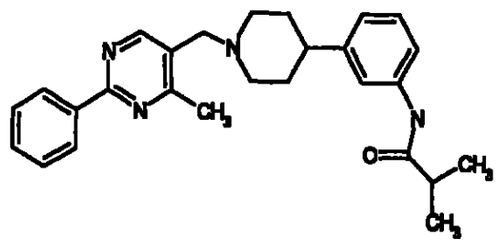
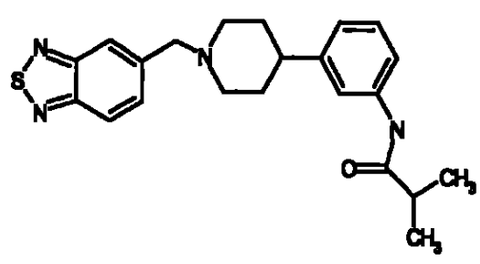
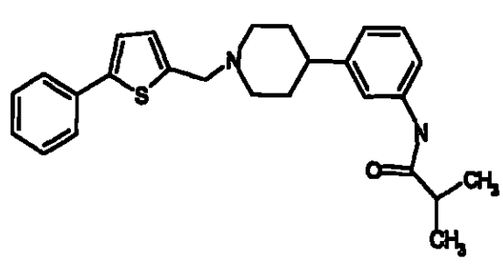
223  318.2

224  48.0

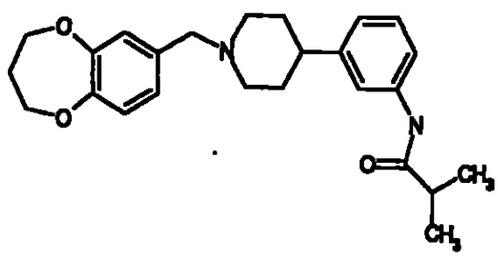
225  213.6

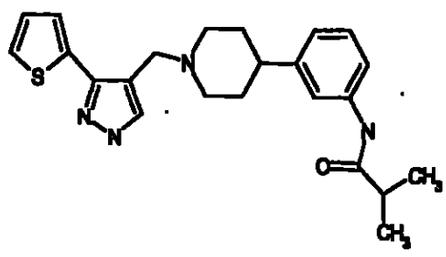
226		238.8
227		261.6
228		841.1
229		884.5

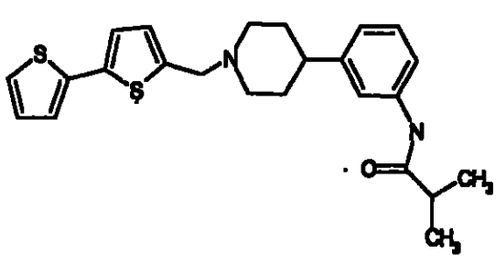
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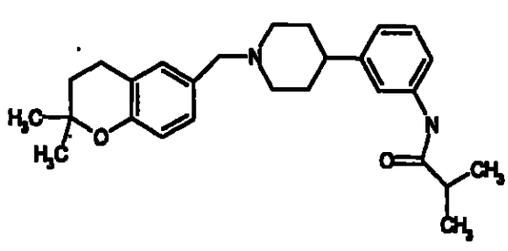
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231		596.4
232		431.2
233		124.7

547

234  116.1

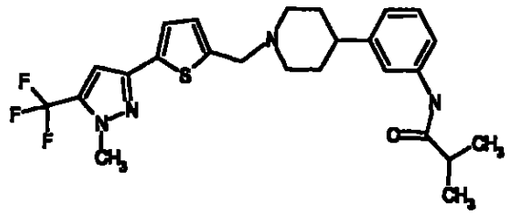
235  411.7

238  97.7

237 

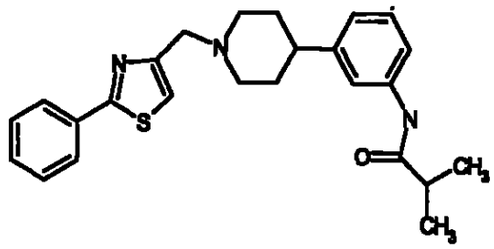
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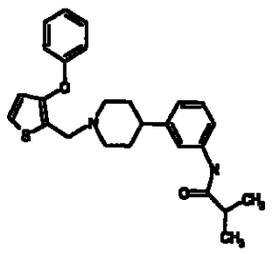


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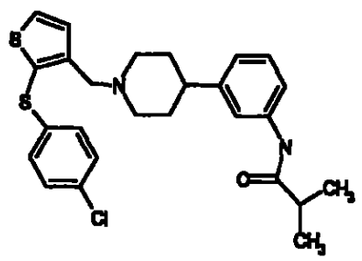
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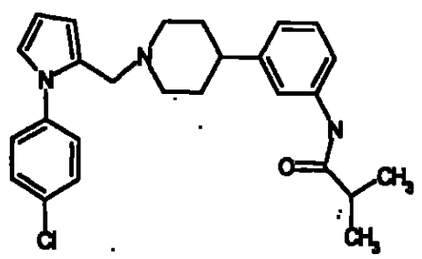
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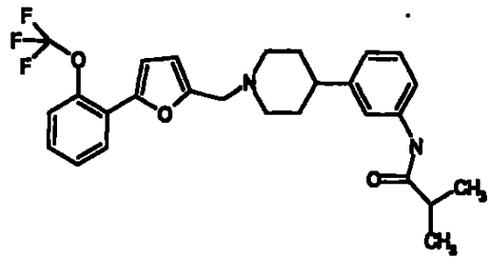
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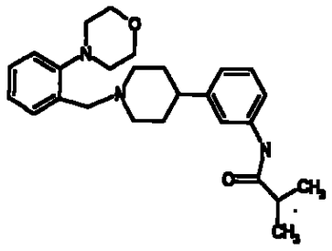
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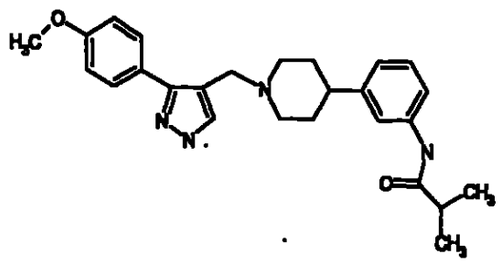
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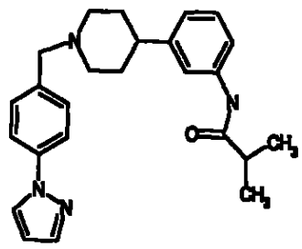


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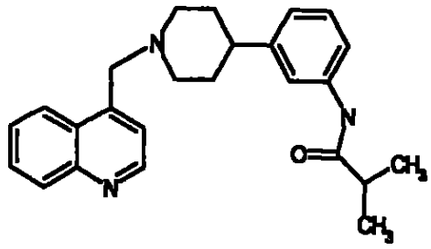


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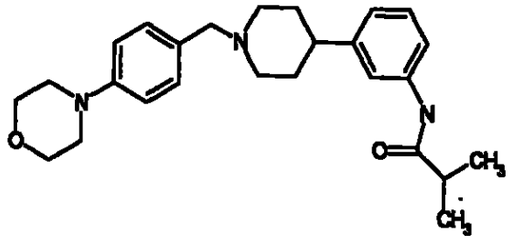
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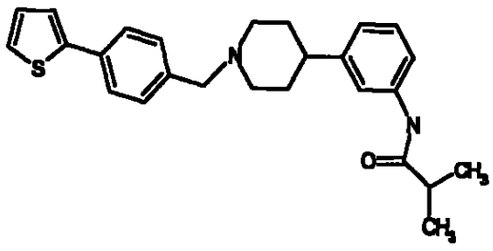
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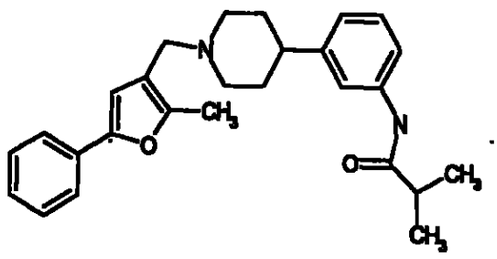


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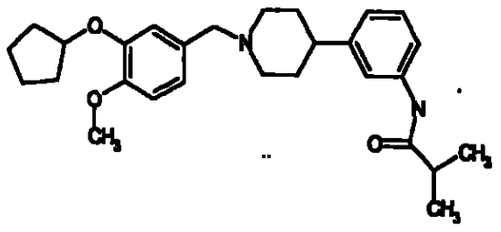


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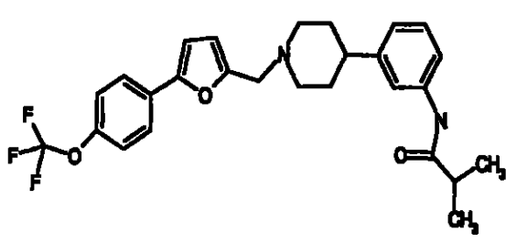
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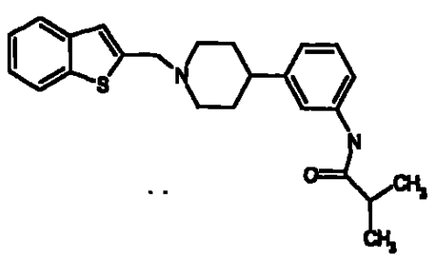
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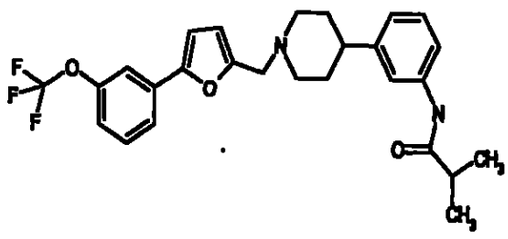
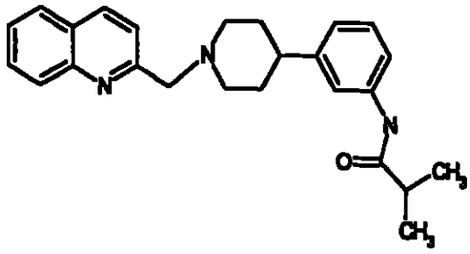
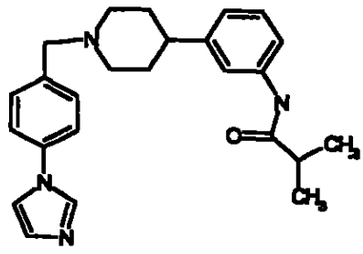
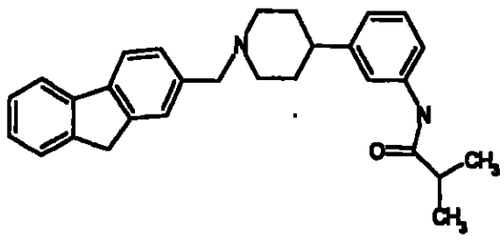


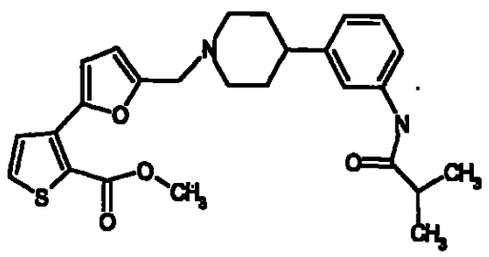
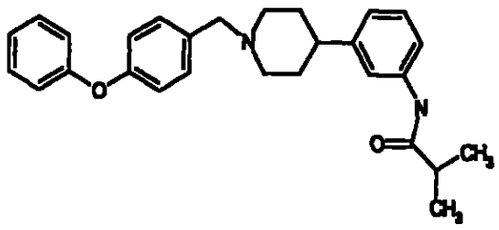
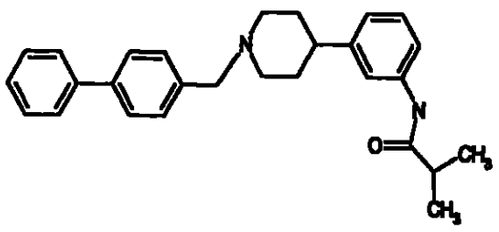
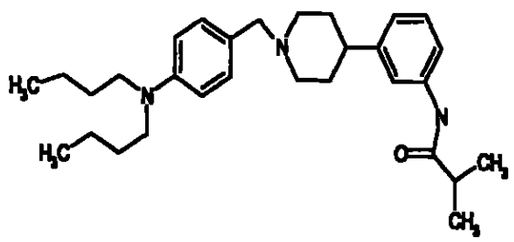
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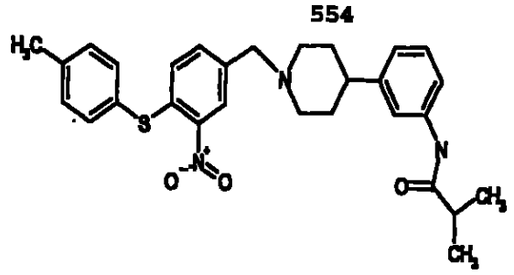


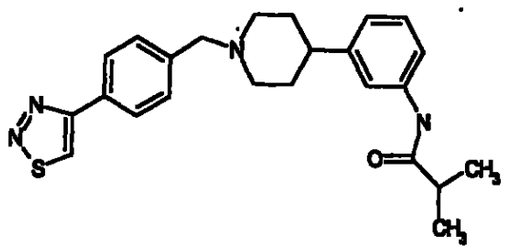
381.8

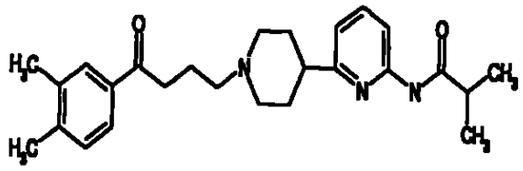
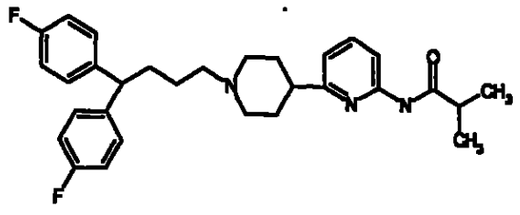
552

254		400.7
255		589.8
256		320.5
257		37.2

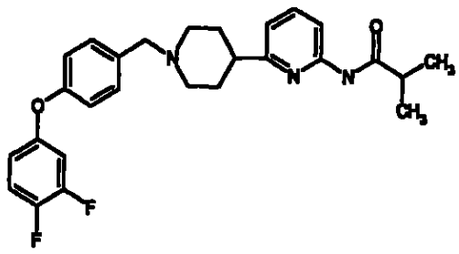
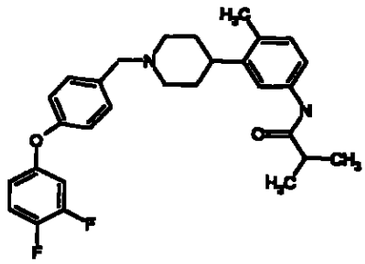
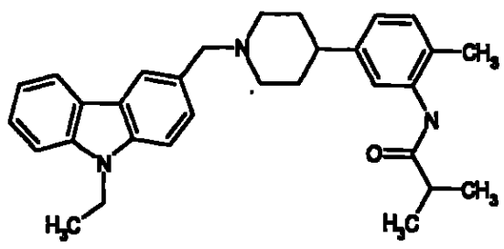
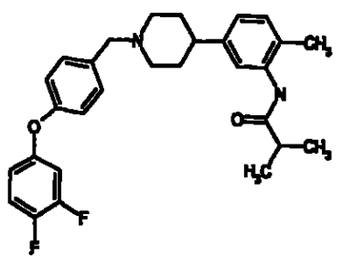
258		110.3
259		15.4
260		77.7
261		6.5

262  64.1

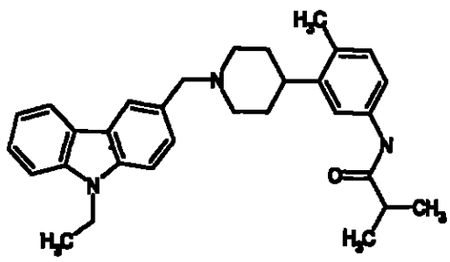
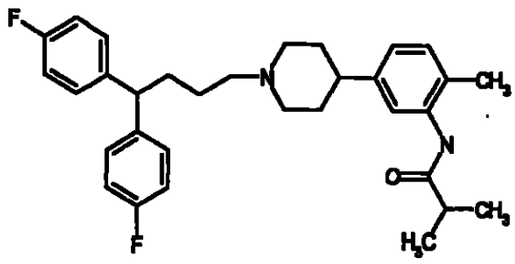
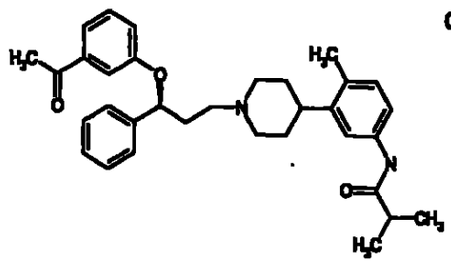
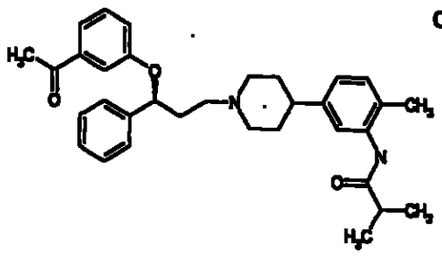
263  156.0

Example	Structure	rMCH-1 Ki (nM)
264		54.7
265		13.5

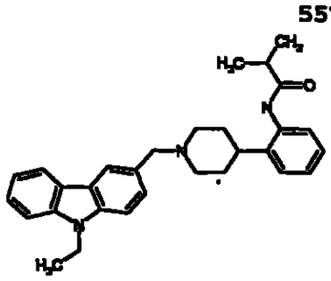
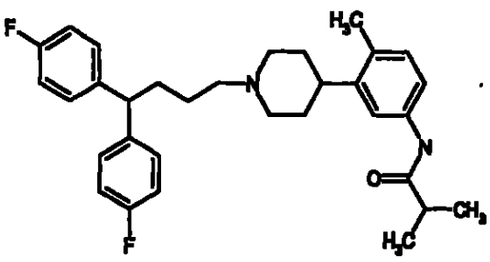
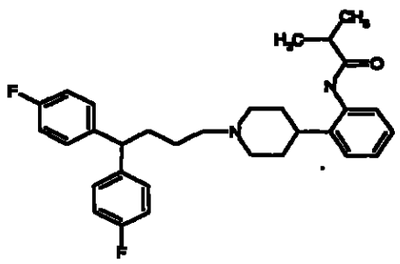
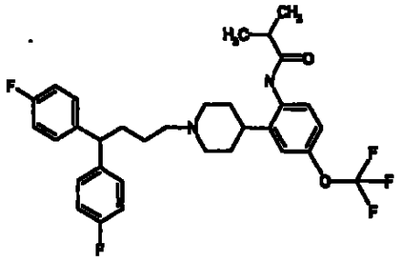
555

266		6.4
267		2.2
268		20.3
269		27.4

556

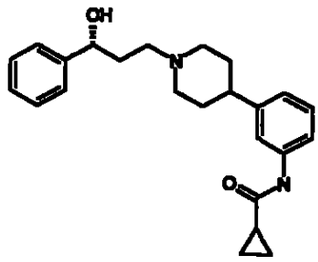
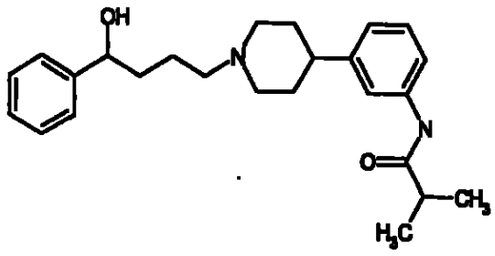
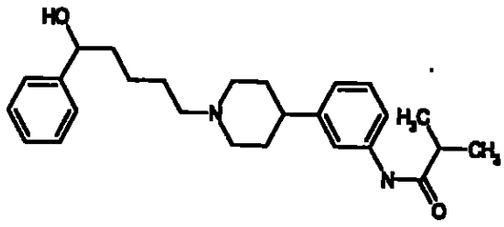
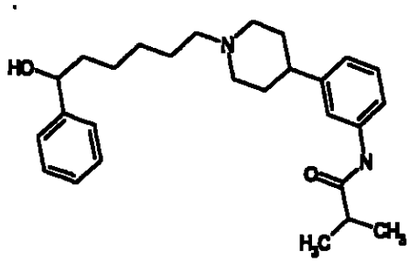
270			3.4
271			40.1
272		Chiral	15.6
273		Chiral	198.4

557

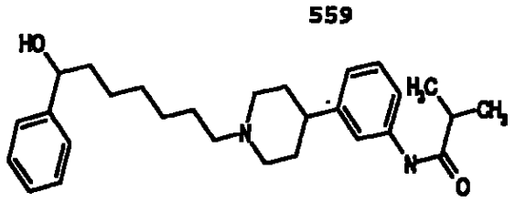
274		843.5
275		3.1
276		734.4
277		117.8

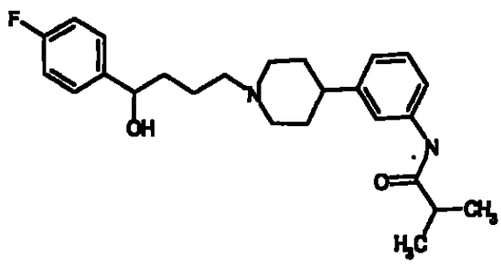
Example	Structure	rMCH-1 Ki (nM)

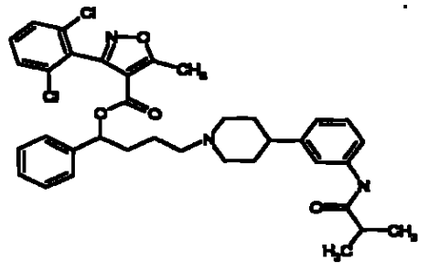
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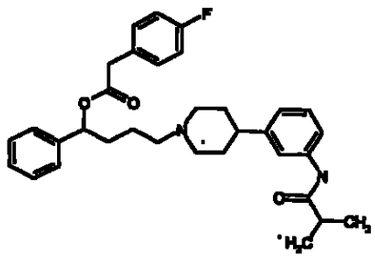
278		Chiral	85.8
279			74.5
280			27.6
281			7.9

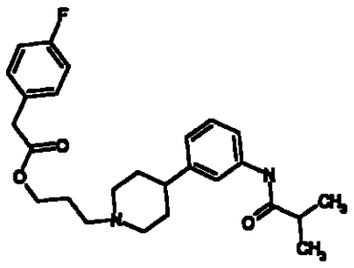
559

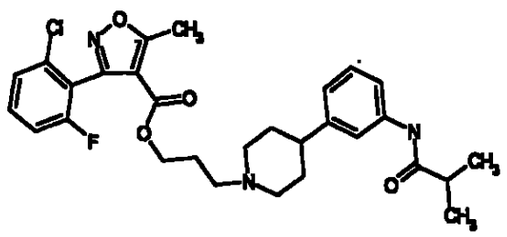
282  23.5

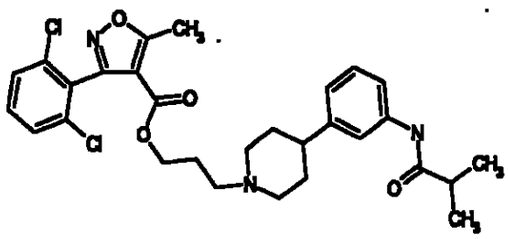
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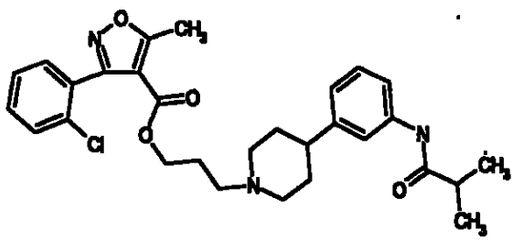
284  18.3

285  10.3

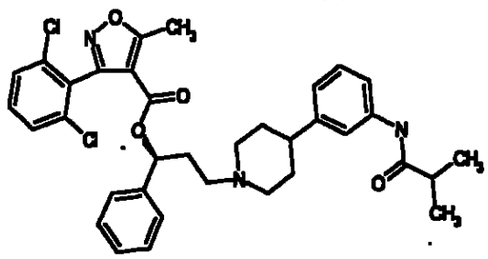
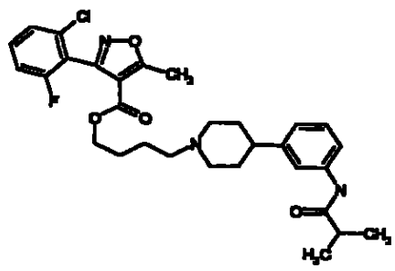
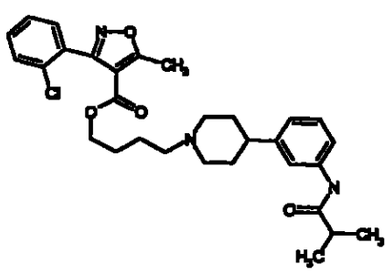
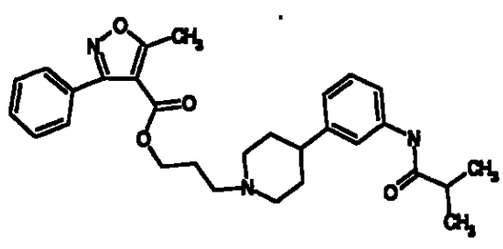
286  67.8

287  34.3

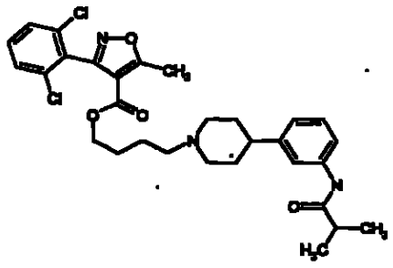
288  30.2

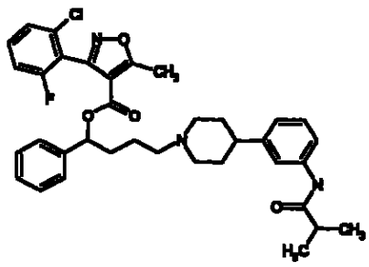
289  31.8

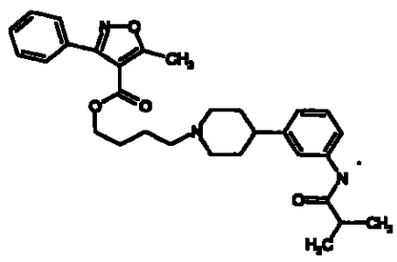
561

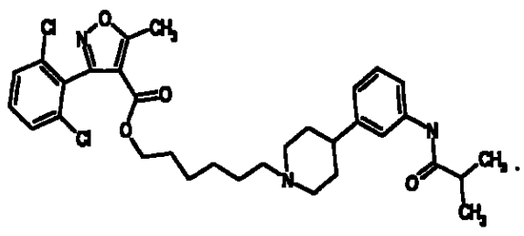
290		51.9
291		24.3
292		18.4
293		39.9

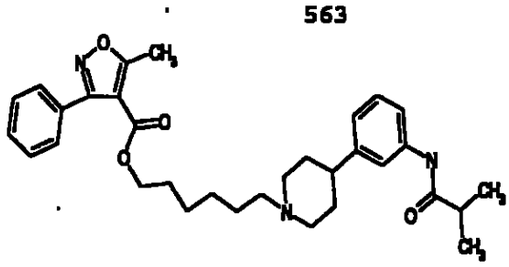
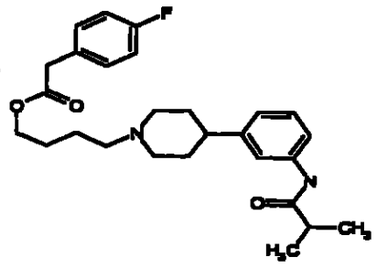
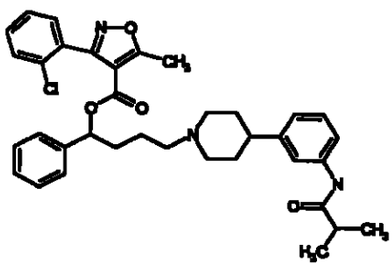
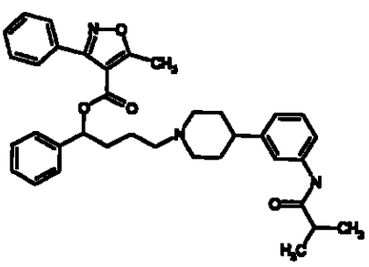
562

294  15.8

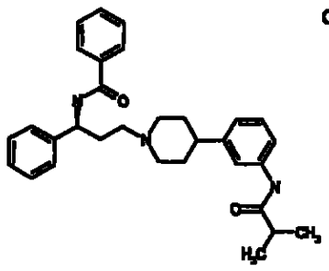
295  8.7

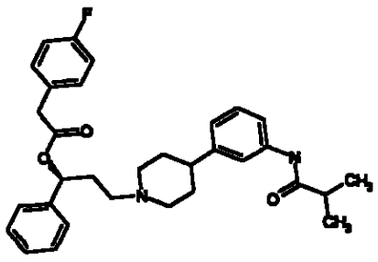
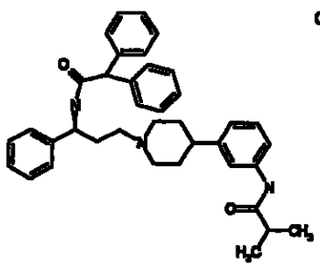
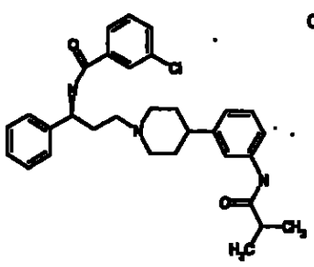
296  20.0

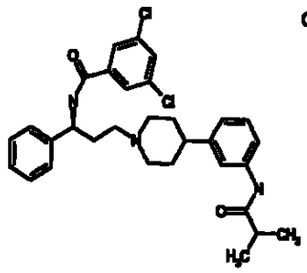
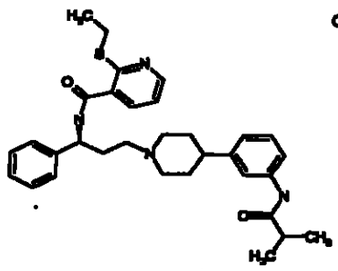
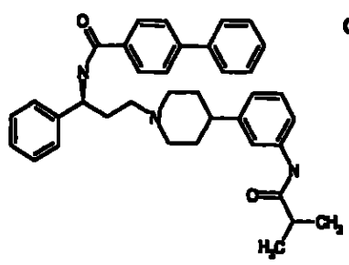
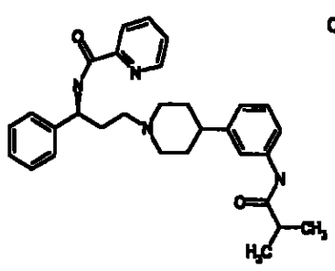
297  11.9

298		40.1
299		37.5
300		7.6
301		

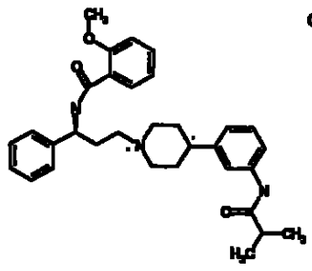
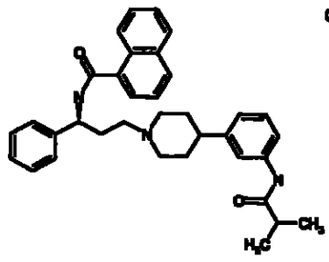
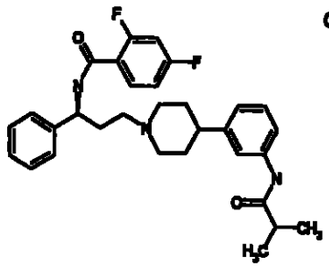
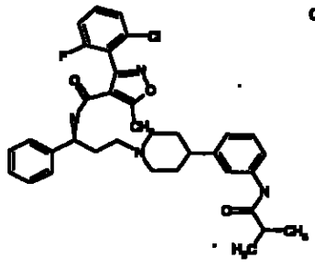
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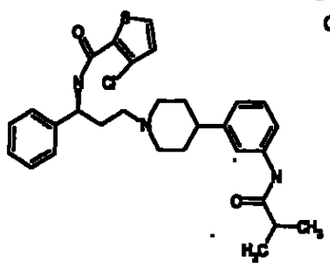
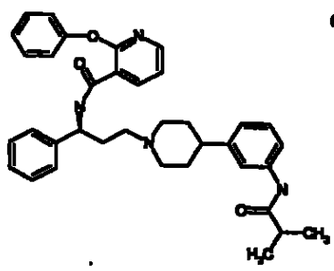
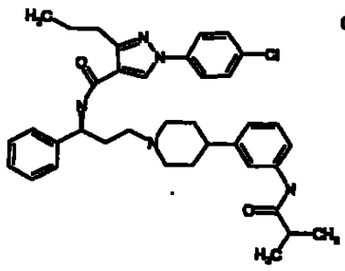
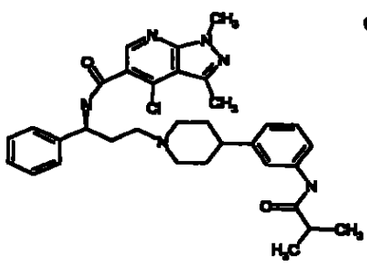
302		Chiral	20.5

Example	Structure		rMCH-1 Ki (nM)
303			9.5
304		Chiral	4.0
305		Chiral	177.2

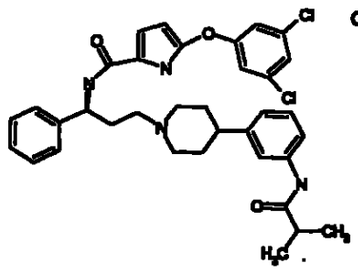
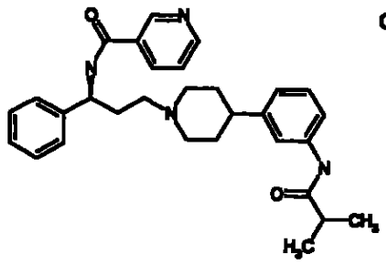
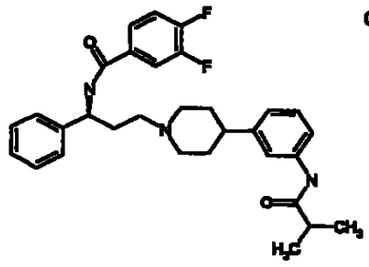
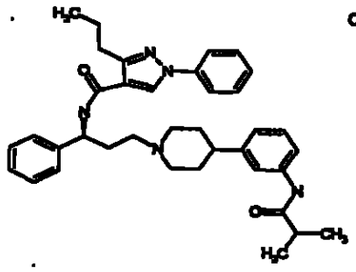
306		Chiral	167.9
307		Chiral	97.4
308		Chiral	401.6
309		Chiral	310.1

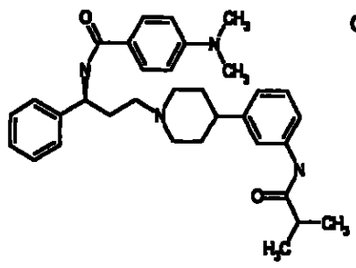
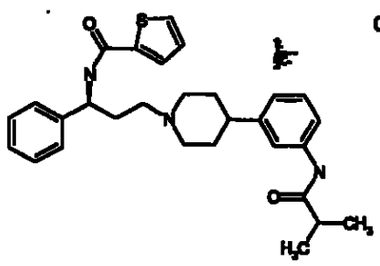
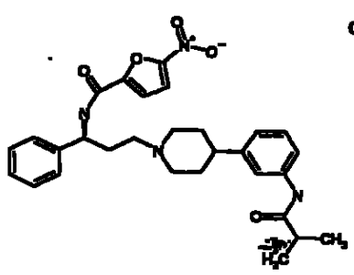
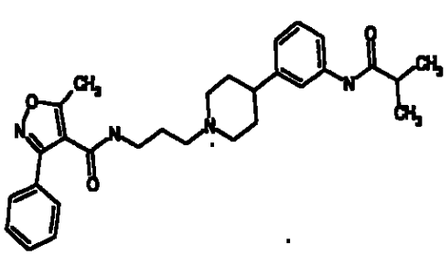
566

310		Chiral	152.2
311		Chiral	43.0
312		Chiral	61.5
313		Chiral	249.3

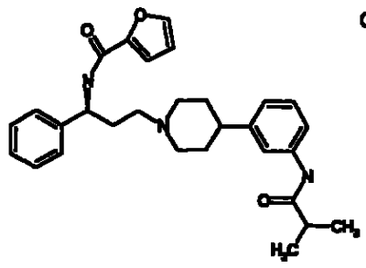
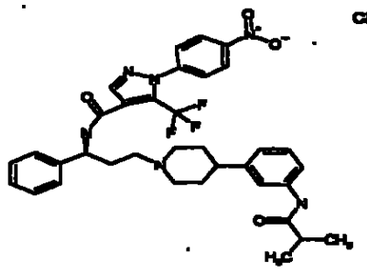
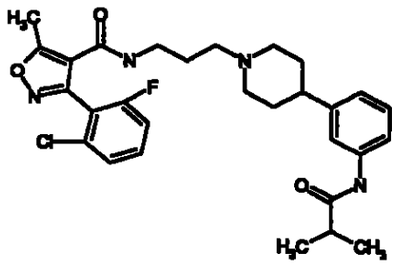
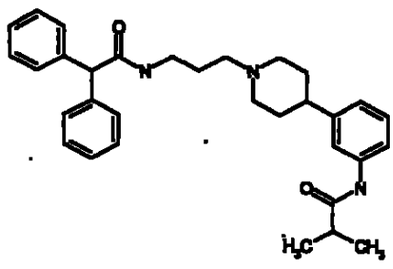
314		Chiral	7.6
315		Chiral	11.4
316		Chiral	8.3
317		Chiral	110.2

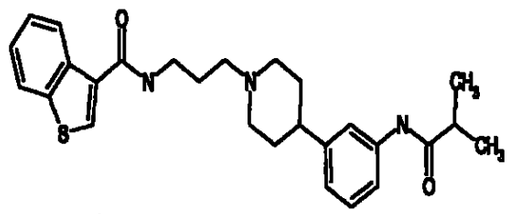
568

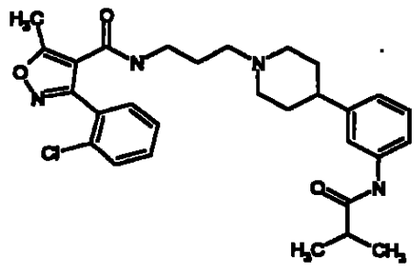
318		Chiral	251.2
319		Chiral	89.8
320		Chiral	10.6
321		Chiral	50.9

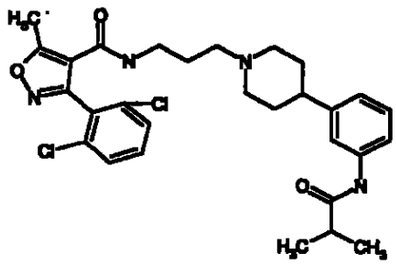
322		Chiral	99.9
323		Chiral	37.0
324		Chiral	76.8
325			29.8

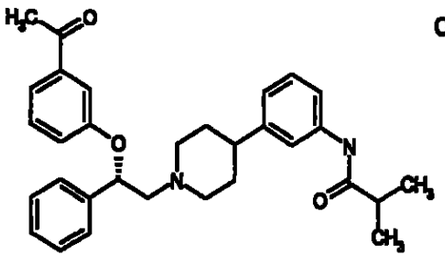
570

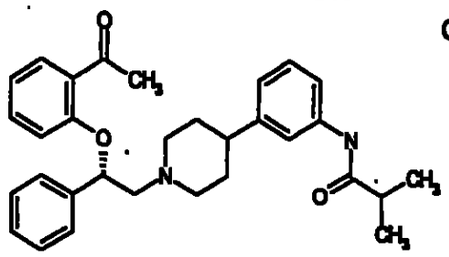
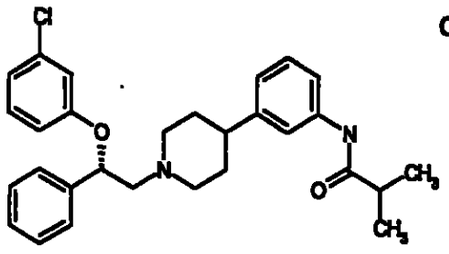
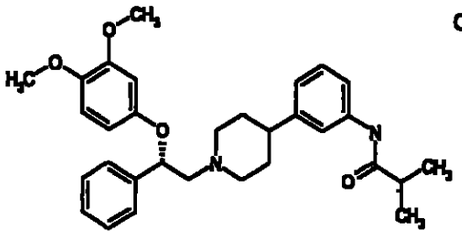
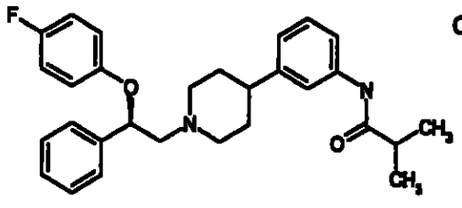
326		Chiral	19.2
327		Chiral	7.7
328			47.6
329			2.9

330  215.0

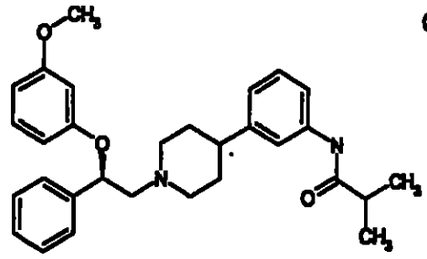
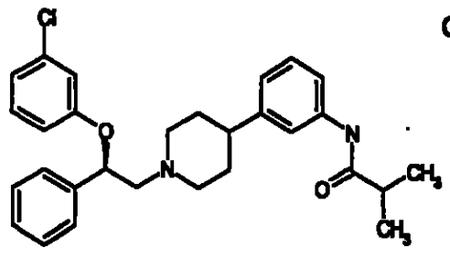
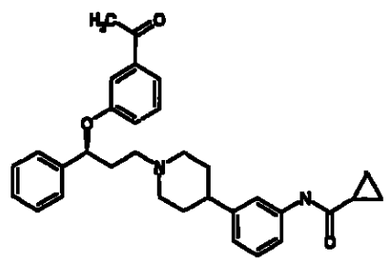
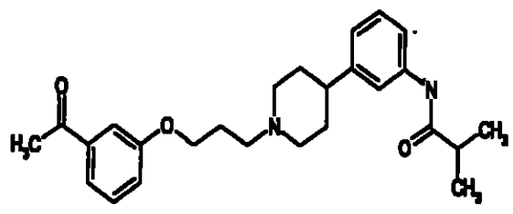
331  51.3

332  29.0

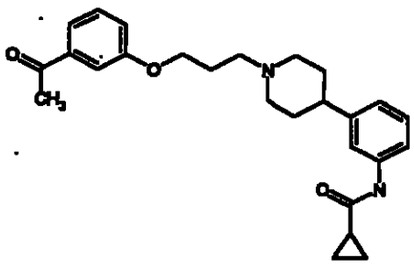
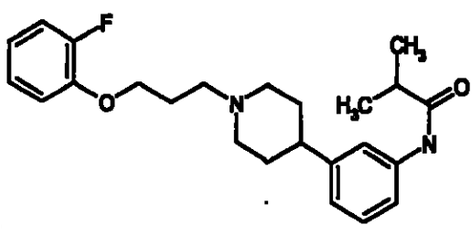
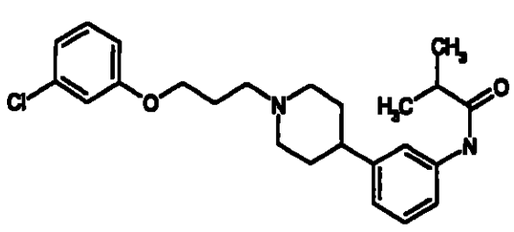
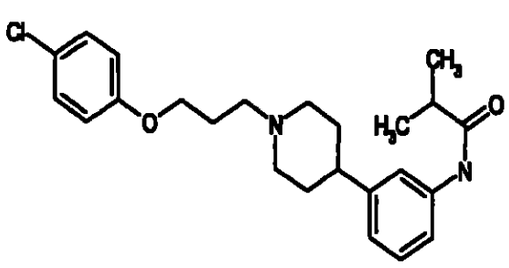
Example	Structure		rMCH-1 Ki (nM)
333		Chiral	587.6

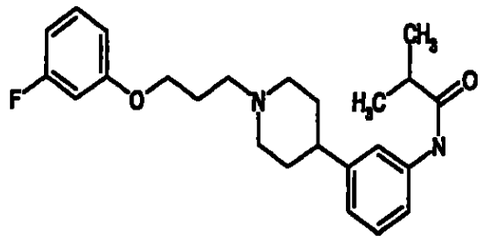
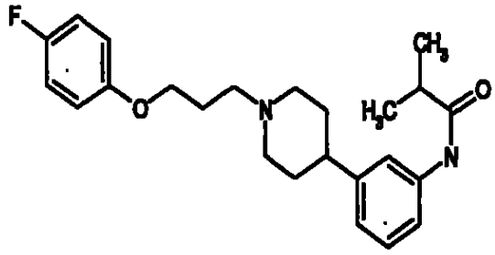
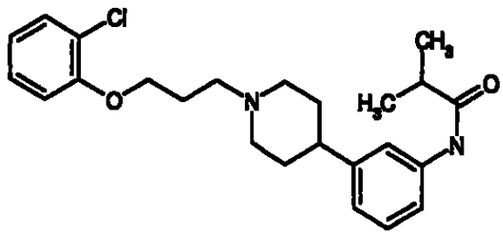
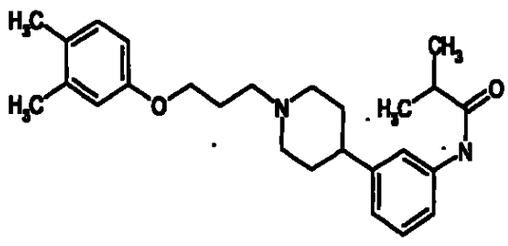
334		Chiral	602.6
335		Chiral	887.7
336		Chiral	693.0
337		Chiral	907.4

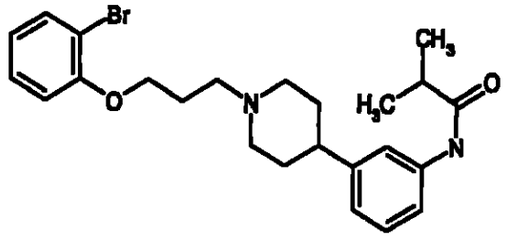
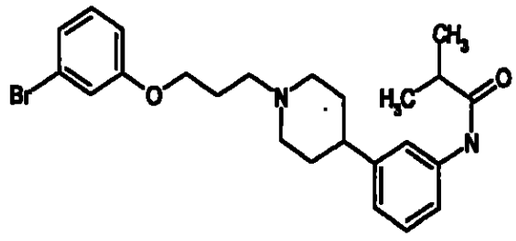
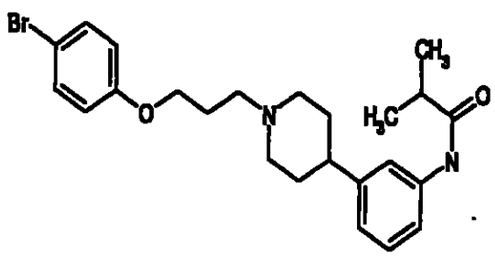
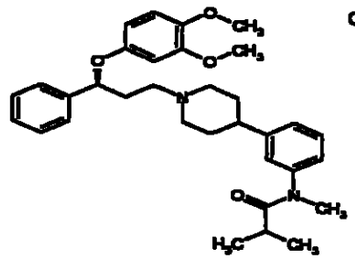
573

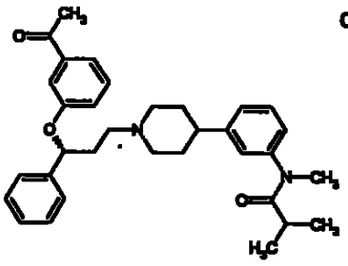
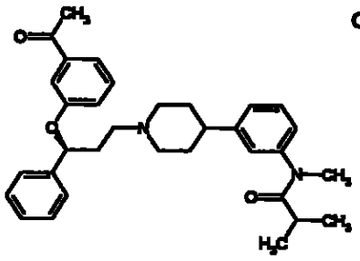
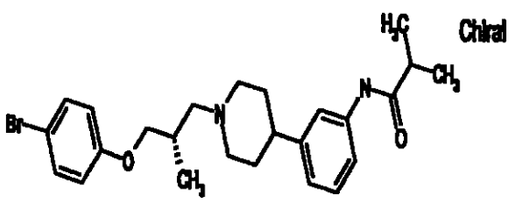
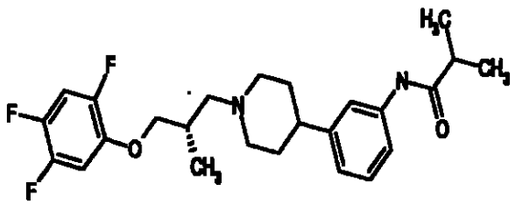
338		Chiral	843.9
339		Chiral	889.9
340		Chiral	15.8
341			255.6

574

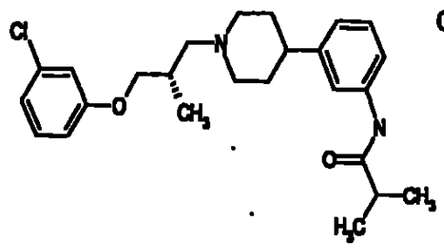
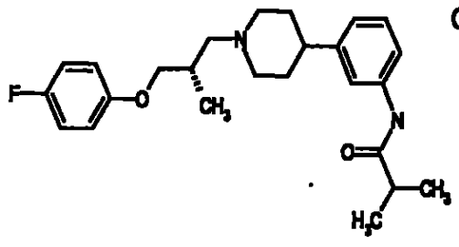
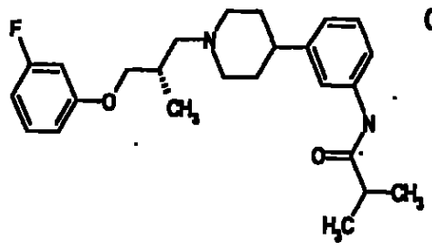
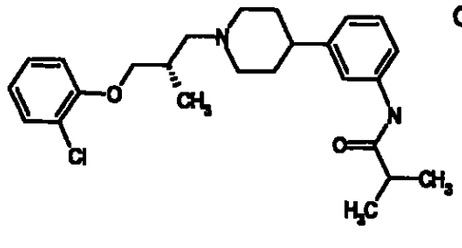
342		183.0
343		194.7
344		44.6
345		15.4

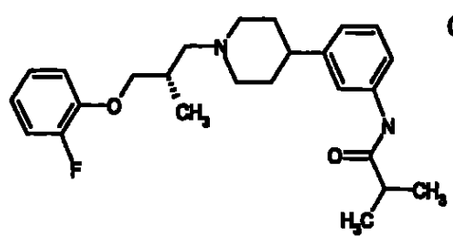
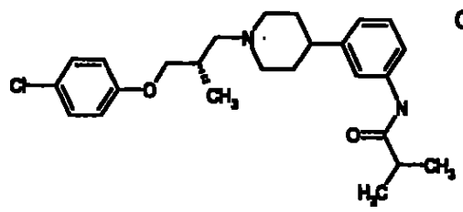
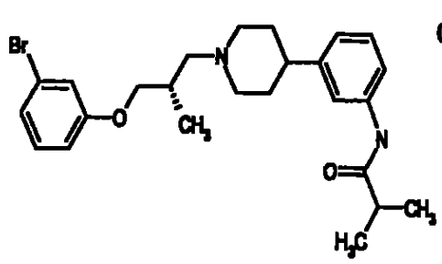
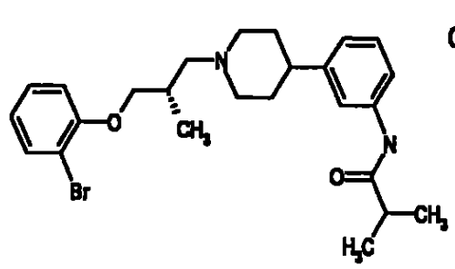
346		106.9
347		54.8
348		84.0
349		20.4

350			12.1
351			61.8
352			13.3
353		Chiral	41.8

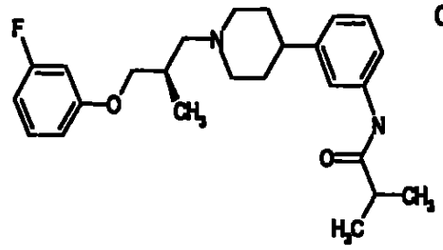
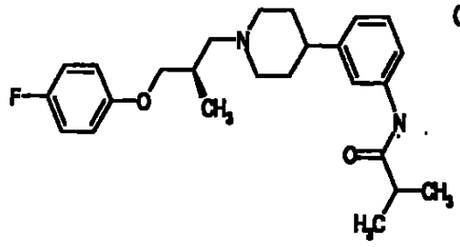
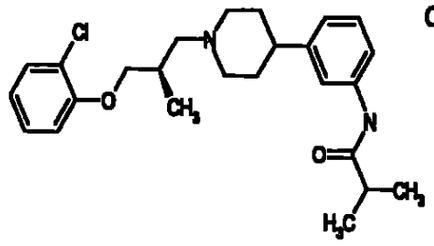
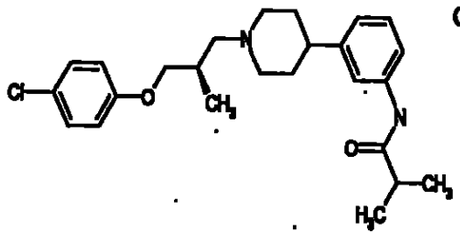
354		Chiral	81.6
355		Chiral	116.6
356		Chiral	54.5
357			115.4

578

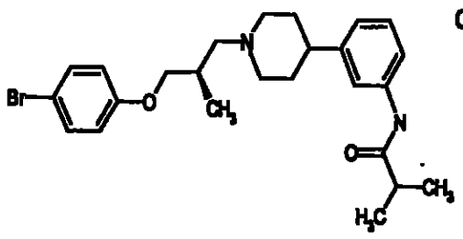
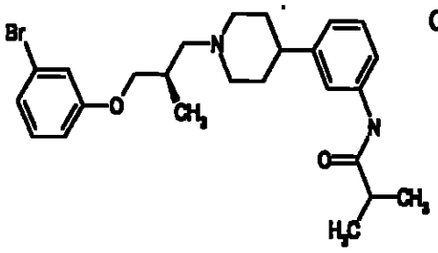
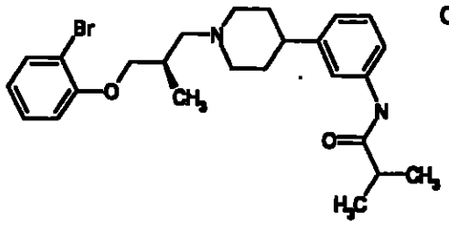
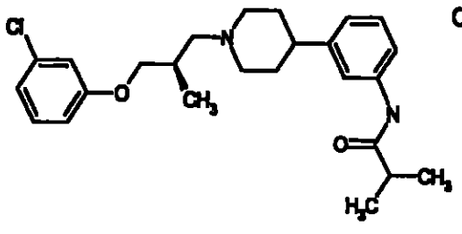
358		Chiral	135.7
359		Chiral	83.2
360		Chiral	163.0
361		Chiral	311.2

362		Chiral	281.2
363		Chiral	31.6
364		Chiral	144.4
365		Chiral	42.9

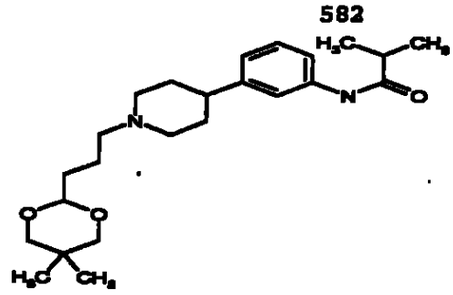
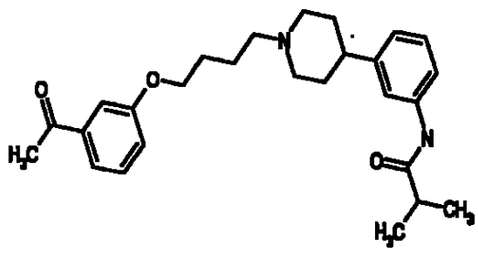
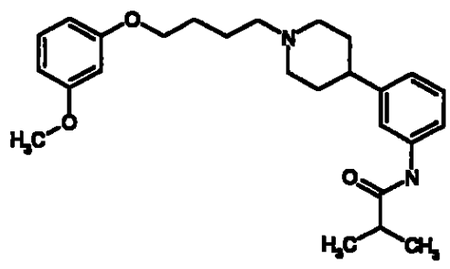
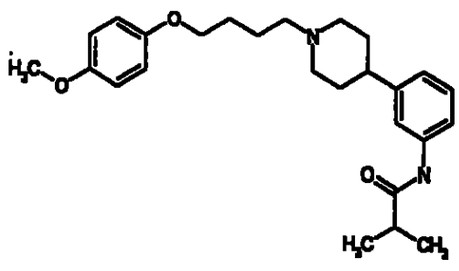
580

366		Chiral	645.5
367		Chiral	235.7
368		Chiral	313.0
369		Chiral	145.0

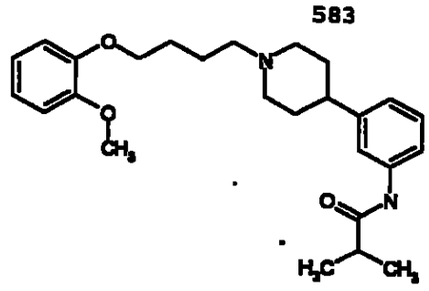
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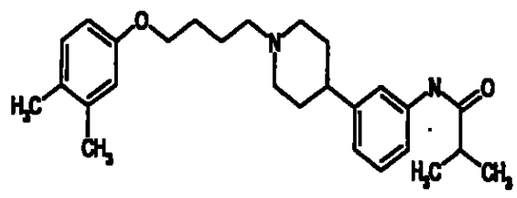
370		Chiral	
371		Chiral	162.7
372		Chiral	357.7
373		Chiral	428.5

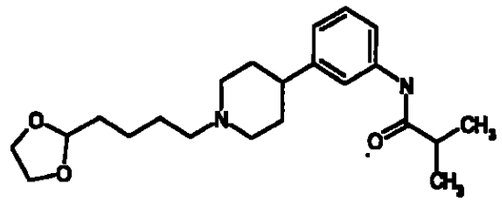
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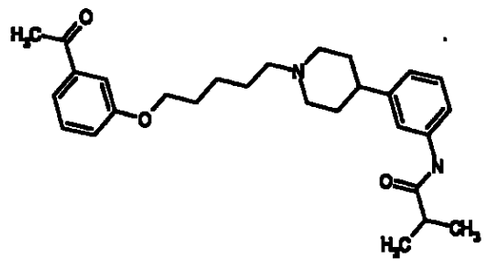
374		96.8
375		185.6
376		887.6
377		711.9

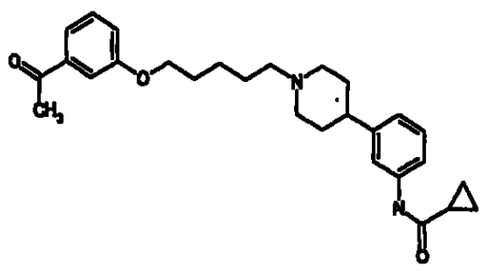
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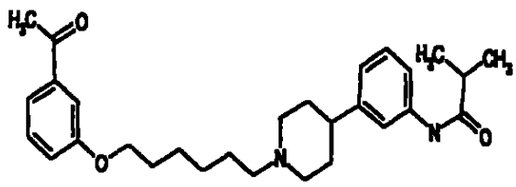
378  307.8

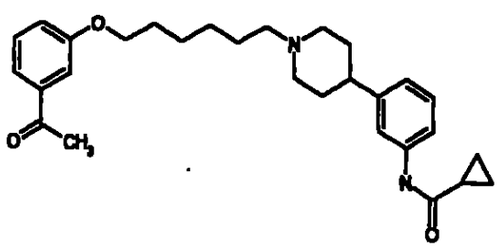
379  203.6

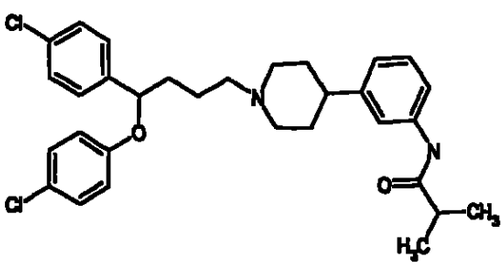
380  309.1

381  235.0

382  318.8

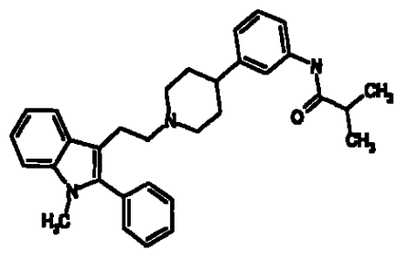
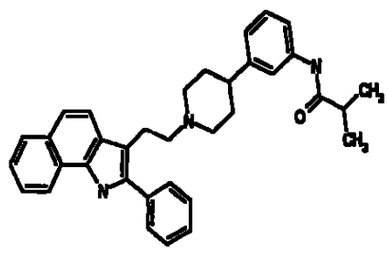
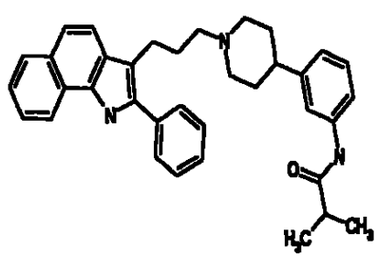
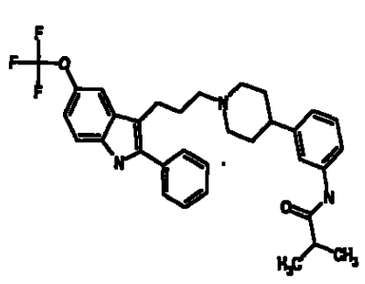
383  289.6

384  69.0

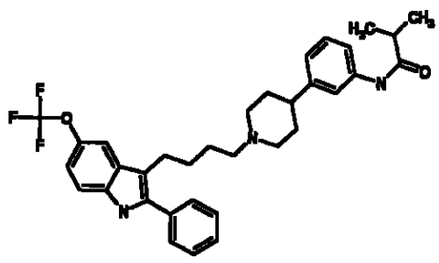
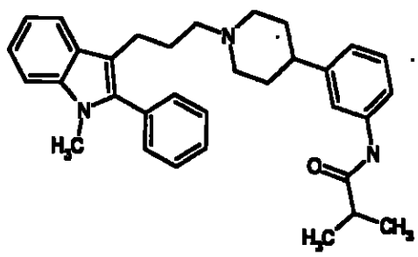
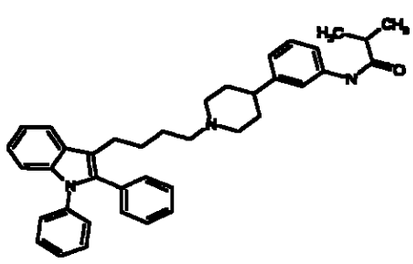
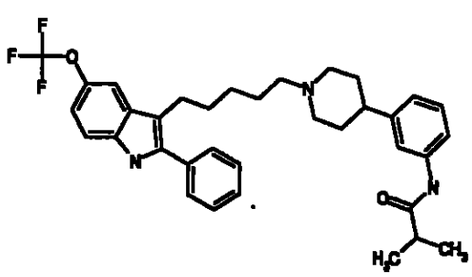
385  324.6

Example	Structure	rMCH1 Ki (nM)

585

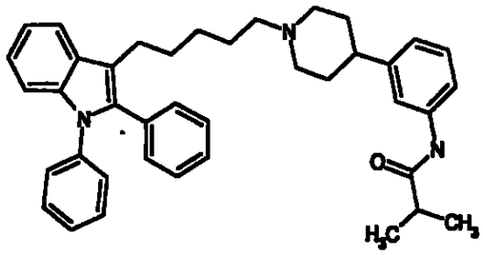
386		26.3
387		19.7
388		20.7
389		2.2

586

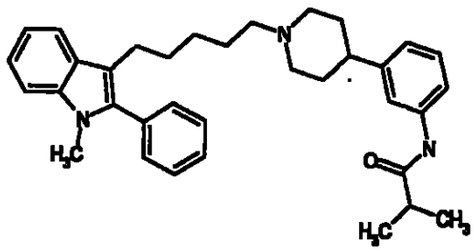
390		1.0
391		21.9
392		18.1
393		9.5

587

394

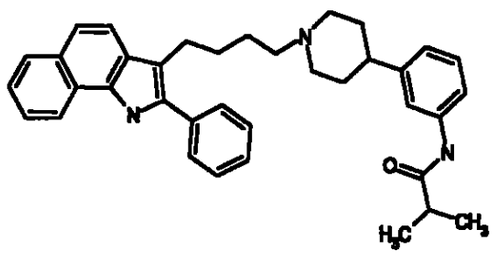


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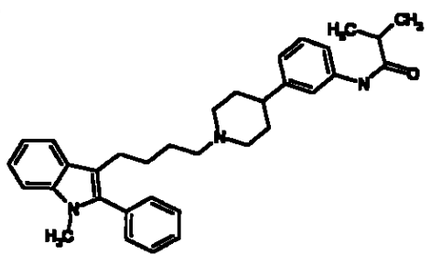


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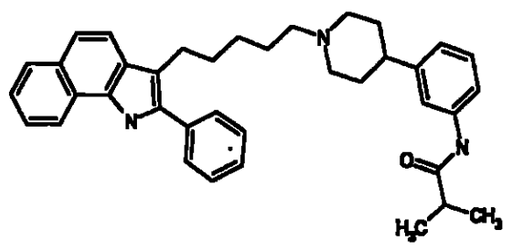
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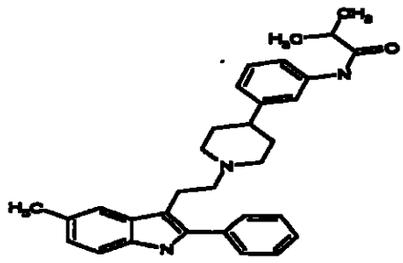


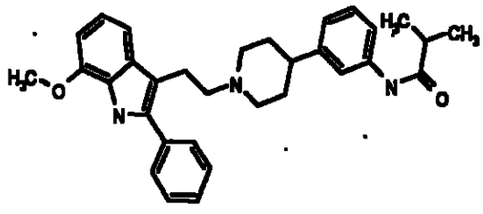
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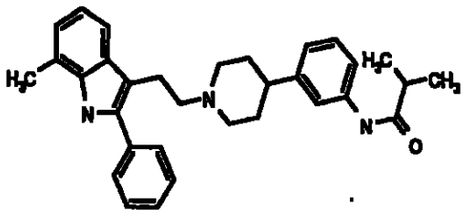


588

398  13.6

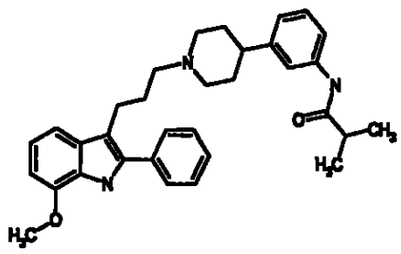
399  31.9

400  43.9

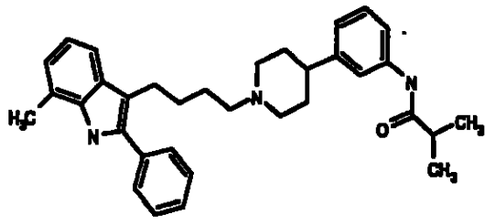
401  44.6

589

402

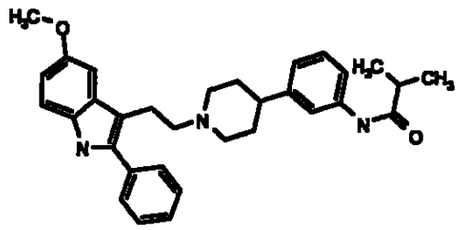


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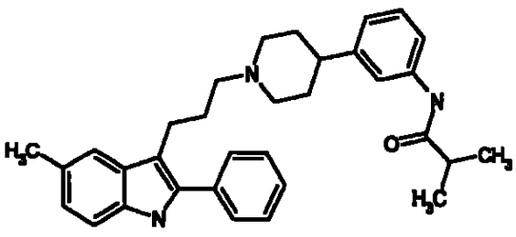


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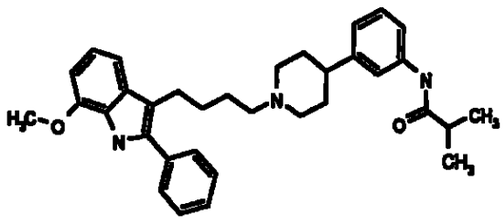
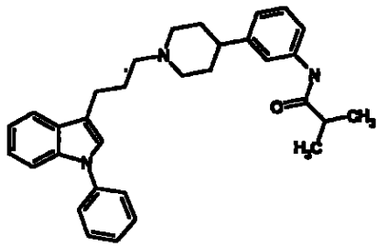
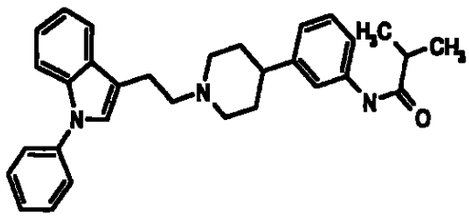
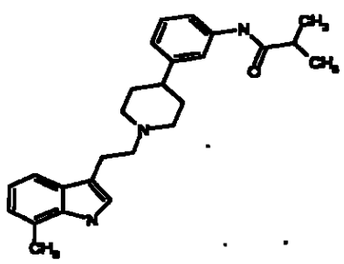
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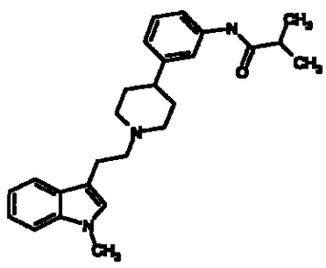
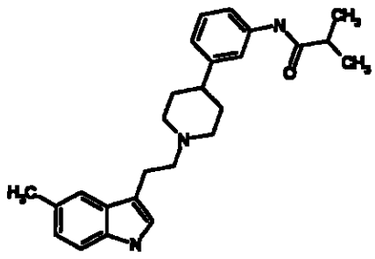
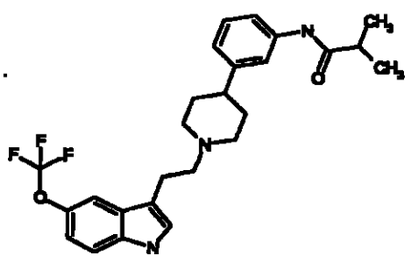
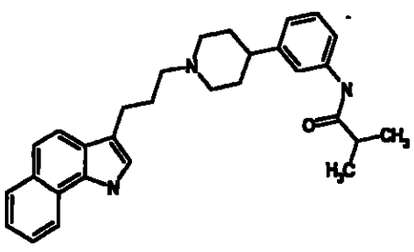


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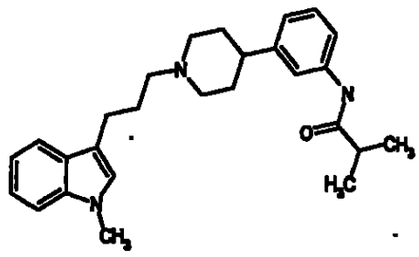
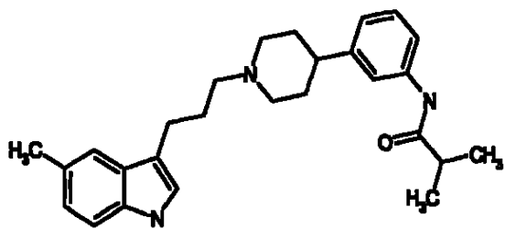
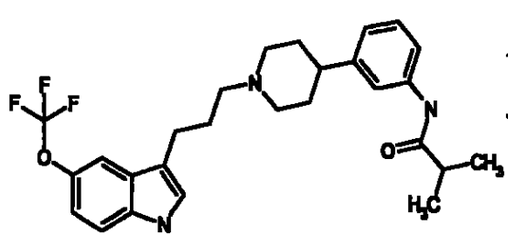
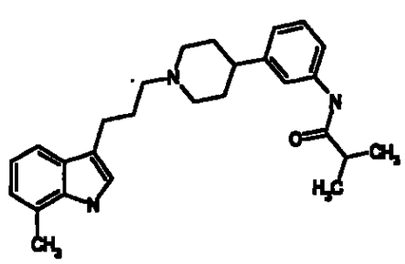


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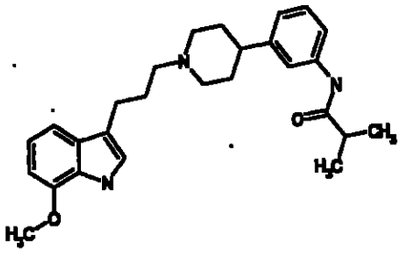
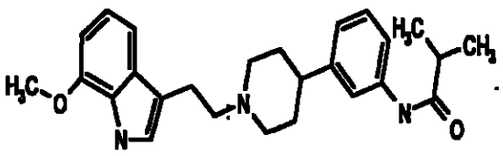
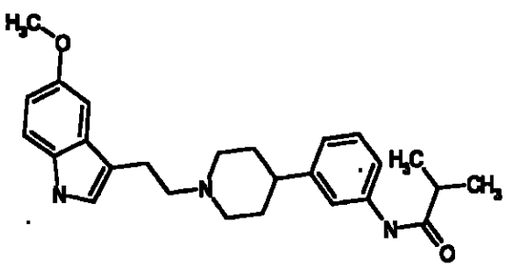
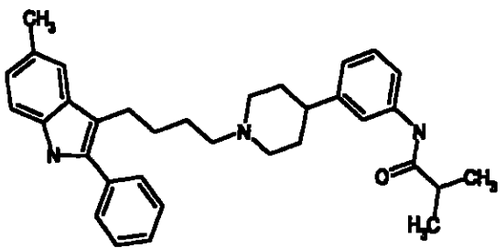
406		12.3
407		16.6
408		21.6
409		96.7

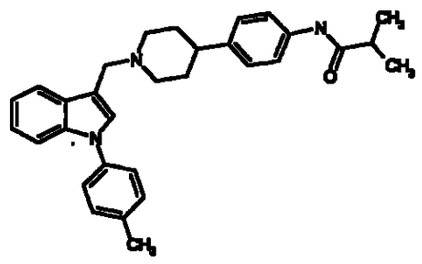
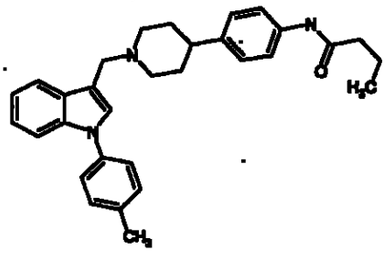
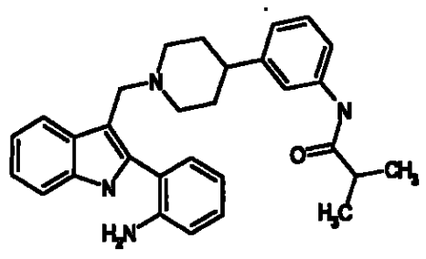
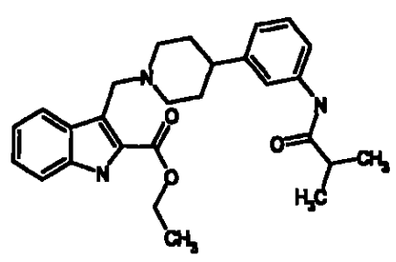
410		591	282.7
411			82.3
412			27.0
413			76.8

592

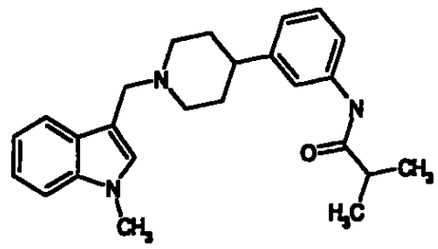
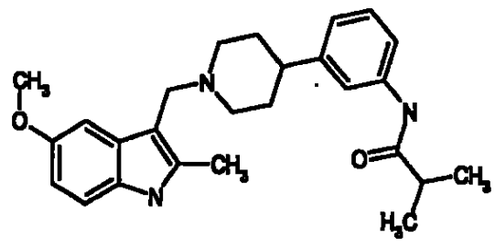
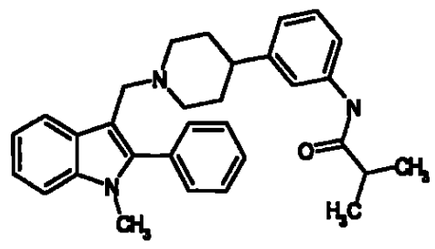
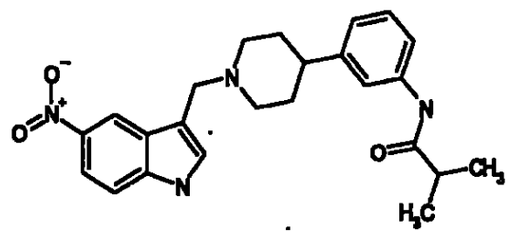
414		2.9
415		8.1
416		12.6
417		20.5

593

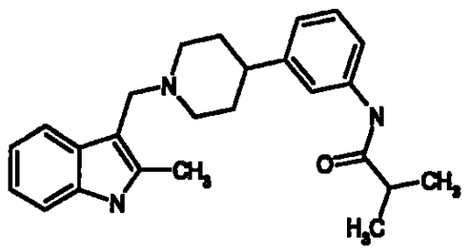
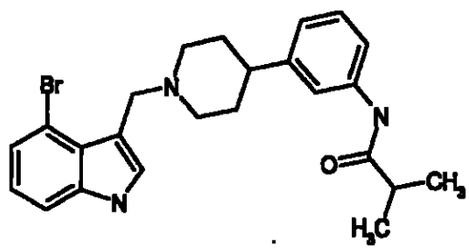
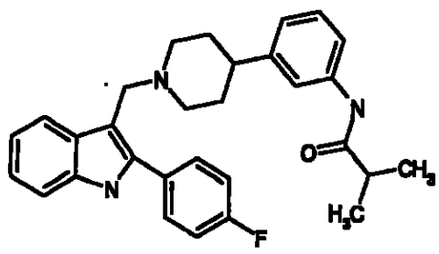
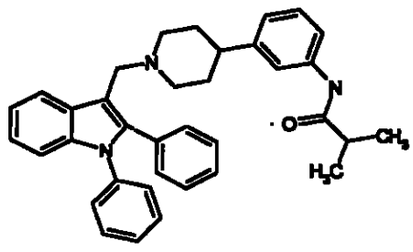
418		51.6
419		83.9
420		
421		1.8

422		173.0
423		405.2
424		114.2
425		599.3

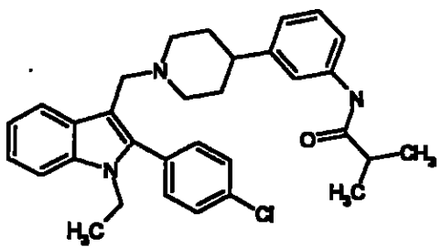
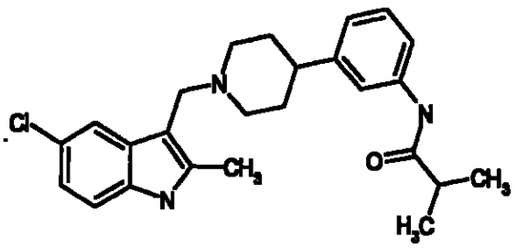
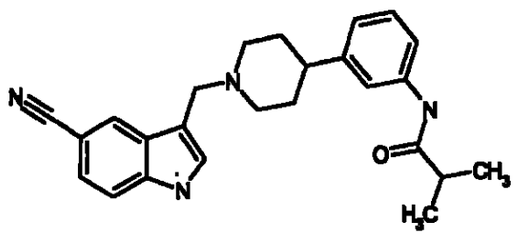
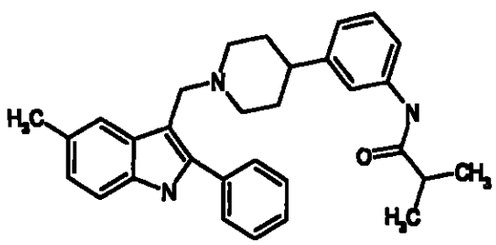
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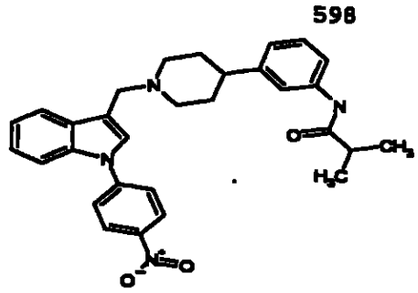
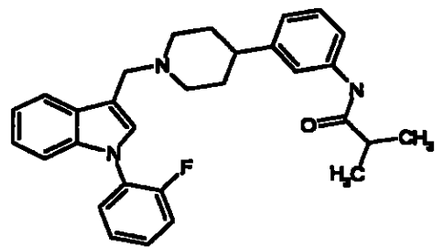
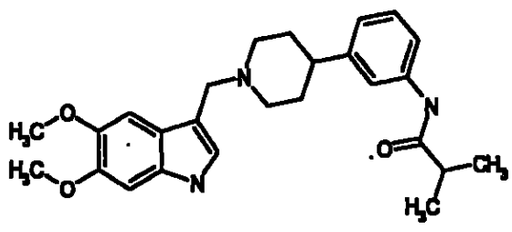
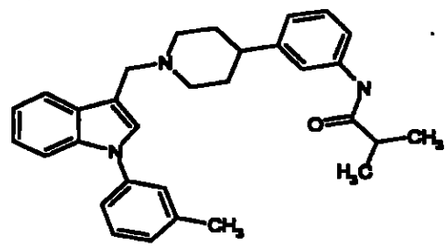
426		556.1
427		248.3
428		132.4
429		121.4

596

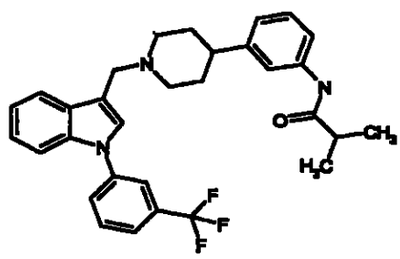
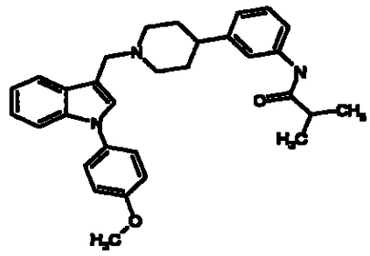
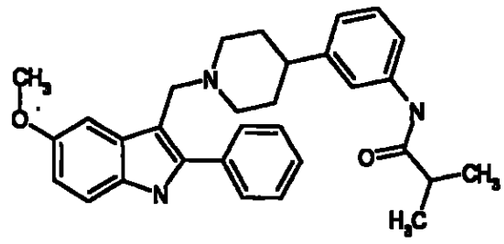
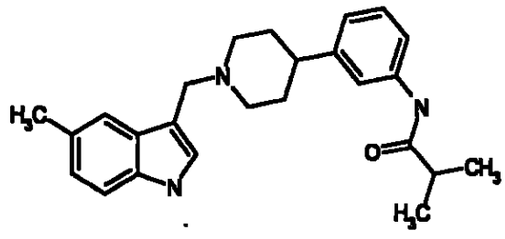
430		647.4
431		967.7
432		198.2
433		30.4

597

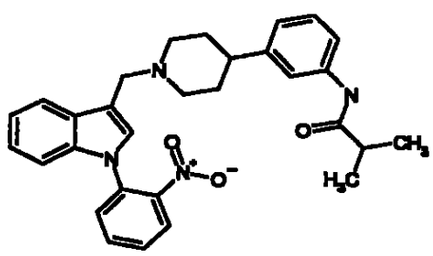
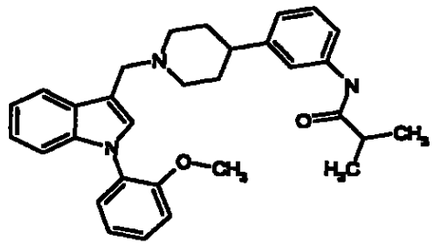
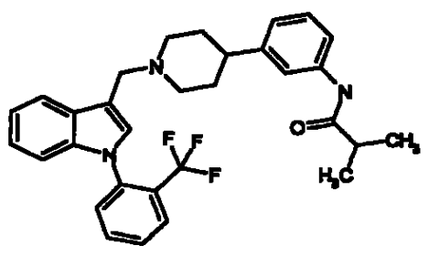
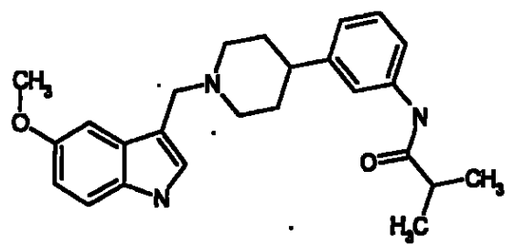
434		214.2
435		215.4
436		434.3
437		552.1

438		598	1.3
439			8.5
440			106.9
441			10.1

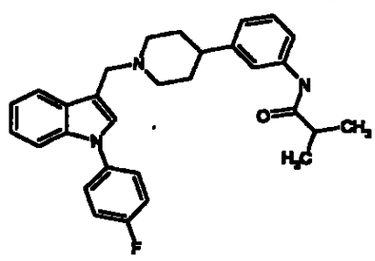
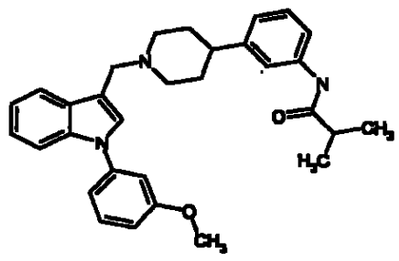
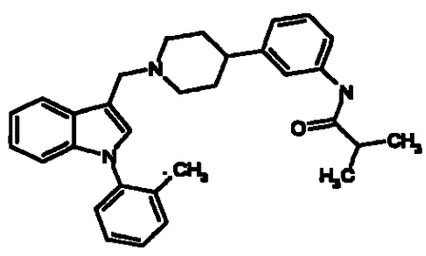
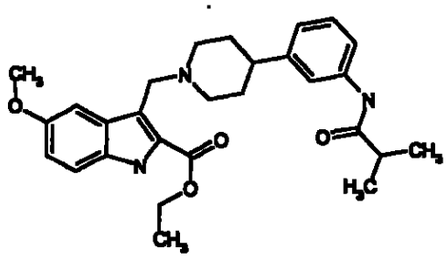
599

442		7.8
443		23.4
444		544.7
445		486.3

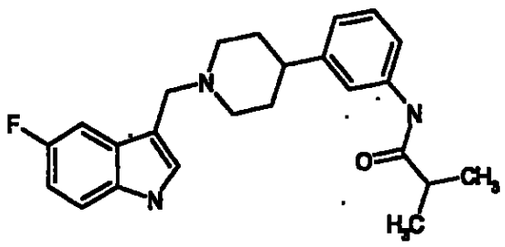
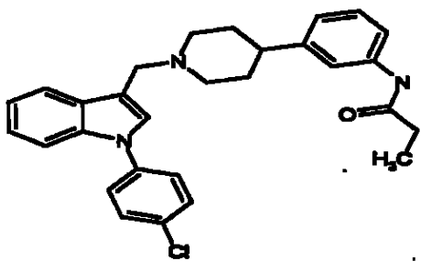
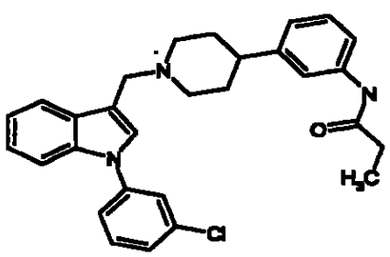
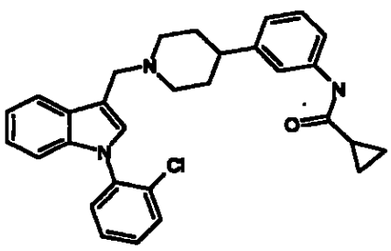
600

446		17.9
447		9.8
448		61.0
449		823.4

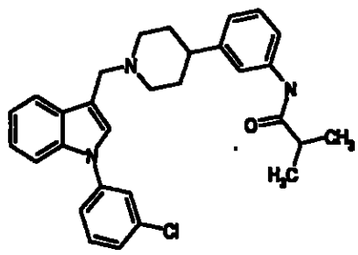
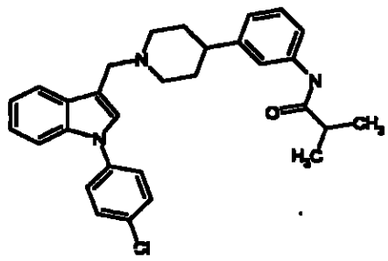
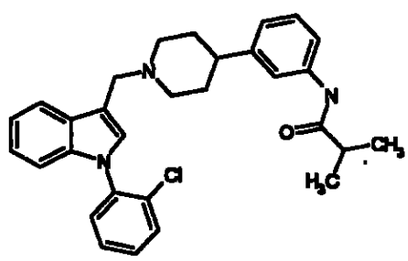
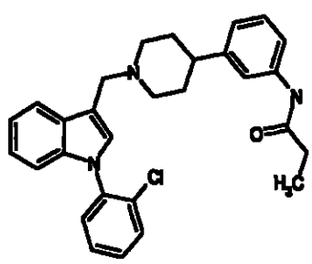
601

450		7.1
451		18.7
452		12.7
453		194.8

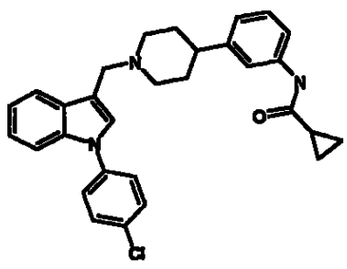
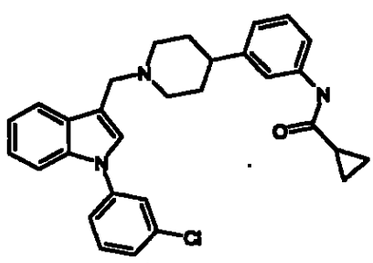
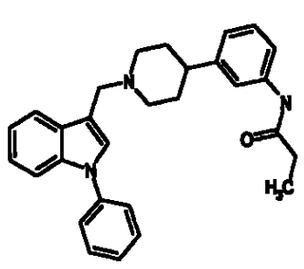
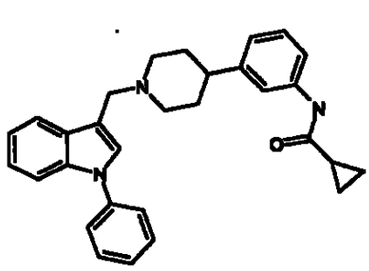
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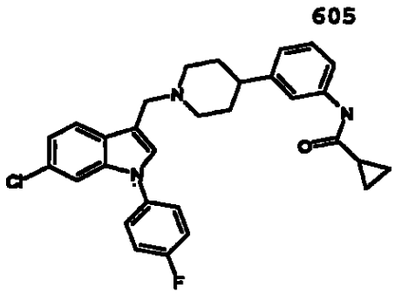
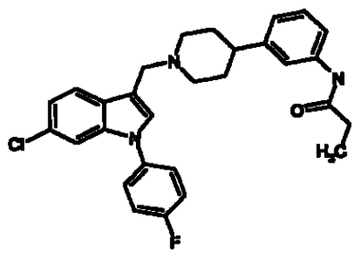
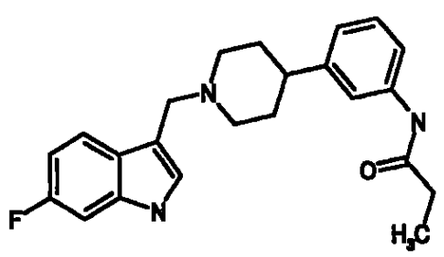
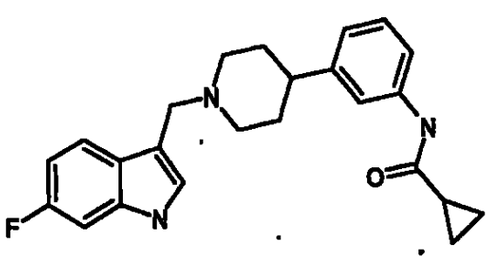
454		772.0
455		10.6
456		28.0
457		27.4

603

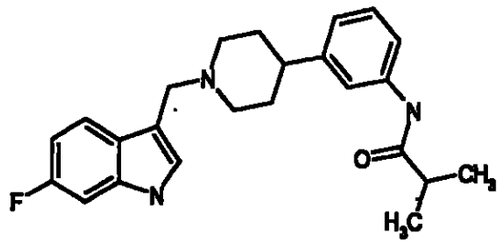
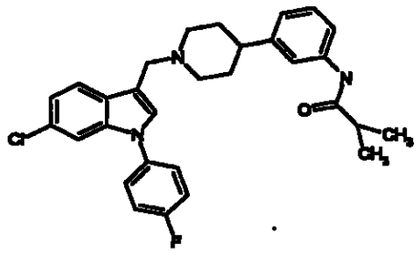
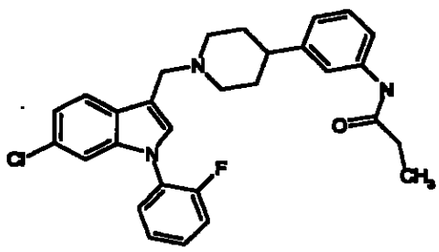
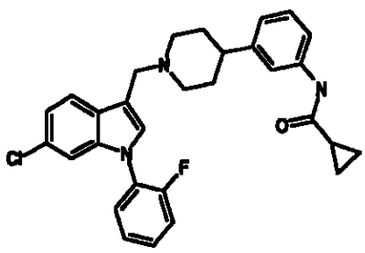
458		15.3
459		10.4
460		9.1
461		35.6

604

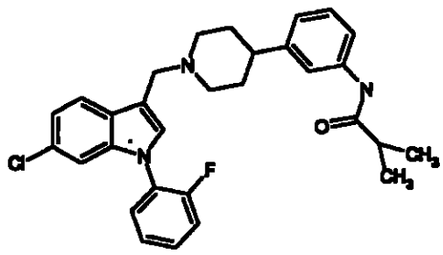
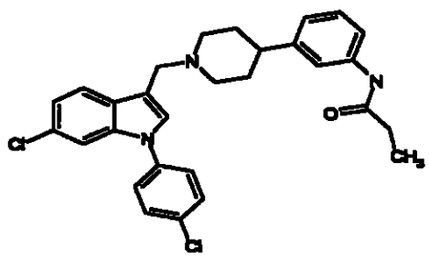
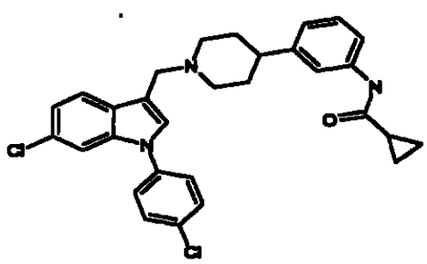
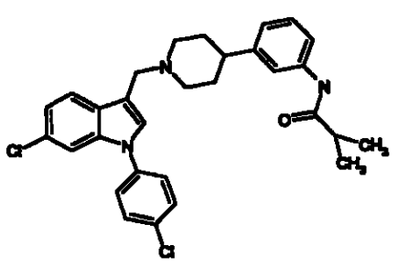
462		12.4
463		17.2
464		84.1
465		10.7

466		605
467		
468		912.3
469		479.5

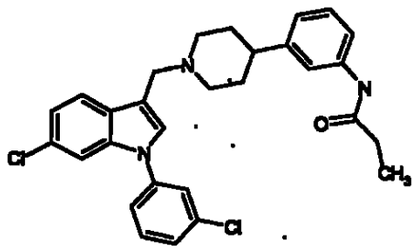
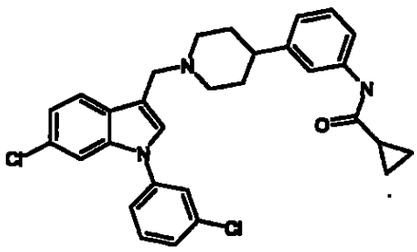
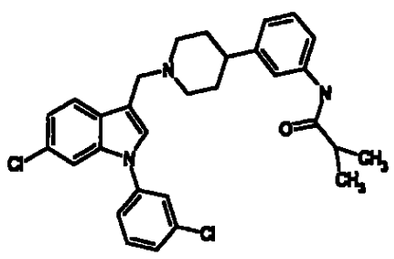
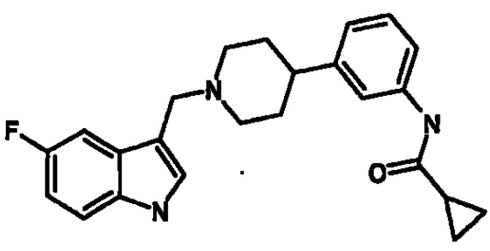
606

470		654.1
471		4.3
472		12.2
473		11.3

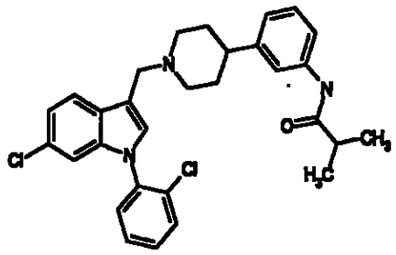
607

474		13.3
475		12.4
476		12.7
477		14.9

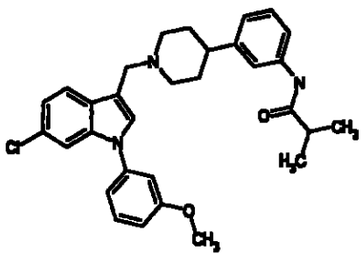
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478		11.7
479		8.1
480		9.0
481		664.0

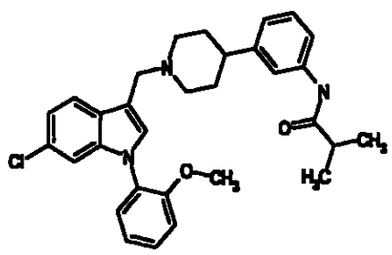
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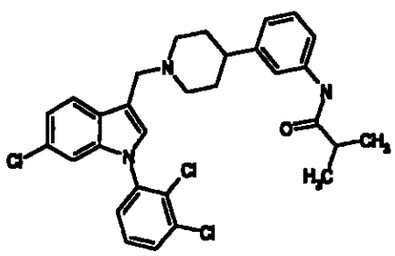
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484

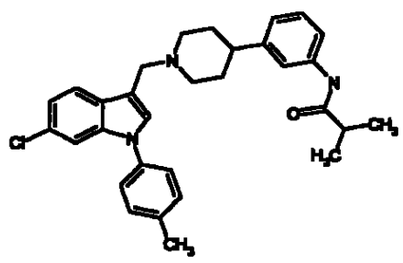


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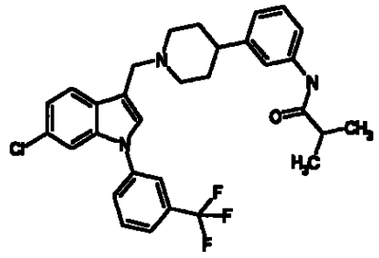


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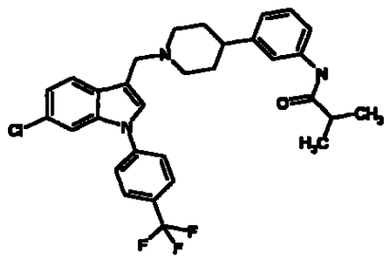
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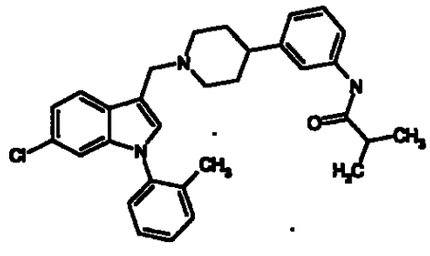
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488

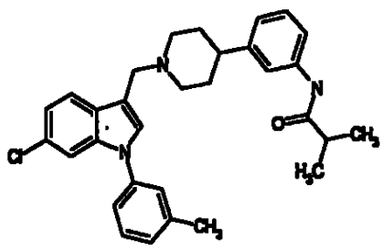


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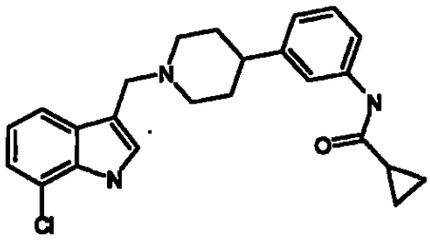


611

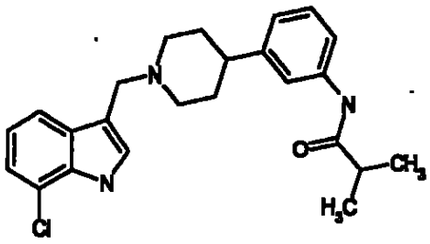
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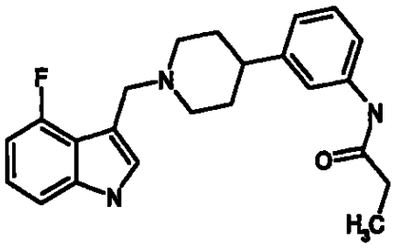
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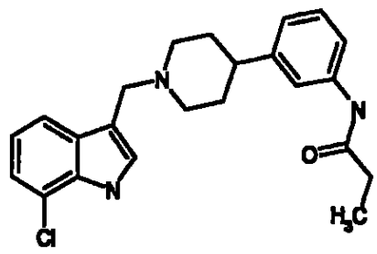
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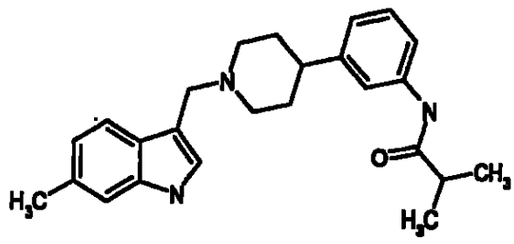
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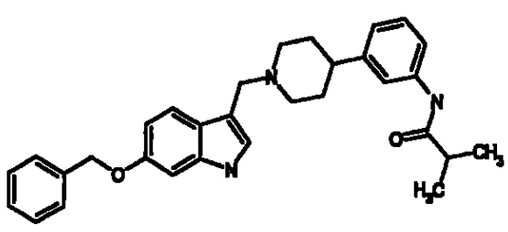
494 612



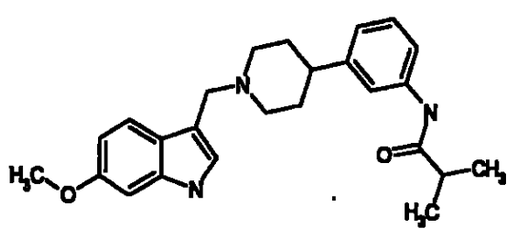
495 95.1



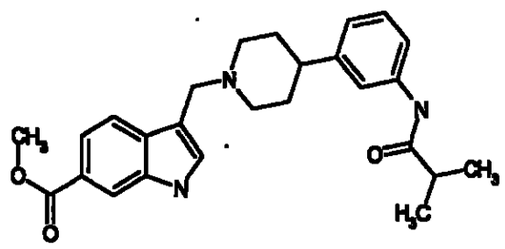
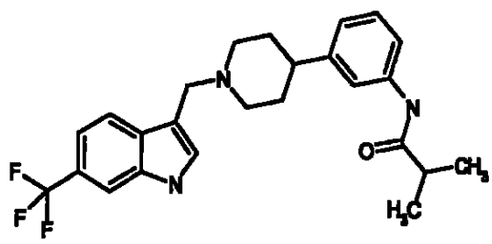
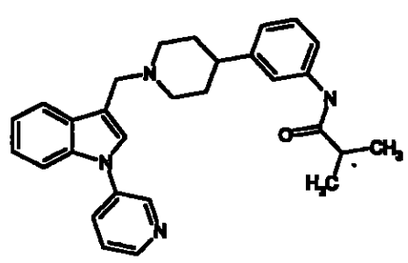
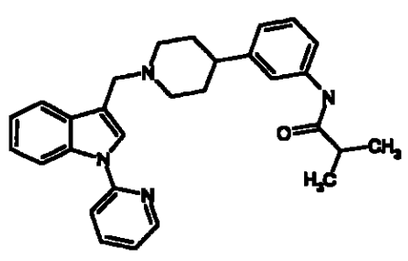
496 286.0



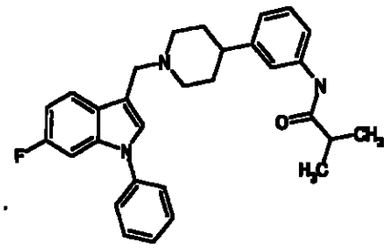
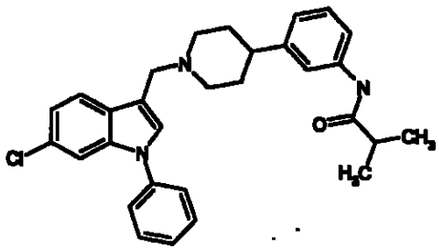
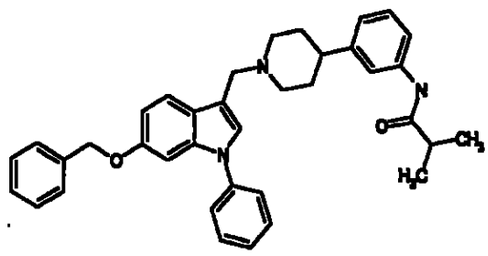
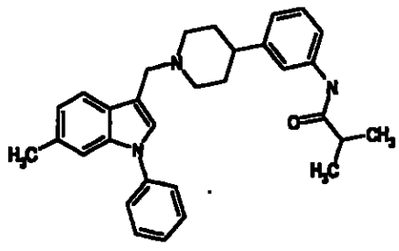
497 97.7



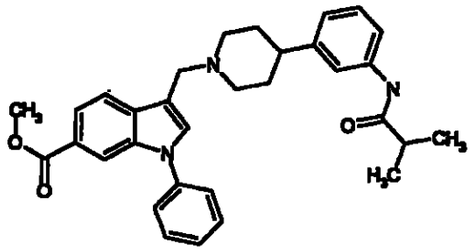
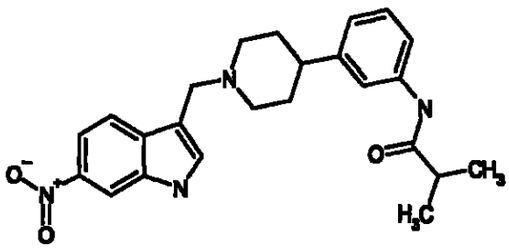
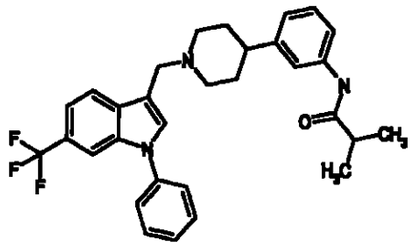
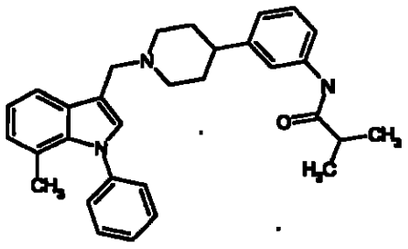
613

498		52.2
499		11.9
500		29.4
501		22.1

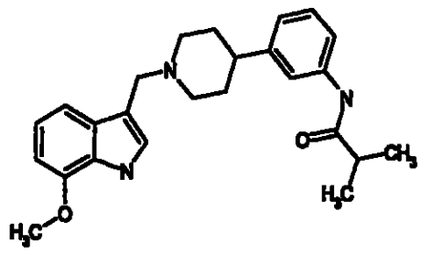
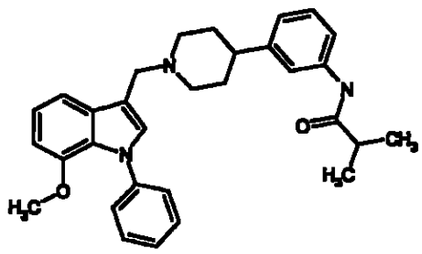
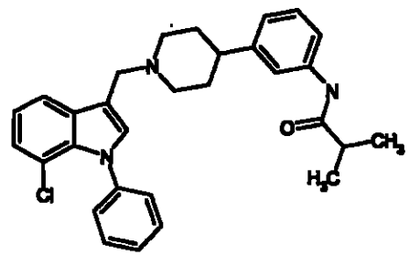
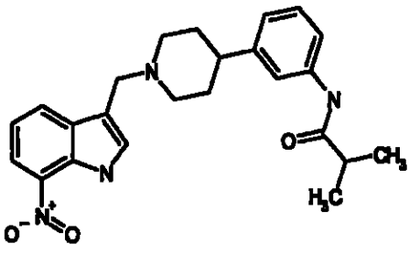
614

502		4.6
503		8.0
504		22.5
505		6.5

615

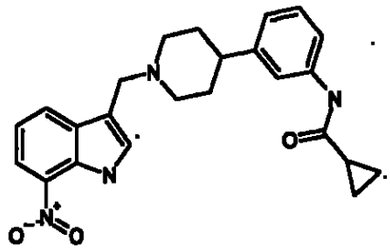
506		2.5
507		57.9
508		8.5
509		24.3

616

510		304.9
511		6.0
512		42.7
513		178.7

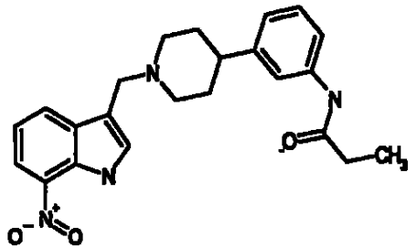
617

514



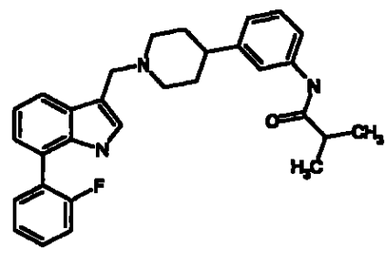
151.4

515



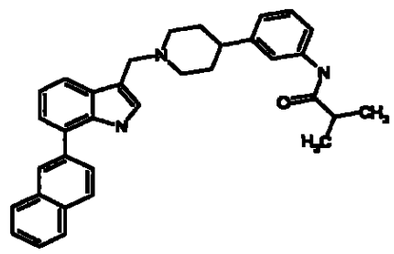
296.2

516



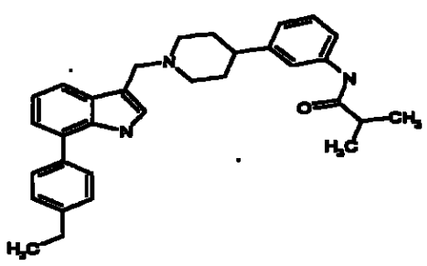
90.9

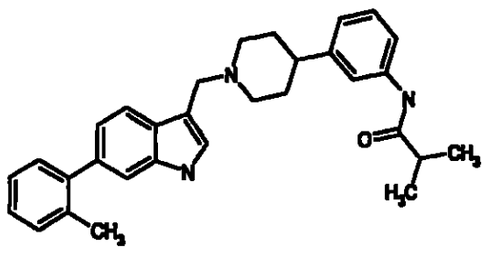
517

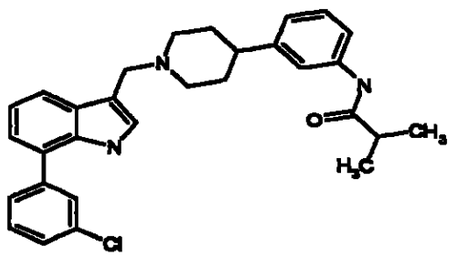


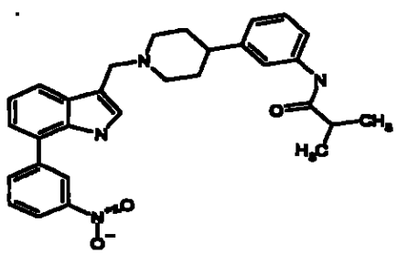
286.9

618

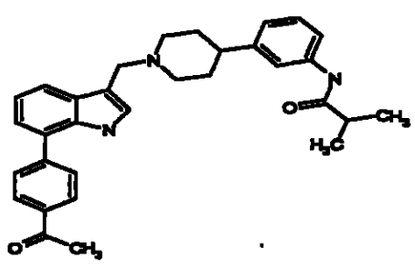
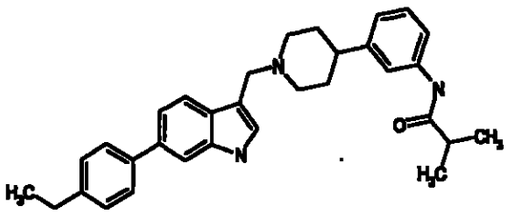
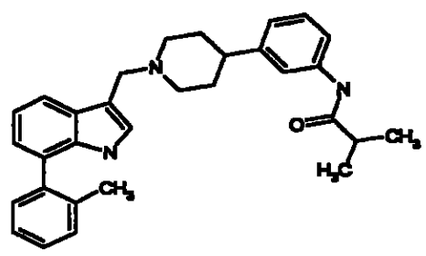
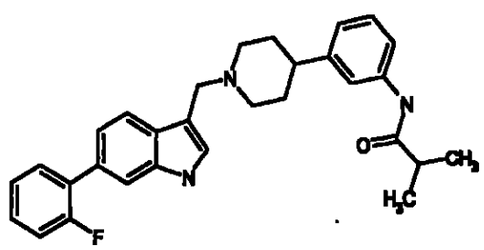
518  226.2

519  80.9

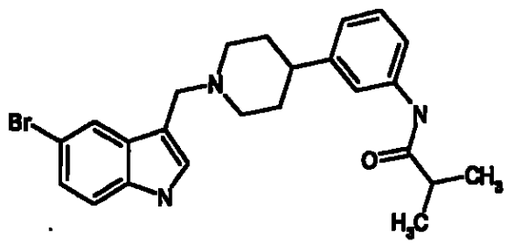
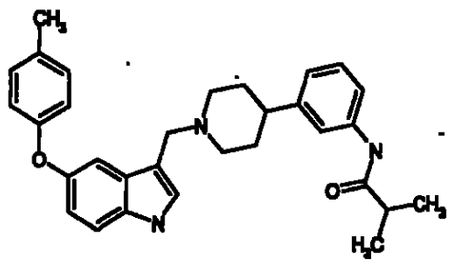
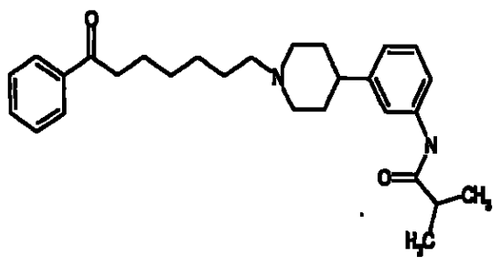
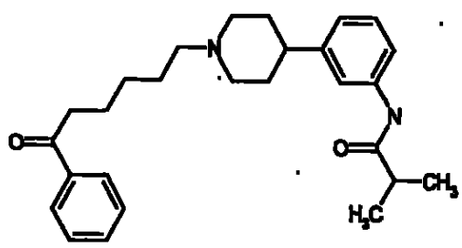
520  135.1

521  27.0

619

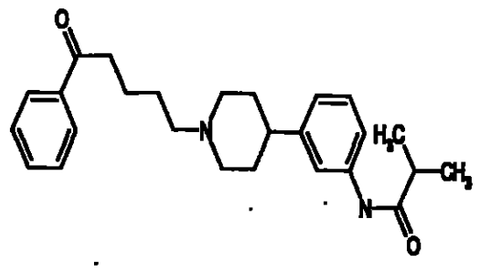
522		247.0
523		54.8
524		198.7
525		91.4

620

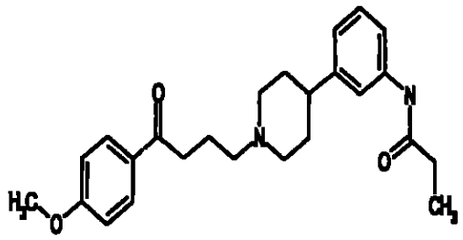
526		410.8
527		226.5
528		115.1
529		42.4

621

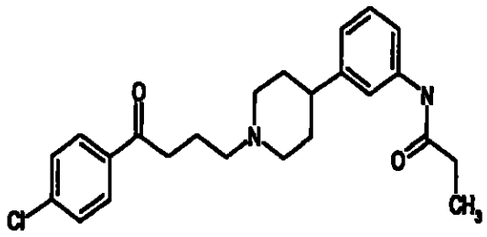
530



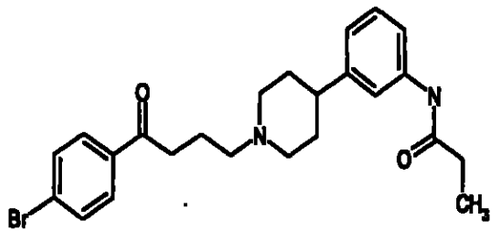
531 105.3



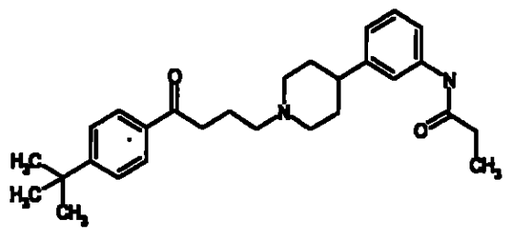
532 8.7



533 10.6

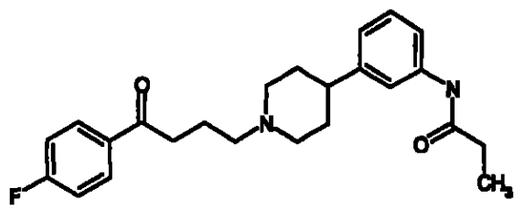


534



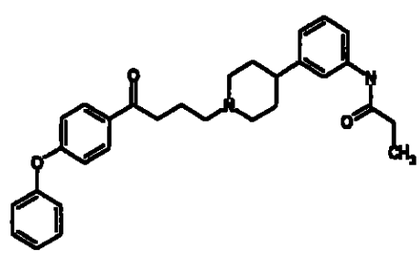
154.9

535



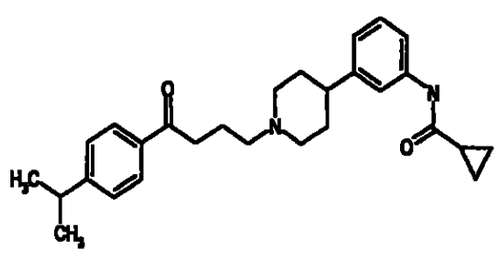
28.1

536

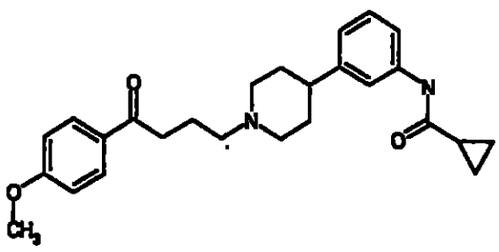
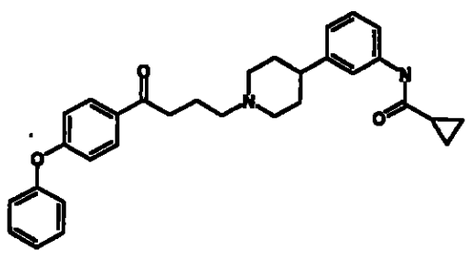
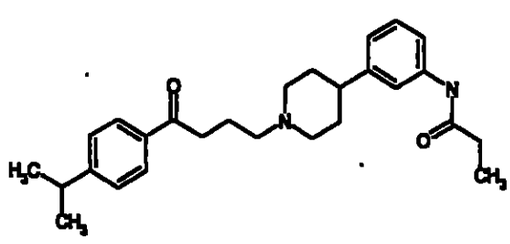
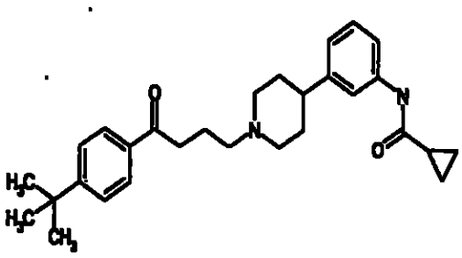


150.4

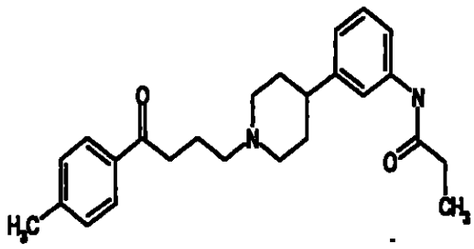
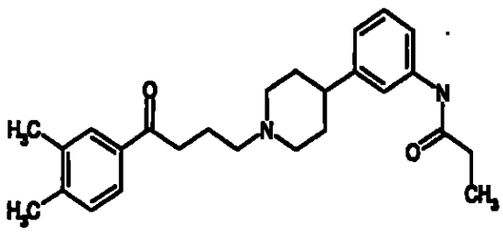
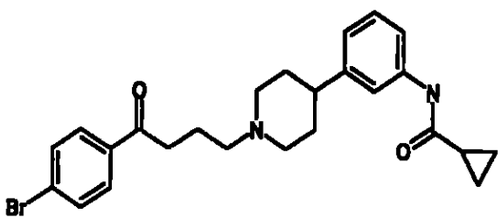
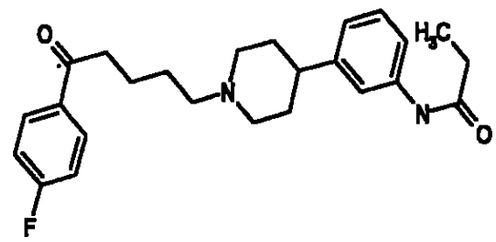
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67.7

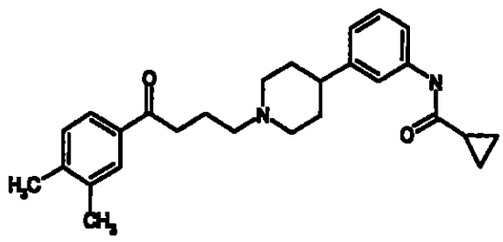
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539		288.4
540		172.3
541		318.6

624

542		31.3
543		27.8
544		16.2
545		52.0

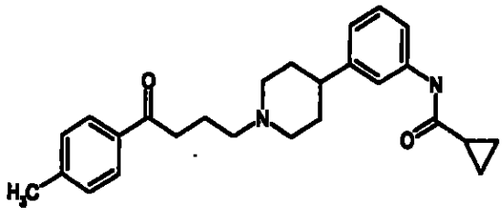
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546



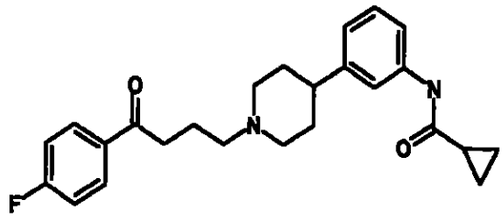
87.9

547



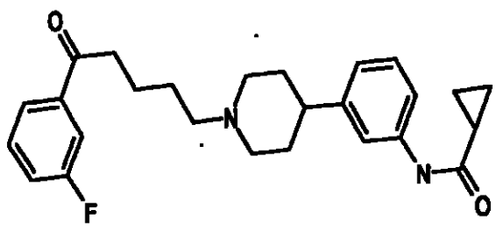
75.5

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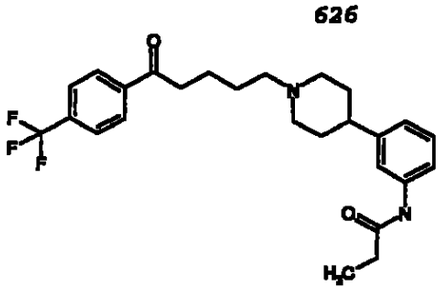
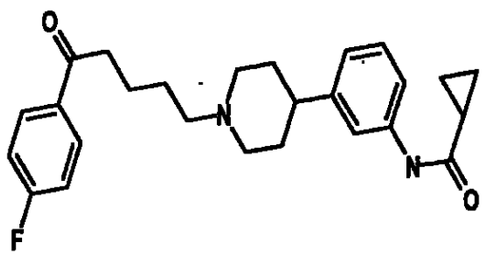
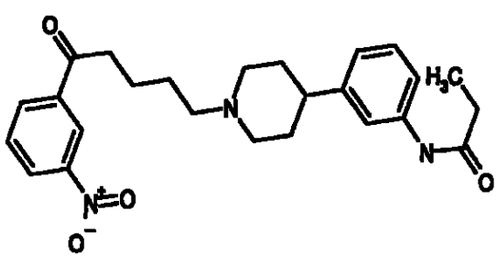
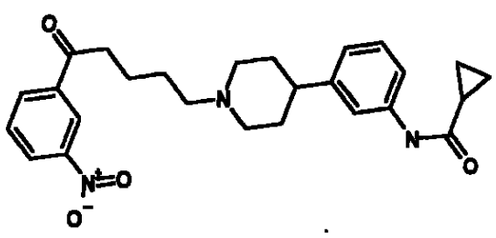


125.6

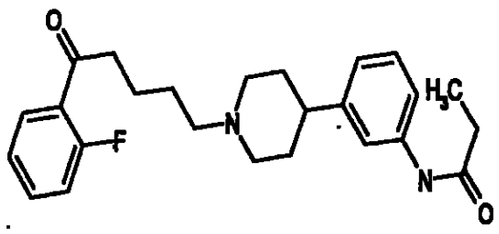
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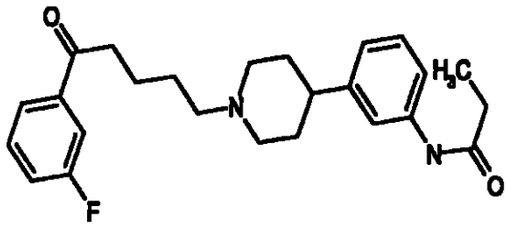


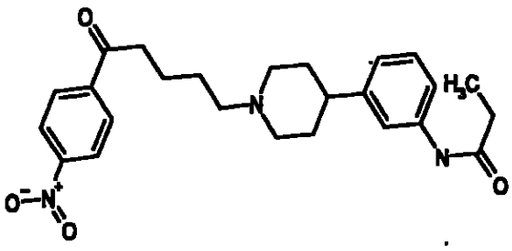
39.7

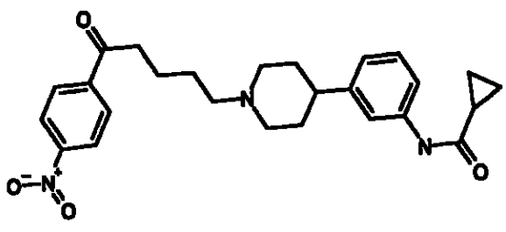
550		60.9
551		21.6
552		24.7
553		27.5

627

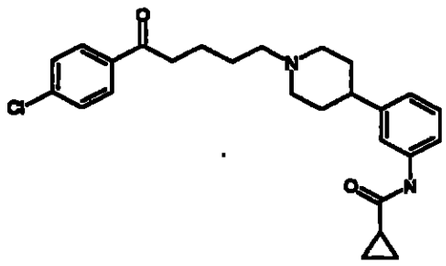
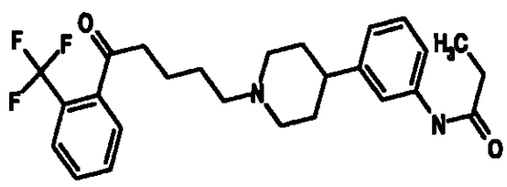
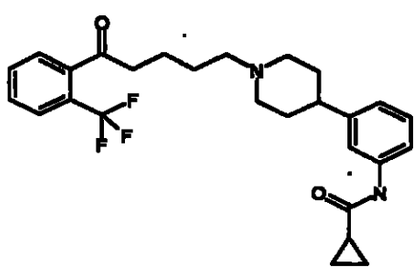
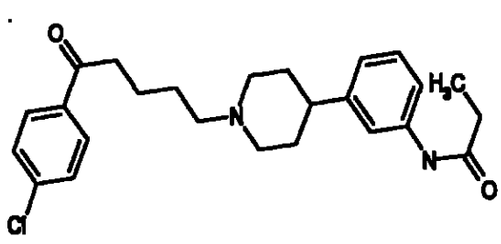
554  70.9

555  50.3

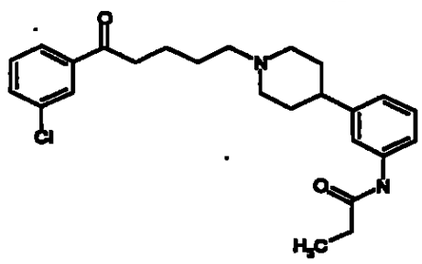
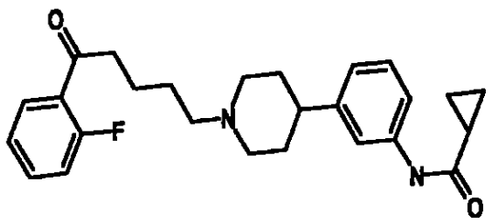
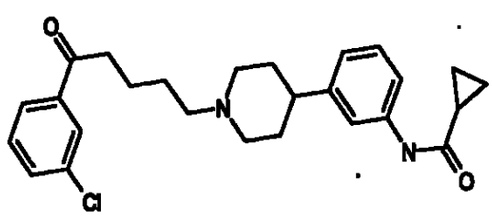
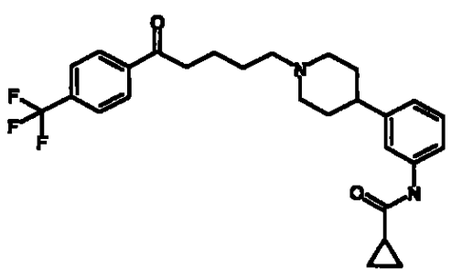
556  35.6

557  25.6

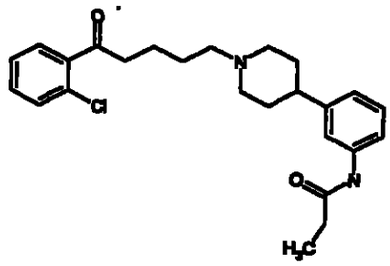
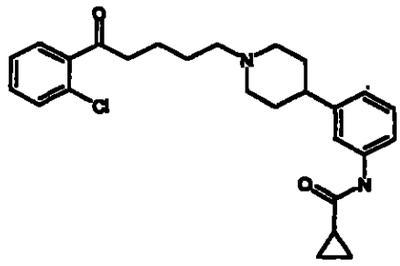
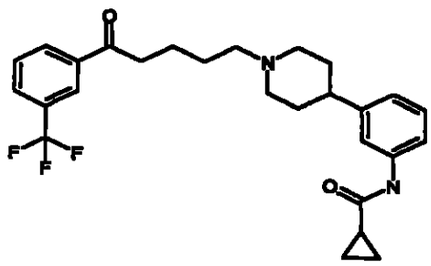
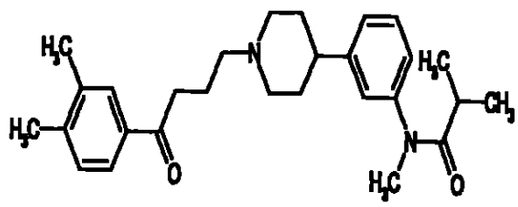
628

558		20.2
559		62.3
560		55.7
561		92.9

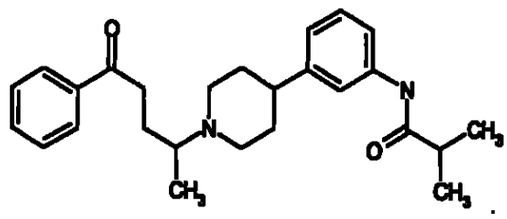
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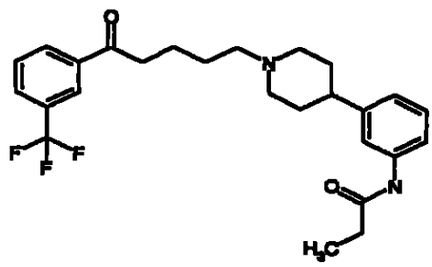
562		48.1
563		50.2
564		28.9
565		49.2

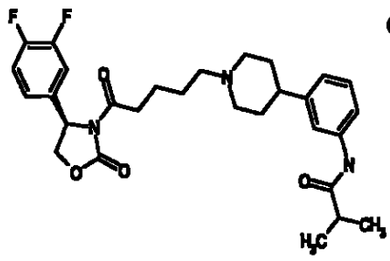
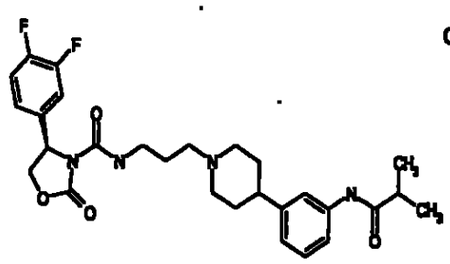
630

566		77.8
567		92.2
568		68.8
569		549.3

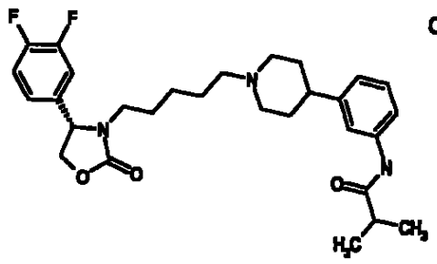
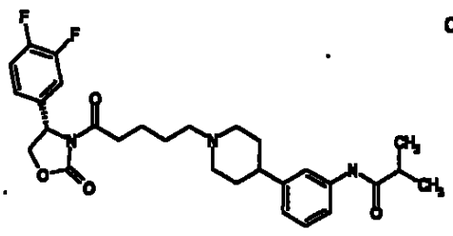
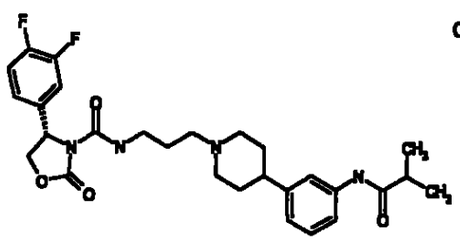
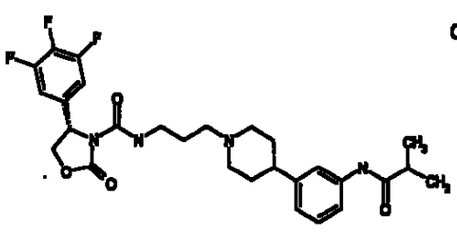
631

570  136.3

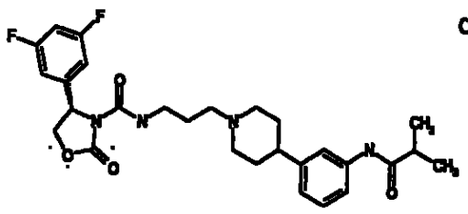
571  88.3

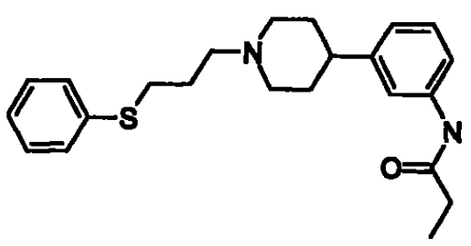
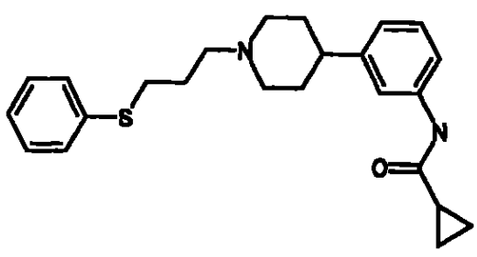
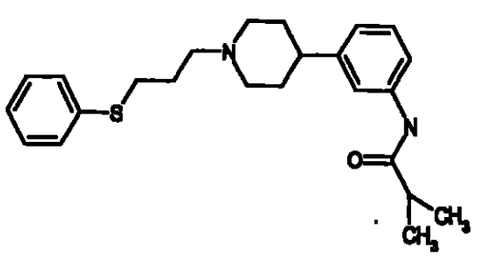
Example	Structure		rMCH1 Ki (nM)
572		Chiral	181.5
573		Chiral	114.3

632

574		Chiral	87.1
575		Chiral	192.6
576		Chiral	74.3
577		Chiral	64.7

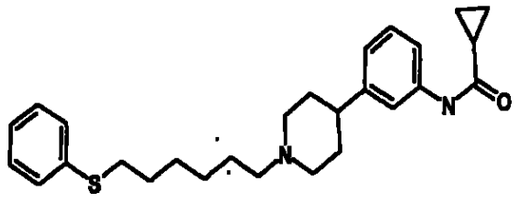
633

578		Chiral	98.8

Example	Structure	rMCH1 Ki (nM)
579		131.1
580		54.0
581		86.4

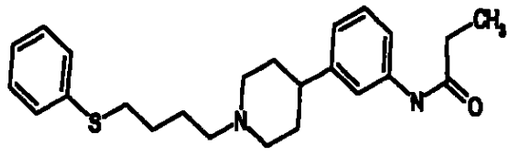
634

582



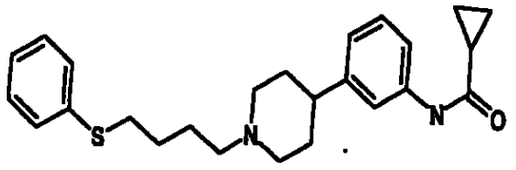
58.3

583



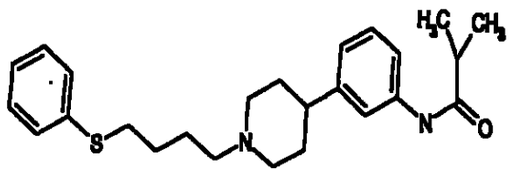
65.6

584



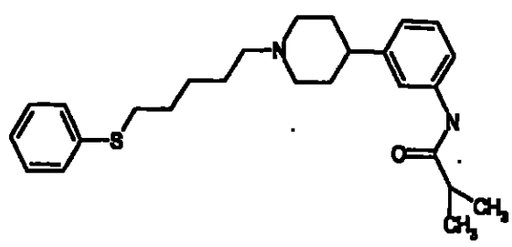
51.8

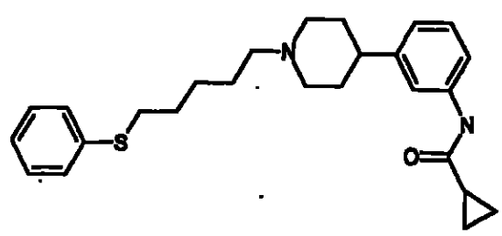
585

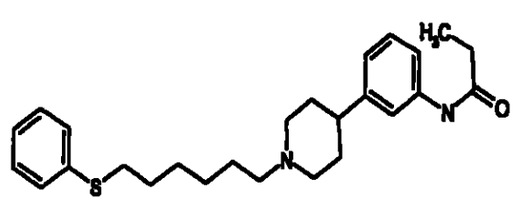


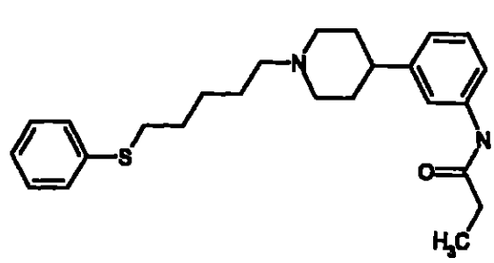
37.2

635

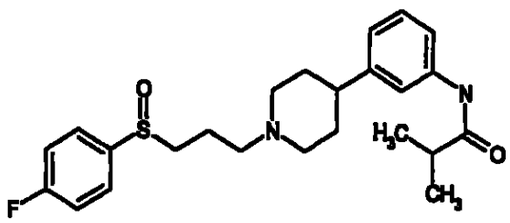
586  42.9

587  46.9

588  283.9

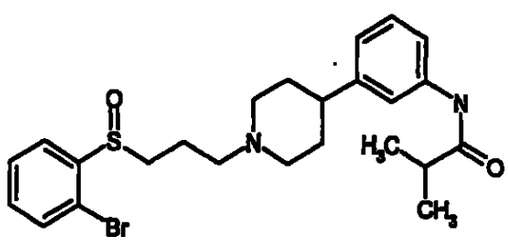
589  66.6

590

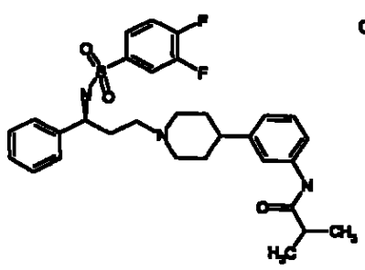
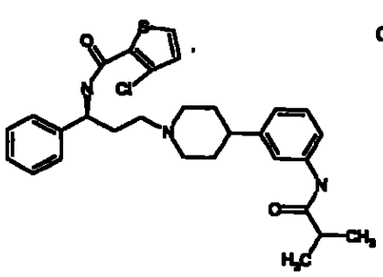


157.1

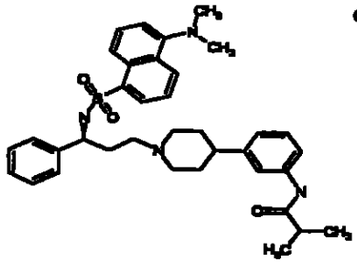
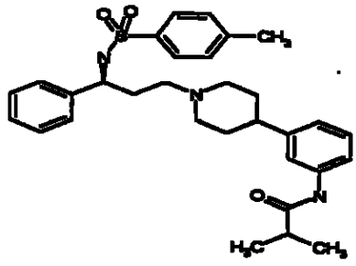
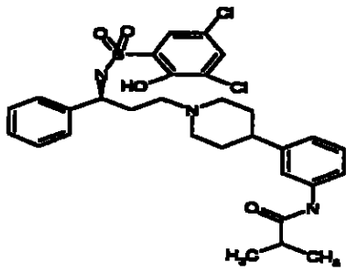
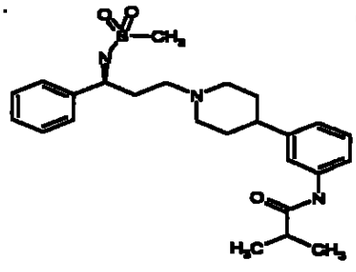
591

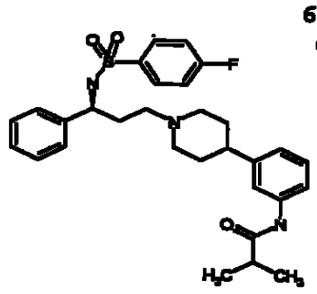
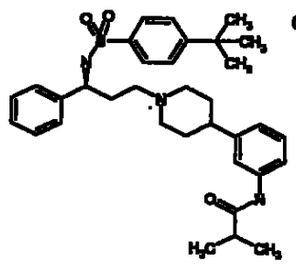
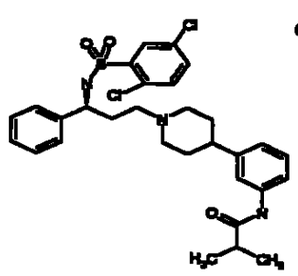
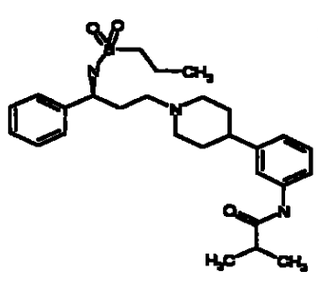


137.5

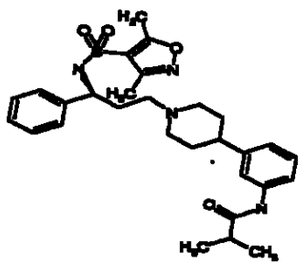
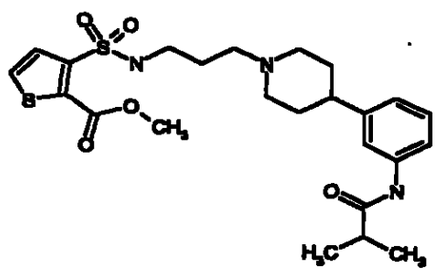
Example	Structure		rMCH1 Ki (nM)
592		Chiral	185.6
593		Chiral	7.6

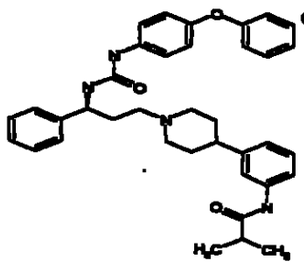
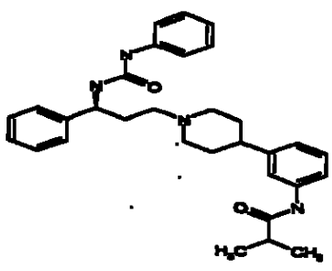
637

594		Chiral	67.0
595		Chiral	38.3
596		Chiral	596.7
597		Chiral	222.7

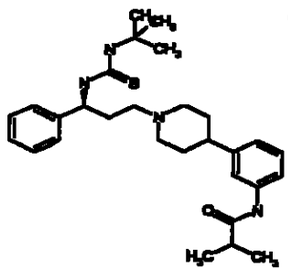
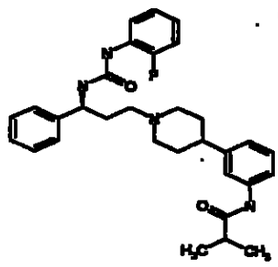
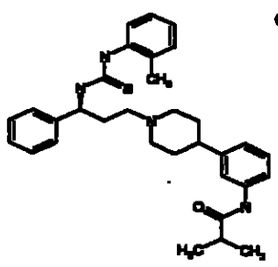
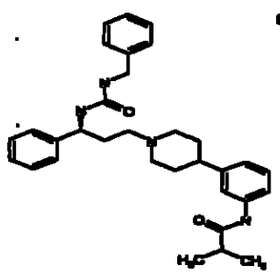
638			
598		Chiral	25.3
599		Chiral	50.0
600		Chiral	41.3
601		Chiral	144.2

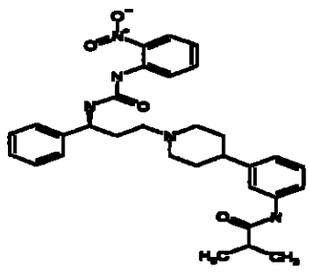
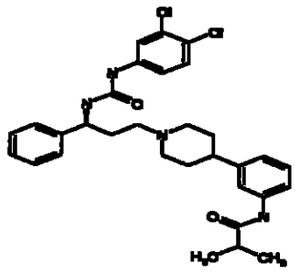
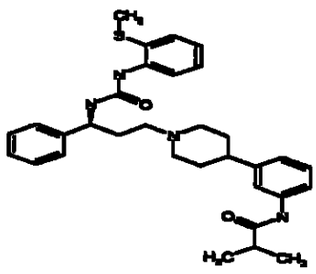
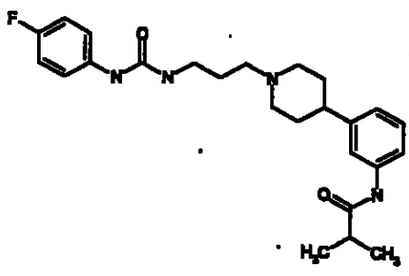
639

602		Chiral	44.6
603			288.8

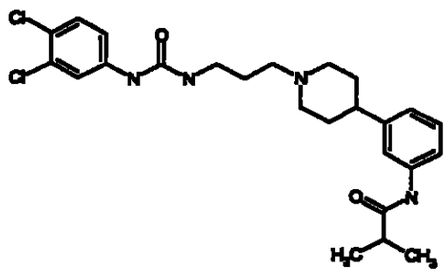
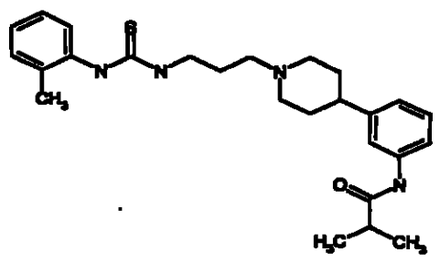
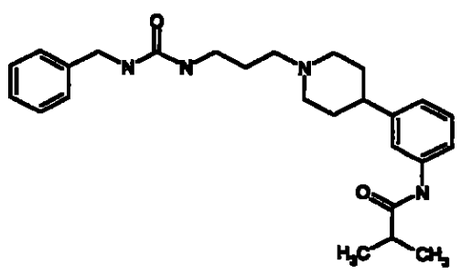
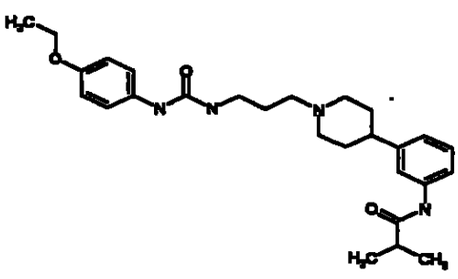
Example	MOLSTRUCTURE		rMCH1 Ki (nM)
604		Chiral	36.8
605		Chiral	94.5

640

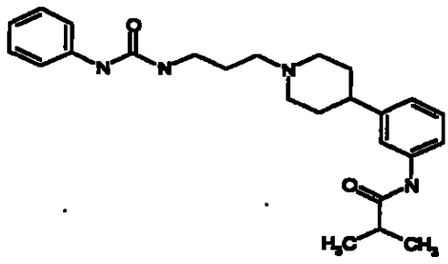
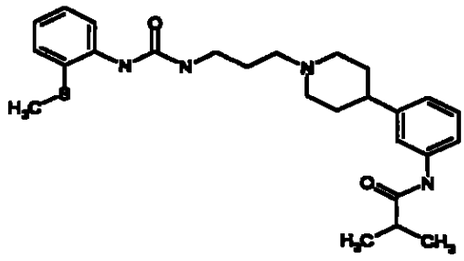
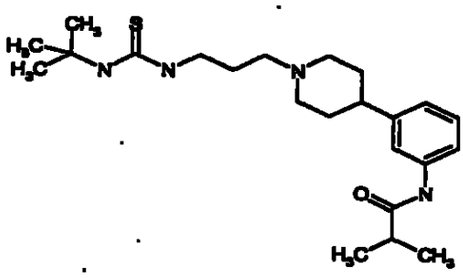
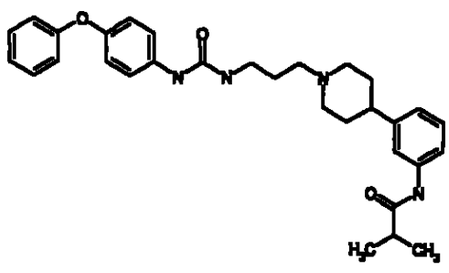
606		Chiral	40.4
607		Chiral	142.1
608		Chiral	34.9
609		Chiral	35.4

610		Chiral	529.8
611		Chiral	85.1
612		Chiral	121.0
613			34.9

642

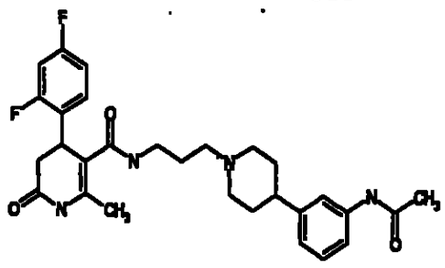
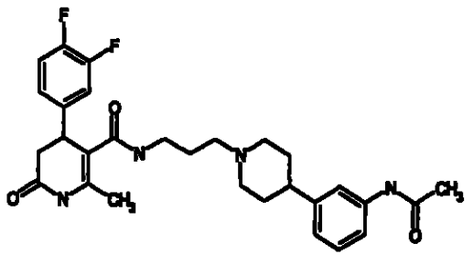
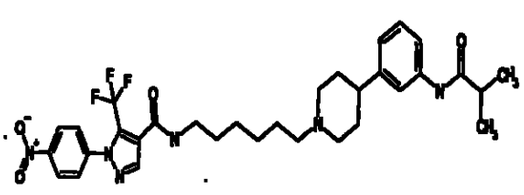
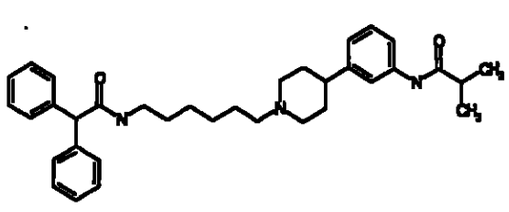
614		84.8
615		210.5
616		405.6
617		608.9

643

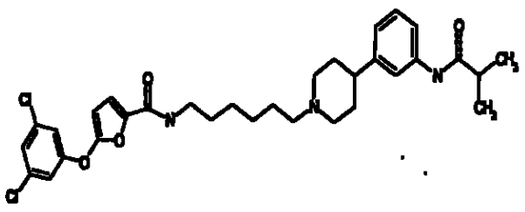
618		399.5
619		177.5
620		223.3
621		204.6

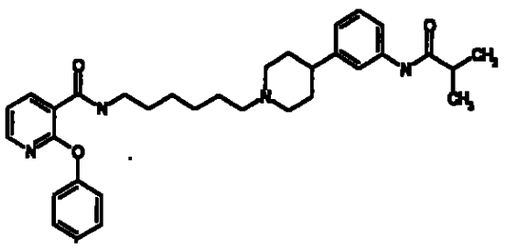
Example	Structure	rMCH1 Ki (nM)

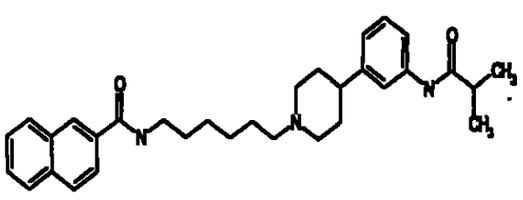
644

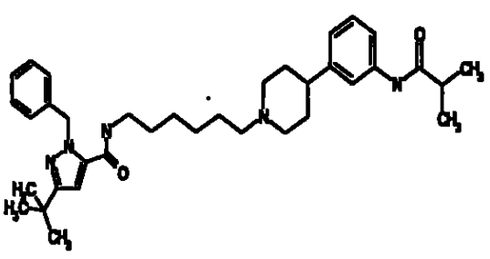
622		162.4
623		23.1
624		47.8
625		29.5

645

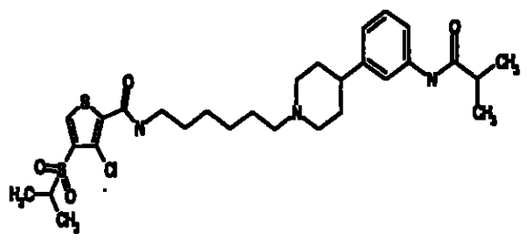
626  20.9

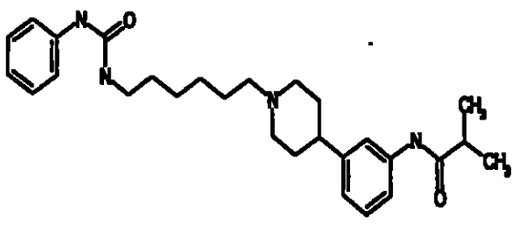
627  109.1

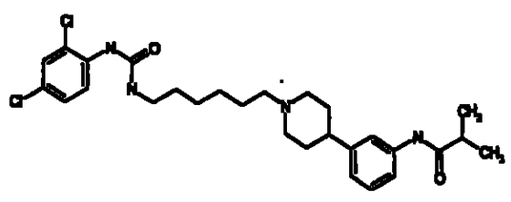
628  160.6

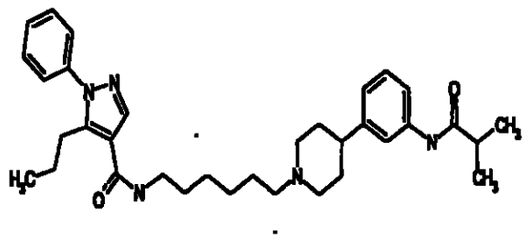
629  42.9

646

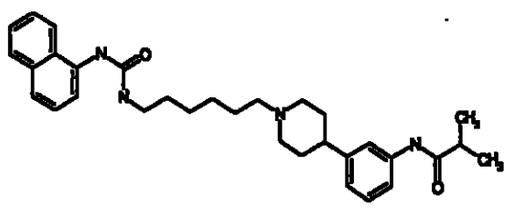
630  201.8

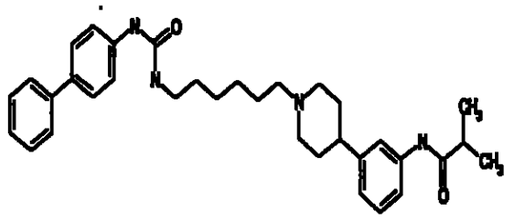
631  256.8

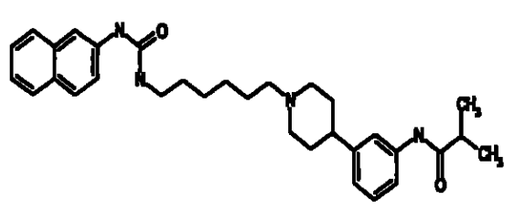
632  76.6

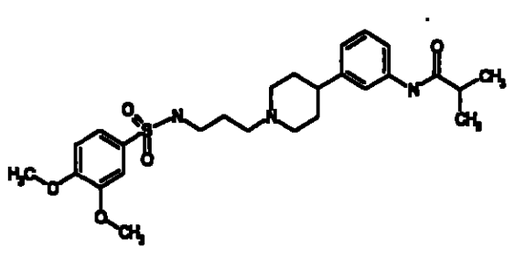
633  107.9

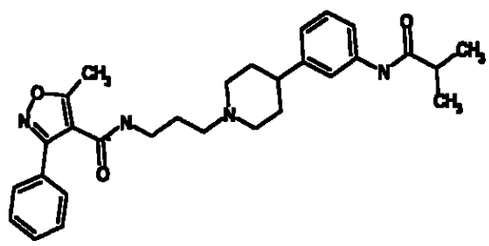
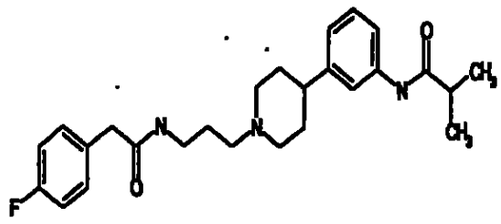
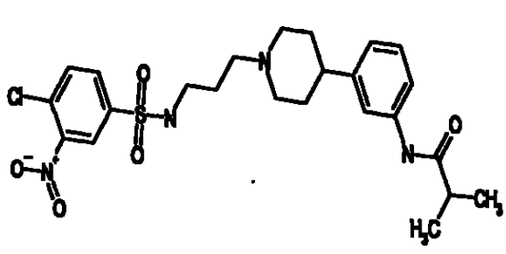
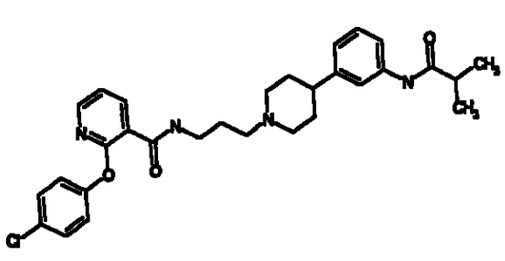
647

634  116.1

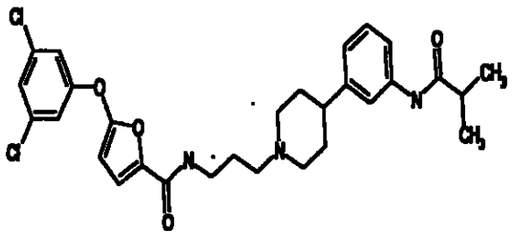
635  73.6

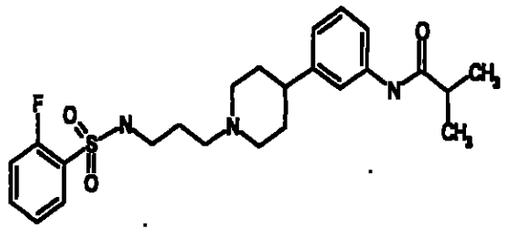
636  40.8

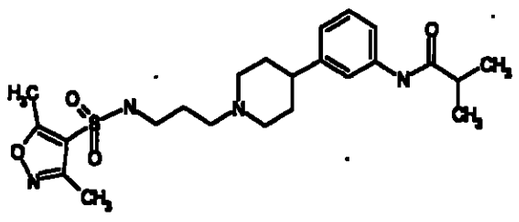
637  105.6

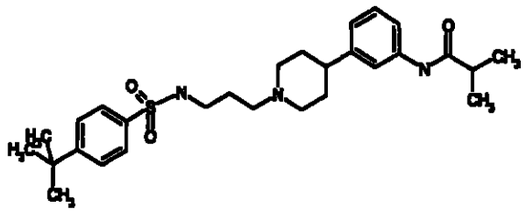
	648	
638		29.8
639		36.3
640		11.2
641		14.2

649

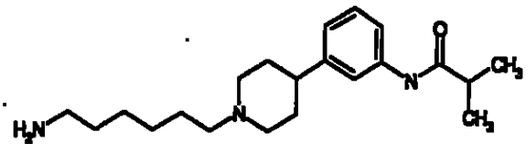
642  8.3

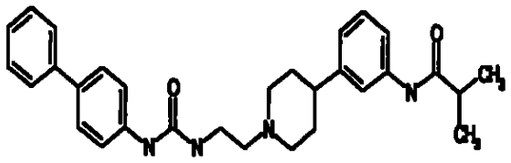
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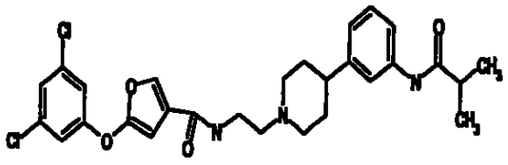
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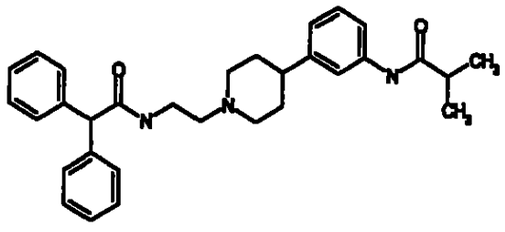
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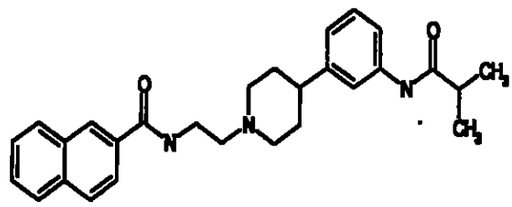
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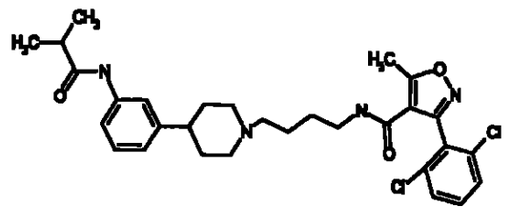
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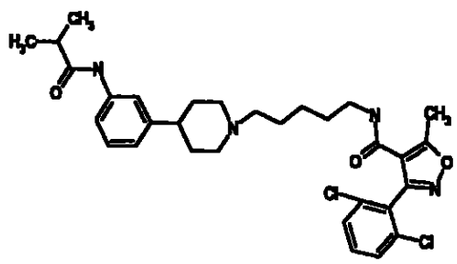
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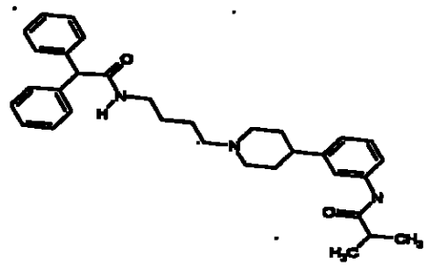
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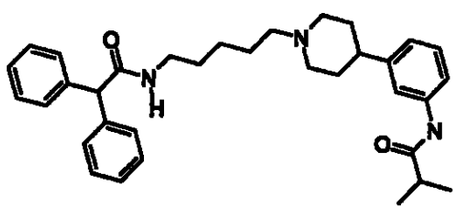
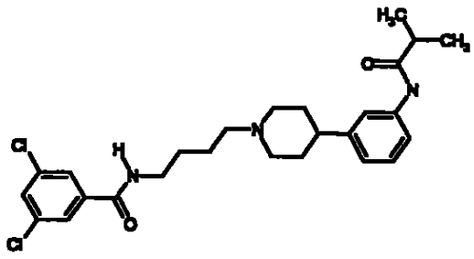
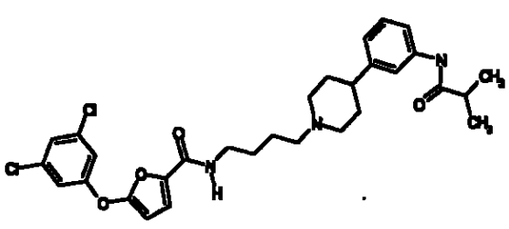
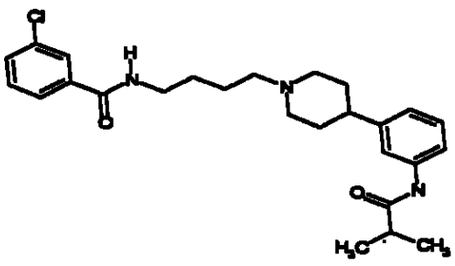
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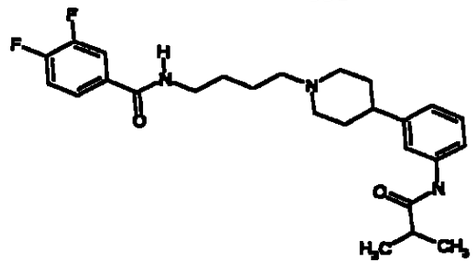
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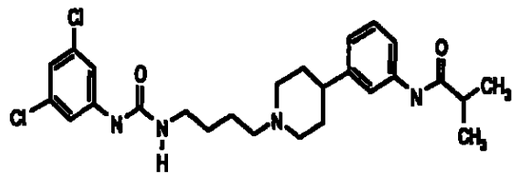
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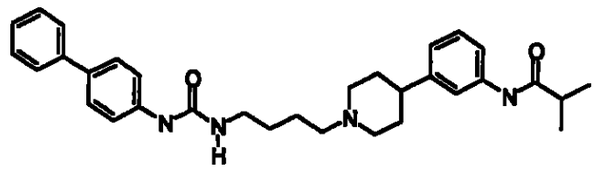
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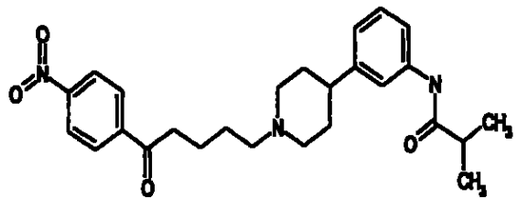
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657		77.9

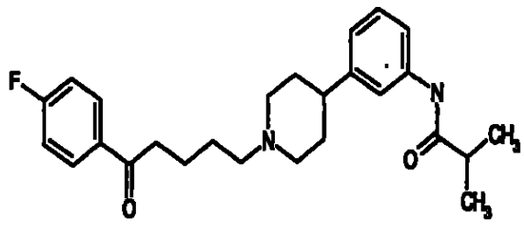
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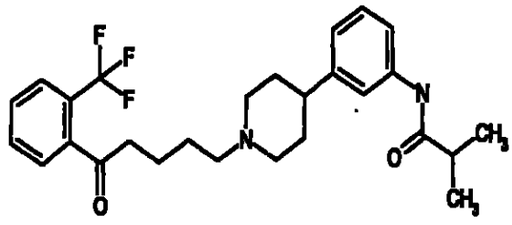
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661  33.3

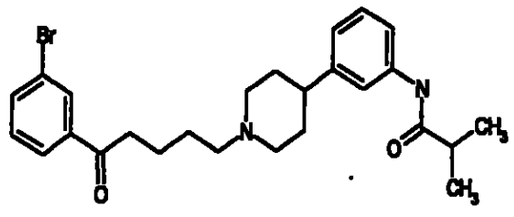
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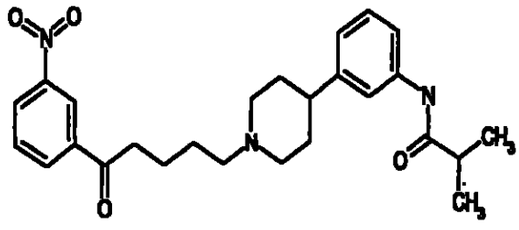
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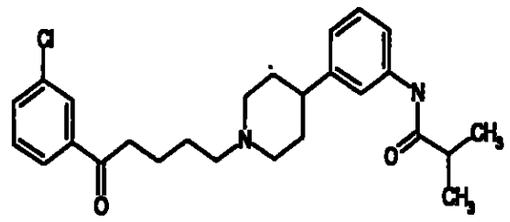
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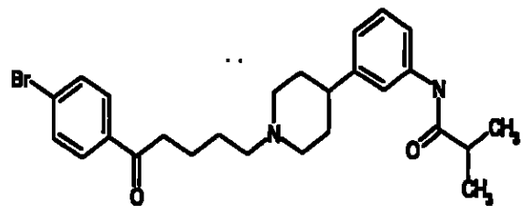
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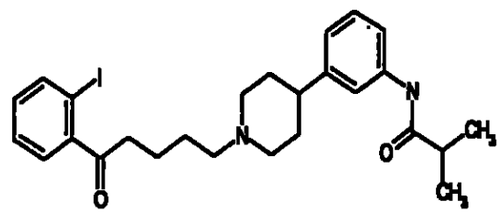


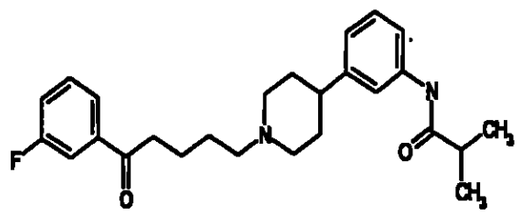
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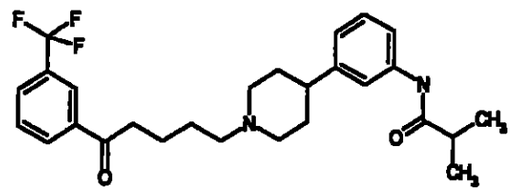
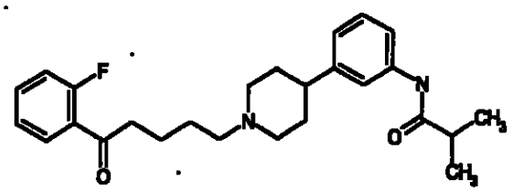
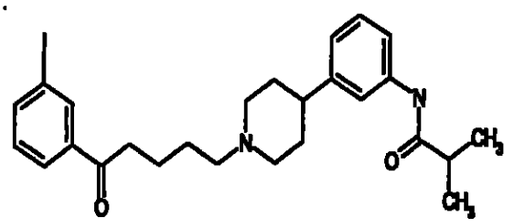
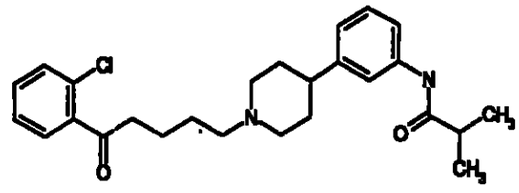
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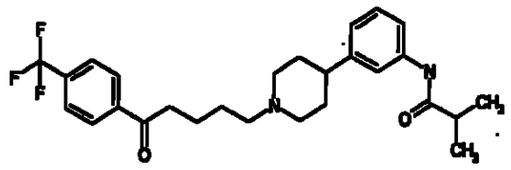
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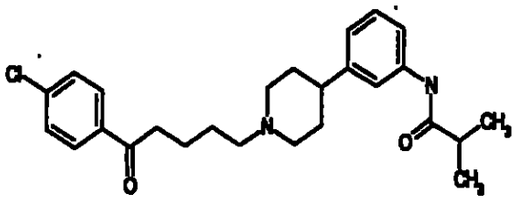
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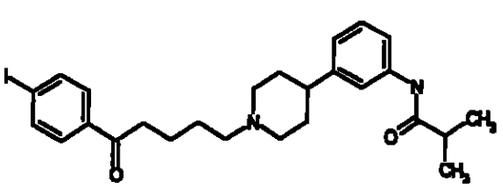
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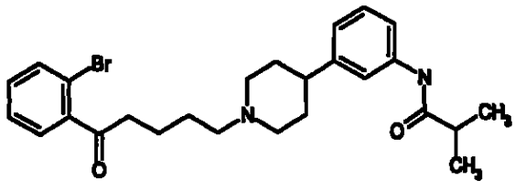
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673		32.5

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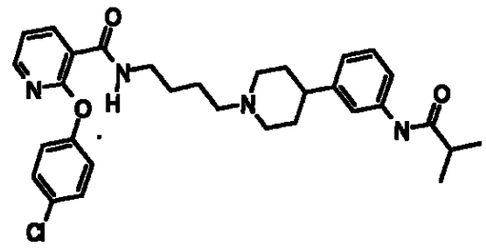
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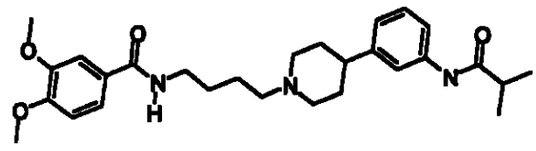
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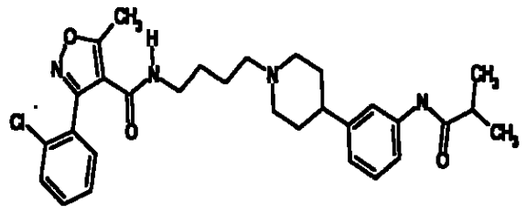
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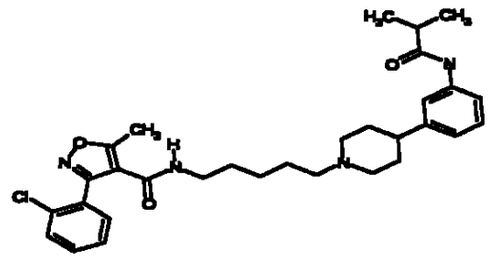
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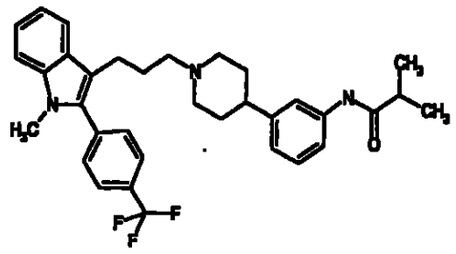
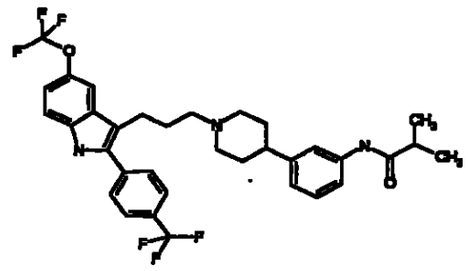
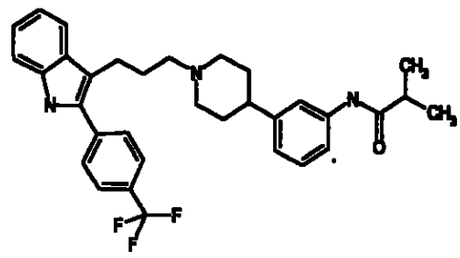
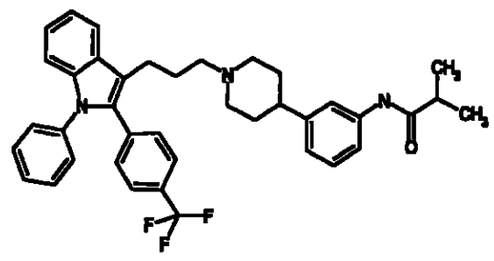
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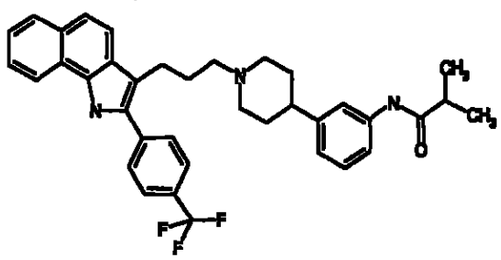
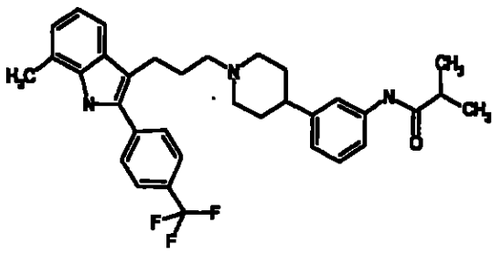
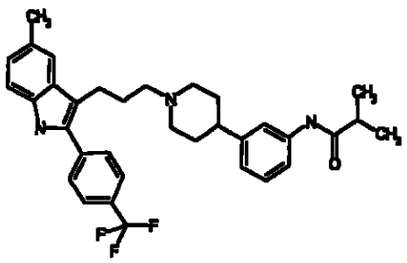
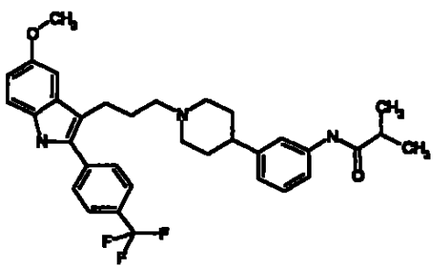
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680  28.1

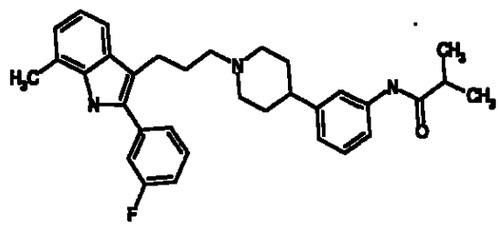
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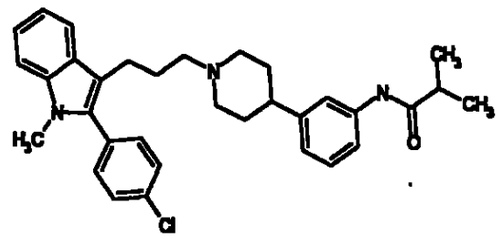
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685		62.4

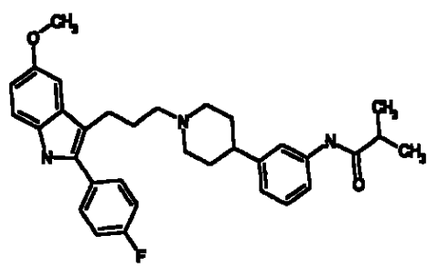
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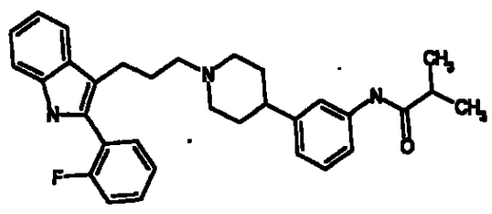
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689		11.3

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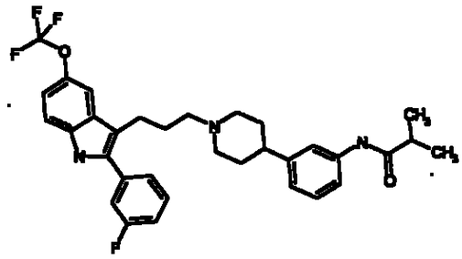
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691  16.3

692  2.0

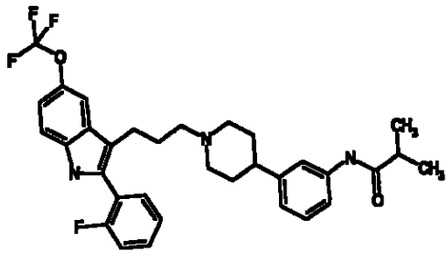
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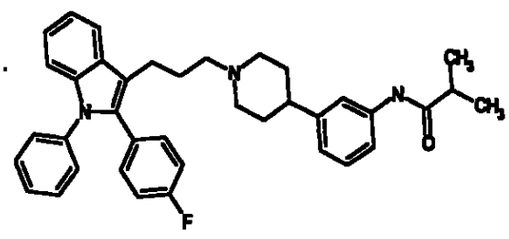
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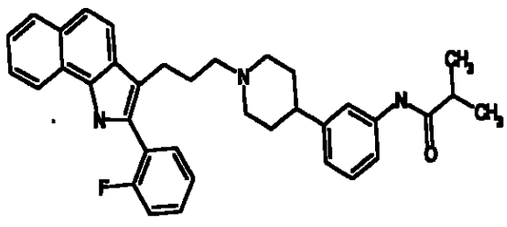
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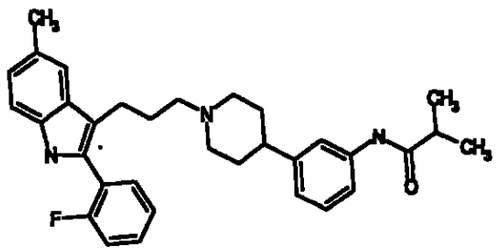
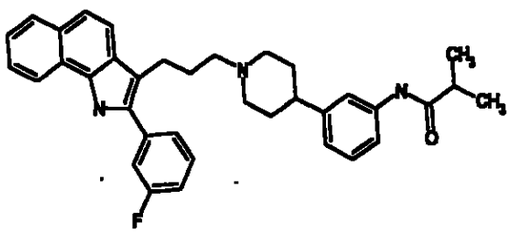
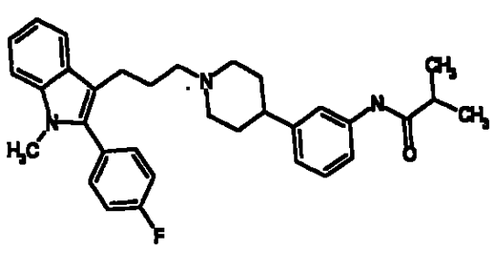
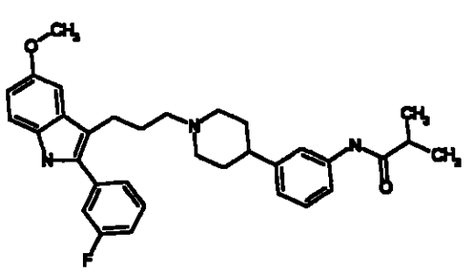


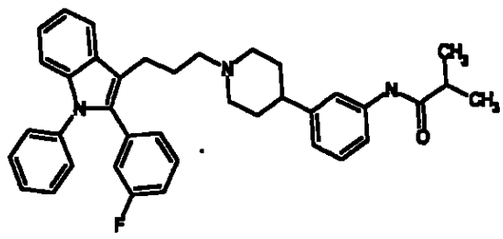
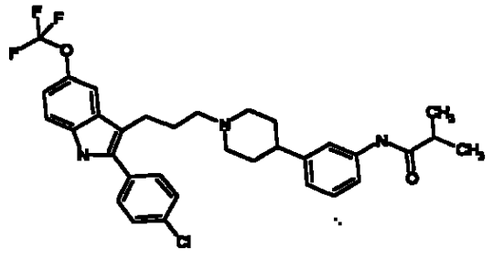
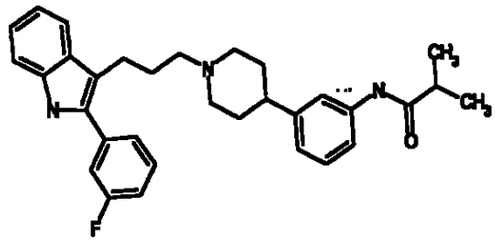
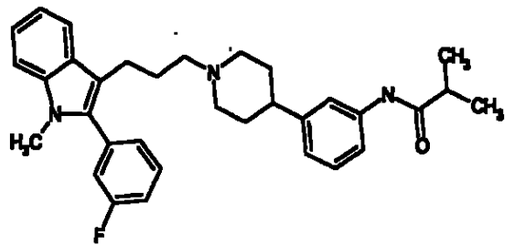
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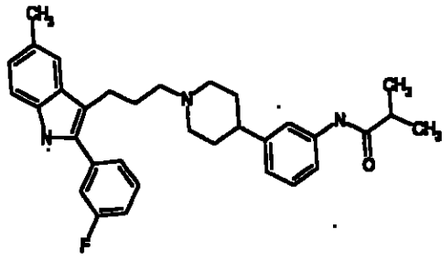
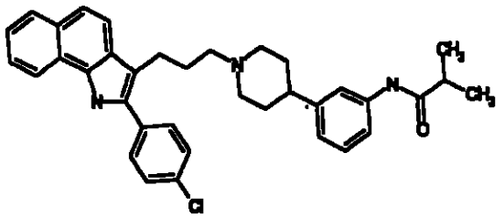
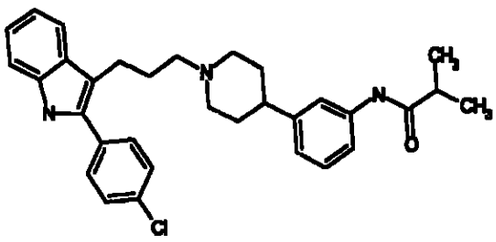
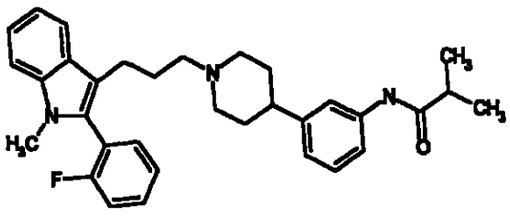
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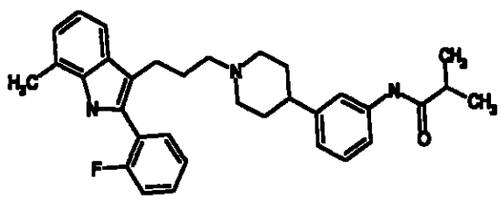


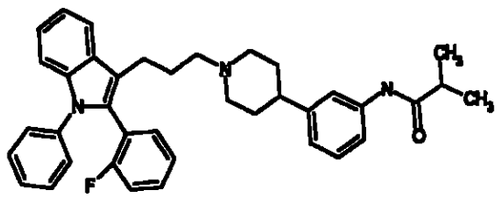
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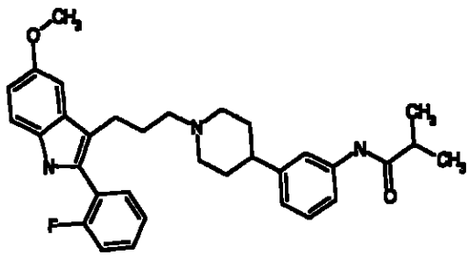
698		3.0
699		5.4
700		2.0
701		2.5

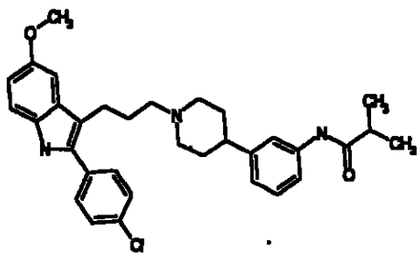
702		27.0
703		16.6
704		1.2
705		8.5

706		4.2
707		19.6
708		3.8
709		1.3

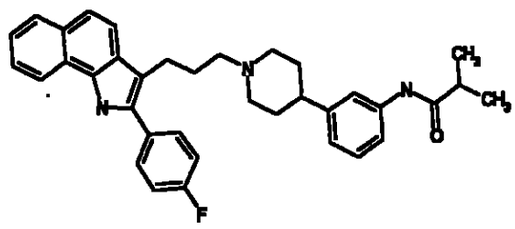
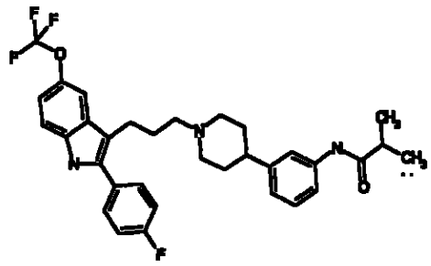
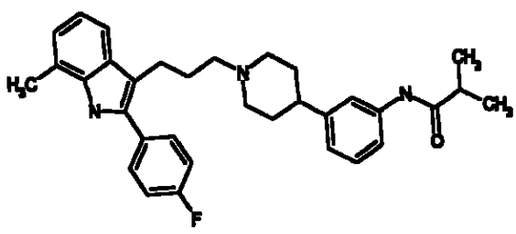
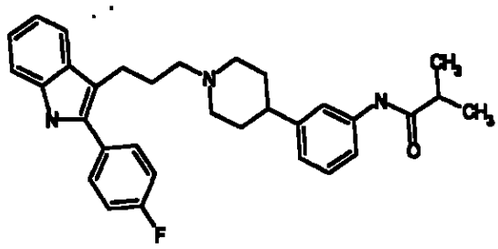
710  6.9

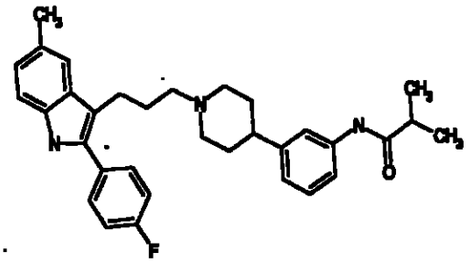
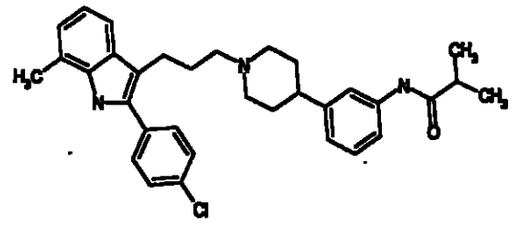
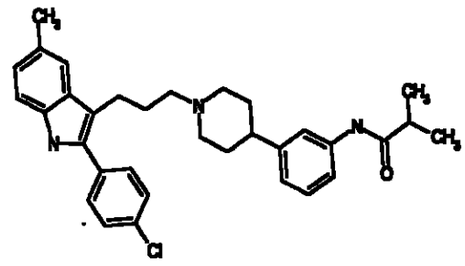
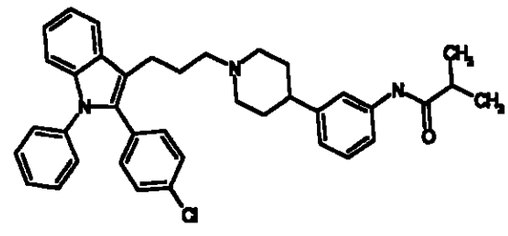
711  90.5

712  8.6

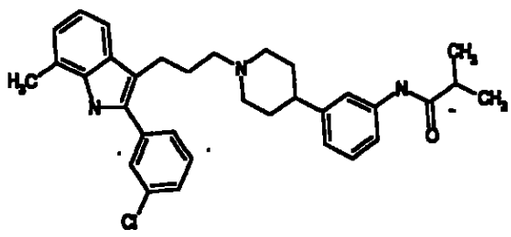
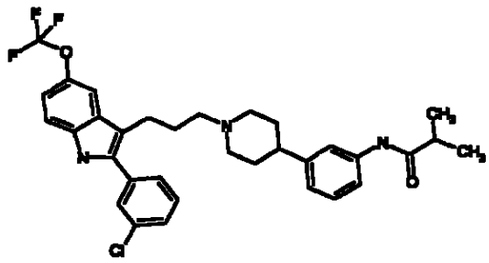
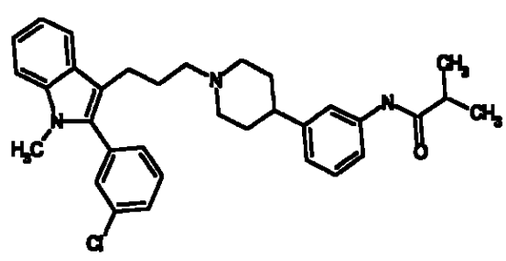
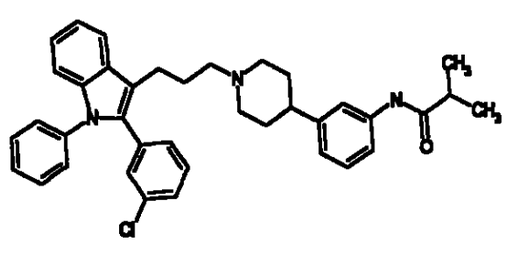
713  7.7

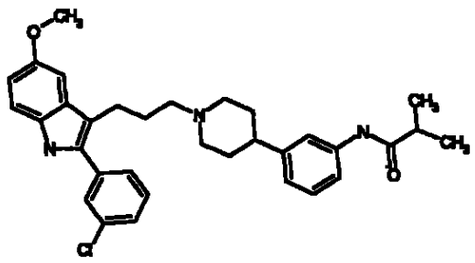
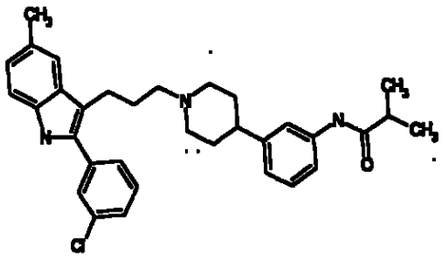
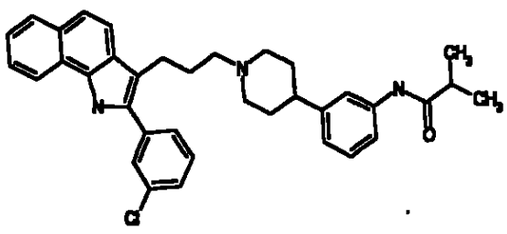
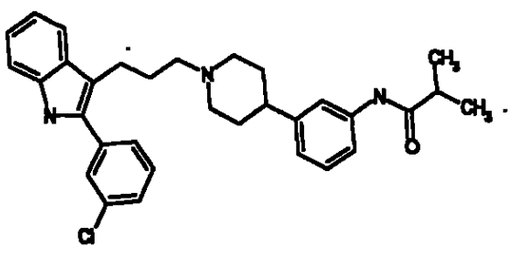
667

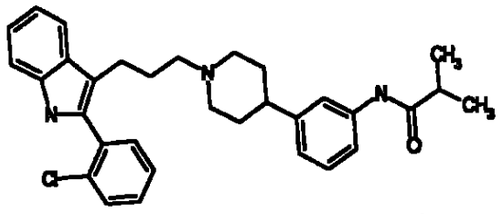
714		4.7
715		4.2
716		4.5
717		1.3

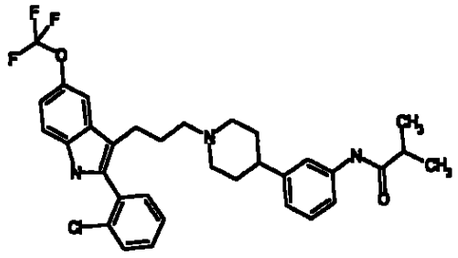
718		3.4
719		14.9
720		12.5
721		75.3

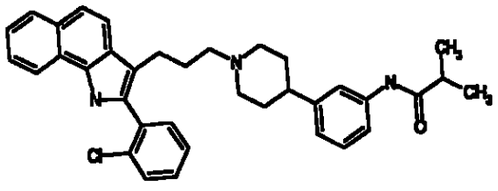
669

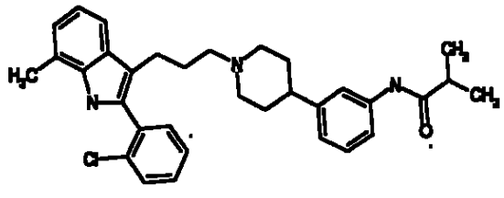
722		6.4
723		9.2
724		5.0
725		151.6

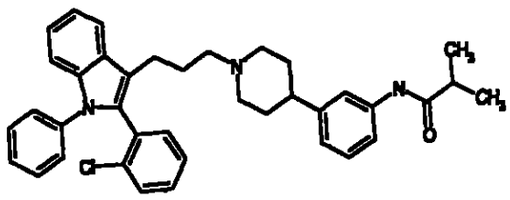
726		5.0
727		3.4
728		16.3
729		1.7

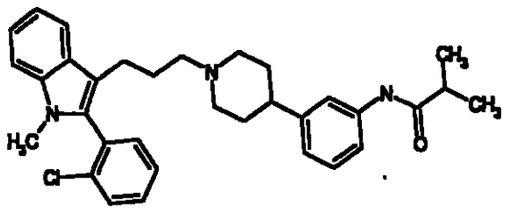
730  0.8

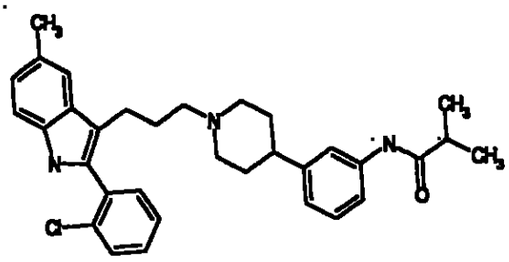
731  9.9

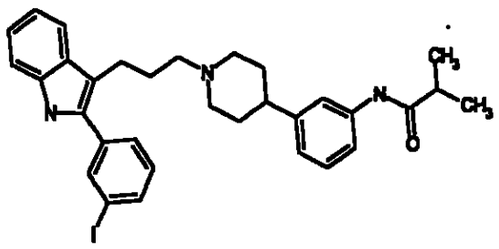
732  5.8

733  10.0

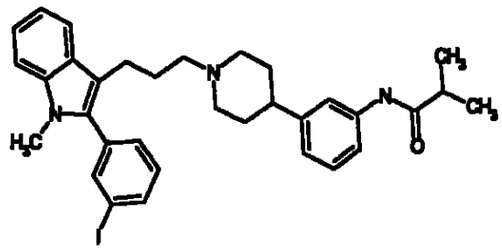
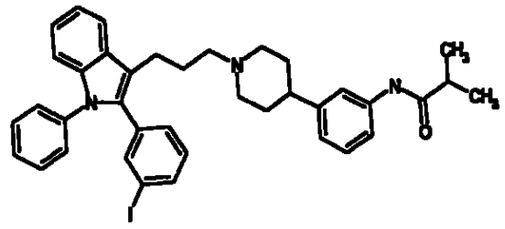
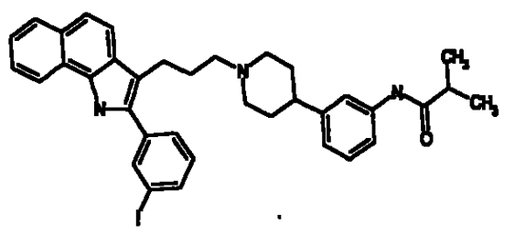
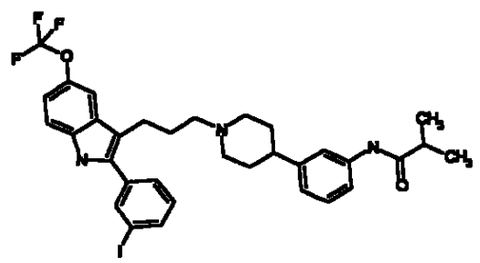
734  28.8

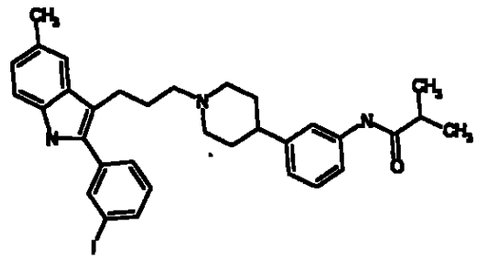
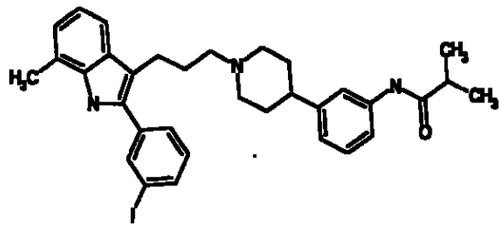
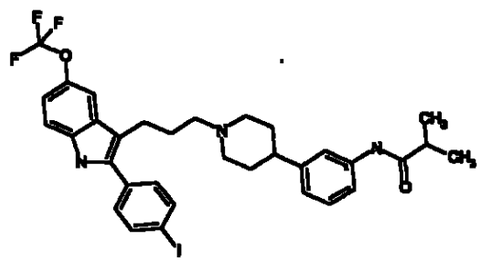
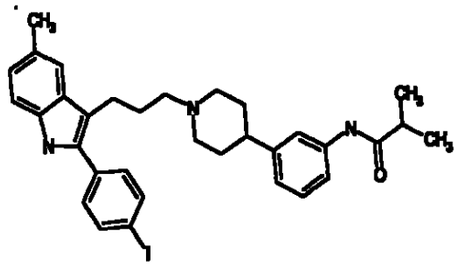
735  1.1

736  5.7

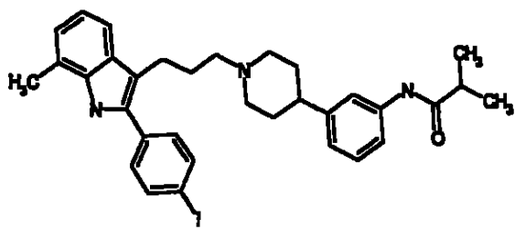
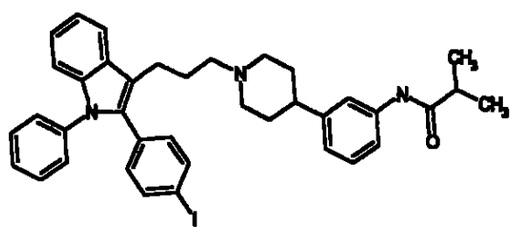
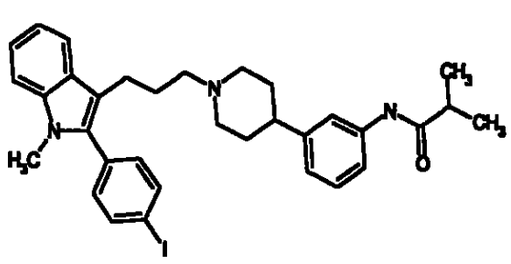
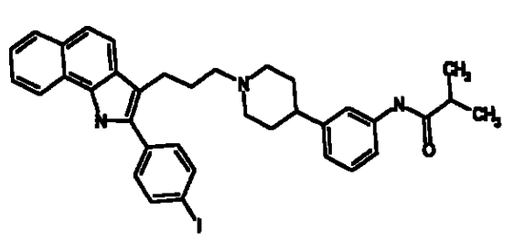
737  1.0

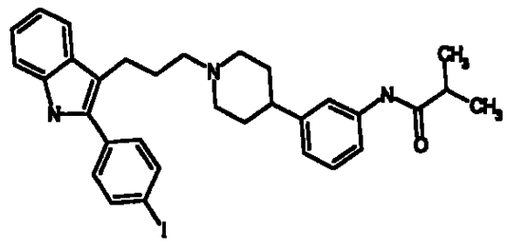
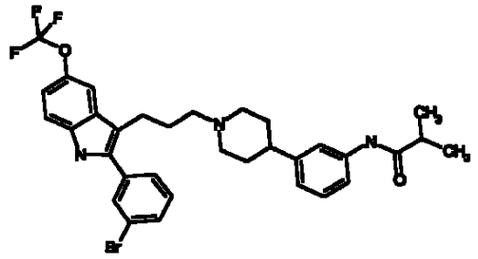
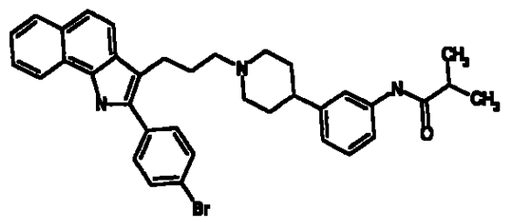
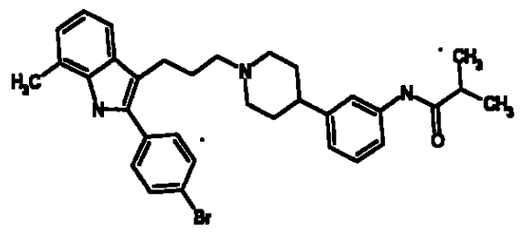
673

738		10.2
739		213.6
740		12.2
741		2.8

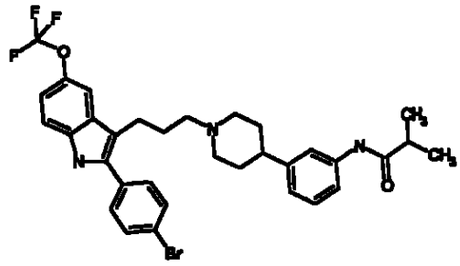
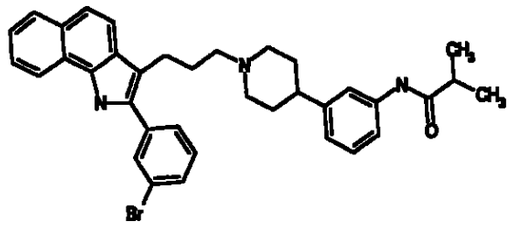
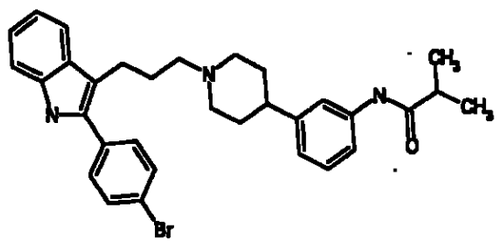
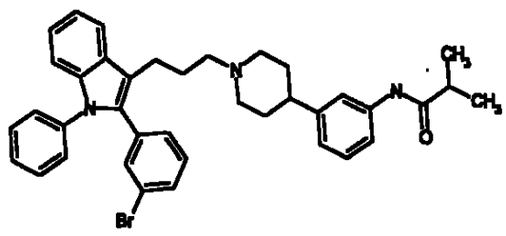
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743		4.1
744		47.1
745		15.8

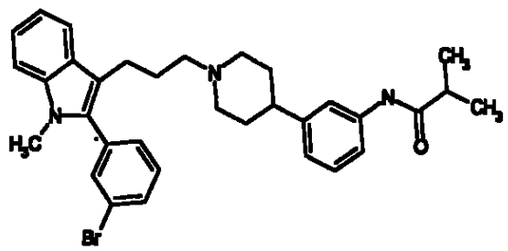
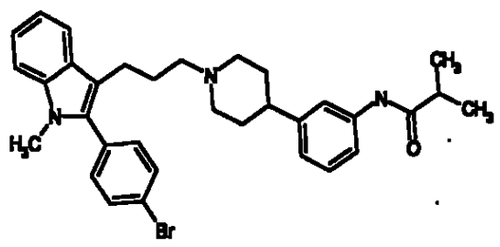
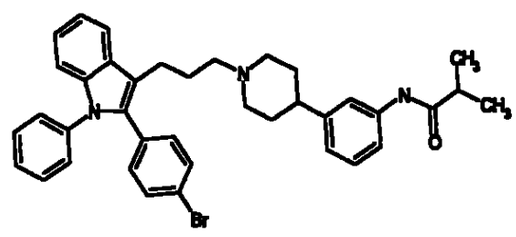
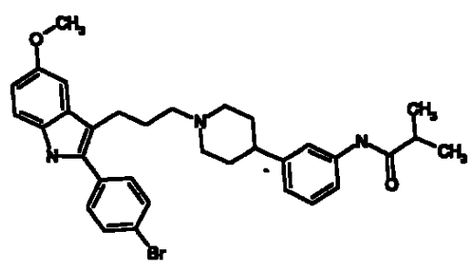
675

746		8.0
747		160.6
748		3.1
749		23.2

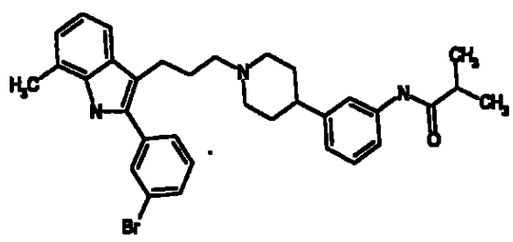
750		2.6
751		12.4
752		21.7
753		16.6

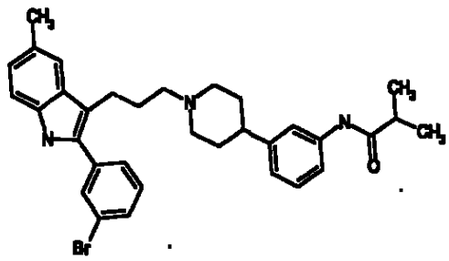
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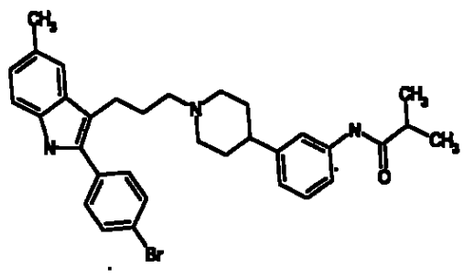
754		49.2
755		23.8
756		4.2
757		6.9

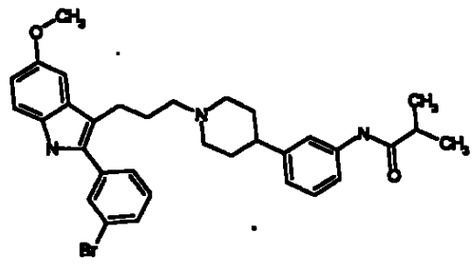
758		110.0
759		9.3
760		92.3
761		15.9

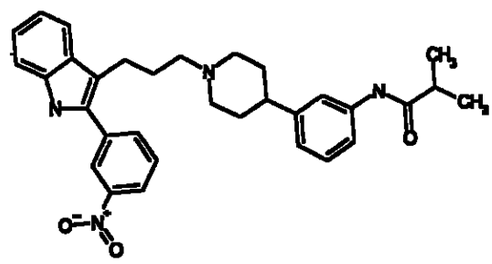
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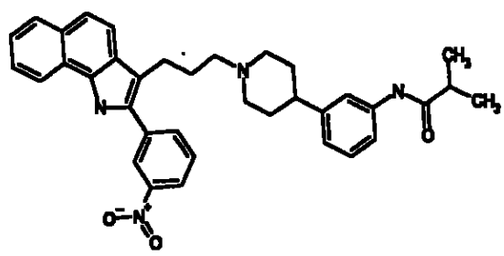
762  8.3

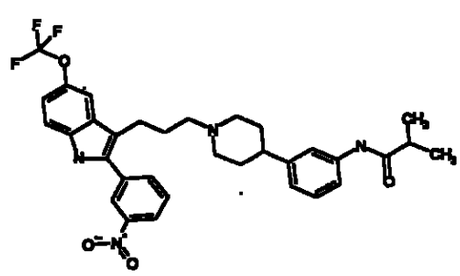
763  1.9

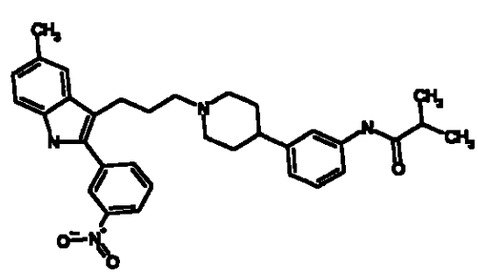
764  14.6

765  6.5

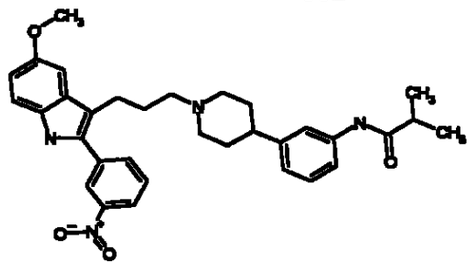
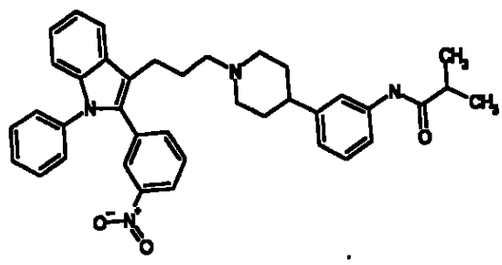
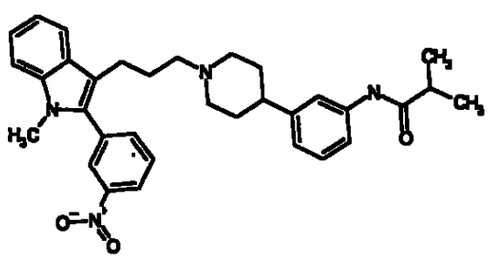
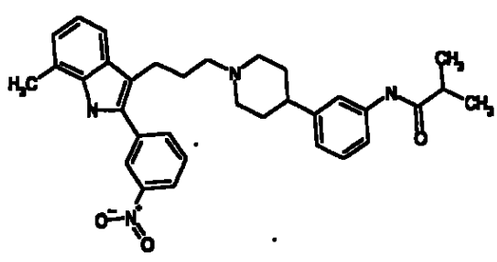
766  7.8

767  34.8

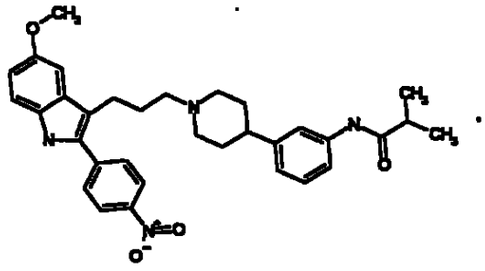
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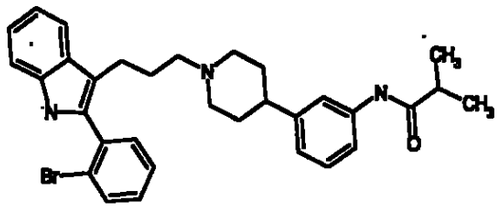
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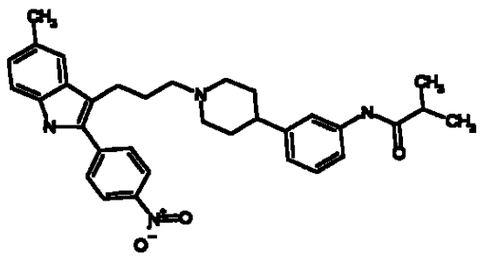
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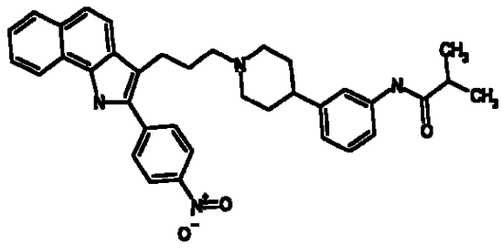
770		12.7
771		189.0
772		14.9
773		23.8

682

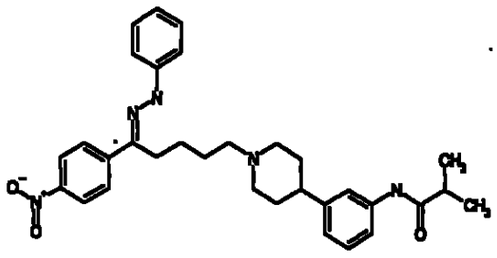
774  7.9

775  4.9

776  18.2

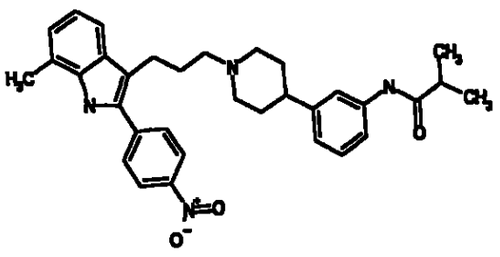
777  8.5

778



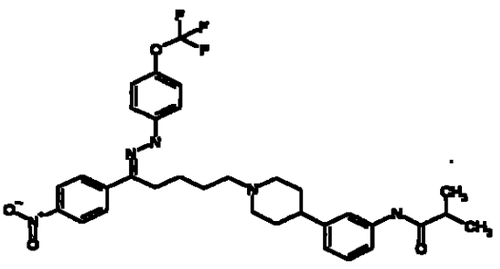
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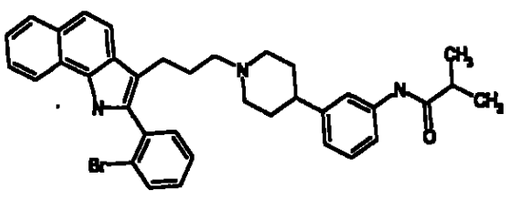
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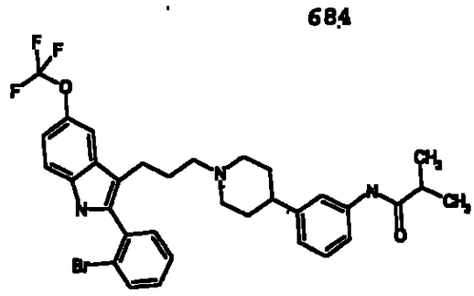


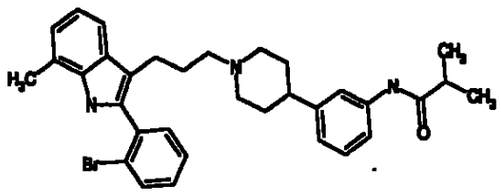
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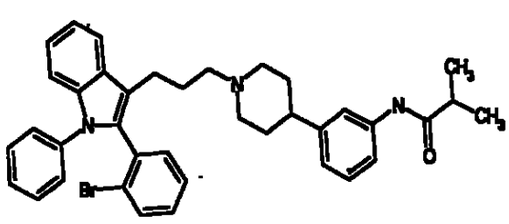
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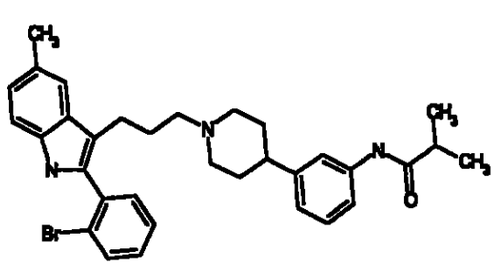


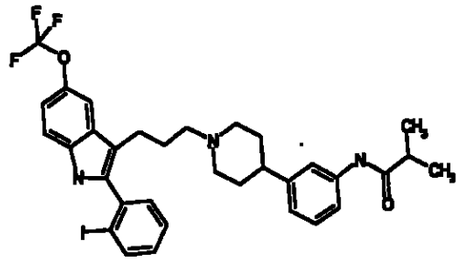
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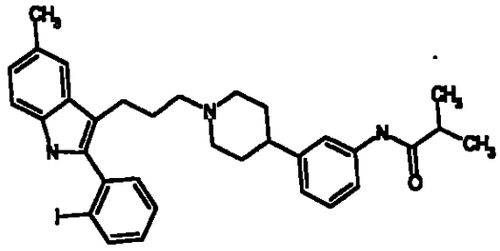
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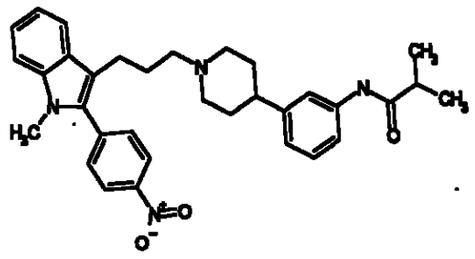
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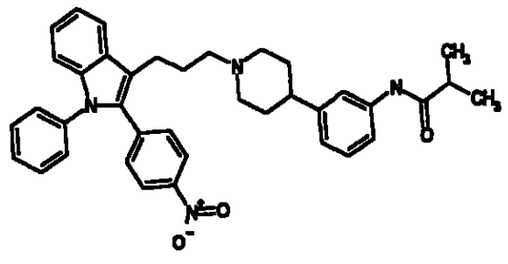
784  121.2

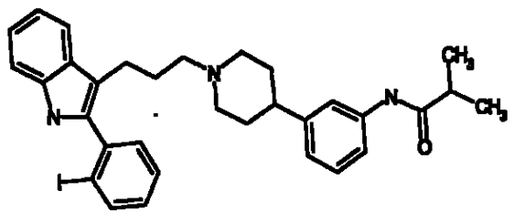
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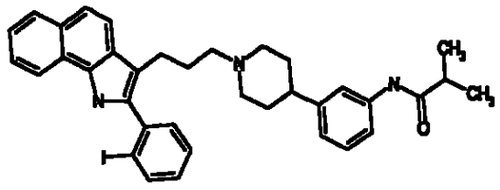
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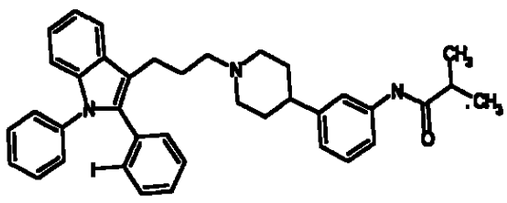
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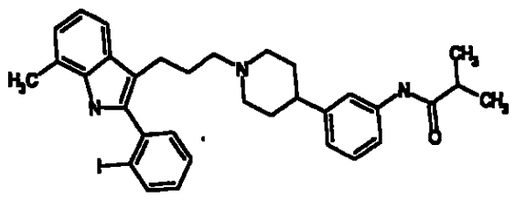
788  11.1

789  36.4

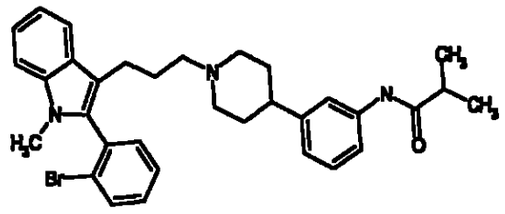
790  4.4

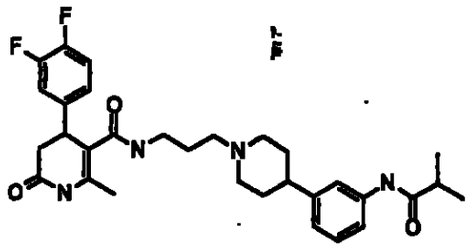
791  12.7

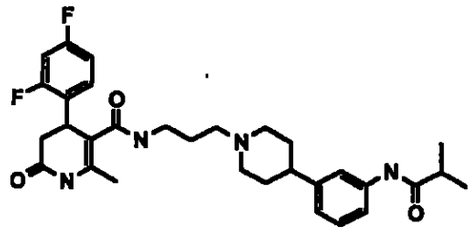
792  122.0

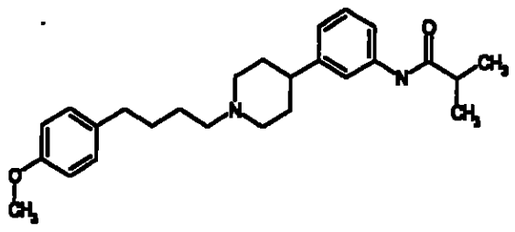
793  18.3

687

794  4.9

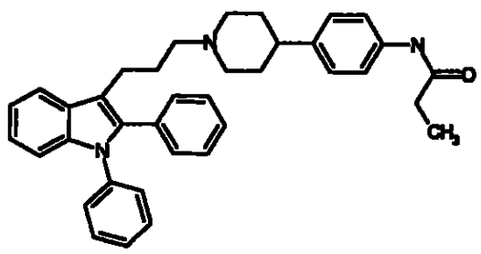
795  51.1

796  43.0

Example	Structure	rMCH1 KI (nM)
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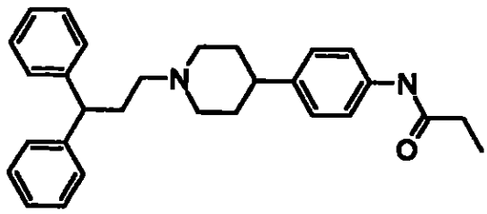
688

798



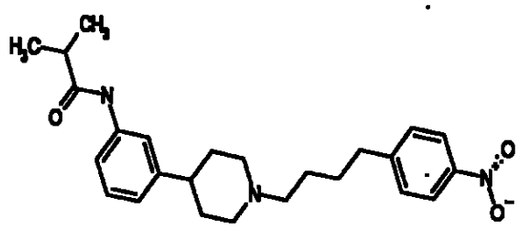
474.7

799



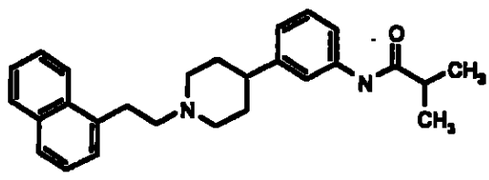
370.6

800



9.9

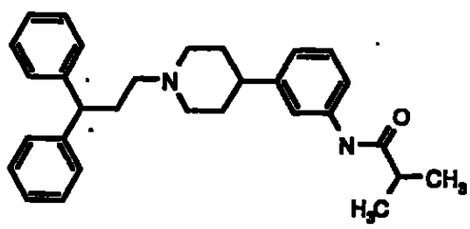
801



311.1

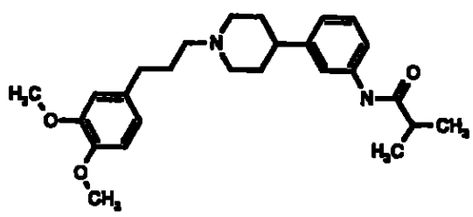
689

802



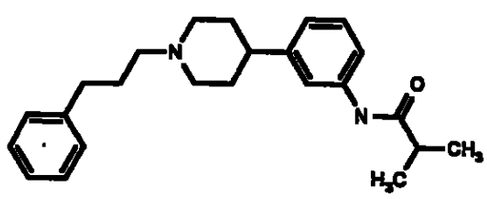
36.7

803



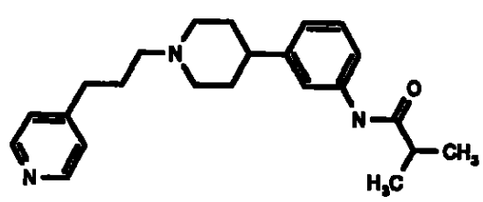
298.6

804



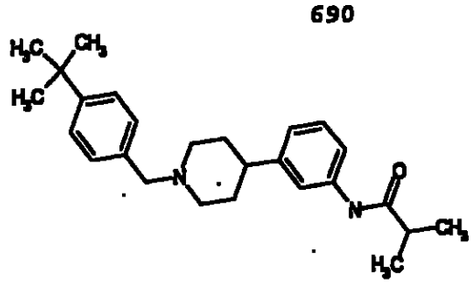
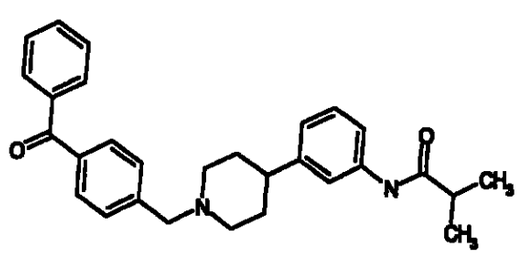
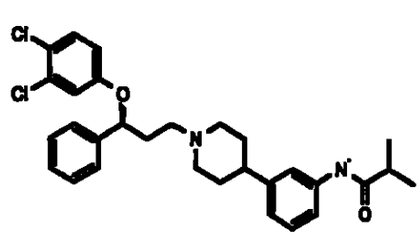
89.2

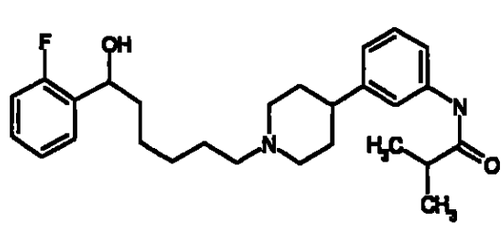
805



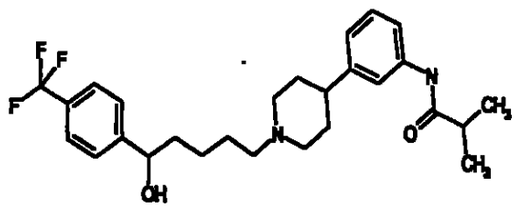
903.9

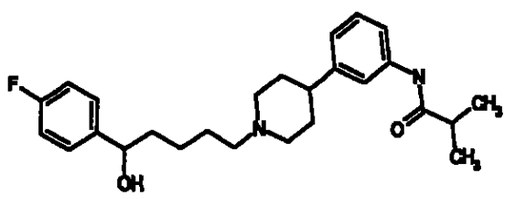
690

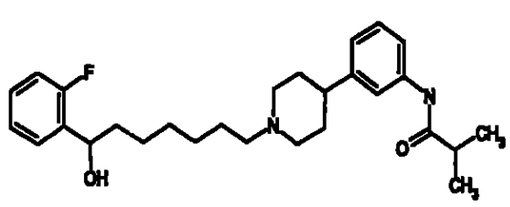
806		14.1
807		2.7
808	 Chiral	10.8

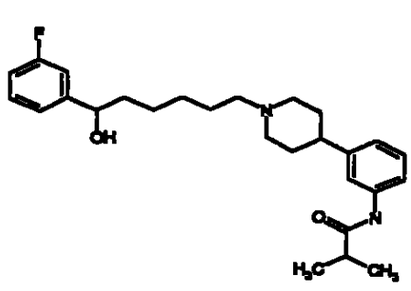
Example	Structure	rMCH1 Ki (nM)
809		56.8

691

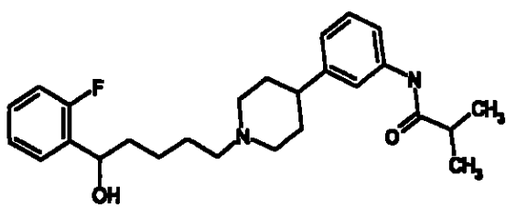
810  191.2

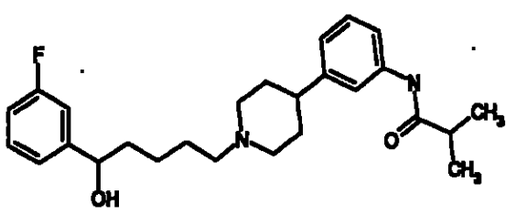
811  190.8

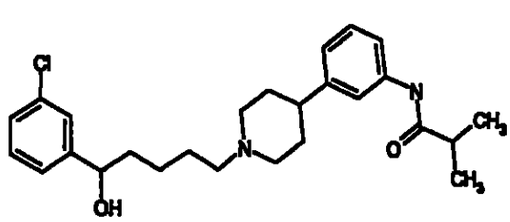
812  244.8

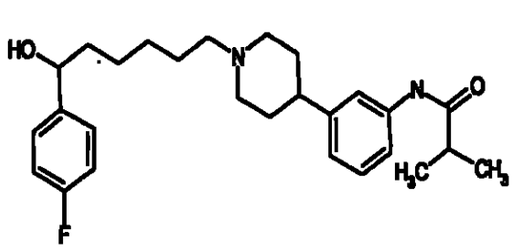
813  57.3

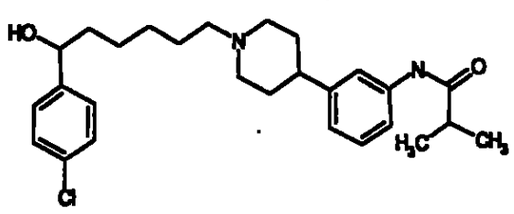
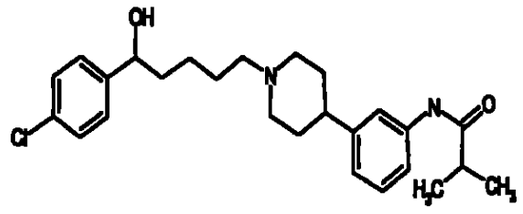
692

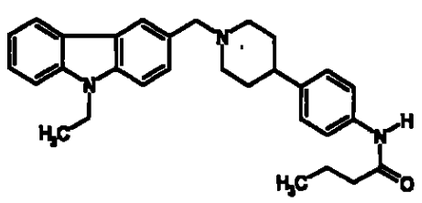
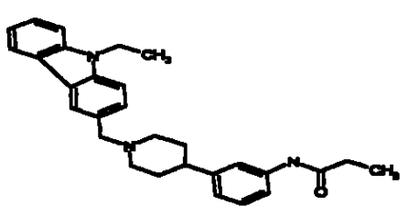
814  159.5

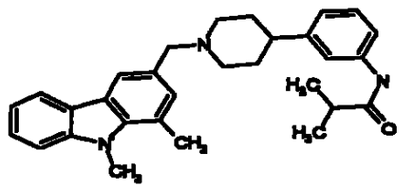
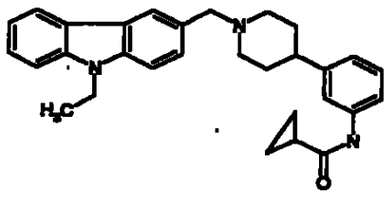
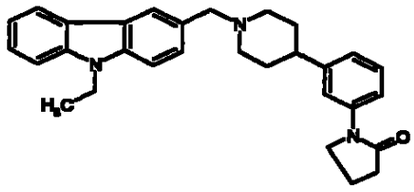
815  126.9

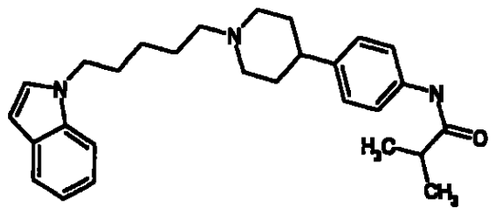
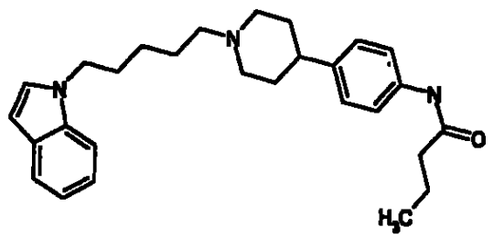
816  89.8

817  34.9

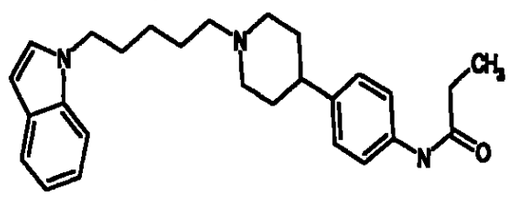
818		38.2
819		80.2

Example	Structure	rMCH1 Ki (nM)
820		108.6
821		12.1

822		1.0
823		2.7
824		36.5

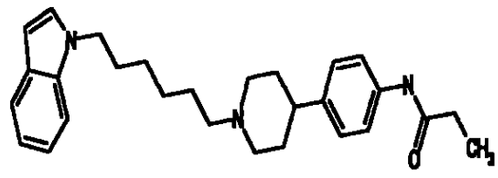
Example	Structure	rMCH1 Ki (nM)
825		600.7
826		785.6

827



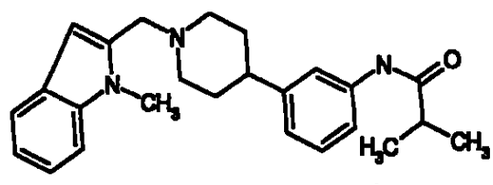
215.4

826



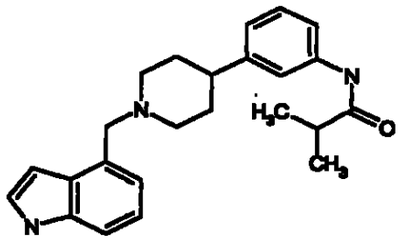
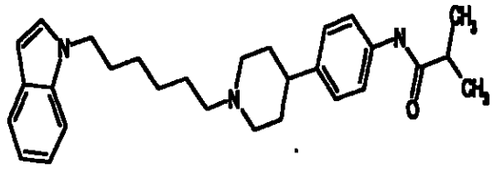
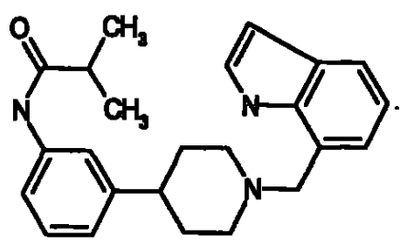
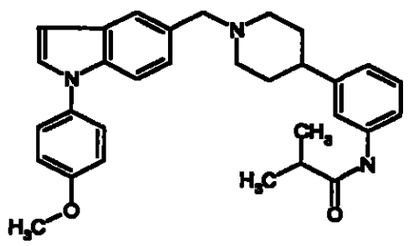
515.9

829

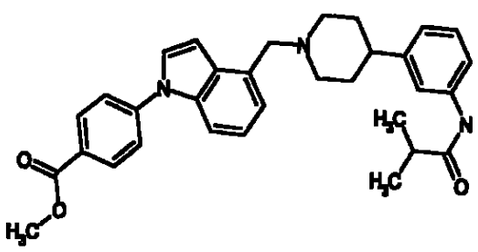
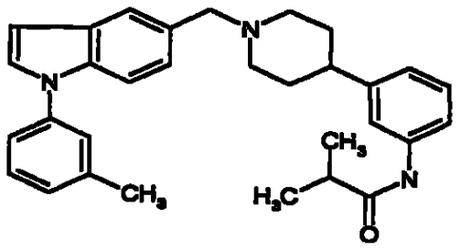
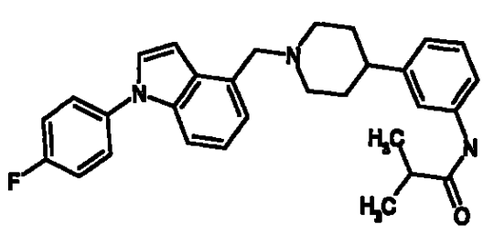
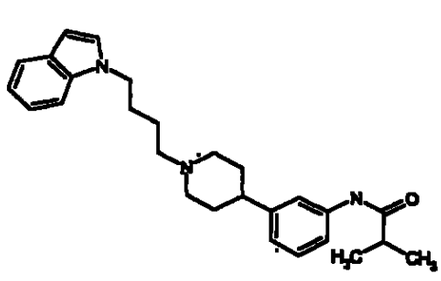


228.0

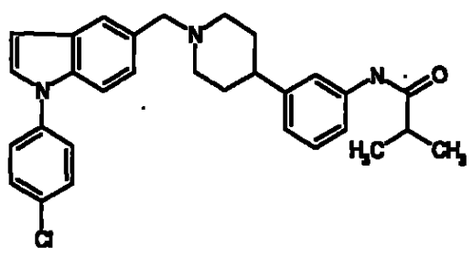
696

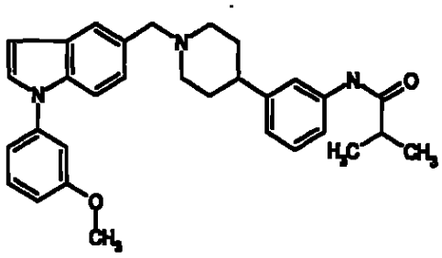
830		488.6
831		569.8
832		614.3
833		27.5

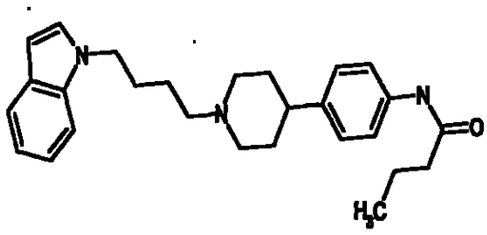
697

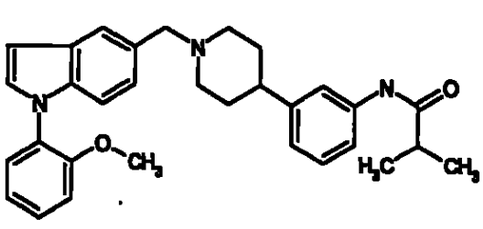
834		38.3
835		21.3
836		7.8
837		35.9

698

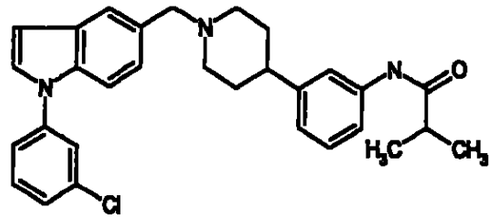
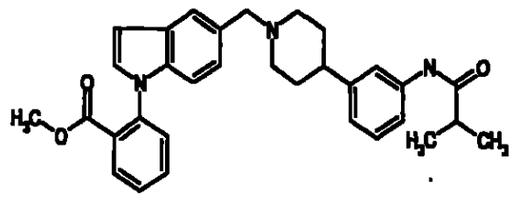
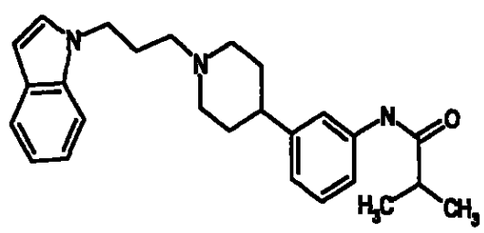
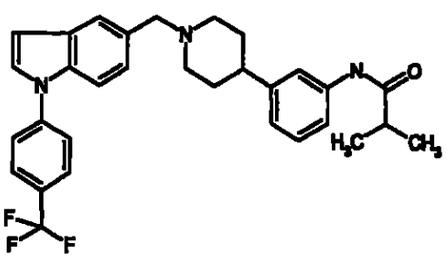
838  11.2

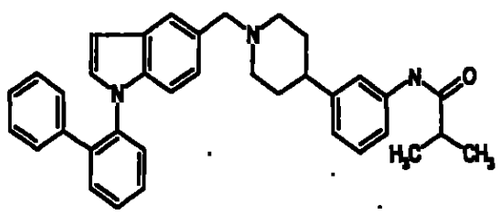
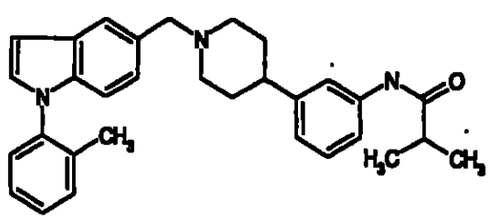
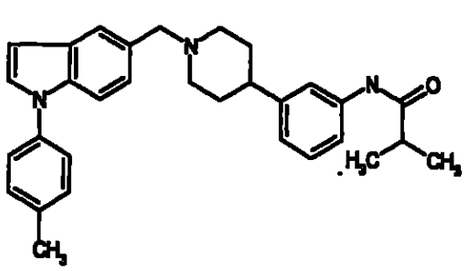
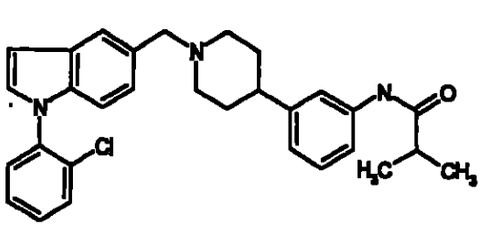
839  82.2

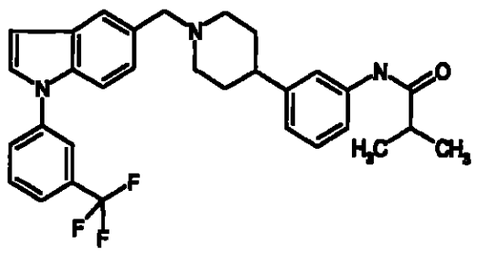
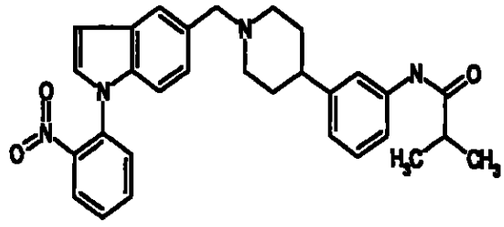
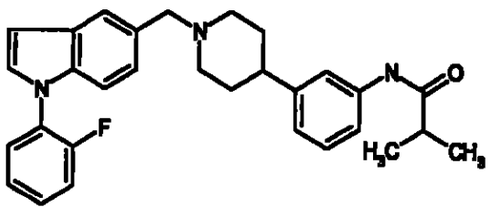
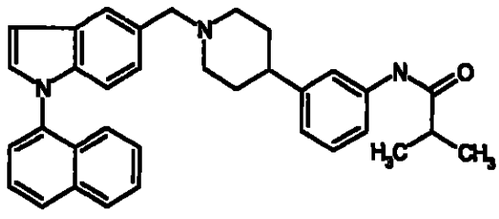
840  663.5

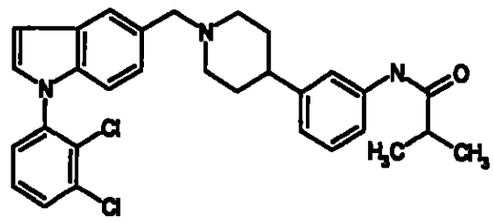
841  25.0

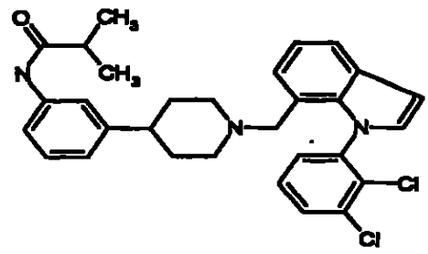
699

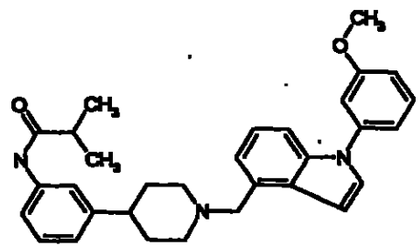
842		16.8
843		15.5
844		37.8
845		43.1

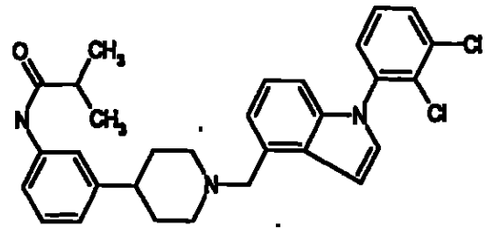
846		18.4
847		10.2
848		19.1
849		9.4

850		9.5
851		27.4
852		14.5
853		48.0

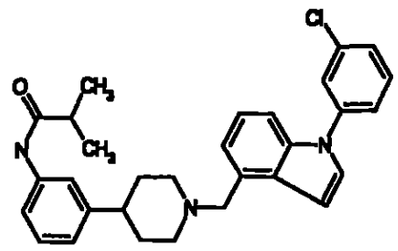
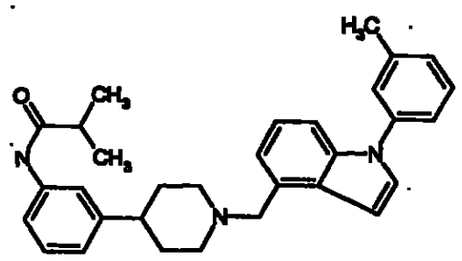
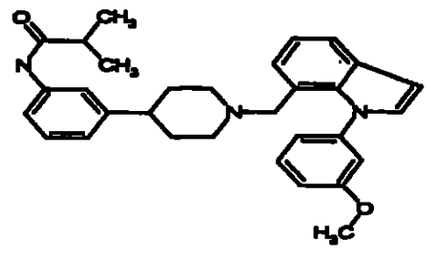
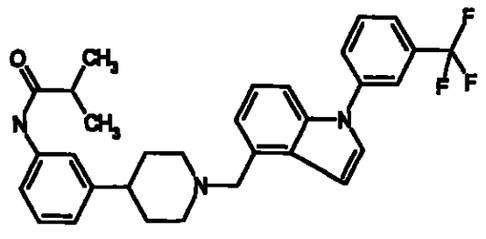
854  13.8

855  256.0

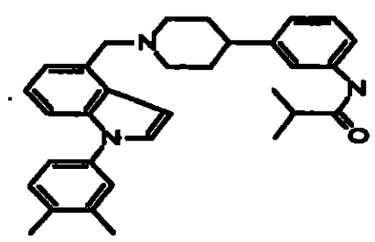
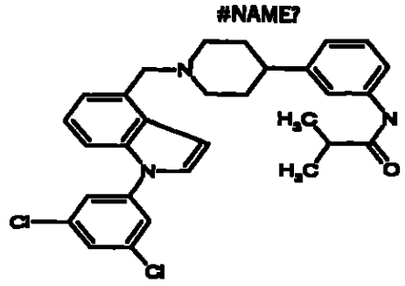
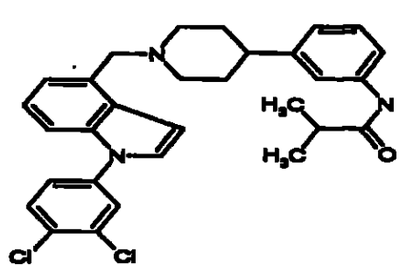
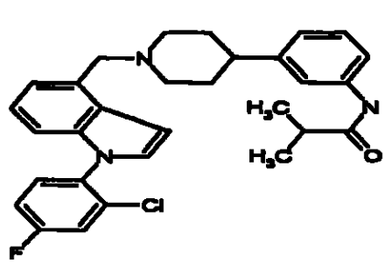
856  122.6

857  89.8

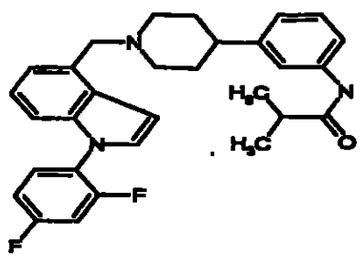
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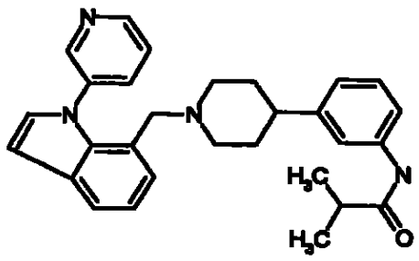
858		44.9
859		320.7
860		40.5
861		94.1

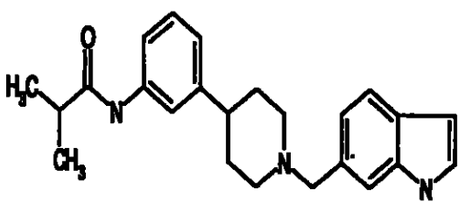
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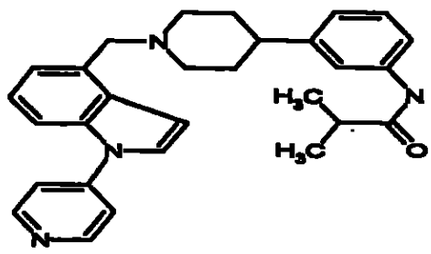
862		437.6
863		289.0
864		292.0
865		94.6

705

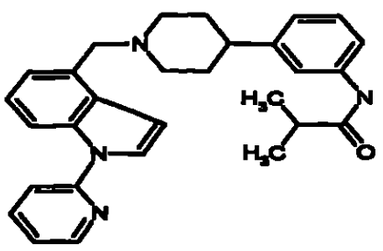
866  169.2

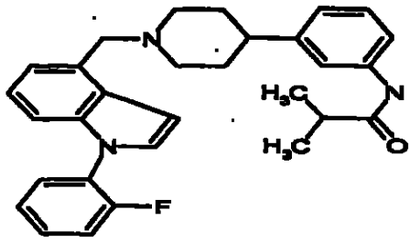
867  891.9

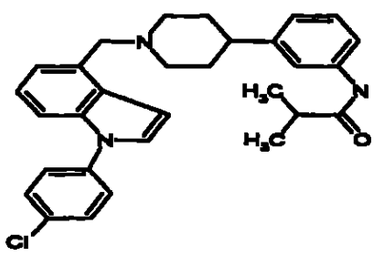
868  403.4

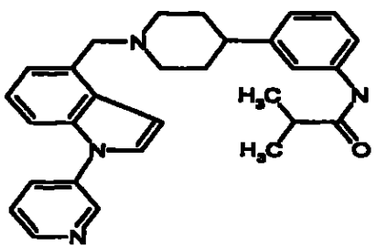
869  430.9

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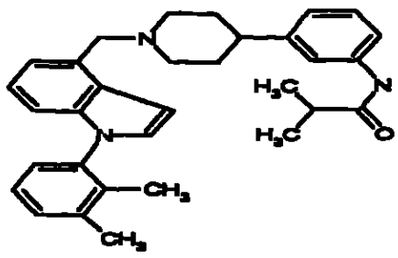
870  166.7

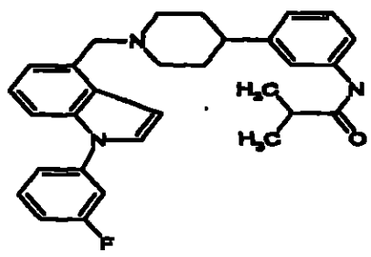
871  251.7

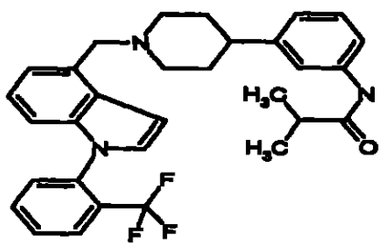
872  306.3

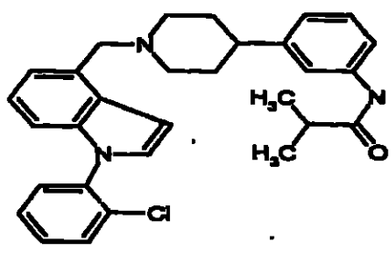
873  345.0

707

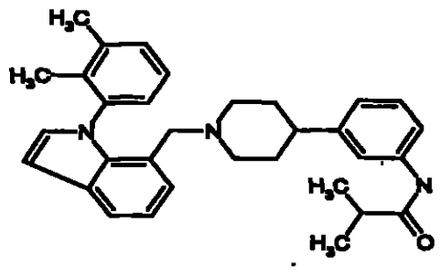
874  247.1

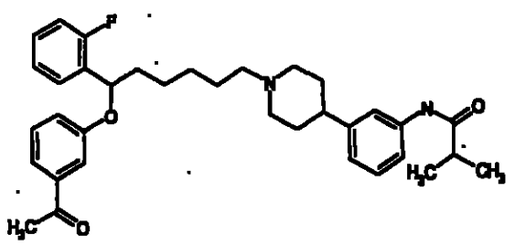
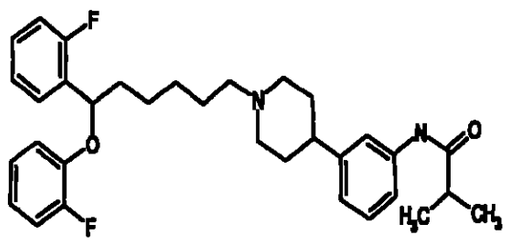
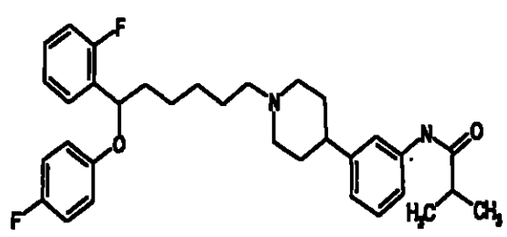
875  130.1

876  758.2

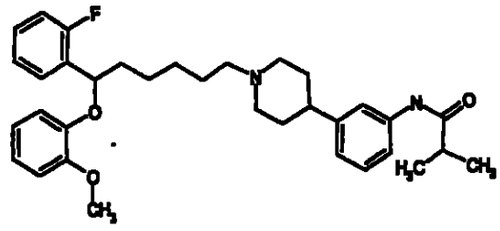
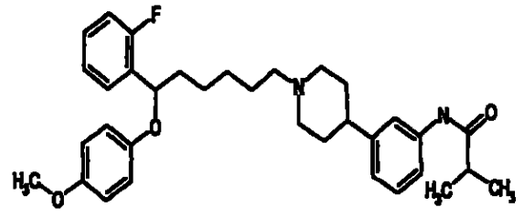
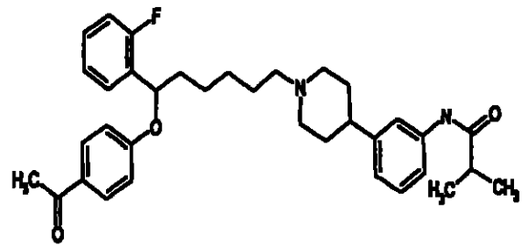
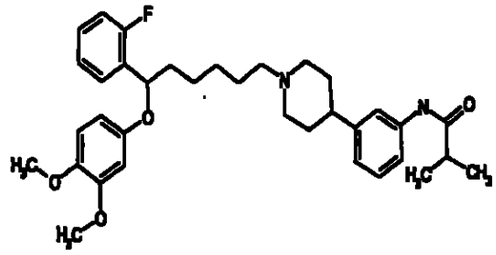
877  245.1

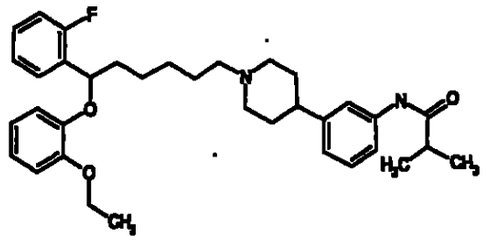
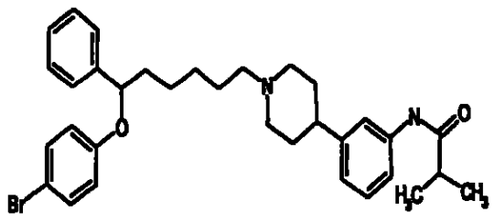
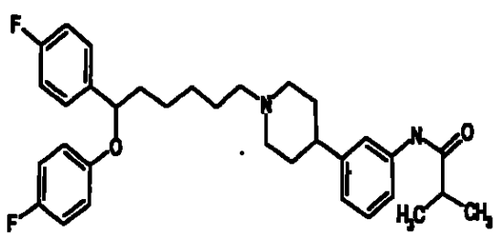
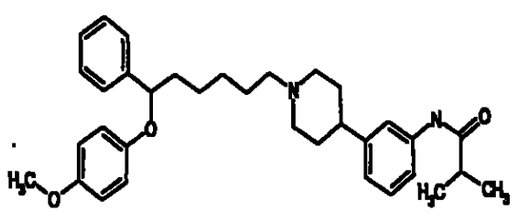
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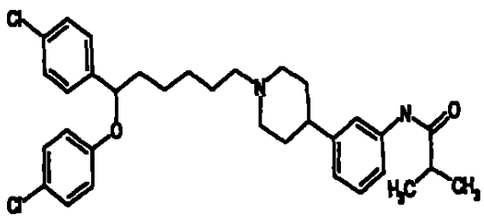
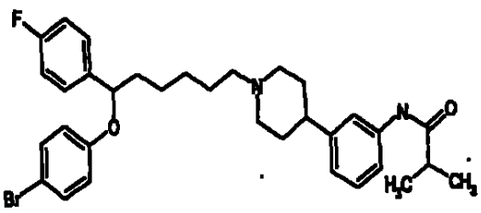
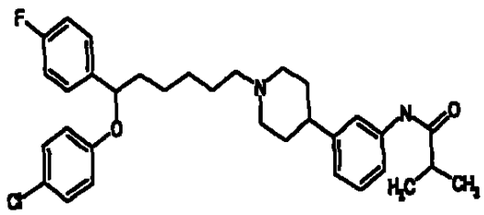
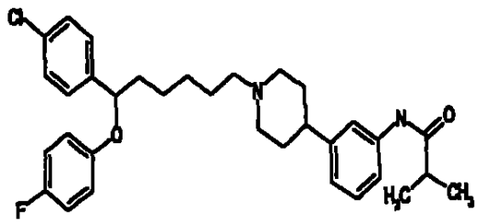
878		188.8

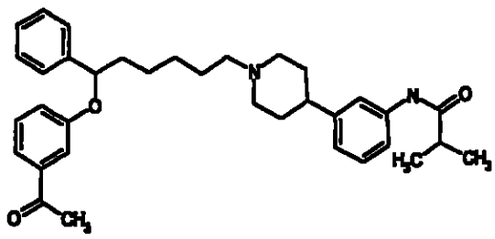
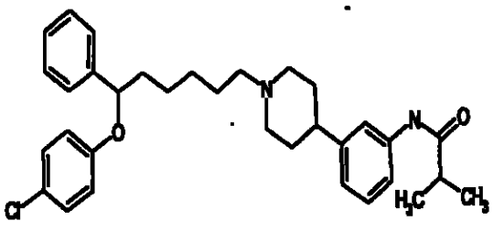
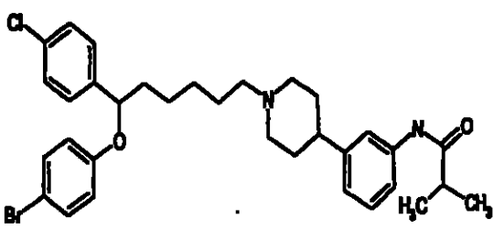
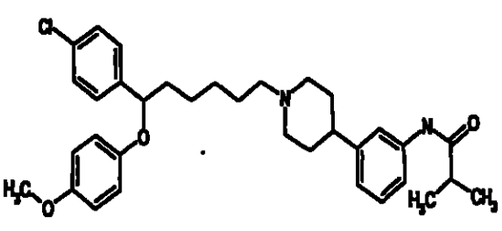
Example	Structure	rMCH1 Ki (nM)
888		19.8
889		8.6
890		11.1

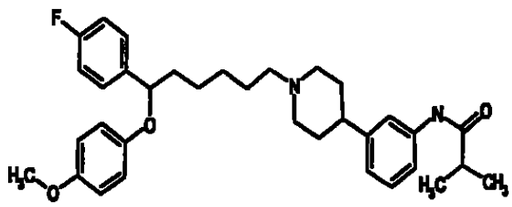
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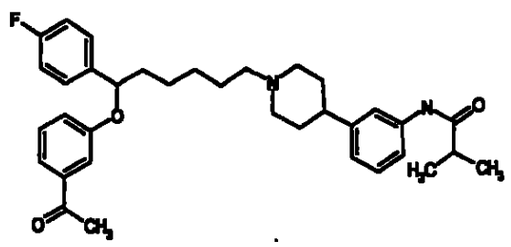
891		6.5
892		17.3
893		23.0
894		41.7

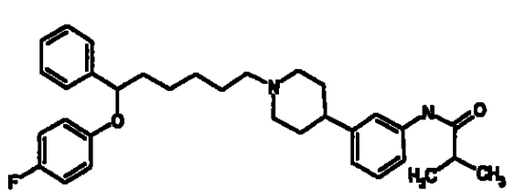
895		6.4
896		30.3
897		6.4
898		33.7

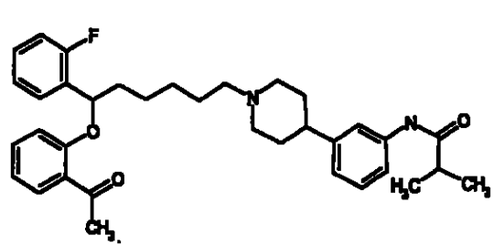
899		18.0
900		11.2
901		8.2
902		11.0

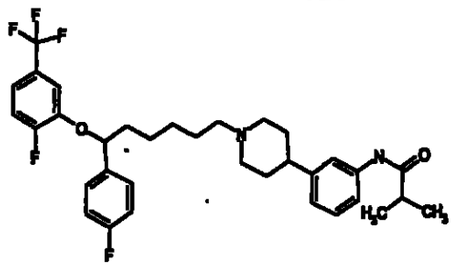
903		12.2
904		14.2
905		5.9
906		5.7

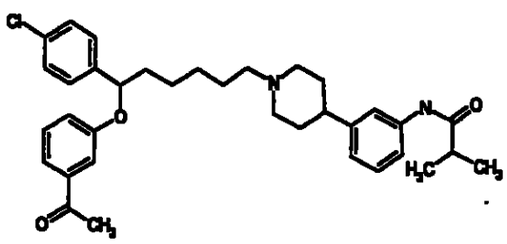
907  3.1

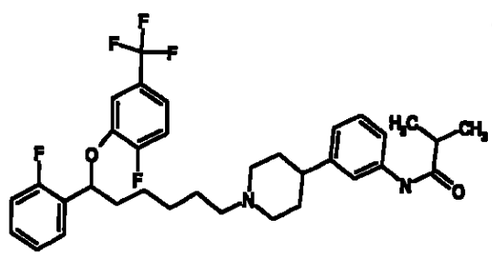
908  3.7

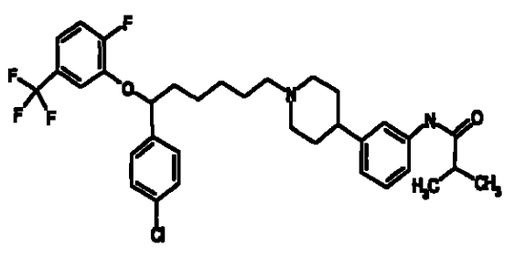
909  10.0

910  10.1

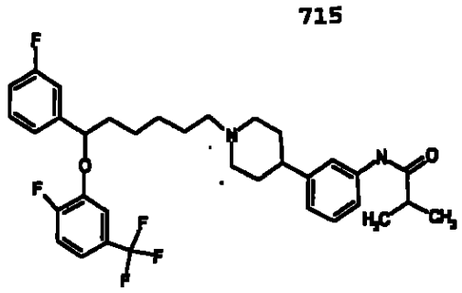
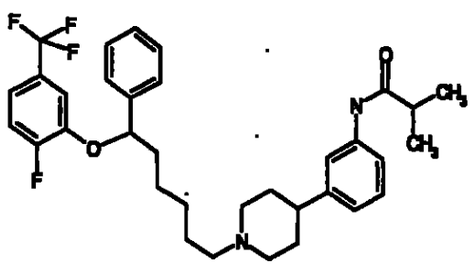
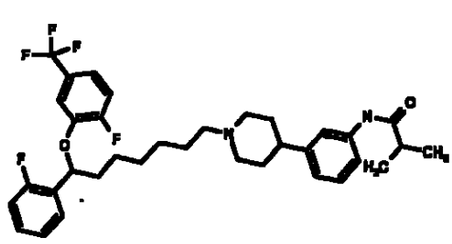
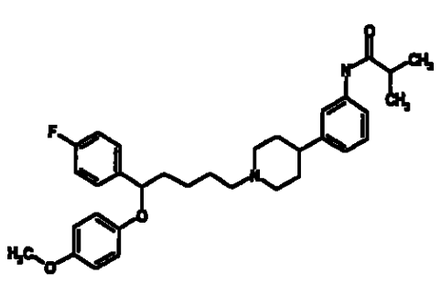
911  7.6

912  5.7

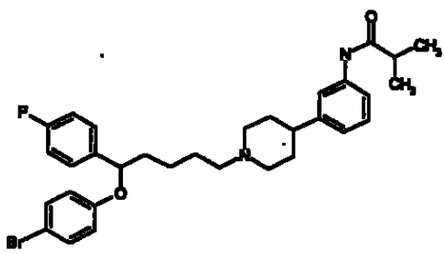
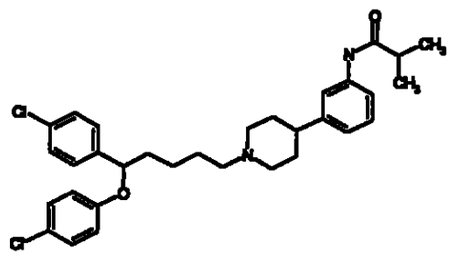
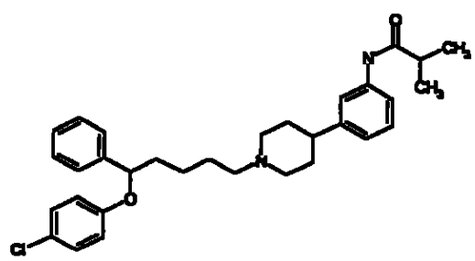
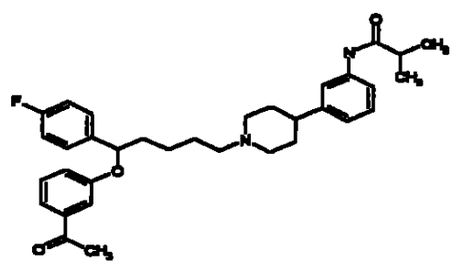
913  12.9

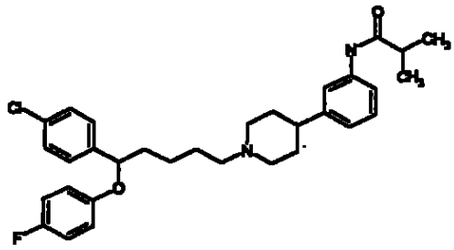
914  17.3

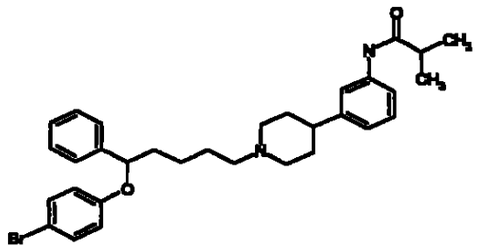
715

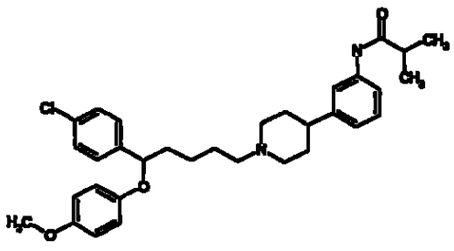
915		22.6
916		20.2
917		78.0
918		29.3

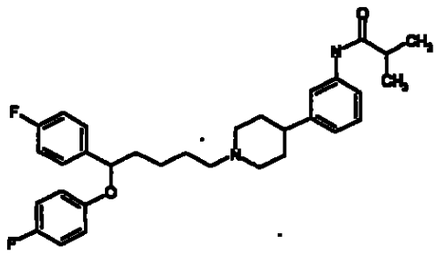
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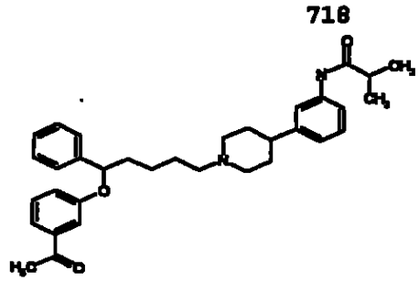
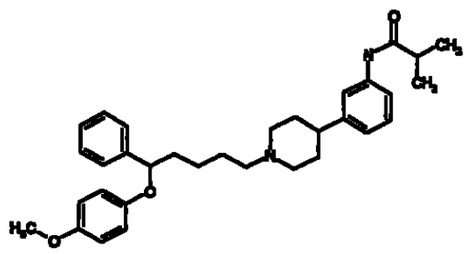
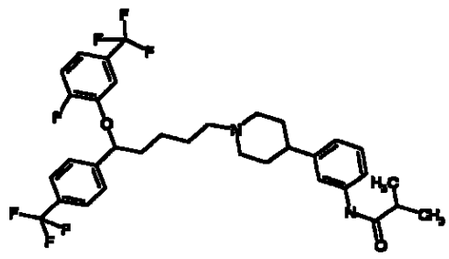
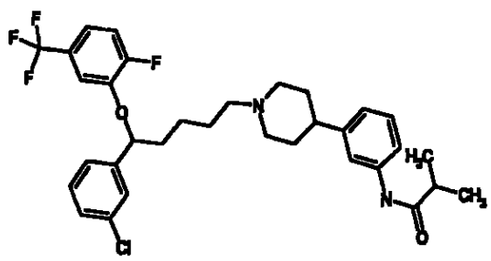
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920		6.9
921		6.8
922		25.0

923  1.3

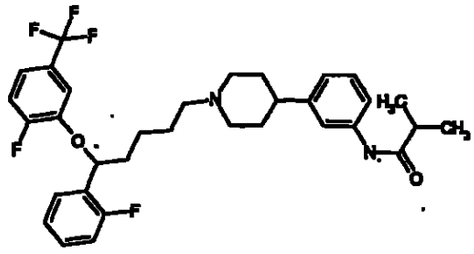
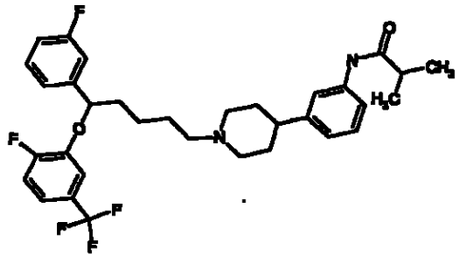
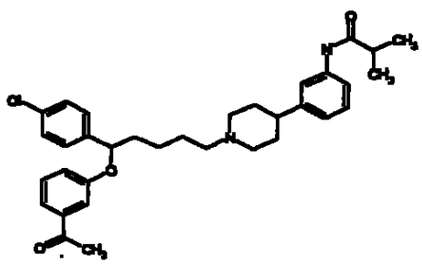
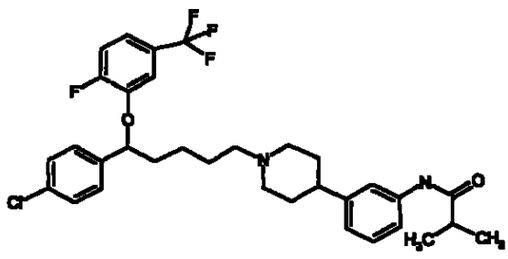
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925  13.4

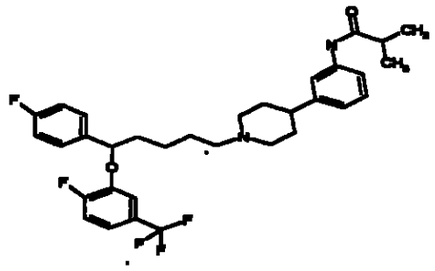
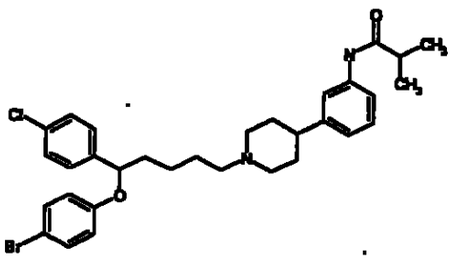
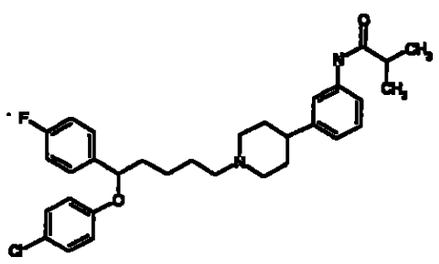
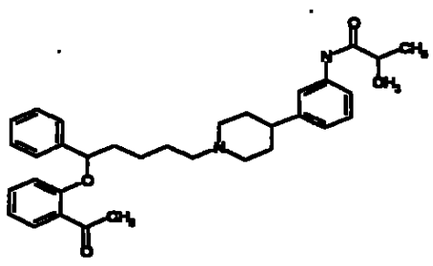
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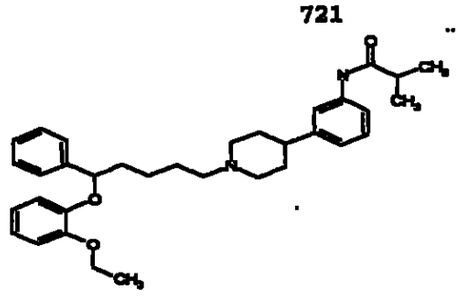
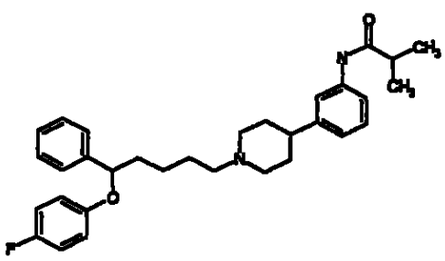
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928			14.9
929			29.9
930			14.6

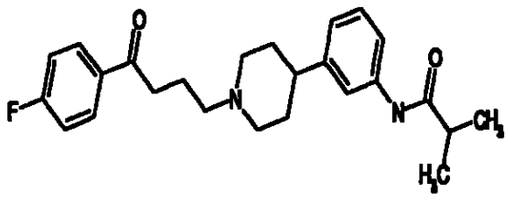
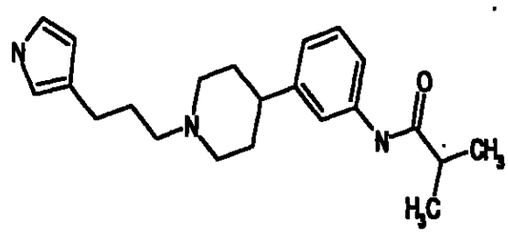
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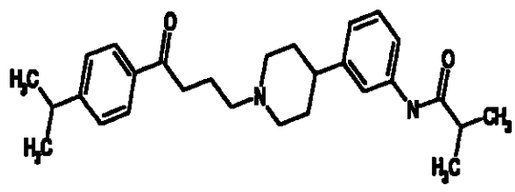
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933		10.9
934		12.3

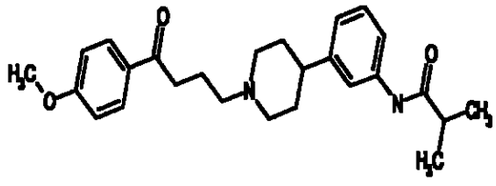
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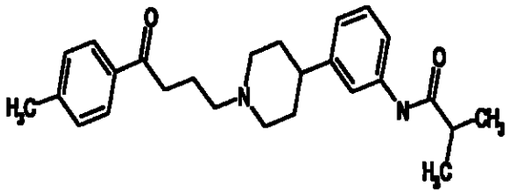
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936		11.8
937		28.4
938		608.6

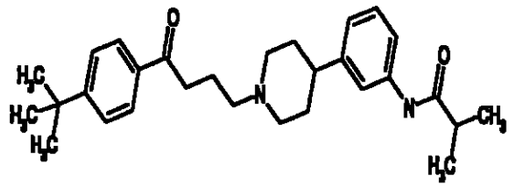
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940		1.8

Example	Structure	rMCH1 Ki (nM)
941		15.2
942		167.9

943  101.7

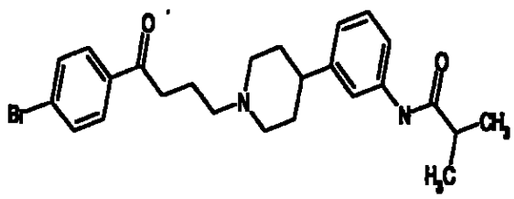
944  38.8

945  31.2

946  336.6

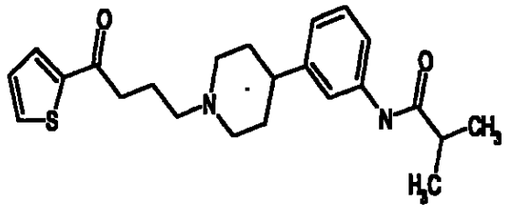
723

947



4.3

948



21.2

Table 2: Binding affinities (Ki) at the rat MCH1, human Dopamine D2, human Histamine H1 and human Alpha-1a Adrenergic receptors.

Compound	rMCH1	hD2	hH1	hAlpha-1a
	Ki (nM)	*Ki (nM)*	*Ki (nM)*	*Ki (nM)*
1	90	6092	823	49
2	3.9	2839	700	32.1
3	766	ND	ND	ND
4	357	ND	ND	ND
5	14.2	1139	1618	9.1
6	274	ND	ND	ND
7	1000	ND	ND	ND
8	627	ND	ND	ND
9	69	1430	1733	26.4
10	2.6	862	461	19.4
11	197	ND	ND	ND
12	84	771	571	57
13	11.9	551	ND	61
14	167	ND	ND	ND
15	720	ND	ND	ND
16	272	ND	ND	ND
17	342	ND	ND	ND
18	29.5	782	ND	115
19	506	ND	ND	ND
20	21	470	ND	41.3
21	630	ND	ND	ND

Table 2: Binding affinities (KI) at the rat MCH1, human Dopamine D2, human Histamine H1 and human Alpha-1a Adrenergic receptors.

22	52	5181	2277	284
23	1036	ND	ND	ND
24	67	1252	ND	127
25	463	ND	ND	ND
26	192	1977	ND	516
27	91	503	ND	130
28	511	ND	ND	ND
29	654	ND	ND	ND
30	382	ND	ND	ND
31	382	ND	ND	ND
32	160	ND	ND	ND
33	815	ND	ND	ND
34	651	ND	ND	ND
35	11.5	9854	2000	533
36	62	12,026	2454	1489
37	29.1	34,993	16,734	1087
38	16.2	>50000	6595	1592
39	11.8	>50000	6401	2937
40	50	7451	273	12.3
41	946	ND	ND	ND
42	118	ND	ND	ND
43	12	10,428	2560	434
44	11.5	8673	11,092	704

Table 2: Binding affinities (KI) at the rat MCH1, human Dopamine D2, human Histamine H1 and human Alpha-1a Adrenergic receptors.

45	1.6	42.2	3.4	18
46	187	ND	ND	ND
47	52	>50000	36,907	>50000
48	6.7	735	6390	452
49	7.1	471	39.1	140
50	3.9	1077	304	161
51	3.1	152	130	33.5
52	3.8	244	264	13.2
53	7.1	191	1320	221
54	4.9	83	283	187
55	5	162	1100	125
56	22.3	435	32.5	55
57	16.6	41,994	48,658	3206
58	20.1	390	590	233
59	12.9	262	46.9	49.1
60	0.923	52	548	22.3
61	13.6	281	969	310
62	12.8	319	25,320	719
63	22.4	766	25,307	1058
64	14.8	313	6994	1142
65	17	331	9390	1720
66	3.3	132	3473	944
67	5.9	133	2148	511

Table 2: Binding affinities (Ki) at the rat MCH1, human Dopamine D2, human Histamine H1 and human Alpha-1a Adrenergic receptors.

68	9.3	66	329	204
69	32.5	46.6	>50000	232
70	50	1050	7998	1521
71	6.6	119	1710	226
72	31.4	41,454	33,096	645
73	22.3	41,454	8522	381
74	48.6	39,511	1882	333
75	11.8	19,041	2844	2469
76	44.6	41,454	39,710	10,985
77	25.7	447	4178	157
78	22.2	37.6	>50000	1313
79	19.4	244	507	722
80	14.3	833	9789	620
81	377	ND	ND	ND
82	11.2	ND	ND	ND
83	48.1	ND	ND	ND
84	121	ND	ND	ND
85	3.2	2449	3816	3021

V. Synthesis of Compound A

Described below is the synthesis of Compound A. Compound A is the radiolabeled compound that was used in the radioligand binding assays described above.

N-[3-(1,2,3,6-TETRAHYDRO-4-PYRIDINYL)PHENYL]ACETAMIDE: The reaction of saturated of aqueous Na_2CO_3 solution (25 mL), tert-butyl 4-{[(trifluoromethyl)sulfonyl]oxy}-1,2,3,6-tetrahydro-1-pyridine-carboxylate (20 mmol), 3-acetamidophenylboronic acid (30 mmol) and tetrakis-triphenylphosphine palladium (0) (1.15 g) in dimethoxyethane (40 mL) at reflux temperature overnight gave tert-butyl 4-[3-(acetylamino)phenyl]-3,6-dihydro-1(2*H*)-pyridinecarboxylate. Deprotection of the BOC group using HCl in dioxane followed by basification (pH 11-12) gave the desired product.

TERT-BUTYL *N*-(3-BROMOPROPYL)CARBAMATE: was prepared from 3-bromopropylamine hydrobromide and BOC_2O in the presence of base in dichloromethane.

N-{3-[1-(3-AMINOPROPYL)-1,2,3,6-TETRAHYDRO-4-PYRIDINYL]PHENYL}ACETAMIDE: The reaction of tert-butyl *N*-(3-bromopropyl)carbamate and *N*-[3-(1,2,3,6-tetrahydro-4-pyridinyl)phenyl]acetamide in refluxing dioxane with catalytic Bu_4NI and base as described in Scheme A gave tert-butyl 3-(4-[3-(acetylamino)phenyl]-3,6-dihydro-1(2*H*)-pyridinyl)propylcarbamate. Deprotection of the BOC group using HCl in dioxane followed by basification (pH 11-12) gave the desired product.

METHYL (4*S*)-3-({[3-(4-[3-(ACETYLAMINO)PHENYL]-3,6-DIHYDRO-1(2*H*)-PYRIDINYL)PROPYL]AMINO}CARBONYL)-4-(3,4-DIFLUOROPHENYL)-6-(METHOXYMETHYL)-2-OXO-1,2,3,4-TETRAHYDRO-5-PYRIMIDINECARBOXYLATE: Prepared from the reaction of 5-methyl 1-(4-nitrophenyl) (6*S*)-6-(3,4-difluorophenyl)-4-(methoxymethyl)-2-oxo-3,6-dihydro-1,5(2*H*)-pyrimidinedicarboxylate (describe in PCT Publication No. WO 00/37026, published June 29, 2000) and *N*-{3-[1-(3-aminopropyl)-1,2,3,6-tetrahydro-4-pyridinyl]phenyl}acetamide: ^{1}H NMR δ 8.90 (t, 1 H, J=3.6 Hz), 7.75 (s, 1 H), 7.50-7.00 (m, 8 H), 6.68 (s, 1 H), 6.03 (br s, 1 H), 4.67 (s, 2 H), 3.71 (s, 3 H), 3.47 (s, 3 H), 3.38 (ABm, 2 H), 3.16 (m, 2 H), 2.71 (t, 2 H, J =5.4 Hz), 2.56 (m, 4 H), 2.35-1.90 (br, 2 H), 2.17 (s, 3 H), 1.82 (p, 2 H, J=7.2 Hz); ESMS, 612.25 $(M+H)^+$.

TRITIATED METHYL (4*S*)-3-{[(3-{4-[3-(ACETYLAMINO)PHENYL]-1-PIPERIDINYL}PROPYL)AMINO]CARBONYL}-4-(3,4-DIFLUOROPHENYL)-6-(METHOXYMETHYL)-2-OXO-1,2,3,4-TETRAHYDRO-5-PYRIMIDINECARBOXYLATE ([^{3}H] COMPOUND A): This radiochemical synthesis was carried out by Amersham Pharmacia Biotech, Cardiff, Wales. A methanolic solution of methyl (4*S*)-3-({[3-(4-[3-(acetylamino)phenyl]-3,6-dihydro-1(2*H*)-pyridinyl)propyl]amino}carbonyl)-4-(3,4-difluorophenyl)-6-(methoxymethyl)-2-oxo-1,2,3,4-tetrahydro-5-pyrimidinecarboxylate was exposed to tritium gas at 1 atmosphere pressure in the presence of 5% palladium on carbon with stirring overnight to give the tritiated methyl (4*S*)-3-{[(3-{4-[3-(acetylamino)phenyl]-1-piperidinyl}propyl)amino]carbonyl}-4-(3,4-difluorophenyl)-6-(methoxymethyl)-2-oxo-1,2,3,4-tetrahydro-5-pyrimidinecarboxylate ((+)-isomer) After

purification by reverse phase HPLC (Hypersil ODS, 4.6 x 100 mm, methanol:H_2O:Et_3N 10:90:1 to 100:0:1 in 15 min at 1.0 mL/min, with radiochemical and UV detection), this product was used as a radioligand in the MCH1 binding assays. The same procedure was carried out with H_2 gas in place of $^3H_2$ to afford the non-radioactive version of Compound A.

VI. In-Vivo Methods

The following *in vivo* methods were performed to predict the efficacy of MCH1 antagonists for the treatment of obesity (3-day body weight and sweetened condensed milk), depression (forced swim test), anxiety (social interaction test), and urinary disorders (DIRC and CSTI).

Effects of MCH1 Antagonists on Body Weight (3 Day)

Male Long Evans rats (Charles River) weighing 180-200 grams were housed in groups of four on a 12-hour light/dark cycle with free access to food and water. Test compounds were administered twice daily *via* i.p. injection, 1 hour before the dark cycle and 2 hours after lights on, for three days. All rats were weighed daily after each morning injection. Overall results were expressed as body weight (grams) gained per day (mean ± SEM) and were analyzed by two-way ANOVA. Data for each time point were analyzed by one-way ANOVA followed by post hoc Newman-Keuls test. The data were analyzed using the GraphPad Prism (v2.01) (GraphPad Software, Inc., San Diego, CA). All data were presented as means ± S.E.M.

Effects of MCH1 Antagonists on Consumption of Sweetened Condensed Milk

Male C57BL/6 mice (Charles River) weighing 17-19 grams at the start of experiments were housed in groups of four or five on a 12 hour light/dark cycle with free access to food and water. For 7 days, mice were weighed, placed in individual cages and allowed to drink sweetened condensed milk (Nestle, diluted 1:3 with water) for 1 hour, 2-4 hours into the light cycle. The amount of milk consumed was determined by weighing the milk bottle before and after each drinking bout. On the test day, mice received i.p. injections of Test Compound (3, 10 or 30 mg/kg in 0.01 % lactic acid), vehicle (0.01 % lactic acid) of d-fenfluramine (10 mg/kg in 0.01 % lactic acid) 30 min. prior to exposure to milk. The amount of milk consumed on the test day (in mls milk/ kg body weight) was compared to the baseline consumption for each mouse determined on the previous 2 days. Data for each time point were analyzed by one-way ANOVA.

Forced Swim Test (FST) in the Rat

Animals

Male Sprague-Dawley rats (Taconic Farms, NY) were used in all experiments. Rats were housed 5 per cage and maintained on a 12:12-h light-dark cycle. Rats were handled for 1 minutes each day for 4 days prior to behavioral testing.

Drug Administration

Animals were randomly assigned to receive a single i.p. administration of vehicle (2.5% EtOH / 2.5% Tween-80), imipramine (positive control; 60 mg/kg), or Test Compound 60 minutes before the start of the 5 minute test period. All injections were given using 1 cc tuberculin syringe with 26 3/8 gauge needles (Becton-Dickinson, VWR Scientific, Bridgeport, NJ). The volume of injection was 1 ml/kg.

Experimental Design

The procedure used in this study was similar to that previously described (Porsolt, et al., 1978), except the water depth was 31 cm in this procedure. The greater depth in this test prevents the rats from supporting themselves by touching the bottom of the cylinder with their feet. Swim sessions were conducted by placing rats in individual plexiglass cylinders (46 cm tall x 20 cm in diameter) containing 23-25°C water 31 cm deep. Swim tests were conducted always between 900 and 1700 hours and consisted of an initial 15-min conditioning test followed 24h later by a 5-minute test. Drug treatments were administered 60 minutes before the 5-minute test period. Following all swim sessions, rats were removed from the cylinders, dried with paper towels and placed in a heated cage for 15 minutes and returned to their home cages. All test sessions were videotaped using a color video camera and recorded for scoring later.

Behavioral Scoring

The rat's behavior was rated at 5-second intervals during the 5-minute test by a single individual, who was blind to the treatment condition. Scored behaviors were:

1. Immobility- rat remains floating in the water without struggling and was only making those movements necessary to keep its head above water;
2. Climbing - rat was making active movements with its forepaws in and out of the water, usually directed against the walls;
3. Swimming - rat was making active swimming motions, more than necessary to merely maintain its head above water, e.g. moving around in the cylinder; and
4. Diving - entire body of the rat was submerged.

Data Analysis

The forced swim test data (immobility, swimming, climbing, diving) were subjected to a randomized, one-way ANOVA and post hoc tests conducted using the Newman-Keuls test. The data were analyzed using the GraphPad Prism (v2.01) (GraphPad Software, Inc., San Diego, CA). All data were presented as means $\pm$ S.E.M. All data were presented as means $\pm$ S.E.M.

Forced Swim Test (FST) in the Mouse

Animals

DBA/2 mice (Taconic Farms, NY) were used in all experiments. Animals were housed 5 per cage in a controlled environment under a 12:12 hour light:dark cycle. Animals were handled 1 min each day for 4 days

prior to the experiment. This procedure included a mock gavage with a 1.5 inch feeding tube.

Drug Administration

Animals were randomly assigned to receive a single administration of vehicle (5% EtOH/5% Tween-80), Test Compound, or imipramine (60 mg/kg) by oral gavage 1 hour before the swim test.

Experimental Design

The procedure for the forced swim test in the mouse was similar to that described above for the rat, with some modifications. The cylinder used for the test was a 1-liter beaker (10.5cm diameter X 15 cm height) fill to 800ml (10cm depth) of 23-25°C water. Only one 5-minute swim test was conducted for each mouse, between 1300 and 1700 hours. Drug treatments were administered 30-60 minutes before the 5-minute test period. Following all swim sessions, mice were removed from the cylinders, dried with paper towels and placed in a heated cage for 15 minutes. All test sessions were videotaped using a Sony color video camera and recorder for scoring later.

Behavioral Scoring

The behavior during minutes 2-5 of the test was played back on a TV monitor and scored by the investigator. The total time spent immobile (animal floating with only minimal movements to remain afloat) and mobile (swimming and movements beyond those required to remain afloat) were recorded.

Data Analysis

The forced swim test data (time exhibiting immobility, mobility; seconds) were subjected to a randomized, one-way ANOVA and post hoc tests conducted using the Newman-Keuls test. The data were analyzed using the GraphPad Prism (v2.01) (GraphPad Software, Inc., San Diego, CA). All data were presented as means ± S.E.M.

Social Interaction Test (SIT)

Rats are allowed to acclimate to the animal care facility for 5 days and are housed singly for 5 days prior to testing. Animals are handled for 5 minutes per day. The design and procedure for the Social Interaction Test is carried out as previously described by Kennett, et al. (1997). On the test day, weight matched pairs of rats (± 5%), unfamiliar to each other, are given identical treatments and returned to their home cages. Animals are randomly divided into 5 treatment groups, with 5 pairs per group, and are given one of the following i.p. treatments: Test Compound (10, 30 or 100 mg/kg), vehicle (1 ml/kg) or chlordiazepoxide (5 mg/kg). Dosing is 1 hour prior to testing. Rats are subsequently placed in a white perspex test box or arena (54 x 37 x 26 cm), whose floor is divided up into 24 equal squares, for 15 minutes. An air conditioner is used to generate background noise and to keep the room at approximately 74°F. All sessions are videotaped using a JVC camcorder (model GR-SZ1, Elmwood Park, NJ) with either TDK (HG ultimate brand) or Sony 30 minute videocassettes. All sessions are conducted between 1300 - 1630 hours. Active social interaction, defined as grooming, sniffing, biting, boxing, wrestling, following and crawling over or under, is scored using a stopwatch

(Sportsline model no. 226, 1/100 sec. discriminability). The number of episodes of rearing (animal completely raises up its body on its hind limbs), grooming (licking, biting, scratching of body), and face washing (i.e. hands are moved repeatedly over face), and number of squares crossed are scored. Passive social interaction (animals are lying beside or on top of each other) is not scored. All behaviors are assessed later by an observer who is blind as to the treatment of each pair. At the end of each test, the box is thoroughly wiped with moistened paper towels.

Animals

Male albino Sprague-Dawley rats (Taconic Farms, NY) are housed in pairs under a 12 hr light dark cycle (lights on at 0700 hrs.) with free access to food and water.

Drug Administration

Test Compound is dissolved in either 100% DMSO or 5% lactic acid, v/v (Sigma Chemical Co., St. Louis, MO). Chlordiazepoxide (Sigma Chemical Co., St. Louis, MO) is dissolved in double distilled water. The vehicle consists of 50% DMSO (v/v) or 100% dimethylacetamide (DMA). All drug solutions are made up 10 minutes prior to injection and the solutions are discarded at the end of the test day. The volume of drug solution administered is 1 ml/kg.

Data Analysis

The social interaction data (time interacting, rearing and squares crossed) are subjected to a randomized, one-way ANOVA and post hoc tests conducted using the

Student-Newman-Keuls test. The data are subjected to a test of normality (Shapiro-Wilk test). The data are analyzed using the GBSTAT program, version 6.5 (Dynamics Microsystems, Inc., Silver Spring, MD, 1997).

In Vivo Models of the Micturition Reflex

The effects of compounds on the micturition reflex were assessed in the "distension-induced rhythmic contraction" (DIRC), as described in previous publications (e.g. Maggi et al, 1987; Morikawa et al, 1992), and Continuous Slow Transvesicular Infusion (CSTI) models in rats.

DIRC Model

Female Sprague Dawley rats weighing approximately 300 g were anesthetized with subcutaneous urethane (1.2 g/kg). The trachea was cannulated with PE240 tubing to provide a clear airway throughout the experiment. A midline abdominal incision was made and the left and right ureters were isolated. The ureters were ligated distally (to prevent escape of fluids from the bladder) and cannulated proximally with PE10 tubing. The incision was closed using 4-0 silk sutures, leaving the PE10 lines routed to the exterior for the elimination of urine. The bladder was canulated via the transurethral route using PE50 tubing inserted 2.5 cm beyond the urethral opening. This cannula was secured to the tail using tape and connected to a pressure transducer. To prevent leakage from the bladder, the cannula was tied tightly to the exterior urethral opening using 4-0 silk.

To initiate the micturition reflex, the bladder was first emptied by applying pressure to the lower abdomen, and then filled with normal saline in 100 increments (maximum = 2 ml) until spontaneous bladder contractions occurred (typically 20-40 mmHg at a rate of one contraction every 2 to 3 minutes. Once a regular rhythm was established, vehicle (saline) or Test Compounds were administered i.v. or i.p. to explore their effects on bladder activity. The 5-HT_{1A} antagonist WAY-100635 was given as a positive control. Data were expressed as contraction interval (in seconds) before drug application (basal), or after the application of vehicle or test article.

Continuous Slow Transvesicular Infusion (CSTI) rat Model

Male Sprague Dawley rats weighing approximately 300 g were used for the study. Rats were anaesthetized with pentobarbitone sodium (50 mg/kg, i.p). Through a median abdominal incision, bladder was exposed and a polyethylene cannula (PE 50) was introduced into the bladder through a small cut on the dome of the bladder and the cannula was secured with a purse string suture. The other end of the cannula was exteriorized subcutaneously at the dorsal neck area. Similarly, another cannula (PE 50) was introduced into the stomach through a paramedian abdominal incision with the free end exteriorized subcutaneously to the neck region. The surgical wounds were closed with silk 4-0 suture and the animal was allowed to recover with appropriate post surgical care. On the following day, the animal was placed in a rat restrainer. The open end of the bladder-cannula was connected to a pressure transducer as well

as infusion pump through a three-way stopcock. The bladder voiding cycles were initiated by continuous infusion of normal saline at the rate of 100 µl/min. The repetitive voiding contractions were recorded on a Power Lab on-line data acquisition software. After recording the basal voiding pattern for an hour, the test drug or vehicle was administered directly into stomach through the intragastric catheter and the voiding cycles were monitored for 5 hours. Micturition pressure and frequency were calculated before and after the treatment (at every 30 min interval) for each animal. Bladder capacity was calculated from the micturition frequency, based on the constant infusion of 100ul/min. The effect of the test drug was expressed as a percentage of basal, pre-drug bladder capacity. WAY 100635 was used as positive control for comparison.

In Vivo Results

Table 2

Effect of MCH1 antagonist (Example No.) in the following *in vivo* models: 3-day Body Weight (3D BW), mouse Sweetened Condensed Milk (mSwCM), mouse Forced Swim Test (mFST), rat Forced Swim Test (rFST), DIRC model, or CSTI model.

Example No.	3D BW	mSwCM	mFST	rFST	DIRC	CSTI
2	A	B	C	D	E	F
10	Not Done	Not Done	C	Not Done	E	F
39	A	B	Not Done	D	Not Done	Not Done
43	Not Done	B	C	Not Done	Not Done	Not Done
44	Not Done	Not Done	No effect	Not Done	Not Done	Not Done
89	Not Done	B	No effect	Not Done	Not-Done	Not Done
90	Not Done	No effect	No effect	Not Done	Not Done	Not Done
91	Not Done	Not Done	C	Not Done	E	F
93	Not Done	Not Done	No effect	Not Done	Not Done	Not Done
95	Not Done	B	No effect	Not Done	Not Done	Not Done
99	A	Not Done	C	Not Done	E	F
105	Not Done	B	C	Not Done	Not Done	Not Done
106	Not Done	B	C	Not Done	E	F
112	Not Done	Not Done	No effect	Not Done	Not Done	Not Done
116	A	Not Done	C	Not Done	E	F

A = Produced a significant reduction in weight gain relative to vehicle-treated controls

B = Produced a significant decrease in consumption of milk relative to vehicle-treated controls

C = Produced a significant decrease in immobility relative to vehicle-treated animals when administered orally.

D = Produced a significant decrease in immobility or a significant increase in swimming activity relative to vehicle-treated animals

E = Produced a significant increase in contraction interval relative to pre-drug interval

F = Produced an increase in bladder capacity in rats relative to baseline capacity.

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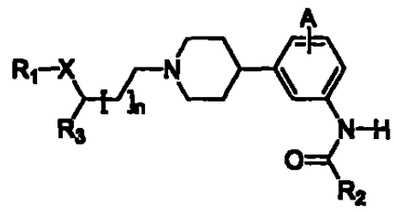
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What is claimed is:

1. A compound having the structure:



;

wherein R_1 is hydrogen, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -F, -Cl, -Br, -I, -CN, -NO_2, -CH_3, -CF_3, -$COCH_3$, -CO_2R_2, phenyl, phenoxy or straight chained or branched C_1-C_7 alkyl;

wherein R_2 is straight-chained or branched C_3-C_4 alkyl or cyclopropyl;

wherein R_3 is aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -F, -Cl, -Br, -I, -CN, -NO_2, straight chained or branched C_1-C_7 alkyl;

wherein A is -H, -F, -Cl, -Br, -CN, -NO_2, -COR_3, -CO_2R_3, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl;

wherein X is O or NH; and

wherein n is an integer from 0 to 5 inclusive.

2. The compound of claim 1, wherein R_1 is aryl optionally substituted with one or more -F, -Cl, -Br, -I, -CN, $-NO_2$, $-COCH_3$, $-CO_2R_2$, straight chained or branched C_1-C_7 alkyl;

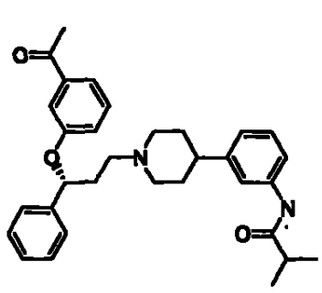
wherein R_3 is phenyl;

wherein A is H; and

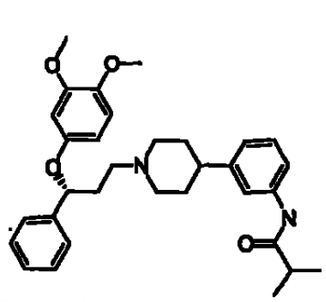
wherein X is O.

3. The compound of claim 2, wherein R_2 is isopropyl.

4. The compound of claim 3, wherein the compound has the structure:



5. The compound of claim 3, wherein the compound has the structure:

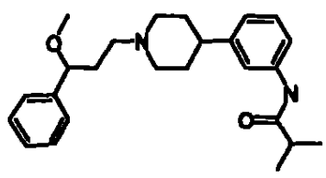


6. The compound of claim 1, wherein R_1 is hydrogen, straight chained or branched C_1-C_7 alkyl; and wherein R_3

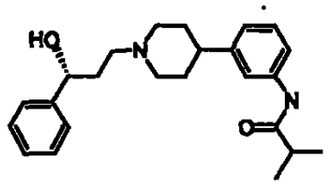
is aryl.

7. The compound of claim 6, wherein R_2 is isopropyl; and A is hydrogen.

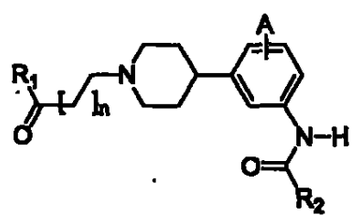
8. The compound of claim 7, wherein the compound has the structure:



9. The compound of claim 7, wherein the compound has the structure:



10. A compound having the structure:



;

wherein R_1 is aryl or heteroaryl optionally substituted with one or more -F, -Cl, -Br, -I, -CN, $-NO_2$, $-OCH_3$, phenoxy, fused cyclopentanyl, straight chained or

branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl;

wherein R_2 is straight-chained or branched C_1-C_4 alkyl or cyclopropyl;

wherein A is -H, -F, -Cl, -Br, -CN, -NO_2, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl; and

wherein n is an integer from 1 to 5 inclusive.

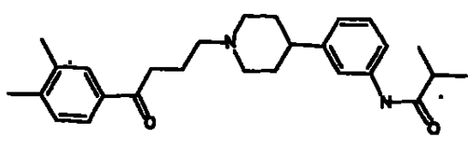
11. The compound of claim 10, wherein R_1 is aryl optionally substituted with one or more -F, -Cl, -Br, -I or straight chained or branched C_1-C_4 alkyl; and

wherein A is H.

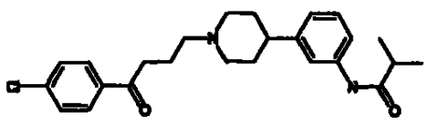
12. The compound of claim 11, wherein R_2 is isopropyl; and

wherein n is 2.

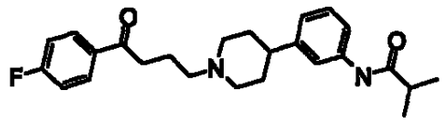
13. The compound of claim 12, wherein the compound has the structure:



14. The compound of claim 12, wherein the compound has the structure:



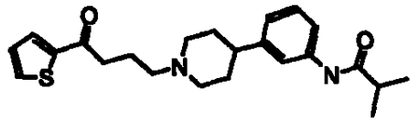
15. The compound of claim 12, wherein the compound has the structure:



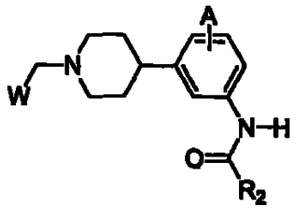
16. The compound of claim 10, wherein R_1 is thienyl; and wherein A is H.

17. The compound of claim 16, wherein R_2 is isopropyl.

18. The compound of claim 17, wherein the compound has the structure:

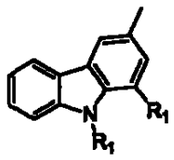
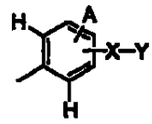


19. A compound having the structure:



;

wherein W is

 or  ;

wherein each R_1 is independently hydrogen, methyl or ethyl;

wherein R_2 is straight-chained or branched C_3-C_4 alkyl or cyclopropyl;

wherein R_3 is hydrogen, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -H, -F, -Cl, -Br, -I, -CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl.

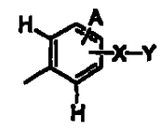
wherein each A is independently -H, -F, -Cl, -Br, -CN, $-NO_2$, $-COR_3$, $-CO_2R_3$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl;

wherein X is O, NR_3, CO or may be absent; and

wherein Y is hydrogen, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -F, -Cl, -Br, -I, -CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl.

20. The compound of claim 19, wherein W is

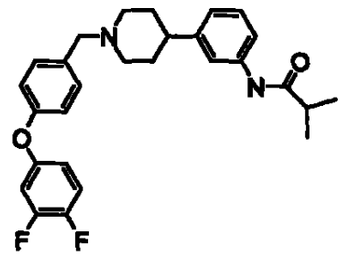
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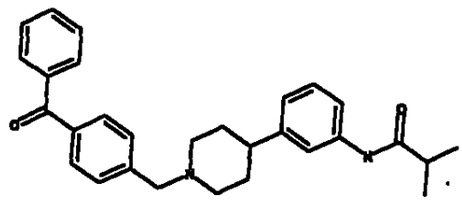
and wherein X is O or may be absent.

21. The compound of claim 20, wherein R_3 is isopropyl.

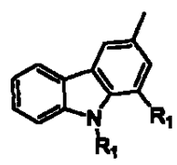
22. The compound of claim 21, wherein the compound has the structure:



23. The compound of claim 21, wherein the compound has the structure:



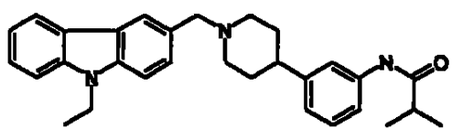
24. The compound of claim 19, wherein W is



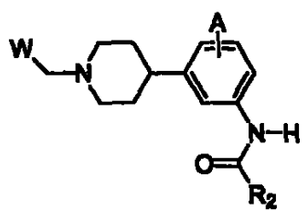
25. The compound of claim 24, wherein A is -H, -F, -Cl, -Br.

26. The compound of claim 25, wherein R_3 is isopropyl; and A is hydrogen.

27. The compound of claim 26, wherein the compound has the structure:

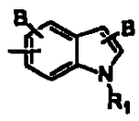
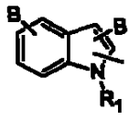


28. A compound having the structure:



;

wherein W is

 or 

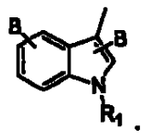
wherein R_1 is hydrogen, straight chained or branched C_1-C_7 alkyl, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -F, -Cl, -Br, -CN, $-NO_2$, $-OCH_3$, $-CO_2CH_3$, $-CF_3$, phenyl, straight chained or branched C_1-C_7 alkyl;

wherein R_2 is straight- chained or branched C_3-C_4 alkyl or cyclopropyl;

wherein A is -H, -F, -Cl, -Br, -CN, $-NO_2$, $-COR_1$, $-CO_2R_1$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl or phenyl.

wherein each B is independently -H, -F, -Cl, -Br, -I, -CN, $-NO_2$, $-COR_1$, $-CO_2R_1$, $-OCH_3$, $-OCF_3$, $-CF_3$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl or aryl, phenoxy or benzyloxy, wherein the aryl, phenoxy or benzyloxy is optionally substituted with one or more -F, -Cl, -Br, -CN, $-NO_2$, $-COR_1$, $-CO_2R_1$, $-OCH_3$, $-OCF_3$, $-CF_3$ or straight chained or branched C_1-C_7 alkyl.

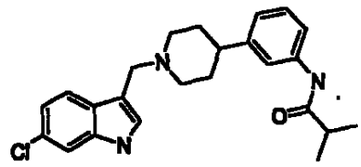
29. The compound of claim 28, wherein W is



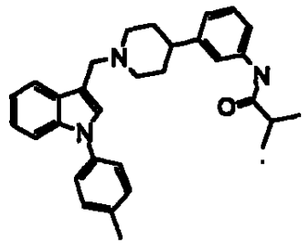
30. The compound of claim 29, wherein R_1 is hydrogen or phenyl optionally substituted with one or more -F, -Cl, -Br, -CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl.

31. The compound of claim 30, wherein R_2 is isopropyl.

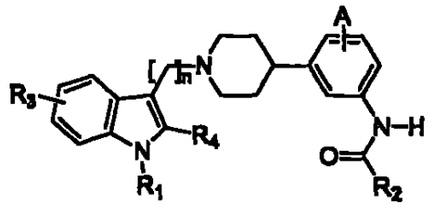
32. The compound of claim 31, wherein the compound has the structure:



33. The compound of claim 31, wherein the compound has the structure:



34. A compound having the structure:



wherein R_1 is hydrogen, straight chained or branched C_1-C_7 alkyl, aryl or heteroaryl, wherein the aryl or heteroaryl is optionally substituted with one or more -F, -Cl, -Br, -CN, -NO_2, -CF_3, -OCH_3, straight chained or branched C_1-C_3 alkyl;

wherein R_2 is straight-chained or branched C_3-C_4 alkyl or cyclopropyl;

wherein R_3 is -H, -F, -Cl, -Br, -I, -CN, -NO_2, -CF_3, -

OCH_3, or straight chained or branched C_1-C_3 alkyl, monofluoroalkyl or polyfluoroalkyl, or a phenyl ring fused to C_6 and C_7 of the indole moiety;

wherein R_4 is hydrogen or aryl optionally substituted with one or more -F, -Cl, -Br, -I, -CN, $-NO_2$, $-CF_3$, straight chained or branched C_1-C_3 alkyl;

wherein A is -H, -F, -Cl, -Br, -CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl; and

wherein n is an integer from 2 to 4 inclusive.

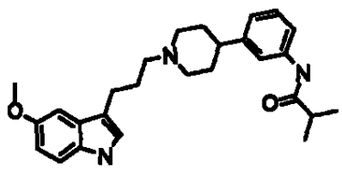
35. The compound of claim 34, wherein R_3 is -H, -F, -Cl, -Br, -I, -CN, $-NO_2$, $-OCF_3$ or $-OCH_3$; and

wherein R_4 is hydrogen or phenyl optionally substituted with one or more -F, -Cl or $-CF_3$.

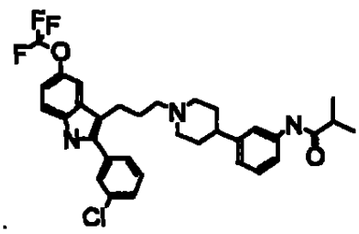
36. The compound of claim 35, wherein R_3 is hydrogen or phenyl optionally substituted with one or more -F, -Cl, -Br, -CN, $-NO_2$, $-CF_3$, $-OCH_3$ or straight chained or branched C_1-C_3 alkyl;

37. The compound of claim 36, wherein R_2 is isopropyl.

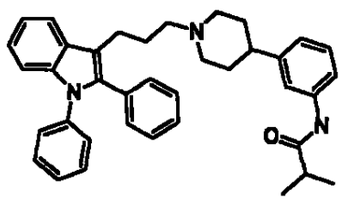
38. The compound of claim 37, wherein the compound has the structure:



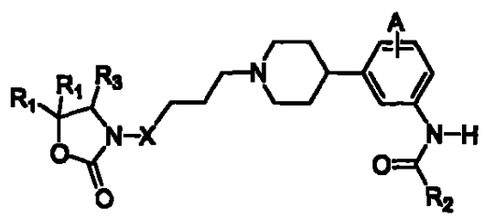
39. The compound of claim 37, wherein the compound has the structure:



40. The compound of claim 37, wherein the compound has the structure:



41. A compound having the structure:



wherein each R_1 is independently hydrogen or CH_3;

wherein R_2 is straight-chained or branched C_1-C_4 alkyl or cyclopropyl;

wherein R_3 is benzyl or phenyl, wherein the benzyl or phenyl is optionally substituted with a methylenenedioxy group or one or more -F or -Cl;

wherein A is -H, -F, -Cl, -Br, -CN, $-NO_2$, straight chained or branched C_1-C_7 alkyl, monofluoroalkyl or polyfluoroalkyl;

wherein X is $(CH_2)_2$, $COCH_2$ or CONH;

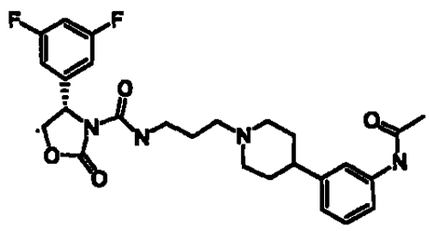
42. The compound of claim 41, wherein R_3 is phenyl optionally substituted with one or more -F; and

wherein A is hydrogen.

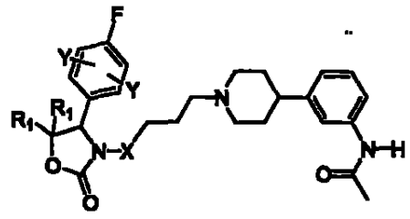
43. The compound of claim 42, wherein X is CONH.

44. The compound of claim 43, wherein R_2 is methyl.

45. The compound of claim 44, wherein the compound has the structure:

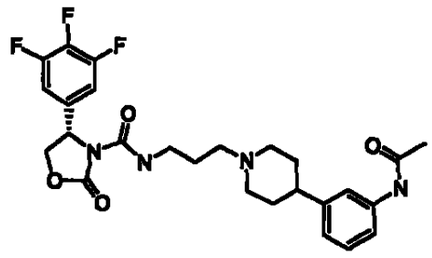


46. The compound of claim 44, wherein the compound has the structure:

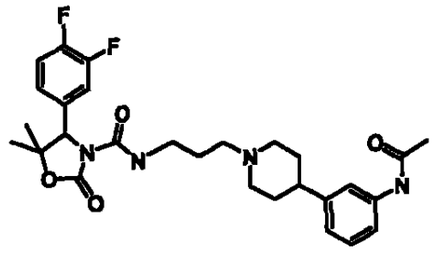


wherein each Y is independently hydrogen or -F.

47. The compound of claim 46, wherein the compound has the structure:

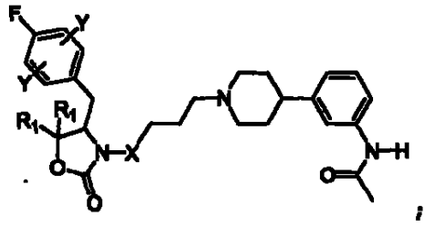


48. The compound of claim 46, wherein the compound has the structure:



49. The compound of claim 41, wherein R_3 is benzyl optionally substituted with a methylenedioxy group or one or more -F or -Cl.

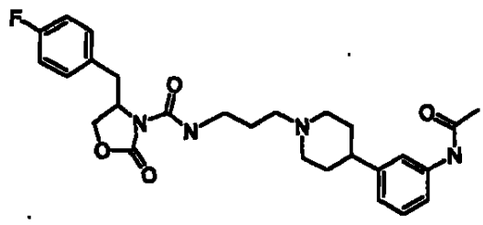
50. The compound of claim 49, wherein the compound has the structure:



wherein each Y is independently hydrogen or -F.

51. The compound of claim 50, wherein the compound has the structure:

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52. A compound of claims 1 to 51, wherein the compound is enantiomerically pure.

53. A compound of claims 1 to 51, wherein the compound is diastereomerically pure.

54. The compound of claims 52 and 53, wherein the compound is enantiomerically and diastereomerically pure.

55. A pharmaceutical composition comprising a therapeutically amount of a compound of any of claims 1 to 51 and a pharmaceutically acceptable carrier.

56. The pharmaceutical composition of claim 55, wherein the amount of the compound is from about 0.01mg to about 500mg.

57. The pharmaceutical composition of claim 56, wherein the amount of the compound is from about 0.1mg to about 60mg.

58. The pharmaceutical composition of claim 57, wherein the amount of the compound is from about 1mg to about 20mg.

59.The pharmaceutical composition of claim 55, wherein the carrier is a liquid and the composition is a solution.

60. The pharmaceutical composition of claim 55, wherein the carrier is a solid and the composition is a tablet.

61. The pharmaceutical composition of claim 55, wherein the carrier is a gel and the composition is a suppository.

62. A process for making a pharmaceutical composition comprising admixing a therapeutically effective amount of the compound of any of claims 1 to 51 and a pharmaceutically acceptable carrier.

63. A method of treating a subject suffering from a disorder selected from the group consisting of depression, anxiety, urge incontinence, or obesity comprising administering to the subject a therapeutically effective amount of the compound of any of claims 1 to 51.

64. The method of claim 63, wherein the therapeutically effective amount is between about 0.03 and about 1000 mg per day.

65. The method of claim 64, wherein the therapeutically effective amount is between about 0.30 and about 300 mg per day.

66. The method of claim 65, wherein the therapeutically effective amount is between about 1.0 and about 100 mg per day.

67. The method of claim 63, wherein the disorder is depression.

68. The method of claim 63, wherein the disorder is anxiety.

69. The method of claim 63, wherein the disorder is obesity.

70. The method of claim 63, wherein the disorder is urge incontinence.

71.A method of reducing the body mass of a subject, which comprises administering to the subject an amount of a compound of any of claims 1 to 51 effective to reduce the body mass of the subject.

72. A method of treating a subject suffering from depression, which comprises administering to the subject an amount of a compound of any of claims 1 to 51 effective to treat the subject's depression.

73. A method of treating a subject suffering from anxiety, which comprises administering to the subject an amount of a compound of any of claims 1 to 51 effective to treat the subject's anxiety.

74.A method of alleviating urge urinary incontinence in a subject suffering from an overactive bladder, which

comprises administering to the subject an amount of the compound of any of claims 1 to 51 effective to alleviate the subject's urge urinary incontinence.

74. A method of managing obesity in a subject in need of weight loss, which comprises administering to the subject an amount of a compound of any of claims 1 to 51 effective to induce weight loss in the subject.

75. A method of managing obesity in a subject who has experienced weight loss, which comprises administering to the subject an amount of a compound of any of claims 1 to 51 effective to maintain such weight loss in the subject.

76. A method of treating overactive bladder in a subject, which comprises administering to the subject an amount of a compound of any of claims 1 to 51 effective to treat the subject's overactive bladder.

78. A method of treating a disorder in a subject, wherein the symptoms of the subject can be alleviated by treatment with an MCH1 antagonist, wherein the MCH1 antagonist is the compound of any of claims 1 to 51.

79. A method of alleviating the symptoms of a disorder in a subject, which comprises administering to the subject an amount of an MCH1 antagonist effective to alleviate the symptoms, wherein the MCH1 antagonist is the compound of any of claims 1 to 51.

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PIPERIDINAS ANÍLINICAS SUSTITUIDAS COMO ANTAGONISTAS SELECTIVOS DE LA HORMONA DE CONCENTRACIÓN DE MELANINA

ANTECEDENTES DE LA INVENCIÓN

Esta solicitud es una continuación en parte de la solicitud estadounidense número de serie 10/042,582, presentada el 9 de enero del 2002, y de la solicitud estadounidense número de serie 09/899,794, presentada el 5 de julio del 2001, cuyo contenido de ambas solicitudes se incorporen la presente para referencia respecto de la solicitud objeto.

A través de esta solicitud, diferentes publicaciones están referidas en paréntesis por el autor y año. Todas las citas de éstas referencias se pueden encontrar al final de la especificación que precede inmediatamente al listado de secuencias y las reivindicaciones. La descripción de estas publicaciones en su totalidad esta incorporada para referencia en esta solicitud, para describir más completamente el estado de la técnica a la cual esta invención pertenece. La hormona de concentración de melanina (MCH, por sus siglas en inglés) es un péptido cíclico originalmente aislado del pescado de teleósto (Kawauchi et al., 1983). En el pescado el péptido de aminoácido 17 provoca agregación de melanina dentro de melanóforos e inhibe la liberación de ACTH, que actúa como

un antagonista funcional de - MSH. La MCH de Mamífero (19 aminoácidos) es altamente conservada entre la rata, el ratón y el humano, exhibiendo 100% de identidad de aminoácido, pero sus papeles fisiológicos son menos claros. La MCH ha sido reportada como que participa en una variedad de procesos incluyen la alimentación, el balance de agua, el metabolismo de la energía, estado general de niveles de alerta/atención, funciones de memoria y conocimiento, y desórdenes psiquiátricos (para revisión, ver Baker, 1991; Baker, 1994; Nahon, 1994; Knigge et al., 1996). Su papel en la alimentación o regulación del peso del cuerpo está soportado por una reciente publicación naturista (Qu et al., 1996) que demuestra que la MCH es sobreexpresada en el hipotálamo del ratón ob/ob comparado con el ratón ob/+, y que en ayuno además incrementa el ARNm de la MCH en ambos ratones obeso/normal durante el ayuno. La MCH también es estimulada por alimentación en ratas normales cuando se les indica en los ventrículos laterales (Rossi et al., 1997). La MCH también ha sido reportada como que antagoniza funcionalmente los efectos de comportamiento de la - MSH (Millar et al., 1993; Gonzalez et al, 1996; Sanchez et al., 1997); además, se ha demostrado que la tensión incrementa los niveles de ARNm del POMC mientras disminuye los niveles de ARNm de la preproMCH (ppMCH) del precursor de la MCH (Presse et al., 1992). Por consiguiente, la MCH puede servir

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como un neuropéptido integral implicado en la reacción de la tensión, así como en la regulación de la actividad alimenticia y sexual (Baker, 1991; Knigge et al., 1996).

Aunque los efectos biológicos de la MCH se cree que son mediados por receptores específicos, sitios de unión para la MCH no han sido bien descritos. Un ligando tritiado ([^{3}H]- MCH) se reportó que exhibe ligando específico a las membranas del cerebro pero era no utilizable para análisis de saturación, de manera que ni la afinidad ni $B_{máx}$ fueron determinadas ((Drozdz and Eberle, 1995). La radioionización de la tirosina en la posición trece resultó en un ligando con actividad biológica dramáticamente reducida (ver Drozdz and Eberle, 1995). En contraste la radioionización del análogo de la MCH ([Phe^{13}, Tyr^{19}]-MCH fue exitosa (Drozdz et al., 1995); el ligando retuvo la actividad biológica y exhibió una unión específica a una variedad de líneas celulares incluyendo el melanoma del ratón (B16-F1, G4F, y G4F-7), células PC12, y COS. En las células G4F-7, el K_D = 0.118nM y el $B_{máx}$ ~1100 sitios/células. En forma importante, la unión no fue inhibida por - MSH pero fue débilmente inhibida por la ANF de rata (Ki=116 nM vs. 12nM para la MCH nativa) (Drozdz et al., 1995). Más recientemente, la unión de la MCH específica se reportó en que queratinocitos transformados (Burgaud et al., 1997) y células de melanoma (Drozdz et al., 1998), en donde estudios de fotoreticulado

sugieren que el receptor es una proteína de membrana con un peso molecular aparente de 45-50 kDaltons, compatible con el intervalo de peso molecular de la superfamilia de GPCR de receptores. Ningún estudio de radioautoradiografía de la localización del receptor de la MCH utilizando este ligando, había sido reportado aún.

Las actividades de localización y biológicas del péptido de la MCH sugiere que la modulación del actividad del receptor de la MCH puede ser útil en un número de aplicaciones terapéuticas. El papel de la MCH en la alimentación, es el mejor caracterizado de sus usos clínicos potenciales. La MCH es expresada en el hipotálamo lateral, un área del cerebro implicada en la regulación de la sed y el hambre (Grillon et al., 1997); recientemente orexinas A y B, las cuales son agentes orexigénicos potentes, han mostrado tener localización muy similar a la MCH en el hipotálamo lateral (Sakurai et al., 1998). Los niveles de ARNm en esta región del cerebro se incrementan en las ratas después de 24 horas de privación de alimento (Hervé and Fellman, 1997); después de la inyección de insulina, un incremento significante en la abundancia e intensidad de manchado de la perikaria y fibras inmunoreactivas a la MCH, se observó concurrente con un incremento significante en el nivel de ARNm de la MCH (Bahjaoui-Bouhaddi et al., 1994). Consistente con la capacidad de la MCH para estimular la

alimentación en ratas (Rossi et al., 1997) es la observación de que los niveles de ARNm de la MCH son regulados en ascendencia en el hipotálamo de ratones ob/ob obesos (Qu et al., 1996), y disminuye en el hipotálamo de ratas tratadas con leptina, cuya captación de alimento y ganancia en el peso del cuerpo, son también disminuidos (Sahu, 1998). La MCH parece que actúa como un antagonista funcional del sistema de melanocortina en su efecto sobre la captación del alimento y sobre la secreción de la hormona dentro del HPA (hipotalamopituitaria/eje adrenal) (Ludwig et al., 1998). Juntos estos datos sugieren un papel para la MCH endógena en la regulación del balance de energía y respuesta a la tensión, y proporcionan una razón para el desarrollo de compuestos específicos que actúan en los receptores de la MCH para utilizarse en el tratamiento de la obesidad y desórdenes relacionados con la tensión.

En todas las especies estudiadas hasta la fecha, una mayor porción de las neuronas del grupo de la célula de MCH ocupa una localización más bien constante en aquellas áreas del hipotálamo lateral y el subtálamo en donde estas caen y pueden ser una parte de alguno de los circuitos de motor llamados "extrapiramidal". Estos implican trayectorias sustanciales estriadas- y pallidofugal que implican el tálamo y la corteza cerebral, áreas hipotalámicas, y conexiones recíprocas para núcleos subtalámicos, sustancia

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negra, y centros de mesencéfalo (Bittencourt et al., 1992). En su localización, el grupo de célula de la MCH puede ofrecer un puente o mecanismo para expresar actividad visceral hipotalámica con actividad apropiada y de motor coordinada. Clínicamente, puede ser de algún valor en consideradas la implicación de éste sistema de la MCH en desórdenes del movimiento, tal como enfermedad de Parkinson y síntoma de Huntingdon en la cual los circuitos extrapiramidales se conoce están implicados.

Los estudios de enlace genética humana han localizado loci de MCHh auténticos en el cromosoma 12 (12q23-24) y la variante de loci de MCHh en el cromosoma 5 (5q12-13) (Pedeutour et al., 1994). Los locus 12q23-24 coinciden con un locus al cual ataxia cerebelosa dominante autosomal tipo II (SCA2) ha sido trazada en mapa (Auburger et al., 1992; Twells et al., 1992). Esta enfermedad comprende desórdenes neurodegenerativos, incluyendo una atrofia olivopontocerebelar. Además, el gen para la enfermedad de Darier, ha sido trazado en mapa al locus 12q23-24 (Craddock et al., 1993). La enfermedad de Darier se caracteriza por anormalidades de adhesión de queratinocito I y enfermedades mentales en algunas familias. En vista de los patrones funcionales y neuroanatómicos del sistema neural de la MCH en los cerebros de ratas y de humanos, el gen de la MCH puede representar un buen candidato para SCA2 o la

enfermedad de Darier. En forma interesante, las enfermedades con alto impacto social han sido trazadas en mapa a este locus. De hecho, el gen responsable para las formas crónicas o agudas de atrofias musculares espinales han sido asignadas al cromosoma 5q12-13 utilizando análisis de enlace genético (Melki et al., 1990; Westbrook et al., 1992). Además, líneas independientes de soporte evidencian la asignación de un mayor locus de esquizofrenia al cromosoma 5q11.2-13.3 (Sherrington et al., 1988; Basset et al., 1998; Gilliam et al., 1989). Los estudios anteriores sugieren que la MCH puede jugar un papel en las enfermedades neurodegenerativas y desórdenes de la emoción.

Aplicaciones terapéuticas adicionales para compuestos relacionados con la MCH, se sugieren para los efectos observados de la MCH en otros sistemas biológicos. Por ejemplo, la MCH puede regular las funciones reproductivas en ratas machos y hembras. Transcripciones de la MCH y el péptido de la MCH se encontraron dentro de células germen en pruebas de ratas adultas, sugiriendo que la MCH puede participar en la renovación de células vástago y/o diferenciación de espermatocitos básicos (Hervieu et al., 1996). La MCH directamente inyectada en las áreas preópticas mediales (MPOA) o núcleos ventromediales (VMN) estimuló la actividad sexual en ratas hembra (Gonzalez et al., 1996). En ratas ovarioctamizadas preinyectadas con

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estradiol, la MCH estimuló la liberación de la hormona (LH) luteinizante mientras el antisuero de la anti-MCH inhibió la liberación de la LH (Gonzalez et al., 1997). La zona incierta, la cual contiene una gran población de los cuerpos de célula de la MCH, previamente ha sido identificada como un sitio de regulación para la oleada de la LH pre-ovulatoria (MacKenzie et al., 1984). La MCH ha sido reportada como que influencia la liberación de hormonas de la pituitaria incluyendo ACTH y oxitocina. Los análogos de la MCH pueden también ser útiles en el tratamiento de epilepsia. En el modelo de crisis epiléptica de PTZ, la inyección de la MCH previo a la inducción de la crisis epiléptica previene la actividad de la crisis epiléptica tanto en ratas como cobayos, sugiriendo que las neuronas que contienen la MCH pueden participar en los circuitos neurales subyacentes a la crisis epiléptica inducida por PTZ (Knigge y Wagner, 1997). La MCH también se ha observado que afecta la correlación del comportamiento de las funciones cognoscitiva. El tratamiento de la MCH acelero la extinción de la respuesta de anulación pasiva en ratas (McBride et al., 1994), aumentando la posibilidad de que los antagonistas del receptor de la MCH pueden ser beneficiosos para el almacenamiento y/o retención de la memoria. Un posible papel para la MCH en la modulación o percepción del dolor, está soportado por la inervación densa del grey

periaqueductal (PAG) por las fibras positivas de la MCH. Finalmente, la MCH puede participar en la regulación de captación de fluidos. La infusión de ICV en la MCH en ovejas concientes produjo cambios diuréticos, natriuréticos y kaliuréticos en respuesta al volumen del plasma incrementado (Parkes, 1996). Junto con datos anatómicos se reportan la presencia de la MCH en áreas regulatorias de fluido del cerebro, los resultados indican que la MCH puede ser un péptido importante involucrado en el control central de la homeostasis de fluido en mamíferos.

La identificación de un receptor acoplado a la proteína G para la MCH ha sido recientemente publicada (Chambers et al., 1999; Saito et al., 1999). Estos grupos identificarón a la MCH como el ligando endógeno para receptor acoplado a la proteína G huérfana de humano SCL1 (Lakaye et al., 1998). El homólogo de rata de este receptor (ahora llamado MCH-1) se reportó estar localizado en regiones del cerebro de rata asociado con el comportamiento alimenticio (e.g., hipotálamo dorsomedial y ventromedial). El enlace entre MCH-1 y los efectos de la MCH sobre la alimentación, ha sido reforzado por reportes recientes en el fenotipo del ratón "bloqueado" (knockout) de MCH-1. Dos grupos han mostrado independientemente (Marsh et al., 2002; Chen et al., 2002) que el rompimiento con el objetivo de gene de receptor MCH-1 ("bloqueado" de MCH-1) en el ratón,

resulta en animales que son hiperfágicos pero son flacos y tienen masa corpórea disminuida respecto a la descendencia inferior el del tipo salvaje. La disminución en la masa corpórea es atribuida a un incremento en el metabolismo. Cada grupo demostró que el ratón "bloqueado" de MCH-1 eran resistentes a la obesidad inducida por dieta, y generalmente exhibían pesos similares a las descendencias inferiores mantenidas con comida regular.

Finalmente, las moléculas de antagonistas sintéticos para el receptor de MCH-1 han sido ahora descritas en la literatura. Bednarek et al. (2002) ha reportado sobre la síntesis de antagonistas de péptido de alta afinidad de MCH-1. Además, un antagonista de molécula pequeña de MCH-1, ha sido descrito por Takekawa et al. (Takekawa et al., 2002). Este compuesto, T-226296, exhibe alta afinidad por el receptor de MCH-1 (~ 5-9 nM para la rata y MCH-1 de humano), y demostró inhibir la captación de alimento inducida por la aplicación intracerebroventricular de MCH. Estos datos validaron la estrategia de utilizar un antagonista del receptor de MCH-1 para tratar la obesidad.

Además, en nuestros propios estudios, se probaron los antagonistas de MCH-1 en varios modelos de animales que son bien conocidos que predicen la eficacia de los compuestos en humanos (Borowsky, et al., en prensa, datos no publicados). Estos experimentos indican que los antagonistas

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de MCH-1 son útiles para tratar la obesidad, depresión ansiedad, así como desórdenes urinarios.

Como se utiliza en esta invención, el término "antagonista" se refiere a un compuesto en cual se une a, y disminuye la actividad de, un receptor en presencia de un agonista. En el caso del receptor acoplado a la proteína G, la activación se puede medir utilizando cualquier sistema de mensajero secundario apropiado, el cual sea acoplado al receptor en una célula o tejido en el cual el receptor sea expresado. Algunos ejemplos específicos, pero que no significa limitativos, de los sistemas de mensajero secundario bien conocidos, son ciclasa de adenilato, movilización de calcio intracelular, activación de canales iónicos, ciclasa de guanilato e hidrólisis de fosfolípido de inositol. Por el contrario, el término "agonista" se refiere a un compuesto que se une a, e incrementa la actividad de, un receptor comparado con la actividad del receptor en ausencia de cualquier agonista.

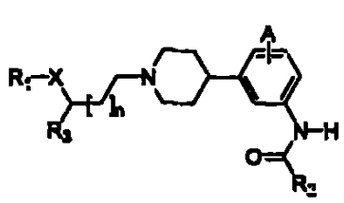
En una modalidad de esta invención, la síntesis de compuestos novedosos que se unen selectivamente al receptor de la hormona de concentración de melanina-1 de humano clonada (MCH1), comparados con otros receptores acoplados a la proteína G clonada, e inhiben la activación de los receptores clonados como se midió en ensayos *in vitro*, está descrita. Los ensayos que unen el receptor *in vitro*

descritos posteriormente, se llevaron a cabo utilizando varias líneas de célula cultivadas, cada una transfectada con y solamente expresando un solo receptor clonado.

Además, los compuestos de la presente invención pueden también ser utilizados para tratar condiciones anormales tal como desórdenes alimenticios (obesidad, bulimia y bulimia nerviosa), desórdenes sexuales/reproductivos, depresión, ansiedad, depresión y ansiedad, ataques epilépticos, hipertensión, hemorragia cerebral, ataque cardiaco congestivo, perturbaciones del sueño, o cualquier condición en la cual el antagonismo de un receptor de MCH1, puede hacer beneficiosos. Además, los compuestos de la presente invención pueden ser utilizados para reducir la masa corpórea de un sujeto. Además, los compuestos de la presente invención pueden ser utilizados para tratar desórdenes urinarios.

LA INVENCIÓN

Esta invención proporciona un compuesto que tiene la estructura:



;

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en donde R_1 es hidrógeno, alquilo de C_1-C_7 de cadena o recta o ramificada, monofluoroalquilo o polifluoroalquilo, arilo o heteroarilo, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más -F, -Cl, -Br, -I,-CN, NO_2, $-CH_3$, $-CF_3$, $-COR_2$, $-CO_2R_2$, fenilo, fenoxi o alquilo de C_1-C_7 de cadena recta o ramificada;

en donde R_2 es alquilo de C_3-C_4 de cadena recta o ramificada o ciclopropilo;

en donde R_3 es arilo o heteroarilo, en donde el arilo o heteroarilo es opcionalmente sustituido con uno o más de -F, -Cl, -Br, -I, -CN, NO_2, alquilo de C_1-C_7 de cadena recta o ramificada;

en donde A es -H, -F, -Cl, -Br, -CN, NO_2, $-COR_3$, $-CO_2R_3$, alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo o polifluoroalquilo;

en donde X es O o NH; y

en donde n es un número entero de 0 a 5, inclusive.

En una modalidad, R_1 es arilo opcionalmente sustituido con uno o más de -F, -Cl, -Br, -I, -CN, NO_2, $-COR_2$, $-CO_2R_2$, alquilo de C_1-C_7 de cadena recta o ramificada;

en donde R_3 es fenilo;

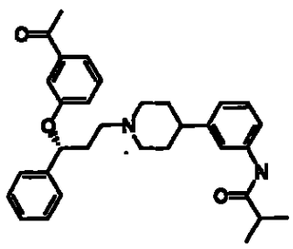
en donde A es H; y

en donde X es 0.

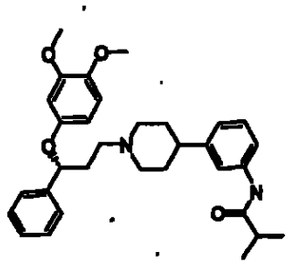
En una modalidad, R_2 es isopropilo.

En una modalidad, R_2 es isopropilo.

En una modalidad, el compuesto tiene la estructura:



En una modalidad, el compuesto tiene la estructura:

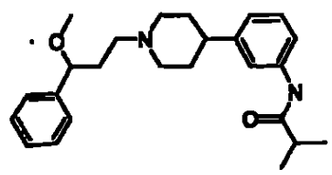


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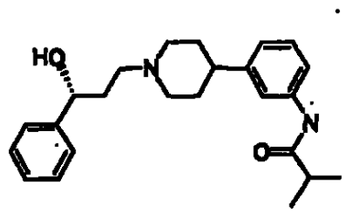
En una modalidad, R_1 es hidrógeno, alquilo de C_1-C_7 de cadena recta o ramificada; en donde R_3 es arilo.

En una modalidad, R_2 es isopropilo; y A es hidrógeno.

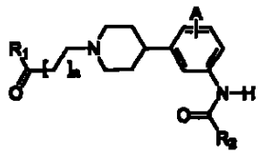
En una modalidad, el compuesto tiene la estructura:



En una modalidad, el compuesto tiene la estructura:



La presente invención también proporciona un compuesto que tiene la estructura:



en donde R_1 es arilo o heteroarilo opcionalmente sustituido con uno o más de -F, -Cl, -Br, -I, -CN, NO_2, -OCH_3, fenoxi, ciclopentanilo fusionado, alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo o polifluoroalquilo;

en donde R_2 es alquilo de C_1-C_4 de cadena recta o ramificada, o ciclopropilo;

en donde A es -H, -F, -Cl, -Br, -CN, -NO_2, alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo o polifluoroalquilo; y

en donde n es un número entero de 1 a 5, inclusive.

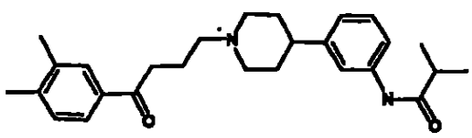
En una modalidad, R_1 es arilo opcionalmente sustituido con uno o más de -F, -Cl, -Br, -I, o alquilo de C_1-C_4 de cadena recta o ramificada; y

en donde A es H.

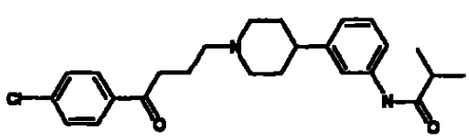
En una modalidad, R_2 es isopropilo; y

en donde n es 2.

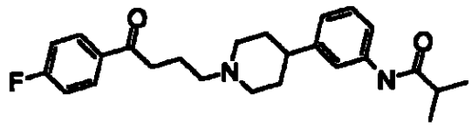
En una modalidad, el compuesto tiene la estructura:



En una modalidad, el compuesto tiene la estructura:



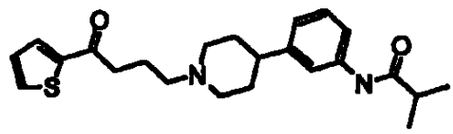
En una modalidad, el compuesto tiene la estructura:



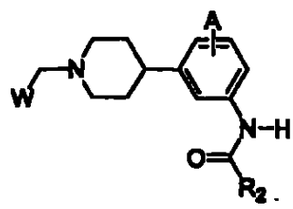
En una modalidad, R_1 es tienilo; y en donde A es H.

En una modalidad, R_2 es isopropilo.

En una modalidad, el compuesto tiene la estructura:

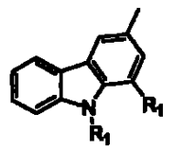


La invención proporciona un compuesto que tiene la estructura:

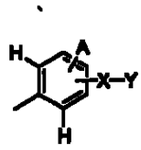


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en donde W es



o



;

en donde cada R_1 es independientemente hidrógeno, metilo o etilo;

en donde R_2 es alquilo de C_3-C_4 de cadena recta o ramificada, o ciclopropilo;

en donde R_3 es hidrógeno, arilo o heteroarilo, en donde el arilo o hetroarilo esta opcionalmente sustituido con uno o más de -H, -F, -Cl, -Br, -I, -CN, NO_2, alquilo de C_1-C_7 de cadena recta o ramificada;

en donde cada una de A es independientemente -H, -F, -Cl, -Br, -CN, $-NO_2$, $-COR_3$, $-CO_2R_3$, alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo o polifluoroalquilo;

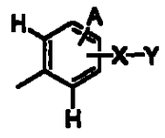
en donde X es O, NR_3, CO o puede estar ausente; y

en donde Y es hidrógeno, arilo o heteroarilo, en donde el arilo o heteroarilo esta opcionalmente sustituido

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con uno o más de -F, -Cl, -Br, -I, -CN, NO_2, alquilo de C_1-C_7 de cadena recta o ramificada.

En una modalidad, W es

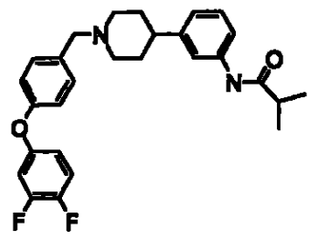


;

y en donde X es O o puede estar ausente.

En una modalidad, R_2 es isopropilo.

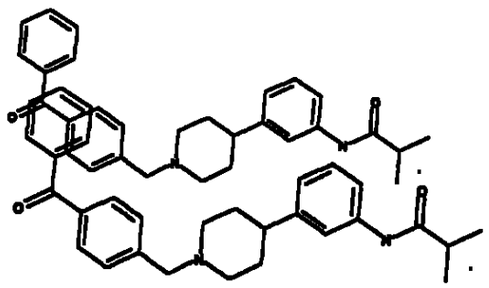
En una modalidad, el compuesto tiene la estructura:



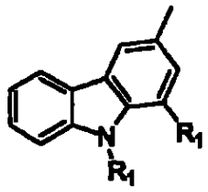
.

En una modalidad, el compuesto tiene la estructura:

820
5/8



En una modalidad, W es



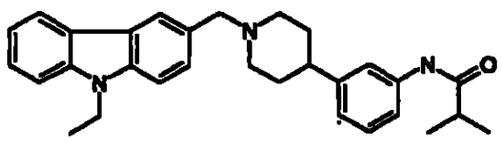
En una modalidad, A es -H, -F, -Cl, -Br.

En una modalidad, R_2 es isopropilo; y A es hidrógeno.

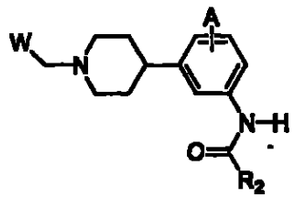
En una modalidad, el compuesto tiene la estructura:

821

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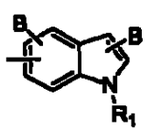


Esta invención proporciona un compuesto que tiene la estructura:

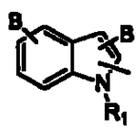


;

en donde W es



o



822
8/20

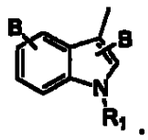
en donde R_1 es hidrógeno, alquilo de C_1 a C_7 de cadena recta o ramificada, arilo o heteroarilo, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más de -F, -Cl, -Br, -CN, $-NO_2$, $-OCH_3$, $-CO_2CH_3$, $-CF_3$, fenilo, alquilo de C_1-C_7 de cadena recta o ramificada;

en donde R_2 es alquilo de C_3-C_4 de cadena recta o ramificada o ciclopropilo;

en donde A es -H, -F, -Cl, -Br, -CN, $-NO_2$, $-COR_1$, $-CO_2R_1$, alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo o polifluoroalquilo o fenilo.

en donde cada una de B es independientemente -H, -F, -Cl, -Br, -I, -CN, $-NO_2$, $-COR_1$, $-OCH_3$, OCF_3, CF_3, alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo o polifluoroalquilo o arilo, fenoxi o benciloxi, esta opcionalmente sustituido con uno o más de -F, -Cl, -Br, -CN, NO_2, $-COR_1$, $-CO_2R_1$, $-OCH_3$, OCF_3, $-CF_3$, alquilo de C_1-C_7 de cadena recta o ramificada.

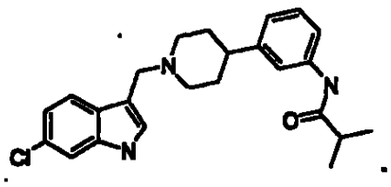
En una modalidad, W es



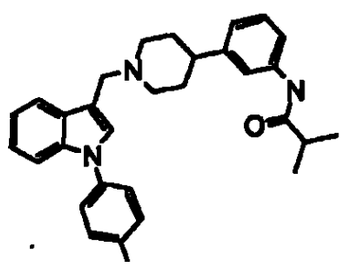
En una modalidad, R_1 es hidrógeno o fenilo opcionalmente sustituido con uno o más de -F, -Cl, -Br, -CN, $-NO_2$, alquilo de C_1-C_7 de cadena recta o ramificada.

En una modalidad, R_2 es isopropilo.

En una modalidad, el compuesto tiene la estructura:

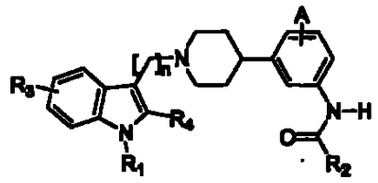


En una modalidad, el compuesto tiene la estructura:



824
8/2

Esta invención proporciona un compuesto que tiene la estructura:



;

en donde R_1 es hidrógeno, alquilo de C_1 a C_7 de cadena recta o ramificada, arilo o heteroarilo, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más de -F, -Cl, -Br, -CN, $-NO_2$, $-CF_3$, $-OCH_3$, alquilo de C_1-C_3 de cadena recta o ramificada;

en donde R_2 es alquilo de C_3-C_4 de cadena recta o ramificada o ciclopropilo;

en donde R_3 es -H, -F, -Cl, -Br, -I, -CN, $-NO_2$, $-CF_3$, $-OCH_3$, alquilo de C_1-C_3 de cadena recta o ramificada, monofluroalquilo o polifluoroalquilo, o un anillo de fenilo fusionado a C_6 y C_7 de la porción de indol;

en donde R_4 es hidrógeno o arilo opcionalmente sustituido con uno o más de -F, -Cl, -Br, -I, -CN, $-NO_2$, $-CF_3$, alquilo de C_1-C_3 de cadena recta o ramificada;

en donde A es -H, -F, -Cl, -Br, -CN, $-NO_2$, alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo o polifluoroalquilo; y

en donde n es un número entero de 2 a 4, inclusive.

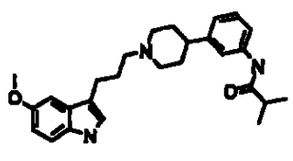
En una modalidad, R_3 es -H, -F, -Cl, -Br, -I, -CN, $-NO_2$, $-OCF_3$ o $-OCH_3$; y

en donde R_4 es hidrógeno o fenilo opcionalmente sustituido con uno o más de -F, Cl, o CF_3.

En una modalidad, R_1 es hidrógeno o fenilo opcionalmente sutiruido con uno o más de -F, -Cl, -Br, -CN, $-NO_2$, $-CF_3$, $-OCH_3$, alquilo de C_1-C_3 de cadena recta o ramificada;

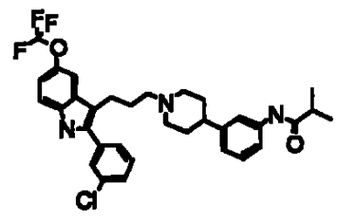
En una modalidad, R_2 es isopropilo.

En una modalidad, el compuesto tiene la estructura:

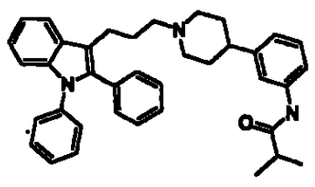


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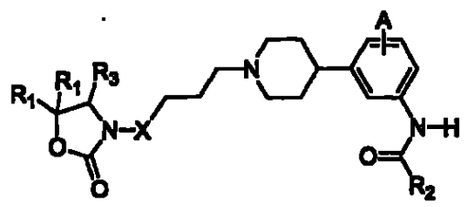
En una modalidad, el compuesto tiene la estructura:



En una modalidad, el compuesto tiene la estructura:



Esta invención proporciona un compuesto que tiene la estructura:



en donde cada R_1 es independientemente hidrógeno o CH_3;

en donde R_2 es un alquilo de C_1-C_4 de cadena recta o ramificada o ciclopropilo;

en donde R_3 es bencilo o fenilo, en donde el bencilo o fenilo esta opcionalemnet sustituido con un grupo metilendioxi o uno o más de -F o -Cl;

en donde A es -H, -F, -Cl, -Br, -CN, $-NO_2$, alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo o polifluoroalquilo;

en donde X es $(CH_2)_2$, $COCH_2$ o CONH.

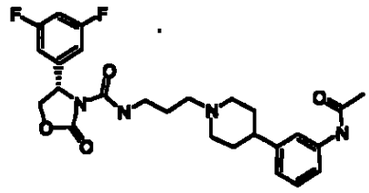
En una modalidad, R_3 es fenilo opcionalmente sustituido con uno o más -F; y

en donde A es hidrógeno.

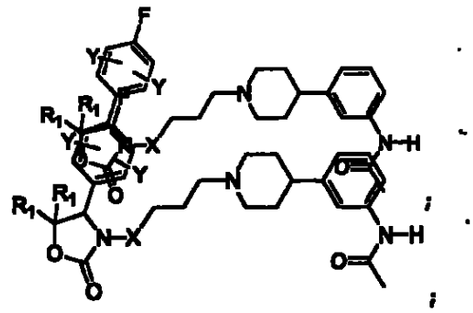
En una modalidad, X es CONH.

En una modalidad, R_2 es metilo.

En una modalidad, el compuesto tiene la estructura:

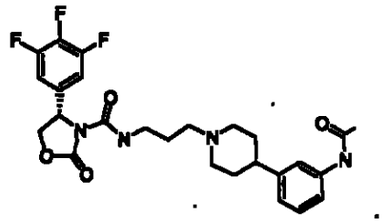


En una modalidad, el compuesto tiene la estructura:

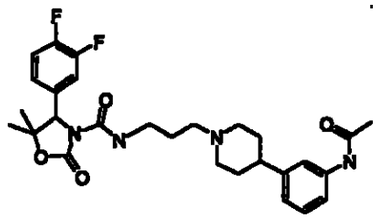


en donde cada Y es independientemente hidrógeno o -F.

En una modalidad, el compuesto tiene la estructura:

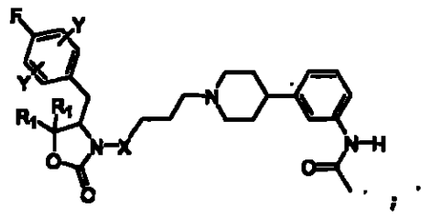


En una modalidad, el compuesto tiene la estructura:



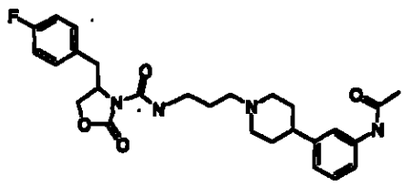
En una modalidad, R_3 es bencilo opcionalmente sustituido con un grupo metilendioxi o uno o más de -F o -Cl.

En una modalidad, el compuesto tiene la estructura:



en donde cada Y es independientemente hidrógeno o -F.

En una modalidad, el compuesto tiene la estructura:



En una modalidad, el compuesto es enantioméricamente puro.

En una modalidad, el compuesto es diastereoméricamente puro.

En una modalidad, el compuesto es enantiomérica y diasteroeméricamente puro.

Esta invención también proporciona una composición farmacéutica que comprende una cantidad en forma terapéutica de un compuesto de la invención y un portador farmacéuticamente aceptable.

En una modalidad, la cantidad del compuesto es desde aproximadamente 0.01mg a aproximadamente 500mg.

En una modalidad, la cantidad del compuesto es desde aproximadamente 0.1mg a aproximadamente 60mg.

En una modalidad, la cantidad del compuesto es desde aproximadamente 1mg a aproximadamente 20mg.

En una modalidad, la composición farmacéutica consiste de un portador que es un líquido y la composición es una solución.

En una modalidad, la composición farmacéutica consiste de un portador que es un sólido y la composición es una tableta.

En una modalidad, la composición farmacéutica consiste de un portador que es un gel y la composición es un supositorio.

La invención también proporciona un proceso para producir una composición farmacéutica que comprende mezclar una cantidad terapéuticamente efectiva del compuesto de cualquiera de la invención y un portador farmacéuticamente aceptable.

Esta invención también proporciona el método para tratar a un sujeto que sufre de un desorden seleccionado del grupo que consiste de depresión, ansiedad, incontinencia insistente, u obesidad que comprende administrar a un sujeto una cantidad terapéuticamente efectiva del compuesto de la invención.

En una modalidad, la cantidad terapéuticamente efectiva esta entre aproximadamente 0.03 y aproximadamente 1000 mg por día.

En una modalidad, la cantidad terapéuticamente efectiva esta entre 0.30 y aproximadamente 300 mg por día.

En una modalidad, la cantidad terapéuticamente efectiva esta entre aproximadamente 1.0 y aproximadamente 100 mg por día.

En una modalidad, el desorden es depresión.

En una modalidad, el desorden es ansiedad.

En una modalidad, el desorden es obesidad.

En una modalidad, el desorden es incontinencia insistente.

La invención proporciona el método de reducir la masa corpórea de un sujeto, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para reducir la masa corpórea del sujeto.

La invención proporciona el método para tratar un sujeto que sufre de depresión, el cual comprende administrar al sujeto una cantidad de un compuesto de cualquiera de las reivindicaciones de la invención, efectiva para tratar la depresión del sujeto.

La invención proporciona el método para tratar un sujeto que sufre de ansiedad, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para tratar la ansiedad del sujeto.

La invención proporciona el método para aliviar la incontinencia urinaria insistente en un sujeto que sufre de una vejiga demasiado activa, el cual comprende administrar a un sujeto una cantidad del compuesto de la invención, efectiva para aliviar la incontinencia urinaria insistente del sujeto.

La invención proporciona el método de manejar la obesidad en un sujeto en necesidad de pérdida de peso, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para inducir la pérdida de peso en el sujeto.

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La invención proporciona el método de manejar la obesidad en un sujeto quien ha experimentado pérdida de peso, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para mantener dicha pérdida de peso en le sujeto.

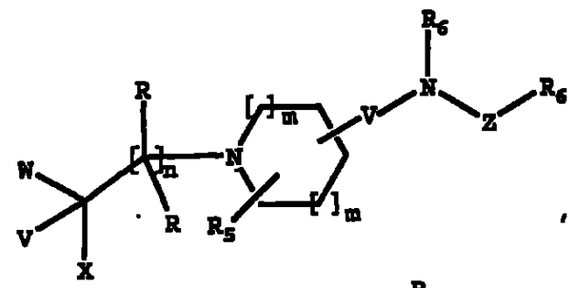
La invención proporciona el método para tratar la vejiga demasiado activa en un sujeto, el cual comprende administrar a un sujeto una cantidad de un compuesto de cualquiera de la invención, efectiva para tratar la vejiga demasiado activa del sujeto.

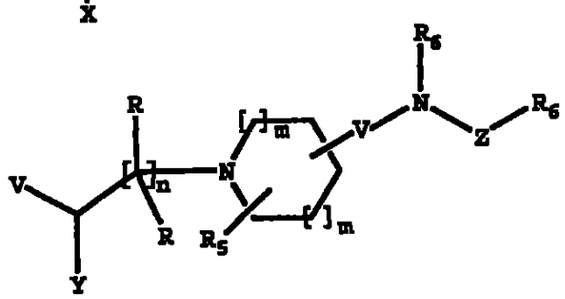
La invención proporciona el método para tratar un desorden en un sujeto, en donde los síntomas del sujeto pueden ser aliviados para el tratamiento con un antagonista de MCH1, en donde el antagonista de MCH1 es el compuesto de la invención.

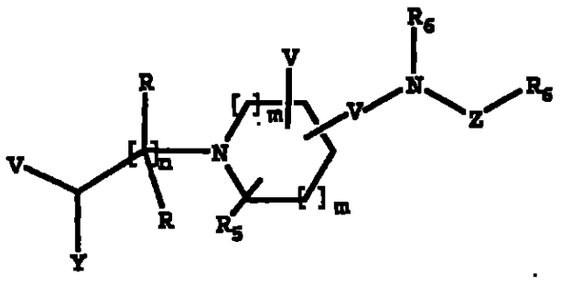
La invención proporciona el método de aliviar los síntomas de un desorden en un sujeto, el cual comprende administrar al sujeto una cantidad de un antagonista de MCH1, efectiva para aliviar los síntomas, en donde el antagonista de MCH1 es el compuesto de la invención.

DESCRIPCION DETALLADA DE LA INVENCION

Esta invención proporciona un compuesto que tiene la estructura:



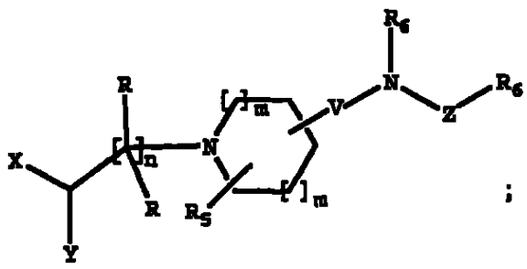




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en donde cada V es independientemente ftalimida, arilo, fenoxi o heteroarilo, en donde le arilo, fenoxi o heteroarilo esta opcionalmente sustituido con uno o más de F; Cl; Br; I; COR_5; CO_2R_5; $-OCOR_5$; $-CON(R_5)_2$; $-N(R_5)COR_5$; CN; $-NO_2$; $-N(R_5)_2$; $-OR_5$; $-SR_5$; $(CH_2)_qOR_5$; $(CH_2)_qR_5$; $(CH_2)_qSR_5$; alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo, polifluoroalquilo, aminoalquilo, o carboxamidoalquilo; alquenilo de C_2-C_7 de cadena recta o ramificada, alquinilo de C_2-C_7; arilo; fenoxi; cicloalquilo de C_3-C_7, monofluorocicloalquilo, polifluorocicloalquilo o cicloalquenilo;

en donde cada W es independientemente arilo o heteroarilo, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más de F; Cl; Br; I; COR_3; CO_2R_3; $-CON(R_3)_2$; $-N(R_3)COR_3$; CN; $-NO_2$; $-N(R_3)_2$; $-OR_3$; $-SR_3$; $(CH_2)_qOR_3$; $(CH_2)_qSR_3$; alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo, polifluoroalquilo, aminoalquilo, o carboxamidoalquilo; alquenilo de C_2-C_7 de

cadena recta o ramificada, alquinilo de C_2-C_7; arilo; fenoxi; cicloalquilo de C_3-C_7, monociclofluoroalquilo, polifluorocicloalquilo o cicloalquenilo;

en donde X es hidrógeno o $-OR_3$, con la condición de que cuando X es $-OR_3$, la V geminal a X no puede ser ftalamida;

en donde Y es hidrógeno, =O (carbonil oxígeno), OR_3, OV, COV, =NNHV, $=NNR_5$, NZV, NCONV (ureas), $NCONR_5$, NR_3, carbazol, indol o ftalamida;

en donde cada R es independientemente -H; -F; alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo o polifluoroalquilo; alquenilo o alquinilo de C_2-C_7 de cadena recta o ramificada; $-N(R_3)_2$; $-NO_2$; -CN; $-CO_2R_3$; $-OCOR_3$; $-OR_3$; o $-N(R_3)COR_3$; $-CON(R_3)_2$;

en donde cada R_3 es independientemente -H; alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo o polifluoroalquilo; alquenilo o alquinilo de C_2-C_7 de cadena recta o ramificada; cicloalquilo de C_3-C_7, monofluorocicloalquilo, polifluorocicloalquilo o cicloalquenilo;

en donde cada R_5 es -H; $-NO_2$; $-N_3$; -CN; alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo o polifluoroalquilo; alquenilo o alquinilo de C_2-C_7 de cadena recta o ramificada; cicloalquilo de C_3-C_7, monofluorocicloalquilo, polifluorocicloalquilo o

cicloalquenilo; $-N(R_3)_2$; $-OR_3$; $(CH_2)_pOR_3$; $-COR_3$; $-CO_2R_3$; $-OCOR_3$; $-CON(R_3)_2$; $-N(R_3)COR_3$; arilo o heteroarilo, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más de F; Cl; Br; I; COR_6; CO_2R_3; $-OCOR_3$; $-CON(R_3)_2$; $-N(R_3)COR_3$; CN; $-NO_2$; $-N(R_3)_2$; $-OR_6$; $-SR_6$; $(CH_2)_qOR_6$; $(CH_2)_qSR_6$; alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo, polifluoroalquilo, aminoalquilo, o carboxamidoalquilo; alquenilo de C_2-C_7 de cadena recta o ramificada, alquenilo de C_2-C_7 de cadena recta o ramificada; alquinilo de C_2-C_7; cicloalquilo de C_3-C_7, monociclofluoroalquilo, polifluorocicloalquilo o cicloalquenilo;

en donde R_6 es -H; alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo o polifluoroalquilo; alquenilo o alquinilo de C_2-C_7 de cadena recta o ramificada, cicloalquilo de C_3-C_7; monofluorocicloalquilo, polifluorocicloalquilo o cicloalquenilo; $-N(R_3)_2$; $-OR_3$; $-(CH_2)_pOR_3$; $-COR_3$; $-CO_2R_3$; $-OCOR_3$; $-CON(R_3)_2$; $-N(R_3)COR_3$; arilo, bencilo o heteroarilo, opcionalmente sustituido con uno o más de F; Cl; Br; I; COR_3; CO_2R_3; $-OCOR_3$; $-CON(R_3)_2$; $-N(R_3)COR_3$, CN; $-NO_2$; $-N(R_3)_2$; $-OR_3$; $-SR_3$; $(CH_2)_qOR_3$; $(CH_2)_qSR_3$; alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo, polifluoroalquilo, aminoalquilo o carboxamidoalquilo; arilo; bencilo; alquenilo de C_2-C_7 de cadena recta o ramificada, alquinilo de C_2-C_7; cicloalquilo

de C_3-C_7, monofluorocicloalquilo, polifluorocicloalquilo o cicloalquenilo;

en donde Z es CO, SO_2 o SO_2NR_6;

en donde cada m es independientemente un número entero de 0 a 3, inclusive;

en donde cada n es independientemente un número entero de 0 a 5, inclusive;

en donde cada p es independientemente un número entero de 1 a 7, inclusive; y

en donde q es un número entero de 1 a 3, inclusive;

o una sal farmacéuticamente aceptable del mismo.

Como se utiliza en la presente invención, el término "cicloalquilo" incluye porciones de C_3-C_7 que pueden ser sustituidas con uno o más de los siguientes: F; CN; -NO_2; alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo de C_1-C_7 de cadena recta o ramificada, polifluoroalquilo de C_1-C_7 de cadena recta o ramificada, alquenilo de C_2-C_7 de cadena recta o ramificada, alquinilo de C_2-C_7 de cadena recta o ramificada; cicloalquilo de C_3-C_7, monofluorocicloalquilo de C_3-C_7, polifluorocicloalquilo de C_3-C_7, cicloalquenilo de C_5-C_7, $-N(R_3)_2$; $-OR_3$; $-NCOR_3$; $-COR_3$; CO_2R_3; $-CON(R_3)_2$ o $-(CH_2)_p-O-(CH_3)_m-CH_3$.

En la presente invención, el término "cicloalquenilo" incluye porciones de cicloalquenilo de C_5-C_7

que pueden ser sustituidas con uno o más de -F; -Cl; -Br; -I; CN; $-NO_2$; alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo de C_1-C_7 de cadena recta o ramificada, polifluoroalquilo de C_1-C_7 de cadena recta o ramificada, alquenilo de C_2-C_7 de cadena recta o ramificada, alquinilo de C_2-C_7 de cadena recta o ramificada; cicloalquilo de C_3-C_7, monofluorocicloalquilo de C_3-C_7, polifluorocicloalquilo de C_3-C_7, cicloalquenilo de C_5-C_7, $-N(R_3)_2$; $-OR_3$; $-NCOR_3$; $-COR_3$; CO_2R_3; $-CON(R_3)_2$ o $-(CH_2)_p-O-(CH_3)_m-CH_3$.

Como se utiliza en la presente invención, el término "heteroarilo" es utilizado para incluir anillos insaturados con cinco y seis miembros que pueden contener uno o más átomos de oxígeno, azufre o nitrógeno. Ejemplos de grupos heteroarilo incluyen pero no están limitados a, furanilo, tienilo, pirrolilo, oxazolilo, tiazolilo, imidazolilo, pirazolilo, isoxazolilo, isotiazolilo, oxadiazolilo, triazolilo, tiadiazolilo, piridilo, piridazinilo, pirimidinilo, pirazinilo, y tiazinilo.

Además, el término "heteroarilo" es utilizado para incluir sistemas de anillo bicíclicos fusionados que pueden contener uno o más heteroátomos, tal como oxígeno, azufre y nitrógeno. Ejemplos de tales grupos heteroarilo incluyen, pero no están limitados a, indolizinilo, indolilo, isoindolilo, benzo[b]furanilo, benzo[b]tiofenilo, indazolilo, bencimidazolilo, purinilo, benzoxazolilo,

bencisoxazolilo, benzo[b]tiazolilo, imidazo[2,1-b]tiazolilo, cinolinilo, quinazolinilo, quinoxalinilo, 1,8-naftiridinilo, pteridinilo, quinolinilo, isoquinolinilo, ftalimidilo y 2,1,3-benzotiazolilo.

El término "heteroarilo" también incluye aquéllas porciones químicas recitadas anteriormente que pueden ser sustituidas con uno o más de los siguientes: -F; -Cl; -Br; -I; CN; $-NO_2$; alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo de C_1-C_7 de cadena recta o ramificada, polifluoroalquilo de C_1-C_7 de cadena recta o ramificada, alquenilo de C_2-C_7 de cadena recta o ramificada, alquinilo de C_2-C_7 de cadena recta o ramificada; cicloalquilo de C_3-C_7, monofluorocicloalquilo de C_3-C_7, polifluorocicloalquilo de C_3-C_7, cicloalquenilo de C_5-C_7, $-N(R_3)_2$; $-OR_3$; $-NCOR_3$; $-COR_3$; CO_2R_3; $-CON(R_3)_2$ o $-(CH_2)_p-O-(CH_3)_m-CH_3$.

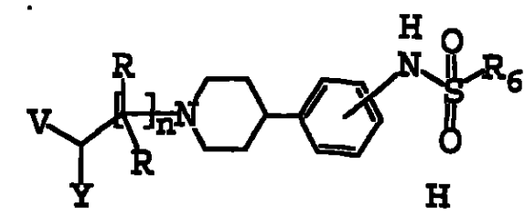
En todavía otra modalidad de la invención antes descrita, el compuesto tiene la estructura:

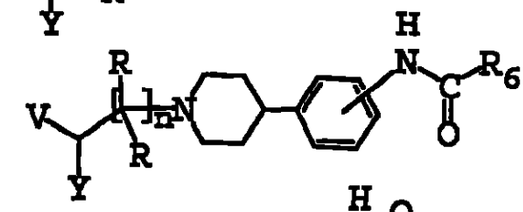
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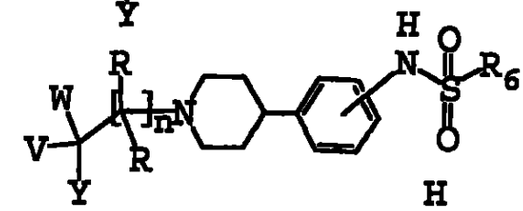
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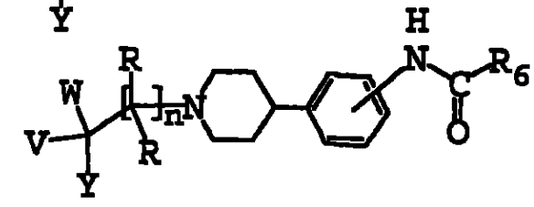
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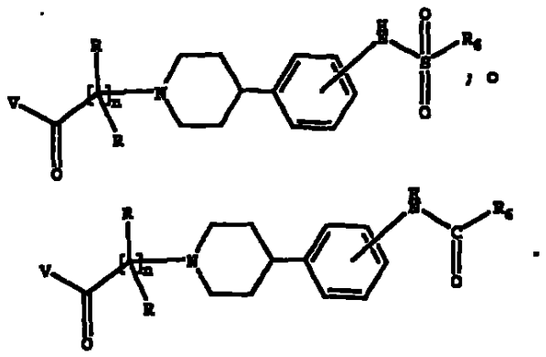

H
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843

3/11

En una modalidad adicional de la presente invención, R_6 es alquilo de C_1-C_7 de cadena recta o ramificada; cicloalquilo de C_3-C_7; $-N(R_3)_2$; $-OR_3$; $-(CH_2)_pOR_3$; $-COR_3$; arilo, bencilo o heteroarilo, opcionalmente sustituido con uno o más de F; Cl; Br; I; OR_3; $(CH_2)_qOR_3$; o alquilo de C_1-C_7 de cadena recta o ramificada.

En una modalidad de la presente invención, el compuesto tiene la estructura:



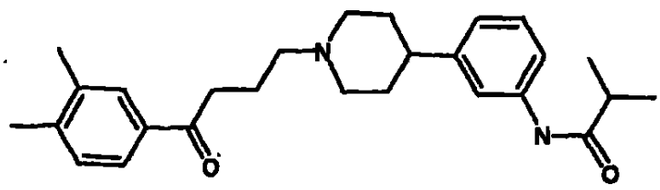
; o

844

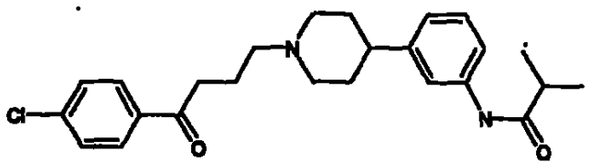
842

En una modalidad adicional de la presente invención, al menos una V es fenilo opcionalmente sustituido con uno o más de F; Cl; Br; OR_3; $(CH_2)_qOR_3$; alquilo de C_1-C_7 de cadena recta o ramificada, polifluoroalquilo de C_1-C_7, o fenoxi.

En una modalidad de la presente invención, el compuesto es:

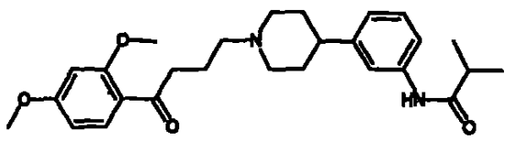


En una modalidad, el compuesto es:

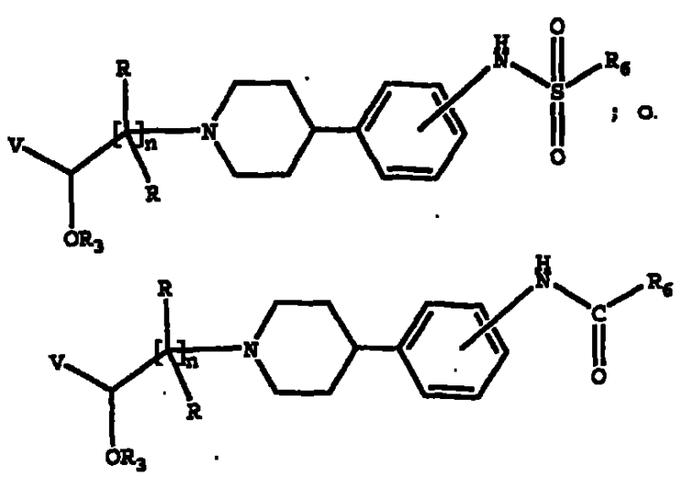


845
8/13

En una modalidad el compuesto es:



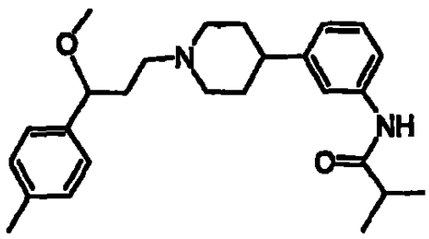
En otra modalidad de la presente invención, el compuesto tiene la estructura:



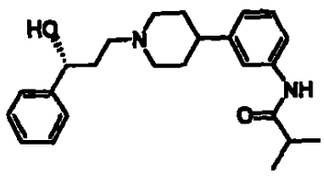
8346
3/14

En una modalidad adicional de la presente invención, al menos una de V es fenilo opcionalmente sustituido con uno o más de F; Cl; Br; OR_3; $(CH_2)_qOR_3$; alquilo de C_1-C_7 de cadena recta o ramificada, polifluoroalquilo de C_1-C_7, o fenoxi.

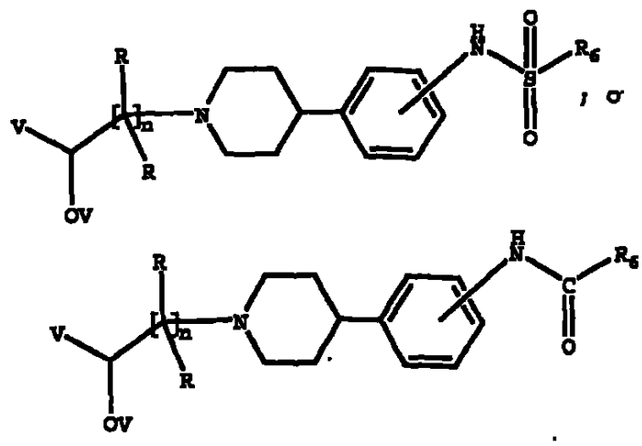
En otra modalidad de la presente invención, el compuesto es:



En una modalidad, el compuesto es:



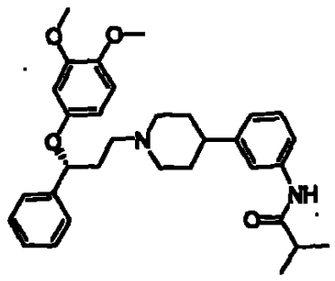
En una modalidad de la presente invención, el compuesto tiene la estructura:



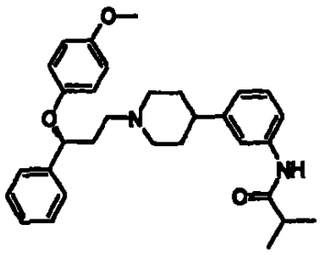
En otra modalidad de la presente invención, al menos una de V es fenilo opcionalmente sustituido con uno o más de F; Cl; Br; $-OR_3$; $-COR_3$; $(CH_2)_qOR_3$; alquilo de C_1-C_7 de cadena recta o ramificada, polifluoroalquilo de C_1-C_7, arilo o fenoxi.

848 3/6

En todavía otra modalidad de la presente invención, el compuesto es:

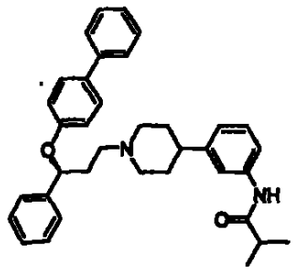


En una modalidad, el compuesto es:

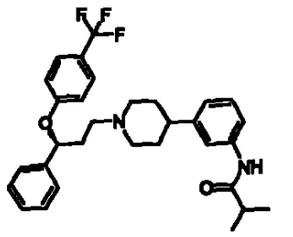


8179

En una modalidad el compuesto es:

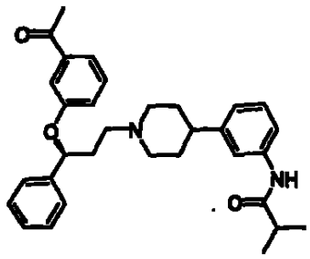


En una modalidad el compuesto es:

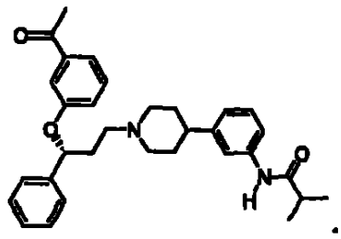


En una modalidad el compuesto es:

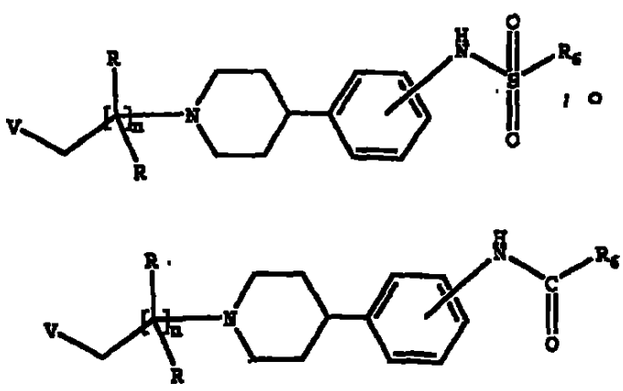
B50
8/18



En una modalidad el compuesto es:

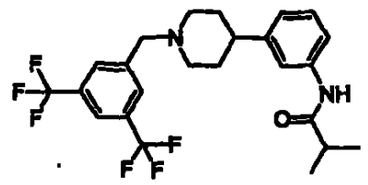


En una modalidad de la presente invención, el compuesto tiene la estructura:

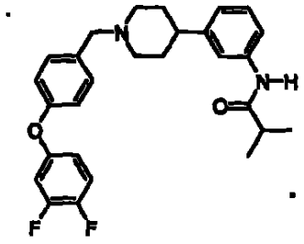


En una modalidad adicional de la presente invención, al menos una de V es fenilo opcionalmente sustituido con uno o más de F; Cl; Br; $-OR_3$; $(CH_2)_qOR_3$; alquilo de C_1-C_7 de cadena recta o ramificada, polifluoroalquilo de C_1-C_7; o fenoxi.

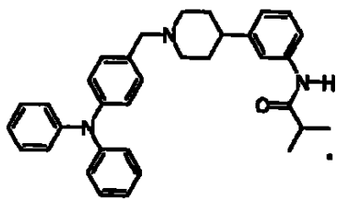
En todavía otra modalidad de la presente invención, el compuesto es:



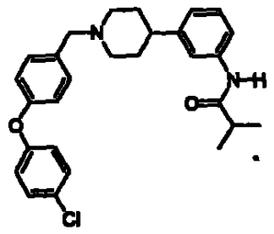
En una modalidad, el compuesto tiene la estructura:



En una modalidad, el compuesto tiene la estructura:

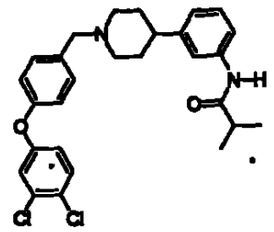


En una modalidad, el compuesto tiene la estructura:

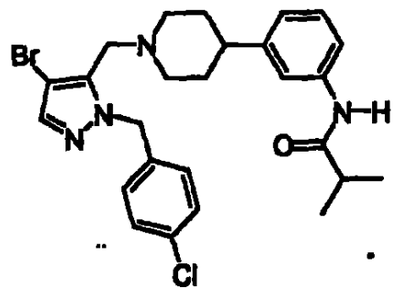


En una modalidad, el compuesto tiene la estructura:

85/2 85

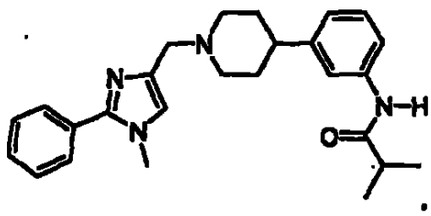


En una modalidad, el compuesto tiene la estructura:

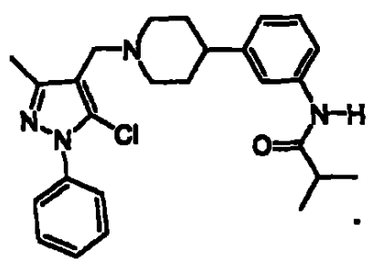


En una modalidad, el compuesto tiene la estructura:

855
373

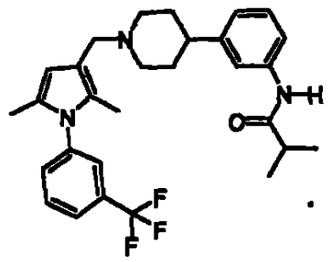


En una modalidad, el compuesto tiene la estructura:



850 8/54

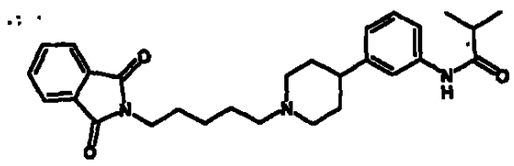
En una modalidad, el compuesto tiene la estructura:



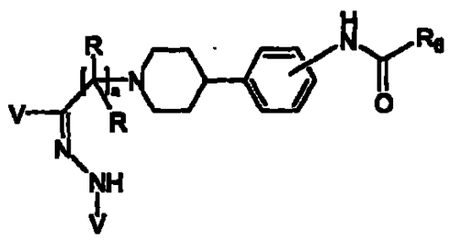
En una modalidad adicional de la presente invención, Y es hidrógeno y V es ftalimida.

En una modalidad adicional de la presente invención, R_6 es alquilo de C_1-C_7 de cadena recta o ramificada, cicloalquilo de C_3-C_7; $-N(R_3)_2$; $-OR_3$; $-(CH_2)_pOR_3$; arilo, bencilo o heteroarilo, opcionalmente sustituido con uno o más de F; Cl; Br; I; OR_3; $(CH_2)_qOR_3$; alquilo de C_1-C_7 de cadena recta o ramificada.

En una modalidad adicional de la presente invención, el compuesto es:



En una modalidad, el compuesto tiene la estructura:

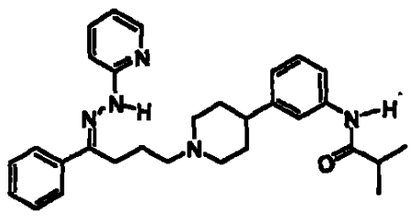


En una modalidad del compuesto, al menos una de V es fenilo o heteroarilo opcionalmente sustituido con uno o más de F; Cl; Br; I; R_5; $-OR_5$; $(CH_2)_qOR_5$; $(CH_2)_qR_5$; alquilo de

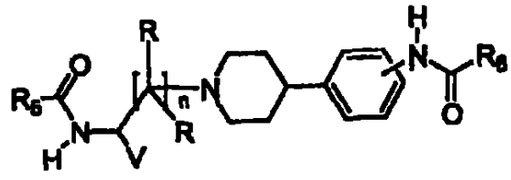
858
356

C_1-C_7 de cadena recta o ramificada, monofluoroalquilo o polifluoroalquilo; o fenoxi.

En una modalidad, el compuesto tiene la estructura:



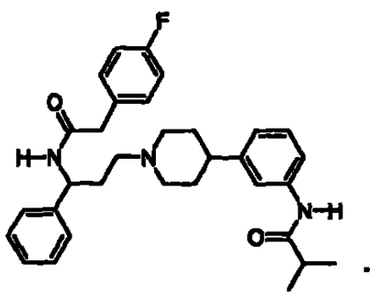
En una modalidad, el compuesto tiene la estructura:



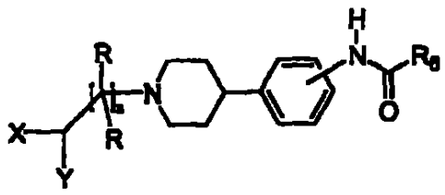
859
857

En una modalidad del compuesto, V es fenilo el cual esta opcionalmente sustituido con uno o más de F; Cl; Br; $-OR_5$; $(CH_2)_qOR_5$; $(CH_2)_qR_5$; alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo o polifluoroalquilo; o fenoxi.

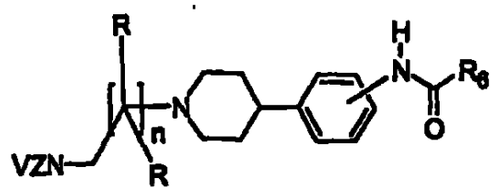
En una modalidad, el compuesto tiene la estructura:



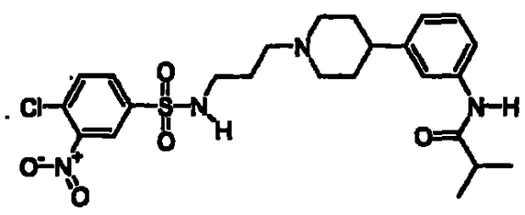
En una modalidad, el compuesto tiene la estructura:



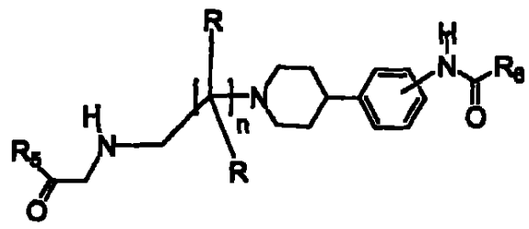
En una modalidad, el compuesto tiene la estructura:



En una modalidad, el compuesto tiene la estructura:

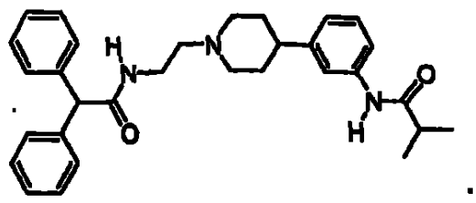


En una modalidad, el compuesto tiene la estructura:

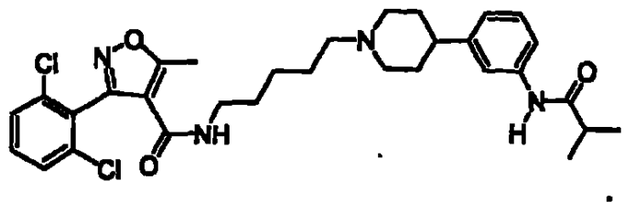


En una modalidad del compuesto, R_5 es alquilo de C_1-C_7 de cadena recta o ramificada; cicloalquilo de C_3-C_7; $-N(R_6)_2$; $-OR_6$; $-(CH_2)_qOR_6$; $-CH(R_6)_2$; $-(CH_2)_qR_6$; o arilo, bencilo o heteroarilo, en donde el arilo, bencilo o heteroarilo esta opcionalmente sustituido con uno o más de F; Cl; Br; I; R_6; $-N(R_6)_2$; $-OR_6$; $-(CH_2)_qOR_6$; $-(CH_2)_qR_6$; o alquilo de C_1-C_7 de cadena recta o ramificada.

En una modalidad, el compuesto tiene la estructura:

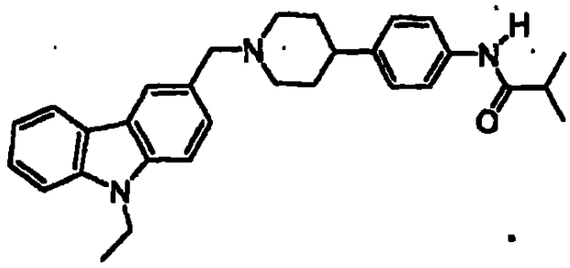


En una modalidad, el compuesto tiene la estructura:

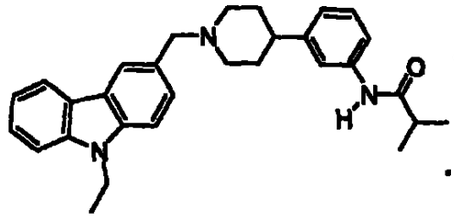


En una modalidad del compuesto, X es hidrógeno y Y es carbazol opcionalmente sustituido con uno o más de F; Cl; Br; R_5; $-OR_5$; $-(CH_2)_qOR_5$; $-(CH_2)_qR_5$; o alquilo de C_1-C_7 de cadena recta o ramificada; monofluoroalquilo o polifluoroalquilo de C_1-C_7; o fenoxi.

En una modalidad, el compuesto tiene la estructura:

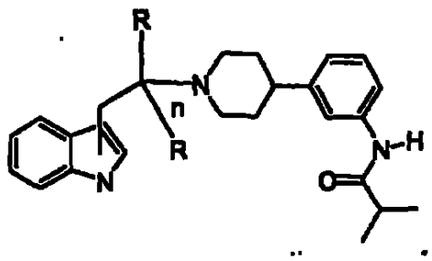


En una modalidad, el compuesto tiene la estructura:

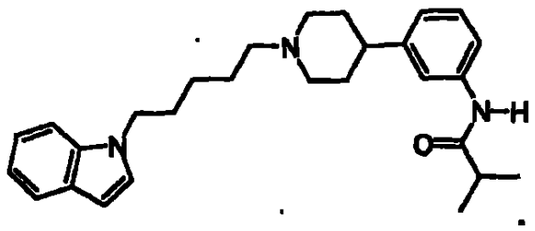


En una modalidad del compuesto, Y es hidrógeno y V es un indol, el cual puede ser opcionalmente sustituido con uno o más de F; Cl; Br; R_5; $-CO_2R_5$; $-OR_5$; $-(CH_2)_qOR_5$; $-(CH_2)_qR_5$; o alquilo de C_1-C_7 de cadena recta o ramificada; monofluoroalquilo o polifluoroalquilo de C_1-C_7; o fenoxi en las posiciones 1, 2, 3, 4, 5, 6 o 7.

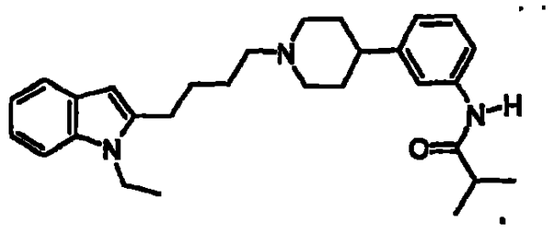
En una modalidad, el compuesto tiene la estructura:



En una modalidad, el compuesto tiene la estructura:



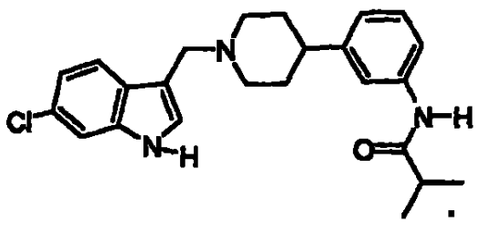
En una modalidad, el compuesto tiene la estructura:



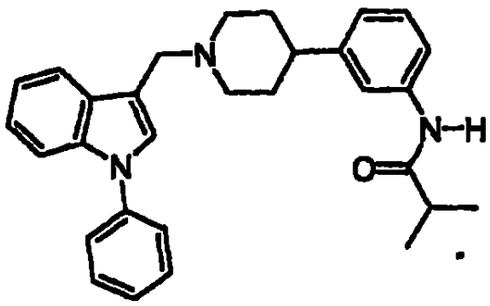
En una modalidad, el compuesto tiene la estructura:

866

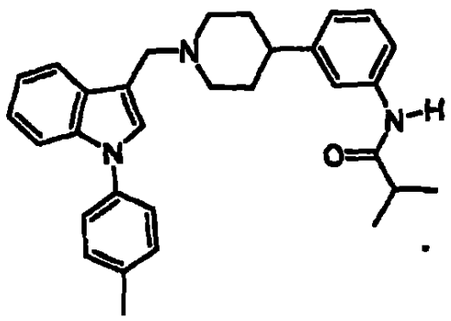
3/4



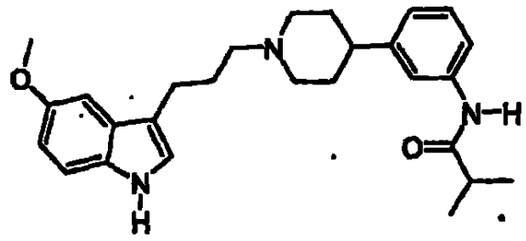
En una modalidad, el compuesto tiene la estructura:



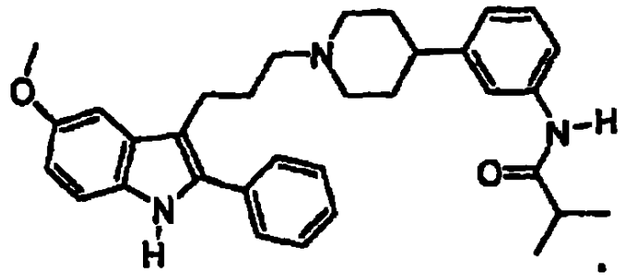
En una modalidad, el compuesto tiene la estructura:



En una modalidad, el compuesto tiene la estructura:

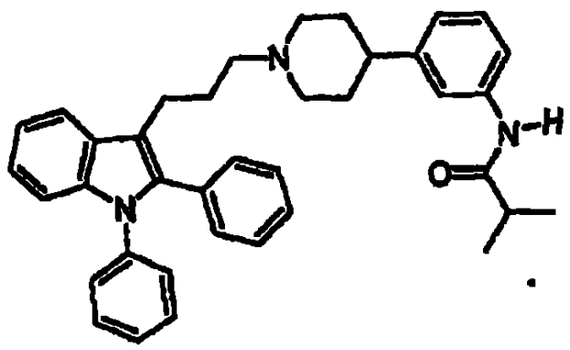


En una modalidad, el compuesto tiene la estructura:

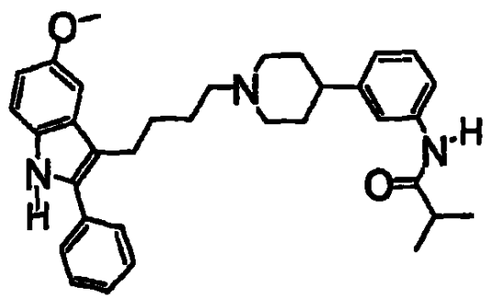


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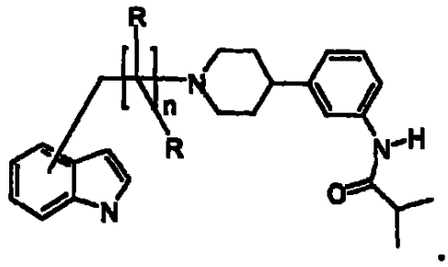
En una modalidad, el compuesto tiene la estructura:



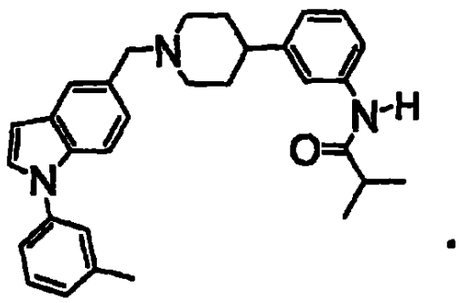
En una modalidad, el compuesto tiene la estructura:



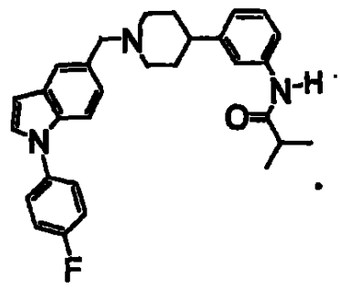
En una modalidad, el compuesto tiene la estructura:



En una modalidad, el compuesto tiene la estructura:

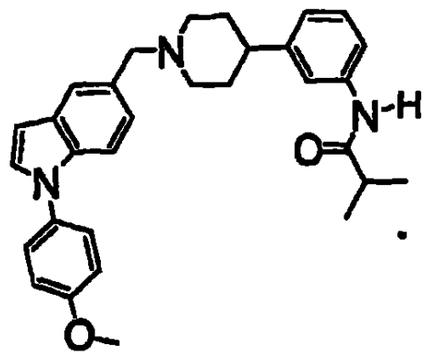


En una modalidad, el compuesto tiene la estructura:



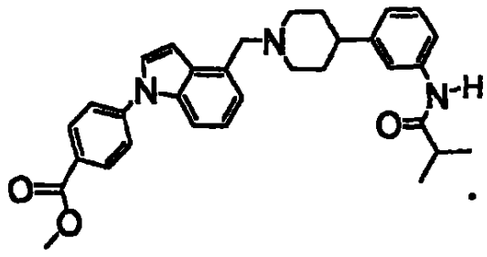
872
S/O

En una modalidad, el compuesto tiene la estructura:



En una modalidad, el compuesto tiene la estructura:

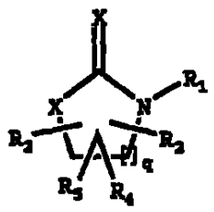
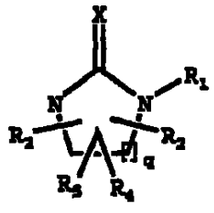
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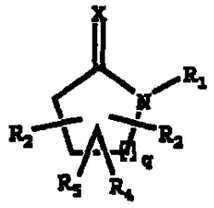
La presente invención proporciona un compuesto que tiene la estructura:

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;

o



en donde cada X es independientemente O o S;

en donde q es 1 ó 2;

en donde cada R_2 es independientemente H; $-(CH_2)_tXR_3$; $-(CH_2)_tC(X)N(R_3)_2$; $-(CH_2)_tCO_2R_3$; $-CO_2R_3$; alquilo de C_1-C_7 de cadena recta o ramificada opcionalmente sustituido con $-N(R_3)_2$; $-CON(R_3)_2$ o $-N(R_3)C(O)R_3$; alquenilo de C_2-C_7 de cadena recta o ramificada, o alquinilo; o cicloalquilo de C_3-C_7 o cicloalquenilo de C_5-C_7;

en donde cada t es independientemente H; alquilo de C_1-C_7 de cadena recta o ramificada, alquenilo de C_2-C_7 de cadena recta o ramificada, o alquinilo; o cicloalquilo de C_3-C_7 o cicloalquenilo de C_5-C_7;

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en donde R_4 es arilo, heteroarilo, alquilo de C_1-C_7 sustituido con uno o dos arilos, o alquilo de C_1-C_7 sustituido con uno o dos heteroarilos; en donde el arilo o heteroarilo puede ser sustituido con uno o más de F, Cl, Br, I, -CN, $-NO_2$, $-N(R_3)_2$, $-COR_3$, $-(CH_2)_nXR_3$, $-(CH_2)_nC(X)NR_3$, $-(CH_2)_nN(R_3)C(X)R_3$, $-(CH_2)_nCO_2R_3$, $-(CH_2)_nOCOR_3$, alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo o polifluoroalquilo o alquinilo, alquenilo o aminoalquilo de C_2-C_7 de cadena recta o ramificada, o cicloalquilo de C_3-C_7 o cicloalquenilo de C_5-C_7;

en donde cada n independientemente es un número entero de 0 a 7, inclusive;

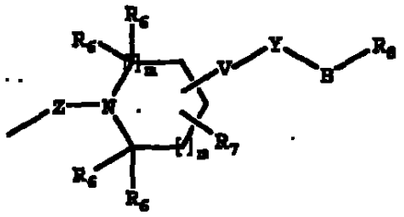
en donde R_5 es H, arilo, alquilo de C_1-C_7 sustituido con arilo, heteroarilo, alquilo de C_1-C_7 sustituido con heteroarilo; en donde el arilo o heteroarilo pueden ser sustituidos con uno o más de F, Cl, Br, I, -CN, $-NO_2$, $-N(R_3)_2$, $-COR_3$, $-(CH_2)_nXR_3$, $-(CH_2)_nC(X)NR_3$, $-(CH_2)_nCO_2R_3$, alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo, polifluoroalquilo o carboxamidoalquilo, o alquinilo, alquenilo o aminoalquilo de C_2-C_7 de cadena recta o ramificada, o cicloalquilo de C_3-C_7 o cicloalquenilo de C_5-C_7;

en donde R_5 y una de R_2 en átomos de carbono adyacentes juntos pueden formar arilo, heteroarilo, indano o tetrahidronaftilo, cicloalquilo de C_3-C_7, o

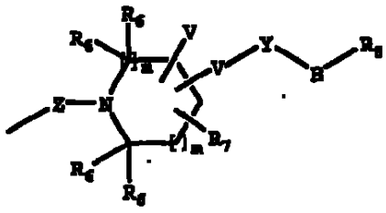
874 876

heterocicloalquilo, en donde uno o dos heteroátomos pueden ser 0, N o S;

en donde R_1 es



, o



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en donde cada V es independientemente arilo, fenoxi o heteroarilo, en donde el arilo, fenoxi o heteroarilo esta opcionalmente sustituido con uno o más de F; Cl; Br; I; COR_5; CO_2R_5; $-OCOR_5$; $-CON(R_5)_2$; $-N(R_5)COR_5$, CN; $-NO_2$; $-N(R_5)_2$; $-OR_5$; $-SR_5$; $(CH_2)_qOR_5$; $(CH_2)_qSR_5$, alquilo de C_1-C_7 de cadena recta o ramificada opcionalmente sustituido con $-CON(R_5)_2$, $-N(R_5)C(O)R_3$ o $N(R_3)_2$, monofluoroalquilo o polifluoroalquilo de cadena recta o ramificada, alquenilo de C_2-C_7 de cadena recta o ramificada, alquinilo de C_2-C_7; fenoxi; o cicloalquilo de C_3-C_7, monofluorocicloalquilo, polifluorocicloalquilo o cicloalquenilo;

en donde R_6 es independientemente H; $(CH_2)_tXR_3$; $-(CH_2)_tC(X)NR_3$; $(CH_2)_tN(R_3)C(X)R_3$; $(CH_2)_tOCOR_3$; alquilo de C_1-C_7 de cadena recta o ramificada opcionalmente sustituido con $-CON(R_3)_2$ o $-NC(O)R_3$; alquilo de C_2-C_7 de cadena recta o ramificada sustituido con $-N(R_3)_2$; alquenilo o alquinilo de C_2-C_7 de cadena recta o ramificada; o cicloalquilo de C_3-C_7 o cicloalquenilo de C_5-C_7;

en donde cada R_7 es independientemente H; F; Cl; Br; I; $-COR_3$; $-CO_2R_3$; $-(CH_2)_nXR_3$, $-(CH_2)_nN(R_3)C(O)R_3$; $-(CH_2)_nC(X)N(R_3)_2$; $-(CH_2)_nCO_2R_3$, $-CN$; $-NO_2$; $-N(R_3)_2$; monofluoroalquilo, polifluoroalquilo, alcoxialquilo, carboxamidolaquilo, aminoalquilo, hidroxialquilo o alquilo de C_1-C_7 de cadena recta o ramificada; alquinilo o alquenilo de C_2-C_7 de cadena recta o ramificada, monofluorociclo-

alquilo, policiclofluoroalquilo, cicloalquilo de C_3-C_7 o cicloalquenilo de C_5-C_7; en donde el alquilo, aminoalquilo, carboxamidoalquilo, hidroxialquilo, alcoxialquilo, alquenilo, alquinilo, cicloalquilo o cicloalquenilo pueden ser sustituidos con uno o más de arilo o heteroarilo, en donde el arilo o heteroarilo puede ser sustituido con uno o más de F, Cl, Br, I, $-(CH_2)_nXR_3$, $-COR_3$, $-(CH_2)_nC(X)N(R_3)_2$; $-(CH_2)_nCO_2R_3$, $-CN$; $-NO_2$; $-(CH_2)_nN(R_3)C(O)R_3$, $-N(R_3)_2$, $-SO_2R_3$, monofluoroalquilo, polifluoroalquilo o alquilo de C_1-C_7 de cadena recta o ramificada, alquinilo o alquenilo de C_2-C_7 de cadena recta o ramificada, o monofluorocicloalquilo, polifluorocicloalquilo, cicloalquilo de C_3-C_7 o cicloalquenilo de C_5-C_7; arilo o heteroarilo, en donde el arilo o heteroarilo puede ser sustituido con uno o más de F, Cl, Br, I, $-(CH_2)_nXR_3$, $-COR_3$, $-(CH_2)_nC(X)N(R_3)_2$; $-(CH_2)_nCO_2R_3$, $-(CH_2)_nN(R_3)C(O)R_3$; $-CN$, $-NO_2$, $-N(R_3)_2$, $-SO_2R_3$, alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo o polifluoroalquilo de C_1-C_7 de cadena recta o ramificada, alquinilo o alquenilo de C_2-C_7 de cadena recta o ramificada o monofluorocicloalquilo, polifluorocicloalquilo, cicloalquilo de C_3-C_7 o cicloalquenilo;

en donde B es CO, SO_2 o SO_2NR_6;

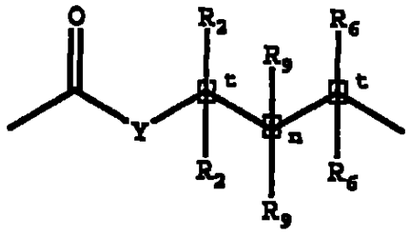
en donde R_6 es -H; monofluoroalquilo, polifluoroalquilo o alquilo de C_1-C_7 de cadena recta o ramificada; alquenilo o alquinilo de C_2-C_7 de cadena recta o ramificada;

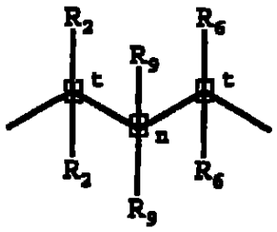
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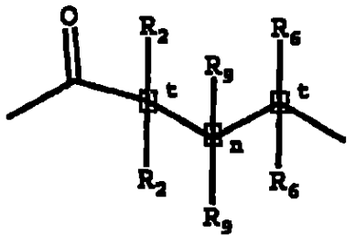
cicloalquenilo, monofluorocicloalquilo, polifluorociclo-alquilo o cicloalquilo de C_3-C_7; $-N(R_3)_2$; $-NR_3C(O)R_3$; $-OR_3$; $-(CH_2)_pOR_3$; $-COR_3$; $-CO_2R_3$; $-OCOR_3$; $-CON(R_3)_2$; arilo o heteroarilo opcionalmente sustituido con uno o más de de F; Cl; Br; I; COR_3; CO_2R_3; $-OCOR_3$; $-NR_3C(O)R_3$; $-CON(R_3)_2$; CN; $-NO_2$; $-N(R_3)_2$; $-OR_3$; $-SR_3$; $(CH_2)_qOR_3$; $(CH_2)_qSR_3$; alquilo de C_1-C_7 de cadena recta o ramificada opcionalmente sustituido con $-CON(R_3)_2$, $-NR_3C(O)R_3$ o $-N(R_3)_2$; monofluoroalquilo o polifluoroalquilo de cadena recta o ramificada, alquenilo de C_2-C_7 de cadena recta o ramificada, alquinilo de C_2-C_7; cicloalquenilo, monofluorocicloalquenilo, polifluorociclo-alquenilo o cicloalquilo de C_3-C_7;

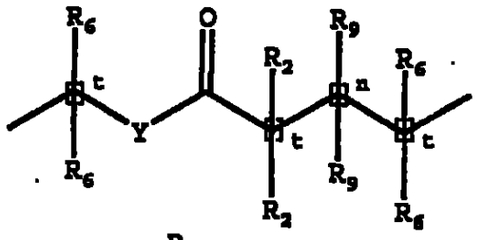
en donde cada m independientemente es un número entero de 0 a 3, inclusive;

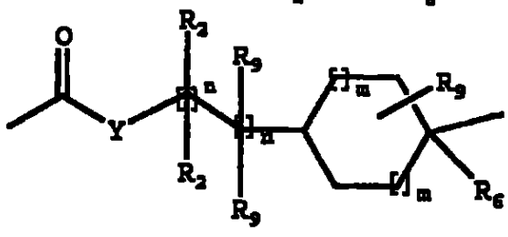
en donde z es

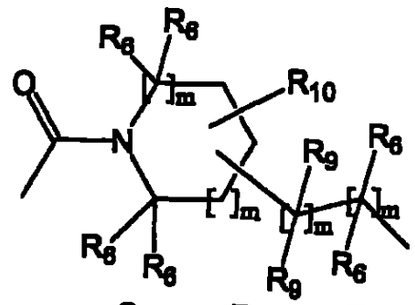




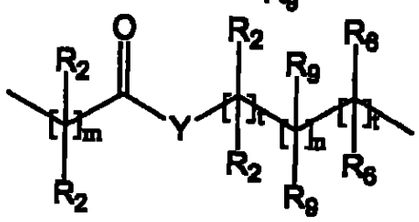




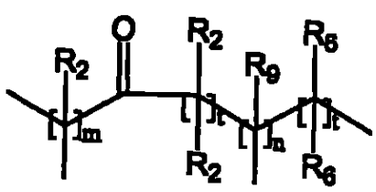




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o alquenilo de C_2-C_7, en donde el alquenilo de C_2-C_7 puede ser insustituido o sustituido con uno o más grupos R_9;

en donde cada R_9 es independientemente H; F; Cl; Br; I; $-(CH_2)_mXR_3$; $(CH_2)_mC(X)NR_3$; $(CH_2)_mCO_2R_3$; carboxamidoalquilo, aminoalquilo, monofluoroalquilo, polifluoroalquilo o alquilo de C_1-C_7 de cadena recta o ramificada; alquinilo o alquenilo de C_2-C_7 de cadena recta o ramificada; cicloalquilo de C_3-C_7 o cicloalquenilo de C_5-C_7;

en donde R_{10} es H; $-(CH_2)_tXR_3$; $-(CH_2)_tC(X)NR_3$; $-(CH_2)_tCO_2R_3$; carboxamidoalquilo, alquilo de C_1-C_7 de cadena recta o ramificada, alquinilo, alquenilo o aminoalquilo de C_2-C_7 de cadena recta o ramificada; o cicloalquilo de C_3-C_7 o cicloalquenilo de C_3-C_7;

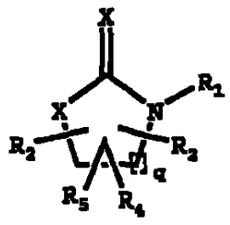
en donde y es S, O o NR_{10};

en donde cada p es independientemente un número entero de 1 a 7, inclusive;

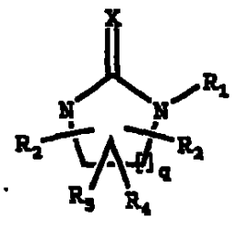
o una sal farmacéuticamente del mismo.

En una modalidad adicional de la presente invención, el compuesto tiene la siguiente estructura:

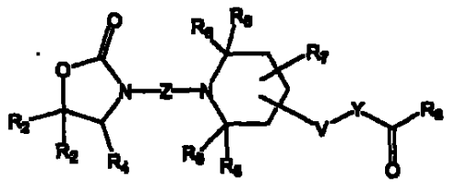
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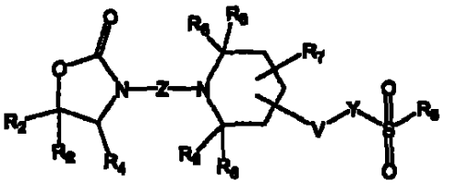
o



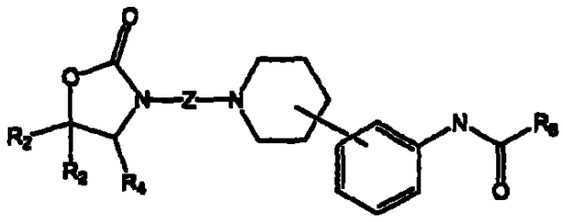
En una modalidad adicional de la presente invención, el compuesto tiene la estructura:



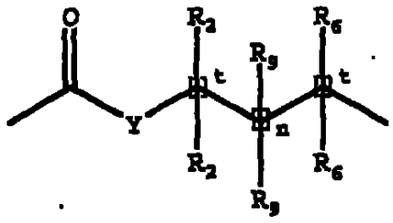
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En una modalidad adicional de la presente invención, el compuesto tiene la estructura:

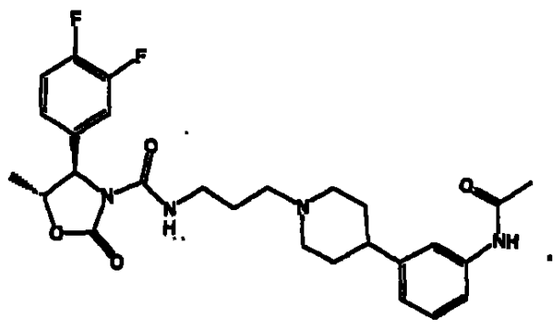


En una modalidad de la presente invención, Z es:

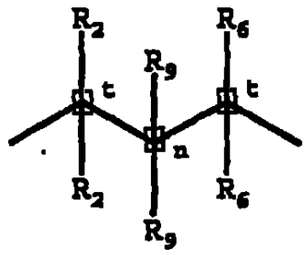


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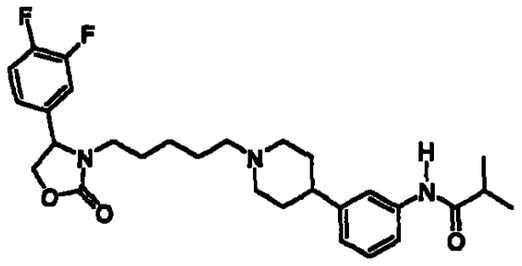
En una modalidad de la presente invención Z es:



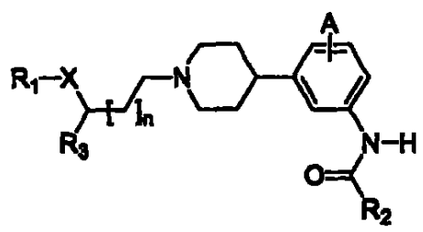
En una modalidad adicional de la presente invención, el compuesto tiene la estructura:



En una modalidad de la presente invención, el compuesto tiene la estructura:



Esta invención proporciona un compuesto que tiene la estructura:



;

en donde R_1 es hidrógeno, monofluoroalquilo, polifluoroalquilo, alquilo de C_1-C_7 de cadena recta o ramificada, arilo o heteroarilo, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más de -F, -Cl, -Br, -I, -CN, $-NO_2$, $-CH_3$, $-CF_3$, $-COCH_3$, $-CO_2R_2$, fenilo, fenoxi o alquilo de C_1-C_7 de cadena recta o ramificada;

en donde R_2 es ciclopropilo o alquilo de C_3-C_4 de cadena recta o ramificada;

en donde R_3 es arilo o heteroarilo, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más de -F, -Cl, -Br, -I, -CN, $-NO_2$, alquilo de C_1-C_7 de cadena recta o ramificada;

en donde A es -H, -F, -Cl, -Br, -CN, $-NO_2$, $-COR_3$, $-CO_2R_3$, monofluoroalquilo, polifluoroalquilo o alquilo de C_1-C_7 de cadena recta o ramificada;

B88 956

en donde X es O o NH;

en donde n es un número entero de 0 a 5, inclusive;

En una modalidad, R_1 es arilo opcionalmente sustituido con uno o más de -F, -Cl, -Br, -I, -CN, $-NO_2$, $-COCH_3$, $-CO_2R_2$, alquilo de C_1-C_7 de cadena recta o ramificada;

en donde R_3 es fenilo;

en donde A es H; y

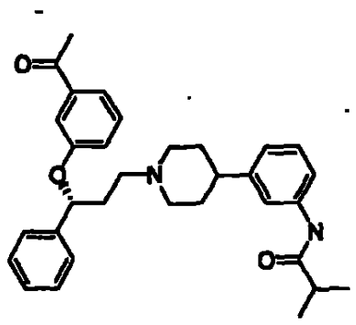
en donde X es O.

En una modalidad, R_2 es isopropilo.

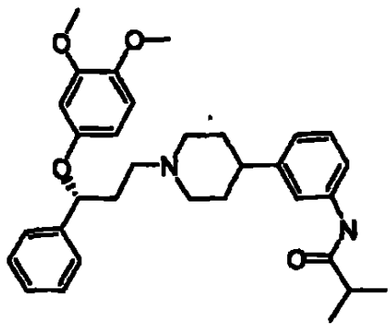
En una modalidad preferida, X es NH, R_1 es alquilo y n es 1 o 2.

En la modalidad más preferida, X es O, R_1 es 3-acetilfenilo, R_2 es isopropilo, R_3 es fenilo y n es 1.

En una modalidad, el compuesto tiene la estructura:



En una modalidad, el compuesto tiene la estructura:

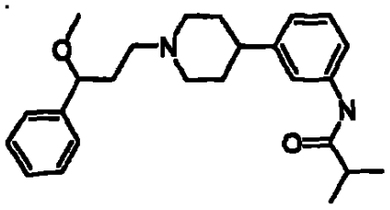


En una modalidad, R_1 es hidrógeno, alquilo de C_1-C_7; y en donde R_3 es arilo.

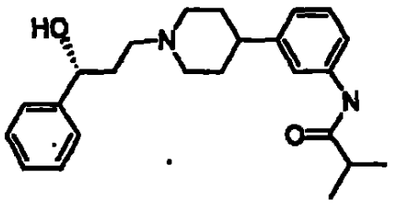
En una modalidad, R_2 es isopropilo; y A es hidrógeno.

En una modalidad, el compuesto tiene la estructura:

BP
3/8

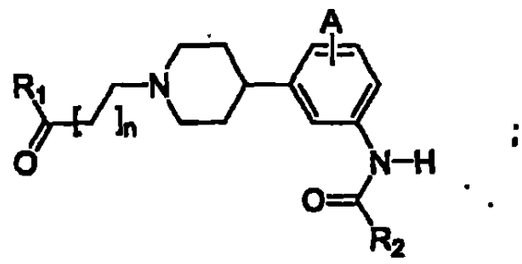


En una modalidad, el compuesto tiene la estructura:



La presente invención también proporciona un compuesto que tiene la estructura:

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en donde R_1 es arilo o heteroarilo opcionalmente sustituido con uno o más de -F, -Cl, -Br, -I, -CN, $-NO_2$, $-OCH_3$, fenoxi, ciclopentanilo, monofluoroalquilo, polifluoroalquilo, alquilo de C_1-C_7 de cadena recta o ramificada; en donde R_2 es ciclopropilo o alquilo de C_1-C_4 de cadena recta o ramificada;

en donde A es -H, -F, -Cl, -Br, -CN, $-NO_2$, monofluoroalquilo, polifluoroalquilo o alquilo de C_1-C_7 de cadena recta o ramificada; y

en donde n es un número entero de 1 a 5, inclusive.

En una modalidad, R_1 es arilo opcionalmente sustituido con uno o más de -F, -Cl, -Br, -I o alquilo de C_1-C_4 de cadena recta o ramificada; y

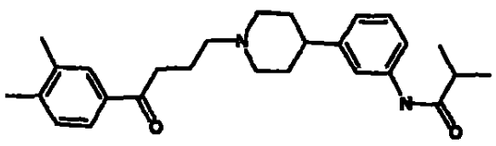
En donde A es H.

En una modalidad, R_2 es isopropilo; y

en donde n es 2.

En una modalidad preferida, n es 2 y R_2 es isopropilo.

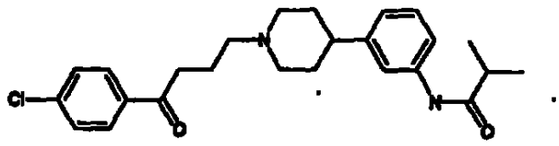
En una modalidad, el compuesto tiene la estructura:



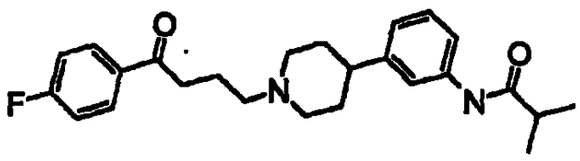
En una modalidad, el compuesto tiene la estructura:

893

951



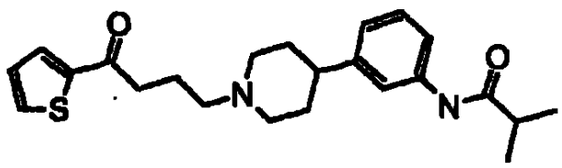
En una modalidad, el compuesto tiene la estructura:



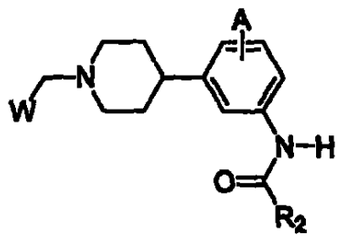
En una modalidad, R_1 es tienilo; y en donde A es H.

En una modalidad, R_2 es isopropilo.

En una modalidad, el compuesto tiene la estructura:

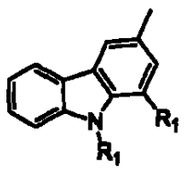


La invención proporciona un compuesto que tiene la estructura:

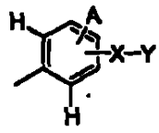


;

en donde W es



o



;

en donde cada R_1 es independientemente hidrógeno, metilo o etilo;

en donde R_2 es alquilo de C_3-C_4 de cadena recta o ramificada o en donde R_2 es ciclopropilo o alquilo de C_3-C_4 de cadena recta o ramificada;

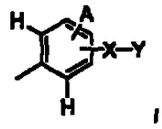
en donde R_3 es hidrógeno, arilo o heteroarilo, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más de -H, -F, -Cl, -Br, -I, -CN, $-NO_2$, alquilo de C_1-C_7 de cadena recta o ramificada.

en donde cada A es independientemente -H, -F, -Cl, -Br, -CN, $-NO_2$, $-COR_3$, $-CO_2R_3$, monofluoroalquilo, polifluoroalquilo o alquilo de C_1-C_7 de cadena recta o ramificada;

en donde X es O, NR_3, CO o puede estar ausente; y

en donde Y es hidrógeno, arilo o heteroarilo, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más de -F, -Cl, -Br, -I, -CN, $-NO_2$, alquilo de C_1-C_7 de cadena recta o ramificada.

En una modalidad, W es

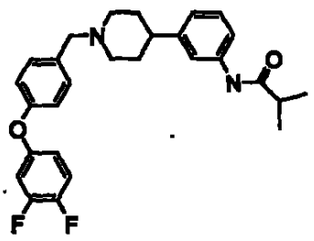


I

y en donde X es O o puede estar ausente.

En una modalidad, R_2 es isopropilo.

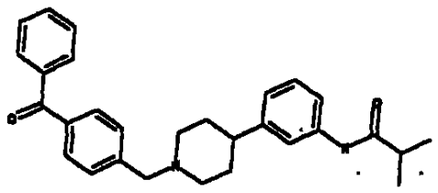
En una modalidad, el compuesto tiene la estructura:



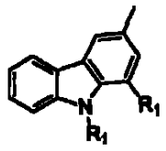
En una modalidad, el compuesto tiene la estructura:

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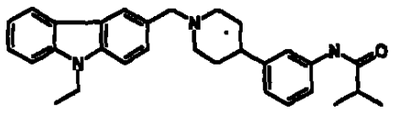
En una modalidad, W es:



En una modalidad, A es -H, -F, -Cl, -Br.

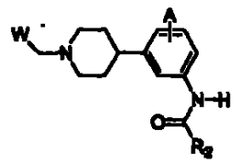
En una modalidad, R_2 es isopropilo; A es hidrógeno.

En una modalidad, el compuesto tiene la estructura:

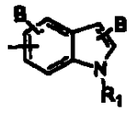


898
8:16

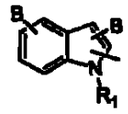
Esta invención proporciona un compuesto que tiene la estructura:



en donde W es



o



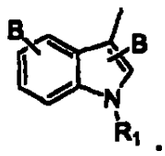
en donde R_1 es hidrógeno, heteroarilo, arilo o alquilo de C_1-C_7 de cadena recta o ramificada, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más de -F, -Cl, -Br, -CN, -NO_2, -OCH_3, -CO_2CH_3, -CF_3, fenilo, alquilo de C_1-C_7 de cadena recta o ramificada;

en donde R_2 es ciclopropilo o alquilo de C_3-C_4 de cadena recta o ramificada;

en donde A es -H, -F, -Cl, -Br, -CN, $-NO_2$, $-COR_1$, $-CO_2R_1$, polifluoroalquilo, monofluoroalquilo o alquilo de C_1-C_7 de cadena recta o ramificada o fenilo;

en donde cada B es independientemente -H, -F, -Cl, -Br, -I, -CN, $-NO_2$, $-COR_1$, $-CO_2R_1$, $-OCH_3$, $-OCF_3$, $-CF_3$, monofluoroalquilo, polifluoroalquilo o arilo o alquilo de C_1-C_7 de cadena recta o ramificada, fenoxi o benciloxi esta opcionalmente sustituido con uno o más de -F, -Cl, -Br, -CN, $-NO_2$, $-COR_1$, $-CO_2R_1$, $-OCH_3$, $-OCF_3$, $-CF_3$, alquilo de C_1-C_3 de cadena recta o ramificada.

En una modalidad, W es

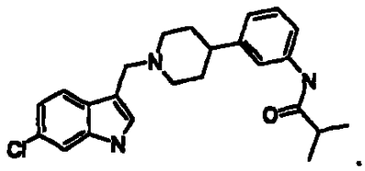


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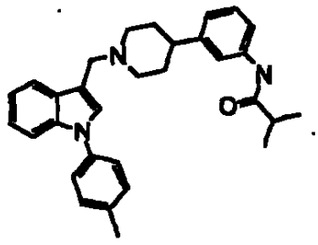
En una modalidad, R_1 es hidrógeno o fenilo opcionalmente sustituido con uno o más de -F, -Cl, -Br, -CN, $-NO_2$, alquilo de C_1-C_7 de cadena recta o ramificada.

En una modalidad, R_2 es isopropilo.

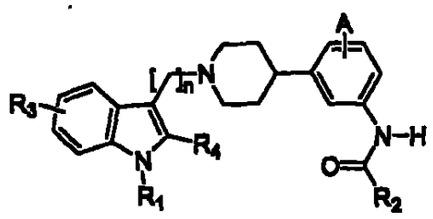
En una modalidad, el compuesto tiene la estructura:



En una modalidad, el compuesto tiene la estructura:



Esta invención proporciona un compuesto que tiene la estructura:



en donde R_1 es hidrógeno, arilo, heteroaerilo o alquilo con C_1-C_7 de cadena recta o ramificada, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más de -F, -Cl, -Br, -CN, $-NO_2$, $-CF_3$, $-OCH_3$, alquilo de C_1-C_3 de cadena recta o ramificada;

en donde R_2 es ciclopropilo o alquilo de C_3-C_4 de cadena recta o ramificada;

en donde R_3 es -H, -F, -Cl, -Br, -I, -CN, $-NO_2$, $-CF_3$, $-OCH_3$, monofluoroalquilo, polifluoroalquilo o alquilo de C_1-C_3 de cadena recta o ramificada, o un anilo de fenilo fusionada a C_6 y C_7 de la porción de indol;

en donde R_4 es hidrógeno o arilo opcionalmente sustituido con uno o más de -F, -Cl, -Br, -I, -CN, $-NO_2$, $-CF_3$, alquilo de C_1-C_3 de cadena recta o ramificada;

en donde A es -H, -F, -Cl, -Br, -CN, $-NO_2$, monofluoroalquilo, polifluoroalquilo o alquilo de C_1-C_7 de cadena recta o ramificada; y

en donde n es un número entero de 2 a 4, inclusive.

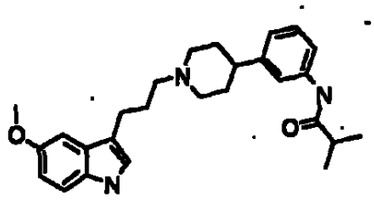
En una modalidad R_3 es -H, -F, -Cl, -Br, -I, -CN, $-NO_2$, $-OCF_3$ o $-OCH_3$; y

En donde R_4 es hidrógeno o fenilo opcionalmente sustituido con uno o más de -F, -Cl, o $-CF_3$.

En una modalidad, R_1 es hidrógeno o fenilo opcionalmente sustituido con uno o más de -F, -Cl, -Br, -CN, $-NO_2$, $-CF_3$, $-OCH_3$, o alquilo de C_1-C_3 de cadena recta o ramificada.

En una modalidad, R_2 es isopropilo.

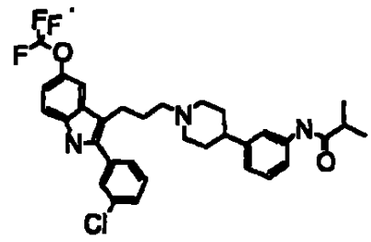
En una modalidad, el compuesto tiene la estructura:



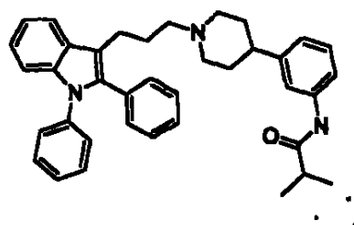
En una modalidad, el compuesto tiene la estructura:

903

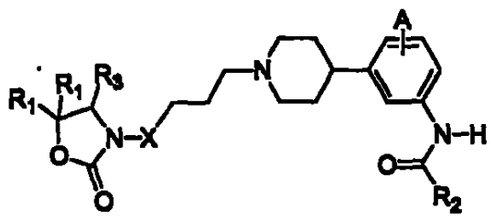
3/1



En una modalidad, el compuesto tiene la estructura:



Esta invención proporciona un compuesto que tiene la estructura:



en donde cada R_1 es independientemente hidrógeno o CH_3;

en donde R_2 es ciclopropilo o alquilo de C_1-C_4;

en donde R_3 es bencilo o fenilo, en donde el bencilo o fenilo esta opcionalmente sustituido con un grupo de metilendioxi o uno o más de -F o -Cl;

en donde A es -H, -F, -Cl, -Br, -CN, $-NO_2$, monofluoroalquilo, polifluoroalquilo o alquilo de C_1-C_7 de cadena recta o ramificada;

en donde X es $(CH_2)_2$, $COCH_2$ o CONH;

En una modalidad, R_3 es fenilo opcionalmente sustituido con uno o más de -F; y

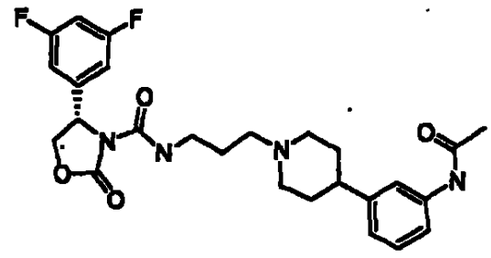
en donde A es hidrógeno.

En una , X es CONH.

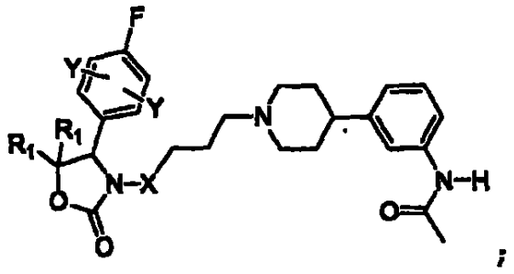
En una modalidad, R_2 es metilo.

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En una modalidad, el compuesto tiene la estructura:

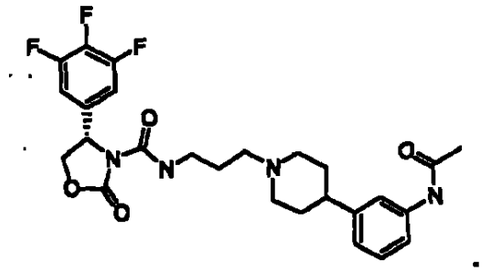


En una modalidad, el compuesto tiene la estructura:

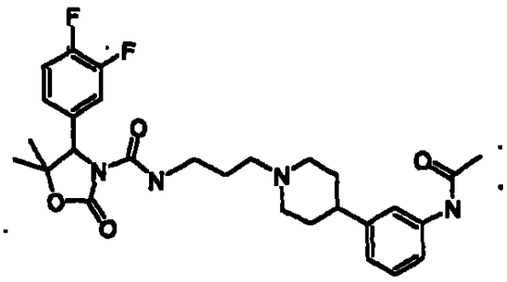


en donde cada Y es independientemente hidrógeno o -F.

En una modalidad, el compuesto tiene la estructura:

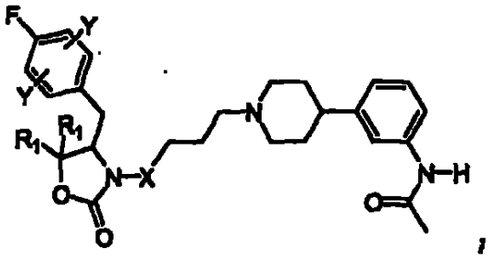


En una modalidad, el compuesto tiene la estructura:



En una modalidad, R_3 es bencilo opcionalmente sustituido con un grupo metilendioxi o uno o más de -F o -Cl.

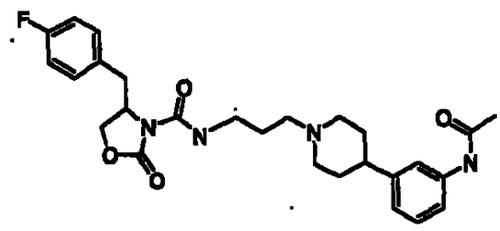
En una modalidad, el compuesto tiene la estructura:



en donde cada Y es independientemente hidrógeno o -F.

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En una modalidad, el compuesto tiene la estructura:



En una modalidad, el compuesto es enantioméricamente puro.

En una modalidad, el compuesto es diastereoméricamente puro.

En una modalidad, el compuesto es enantiomérica y diastereoméricamente puro.

Esta invención también proporciona una composición farmacéutica que comprende una cantidad en forma terapéutica de un compuesto de la invención y un portador farmacéuticamente aceptable.

En una modalidad, la cantidad del compuesto es desde aproximadamente 0.01mg a aproximadamente 500mg.

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En una modalidad, la cantidad del compuesto es desde aproximadamente 0.1mg a aproximadamente 60mg.

En una modalidad, la cantidad del compuesto es desde aproximadamente 1mg a aproximadamente 20mg.

En una modalidad, la composición farmacéutica consiste de un portador que es un líquido y la composición es una solución.

En una modalidad, la composición farmacéutica consiste de un portador que es un sólido y la composición es una tableta.

En una modalidad, la composición farmacéutica consiste de un portador que es un gel y la composición es un supositorio.

La invención también proporciona un proceso para la elaboración de una composición farmacéutica que comprende mezclar una cantidad terapéuticamente efectiva de un compuesto cualesquiera de la invención y un portador farmacéuticamente aceptable.

Esta invención también proporciona el método para tratar un sujeto que sufre de un desorden seleccionado de un grupo que consiste de depresión, ansiedad, incontinencia persistente, u obesidad que comprende administrar a un sujeto una cantidad terapéuticamente efectiva del compuesto de la invención.

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En una modalidad, la cantidad terapéuticamente efectiva esta entre aproximadamente 0.03 y aproximadamente 1000mg por día.

En una modalidad, la cantidad terapéuticamente efectiva esta entre aproximadamente 0.30 y aproximadamente 300mg por día.

En una modalidad, la cantidad terapéuticamente efectiva esta entre aproximadamente 1.0 y aproximadamente 100mg por día.

En una modalidad, el desorden es depresión.

En una modalidad, el desorden es ansiedad.

En una modalidad, el desorden es obesidad.

En una modalidad, el desorden es incontinencia persistente.

La invención proporciona el método de reducir la masa corpórea de un sujeto, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para reducir la masa corpórea del sujeto.

La invención proporciona el método para tratar un sujeto que sufre de depresión, el cual comprende administrar al sujeto una cantidad de un compuesto de cualesquiera de las reivindicaciones de la invención, efectiva para tratar la depresión del sujeto.

La invención proporciona el método para tratar un sujeto que sufre de ansiedad, el cual comprende administrar

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al sujeto una cantidad de un compuesto de la invención, efectiva para tratar la ansiedad del sujeto.

La invención proporciona el método para aliviar la incontinencia urinaria persistente en un sujeto que sufre de una vejiga demasiado activa, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para aliviar la incontinencia urinaria persistente del sujeto.

La invención proporciona el método para manejar la obesidad en un sujeto que necesita perder peso, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para inducir la perdida de peso en el sujeto.

La invención proporciona el método para manejar la obesidad en un sujeto quien ha experimentado perdida de peso, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para mantener dicha perdida de peso en el sujeto.

La invención proporciona el método para tratar la vejiga demasiado activa en un sujeto, el cual comprende administrar al sujeto una cantidad de un compuesto cualesquiera de la invención, efectiva para tratar la vejiga demasiado activa del sujeto.

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La invención proporciona el método para tratar un desorden en un sujeto, en donde los síntomas del sujeto pueden ser aliviados por tratamiento con un antagonista de MCH1, en donde el antagonista MCH1 es el compuesto de la invención.

La invención proporciona el método para aliviar los síntomas de un desorden en un sujeto, el cual comprende administrar al sujeto una cantidad de un antagonista MCH1, efectiva para aliviar los síntomas, en donde el antagonista de MCH1 es el compuesto de la invención.

Como se utiliza en la presente invención, el término "heteroarilo" es utilizado para incluir anillos insaturados con cinco o seis miembros, que pueden contener uno o más átomos de oxígeno, azufre o nitrógeno. Ejemplos de grupos heteroarilo incluyen, pero no están limitados a, carbazol, furanilo, tienilo, pirrolilo, oxazolilo, tiązolilo, imidazolilo, pirazolilo, isoxazolilo, isotiazolilo, oxadiazolilo, triazolilo, tiadiazolilo, piridilo, piridazinilo, pirimidinilo, pirazinilo, y triazinilo.

Además, el término "heteroarilo es utilizado para incluir sistemas de anillo bicíclicos fusionados que pueden contener uno o más heteroátomos, tal como oxígeno, azufre y nitrógeno. Ejemplos de tales grupos heteroarilo incluyen, pero no están limitados a, indolizinilo, indolilo,

isoindolilo, benzo[b]furanilo, benzo[b]tiofenilo, indazolilo, bencimidazolilo, purinilo, benzoxazolilo, bencisoxazolilo, benzo[b]tiazolilo, imidazo[2,1-b]tiazolilo, cinolinilo, quinazolinilo, quinoxalinilo, 1,8-naftiridinilo, pteridinilo, quinolinilo, isoquinolinilo, ftalimidilo y 2,1,3-benzotiazolilo.

El término "heteroarilo" también incluye aquéllas porciones químicas recitadas anteriormente que pueden ser sustituidas con uno o más de los siguientes: -F; -Cl; -Br; -I; CN; $-NO_2$; alquilo de C_1-C_7 de cadena recta o ramificada, monofluoroalquilo de C_1-C_7 de cadena recta o ramificada, polifluoroalquilo de C_1-C_7 de cadena recta o ramificada, alquenilo de C_2-C_7 de cadena recta o ramificada, alquinilo de C_2-C_7 de cadena recta o ramificada; cicloalquilo de C_3-C_7, monofluorocicloalquilo de C_3-C_7, polifluorocicloalquilo de C_3-C_7, cicloalquenilo de C_5-C_7.

El término "heteroarilo" además incluye los N-óxidos de aquellas porciones químicas recitadas anteriormente que incluyen al menos un átomo de nitrógeno.

En la presente invención, el término "arilo" es fenilo o naftilo.

La invención se proporciona para cada estereoisómero puro de cualesquiera de los compuestos descritos en la presente. Dichos estereoisómeros pueden incluir enantiómeros, diastereómeros, o isómeros E o Z

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alqueno o de imina. La invención también se proporciona para mezclas diatereoméricas, mezclas isoméricas de E/Z. Estereoisómeros pueden ser sintetizados en forma pura (Nógrádi, M.; Stereoselective Synthesis, (1987) VCH Editor Ebel, H. and Asymetric Synthesis, Volumes 3 B 5, (1983) Academic Press, Editor Morrison, J.) o pueden ser resueltos por una variedad de métodos tales como cristalización y técnicas de cromatografía (Jaques, J.; Collet, A.; Wilen, S.; Enantiomer, Racemates, and Resolutions, 1981, John Wiley and Sons and Asymetric Synthesis, Vol. 2, 1983, Academic Press, Editor Morrison, J.).

Además los compuestos de la presente invención pueden estar presentes como enantiómeros, diasteriómeros, isómeros o dos o más de los compuestos pueden estar presentes para formar una mezcla racémica o diastereomérica.

Los compuestos de la presente invención son preferiblemente 80% puros, más preferiblemente 90% puros, y aún más preferiblemente 95% puros. Incluidas en esta invención están sales farmacéuticamente aceptables y complejos de todos los compuestos descritos en la presente. Los ácidos y bases a partir de los cuales éstas sales son preparadas incluyen pero no están limitadas a los ácidos y bases listados en la presente. Los ácidos incluyen, pero no están limitados a, los siguientes ácidos inorgánicos: ácido clorhídrico, ácido bromhídrico, ácido iodhídrico, ácido

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sulfúrico y ácido bórico. Los ácidos incluyen, pero no están limitados a, los siguientes ácidos orgánicos: ácido acético, ácido malónico, ácido succínico, ácido fumárico, ácido tartárico,. ácido maléico, ácido cítrico, ácido metanosulfónico, ácido benzóico, ácido glicólico, ácido láctico y ácido mandélico. Las bases incluyen, pero no están limitadas a amonio, metilamina, etilamina, propilamina, dimetilamina, dietilamina, trimetilamina, trietilamina, etilendiamina, hidroxietilamina, morfolina, piperazina y guanidina. Esta invención además se proporciona para los hidratos y polimorfos de todos los compuestos descritos en la presente.

La presente invención incluye dentro de su alcance profármacos de los compuestos de la invención. En general, tales profármacos serán derivados funcionales de los compuestos de la invención que son fácilmente convertibles *in vivo* en el compuesto requerido. Por consiguiente, en la presente invención, el término "administrado" deberá de abarcar el tratamiento de las diferentes condiciones descritas con el compuesto específicamente descrito o con un compuesto que no este específicamente descrito, pero que se convierte al compuesto especificado *in vivo* después de la administración al paciente. Procedimientos convencionales para la selección y preparación de derivados de profármacos

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adecuados están descritos, por ejemplo, en Design of Prodrugs, ed. H. Bundgaard, Elsevier, 1985.

La presente invención además incluye metabolitos de los compuestos de la presente invención. Los matabolitos incluyen especies producidas durante la introducción de compuestos de esta invención en el medio ambiente biológico.

Esta invención además proporciona una composición farmacéutica que comprende una cantidad terapéuticamente efectiva del compuesto de la invención y un portador farmacéuticamente aceptable. En una modalidad, la cantidad del compuesto es desde aproximadamente 0.01 mg a aproximadamente 800 mg. En otra modalidad, la cantidad del compuesto es desde aproximadamente 0.01 mg a aproximadamente 500 mg. En todavía otra modalidad, la cantidad del compuesto es desde aproximadamente 0.1 mg a aproximadamente 250 mg. En otra modalidad, la cantidad del compuesto es desde aproximadamente 0.1 mg a aproximadamente 60 mg. En todavía otra modalidad, la cantidad del compuesto es desde aproximadamente 1 mg a aproximadamente 20 mg. En una modalidad adicional, el portador es un líquido y la composición es una solución. En otra modalidad, el portador es un sólido y la composición es una tableta. En otra modalidad, el portador es un gel y la composición es una cápsula, supositorio o una crema. En una modalidad adicional, el compuesto puede ser formulado como una parte

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de un parche transdérmico farmacéuticamente aceptable. En aún otra modalidad adicional, el compuesto puede ser suministrado al sujeto por medio de un pulverizador o inhalador.

Esta invención también proporciona una composición farmacéutica elaborada al combinar una cantidad terapéuticamente efectiva del compuesto de esta invención y un portador farmacéuticamente aceptable.

Esta invención proporciona un proceso para elaborar una composición farmacéutica que comprende combinar una cantidad terapéuticamente efectiva del compuesto de ésta invención y un portador farmacéuticamente aceptable.

Un portador sólido puede incluir una o más sustancias que pueden también actuar como portadores endógenos (e.g., portadores nutrientes o micronutrientes), agentes saborizantes, lubricantes, solubilizantes, agentes de suspensión, rellenadores, deslizantes, auxiliares de compresión, aglutinantes o agentes desintegradores de tableta; también puede ser un material de encapsulación. En polvos, el portador es un sólido finamente dividido que es una mezcla con el ingrediente activo finamente dividido. En tabletas, el ingrediente activo se mezcla con un portador que tiene las propiedades de compresión necesarias en proporciones adecuadas y se compacta en una forma y tamaño deseados. Los polvos y tabletas preferiblemente contienen

hasta 99% del ingrediente activo. Los portadores sólidos adecuados incluyen, por ejemplo, fosfato de calcio, estearato de magnesio, talco, azúcares, lactosa, dextrina, almidón, gelatina, celulosa, polivinilpirrolidina, ceras de fusión baja y resinas de intercambio iónico.

Portadores líquidos son utilizados en la preparación de soluciones, suspensiones, emulsiones, jarabes, elixires y composiciones presurizadas. El ingrediente activo puede ser disuelto o suspendido en un portador líquido farmacéuticamente aceptable, tal como agua, un solvente orgánico, una mezcla de ambos o aceites o grasas farmacéuticamente aceptables. El portador líquido puede contener otros aditivos farmacéuticos adecuados, tal como solubilizantes, emulsificantes, amortiguadores, preservativos, edulcorantes, agentes saborizantes, agentes de suspensión, agentes espesantes, agentes colorantes, reguladores de viscosidad, estabilizadores u osmoreguladores. Ejemplos adecuados de portadores líquidos para administración oral y parenteral incluyen agua (que contienen parcialmente aditivos como los mencionados anteriormente, e.g., derivados de celulosa, preferiblemente solución de carboximetilcelulosa de sodio), alcoholes (que incluyen alcoholes monohídricos y alcoholes polihídricos, e.g.,glicoles) y sus derivados, y aceites (e.g., aceite de coco y aceite de cacahuate fraccionados). Para

administración parenteral, el portador puede también ser un éster aceitoso tal como oleato de etilo o miristato de isopropilo. Portadores líquidos estériles son útiles en composiciones de forma líquida estéril para administración parenteral. El portador líquido para composiciones presurizadas pueden ser un hidrocarbono halogenado u otro propelente farmacéuticamente aceptable.

Composiciones farmacéuticas líquidas que son soluciones o suspensiones estériles, pueden ser utilizadas vía por ejemplo, intramuscular, intratecal, epidural, intraperitoneal o inyección subcutánea. Las soluciones estériles pueden ser también administradas en forma intravenosa. Los compuestos pueden ser preparados como una composición sólida estéril que puede ser disuelta o suspendida al tiempo de la administración utilizando agua estéril, solución salina u otros medios inyectables estériles apropiados. Los portadores se proponen para incluir aglutinantes inertes y necesarios, agentes de suspensión, lubricantes, saborizantes, edulcorantes, preservativos, colorantes y revestimientos. El compuesto puede ser administrado oralmente en la forma de una solución o suspensión estéril que contiene otros solutos o agentes de suspensión (por ejemplo, solución salina o glucosa suficiente para elaborar la solución isotónica), sales biliares, acacia, gelatina, monoleato de sorbitan,

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polisorbato 80 (ésteres de oleato de sorbitol y sus anhídridos copolimerizados con óxido de etileno) y similares.

El compuesto también puede ser administrado oralmente ya sea en líquido o en composición en forma sólida. Las composiciones adecuadas para administración oral incluyen formas sólidas, tal como píldoras, cápsulas, granulos, tabletas, y polvos, y formas líquidas, tal como soluciones, jarabes, elixires y suspensiones. Las formas útiles para administración parenteral incluyen soluciones estériles, emulsiones, y suspensiones.

Dósis óptimas a ser administradas pueden ser determinadas por aquellos diestros en la técnica, y variarán con el compuesto particular en uso, la solidez de la preparación, el modo de administración y el avance de la condición de la enfermedad. Factores adicionales que dependen del sujeto en particular que es tratado, resultarán en una necesidad de ajustar la dosis, incluyendo la edad del sujeto, peso, sexo, dieta, y tiempo de administración.

En la aplicación al sujeto, una "cantidad terapéuticamente efectiva", es cualquier cantidad de un compuesto que, cuando se administra a un sujeto que sufre de una enfermedad contra la cual los compuestos son efectivos, causa reducción, remisión, o regresión de la enfermedad. En

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una aplicación al sujeto, un "sujeto" es un vertebrado, un mamífero o un humano.

Esta invención proporciona un método para tratar un sujeto que sufre de una anormalidad, en donde dicha anormalidad se alivia al disminuir la actividad de un receptor de MCH1 que comprende administrar al sujeto una cantidad de un compuesto de la invención que es un antagonista del receptor de MCH1, efectivo para tratar la anormalidad del sujeto.

En modalidades separadas, la anormalidad es una regulación de un esteroide o desorden de la hormona pituitaria, un desorden de liberación de epinefrina, un desorden gastrointestinal, un desorden cardiovascular, un desorden de balance de electrolito, hipertensión, diabetes, un desorden respiratorio, asma, un desorden de función reproductiva, un desorden inmune, un desorden endocrino, un desorden musculoesquelético, un desorden neuroendócrino, un desorden conocitivo, un desorden de la memoria, tal como la enfermedad de Alzheimer, un desorden de modulación y transmisión sensitiva, un desorden de coordinación motora, un desorden de integración sensitiva, un desorden de integración motora, un desorden de la función dopaminérgica, tal como enfermedad de Parkinson, un desorden de transmisión sensitiva, un desorden olfativo, un desorden de inervación simpática, un desorden afectivo, tal como depresión y

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ansiedad, un desorden relacionado con la tensión, un desorden de balance de fluido, un desorden de ataque, dolor, comportamiento psicótico, tal como esquizofrenia, tolerancia a la morfina, adicción a narcótico, migraña o desorden urinario, tal como incontinencia urinaria.

La siguiente descripción de desordenes depresivos y de ansiedad, es para propósito de ilustrar la utilidad de los compuestos de esta invención. Las definiciones de desordenes depresivos y de ansiedad dados enseguida, son aquéllos listados en Diagnostic and Statistical Manual of Mental Disorders. 4th ed. (DSM-IV; American Psychiatric Association, 1994a) o Diagnostic and Statistical Manual of Mental Disorders. 3rd ed. Revised (DSM-III-R; American Psychiatric Association, 1987). Información adicional respecto a éstos desordenes se puede encontrar en esta referencia, así como las otras citadas enseguida, todas las cuales están incorporadas en la presente para referencia.

Desordenes depresivos incluyen desorden depresivo mayor y desorden distímico (American Psychiatric Association, 1994a; American Psychiatric Association, 1994b). El desorden depresivo mayor esta caracterizado por la ocurrencia de uno o más episodios depresivos mayores sin episodios hipománicos o mánicos. Un episodio depresivo mayor esta definido como un estado de humor prominente y depresivo relativamente persistente o disfórico que usualmente

interfiere con funcionamiento diario (casi cada día durante al menos 2 semanas); se debe incluir al menos 4 de los siguientes 8 síntomas: cambio en el apetito, cambio en el sueño, agitación psicomotora o retardación, perdida de interés en actividades usuales o disminución en el impulso sexual, fatiga incrementada, sentimientos de culpabilidad o falta de valor, pensamiento lento o concentración deteriorada, y un intento de suicidio o idea de suicidio (Medical Economics Company, 2002). El desorden distímico implica un tipo de depresión que no es lo suficientemente severa para ser llamada un episodio depresivo mayor, pero que es al menos mucho más grande que el desorden depresivo mayor, sin fases altas.

Esta contemplado que los compuestos de esta invención serán efectivos en el tratamiento de depresión en pacientes quienes hayan sido diagnosticados con depresión al administrar cualesquiera de las siguientes pruebas: Escala de Valoración de Depresión de Hamilton (Hamilton Depression Rating Scale (HDRS)), punto de estado de humor de depresión de Hamilton (Hamilton depressed mood item), Severidad de Impresiones Globales Clínicas (CGI) de la Enfermedad. Esta además contemplado que los compuestos de la invención serán efectivos en inducir las mejoras en ciertos factores medidos en éstas pruebas, tal como puntuaciones del subfactor de la HDRS, incluyendo el punto de estado de humor de depresión,

el factor de perturbación del sueño y el factor de ansiedad, y la valoración de Severidad de CGI de la enfermedad. También esta contemplado que los compuestos de ésta invención serán efectivos para prevenir recaídas de episodios de depresión mayores.

Los desordenes de ansiedad incluyen desorden de pánico, agorafobia con o sin historia de desorden de pánico, fobia específica, fobia social, desorden de obesidad compulsiva, desorden de tensión post-traumática, desorden de tensión y deosrden de ansiedad generalizada. Esta contemplado que los compuestos de ésta invención serán efectivos en el tratamiento de cualesquiera de todos éstos desordenes en pacientes quienes hayan sido diagnosticados con éstos desordenes.

El desorden de obesidad compulsiva esta caracterizado por ideas recurrentes y persistentes, pensamientos, impulsos o imágenes (obsesiones), que son ego-distónicas y/o repetitivas, comportamientos decididos e intencionales (compulsiones) que son reconocidos por la persona como excesivos o inrasonables (American Psychiatric Association, 1994a). Las obsesiones o compulsiones que provocan marcado agotamiento, son consumidores de tiempo, o interfieren significativamente con funcionamiento social u ocupacional.

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Esta contemplado que los compuestos de ésta invención serán efectivos en el tratamiento de obsesiones e impulsos en pacientes quienes hayan sido diagnosticados con desorden compulsivo obsesivo por administración de pruebas apropiadas, que pueden incluir, pero no están limitadas a cualesquiera de las siguientes: Escala Compulsiva de Obesidad de Yale Brown (Yale Brown Obsessive Compulsive Scale (YBOCS))(Goodman, 1989) (para adultos), National Institute of Mental Health Global OCD Scale (NIMH GOCS), Escala de Severidad de CGI de la Enfermedad (CGI-Severity of Illeness scale). Esta además contemplado que los compuestos de la invención serán efectivos en inducir mejoras en ciertos factores medidos en éstas pruebas, tal como una reducción de varios puntos en la puntuación total de YBOCS. También esta contemplado que los compuestos de esta invención serán efectivos en prevenir recaídas de desorden compulsivo de obesidad.

El desorden de pánico esta caracterizado por ataques recurrentes de pánico inesperados y casos cercanos relacionados que tienen ataques adicionales, preocupación acerca de implicaciones o consecuencias de los ataques, y/o un cambio significante en el comportamiento relacionados con los ataques (American Psychiatric Association, 1994a). Un ataque de pánico esta definido como un período discreto de temor o incomodidad, en el cual cuatro (o más) de los

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siguientes síntomas se desarrollan abruptamente y alcanzan un pico dentro de 10 minutos: (1) palpitaciones, corazón que palpita violentamente o velocidad de corazón acelerada; (2) sudoración; (3) temblor o sacudimiento; (4) sensaciones de falta de respiración o asfixia ; (5) sentimiento de asfixia; (6)dolor de pecho o incomodidad; (7) nauseas o agotamiento abdominal; (8) sentimiento de vértigo, inestabilidad, mareo, o debilitamiento; (9) desrealización (sentimientos de perdida de la realidad) o despersonalización (que se desliga de uno mismo); miedo del control de la derrota; (11)miedo de morir; (12) parestesias (sensaciones de entumecimiento o hormigueo); (13) abundantes escalofríos o acaloramientos. El desorden de pánico puede o no estar asociado con agarofobia, o un miedo de incapacidad irracional y frecuente de estar frente al público.

Esta contemplado que los compuestos de ésta invención serán efectivos en el tratamiento de desorden de pánico en pacientes quienes hayan sido diagnosticados con desorden de pánico en base de la frecuencia de ocurrencia de ataques de pánico, o por medio de la escala de Severidad de CGI de la Enfermedad. Esta además contemplado que los compuestos de la invención serán efectivos en inducir mejoras en ciertos de los factores medidos en estas evaluaciones, tal como una reducción en la frecuencia o eliminación de ataques de pánico, una mejora en la escala de

Severidad de CGI de la Enfermedad o una puntuación de Mejora en la CGI Global de 1 (mucho muy mejorada), 2 (muy mejorada) o 3 (mejorada en forma mínima). Esta también contemplado que los compuestos de ésta invención serán efectivos en prevenir recaídas del desorden de pánico.

El desorden de ansiedad social, también conocido como fobia social, esta caracterizado por un miedo marcado y persistente de una o más situaciones sociales o desempeño en las que la persona esta expuesta a gente que no le es familiar o a posible escrutinio por otroas pesonas (American Psychiatric Association, 1994a). La exposición a la situación con miedo provoca también invariablemente ansiedad, que puede acercarse a la intensidad de un ataque de pánico. Las situaciones con miedo son evitadas o soportadas con ansiedad intensa o agotamiento. El evitar la anticipación de ansiedad, o agotamiento en la(s) situación(es) con miedo, interfiere significativamente con la rutina normal de la persona, desempeño ocupacional o académico, o actividades sociales o de relación, o casi existe agotamiento marcado que tienen las fobias. Grados más bajos de ansiedad o timidez en el desempeño, generalmente no requieren tratamiento psicofarmacológico.

Esta contemplado que los compuestos de ésta invención serán efectivos en el tratamiento del desorden de ansiedad social en pacientes quienes hayan sido

diagnosticados con desorden de ansiedad social al administrar cualesquiera de las siguientes pruebas: La Escala de Ansiedad Social de Liebowitz (Liebowitz Social Scale (LSAS)), la escala de Severidad de CGI de la Enfermedad (CGI-Severity of Illness scale), la Escala de Valoración de Hamilton para la Ansiedad (Hamilton Rating Scale for Anxiety (HAM-A)), la Escala de Valoración de Hamilton para la Depresión (Hamilton Rating Scale for Depression (HAM-D)), la Escala de Evaluación del uncionamiento Social y Ocupacional del eje V de DSM-IV (axis V Social and Occupational Functioning Assesstment Scale od DSM-IV)), la Evaluación de Discapacidad de la Organización Mundial de la Salud del eje II (ICD-10)(axis II(ICD-10) World Health Organization Disability Assesstment)), Programa 2 (DAS-2) (Schedule 2), las Escalas de Discapacidad de Sheehan (Sheehan Disability Scales), el Perfil de discapacidad de Schneier (Schneier Disability Profile), la Calidad de Vida-100 de la Organización Mundial de la Salud (World Health Organization Quality of Life-100 (WHOQOL-100)), u otras pruebas como las que se describen en Bobes, 1998, que se incorporan en la presente para referencia. Esta además contemplado que los compuestos de la invención serán efectivos en inducir mejoras conforme se miden por éstas pruebas, tal como el cambio de la línea basal en la Escala de Ansiedad Social de Liebowitz (Liebowitz Social Anxiety

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Scale (LSAS)), o una puntuación de Mejora Global de CGI (CGI-Global Improvement score) de i (mucho muy mejorada), 2 (muy mejorada), o 3 (mejorada en forma mínima). También esta contemplado que los compuestos de ésta invención serán efectivos en prevenir recaídas del desorden de ansiedad social.

El desorden de ansiedad generalizada esta caracterizado por excesiva ansiedad y preocupación (expectativa aprehensiva) que es persistente por al menos 6 meses y que la persona encuentra dificultad para controlar (American Psychiatric Association, 1994a). Este debe de ser asociada con al menos 3 meses de los siguientes 6 síntomas: impaciencia o sentimiento de emoción o de nervios, que fácilmente se fatiga, difícilmente se concentra o su mente esta en blanco, irritabilidad, tensión muscular, perturbación del sueño. El criterio de diagnóstico para éste desorden esta descrito en mayor detalle en DSM-IV, la cual esta incorporada en la presente para referencia (American Psychiatric Association, 1994a).

Esta contemplado que los compuestos de ésta invención serán efectivos en el tratamiento del desorden de ansiedad generalizado en pacientes quienes hayan sido diagnosticados con éste desorden de acuerdo al criterio de diagnóstico descrito en DSM-IV. Esta además contemplado que los compuestos de la invención serán efectivos en reducir

los síntomas de éste desorden, tal como los siguientes: preocupación y ansiedad excesiva, dificultad para controlar la preocupación, impaciencia o sentimiento de emoción o de nervios, fácilmente se fatiga, difícilmente se concentra o su mente esta en blanco, irritabilidad, tensión muscular, o perturbación del sueño. También esta contemplado que los compuestos de ésta invención serán efectivos en prevenir recaídas del desorden de ansiedad general.

Desorden de tensión post-traumático (PTSD, por sus siglas en inglés), como esta definido en DSM-III-R/IV (American Psychiatric Association, 1987, American Psychiatric Association, 1994a), requiere exposición a un evento traumático que implica amenaza de muerte o muerte real o daño serio, o amenaza a la integridad física de uno mismo u otros, y una respuesta que implica miedo intenso, impotencia, u horror. Los síntomas que ocurren como un resultado de exposición al evento traumático incluyen el volver a experimentar el evento en forma de pensamientos intrusivos, escenas o sueños, y agotamiento psicológico intenso y reactividad psicológica a exposición a estímulos de evento; el evitar situaciones evocadas del evento traumático, inabilitar el llamar detalles del evento, y/o el paralizar la sensibilizar general manifestada como la disminución del interés en actividades significantes, alejamiento de otros, intervalo restringido de afecto, o

sentido del futuro a corto plazo; y síntomas de despertar autonómicos que incluyen hipervigilancia, respuesta de sobresalto exagerada, perturbación del sueño, concentración deteriorada, e irritabilidad o arrebatos de enojo. Un diagnóstico PTSD requiere que los síntomas estén presentes por al menos un mes y que éstos provoquen agotamiento clínicamente significante o deterioro en lo social, ocupacional, u otras áreas importantes de funcionamiento. Esta contemplado que los compuestos de ésta invención serán afectivos en el tratamiento de PTSD en pacientes quienes hayan sido diagnosticados con PTSD al administrar cualesquiera de las siguientes pruebas: Clinician-Administered PTSD Scale Part 2 (CAPS, por sus siglas en inglés), el Impacto valorado del paciente de la Escala de Evento (patient-rated Impact of Event Scale (IES)) (Medical Economics Company, 2002, p. 2752). Esta además contemplado que los compuestos de la invención serán efectivos en inducir mejoras en las puntuaciones de las pruebas de CAPS, IES, Severidad de CGI de la Enfermedad (CGI-Severity of Illness) o Mejora Global de CGI (CGI-Global Improvement). También esta contemplado que los compuestos de ésta invención serán efectivos en prevenir recaídas de PTSD.

En una modalidad preferida, la materia de la invención proporciona un método de tratamiento o manejo de las siguientes indicaciones: desordenes depresivos,

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desordenes de ansiedad, desordenes de peso corporal /comida, y desordenes urinarios. Ejemplos de desordenes depresivos son el desorden depresivo mayor o desorden distímico. Ejemplos de desordenes de ansiedad son el desorden de pánico, agorafobia sin historia de desorden de pánico, fobia específica, fobia social, desorden de obesidad compulsiva, desorden de tensión post-traumática, desorden de tensión aguda o desorden de ansiedad generalizada. Ejemplos de desordenes de peso corporal/comida, son la obesidad, ganancia de peso, bulimia, bulimia nerviosa o anorexia nerviosa. Ejemplos de desordenes urinarios incluyen, pero no están limitados a, incontinencia urinaria, vejiga demasiado activa, incontinencia persistente, frecuencia urinaria, urgencia urinaria, nicturia o enuresis. Vegija demasiada activa y urgencia urinaria pueden o no estar asociados con la hiperplasia prostática benigna.

Esta invención proporciona un método para modificar el comportamiento de alimentación de un sujeto, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para disminuir el consumo de alimento por el sujeto. Esta invención también proporciona un método para tratar un desorden de comida en un sujeto, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para tratar el desorden de comida. En una modalidad de la

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presente invención, el desorden de comida es obesidad, bulimia, bulimia nerviosa o anorexia nerviosa.

La presente invención además proporciona un método para reducir la masa corporal de un sujeto, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para reducir la masa corporal del sujeto. Esta invención también proporciona un método para manejar la obesidad en un sujeto que necesita perder peso, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para inducir la perdida de peso en el sujeto. Esta invención también proporciona un método para manejar la obesidad en un sujeto quien ha experimentado perdida de peso, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para mantener la perdida de peso en el sujeto.

La presente invención también proporciona un método para tratar la depresión en un sujeto, el cual comprende el administrar al sujeto una cantidad de un compuesto de la invención, efectiva para tratar la depresión del sujeto. Esta invención también proporciona un método para tratar la ansiedad en un sujeto, el cual comprende el administrar al sujeto una cantidad de un compuesto de la invención, efectiva para tratar la ansiedad del sujeto. Esta invención también proporciona un método para tratar la depresión y ansiedad en un sujeto, el cual comprende

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administrar al sujeto una cantidad de un compuesto de la invención, efectiva para tratar la ansiedad y depresión del sujeto. Esta invención también proporciona un método para tratar un desorden depresivo mayor en un sujeto, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para tratar el desorden depresivo mayor del sujeto. Esta invención también proporciona un método para tratar un desorden distémico en un sujeto, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para tratar el desorden distémico del sujeto. Esta invención también proporciona un método para tratar obsesiones y compulsiones en un sujeto con desorden compulsivo obsesivo, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para tratar las obsesiones y compulsiones del sujeto. Esta invención también proporciona un método para tratar un desorden de pánico, con o sin agorafobia, en un sujeto, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para tratar el desorden de pánico del sujeto. Esta invención también proporciona un método para tratar un desorden de ansiedad social en un sujeto, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para tratar el desorden de ansiedad social del sujeto. Esta invención también proporciona un

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método para tratar un desorden de ansiedad generalizado en un sujeto, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para tratar el desorden de ansiedad generalizada del sujeto. Esta invención también proporciona un método para tratar el desorden de tensión post-traumático en un sujeto, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para tratar el desorden de tensión post-traumático del sujeto.

Esta contemplado que los compuestos de ésta invención serán efectivos en el tratamiento de la obesidad, incluyendo perdida de peso y mantenimiento de la perdida de peso en los pacientes, quienes hayan sido diagnosticados con obesidad por una o más de las siguientes medidas: un índice de masa corpórea incrementado, circunferencia de cintura incrementada (como indicador de grasa intra-adominal), absortiometría de Rayos X de Doble Energía (Dual Energy X-Ray Absorptiometry (DEXA)) y masa grasa trucal (androide). Esta además contemplado que los compuestos de la invención serán efectivos en inducir mejoras en ciertos factores medidos en estas pruebas.

Esta contemplado que los compuestos de ésta invención serán efectivos en el tratamiento de desordenes urinarios en pacientes quienes tienen incontinencia persistente o mezclada (con una predominancia de

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persistencia), como se evidencia por el número de episodios inecesarios por semana, el número de micciones por día y un volumen bajo vaciado por micción. Esta además contemplado que los compuestos de la invención serán efectivos en inducir mejoras en ciertos factores medidos en éstas pruebas.

La presente invención también proporciona un método para tratar un sujeto que sufre de desorden bipolar I y II, desorden esquizoafectivo, un desorden de conocimiento con estado de humor depresivo, un desorden de personalidad, insomnio, hipersomnio, narcolepsia, desorden de sueño del ritmo circadiano, desorden de pesadillas, desorden de terror de sueño o desorden de sonanbulismo.

La presente invención proporciona un método para tratar vejiga demasiado activa con síntomas de incontinencia urinaria persistente, urgencia y/o frecuencia en un sujeto, que comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para tratar la vejiga demasiado activa del sujeto. Esta invención también proporciona un método para aliviar la incontinencia urinaria persistente en un sujeto que sufre de vejiga demasiado activa, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para aliviar la incontinencia urinaria persistente. Esta invención además proporciona un método para aliviar la urgencia urinaria en

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un sujeto que sufre de vejiga demasiado activa, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para aliviar la urgencia urinaria . del sujeto. Adicionalmente, esta invención proporciona un método para aliviar la frecuencia urinaria en un sujeto que sufre de vejiga demasiado activa, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para aliviar la frecuencia urinaria del sujeto.

La presente invención también proporciona un método para tratar un sujeto que sufre de desorden urinario, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para tratar el desorden urinario del sujeto. En alguna modalidad el desorden urinario es incontinencia urinaria, vejiga demasiado activa, incontinencia persistente, frecuencia urinaria, urgencia urinaria, nicturia o enuresis.

La presente invención proporciona un método para aliviar los síntomas de un desorden en un sujeto, el cual comprende administrar al sujeto una cantidad de un antagonista de MCH1, efectiva para aliviar los síntomas, en donde el antagonista de MCH1 es cualesquiera de los compuestos de la invención.

En una modalidad de la invención, el sujeto es un vertebrado, un mamífero, un humano o un canino. En otra

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modalidad, el compuesto es administrado oralmente. En todavía otra modalidad, el compuesto es administrado en combinación con alimento.

Esta invención será mejor entendida a partir de los Detalles Experimentales en una modalidad preferida, la materia de la invención proporciona un método de tratamiento para las siguientes indicaciones: depresión, ansiedad, desordenes de comida/peso corporal, y desordenes urinarios. Ejemplos de desordenes de comida/peso corporal son la obesidad, bulimia, o bulimia nerviosa. Ejemplos de desordenes urinarios incluyen, pero no están limitados a, incontinencia urinaria, vejiga demasiado activa, incontinencia persistente, frecuencia urinaria, urgencia urinaria, nicturia, o enuresis. La vejiga demasiado activa y la urgencia urinaria pueden o estar asociadas con hiperplasia prostática benigna.

Esta invención proporciona un método para modificar el comportamiento alimenticio de un sujeto, el cual comprende administrar a un sujeto una cantidad de un compuesto de la invención, efectiva para disminuir el consumo de alimento por el sujeto.

Esta invención también proporciona un método para tratar un desorden de comida en un sujeto, el cual comprende administrar al sujeto una cantidad de un compuesto de ésta invención, efectiva para disminuir el consumo de alimento

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por el sujeto. En una modalidad de la presente invención, el desorden de comida es bulimia, obesidad o bulimia nerviosa. En una modalidad de la presente invención, el sujeto es un vertebrado, un mamífero, un humano o un canino. En una modalidad adicional, el compuesto es administrado en combinación con alimento.

La presente invención además proporciona un método para reducir la masa corpórea de un sujeto, el cual comprende administrar al sujeto una cantidad de un compuesto de la invención, efectiva para reducir la masa corpórea del sujeto.

La presente invención también proporciona un método para tratar un sujeto que sufre de depresión, el cual comprende administrar al sujeto una cantidad de un compuesto de ésta invención, efectiva para tratar la depresión del sujeto. La presente invención además proporciona un método para tratar un sujeto que sufre de ansiedad, el cual comprende administrar al sujeto una cantidad de un compuesto de ésta invención, efectiva para tratar la ansiedad del sujeto. La presente invención también proporciona un método para tratar un sujeto que sufre de depresión y ansiedad, el cual comprende administrar al sujeto una cantidad de un compuesto de ésta invención, efectiva para tratar la depresión y ansiedad del sujeto.

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La presente invención también proporciona un método para tratar un sujeto que sufre de desorden depresivo mayor, desorden distímico, desordenes bipolar I y II, desorden esquizoafectivo, un desorden de conocimiento con estado de humor depresivo, desordenes de personalidad, insomnio, hipersomnio, narcolepsia, desorden de sueño del ritmo circadiano, desorden de pesadillas, desorden de terror de sueño, desorden de sonanbulismo desorden de obesidad compulsiva, desorden de pánico, con o sin agorafobia, desorden de tensión post-traumático, desorden de ansiedad social, desorden de fobia social y ansiedad generalizada.

La presente invención también proporciona un método para tratar un sujeto que sufre de desorden urinario, el cual comprende administrar al sujeto una cantidad de un compuesto de ésta invención, efectiva para tratar un desorden urinario del sujeto. En algunas modalidades, el desorden urinario es incontinencia urinaria, vejiga demasiado activa, incontinencia persistente, frecuencia urinaria, urgencia urinaria, nicturia o enuresis.

Esta invención será mejor entendida a partir de los Detalles Experimentales que siguen. Sin embargo, un experto en la técnica apreciará fácilmente que los métodos y resultados discutidos, son meramente ilustrativos de la invención, como se describe más completamente en las reivindicaciones que siguen posteriormente.

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Sección Experimental

I. Métodos Sintéticos para Ejemplos

Métodos Generales: Todas las reacciones (excepto para aquellas hechas para formar reacciones de síntesis paralelas) fueron realizadas bajo atmósferas de Argón y los reactivos, limpios o en solventes apropiados, fueron transferidos al recipiente de reacción vía técnicas de jeringa y cánula. Las formaciones de reacción de síntesis paralela se realizaron en frascos (sin una atmósfera inerte) utilizando agitadores de calor J-KEM (Saint Louis, MO). Solventes anhídros fueron obtenidos de Aldrich Chemical Company y utilizados como se recibieron. Los ejemplos descritos en la patente fueron nombrados utilizando el programa de ACD/Name (versión 2.51, Advanced Chemistry Development Inc., Toronto, Ontario, M5H2L3, Canadá). A menos de que se indique de otra manera, los espectros ^{1}H fueron registrados a 300 y 400 MHz (QE Plus and Brûker, respectivamente) con tetrametilsilano como estándar interno. s = singlete; d = doblete; t = triplete; q = cuarteto; p = penteto; sexteto; septeto; br = amplio; m = multiplete. Análisis elementales fueron realizados por Robertson Microlit Laboratories, Inc. A menos de que se indique de otra manera, los espectros de masa se obtuvieron utilizando electropulverizado de baja resolución (ESMS) y MH^{+} es

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reportado. Cromatografía de capa delgada (TLC, por sus siglas en inglés) se llevó a cabo en placas de vidrio prerevestido con gel de sílice 60 F_{254} (0.25 mm, EM Separations Tech.). Cromatografía de capa delgada preparatoria se llevó a cabo en hojas de vidrio prerevestidas con gel de sílice GF (2 mm, Analtech). Cromatografía de columna instantánea se realizó en gel de sílice 60 de Merck (malla 230-400). Los puntos de fusión fueron determinados (pf) en tubos capilares abiertos en un aparto Mel-Temp y están sin corregir.

Intermediarios de Cadena Lateral de Piperidina

4-{[(TRIFLUOROMETIL)SULFONIL]OXI}-1,2,3,6-TETRAHIDRO-1-PIRIDINCARBOXILATO DE TERT-BUTILO: n-Butil litio (17.6 mL, 44.2 mmol, 2.5 en hexanos) se adicionó a una solución de diisopropilamina (96.2 mL, 44.2 mmol) en 40 mL de THF seco a 0°C y se agitó durante 20 minutos. La mezcla de reacción se enfrió a -78°C y 4-oxo-1piperidincarboxilato de tert-butilo (Aldrich chemical Company, 40.0 mmol) en THF, se adicionó gota a gota a la mezcla de reacción y se agitó durante 30 minutos. Tf_2NPh (42.0 mmol, 15.0 g) en THF (40 mL) se adicionó gota a gota a la mezcla de reacción y se agitó a temperatura ambiente durante la noche. La mezcla de reacción se concentró *in vacuo*, se volvió a disolver en hexanos: EtOAc (9:1), se pasó a través de una solución tampón de alumina, y la solución

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tampón de alúmina se lavó con hexanos:EtOAc (9:1). Los extractos combinados se concentraron para producir 16.5 g del producto deseado que fue contaminado con algo de Tf_2NPh de partida.

RMN ^1H (400 MHz, 400 MHz, $CDCl_3$) 5.77 (s, 1 H), 4.05 (dm, 2 H, J=3.0 Hz), 3.63 (t, 2 H, J=5.7 Hz), 2.45 (m, 2 H), 1.47 (s, 9 H).

4-[3(AMINO)FENIL]-1,2,3,6-TETRAHIDRO-1-PIRI-DINCARBOXILATO DE TERT-BUTILO: Una mezcla de una solución de Na_2CO_3 acuosa 2 M (4.2 mL), 4-{[(trifluorometil)-sulfonil]oxi}-1,2,3,6-tetrahidro-1-piridincarboxilato de tert-butilo (0.500 g, 1.51 mmol), hemisulfato de ácido 3-aminofenilborónico (0.393 g, 2.11 mmol), cloruro de litio (0.191 g, 4.50 mmol) y tetrakis-trifenilfosfin paladio (0) (0.080 g, 0.075 mmol)) en dimetoxietano (5 mL), se calentó a temperatura de reflujo durante 3 horas, bajo una atmósfera inerte (se recomendó un desgaseado inicial de la mezcla para prevenir la formación de óxido de trifenilfosfina). La capa orgánica de la mezcla de reacción enfriada se separó y la capa acuosa se levó con acetato de etilo (3X). Los extractos orgánicos combinados se secaron y concentraron *in vacuo*. El producto crudo se cromatografió (sílice, hexanos:EtOAc:diclorometano (6:1:1) con isopropilamina adicionada al 1%, para proteger el grupo BOC de hidrólisis), para dar 0.330 g del producto deseado en

una producción de 81%. RMN ^1H (400 MHz, $CDCl_3$) 7.12 (t, 1H, J=7.60 Hz), 6.78 (d, 1H, J=8.4 Hz), 6.69 (t, 1H, J= 2.0 Hz), 6.59 (dd, 1H, J = 2.2, 8.0 Hz), 6.01 (m, 1H), 4.10 - 4.01 (d, 2H, J= 2.4 Hz), 3.61 (t, 2H, J= 5.6 Hz), 2.52 - 2.46 (m, 2H), 1.49 (s, 9H); ESMS m/e: 275.2 $(M + H)^+$. Calc. Anal. para $C_{16}H_{24}N_2O_2$: C, 70.04; H, 8.08; N, 10.21. Encontrado: C, 69.78; H, 7.80; N, 9.92.

4-[3(AMINO)FENIL]-1-PIRIDINCARBOXILATO DE TERT-BUTILO: Una mezcla de de 3.10 g de 4-(3-aminofenil)-1,2,3,6-tetrahidro-piridin-1-carboxilato de tert-butilo (11.3 mmol) y 1.0 g de Pd/C al 10% en 200 mL de etanol, se hidrogenó a temperatura ambiente utilizando el método de matraz durante 2 días. La mezcla de reacción se filtró y se lavó con etanol. Los extractos de etanol combinados se concentraron *in vacuo* y el residuo se cromatografió sobre sílice (diclorometano:metanol 95:5, con isopropilamina al 1% adicionada para proteger el grupo BOC de hidrólisis), para dar 2.63 g del producto deseado (84%). RMN ^1H (400 MHz, $CDCl_3$) 7.10 (t, 1H, J=7.60 Hz), 6.62 (d, 1H, J= 8.4 Hz), 6.60 - 6.59 (m, 2H), 4.27 - 4.18 (m, 2H), 3.62 - 3.58 (m, 2H), 2.80 - 2.72 (m, 2H), 2.62 - 2.59 (m, 1H), 1.89 - 1.52 (m, 4H), 1.49 (s, 9H); ESMS m/e: 277.2 $(M + H)^+$.

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4-[3(ACETILAMINO)FENIL]-1,2,3,6-TETRAHIDRO-1-PIRIDINCARBOXILATO DE TERT-BUTILO: Una mezcla de una solución de Na_2CO_3 acuosa saturada (25 mL), 4-{[(trifluorometil)-sulfonil]oxi}-1,2,3,6-tetrahidro-1-piridincarboxilato de tert-butilo (20 mmol), ácido 3-acetamidofenilborónico (30 mmol) y tetrakis-trifenilfosfin-paladio (0) (1.15 g) y dimetoxietano (40 mL), se calentó a temperatura de reflujo durante la noche. La capa orgánica de la mezcla de reacción enfriada se separó y la capa acuosa se lavó con acetato de etilo (3X). Los extractos orgánicos combinados se secaron y concentraron *in vacuo*. El producto crudo se cromatografió, dando el producto deseado: RMN ^1H (400 MHz, $CDCl_3$) 8.11 (br s, 1 H), 7.57 (br s, 1 H), 7.41 (br d, 1 H, J= 7.8 Hz), 7.25 (t aparente, 1 H, J= 7.8 Hz), 7.08 (br d, 1 H, J= 7.8 Hz), 5.99 (br s, 1 H), 4.03 (br m, 2 H, J= 2.7 Hz), 3.59 (t, 2 H, J= 5.7 Hz), 2.46 (m, 2 H), 2.16 (s, 3 H), 1.49 (s, 9 H).

N1-[3-(1,2,3,6-TETRAHIDRO-4-PIRIDINIL)FENIL]ACETAMIDA:

Una solución de HCl 4 M en dioxano (10 mL) se adicionó a 4-[3-(acetilamino)fenil]-1,2,3,6-tetrahidro-1-piridincarboxilato de tert-butilo (8.25 mmol) en diclorometano (30 mL). La mezcla de reacción se agitó a temperatura ambiente durante la noche, se concentró *in vacuo*, dando el producto deseado como la sal de clorohidrato (2.1 g): RMN ^1H ($CDCl_3$) 7.47 - 7.00 (m, 4 H), 6.10 (br, 1

H), 3.55 (m, 2 H), 3.16 (t, 2 H, J= 5.7 Hz), 2.44 (m, 2 H), 2.19 (s, 3 H).

N-(3-BROMOPROPIL)CARBAMATO DE TERT-BUTILO: Se preparó a partir de hidrobromuro de 3-bromopropilamina y BOC_2O, en presencia de la base en diclorometano, 9.89 mmol: RMN ^1H ($CDCl_3$) 5.07 (br, 1 H), 3.31 (t, 2 H, J=6.6 Hz), 3.12 (br q aparente, 2 H, J=6.0 Hz), 1.92 (p, 2 H, J=6.6 Hz), 1.30 (s, 9 H).

N-(3-{4-[3-ACETILAMINO)FENIL]-1,2,3,6-TETRAHIDRO-1-PIRIDINIL}PROPIL)CARBAMATO DE TERT-BUTILO: Una solución de N1-[3-(1,2,3,6-tetrahidro-4-piridinil)fenil]acetamida.HCl (8.24 mmol), N(3-bromopropil)carbamato de tert-butilo y carbonato de potasio (33 mmol) en dioxano seco (30 mL) se calentó a temperatura de reflujo durante la noche. Los sólidos se retiraron por filtración, la solución se concentró *in vacuo* y el producto se cromatografió, dando el producto deseado (110 mg). RMN ^1H ($CDCl_3$) 7.65 (s, 1 H), 6.98 (s, 1 H), 7.45 (d, 1 H, J=7.8 Hz), 7.16 (t aparente, 1 H, J=7.8 Hz), 7.10 (d, 1 H, J=7.8 Hz), 6.02 (s, 1 H), 5.23 (b, 1H), 3.40 (b, 2 H), 3.30-1.80 (m, 10 H), 2.18 (s, 3 H), 1.45 (s, 9 H).

N1-{3-[1-(3-AMINOPROPIL)-1,2,3,6-TETRAHIDRO-4-PIRIDINIL]FENIL}ACETAMIDA: Una solución 1:1 de TFA:CH_2Cl_2 (5 mL) se

adicionó a N-(3-{4-[3-acetilamino)fenil]-1,2,3,6-tetrahidro-1-piridinil}propil)carbamato de tert-butilo en diclorometano (5mL). La solución resultante se agitó a temperatura ambiente durante 1-3 días, $NaHCO_3$ saturado se adicionó hasta pH > 6, la capa orgánica se separó, y se secó *in vacuo*, dando el producto deseado (45 mg): RMN ^1H ($CDCl_3$) 7.68 (br, 1 H), 7.35 (dm, 1 H, J=7.8 Hz), 7.25 (t aparente, 1 H, J=7.8 Hz), 7.15 (dm, 1 H, J=7.8 Hz), 6.12 (m, 1 H), 3.22 (m, 2 H), 3.03 (t, 2 H, J=7.3 Hz), 2.78 (t, 2 H, J=5.5 Hz), 2.70-2.50 (m, 4 H), 2.10 (s, 3 H), 1.87 (p, 2 H, J=7.3 Hz).

4-[3-(ACETILAMINO)FENIL]-1-PIPERIDINCARBOXILATO DE TERT-BUTILO: Una mezcla de 4-[3-(acetilamino)fenil]-1,2,3,6-tetrahidro-1-piridincarboxilato (710 mg) y Pd/C al 5 5 (100 mg) en EtOH (10 mL), se hidrogenó (técnica de matraz) a temperatura ambiente durante la noche. La mezcla de reacción se pasó a través de una almohadilla de Celite 5454 y la almohadilla de Celite se lavó con etanol. Los extractos de etanol combinados se concentraron y cromatografiaron, dando el producto deseado (660 mg): RMN ^1H ($CDCl_3$) 7.80 (s, 1 H), 7.41-7.20 (m, 3 H), 6.94 (d, 1 H, J=7.5 Hz), 4.21 (m, 2 H), 2.75 (m, 2 H), 2.62 (m, 1 H), 2.16 (s, 3 H), 1.78 (m, 2 H), 1.56 (m, 2 H), 1.48 (s, 9 H).

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N1-[3-(4-PIPERIDINIL)FENIL]ACETAMIDA: Una solución de HCl en dioxano (4N, 5 mL) se adicionó a 4-[3-(acetilamino)fenil]-1-piperidinilcarboxilato de tert-butilo (660 mg) en diclorometano seco (15 mL). La mezcla de reacción se agitó a temperatura ambiente durante la noche y se concentró *in vacuo*, dando el producto deseado (550 mg): pf 102-104°C; RMN ^1H ($CDCl_3$) 2.02 (d, J=13.2 Hz,2H), 2.11-2.45 (m, 5H), 2.67-2.77 (m, 1H), 3.00-3.10 (m, 2H), 3.51 (d, J=10.5 Hz, 2H), 6.94 (d, J=7.5 Hz, 1H), 7.20-7.46 (m, 3H), 7.60 (s, 1H); Calc. Anál. para $C_{13}H_{19}N_2OCl+0.86\ CH_2Cl_2$: C, 50.78; H, 6.37; N, 8.55. Encontrado: C, 50.80; H, 7.55; N, 7.01.

N(3-{4-[3-(ACETILAMINO)FENIL]PIPERIDINO}PROPIL)CARBAMATO DE TERT-BUTILO: Una solución de N1-[3-(4-piperidil)fenil]-acetamida (550 mg, 0.210 mmol), N-(3-bromopropil)carbamato de tert-butilo (550 mg, 0.230mmol), K_2CO_3 (1.10 g, 0.890 mmol), diisopropiletilamina (1.50 mL) y unos pocos cristales de KI en dioxano (20 mL), se calentó a temperatura de reflujo durante 2 días. Las sales precipitadas se retiraron por filtración, se concentraron *in vacuo*, y el producto crudo se cromatografió, dando el producto deseado (340 mg): RMN ^1H ($CDCl_3$) 8.15 (s, 1 H), 7.47-7.44 (m, 2 H), 7.22 (t, 1 H, J=7.8 Hz), 6.94 (d, 1 H, J=7.8 Hz), 5.53 (b, 1 H), 3.23 (b, 6 H), 2.80-1.60 (m, 9 H), 2.20 (s, 3 H), 1.45 (s, 9 H).

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N1-{3-[1-(3-AMINOPROPIL)-4-PIPERIDINIL]FENIL}ACETAMIDA: TFA (1.0 mL) se adicionó a una solución de N(3-{4-[3-(acetilamino)fenil]piperidino}propil)carbamato de tert-butilo (340 mg) en diclorometano seco (10 mL) y se agitó a temperatura ambiente durante 5 h. Una solución acuosa al 10% de KOH se adicionó a la mezcla de reacción hasta pH > 6, y después el diclorometano se retiró *in vacuo*. La capa acuosa se congeló y liofilizó para dar un sólido, el cual se extrajo con metanol. La remoción del solvente dio el producto deseado (120 mg) como un aceite: RMN ^1H ($CDCl_3$) 7.23-7.16 (t aparente, 1H, J=7.5 Hz), 6.95-6.92 (m, 1H), 3.03-2.99 (m, 2H), 2.77-2.73 (t, 2H, J=6.6 Hz), 2.50-1.60 (m, 10 H), 2.13 (s, 3 H).

4-(3-NITROFENIL)-3,6-DIHIDRO-1(2H)-PIRIDINCARBOXILATO: De acuerdo al procedimiento utilizado para la síntesis de 4-[3-(amino)fenil]-1,2,3,6-tetrahidro-1-piridincarboxilato de tert-butilo, una mezcla de una solución de Na_2CO_3 acuosa 2 M (2.2 mL), 4-{[(trifluorometil)sulfonil]oxi}-1,2,3,6-tetrahidro-1-piridin-carboxilato de tert-butilo (0.500 g, 1.51 mmol), ácido 3-nitrofenilborónico (0.353 g, 2.11 mmol), cloruro de litio (0.191 g, 4.50 mmol) y tetrakis-trifenilfosfin-paladio (0) (0.080 g, 0.075 mmol) en dimetoxietano (5 mL), produciendo 0.380g del producto deseado.

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RMN ^1H (400 MHz, $CDCl_3$) 8.23 (s, 1H), 8.11 (d, 1H, J=8.0 Hz), 7.69 (d, 1H, J=8.0 Hz), 7.51 (t, 1H, J=8.0 Hz), 6.20 (m, 1H), 4.17-4.08 (m, 2H), 3.67 (t, 2H, J=5.6 Hz), 2.61-2.52 (m, 2H), 1.50 (s, 9H); ESMS m/e: 249.1 $(M + H - C_4H_8)^+$.

1,2,3,6-TETRAHIDRO-4-(3-NITROFENIL)PIRIDINA: En una solución agitada de 5.00 g (16.0 mmol) de 1,2,3,6-tetrahidro-4(3-nitrofenil)piridina-1-carboxilato de tert-butilo en 100 ml de 1,4-dioxano a 0°C, se burbujeo gas de HCl durante 10 minutos. La mezcla de reacción se permitió que se calentará a temperatura ambiente y el burbujeo de gas de HCl se continuo durante 1 hora adicional. El solvente se removió *in vacuo*, se disolvió el residuo en 50 mL de agua y se neutralizó mediante la adición de pelotillas de KOH. La solución acuosa se extrajo con 3 X 80 mL de diclorometano y los extractos orgánicos combinados se secaron ($MgSO_4$), se filtró y se concentró *in vacuo*. El residuo se purificó por cromatografía de columna (sílice, 9:1, diclorometano:metanol + isopropilamina al 1%) para dar 2.85 g (rendimiento 87.5%) del producto deseado: RMN ^1H (400 MHz, $CDCl_3$) 8.24 (s, 1H), 8.09 (d, 1H, J=8.4 Hz), 7.71 (d, 1H, J=8.0 Hz), 7.49 (t, 1H, J=8.0 Hz), 6.35-6.25 (m, 1H), 3.58 (q aparente, 2H, J=3.0 Hz), 3.14 (t, 2H, J=5.6 Hz), 2.54-2.46 (m, 2H).

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3-(4-(3-NITROFENIL)-3,6-DIHIDRO-1(2H)-PIRIDINIL)PROPILCARBAMATO DE TERT-BUTILO: Una mezcla de 2.80 g (14.0 mmol) de 1,2,3,6-tetrahidro-4-(3-nitrofenil)piridina, 3.60 g (15.0 mmol) de N-(3-bromopropil)carbamato de tert-butilo, 11.6 g de K_2CO_3, 14.6 mL (84.0 mmol) de diisopropilamina y 0.78 g (2.00 mmol) de yoduro de tetrabutilamonio en 250 mL de 1,4-dioxano, se calentó a temperatura de reflujo durante 14 horas. La mezcla de reacción se filtró y el filtrado se secó ($MgSO_4$), se concentró *in vacuo* y el residuo se purificó por cromatografía de columna (sílice, 9:1, diclorometano:metanol + isopropilamina al 1%) para producir 4.35 g (rendimiento 85.7%) del producto deseado: RMN ^1H (400 MHz, $CDCl_3$) 8.24 (t, 1H, J=1.9 Hz)), 8.09 (dd, 1H, J=1.9, 8.0 Hz), 7.70 (d aparente, 1H, J=8.0 Hz), 7.49 (t, 1H, J=8.0 Hz), 6.23 (m, 1H), 3.29-3.18 (m, 4H), 2.75 (t, 2H, J=5.6 Hz), 2.64-2.54 (m, 4H), 1.82-1.70 (m, 2H), 1.44 (s, 9H); ESMS m/e: 362.2 $(M + H)^+$.

3-(4-(3-NITROFENIL)-3,6-DIHIDRO-1(2H)-PIRIDINIL)-1-PROPANAMINA: En una solución agitada de 4.35 g (12.0 mmol) de 3-(4-(3-nitrofenil)-3,6-dihidro-1(2H)-piridinil)propil-carbamato de tert-butilo en 100 ml de 1,4-dioxano a 0°C, se burbujeo gas de HCl durante 10 minutos. A la mezcla de reacción se le permitió calentar a temperatura ambiente y se continuó el burbujeo durante 1 hora adicional. El solvente

se retiro *in vacuo*, se disolvió el residuo en 50 mL de agua y se neutralizó por medio de la adición de pelotillas de KOH. La solución acuosa se extrajo con 3 X 80 mL de diclorometano, los extractos orgánicos combinados se secaron ($MgSO_4$), se filtró y se concentró *in vacuo*. El residuo se purificó por cromatografía de columna (sílice, 9:1, diclorometano:metanol + isopropilamina al 1%) para producir 3.05 g (rendimiento 97.0%) del producto deseado: RMN ^1H (400 MHz, $CDCl_3$) 8.24 (t, 1H, J=1.8 Hz), 8.09 (dd, 1H, J=1.8, 8.2 Hz), 7.69 (dd, 1H, J=1.8, 8.2 Hz), 7.48 (t, 1H, J=8.2 Hz), 6.24 (m, 1H), 3.21 (d, 2H, J=3.6 Hz), 2.84 (t, 2H, J=6.6 Hz), 2.75 (t, 2H, J=5.8 Hz), 2.64-2.54 (m, 4H), 1.76 (m, 2H); ESMS m/e: 262.2 $(M + H)^+$; Calc. Anál. para $C_{14}H_{19}N_3O_2$ (0.06 $CHCl_3$): C, 62.90; H, 7.16; N, 15.65. Encontrado: C, 63.20; H, 7.16, N, 15.65.

(4S)-3-[({3-[4-(3-AMINOFENIL)-1-PIPERIDINIL]PROPIL}AMINO)-CARBONIL]-4-(3,4-DIFLUOROFENIL)-6-(METOXIMETIL)-2-OXO-1,2,3,4-TETRAHIDRO-5-PIRIMIDINCARBOXILATO DE METILO: Una mezcla de 3.02 g (6.33 mmol) de 1-(4-nitrofenil) (6S)-6-(3,4-difluorofenil)-4-(metoximetil)-2-oxo-3,6-dihidro-1,5-(2H)-pirimidindicarboxilato de 5-metilo, 1.50 g (5.80 mmol) de 3-(4-(3-nitrofenil)-3,6-dihidro-1(2H)-piridinil)-1-propanamina, 7.94 g (75.5 mmol) de K_2CO_3 y 1.00 mL de metanol en 200 mL de diclorometano (bajo argón), se agitó a temperatura

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ambiente durante 1 hora. La mezcla de reacción se filtró y se concentró *in vacuo*. El residuo se disolvió en 100 mL de acetato de etilo y se lavó con 3 X 50 mL de una solución de NaOH acuosa al 5%, la capa orgánica se secó ($MgSO_4$) y se concentró *in vacuo*. El residuo se disolvió en 100 mL de etanol anhidro que contiene 0.50 g de Pd/C al 10% y la mezcla de reacción se agitó bajo un matraz de hidrógeno durante 24 horas. La mezcla de reacción se pasó a través de una columna de agente de filtración de Celite 545, se lavó con etanol, el filtrado se secó ($MgSO_4$) y se concentró *in vacuo*. El residuo se purificó por cromatografía de columna (sílice, 9.5:0.5, diclorometano:metanol + isopropilamina al 1%) para producir el compuesto deseado: RMN ^1H (400 MHz, $CDCl_3$) 7.80 (s, 1H), 7.22-7.02 (m, 2H), 6.95 (t, J=8.70 Hz, 1H), 6.63-6.44 (m, 4H), 4.56 (Abq, 2H), 3.62 (s, 3H), 3.33 (s, 3H), 3.32-3.20 (m, 4H), 2.96 (br s, 2H), 2.33 (t, J=7.50 Hz, 2H), 2.11-1.94 (m, 3H), 1.81-1.64 (m, 4H); ESMS m/e: 572.3 $(M + H)^+$.

4-[3-(ISOBUTIRILAMINO)FENIL]-3,6-DIHIDRO-1(2H)-PIRIDINCARBOXILATO DE TERT-BUTILO: En una solución de 4.00 g (16.0 mmol) de 4-(3-aminofenil)-3,6-dihidro-1(2H)-piridincarboxilato de tert-butilo y 5.60 mL (32.0 mmol) de diisopropiletilamina en 100 mL de diclorometano, se adicionó lentamente 1.90 mL (19.0 mmol) de cloruro de isobutirilo. La mezcla de

reacción se agitó a temperatura ambiente durante 2 horas, se lavó con agua, se secó ($MgSO_4$), y se concentró *in vacuo*. El residuo se purificó por cromatografía de columna (sílice, 50:46:3:1, hexanos:diclorometano:metanol:isopropilamina) para producir 2.90 g (rendimiento 52.0%) del producto deseado: RMN ^1H (400 MHz, $CDCl_3$) 7.69 (s, 1 H), 7.34 (d, 1 H, J=7.8 Hz), 7.27 (t, 1H, J=7.8 Hz), 7.11 (d, 1H, J=7.8 Hz), 6.04 (s, 1H), 4.05 (s, 2H), 3.62 (t aparente, 2 H, J=4.9 Hz), 2.51 (m, 3H), 1.49 (s, 9H), 1.25 (d, 6H, J=7.4 Hz); ESMS m/e: 345.5 $(M + H)^+$. Calc. Anál. para $C_{20}H_{28}N_2O_3$ + 0.175 $CHCl_3$: C, 66.33; H, 7.77; N, 7.67. Encontrado: C, 66.20; H, 7.41, N, 7.88.

4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINCARBOXILATO DE TERT-BUTILO: Una mezcla de 2.90 g (8.40 mmol) de 4-[3-(isobutirilamino)fenil]-3,6-dihidro-1(2H)-piridincarboxilato de tert-butilo y 0.80 g de Pd/C de rendimiento al 10% en 100 mL de etanol se agitó bajo un matraz de hidrógeno durante 24 horas. La mezcla de reacción se pasó a través de una columna de agente de filtración de Celite 545, el filtrado se secó ($mgSO_4$) y se concentró *in vacuo*. El residuo se purificó por cromatografía de columna (sílice, 9.5:0.5, diclorometano:metanol + isopropilamina al 1%) para producir 2.40 g (rendimiento 84%) del producto deseado: RMN ^1H (400 MHz, $CDCl_3$) 7.49-7.44 (m, 2H), 7.24 (t, 1H, J=7.6 Hz), 6.93 (d,

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1H, J=7.6 Hz), 4.20-4.10 (m, 2H), 2.86-2.45 (m, 4H), 1.86-1.75 (m, 4H), 1.48 (s, 9H), 1.24 (d, 6H, J=6.8 Hz); ESMS m/e: 345.2 $(M + H)^+$; Calc. Anál. para $C_{20}H_{30}N_2O_3$ +0.3 H_2O: C, 68.27; H, 8.77; N, 7.96. Encontrado: C, 68.25; H, 8.54, N, 7.84.

2-METIL-N-[3-(4-PIPERIDINIL)FENIL]PROPANAMIDA: En una solución agitada de 2.20 g (6.50 mmol) de 4-[3-(isobutirilamino)fenil]-1-piperidincarboxilato de tert-butilo en 100 mL de 1,4-dioxano a °C, se burbujeo gas de HCl durante 10 minutos. Se permitió a la mezcla de reacción calentarse a temperatura ambiente y se continuó el burbujeo del gas de HCl durante 1 hora. El solvente se retiro *in vacuo*, el residuo se disolvió en 50 Ml de agua y se neutralizó por adición de pelotillas de KOH. La solución acuosa se extrajo con 3 X 80 mL de diclorometano, los extractos orgánicos combinados se secaron ($MgSO_4$), se filtró y se concentró *in vacuo*. El residuo se purificó por cromatografía de columna (sílice, 9:1, diclorometano:metanol + isopropilamina al 1%) para producir 0.700 g (rendimiento 46.0%) del producto deseado: RMN ^1H (400 MHz, $CDCl_3$) 7.47 (s, 1H), 7.40 (d, 1H, J=7.8 Hz), 7.24 (t, 1H, J=7.8 Hz), 7.00 (d, 1H, J=7.8 Hz), 3.23-3.14 (m, 5H), 2.82-2.57 (m, 4H), 1.20 (d, 6H, J=6.8 Hz); ESMS m/e: 247.2 $(M + H)^+$. La sal de clorhidrato se utilizó para el análisis de

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combustión: Calc. Anál. para $C_{15}H_{22}N_2O$ + HCl + 0.15 $CHCl_3$: C, 60.51; H, 7.76; N, 9.32. Encontrado: C, 60.57; H, 7.83, N, 8.88.

3-(4-PIPERIDINIL)ANILINA: Una solución de HCl 4M en dioxano (25 mL) se adicionó a 4-(3-amino)fenil]-1-piperidincarboxilato de tert-butilo (2.60 g, 9.00 mmol) en diclorometano (250 mL). La mezcla de reacción se agitó a temperatura ambiente durante la noche, se concentró *in vacuo*, y el residuo se disolvió en agua (50 mL). La mezcla se neutralizó utilizando pelotillas de KOH y se extrajo con cloruro de metileno (3 X 50 mL). Los extractos orgánicos combinados se secaron ($MgSO_4$), se concentraron y cromatografiaron, para dar el producto deseado (1.03 g). RMN ^1H (400 MHz, $CDCl_3$) 7.01 (t, 1H, J=7.6 Hz), 6.62-6.54 (m, 3H), 3.16 (br d, 2H, J=10.3 Hz), 2.75 (dt, 2H, J=2.7, 12.3 Hz), 2.56 (tt, 1H, J=3.6, 12.3 Hz), 1.81 (br d, 2H, J=12.3 Hz), 1.65 (dq, 2H, J=4.0, 12.3 Hz); ESMS m/e: 177.2 $(M + H)^+$.

4-[4-NITROFENIL)-3,6-DIHIDRO-1(2H)-PIRIDINCARBOXILATO DE TERT-BUTILO: A un matraz RB de 25 mL, equipado con un condensador, se adicionó 4{[trifluorometil)sulfonil]oxi}-3,6-dihidro-1(2H)-piridincarboxilato de tert-butilo (1.0 g), ácido 4-nitrofenilborónico (0.71 g), carbonato de sodio (0.430 mL de solución 2M), cloruro de litio (0.382 g),

tetrakis(trifenilfosfin)-paladio (0) (0.173 g) y dimetiléter de etilenglicol (10 mL). La mezcla de reacción se sofoco con argón tres veces, después la mezcla de reacción se calentó a 100°C durante 3 horas. Después de enfriarse a temperatura ambiente, la mezcla de reacción se diluyó con cloruro de metileno (30 mL) y agua (30 mL) y la capa orgánica se separó. La capa acuosa se extrajo con cloruro de metileno (3x20mL) y los extractos orgánicos combinados se lavaron con NH_4Cl saturado (20 mL) y salmuera (20 mL), se secó sobre $MgSO_4$, y se concentró bajo presión reducida. El residuo se purificó por cromatografía (6:1=hexano:acetato de etilo con NH_3 al 1%), para producir el producto (0.55 g, 59.9%) como un aceite amarillo. El compuesto no es estable a temperatura ambiente y deberá de ser utilizado tan pronto como sea práctico: RMN ^1H (400 MHz, $CDCl_3$) 8.20 (d, 2H, J=8.6 Hz), 7.51 (d, 2H, J=8.6 Hz), 6.24 (m, 1H), 4.13 (m, 2H), 3.67 (t aparente, 2H, J=5.5 Hz), 2.55 (m, 2H), 1.49 (s 9H).

4-(4-NITROFENIL)-1,2,3,6-TETRAHIDROPIRIDINA: 4-(4-Nitrofenil)-1,2,3,6-tetrahidropiridina se preparó mediante un procedimiento similar a aquel utilizado para la preparación de 2-metil-N-[3-(4-piperidinil)fenil]propanamida utilizando gas de HCl y 4-(4-Nitrofenil)-3,6-dihidro-1(2H)-piridincarboxilato (130 mg) en dioxano (5.0 mL) a temperatura ambiente. La mezcla de reacció se concentró *in*

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vacuo para dar el producto crudo (69.8 mg), el cual se utilizó en la siguiente reacción sin purificación adicional.

Intermediarios de Oxazolidinona:

AMINO-(3,4-DIFLUOROFENIL)-ACETONITRILO: A través de una solución de 3,4-difluorobenzaldehido (25.0 g, 0.176 mol) en MeOH (500 mL) en un matraz de fondo redondo, se hizo burbujear gas de amoniaco durante dos horas a temperatura ambiente. El matraz fue después enfriado a 0°C y cianuro de trimetilsililo fue después lentamente adicionado. La mezcla de reacción se agitó durante 2 h, en el cual tiempo el análisis de TLC indicó que la reacción estaba completa (R_f = 0.35, 3:2 hexano/EtOAc). El solvente se removió *in vacuo* y el residuo se sometió a cromatografía de columna de instantánea sobre gel de sílice, para obtener el producto deseado, el cual se utilizó en la siguiente etapa sin purificación.

METIL ESTER DEL ACIDO AMINO-(3,4-DIFLUOROFENIL)ACETICO: En una solución bien agitada de amino-(3,4-difluorofenil)acetonitrilo (22.0 g, 0.130 mol), se adicionó una solución de HCl en MeOH (200 mL), a temperatura ambiente. La solución amarilla resultante se agitó atemperatura ambiente durante 10 h y se calentó a temperatura de reflujo durante 1.5 h. Después de enfriarse,

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el solvente se retiró *in vacuo* y el sólido amarillo resultante se disolvió en agua (200 mL). La solución acuosa fue después cuidadosamente basificada con una solución de NaOH al 20% a pH 9. La capa acuosa se extrajo con CH_2Cl_2 (3 x 100 mL). La capa orgánica se separó y secó sobre Na_2SO_4, se filtró y el solvente se removió *in vacuo*, para obtener el producto deseado que se utilizó en la siguiente etapa sin purificación.

2-AMINO-2-(3,4-DIFLUOROFENIL)-ETANOL: En una suspensión bien agitada de $LiAlH_4$ (4.7 g, 0.125 mol) en THF (120 mL), en un matraz de fondo redondo de 3 cuellos fijado con un condensador y un embudo de goteo, se adicionó una solución de metil éster del ácido amino-(3,4-difluorofenil)acético (10.0 g, 0.05 mol) en THF (100 mL) gota a gota, a 0°C. La suspensión café verdosa se calentó a temperatura de reflujo durante 2 h. La mezcla de reacción se enfrió a 0°C y después cuidadosamente se enfrió rápidamente en forma secuencial con 5 mL de agua, 5 mL de NaOH 3N, seguidos por 15 mL de agua. La suspensión resultante se filtró a través de un embudo de vidrio sinterizado. A la torta de filtro se adicionaron 100 mL de Et_2O y la suspensión se calentó a temperatura de reflujo durante 20 minutos. La suspensión se filtró y los filtrados combinados se secaron sobre $MgSO_4$, se filtró y se removió el solvente *in vacuo*. Se obtuvo 2-amino-2-(3,4-

difluorofenil)-etanol como un jarabe vidrioso amarillo que se utilizó en la siguiente etapa sin purificación adicional.

TERT-BUTIL ESTER DEL ACIDO [1-(3,4-DIFLUOROFENIL)-2-HIDROXI-ETIL]-CARBAMICO: En una solución de 2-amino-2-(3,4-difluorofenil)-etanol (8.6 g, 49.7 mmol) en $CHCl_3$ (150 mL) a 0°C, se adicionó una solución de dicarbonato de di-tert-butilo (11.4 g, 52.0 mmol) en $CHCl_3$ (50 mL) en una porción y la solución resultante se agitó durante la noche a temperatura ambiente. El solvente se removió *in vacuo* y el residuo se sometió a cromatografía de columna sobre gel de sílice (2:1 hexano:EtOAc seguido por EtOAc), para obtener tert-butil éster del ácido [1-(3,4-difluorofenil)-2-hidroxi-etil]carbámico como un sólido blanco (10.0 g, rendimiento 74%).

(+)-4-(3,4-DIFLUOROFENIL)-OXAZOLIDIN-2-ONA: En una suspensión bien agitada de NaH (1.1 g, 45.8 mmol) en THF (40 mL) a temperatura ambiente, se adicionó una solución de tert-butil éster del ácido [1-(3,5-difluorofenil)-2-hidroxi-etil]carbámico (5.0 g, 18.3 mmol) en THF (20 mL), vía un embudo de goteo, a temperatura ambiente. La suspensión resultante se agitó durante 3 h y después cuidadosamente se enfrió rápidamente con 10 mL de agua. La mezcla bifásica se extrajo con 100 mL de Et_2O, se lavó con salmuera, se filtró

y el solvente se removió *in vacuo*. El residuo gomoso así obtenido, se purificó por cromatografía de columna sobre gel de sílice (R_f = 0.15, 3:2 hexano:EtOAc), para obtener 4-(3,5-difluorofenil)-oxazolidin-2-ona, como un sólido escamoso blanco (2.8 g, rendimiento 77%). P.F 81-83°C; RMN ^1H (300 MHz, $CDCl_3$) 7.23-7.03 (m, 3H), 6.08 (br s, 1H), 4.94 (dd, J=6.6 Hz, J=8.7 Hz, 1H), 4.73 (t, J=8.7 Hz, 1H), 4.13 (dd, J=6.6 Hz, J=8.7 Hz, 1H). Los enantiómeros se separaron por CLAP en una columna Chiracel OD (20 x 250 mm), utilizando 80% de hexano/20% de alcohol isopropílico como el sistema eluyente a 12.0 mL/min (U.V 254 nm). Los tiempos de retención para los dos isómeros fueron de 16.19 min y 20.08 min, respectivamente.

(4S)-4-(3,4-DIFLUOROFENIL)-2-OXO-1,3-OXAZOLIDIN-3-CARBOXILATO DE 4-NITRODFENILO: En una suspensión de NaH (0.14 g, 5.30 mmol) en 20 mL de THF anhidro bajo argón, una solución de (+)-4(3,4-difluorfenil)oxazolidin-2-ona (0.88 g, 4.42 mmol) en THF, se adicionó gota a gota (embudo de goteo). La suspensión resultante se agitó a temperatura ambiente durante 30 minutos. Esta suspensión fue después adicionada gota a gota, vía una cánula en otro matraz de fondo redondo que contiene una solución de 4-nitrofenilcloroformato (1.11 g, 5.30 mmol) en 25 mL de THF y se enfrió a -78°C en un periodo de 15 minutos. Se continuó la agitación durante 2 h

después de las cuales el solvente se retiró y el residuo se purificó por cromatografía de columna en gel de sílice con 1:1 hexano/CH_2Cl_2 seguido por CH_2Cl_2 (R_f = 0.4, CH_2Cl_2), para obtener el producto deseado como un sólido blanco (1.55 g, rendimiento 86%).

En forma similar, siguiendo el procedimiento anterior, 4-nitrofenil éster del ácido 4-(3,5-difluorofenil)-2-oxo-oxazolidin-3-carboxílico y 4-nitrofenil éster del ácido 4-(3,4,5-trifluorofenil)-2-oxo-oxazolidin-3-carboxílico, se obtuvieron al sustituir 3,4-difluorobenzaldheido en la primera etapa con 3,5-difluorobenzaldehido o 3,4,5-trifluorbenzaldehido, respectivamente. Los enantiómeros de oxazolidinona se resolvieron por CLAP en una columna Chiracel OD (como en el ejemplo previo) y los carbamatos de 4-nitrofenilo se prepararon utilizando 4-nitrofenilcloroformato.

(4S)-4-(3,5-DIFLUOROFENIL)-2-OXO-1,3-OXAZOLIDIN-3-CARBOXILATO DE 4-NITROFENILO: Siguiendo el procedimiento para la síntesis de 4-nitro-fenil éster del ácido 4-(3,4-difluorofenil)-2-oxo-oxazolidin-3-carboxílico, 3,5-difluorobenzaldehido produjo el producto deseado.

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RMN ^1H (400 MHz, $CDCl_3$) 8.26 (d, 2H, J=9.3 Hz), 7.33-6.81 (m, 5H), 5.41 (dd, 1H, J=4.1, 8.7 Hz), 4.81 (t, 1H, J=9.3 Hz, 1H), 4.33 (dd, 1H, J=4.1, 9.3 Hz); Calc. Anál. para $C_{16}H_{10}F_2N_2O_6$+0.2EtOAc: C,52.84; H, 3.06; N, 7.34. Encontrado: C, 53.26; H, 2.83; N, 7.73.

(4S)-2-OXO-4-(3,4,5-TRIFLUOROFENIL)-1,3-OXAZOLIDIN-3-CARBOXILATO DE 4-NITROFENILO: Siguiendo el procedimiento para la síntesis de 4-nitro-fenil éster del ácido 4-(3,4-difluorofenil)-2-oxo-oxazolidin-3-carboxílico, 3,4,5-trifluorobenzaldehido produjo el producto deseado.

RMN ^1H (400 MHz, $CDCl_3$) 8.27 (d, 2H, J=9.0 Hz), 7.31 (d, 2H, J=9.0 Hz), 7.11-7.02 (m, 2H), 5.37 (dd, 1H, J=4.1, 9.0 Hz), 4.81 (t aparente, 1H, J=9.0 Hz), 4.33 (dd, 1H, J=4.1, 9.0 Hz); Calc. Anál. para $C_{16}H_9F_3N_2O_6$: C, 50.27; H, 2.37; N, 7.33. Encontrado: C, 50.56; H, 2.50; N, 7.49.

1-(3,4-DIFLUOROFENIL)-2-METIL-2-HIDROXIPROPILAMINA: En una solución bien agitada de 2-amino-2-(3,4-difluorofenil)acetato (10.5 g, 52.19 mmol) en éter anhidro (200 mL) a 0°C, se adicionó una solución de bromuro de metilmagnesio (3M, 87 mL, 261 mmol) en éter, se adicionó durante 10 minutos. La mezcla de reacción se agitó a 0°C durante 2.5 h y se le dejó calentar a temperatura ambiente. Después de 12

h, la mezcla de reacción fue cuidadosamente vaciada en una mezcla de hielo (300 g) y cloruro de amonio acuoso saturado (50 g). La capa de éter se separó y la capa acuosa se extrajo con más éter (4 X 200 mL). Los extractos combinados se secarón con sulfato de magnesio y se evaporó el solvente. El producto crudo se purificó por columna de cromatografía de columna en gel de sílice, utilizando cloroformo/metanol/amonio 2M en metanol (1000:20:10, 1000:40:20, 1000:80:40) como el eluyente para dar el cproducto como un aceite (6.5 g, rendimiento 62%), el cual fue utilizado en la siguiente etapa sin purificación adicional.

4-(3,4-DIFLUOROFENIL)-5,5-DIMETIL-2-OXO-OXAZOLIDINA: Una mezcla de 1(3,4-difluorofenil)-2-metil-2-hidroxipropilamina (3.00 g, 14.9 mmol) y carbonildiimidazol (2.418 g, 14.9 mmol) en diclorometano (150 mL), se calentó a temperatura de reflujo durante 36 h y se evaporó el solvente. El residuo se purifico por cromatografía de columna en gel de sílice, utilizando cloroformo/acetato de etilo (9:1) para dar el producto como un aceite viscoso que solidifica en posición vertical (1.80 g, rendimiento 50%). El producto se utilizó en la siguiente etapa sin caracterización adicional.

4-(3,4-DIFLUOROFENIL)-5,5-DIMETIL-2-OXO-1,3-OXAZOLIDIN-3-CARBOXILATO DE 4-NITROFENILO: En una suspensión agitada de

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hidruro de sodio (suspensión al 60% en 203 mg de parafina, 1.4 eq.) en THF (20 mL) a 0°C, una solución de 4-(3,4-difluorofenil)-5,5-dimetil-2-oxo-oxazolidina (870 mg, 3.622 mmol) en THF (5 mL), se adicionó seguida de agitación durante 30 minutos. Esta suspensión se adicionó a una solución de 4-nitrofenil cloroformato (950 mg, 4.71 mmol) en THF (20 mL) a -78°C bajo argón y se continuó la agitación durante 2 h. Esta fue lentamente calentada a temperatura ambiente y después de 4 h se evaporó el solvente. El residuo se mezclo con diclorometano (150 mL), se lavó con hidróxido de sodio 0.05 N (3 X 10 mL), y se secó (sulfato de sodio). El solvente se evaporó y el residuo se purificó por cromatografía de columna en gel de sílice, utilizando cloroformo/acetato de etilo (9:1) como el eluyente, para dar el producto como un polvo blanco (860 mg, rendimiento 59%). RMN ^1H (400 MHz, $CDCl_3$) 8.24 (d, 2H, J=9.0 Hz), 7.29-6.97 (m, 5H), 5.04 (s, 1H), 1.09 (s, 6H); Calc. Anál. para $C_{18}H_{14}F_2N_2O_6$+0.2% de H_2O: C, 54.61; H, 3.67; N, 7.08. Encontrado: C, 54.89; H, 3.59; N, 7.41.

(3,4-DIFLUOROFENIL)-N-(DIFENILMETILEN)METANAMINA: En una solución de 3,4-difluorbencilamina (9.8 g, 69 mmol) y benzofenona (13.0 g, 71.0 mmol) en tolueno (200 mL), se adicionó una cantidad catalítica de $BF_3.OEt_2$ y la solución resultante se calentó a temperatura de reflujo durante 12 h.

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La mezcla de reacción se concentró *in vacuo*, produciendo un aceite (21 g, >95%), el cual fue caracterizado por análisis de RMN y sometido a la siguiente reacción sin ninguna purificación adicional. RMN ^1H (400 MHz, $CDCl_3$) 4.57 (s, 2H), 7.80-6.80 (m, 13H).

1-(3,4-DIFLUOROFENIL)-1-[(DIFENILMETILEN)AMINO]PROPAN-2-OL: En una solución de benzhidrilinden-(3,4.difluoro-bencil)-amina 821 g, 69 mmol) en 250 ml de THF seco, se adicionó tert-butillitio (1.7 M, 60 ml) gota a gota y la solución resultante se agitó a -78°C durante 0.5 h. A la solución se adicionó acetaldehido (10 ml, 180 mmol) en 100 ml de THF y la solución se agitó a -78°C durante 2 h y 25°C durante 1 h. La mezcla de reacción se enfrió rápidamente al adicionar salmuera. La mezcla de reacción se diluyo con 500 ml de ET_2O y se lavó con salmuera. La capa orgánica se secó sobre Na_2SO_4 y se concentró *in vacuo* para dar un aceite, el cual se tomo en la siguiente etapa sin ninguna purificación adicional. RMN ^1H ($CDCl_3$) 1.04 (d, 3H), 2.77 (br s, 1H), 4.08 (m, 1H), 4.15 (d, 1H), 7.80-6.80 (m, 13H).

1-AMINO-1-(3,4-DIFLUORO-FENIL)PROPAN-2-OL: Una solución de producto crudo del procedimiento previo y $MeONH_2.HCl$ (10 g, 120 mmol), se diluyó en 200 ml de MeOH y se agitó durante 12 h. La mezcla de reacción se concentró *in vacuo*, produciendo solamente un residuo aceitoso, el cual se volvió a disolver

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en 200 ml de EtOAc y se lavó con salmuera. La capa orgánica se concentró *in vacuo* para producir una mezcla aceitosa, la cual se sometió a cromatografía de columna [NH_3 al 5% (2.0 M en MeOH) en $CHCl_3$], para producir el producto deseado (8.8 g, rendimiento 68% de 3,4-difluorobencilamina) como una mezcla de diastereómeros. RMN ^1H ($CDCl_3$) (~ 4:1 mezcla de los diastereómeros) 1.02 (d, J=6.0 Hz, 3 H), 1.04 (d, J=6.3 Hz, 3 H), 2.10 (br, 6 H), 3.56-3.69 (m, 2 H), 3.88-3.92 (m, 2 H), 7.02-7.17 (m, 6 H).

TERT-BUTIL ESTER DEL ACIDO [1-(3,4-DIFLUOROFENIL)-2-HIDROXI-PROPIL]CARBAMICO: En una solución de 1-amino-1(3,4-difluorofenil)-propan-2-ol (13.1 g, 70.21 mmol) en $CHCl_3$ (150 mL) a 0°C, se adicionó una solución de dicarbamato de di-tert-butilo (19.3g, 87.6 mmol) en $CHCl_3$ (50 mL) en una porción y la solución resultante se agitó durante la noche a temperatura ambiente. Se removió el solvente *in vacuo* y el residuo resultante se sometió a cromatografía de columna en gel de sílice (2:1 hexano-EtOAc seguido por EtOAc) para obtener tert-butil éster del ácido [1-(3,4-difluorofenil)-2-hidroxi-propil]carbámico como un aceite viscoso (18.4 g, rendimiento 91%). RMN ^1H ($CDCl_3$) (~ 4:1 mezcla de los diastereómeros) 1.05 (d, J=6.6 Hz, 3 H), 1.25 (d, J=6.0 Hz, 3 H), 1.41 (br, 20 H), 3.92-4.19 (br, 2 H), 4.45-4.60 (m, 2 H), 5.41-5.49 (br, 2 H), 7.02-7.17 (m, 6H).

4-(3,4-DIFLUOROFENIL)-5-METIL-OXALIDIN-2-ONA: En una solución bien agitada de tert-butil éster del ácido [1-(3,4-difluorofenil)-2-hidroxi-propil]carbámico (0.43 g, 1.5 mmol) en THF (20 mL), se adicionó NaH al 95% (0.09 g, 3.8 mmol) a temperatura ambiente. Cuando la reacción se llevó a cabo en una gran escala (> 5 g), 1.0 equivalente de KH y 1.5 eq. De NaH se utilizaron como la base. La suspensión resultante se agitó durante 3 h a aproximadamente 35°C (baño de agua caliente) y después se enfrió rápidamente en forma cuidadosa con hielo. La mezcla bifásica se extrajo con 100 mL de EtOAc, se lavó con salmuera, se secó sobre Na_2SO_4, se filtró y el solvente se retiró *in vacuo*. Los dos diasterómeros fueron separados por cromatografía de columna sobre gel de sílice (Primer isómero: 0.16 g, R_f = 0.6, 3:1 hexano-EtOAc; segundo isómero: 0.18 g, R_f = 0.5, 3:1 hexano-EtOAc). Experimentos NOE sugirieron que el primer diaterómero tiene el grupo metilo y arilo en configuración trans, mientras que el segundo diasterómero tiene la relación cis entre los dos grupos. El espectro de RMN ^1H para el diasterómero trans es como sigue. RMN ^1H ($CDCl_3$) 1.49 (d, J=6.0 Hz, 3H), 4.37 (dq, J=6.0 Hz, J= 7.2 Hz, 1H), 4.45 (d, J=7.2 Hz, 1H), 6.63 (br s, 1H), 7.08-7.28 (m, 3H).

4-NITRO-FENIL ESTER DEL ACIDO 4-(3,4-DIFLUOROFENIL)5-METIL-2-OXO-OXAZOLIDIN-3-CARBOXILICO: En una solución de uno de los diaterómeros de 4-(3,4-difluorofenil)-5-metil.oxazolidin-2-ona (0.97 g, 4.55 mmol) en 60 mL de THF, se adicionó una solución de n-butillitio en hexano (3.06 mmol, 4.9 mmol) gota a gota, vía una jeringa bajo atmósfera de argón a -78°C. La solución amarilla resultante se agitó a -78°C durante 40 minutos. Después, esta solución se adicionó gota a gota vía una cánula dentro de otro matraz de fondo redondo que contiene una solución de 4-nitrofenil-cloroformato (1.03 g, 5.1 mmol) en 60 mL de THF, se enfrió a -78°C, durante un período de 15 minutos. Después de cinco minutos, el matraz se retiró del baño de enfriamiento y se continuó agitando durante 1 h. La mezcla de reacción se enfrió rápidamente al adicionar hielo y se extrajo con EtOAc. Los extractos orgánicos se lavaron con salmuera y la capa orgánica se secó sobre Na_2SO_4. Se retiró el solvente después de la filtración y el residuo se purificó por cromatografía de columna en gel de sílice con 1:1 hexano/CH_2Cl_2 seguida por CH_2Cl_2 para dar el compuesto deseado.

Las configuraciones relativas de los isómeros cis y trans se asignaron en base de los análisis de RMN ^1H de los derivados de p-nitrofeniloxicarbonilo respectivos. Para el isómero trans, un NOE se observó entre los protones del

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grupo metilo C-5 y el protón en C-4. No se observó ningún NOE entre los protones en las posiciones C-4 y C-5 de éste isómero, lo cual fue después asignado con estereoquímica trans. Para el isómero cis, no se observó ningún NOE entre los protones del grupo metilo C-5 y el protón en C-4. Sin embargo, se observó un NOE entre los protones en las posiciones C-4 y C-5, conduciendo a asignar a éste con estereoquímica del isómero cis. Las constantes de acoplamiento vecinal de los protones C-4 de cis (J=7.8 Hz) y trans (J=5.1 Hz),son también consistentes con los valores reportados para oxazolidinonas similares, y fueron así útiles en elaborar las asignaciones estereoquímicas (Dondoni, A.; Perrone, D.; Semola, T. Synthesis 1995, 181).

Los enantiómeros de los disterómeros se separaron por CLAP al utilizar una columna Chiracel OD (20 x 250 mm) con 80% de hexano/ 20% de alcohol isopropílico/0.1 % de dietilamina como el sistema eluyente (12 mL/min) bajo condiciones isocráticas (U.V. 254 nm).

A fin de asignar las configuraciones absolutas en los centros esterogénicos de los anillos de oxazolidinona, una nueva ruta sintética se designó, la cual emplea un sustrato enantioméricamente puro derivado del grupo quiral. (S)-(+)-metil lactato comercialmente disponible se convirtió en su

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pirrolidinamida de acuerdo al método de Martin et al (Martin, R.; Pascual, O.; Romea, P.; Rovira, R.; Urpi, F.; Vilarrasa, J. Tetrahedron Lett. 1997, 38, 16333). Enseguida de la protección del grupo hidroxi de (2S)-1-oxo-1-(1-pirrodinil)-2-propanol a un grupo de TBDMS, el tratamiento de (1S)-1-metil-2-oxo-2-(1-pirrolidinil)etil éter de butil(dimetil)sililo con 3,4-difluorofenillitio produjo (2S)-2-{[tert-butil(dimetil)silil]oxi}-1-(3,4-difluorofenil)-1-propanona como el producto solo, el cual fue después convertido a (2S)-2-{[tert-butil(dimetil)-silil]oxi}-1-(3,4-difluorofenil)-1-propano oxima. La reducción del (2S)-2-{[tert-butil(dimetil)silil]oxi}-1-(3,4-difluorofenil)-1-propano oxima con $LiAlH_4$, N-acilación, y base, indujo a la ciclización proveyendo disterómeros de oxazolidinona, los cuales se separarón por cromatografía de columna instantánea. La pureza enentiomérica de éstos isómeros se confirmó por análisis de cLAP quiral y sus configuraciones relativas se asignaron por comparación de sus espectros de RMN ^1H con aquellos de los isómeros racémicos. Como las configuraciones absolutas en C-5 del ácido láctico derivado de oxazolidinona descritas anteriormente es (S), el centro C-4 en compuestos trans, también tiene la configuración (S). Por consiguiente, las configuraciones absolutas para los centros esterogénicos en los compuestos cis están asignados por consiguiente como (4R, 5S).

(4S,5R)-4-(3,4-DIFLUOROFENIL)-5-METIL-2-OXO-1,3-OXAZOLIDINA-3-CARBOXILATO DE 4-NITROFENIL: RMN ^1H (400 MHz, $CDCl_3$) 8.25 (d, 2H, J=8.8 Hz), 7.30-6.99 (m, 5H), 5.35 (d, 1H, J=7.7 Hz), 5.07 (quinteto aparente, 1H), 1.17 (d, 3H, J=6.5 Hz); Calc. Anál. para $C_{17}H_{12}F_2N_2O_6$+0.5 de H_2O: C, 52.72; H, 3.38; N, 7.23. Encontrado: C, 53.09; H, 3.19; N, 7.50.

(+)-2-AMINO-3-(3,4-DIFLUORO)-FENIL-PROPAN-1-OL: (+)-3,4-difluorofenil alanina (1.0 g, 5.0 mmol) se adicionó en porciones pequeñas a una suspensión agitada de $LiAlH_4$ (0.480 g, 12.5 mmol) en THF (30 mL) a 0°C. La suspensión gris resultante fue después calentada a reflujo durante 2 horas. La mezcla de reacción se enfrió a 0°C y después se enfrió en forma rápida cuidadosamente en forma secuencial con agua (0.5 mL), 3 N NaOH (0.5 mL), y agua (1.50 mL). La suspensión resultante se filtró a través de un embudo de vidrio sinterizado. Se adicionó éter (50 mL) a la torta de filtro y la suspensión se calentó a temperatura de reflujo durante 20 minutos. La suspensión se filtró y se combinó con el filtrado previo. Los orgánicos combinados se secaron sobre $MgSO_4$, se filtraron y el solvente se retiró *in vacuo*. 2-Amino-3-(3,4-difluoro)-fenil-propan-1-ol se obtuvo como un sólido blanco (0.500 g, 100%), el cual fue utilizado en la siguiente etapa sin purificación adicional.

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TERT-BUTIL ESTER DEL ACIDO (+)-[1-(3,4-DIFLUOROBENCIL)-2-HIDROXI-ETIL]CARBAMICO: Una solución de dicarbamato de di-tert-butilo (0.640 g, 2.90 mmol) en $CHCl_3$ (10 mL) se adicionó en una porción a una solución de (+)-2-amino-3-(3,4-difluoro)-fenil-propan-1-ol (0.500 g, 2.62 mmol) en $CHCl_3$ (20 mL) a 0°C y la solución resultante se agitó durante la noche a temperatura ambiente. Se retiró el solvente *in vacuo* y se cromatografio el residuo (2:1 hexano-EtOAc, seguido por EtOAc), dando tert-butil éster del ácido (+)-[1-(3,4-difluorobencil)-2-hidroxi-etil]-carbámico como un sólido blanco (0.640 g, 99%).

(+)-4-(3,4-DIFLUORO-BENCIL)-OXAZOLIDIN-2-ONA: Una solución de tert-butil éster del ácido (+)-[1-(3,4-difluorobencil)-2-hidroxi-etil]-carbámico (1.00 g, 4.00 mmol) en THF (10 mL), se adicionó vía un embudo de goteo a una suspensión agitada de NaH al 95% (0.12 g, 5.0 mmol) en THF (20 mL) a temperatura ambiente. La suspensión resultante se agitó durante 3 h y después se enfrió en forma rápida cuidadosamente con agua (10 mL). La mezcla bifásica se extrajo con Et_2O (50 mL), se lavó con salmuera, se filtró y el solvente se retiró *in vacuo*. El residuo gomoso resultante se purificó por cromatografía de columna (R_f = 0.25, 3:2

hexano-EtOAc), para dar el producto deseado como un sólido blanco (0.320 g, 76%).

4-NITRO-FENIL ÉSTER DEL ÁCIDO (+)-4-(3,4-DIFLUORO-BENCIL)-OXAZOLIDIN-2-ONA-3-CARBOXÍLICO: Una solución de (+)-4-(3,4-difluoro-bencil)-oxazolidin-2-ona (0.210 g, 1.0 mmol) en THF (10 mL) se adicionó gota a gota vía un embudo de goteo a una suspensión agitada de NaH (30.0 mg, 1.30 mmol) en THF anhidro (10 mL) bajo argón. La suspensión resultante se agitó a temperatura ambiente durante 30 minutos. Esta suspensión fue después adicionada gota a gota vía una cánula a una solución de 4-nitrofenilcloroformato (0.300 g, 1.50 mmol) en THF (20 mL) a -78°C durante 15 minutos. Se continuó la agitación durante 2 h después de lo cual el solvente se retiró y el residuo se purificó por cromatografía de columna (1:1 hexano/CH_2Cl_2, seguido por CH_2Cl_2; R_f = 0.4, CH_2Cl_2), para dar el producto deseado como un sólido amarillo (0.350 g, 82%).

En forma similar, siguiendo el procedimiento anterior, 4-(4-fluorobencil)-2-oxo-1,3-oxazolidin-3-carboxilato de 4-nitrofenilo se obtuvo al sustituir (+)-3,4-difluorofenil alanina con p-fluorofenil alanina.

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4-(4-FLUOROBENCIL)-2-OXO-1,3-OXAZOLIDIN-3-CARBOXILATO DE 4-NITROFENILO: RMN ^1H (400 MHz, $CDCl_3$) 8.32 (d, 2H, J=9.3 Hz), 7.42 (d, 2H, J=8.9 Hz), 7.24-6.99 (m, 4H), 4.69-4.59 (m, 1H), 4.35 (t, 1H, J=8.6 Hz), 4.23 (dd, 1H, J=2.7, 9.3 Hz), 3.37 (dd, 1H, J=3.8, 13.6 Hz), 2.94 (dd, 1H, J=9.3, 13.6 Hz); Calc. Anál. para $C_{17}H_{13}FN_2O_6$: C, 56.67; H, 3.64; N, 7.77. Encontrado: C, 56.94; H, 3.76; N, 7.71.

2-[6-(4-FENIL-1-PIPERIDINIL)HEXIL]-1H-ISOINDOL-1,3(2H)-DIONA: Al matraz de RB de 500 ml se adicionó clorohidrato de fenilpiperidina (5 g, 25 mmol), N-(6-bromohexil)ftalimida (15.5 g, 50 mmol), N,N-diisopropiletilamina (21.8 ml, 125 mmol), yoduro de tetrabutilamonio (0.2 g), y dioxano (250 ml) a temperatura ambiente. La mezcla de reacción se agitó a 100°C durante 72 h. Se retiró el solvente *in vacuo* y el producto crudo se purificó por cromatografía instantánea (98:2 = cloroformo: amoniaco 2N en metanol) para producir 7.67 g del producto deseado (rendimiento 77%). RMN ^1H (400 MHz, $CDCl_3$) 7.78-7.79 (m, 2H), 7.74-7.65 (m, 2H), 7.32-7.14 (m, 5H), 3.69 (t, 2H, J=7.35 Hz), 3.06 (d, 2H, J=11.0 Hz), 2.02 (t, 2H, J=12.5 Hz), 1.82 (br s, 4H), 1.69 (t, 2H, J=6.3 Hz), 1.54 (br s, 2H), 1.37 (br s, 4H); ESMS m/e: 391.3 $(M + H)^+$; Calc. Anál. para $C_{25}H_{30}N_2O_2$+0.2 de H_2O: C, 76.19; H, 7.77; N, 7.11. Encontrado: C, 76.14; H, 7.38; N, 7.13.

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METODO I. Procedimiento general para la Preparación de 4-[4-3-aminofenil)-1-piperidinil]-1-(fenil)-1-butanonas sustituidas: Una mezcla de 4-(3-aminofenil)piperidina (2.0 mmol), 2.4 mmol de cloruro de fenilbutirilo sustituido apropiado (e.g., 4-cloro-4'-fenoxibutirofenona, 4-cloro-3',4'-dimetilbutirofenona, 4-cloro-4'-clorobutirofenona, -clorobutirofenona, 4-cloro-3',4'-dimetoxibutirofenona), 3.0 mmol de K_2CO_3 y 10 mg de 18-corona-16 en 5 mL de tolueno, se calentaron a 110°C durante 2.5 días. La mezcla de reacción se concentró y cromatografió en sílice (metanol al 5% en diclorometano) para dar el compuesto deseado:

4-[4-(3-AMINOFENIL)-1-PIPERIDINIL]-1-(4-FENOXIFENIL)-1-BUTANONA: Utilizando el Método I, se obtuvo el producto deseado. 305 mg; ESMS m/e: 415.4 $(M + H)^+$.

4-[4-(3-AMINOFENIL)-1-PIPERIDINIL]-1-(3,4-DIMETILFENIL)-1-BUTANONA: Utilizando el Método I, se obtuvo el producto deseado. 320 mg; ESMS m/e: 351.3 $(M + H)^+$.

4-[4-(3-AMINOFENIL)-1-PIPERIDINIL]-1-(4-CLOROFENIL)-1-BUTANONA: Utilizando el Método I, se obtuvo el producto deseado. 500 mg; Calc. Anál. para $C_{21}H_{25}ClN_2O$+0.3 de H_2O: C, 69.62; H, 7.12; N, 7.73. Encontrado: C, 69.63; H, 7.34; N, 7.60; ESMS m/e : 357.3 $(M + H)^+$.

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4-[4-(3-AMINOFENIL)-1-PIPERIDINIL]-1-FENIL-1-BUTANONA: Utilizando el Método I, se obtuvo el producto deseado. 250 mg; Calc. Anál. para $C_{21}H_{25}N_2O$+0.2 de H_2O: C, 77.36; H, 8.16; N, 8.59. Encontrado: C, 77.55; H, 8.12; N, 8.75; ESMS m/e : 323.3 $(M + H)^+$.

4-[4-(3-AMINOFENIL)-1-PIPERIDINIL]-1-(2,4-DIMETOXIFENIL)-1-BUTANONA: Utilizando el Método I, se obtuvo el producto deseado. 330 mg; Calc. Anál. para $C_{23}H_{30}N_2O_3$+0.5 de H_2O: C, 70.56; H, 7.98; N, 7.16. Encontrado: C, 70.69; H, 7.87; N, 6.99; ESMS m/e : 383.3 $(M + H)^+$.

METODO II. Procedimiento General para la Acilación o Sulfonilación de las 4-[4-(3-Aminofenil)-1-piperidinil]-1-(4-fenil)-1-butanonas Sustituidas: Una mezcla de 1 equivalente de una 4-[4-(3-aminofenil)-1-piperidinil]-1-(4-fenil)-1-butanona, 1.5 equivalentes de un cloruro ácido o un cloruro de sulfonilo, y 5 equivalentes de diisopropil-etilamina, en diclorometano se agitó a temperatura ambiente durante dos días. La mezcla de reacción se aplicó a una placa de TLC preparatoria y se eluyó con diclorometano: metanol (15:1, que contenía isopropilamina al 1%) para dar el producto deseado.

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METODO III. Procedimiento general para la Preparación de las 4-N-(3{1-[4-(fenil)-4-oxobutil]-4-piperidinil}acetamidas sustituidas: Una mezcla de N-[3-(4-piperidinil)fenil]-acetamida (1.0 eq) y una clorobutirofenona sustituida en arilo (2.0 eq), K_2CO_3 (5.0 eq), diisopropil-etilamina (3.0 eq) y yoduro de tetrabutilamonio(cat. 5-10%) en dioxano (0.5 a 1.0 M), se calentarón a temperatura de reflujo durante 16 h. La mezcla de reacción se filtró y se concentró *in vacuo*. El producto crudo se cromatografió utilizando TLC preparatoria de sílice (cloroformo: metanol que contenía isopropil amina al 0.5%) para dar el producto deseado.

Ejemplo 1

N-(3-{1-[4-(3,4-DIMETILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)ACETAMIDA: Utilizando el Método III, se obtuvo el producto deseado. RMN ^1H ($CDCl_3$) 7.75 (s, 1H), 7.71 (d, 1H, J=7.6 Hz), 7.45 (d, 2H, J=7.2 Hz), 7.35 (s, 1H), 7.26-7.22 (m, 2H), 6.93 (d, 1H, J=7.6 Hz), 3.24-3.21 (m, 2H), 3.04 (t, 2H, J=7.0 Hz), 2.67-2.63 (m, 2H), 2.59-2.48 (m, 1H), 2.32 (s, 6H), 2.30-2.27 (m, 2H), 2.18 (s, 3H), 2.14-2.06 (m, 2H), 2.00-1.80 (m, 4H); ESMS m/e: 393.3 $(M + H)^+$.

Ejemplo 2

N-(3-{1-[4-(3,4-DIMETILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Una mezcla de 0.0500 g (0.200

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mmol) de 2-metil-N-[3-(4-piperidinil)fenil]propanamida, 0.100 g (0.480 mmol) de 4-cloro-3',4'-dimetilbutirofenona, 0.080 g (0.600 mmol) de K_2CO_3 y 0.090 g (0.600 mmol) de NaI en 5 mL de DMF, se calentó a temperatura de reflujo durante 18 horas. La mezcla de reacción se filtró, el filtrado se vació en 5 mL de agua y se lavó con 3 X 5 mL de acetato de etilo. Los extractos orgánicos combinados se secaron ($MgSO_4$), se concentró *in vacuo* y se purificó por TLC preparatoria (sílice; 9.5:0.5, diclorometano:metanol + isopropilamina al 1%) para producir 0.067 g (rendimiento 80%) del producto deseado: RMN ^1H (400 MHz, $CDCl_3$) 7.72 (d, 1H, J=8.0 Hz), 7.44 (s, 1H), 7.38 (d, 1H, J=8.0 Hz), 7.23-7.20 (m, 2H), 7.16 (s, 1H), 6.95 (d, 1H, J=6.8 Hz), 3.13-3.11 (m, 2H), 3.02 (t, 2H, J=7.0 Hz), 2.56-2.40 (m, 4H), 2.32 (s, 6H), 2.17-2.15 (m, 2H), 2.04-1.78 (m, 6H), 1.25 (d, 6H, J=6.8 Hz); ESMS m/e: 421.3 $(M + H)^+$.

Ejemplo 3

N-(3-{1-[4-(3,4-DIMETILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)CICLOHEXANOCARBOXAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.80-6.81 (m, 7H), 3.41-3.00 (m, 4H), 2.95-2.41 (m, 4H), 2.32 (s, 6H), 2.22-1.05 (m, 18H); ESMS m/e: 461.4 $(M + H)^+$.

Ejemplo 4

N-(3-{1-[4-(3,4-DIMETILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)-2FENILACETAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^{1}H (400 MHz, $CDCl_3$) 7.85-7.65 (m, 2H), 7.45-6.92 (m, 10H), 3.76 (s, 2H), 3.10-2.90 (m, 4H), 2.50-2.35 (m, 3H), 2.32 (s, 6H), 2.10-1.85 (m, 4H), 1.80-1.60 (m, 4H); ESMS m/e: 469.4 $(M + H)^+$.

Ejemplo 5

N-(3-{1-[4-(3,4-DIMETILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)-2-(3-METOXIFENIL)ACETAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^{1}H (400 MHz, $CDCl_3$) 7.76-7.65 (m, 2H), 7.38-7.12 (m, 6H), 6.95-6.80 (m, 3H), 3.82 (s, 3H), 3.70 (s, 2H), 3.10-2.90 (m, 4H), 2.50-2.38 (m, 3H), 2.32 (s, 6H), 2.10-1.85 (m, 4H), 1.80-1.60 (m, 4H); ESMS m/e: 499.4 $(M + H)^+$.

Ejemplo 6

N-(3-{1-[4-(3,4-DIMETILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)-2-METOXIACETAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^{1}H (400 MHz, $CDCl_3$) 7.80-7.75 (m, 2H), 7.50-7.38 (m, 2H), 7.34-6.90 (m, 3H), 4.00 (s, 2H), 3.51 (s, 3H), 3.30-2.95 (m, 4H), 2.70-2.50 (m, 3H), 2.32 (s, 6H), 2.15-1.80 (m, 8H); ESMS m/e: 423.3 $(M + H)^+$.

Ejemplo7

N-(3-{1-[4-(3,4-DIMETILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)METANOSULFONAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.82-7.10 (m, 7H), 3.41 (s, 3H), 3.40-2.85 (m, 4H), 2.82-2.35 (m, 5H), 2.32 (s, 6H), 2.22-1.80 (m, 6H); ESMS m/e: 429.3 $(M + H)^+$.

Ejemplo 8

N-(3-{1-[4-(3,4-DIMETILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)ETANOSULFONAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.75 (S, 1H), 7.71 (D, 1H, J=7.6 Hz), 7.30-7.09 (m, 4H), 7.02 (d, 1H, J=7.2 Hz), 3.36-3.05 (m, 6H), 2.77-2.52 (m, 3H), 2.32 (s, 6H), 2.15-1.82 (m, 8H), 1.37 (t, 3H, J=7.4 Hz); ESMS m/e: 443.3 $(M + H)^+$.

Ejemplo 9

N-(3-{1-[4-(4-CLOROFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)-ACETAMIDA: Utilizando el Método III, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.92 (d, 2H, J=8.8 Hz), 7.55-7.40 (m, 3H), 7.35 (s, 1H), 7.22 (t, 1H, J=8.0 Hz), 6.92 (d, 1H, J=8.0 Hz), 3.30-3.27 (m, 2H), 3.09 (t, 2H, J=7.0 Hz), 2.76-2.39 (m, 5H), 2.20 (s, 3H), 2.17-1.85 (m, 6H); ESMS m/e: 399.3 $(M + H)^+$.

Ejemplo 10

N-(3-{1-[4-(4-CLOROFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^{1}H (400 MHz, $CDCl_3$) 7.93 (d, 2H, J=8.6 Hz), 7.45 (d, 2H, J=8.6 Hz), 7.39 (d, 1H, J=7.2 Hz), 7.32 (s, 1H), 7.24 (t, 1H, J=7.8 Hz), 6.94 (d, 1H, J=8.4 Hz), 3.21-3.18 (m, 2H), 3.05 (t, 2H, J=7.0 Hz), 2.64-2.51 (m, 4H), 2.28-1.86 (m, 8H), 1.26 (d, 6H, J=6.8 Hz); ESMS m/e: 427.3 $(M + H)^+$.

N-(3-{1-[4-(4-CLOROFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)-CICLOHEXANOCARBOXAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^{1}H (400 MHz, $CDCl_3$) 7.93 (d, 2H, J=8.4 Hz), 7.55-7.19 (m, 5H), 6.93 (d, 1H, J=7.6 Hz), 3.25-3.00 (m, 4H), 2.65-2.45 (m, 4H), 2.30-1.50 (m, 18H); ESMS m/e : 467.3 $(M + H)^+$.

Ejemplo 12

N-(3-{1-[4-(4-CLOROFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)-2-FENILACETAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^{1}H (400 MHz, $CDCl_3$) 7.92 (d, 2H, J=8.4 Hz), 7.46-7.26 (m, 9H), 7.20 (t, 1H, J=7.6 Hz), 6.92 (d, 1H, J=7.6 Hz), 3.75 (s, 2H), 3.15-3.13 (m, 2H), 3.03 (t, 2H, J=7.0 Hz), 2.64-2.46 (m, 3H), 2.22-1.60 (m, 8H); ESMS m/e : 475.3 $(M + H)^+$.

Ejemplo 13

N-(3-{1-[4-(4-CLOROFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)-2-(3-METOXIFENIL)ACETAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.92 (d, 2H, J=8.4 Hz), 7.44 (d, 2H, J=8.4 Hz) 7.38 (s, 1H), 7.35-7.25 (m, 3H), 7.19 (t, 1H, J=7.8 Hz), 6.94-6.86 (m, 3H), 3.81 (s, 3H), 3.72 (s, 2H), 3.12-3.09 (m, 2H), 3.02 (t, 2H, J=6.8 Hz), 2.57-2.44 (m, 3H), 2.20-1.60 (m, 8H); ESMS m/e : 505.3 $(M + H)^+$.

Ejemplo 14

N-(3-{1-[4-(4-CLOROFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)-2-METOXIACETAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.93 (d, 2H, J=8.4 Hz), 7.50-7.25 (m, 5H), 6.98 (d, 1H, J=7.8 Hz), 4.01 (s, 2H), 3.57 (s, 3H), 3.30-3.15 (m, 2H), 3.06 (t, 2H, J=6.8 Hz), 2.70-2.50 (m, 3H), 2.35-1.80 (m, 8H); ESMS m/e : 429.3 $(M + H)^+$.

Ejemplo 15

N-(3-{1-[4-(4-CLOROFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)-METANOSULFONAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.95-6.96 (m,

8H), 3.48 (s, 3H), 3.28-2.90 (m, 6H), 2.80-2.57 (m, 3H), 2.38-1.86 (m, 6H); ESMS m/e : 435.2 $(M + H)^+$.

Ejemplo 16

N-(3-{1-[4-(4-CLOROFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)-ETANOSULFONAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.93 (d, 2H, J=8.2 Hz), 7.45 (d, 2H, J=8.2 Hz), 7.30-7.08 (m, 3H), 6.99 (d, 1H, J=7.6 Hz), 3.26-3.02 (m, 6H), 2.69-2.45 (m, 3H), 2.32-1.75 (m, 8H), 1.36 (t, 3H, J=7.4 Hz) ; ESMS m/e : 449.3 $(M + H)^+$.

Ejemplo 17

N-{3-[1-(4-OXO-4-FENILBUTIL]-4-PIPERIDINIL}FENIL)-ACETAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 8.10-6.80 (m, 9H), 3.40-2.95 (m, 4H), 2.85-2.20 (m, 3H), 2.19 (s, 3H), 2.15-1.70 (m, 8H); ESMS m/e: 365.3 $(M + H)^+$.

Ejemplo 18

2-METIL-N-{3-[1-(4-OXO-4-FENILBUTIL]-4-PIPERIDINIL}FENIL)-PROPANAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.99 (d, 2H, J=7.4 Hz), 7.57 (t, 1H, J=7.4 Hz), 7.48 (t, 2H, J=7.4 Hz), 7.45-7.20 (m, 2H), 7.24 (t, 1H, J=8.0 Hz), 6.94 (d, 1H, 8.0 Hz),

3.24-3.21 (m, 2H), 3.09 (t, 2H, J=7.0 Hz), 2.57-2.25 (m, 4H), 2.31-1.84 (m, 8H), 1.26 (d, 6H, J=7.2 Hz); ESMS m/e : 393.3 $(M + H)^+$.

Ejemplo 19

N-{3-[1-(4-OXO-4-FENILBUTIL]-4-PIPERIDINIL}FENIL)-2-FENILACETAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.98 (d, 2H, J=7.6 Hz), 7.65-7.15 (m, 11H), 6.92 (d, 2H, J=7.2 Hz), 3.74 (s, 2H), 3.20-2.95 (m, 4H), 2.65-2.40 (m, 3H), 2.25-1.70 (m, 8H); ESMS m/e : 441.3 $(M + H)^+$.

Ejemplo 20

2-(3-METOXIFENIL)-N-{3-[1-(4-OXO-4-FENILBUTIL]-4-PIPERIDINIL}FENIL)ACETAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.98 (d, 2H, J=7.6 Hz), 7.56 (t, 1H, J=7.62 Hz), 7.46 (t, 2H, J=7.6 Hz), 7.40 (s, 1H), 7.37-7.26 (m, 2H), 7.19 (t, 1H, J=7.8 Hz), 6.94-6.86 (m, 3H), 3.81 (s, 3H), 3.71 (s, 3H), 3.12-3.03 (m, 4H), 2.57-2.44 (m, 3H), 2.16-1.77 (m, 8H); ESMS m/e : 471.3 $(M + H)^+$.

Ejemplo 21

N-{3-[1-(4-(2,4-DIMETOXIFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)ACETAMIDA: Utilizando el Método III, se obtuvo el

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producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.82 (d, 1H, J=8.8 Hz), 7.54 (d, 1H, J=7.6 Hz), 7.33 (s, 1H), 7.22 (t, 1H, J=7.6 Hz), 6.93 (d, 1H, J=7.6 Hz), 6.53 (d, 1H, J=8.8 Hz), 6.46 (s, 1H), 3.90 (s, 3H), 3.86 (s, 3H), 3.48-3.27 (m, 2H), 3.05 (t, 2H, J=6.8 Hz), 2.90-2.68 (m, 2H), 2.65-2.38 (m, 3H), 2.25 (s, 3H), 2.18-1.80 (m, 6H); ESMS m/e : 425.3 $(M + H)^+$.

Ejemplo 22

N-(3-{1-[4-(2,4-DIMETOXIFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.98 (d, 1H, J=8.6 Hz), 7.41-7.37 (m, 2H), 7.24 (t, 1H, J=7.8 Hz), 6.96 (d, 1H, J=7.8 Hz), 6.54 (d, 1H, J=8.6 Hz), 6.46 (s, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 3.11-3.08 (m, 2H), 2.98 (t, 2H, J=7.2 Hz), 2.53-2.46 (m, 4H), 2.13-1.79 (m, 8H), 1.25 (d, 6H, J=6.8 Hz); ESMS m/e : 453.3 $(M + H)^+$.

Ejemplo 23

N-(3-{1-[4-(2,4-DIMETOXIFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)-2-FENILACETAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.85 (m, 12H), 3.89 (s, 3H), 3.86 (s, 3H), 3.74 (s, 2H), 3.22-2.90 (m, 4H), 2.64-2.40 (m, 3H), 2.25-1.70 (m, 8H); ESMS m/e : 501.3 $(M + H)^+$.

Ejemplo 24

N-(3-{1-[4-(2,4-DIMETOXIFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)-2-(3-METOXIFENIL)ACETAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^{1}H (400 MHz, $CDCl_3$) 7.82 (d, 1H, J=8.8 Hz), 7.48-7.15 (m, 5H), 6.95-6.80 (m, 3H), 6.58-6.45 (m, 2H), 3.89 (s, 3H), 3.86 (s, 3H), 3.81 (s, 3H), 3.72 (s, 2H), 3.25-2.95 (m, 4H), 2.65-2.40 (m, 3H), 2.30-1.95 (m, 4H), 1.93-1.72 (m, 4H); ESMS m/e : 531.3 $(M + H)^+$.

Ejemplo 25

N-(3-{1-[4-OXO-4-(4-FENOXIFENIL)BUTIL]-4-PIPERIDINIL}-FENIL)ACETAMIDA: Utilizando el Método III, se obtuvo el producto deseado. RMN ^{1}H (400 MHz, $CDCl_3$) 8.15-6.75 (m, 13H), 3.30-2.80 (m, 4H), 2.75-2.10 (m, 5H), 2.03 (s, 3H), 2.00-1.60 -(m, 6H); ESMS m/e : 457.3 $(M + H)^+$.

Ejemplo 26

2-METIL-N-(3-{1-[4-OXO-4-(4-FENOXIFENIL)BUTIL]-4-PIPERIDINIL}-FENIL)PROPANAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^{1}H (400 MHz, $CDCl_3$) 7.96 (d, 2H, J=8.8 Hz), 7.43-7.15 (m, 6H), 7.10-6.93 (m, 5H), 3.42-2.95 (m, 4H), 2.80-2.45 (m, 4H), 2.20-1.80 (m, 8H), 1.14 (d, 6H, J=68 Hz); ESMS m/e : 485.4 $(M + H)^+$.

Ejemplo 27

2-(3-METOXIFENIL)-N-(3-{1-[4-OXO-4-(4-FENOXIFENIL)BUTIL]-4-PIPERIDINIL}-FENIL)ACETAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.97 (d, 2H, J=8.8 Hz), 741-7.18 (m, 7H), 7.08-6.99 (m, 5H), 6.94-6.87 (m, 3H), 3.82 (s, 3H), 3.70 (s, 2H), 3.10-2.95 (m, 4H), 2.55-2.40 (m, 3H), 2.15-1.95 (m, 4H), 1.81-1.70 (m, 4H); ESMS m/e : 563.4 $(M + H)^+$.

Ejemplo 28

N'-(3-{1-[4-(4-CLOROFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)-N,N-DIMETILSULFAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.93 (d, 2H, J=8.8 Hz), 7.44 (d, 2H, J=8.8 Hz), 7.27 (s, 1H), 7.25-7.10 (m, 2H), 6.94 (d, 1H, J=7.6 Hz), 3.30-3.10 (m, 2H), 3.04 (t, 2H, J=6.8 Hz), 2.83 (s, 6H), 2.68-2.45 (m, 3H), 2.30-1.75 (m, 8H); ESMS m/e : 464.3 $(M + H)^+$.

Ejemplo 29

N-(3-{1-[4-OXO-4-(2-TIENIL)BUTIL]-4-PIPERIDINIL}-FENIL)-ACETAMIDA: Utilizando el Método III, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.90-6.78 (m, 7H), 3.22-2.88 (m, 4H), 2.69-2.25 (m, 5H), 2.02 (s, 3H), 2.00-1.64 (m, 6H); ESMS m/e : 371.2 $(M + H)^+$.

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Ejemplo 30

N-(3-{1-[4-(4-ISOPROPILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)ACETAMIDA: Utilizando el Método III, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 8.00-6.78 (m, 8H), 3.15-2.98 (m, 4H), 2.77-2.15 (m, 4H), 2.03 (s, 3H), 2.00-1.62 (m, 8H), 0.927 (d, 6H, J=6.0 Hz); ESMS m/e : 407.3 $(M + H)^+$.

Ejemplo 31

N-(3-{1-[4-(4-METILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)ACETAMIDA: Utilizando el Método III, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.90-6.80 (m,8H), 3.10-2.45 (m, 7H), 2.32 (s, 3H), 2.02 (s, 3H), 2.01-1.68 (m, 8H); ESMS m/e : 379.3 $(M + H)^+$.

Ejemplo 32

N-(3-{1-[4-(4-BROMOFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)-ACETAMIDA: Utilizando el Método III, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.90-6.80 (m, 8H), 3.30-3.05 (m, 4H), 270-2.45 (m, 3H), 2.05 (s, 3H), 1.98-1.65 (m, 8H); ESMS m/e : 444.0 $(M + H)^+$.

Ejemplo 33

N-(3-{1-[4-(3,4-DIMETILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)-2-PROPANSULFONAMIDA: Utilizando el Método II, se

obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.75 (s, 1H), 7.71 (d, 1H, J=7.6 Hz), 7.27-7.00 (m, 5H), 3.32-3.24 (m, 3H), 3.10-3.02 (m, 2H), 2.78-2.50 (m, 3H), 2.32 (s, 6H), 2.19-1.84 (m, 8H), 1.39 (d, 6H, J=6.8 Hz); ESMS m/e : 457.4 $(M + H)^+$.

Ejemplo 34

N-(3-{1-[4-OXO-4-(4-FENOXIFENIL)BUTIL]-4-PIPERIDINIL}-FENIL)-2-PROPANSULFONAMIDA: Utilizando el Método II, se obtuvo el producto deseado. RMN ^1H (400 MHz, $CDCl_3$) 7.97 (d, 2H, J=7.6 Hz), 7.44 (t, 2H, J=7.6 Hz), 7.27-7.00 (m, 9H), 3.35-2.96 (m, 5H), 2.69-2.45 (m, 3H), 2.14-1.79 (m, 8H), 1.39 (d, 6H, J=6.8 Hz); ESMS m/e : 521.4 $(M + H)^+$.

Ejemplo 35

N-(3-{1-[3-(4-CLOROFENIL)-3-METOXIPROPIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Una mezcla de 3-metoxi-3-(p-clorofenil9-1-cloropropano (27.4 mg, 0.125 mmol), 2-metil-N-[3-(4-piperidinil9fenil]propanamida (28.3 mg, 0.125 mmol), diisopropiletilamina (0.50 mL) y cantidad catalítica de yoduro de tetrabutilamonio en dioxano (2.0 mL), se agitó a 90°C durante 72 hrs. La mezcla de reacción se concentró a un volumen pequeño y se cromatografió utilizando placas de TLC preparativas [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dando N-(3-{1-[3-(4-clorofenil)-3-metoxipropil]-4-piperidinil}

fenil)-2-metilpropanamida (39.5 mg, rendimiento 73.8%) como un aceite espeso: RMN ^1H 7.48 (s, 1 H), 7.34-7.3 (m, 2H), 7.25 (m, 4H), 6.96 (d, 1H, J=7.4 Hz), 4.20 (dd aparente, 1H, J=5.9, 7.6 Hz), 3.2 (s, 3H), 3.04 (d, 1H, J=10.1 Hz), 2.99 (d, 1H, J=10.1 Hz), 2.49 (h, 4H, J=6.6 Hz), 2.20-2.10 (m, 4H), 1.82 (m, 4H), 1.25 (d, 6H, J=7.1 Hz); ESMS m/e: 429.4 $(M + H)^+$.

Ejemplo 36

N-(3-{1-[6-(1,3-DIOXO-1,3-DIHIDRO-2H-ISOINDOL-2-IL)HEXIL]-4-PIPERIDINIL}FENIL}-2-METILPROPANAMIDA: El método sintetico es el mismo como el descrito para 2-[6-(4-fenil-1-piperidinil)hexil]-1H-isoindol-1,3(2H)-diona. N-(3-{1-[1,3-dioxo-1,3-dihidro-2H-isoindol-2-il)hexil]-4-piperidinil}fenil)-2-metilpropanamida: 506 mg (rendimiento 56%); RMN ^1H (400 MHz, $CDCl_3$) 7.86-7.80 (m, 2H), 7.73-7.68 (m, 2H), 7.44 (s, 1H), 7.37 (d, 1H, J=8.3 Hz), 7.22 (t, 1H, J=7.7Hz), 6.96 (d, 1H, J=7.7 Hz), 3.69 (t, 2H, J=7.2 Hz), 3.01 (d aparente, 2H, J=11.3 Hz), 2.58-2.40 (m, 2H), 2.33 (m, 2H) 1.98 (dt, 2H, J=3.2, 11.3 Hz), 1.84-1.64 (m, 4H), 1.51 (q, 2H, J=7.1 Hz), 1.43-1.30 (m, 6H), 1.24 (d, 6H, J=6.8 Hz); ESMS m/e: 476.4 $(M + H)^+$.

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Ejemplo 37

N-{3-(1-(3-METOXI-3-FENILPROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Una mezcla de 3-metoxi-3-fenil-1-cloropropano (23.1 mg, 0.126 mmol), 2-metil-N-[3-(4-piperidinil)fenil]propanamida (28.3 mg, 0.126 mmol), diisopropiletilamina (0.50 mL) y una cantidad catalítica de yoduro de tetrabutilamonio en dioxano (2.0 mL), se agitó a 90°C durante 72 hrs. La cromatografía utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$ dió N-{3-[1-(3-metoxi-3-fenilpropil)-4-piperidini]fenil}-2-metilpropanamida (45.4 mg, rendimiento 91.2%) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 7.45 (S, 1 H), 7.34-7.25 (m, 5H), 7.25 (m, 2H), 6.96 (d, 1H, J=7.4 Hz), 4.20 (dd aparente, 1H, J=5.9, 7.6 Hz), 3.2 (s, 3H) ¡ 3.04 (d, 1H, J=10.1 Hz), 2.99 (d, 1H, J=10.1Hz), 2.49 (sept aparente, parcialmente oculto, 4H, J=6.6 Hz), 2.3-2.1 (m, 4H), 1.82 (m, 4H), 1.25 (d, 6H, J=7.1 Hz); ESMS m/e: 395.4 $(M + H)^+$.

Ejemplo 38

N-(3-{1-[4-(1,3-DIOXO-1,3-DIHIDRO-2H-ISOINDOL-2-IL)BUTIL]-4-PIPERIDINIL}FENIL)-2 -METILPROPANAMIDA: El método sintético es el mismo como el decrito para 2-[6-(4-fenil-1-piperidinil)hexil]-1H-isoindol-1,3(2H)-diona. N-(3-{1-[4-(1,3-dioxo-1,3-dihidro-2H-isoindol-2-il)butil]-4-piperidi-

nil}fenil)-2-metilpropanamida: 664 mg (rendimiento 74%); RMN ^1H (400 MHz, $CDCl_3$) 7.87-7.78 (m, 2H), 7.76-7.64 (m, 2H), 7.47 (s, 1H), 7.39 (d, 1H, J=7.6 Hz), 7.21 (t, 1H, J=8.1 Hz), 6.94 (d, 1H, J=7.6 Hz), 3.72 (t, 2H, J=6.8 Hz), 3.37-3.22 (m, 2H) , 3.0 (d aparente, 2H, J=10.7 Hz), 2.75 (q, 2H, J=7.0 Hz), 2.64-2.33 (m, 4H), 1.99 (dt, 2H, J=2.6, 11.7 Hz), 1.86-1.65 (m, 2H), 1.63-1.50 (m, 2H), 1.23 y 1,21 (dble d, 6H, J=5.5 Hz); ESMS m/e : 448.4 $(M + H)^+$; Calc. Anál. para $C_{27}H_{34}N_3ClO_3$+0.4 de H_2O: C, 66.02; H, 7.14; N, 8.55. Encontrado: C, 66.07; H, 6.78; N, 8.65.

Ejemplo 39

N-(3-{1-(4-(1,3-DIOXO-1,3-DIHIDRO-2H-ISOINDOL-2-IL)BUTIL]-4-PIPERIDINIL}FENIL-2-METILPROPANAMIDA: El método sintético es el mismo como el descrito para 2-[6-(4-fenyl-1-piperidinil)hexil]-1H-isoindol-1,3(2H)-diona. N-(3-{1-[5-(1,3-dioxo-1,3-dihidro-2H-isondol-2-il)pentil]-4-piperidinil}fenil)-2-metilpropanamida: 614 mg (rendimiento 64%); RMN ^1H (400 MHz, $CDCl_3$) 7.87-7.8 (m, 2H), 7.76-7.68 (m, 2H), 7.48 (s, 1H), 7.41 (d, 1H, J=7.6 Hz), 7.21 (t, 1H, J=7.6 Hz), 6.95 (d, 1H, J=7.6 Hz), 3.69 (t, 2H, J=7.2 Hz), 3.39-3.28 (m, 2H) , 3.02 (d aparente, 2H, J=11.6 Hz), 2.78 (q, 2H, J=7.2 Hz), 2.64-2.52 (m, 1H), 2.52-2.40 (m, 1H), 2.40-2.31 (m, 2H), 2.01 (dt, 2H, J=3.7, 11.1 Hz), 1.85-1.64 (m, 2H), 1.58 (q, 2H, J=7.6 Hz), 1.45-1.32 (m, 2H), 1.23 (d, 6H,

J=6.9 Hz); ESMS m/e: 462.4 $(M + H)^+$; Cálc. Anál. para $C_{28}H_{36}N_3ClO_3$: C, 67.52; H, 7.29; N, 8.44. Encontrado: C, 67.04; H, 7.06; N, 8.38.

Ejemplo 40

2-METIL-N-{3-[1-(4-FENILBUTIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Una mezcla de 2-metil-N-[3-(4-piperidinil)fenil]propanamida (28.3 mg, 0.100 mmol), 4-fenil-1-clorobutano (21.1 mg, 0.125 mmol), diisopropiletilamina (0.50 mL), cantadidad catalítica de yoduro de tetrabutilamonio y dioxano (2.0 mL), se calentó a temperatura de reflujo durante 3 días. La mezcla de reacción se concentró y cromatografió utilizando placas de TLC preparatorias [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], produciendo el producto, 2-metil-N-{3-[1-(4-fenilbutil)-4-piperidinil]fenil}propanamida (9.50 mg, rendimiento 25.1%) como un aceite espeso: RMN ^1H 7.37 (s, 1H), 7.29 (d aparente, 1H, J=7.9 Hz), 7.18 (m, 3H), 7.11 (m, 3H), 6.90 (d aparente, 1H, J=7.9 Hz), 3.02 (d, 2H, J=6.8 Hz), 2.41 (m, 4H, parcialmente oculto), 2.01 (m, 2H), 1.78 (m, 4H), 1.57 (m, 4H), 1.18 (d, 6H, J=7.7 Hz); ESMS m/e: 379.4 $(M + H)^+$.

Ejemplo 41

N-(3-{1-[3-(1,3-DIOXO-1,3-DIHIDRO-2H-ISOINDOL-2-IL)PROPIL]-4-PIPERIDINIL}-2-METILPROPANAMIDA: El método sintético es el

mismo como el descrito para 2- [6-(4-fenil-1-piperidinil)-hexil]-1H-isoindol-1,3(2H)-diona. N-(3-{1-[3-(1,3-dioxo-1,3-dihidro-2H-isoindol-2-il)propil]-4-piperidinil}fenil)-2-metilpropanamida: 810 mg. (rendimiento 93%); RMN ^1H (400 MHz, $CDCl_3$) 7.87-7.82 (m, 2H), 7.73-7.68 (m, 2H), 7.57 (s, 1H), 7.36 (d, 1H, J=8.5 Hz), 7.18 (t, 1H, J=7.7 Hz), 6.79 (d, 1H, J=7.1 Hz), 3.78 (t, 2H, J=6.8 Hz), 3.06 (quinteto, 2H, J=6 Hz), 2.95 (d aparente, 2H, J=12.2 Hz), 2.58-2.31 (m, 4H), 1.96-1.83 (m, 2H), 1.70 (d aparente, 2H, J=12.1 Hz), 1.52 (dt, 2H, J=3.5, 12.5 Hz), 1.03 (d, 6H, J=6.5 Hz), ESMS m/e: 434.4 $(M + H)^+$.

Ejemplo 42

N-(3-{1-[(3S)-3-HIDROXI-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de (S)-(-)-3-cloro-1-fenil-1-propanol (0.426 g, 2.50 mmol, 99%ee), 2-metil-N-[3-(4-piperidinil)fenil]propanamida (0.565 g, 2.00 mmol), diisopropiletilamina (1.29 g, 10.0 mmol), dioxano (5.0 mL) y una cantidad catalítica de yoduro de tetrabutilamonio, se agitó a 90°C durante 72 hrs. La cromatografía utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$ dio el producto deseado (306 mg, rendimiento 39.3%) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 7.46 (S, 1 H), 7.42 (d, 4H, J=8.1 Hz), 7.35 (m, 1 H), 7.30 (d, 1 H, J=8.0 Hz), 7.23 (t, 1H, J=8.1 Hz), 7.12

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(s, 1H) , 6.96 (dd aparente, 1H, J=8.0 Hz), 5.0 (dd aparente, 1H, J=4.4, 8.3 Hz), 3.18 (dd aparente, 2H, J=2.5, 12.5 Hz), 2.74 (m, 2 H) , 2.50 (m, 2H), 2.3-2.1 (m, 6H), 1.8 (m, 2H), 1.25 (d, 6H, J=7.1 Hz); ESMS m/e: 389.2 $(M + H)^+$.

Ejemplo 43

N-(3-{1-[3-METOXI-3-(4-METIFENIL)PROPIL-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de 3-metoxi-3-(p-tolil)-1-cloropropano (24.9 mg, 0.126 mmol), 2-metil-N-[3-(4-piperidinil)fenil]propanamida (28.3 mg, 0.126 mmol), diisopropiletilamina (0.50 mL) y cantidad catalítica de yoduro de tetrabutilamonio en dioxano (2.0 mL), se agitó a 90°C durante 72 hrs. La cromatografía utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dio el producto deseado (10.9 mg, rendimiento 21.2%) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 7.44 (s, 1 H), 7.38 (m, 1H), 7.3-7.1 (m, 5 H), 6.96 (d, 1H, J=7.4 Hz), 4.18 (dd aparente, 1H, J=5.6, 7.9 Hz), 3.24 (d, 1H, J=8.2 Hz), 3.2 (s, 3H), 3.11 (m, 2H, J=10.1Hz), 2.49 (m, 4H), 2.35 (s, 3H), 2.3-2.1 (m, 3H), 1.92 (d, 4H), 1.25 (d, 6H, J=7.1 Hz); ESMS m/e: 409.4 $(M + H)^+$.

Ejemplo 44

N-{3-(1-(3-ISOPROPOXI-3-FENILPROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Una mezcla de 3-isopropil-3'fenil-1-

cloropropano (25.6 mg, 0.126 mmol),. 2-metil-N-[3-(4-piperidinil)fenil]propanamida (28.3 mg, 0.126 mmol), diisopropiletilamina (0.50 mL) y cantidad catalítica de yoduro de tetrabutilamonio en dioxano (2.0 mL), se agitó a 90°C durante 72 hrs. La cromatografía utilizando placas de TLC preparatorias de sílice [2.5 % de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (14.1 mg, rendimiento 26.5%) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 7.46 (s, 1H), 7.43-7.37 (m, 2H), 7.33 (m, 3H), 7.23 (m, 2H), 6.95 (d, 1H, J=8.4 Hz), 4.46 (dd aparente, 1H, J=5.0, 8.3 Hz), 3.49 (sept aparente, 1H, J=7.1 Hz), 3.10 (s, 2H), 2.70 (m, 2H), 2.52 (sept aparente, parcialmente oculto, 4H, J=6.6 Hz), 2.30-2.10 (m, 2H), 1.90-1.80 (d, 4H), 1.25 (d, 6H, J=7.1 Hz), 1.15 (d, 3H, J=6.4 Hz), 1.08 (d, 3H, J=6.4 Hz); ESMS m/e: 423.4 $(M + H)^+$.

Ejemplo 45

N-(3-{1-[4,4-BIS(4-FLUOROFENIL)BUTIL)-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de 4,4-bis(4-fluoro-fenil)-1-cloro-butano (39.0 mg, 0.126 mmol), 2-metil-N-[3-(4-piperidinil)fenil]propanamida (28.3 mg, 0.126 mmol), diisopropiletilamina (0.50 mL) y cantidad catalítica de yoduro de tetrabutilamonio en dioxano (2.0 mL), se agitó a 90°C durante 72 hrs. La cromatografía utilizando placas de TLC preparatorias de sílice [2.5 % de NH_3 (2.0 M en metanol)

en $CHCl_3$], dió el producto deseado (15.9 mg, rendimiento 25.2%) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 8.02 (s, 1H), 7.41 (s, 1H), 7.3-7.15 (m, 4H), 7.10 (m, 3H), 6.89 (t aparente, 5H), 3.81 (t, 1H, J=7.8 Hz), 3.30 (s, 1H), 2.91 (d, 1H, J=12,5 Hz), 2.80 (m, 1H), 2.40 (m, 2H), 2.31 (t, 1H, J=8.0 Hz), 1.93 (q aparente, 3H, J=8.0 Hz), 1.72 (m, 3H), 1.40 (m, 2H), 1.20 (m, 2H), 1.15 (d, 6H, J=8.1 Hz); ESMS m/e: 491.4 $(M + H)^+$.

Ejemplo 46

N-{3-[1-(3-METOXIBENCIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Una mezcla de 2-metil-N-[3-(4-piperidinil)fenil]-propanamida (28.3 mg, 0.100 mmol), cloruro de 3-metoxibencilo (19.6 mg, 0.125 mmol), diisopropiletilamina (0.50 mL), cantidad catalítica de yoduro de tetrabutilamonio y dioxano (2.0 mL). La cromatografía utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], produjo el producto deseado (10.2 mg, rendimiento 27.9%) como un sólido amarillo: RMN ^1H (400 MHz, $CDCl_3$) 7.46 (s, 1H), 7.35 (d aparente, 1H, J=8.3 Hz), 7.27-7.21 (m, 2H), 6.95 (t aparente, 3H, J=6.9 Hz), 6.82 (dd aparente 1H, J=2.4, 8.3 Hz), 3.84 (m, 3H), 3.56 (s, 2H), 3.05 (d, 2H, J=10.5 Hz), 2.51 (sept aparente, parcialmente oculto, 4H, J=7.2 Hz), 2.13 (t aparente, 2H, J=9.7 Hz), 1.88(m, 2H), 1.25 (d, 6H, J=6.7 Hz); ESMS m/e: 367.3 $(M + H)^+$.

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Ejemplo 47

N-(3-{1-[3,5-BIS(TRIFLUOROMETIL)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de 2-metil-N-[3-(4-piperidinil)fenil]propanamida (28.3 mg, 0.100 mmol), bromuro de 3,5-bis(trifluorometil)bencilo (38.4 mg, 0.125 mmol), diisopropiletilamina (0.50 mL), cantidad catalítica de yoduro de tetrabutilamonio y dioxano (2.0 mL). La cromatografía utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (12.2 mg, rendimiento 25.8%) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 7.83 (s, 2H), 7.77 (s, 1H), 7.53 (s, 1H), 7.30-7.21 (m, 2H), 7.16 (s, 1H), 6.98 (d aparente, 1H, J=7.6 Hz), 3.62 (s, 2H), 2.94 (d, 2H, J=9.4 Hz), 2.51 (sept aparente, parcialmente oculto, 2H, J=6.6 Hz), 2.14 (m, 2H), 1.82 (m, 4H), 1.25 (d, 6H, J=6.6 Hz); ESMS m/e: 473.2 $(M + H)^+$.

Ejemplo 48

N-(3-{1-[(3R)-3-(3,4-DIMETOXIFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA

Método A

4-{[1R)-3-cloro-1-fenilpropil]oxy}-1,2-dimetoxibenceno: Una mezcla de 3,4-dimetoxifenol (4.07 g, 26.4 mmol), (S)-(-)-3-

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cloro-fenil-1-propanol (4.50 g, 26.4 mmol, 99%ee, Aldrich Chemical Co.), trifenilfosfina (6.92 g, 26.4 mmol) y azodicarboxilato de dietilo (4.59 g, 26.4 mmol) en THF (110 mL), se agitó a temperatura ambiente durante 24 h. La mezcla de reacción se ocncentró *in vacuo*. En este punto, el residuo puede ser ya sea lavado con pentano (x3) y los extracos de pentano combinados se concentraron y se cromatografiaron (sílice con hexanos–EtOAc 8:1 como el eluyente) para dar el producto deseado (como procedimiento general como esta descrito por: Srebnik, M.; Ramachandran, P.V.; Brown, H.C. J. Org. Chem. 1988, 53, 2916-2920). Este procedimiento se llevo a cabo en una escala de reacción más pequeña y solamente un rendimiento de 40% del producto se realizó.

Alternativamente, a una escala mayor (26.4 mmol), el producto crudo se trituró con una pequeña cantidad de diclorometano y el óxido de trifenilfosphina precipitado se filtró. El filtrado se concentró y el producto crudo se cromatografió para dar el producto deseado como un aceite amarillo espeso (7.30 g, rendimiento 88.9%): RMN ^1H (400 MHz, $CDCl_3$) 7.39-7.32 (m, 4H), 7.20 (m, 1H), 6.64 (d, 1H, J=8.7 Hz), 6.51 (d, 1H, J=2.7 Hz), 6.30 (dd, 1H, J=2.7, 8.7 Hz), 5.27 (dd aparente,1H, J=4.5, 8.7 Hz), 3.79 (s, 3H), 3.77 (s, 3H), 3.61 (m, 1H) , 2.45 (m, 1 H) , 2.20 (m, 1H) 1.80 (s, 1H) ; ESMS m/e: 307.11 $(M+H)^+$.

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N-(3-{1-[(3R)-3-(3,4-DIMETOXIFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL-2METILPROPANAMIDA: Una mezcla de carbonato de potasio (321 mg, 2.32 mmol), yoduro de sodio (522 mg, 3.48 mmol), 2-metil-N-[3-(4-piperidinil)fenil]propanamida (570 mg, 2.32 mmol) y 4-{[(1R)-3-cloro-1-fenilpropil]oxi}-1,2-dimetoxibenceno (712mg, 2.32 mmol) en DMF (5.0 mL), se agitó a 100°C durante 3 hrs, tiempo en el cual la TLC indicó que la reacción fue completa. La mezcla de reacción se vació en agua (50 mL) y la capa acuosa se extrajo con cloruro de metileno (3x30 mL). Los extractos orgánicos combinados se lavaron con salmuera (30 mL), se secaron sobre $MgSO_4$ y se concentraron bajo presión reducida. El producto crudo se purificó por medio de placas de TLC preparatorias [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$] para producir el producto (970 mg, 90.1%) como un aceite espeso.

Método B

En un matraz RB de 25-mL se adicionó trifenilfosfina (9.80 mg, 0.0375 mmol), azodicarboxilato de dietilo (5.22 mg, 0.0300 mmol), N-(3-{1-[(3S)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (9.53 mg, 0.0250 mmol), 3,4-dimetoxifenol (7.70 mg, 0.050 mmol) y THF (1.0 mL) a temperatura ambiente. La mezcla de reacción se agitó a temperatura ambiente durante la noche (16 hrs).

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El solvente se retiró bajo presión reducida y se purificó el residuo por medio de placas de TLC preparatorias[2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$] para producir el producto deseado (4.4 mg, rendimiento 34.1 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 7.46 (s, 1H),7.40-7.30 (m, 4H),7.25 (m, 3H), 6.97 (d, 1H, J=7.8 Hz), 6.64 (d, 1H, J=9.1 Hz), 6.51 (d, 1H, J=2.6 Hz), 6.29 (d, 1H, J=2.6, 9.1 Hz), 5.20 (dd aparente, 1H, J=4.4, 8.5 Hz), 3.80 (s, 3H) , 3.77 (s, 3H) , 3.23 (m, 2H) , 2.77 (m, 2 H), 2.5 (m, 2H) , 2.3-2.1 (m, 6H), 1.80 (m, 2H), 1.25 (d, 6H, J=7.9 Hz); ESMS m/e: 517.4 $(M + H)^+$.

Ejemplo 49

2-METIL-N-(3-{1-[(3S)-3-FENOXI-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil)-4-piperidinil}fenil)-2-metilpropanamida (9.53 mg, 0.0250 mmol), fenol (4.70 mg, 0.050 mmol), trifenilosfina (9.80 mg, 0.0375 mmol) y azodicarboxilato de dietilo (5.22 mg, 0.0300 mmol) en THF (1.0 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (2.7 mg, rendimiento 23.6 %) como un aceite espeso: RMN ^1H 7.46 (s, 2H), 7.40-7.30 (m, 4H), 7.25 (m, 3 H), 7.20 (m, 2H), 6.97 (d aparente, 1H, J=7.4 Hz), 6.89 (tt aparente, 1H,

J=0.8, 7.6 Hz), 6.84 (dt aparente, 1H, J=0.8, 8.0 Hz), 5.20 (dd aparente, 1H, J=4.4, 8.5 Hz), 3.35 (m, 2H) , 2.91 (m, 2H) , 2.60 (m, 2H) , 2.30-2.10 (m, 6H), 1.90 (m, 2H), 1.25 (d, 6H, J=7.9 Hz) ESMS m/e: 457.4 $(M + H)^+$.

Ejemplo 50

N-(3-{1-[(3S)-3-(4-METOXIFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (9.53 mg, 0.0250 mmol), 4-metoxifenol (6.20 mg, 0.050 mmol), trifenilfosfina (9.80 mg, 0.0375 mmol) y azodicarboxilato de dietilo (5.2 mg, 0.0300 mmol) en THF (1.0 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (4.6 mg, rendimiento 37.9 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 7.38-7.14 (m, 8H), 6.90 (d aparente, 1H, J=7.7 Hz), 6.72-6.46 (m, 4H), 5.09 (dd aparente, 1H, J=4.8, 8.1 Hz), 3.64 (s, 3H) , 3.18 (m, 2H), 2.73 (m, 2H) , 2.50 (m, 2H), 2.37-1.72 (m, 8H), 1.25 (d, 6H, J=7.4 Hz); ESMS m/e: 487.4 $(M + H)^+$.

Ejemplo 51

N-(3-{1-[(3S)-3-(3-CLOROFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-

3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (9.53 mg, 0.0250 mmol), 3-clorofenol (6.40 mg, 0.050 mmol), trifenilfosina (9.80 mg, 0.0375 mmol) y azodicarboxilato de dietilo (5.22 mg, 0.0300 mmol) en THF (1.0 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (4.9 mg, rendimiento 40.0 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 7.39 (s, 1H), 7.35-7.10 (m, 7H), 7.02 (t, 1H, J=8.0 Hz), 6.90 (d, 1H, J=7.6 Hz), 6.84-6.75 (m, 2H), 6.65 (m, 1H), 5.09 (dd aparente, 1H, J=4.99, 8.1 Hz), 3.10 (m, 2H), 2.60 (m, 2H), 2.50 (m, 2H), 2.30-1.70 (m, 8H), 1.18 (d, 6H, J=6.8 Hz); ESMS m/e: 491.4 $(M + H)^+$.

Ejemplo 52

N-(3-{(3S)-3-(4-CLOROFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (9.53 mg, 0.0250 mmol), 4-clorofenol (6.40 mg, 0.050 mmol), trifenilfosfina (9.80 mg, 0.0375 mmol) y azodicarboxilato de dietilo (5.22 mg, 0.0300 mmol) en THF (1.0 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$), dió el producto deseado (3.3 mg, rendimiento 26.9 %) como un aceite

espeso: RMN ^1H 7.36 (s, 1H), 7.35-7.22 (m, 7H), 7.12 (m, 2H), 6.97 (d aparente, 1H, J=7.2 Hz), 6.77 (m, 2H), 5.23 (m, 1H), 3.18 (m, 2H), 2.70 (m, 2H), 2.50 (m, 2H), 2.40-1.80 (m, 8H), 1.25 (d, 6H, J=6.8 Hz); ESMS m/e: 491.4 $(M + H)^+$.

Ejemplo 53

2-METIL-N-[3-(1-{(3S)-3-FENIL-3-[4-(TRIFLUOROMETIL)FENOXI]-PROPIL}4-PIPERIDINIL)FENIL]PROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (9.53 mg, 0.0250 mmol), 4-trifluorometilfenol (8.100 mg, 0.050 mmol), trifenilfosina (9.8 mg, 0.0375 mmol) y azodicarboxilato de dietilo (5.22 mg, 0.0300 mmol) en THF (1.0 mL), se agitó a temperatura ambiente durante 3 días. La cromatografía utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (5.10 mg, rendimiento 38.9 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 8.06 (s, 1H), 7.49 (s, 1H), 7.44 (d aparente, 2H, J=6 Hz), 7.38-7.30 (m, 4H), 7.30—7.20 (m, 3H), 6.96 (d aparente, 1H, J=7.6 Hz), 6.91 (d aparente, 2H, J=8.6 Hz), 5.34 (m, 1H), 3.19 (m, 2H), 2.72 (m, 2H), 2.53 (m, 2H), 2.40-1.80 (m, 8H), 1.25 (d, 6H, J=6.8 Hz); ESMS m/e: 525.4 $(M + H)^+$.

Ejemplo 54

N-(3-{1-[(3R)-3-(2,5-DIFLUOROFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (9.53 mg, 0.0250 mmol), 2,5 difluorofenol (6.50 mg, 0.050 mmol), trifenilfosina (9.80 mg, 0.0375 mmol) y azodicarboxilato de dietilo (5.22 mg, 0.0300 mmol) en THF (1.0 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (3.60 mg, rendimiento 29.3 %) como un aceite espeso: RMN ^1H 7.46 (s, 1H), 7.40-7.32 (m, 4H), 7.31-7.20 (m, 2H), 7.17 (s, 1H), 7.01-6.92 (m, 2H), 6.65-6.42 (m, 2H) , 5.27 (m, 1H), 3.13 (m, 2H), 2.64 (m, 2H), 2.51 (m, 2H), 2.28-1.80 (m, 8 H), 1.25 (d, 6H, J=7.1 Hz); ESMS m/e: 493.4 $(M + H)^+$.

Ejemplo 55

N-(3-{1-[(3R)-3-(3,4-DICLOROFENOXI)-3-FENILPROPIL)-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (9.53 mg, 0.0250 mmol), 3,4diclorofenol (8.20 mg, 0.050 mmol), trifenilfosina (9.80 mg, 0.0375 mmol) y azodicarboxilato de dietilo (5.22 mg, 0.0300 mmol) en THF (1.0 mL), se agitó a temperatura ambiente durante 3 días. La

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cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (5.20 mg, rendimiento 39.7 %) como un aceite espeso: RMN ^1H ($CDCl_3$) 7.70-7.63 (m, 2H), 7.55 (m, 1H), 7.47-7.43 (m, 3H), 7.40-7.19 (m, 3H.), 7.00-6.50 (m, 2H), 6.69 (dd, 1H, J=2.2, 8.8 Hz), 5.25 (m, 1H), 3.20 (m, 2H), 2.70 (m, 2H), 2.53 (m, 2H), 2.40-2.20 (m, 4H), 2.10-1.80 (m, 4H), 1.25 (d, 6H, J=7.1 Hz); ESMS m/e: 525.4 $(M + H)^+$.

Ejemplo 56

2 METIL-N-(3-{1-[(3R)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-PROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (9.53 mg, 0.0250 mmol), fenol (4.70 mg, 0.050 mmol), trifenilfosina (9.80 mg, 0.0375 mmol) y azodicarboxilato de dietilo (5.22 mg, 0.0300 mmol) en THF (1.0 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (4.1 mg, rendimiento 36.0 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 7.45 (s, 1H), 7.40-7.15 (m, 10H), 6.97 (d, 1H, J=7.6 Hz), 6.88-6.82 (m, 2H), 5.26 (m, 1H) 3.18 (m, 2H), 2.75 (m, 2H), 2.53 (m, 2H), 2.40-2.10 (m, 4H), 2.10-

1.80 (m, 4H), 1.25 (d, 6H, J=6.9 Hz); ESMS m/e: 457.4 $(M + H)^+$.

Ejemplo 57

N-(3-{1-[(3R)-3-HIDROXI-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA

Método A

En un matraz RB de 25 mL se adicionó (R)-(+)-3-cloro-1-fenil-1-propanol (0.545 g, 3.19 mmol, 99%ee, Aldrich Chemical Co.), 2-metil-N-[3-(4-piperidinil)fenil]propanamida (0.748 g, 3.04 mmol), carbonato de potasio (0.420 g, 3.04 mmol) y yoduro de sodio (0.684 g, 4.56 mmol) y DMF (6.0 mL) a temperaura ambiente. Después de la agitación a 100°C durante 3 hrs, la TLC mostró que la reacción estaba completa. La mezcla de reacción se vació en agua (50 mL) y la capa acuosa se extrajo con cloruro de metileno (3x20 mL). Los extractos orgánicos combinados se lavaron con salmuera (20 mL), se secarón sobre Na_2SO_4 y se concentraron bajo presión reducida. El residuo se purificó por cromatografía instantánea (1:1= hexano:acetato de etilo con isopropilamina al 1%) para producir el producto deseado (1.09 g, rendimiento 94.3 %) como un sólido amarillo ligero: RMN ^1H (400 MHz, $CDCl_3$) 8.10 (s, 1H), 7.46-7.35 (m, 6H), 7.27 (m, 2H), 6.98 (d aparente, 1H, J=7.6 Hz), 5.02 (dd aparente, 1H,

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J=4.4, 8.1 Hz), 3.18 (dd aparente, 2H, J=2.5, 12.5 Hz), 2.74 (m, 2 H), 2.50 (m, 2H), 2.30-2.10 (m, 6H), 1.80 (m, 2H), 1.25 (d, 6H, J=7.1 Hz); ESMS m/e: 381.2 $(M + H)^+$.

La sal hidroclórica se preparó al adicionar un ligero exceso de HCl 1N en éter (1.2 eq.) auna solución de la base libre en diclorometano. El solvente se retiró bajo presión reducida, el residuo se lavó con éter y se secó bajo prsesión reducida: Cálc. Anál. para $C_{24}H_{32}N_2O_2+0.8H_2O$: C, 66.82; H, 8.08; N, 6.49; Cl, 8.22. Encontrado: C, 66.90; H, 7.78; N, 6.63; Cl, 8.52.

Método B

En un matraz RB de 25 mL se adicionó (R)-(+)-3-cloro-1-fenil-1-propanol (0.426 g, 2.50 mmol, 2-metil-N-[3-(4-piperidinil)fenil]propanamida (0.565 g, 2.00 mmol), diisopropiletilamina (1.29 g, 10.0 mmol), dioxano (5.0mL) y cantidad catalítica de yoduro de tretrabutilamonio a temperatura ambiente. Después de la agitación a 90°C durante 72 hrs, la mezcla de reacción se vació en agua (50 mL) y la capa acuosa se extrajo con cloruro de metileno (3x20 mL). Los extractos orgánicos combinados se lavaron con salmuera (20 mL), se secaron sobreNa_2SO_4 y se concentraron bajo presión reducida. El residuo se purificó por medio de placas de TLC preparatorias (1:5:100=isopropilamina:metanol:acetato

de etilo) para producir el producto deseado (0.260 g, rendimiento 34.2 %) como sólido amarillo ligero.

Ejemplo 58

N-(3-{1-[(3S)-3-(4-CIANO-FENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: N-(3-{1-[(3S)-3-(4-cianofenoxi)-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida.

Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.20 mg, 0.0137 mmol), 4-cianofenol (100 mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografía utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (4.70 mg, rendimiento 71.3 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 7.54 (m, 2H), 7.48 (d, 2H, J=8.4 Hz), 7.30-7.20 (m, 3H), 7.20 (m, 3H), 6.97 (d aparente, 1H, J=8.4 Hz), 6.92 (d aparente, 2H, J=8.4 Hz), 5.36 (dd aparente, 1H, J=3.9, 7.6 Hz), 3.12 (m, 2H), 2.61 (m, 2H), 2.53 (sept aparente, parcialmente oculto, 2H, J=7.6 Hz), 2.30-2.10 (m, 6H) 1.82 (m, 2H), 1.25 (d, 6H, J=6.8 Hz); ESMS m/e: 482.2 $(M + H)^+$.

Ejemplo 59

N-(3-{1-[(3S)-3-(4-FLUOROFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.20 mg, 0.0137 mmol), 4-fluorofenol (100 mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (4.20 mg, rendimiento 64.7 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) δ 7.40 (m, 2H), 7.30-7.20 (m, 5H), 7.20 (m, 3H), 6.97 (d aparente, 1H, J=7.7 Hz), 6.87 (m, 1H), 6.76 (m, 1H), 5.26 (dd aparente, 1H, J=4.0, 8.1 Hz), 3.09 (m, 2H), 2.66 (m, 2H), 2.51 (m, 2H), 2.3-2.1 (m, 6H), 1.82 (m, 2H), 1.25 (d, 6H, traslapado); ESMS m/e: 475.2 $(M + H)^+$.

Ejemplo 60

N-(3-{1-[(3S)-3-(4-BROMOFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.20 mg, 0.0137 mmol), 4-bromofenol (100 mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia

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utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (0.70 mg, rendimiento 9.6 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.48 (m, 2H), 7.30-7.20 (m, 5H), 7.20 (m, 3H), 6.97 (d aparente, 1H, J=8.5 Hz), 6.73 (d aparente, 2H, J=8.5 Hz), 5.22 (dd aparente, 1H, J=4.9, 7.8 Hz), 3.15 (m, 2H), 2.65 (m 2H), 2.51 (sept aparente, parcialmente oculto, 2H, J=7.6 Hz), 2.30-2.10 (m, 6H), 1.82 (m, 2H), 1.25 (d, 6H, J=6.8 Hz); ESMS m/e: 535.1 $(M + H)^+$.

Ejemplo 61

N-(3-{1-[(3S)-3-(3-METOXIFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.20 mg, 0.0137 mmol), 3-metoxifenol (100 mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (3.1 mg, rendimiento 46.6 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) δ 7.47 (d, 1H, J=6.7 Hz), 7.42 (s, 1H), 7.3-7.20 (m, 3H), 7.20 (m, 3H), 7.07 (t, 1H, J=8.4 Hz), 6.97 (d aparente, 1H, J=6.7 Hz), 6.40 (m, 3H), 5.27 (dd aparente, 1H, J=5.3, 8.0 Hz), 3.74 (s, 3H), 3.38 (m, 2H), 2.93 (m,

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2H), 2.61 (s, 1H), 2.53 (sept aparente, parcialmente oculto, 1H, J=6.5 Hz), 2.30-2.10 (m, 6H), 1.82 (m, 2H), 1.25 (d, 6H, J=6.9 Hz); ESMS m/e: 487.3 $(M + H)^+$.

Ejemplo 62

N-(3-{(3S)-3-(4-CIANO-2-METOXIFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metil-propanamida (5.20 mg, 0.0137 mmol), 2-metoxi-4-cianofenol (100 mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (5.50 mg, rendimiento 76.5 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) δ 7.51 (s, 1H), 7.38 (s, 1H), 7.37 (d, 2H, J=2.4 Hz), 7.20 (m, 4H), 7.10 (d, 1H, J=2.4 Hz), 7,08 (s, 1H), 6.99 (d aparente, 1H, J=8.3 Hz), 6.76 (d aparente, 1H, J=8.3 Hz), 5.43 (dd aparente, 1H, J=5.1, 8.0 Hz), 3.91 (s, 3H), 3.34 (m, 2H), 2.63 (m, 2H), 2.63 (s, 1H), 2.53 (sept aparente, parcialmente oculto, 1H, J=7.7 Hz), 2.30-2.10 (m, 6H), 1.82 (m, 2H), 1.28 (d, 6H, J=6.8 Hz); ESMS m/e: 512.2 $(M + H)^+$.

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Ejemplo 63

N-(3-{1-[(3S)-3-(5-ACETIL-2-METOXIFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.20 mg, 0.0137 mmol), 2-metoxi-5-acetilfenol (100 mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (1.60 mg, rendimiento 22.2 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) δ 7.52 (d, 2H, J=2.4 Hz), 7,3-7,2 (m, 5H), 7.20 (m, 3H), 6.97 (d aparente, 1H, J=6.7 Hz), 6.69 (d aparente, 1H, J=8.0 Hz), 5,47 (dd aparente, 1H, J=4.3, 7.8 Hz), 3.95 (s, 3H), 3,38 (m, 2H), 2.93 (m, 2H), 2.61 (s, 1H), 2.53 (sept aparente, parcialmente oculto, 1H, J=7.6 Hz), 2.50 (s, 3H), 2.30-2.10 (m, 6H), 1.82 (m, 2H), 1.25 (d, 6H, J=6.8 Hz); ESMS m/e: 529.6 $(M + H)^+$.

Ejemplo 64

N-(3-{1-[(3R)-3-(2-ACETILFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3S)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.2 mg, 0.0137 mmol), 2-acetilfenol (100

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mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (1.70 mg, rendimiento 24.9 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) δ 7.65 (m, 1H), 7.55 (s, 1H), 7,30-7.20 (m, 5H), 7.20 (m, 3H), 6.97 (m, 2H), 6.76 (d aparente, 1H), 5.49 (dd aparente, 1H, J=4.3, 8,0 Hz), 3.38 (m, 2H) 2.93 (m, 2H), 2.71 (s, 3H), 2.60 (s, 1H), 2.53 (sept aparente, parcialmente oculto, 1H, J=7.6 Hz), 2.30-2.10 (m, 6H), 1.82 (m, 2H) 1.25 (d, 6H, J=6.9 Hz); ESMS m/e: 498.8 (M^+).

Ejemplo 65

N-(3-(1-{(3R)-3-[2-FLUORO-5-(TRIFLUOROMETIL)FENOXI]-3-FENILPROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3S)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.20 mg, 0.0137 mmol), 2-fluoro-5-trifluorometilfenol (100 mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (2.50 mg, rendimiento 33.7 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) δ 8.07 (s,

1H), 7.67 (m, 1H), 7.54 (m, 1H), 7.45 (m, 2H), 7.30-7.10 (m, 6H), 7.14 (d, 1H, J=7.4 Hz), 6.97 (d aparente, 1H, J=7,7 Hz), 5.37 (dd aparente, 1H, J=5.0, 8.5 Hz), 3.4 (m, 2H), 2.8 (m,2H), 2.6 (s, 1H), 2.53 (sept aparente, parcialmente oculto, 1H, J=7.4 Hz), 2.30-2.10 (m, 6H), 1.80 (m, 2H), 1.25 (d, 6H, J=7.1 Hz, traslapado); ESMS m/e: 542.6 (M^+), 543.54 ($M + H^+$).

Ejemplo 66

N-[3-(1-{(3S)-3-[2-FLUORO-5-(TRIFLUOROMETIL)FENOXI]-3-FENILPROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.20 mg, 0.0137 mmol), 2-fluoro-5-trifluorometilfenol (100 mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (3.00 mg, rendimiento 40.4 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.67 (m, 2H), 7.55 (m, 2H), 7.50-7.40 (m, 3H), 7.30-7.10 (m, 3H), 7,17 (d, 1H, J=8.9 Hz), 7.07 (d aparente, 1H, J=6.7 Hz), 6.97 (d aparente, 1H, J=7.8 Hz), 5.37 (dd aparente, 1H, J=4.2, 8.1 Hz), 3.37 (m, 2H), 2.93 (m, 2H), 2.63 (s, 1H), 2.50 (sept aparente,parcialmente oculto, 1H,

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J=7.9 Hz), 2.30-2.10 (m, 6H), 1.85 (m, 2H), 1.25 (d, 6H, J=6.9 Hz); ESMS m/e: 542.7 $(M + H)^+$.

Ejemplo 67

N-(3-{1-[(3S)-3-(2,5-DIFLUOROFENOXI)-3-FENILPROPIL-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.20 mg, 0.0137 mmol), 2,5-difluorofenol (100 mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (2.70 mg, rendimiento 40.1 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.40-7.30 (m, 4H), 7.20 (m, 2H), 7.17 (s, 1H), 6.97 (m, 2H), 6.58 (m, 1H), 6.51 (m, 1H), 5.27 (dd aparente, 1H, J=5.1, 8.2 Hz), 3.13 (d aparente, J=9.7 Hz, 2H), 2.64 (m, 2H), 2,51 (m, 2H), 2.34 (sept aparente, parcialmente oculto, J=7.1 Hz, 1H), 2.17 (m, 3H), 1.90-1.80 (m, 4H), 1.25 (d, 6H, J=7.1 Hz); ESMS m/e: 493.1 $(M + H)^+$.

Ejemplo 68

N-(3-{1-[(3R)-3-(3-CLOROFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3S)-

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3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.20 mg, 0.0137 mmol), 3-clorofenol (100 mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (2.4 mg, rendimiento 35.8 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) δ 7.30 (m, 2H), 7.30-7.20 (m, 3H), 7.20 (m, 3H), 6.90 (d aparente, 1H, J=7.7 Hz), 6.71 (d aparente, 1H, J=2.9 Hz), 6.69 (t aparente, 1H, J=2.9 Hz), 6,67 (t aparente, 1H, J=2.9 Hz), 6.65 (d aparente, 1H, J=2.9 Hz), 5.09 (dd aparente, 1H, J=4.8, 8.1 Hz), 3.18 (m, 2H), 2.73 (m, 2H), 2.50 (sept aparente, parcialmente oculto, 2H, J=7.1 Hz), 2.30-2.10 (m, 6H), 1.89 (m, 2H), 1.25 (d, 6H, traslapado); ESMS m/e: 491.1 $(M + H)^+$.

Ejemplo 69

1-NAFTOATO DE (1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL: En un matraz RB de 25 mL se adicionó N-(3-{1-[(3S)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.20 mg, 0.0137 mmol),cloruro de 1-naftalencabonilo (100 mg), diisopropiletilamine (0.30 mL) en THF (0,50 mL) a temperatura ambiente. Después de que se agitó durante 16 hrs a temperatura ambiente, la mezcla de

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reacción se concentró bajo presión reducida. El residuo se purificó utilizando placas de TLC preparatorias [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dando el producto deseado (4.70 mg, rendimiento 71.3 %) como un aceite espeso: RMN ^{1}HNMR (400 MHz, $CDCL_3$) δ 8.90 (d, 1H, J=8.9 Hz), 8.28 (dd aparente, 1H, J=1.5, 7.2 Hz), 8.03 (d, 1H, J=8.7 Hz), 7.88 (dm, 2H, J=8.7 Hz), 7.60-7.48 (m, 7H), 7.40-7.32 (m, 3H), 7,25 (m, 1H), 6.90 (d aparente, 1H, J=7.4 Hz), 6.18 (dd aparente, 1H, J=5.7, 7.8 Hz), 3.42 (m, 2H), 2.84 (m, 2H), 2.53 (m, 2H), 2.44 (sept aparente, parcialmente oculto 4H, J=7.5 Hz), 2.30-2.10 (m, 2H), 1.82 (m, 2H), 1.25 (d, 6H, J=6.8 Hz); ESMS m/e: 535.6 $(M + H)^+$.

Ejemplo 70

N-(3-{1-[(3S)-3-(3-ACETILFENOXI)-3-FENILPROPIL-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.20 mg, 0.0137 mmol), 2-acetilfenol (100 mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (1.50 mg, rendimiento 22.0 %) como un aceite espeso: RMN ^{1}H (400 MHz, $CDCl_3$) δ 7.65 (m, 1H), 7.55 (s, 1H), 7.30-7.20 (m,

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5H), 7.20 (m, 3H), 6.97 (m, 2H), 6,76 (d aparente, 1H), 5.49 (dd aparente, 1H, J=4.3, 8.0 Hz), 3.38 (m, 2H), 2.93 (m, 2H), 2.75 (s, 3H), 2.53 (sept aparente, parcialmente oculto, 2H, J=7.6 Hz), 2.30-2.10 (m, 6H), 1.92 (m, 2H), 1.25 (d, 6H, J=6.9 Hz); ESMS m/e: 498.81 (M^+), 499.6 $(M + H)^+$.

Ejemplo 71

N-(3-{1-[(3S)-3-(2-FLUOROFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.20 mg, 0.0137 mmol), 2-fluorofenol (100 mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (3.5 mg, rendimiento 53.9 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.65 (m, 1H), 7.41 (s, 1H), 7.40-7.10 (m, 5H), 7.05 (m, 2H), 6.97 (d aparente, 1H, J=8.7 Hz), 6.86 (m, 2H), 6.79 (dt aparente, 1H, J=2.4, 7.9 Hz), 5.31 (dd aparente, 1H, J=4 5, 8.0 Hz), 3.39 (m, 2H), 2.97 (m, 2H), 2.53 (sept aparente, parcialmente oculto, 2H, J=7.5 Hz), 2.3-2.1 (m, 6H), 1.92 (m, 2H), 1.25 (d, 6H, J=6.7 Hz); ESMS m/e: 475.7 $(M + H)^+$.

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Ejemplo 72

(4S)-N-(3-{4-[3-(ACETILAMINO)FENIL]-1-PIPERIDINIL}-4-(3,5-DIFLUOROFENIL)-2-OXO-1,3-OXAZOLIDIN-3-CARBOXAMIDA :

Método: En un frasco de 20 ml. se adicionó N1-{3-[1-(3-aminopropil)-4-piperdinil]fenil}acetamida (15 mg; 0,054 mmol), 4-nitrofenil éster del ácido (4S)-4-(3,5-difluorofenil)-2-oxo-oxazolidin-3-carboxílico (39.3 mg, 1.08 mmol, 2 eq) y diclorometano con 0.6% de metanol (3 ml) a temperatura ambiente. Después de que se agitó a temperatura ambiente durante 3 hrs, la mezcla de reacción se filtró y se purificó por medio de TLC preparatoria de sílice (19:1 = cloroformo:metanol), para producir el producto deseado (18.3 mg, rendimiento 68%); RMN ^1H (400 MHz, $CDCl_3$) δ 8.09 (br s, 1H), 7.40 (d, 1H, J=8.0 Hz), 7.36-7.28 (m, 2H), 7.24 (t, 1H, J=8.0 Hz), 6.99 (d, 1H, J=8.0 Hz), 6.86-6.82 (m, 2H), 5,41 (dd, 1H, J=4.1, 9.0 Hz), 4.72 (t, 1H, J=9.0 Hz), 4.22 (dd, 1H, J=3.9, 9.1 Hz), 3.42-3.29 (m, 2H), 3.02 (d, 2H J=11.1 Hz), 2.52-2.38 (m, 3H), 2.16 (s, 3H), 2.08-1.98 (m, 2H), 1.86-1,70 (m, 6H); ESMS m/e: 501.2 $(M + H)^+$; Calc. Anál. para $C_{26}H_{30}F_2N_4O_4+0.5H_2O$: C, 60.64; H, 6.18; N, 10.88. Encontrado: C, 60.67; H, 5.79; N, 10.86.

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Ejemplo 73

El método sintético es el mismo como el descrito para la síntesis de (4S)-N-(3-{4-[3-(acetilamino)fenil]-1-piperidinil}propil)-4-(3,5-difluorofenil)-2-oxo-1,3-oxazolidin-3-carboxamida.

(4S)-N-(3-{4-[3-(ACETILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-2-OXO-4-(3,4,5-TRIFLUOROFENIL)-1,3-OXAZOLIDIN-3-CARBOXAMIDA: 18.8 mg (rendimiento 67%); RMN ^1H (400 MHz, $CDCl_3$) δ 8.09 (br s, 1H), 7.41-7.20 (m, 3H), 7.02-6.91 (m, 3H), 5.37 (dd, 1H, J=3.8, 8.9 Hz), 4.71 (t, 1H, J=9 Hz), 4.21 (dd, 1H, J=4, 9.3 Hz), 3.43-3,27 (m, 2H), 3.02 (d, 2H, J=11.0 Hz), 2.53-2.37 (m, 3H), 2.16 (s, 3H), 2.08-1,97 (m, 2H), 1.85-1.69 (m, 6H); ESMS m/e: 519.2 $(M + H)^+$; Calc. Anál. para $C_{26}H_{29}F_3N_4O_4+0.5H_2O$: C, 59,20; H, 5.73; N, 10.62. Encontrado: C, 59.40; H, 5.35; N, 10.65.

Ejemplo 74

El método sintético es el mismo como el descrito para la síntesis de (4S)-N-(3-{4-[3-(acetilamino)fenil]-1-piperidinil}propil)-4-(3,5-difluorofenil)-2-oxo-1,3-oxazolidin-3-carboxamida.

N-(3-{4-[3-(ACETILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-4-(3,4-DIFLUOROFENIL)-5,5,-DIMETIL-2-OXO-1,3-OXAZOLIDIN-3-CARBOXA-

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MIDA: 19.6 mg (rendimiento 68%); RMN ^1H (400 MHz, $CDCl_3$) 8.18 (t, 1H, J=5.9 Hz), 7.41 (d, 1H, J=8,8 Hz), 7.33 (s, 1H), 7.27-7.14 (m, 2H), 7.02-6,88 (m, 3H), 5.04 (s, 1H),3.34 (qm, 2H, J=6.3 Hz), 3.02 (dm, 2H, J=10.9 Hz), 2.53-2.38 (m, 3H), 2.16 (s, 3H), 2.07-1.96 (m, 2H), 1.87-1.69 (m, 6H), 1.62 (s, 3H), 1.02 (s, 3H); ESMS m/e: 529.3 $(M + H)^+$; $)^+$; Calc. Anál. para $C_{28}H_{34}F_2N_4O_4$:C 0, 63.62; H, 6.48; N, 10.60. Encontrado: C, 63.15; H, 6,27; N, 10.48.

Ejemplo 75

El método sintético es el mismo como el descrito para la síntesis de (4S)-N-(3-{4-[3-(acetilamino)fenil]-1-piperidinil}propil)-4-(3,5-difluorofenil)-2-oxo-1,3-oxazolidin-3-carboxamida.

(4S,5R)-N-(3-{4-[3-(ACETILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-4-(3,4-DIFLUOROFENIL)-5-METIL-2-OXO-1,3-OXAZOLIDIN-3-CARBOXAMIDA: 20. 5 mg (rendimiento 74%); RMN ^1H (400 MHz, $CDCl_3$) δ 8.14 (t, 1H, J=5 Hz), 7.40 (d, 1H, J=7.8 Hz), 7.37-6.89 (m, 6H), 5,35 (d, 1H, J=7.5 Hz), 5,02-4.93 (m, 1H), 3.41-3.25 (m, 2H), 3.02 (d, 2H, J=10.8 Hz), 2.53-2.37 (m, 3H), 2.16 (s, 3H), 2.07 (m, 2H), 1.89-1.68 (m, 6H), 1.04 (d 3H, J=6.4 Hz) ; ESMS m/e: 515.3 $(M + H)^+$. Calc. Anál. para $C_{27}H_{32}F_2N_4O_4+0.5H_2O$: C, 61.94; H, 6.35; N, 10.70. Encontrado: C, 61.90; H, 6.13; N, 10,64.

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Ejemplo 76

El método sintético es el mismo como el descrito para la síntesis de (4S)-N-(3-{4-[3-(acetilamino)fenil]-1-piperidinil}propil)-4-(3,5-difluorofenil)-2-oxo-1,3-oxazolidin-3-carboxamida.

N-(3-{4-[3-(ACETILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-4-(FLUOROBENCIL)-2-OXO-1,3-OXAZOLIDIN-3-CARBOXAMIDA:

17.4 mg (rendimiento 65%); RMN ^1H (400 MHz, $CDCl_3$) 8.08 (t, 1H, J=5.6 Hz), 7.4 (d, 1H, J=7 2 Hz), 7.34 (s, 1H), 7.28-7.14 (m, 3H), 7.05-6.95 (m, 3H), 4.69-4.60 (m, 1H), 4.26 (t, 1H, J=8.8 Hz), 4.15 (dd, 1H, J=3.2, 9 Hz), 3.43 (q, 2H, J=6.2 Hz), 3.3 (dm 1H, J=13.6 Hz), 3.04 (dm 2H, J=11 Hz), 2.87 (dd, 1H, J=9.3, 14.4 Hz), 2.53-2.42 (m, 3H), 2.16 (s, 3H), 2.09-1.99 (m, 2H), 1.87-1.65 (m, 6H); ESMS m/e: 497.3 $(M + H)^+$. $)^+$. Calc. Anál. para $C_{27}H_{33}FN_4O_4+0.5H_2O$: C, 64.14; H, 6.78; N, 11.08. Encontrado: C, 64.26; H, 6.39; N, 11.12.

Ejemplo 77

2-METIL-N-(3-{1-[(3R)-3-(2-NITROFENOXI)-3-FENILPROPIL]PROPANAMIDA: Una mezcla de N-(3-{1-[(3S)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.20 mg, 0.0137 mmol), 2-nitrofenol (100 mg), trifenilfosina

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(30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$] dió el producto deseado (2.37 mg, rendimiento 34.5 %) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 7.84 (d, 1H), 7.90 (m 1H) , 7.45 (m 1H), 7.30-7.20 (m, 2H), 7.20 (m, 2H), 6.98 (m, 2H), 6,89 (d aparente, 1H, J=7.7 Hz), 5.62 (dd aparente, 1H, J=4,1, 8.9 Hz), 3.10 (m, 2H), 2.60 (m, 2H), 2.53 (m, 2H), 2.30-2.10 (m, 6H), 1,90 (m, 2H), 1.25 (d, 6H, traslapado); ESMS m/e: 502.3 $(M + H)^+$.

Ejemplo 78

N-(3-{1-[(3S)-3-([1,1'-BIFENIL]-4-ILOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metil-propanamida (5.20 mg, 0.0137 mmol), 4-fenilfenol (100 mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$] dió el producto deseado (3.00 mg, rendimiento 41.2%) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 8.06 (s, 1H), 7.48 (m, 2H), 7.40-7.30 (m, 8H), 7.30-7.25 (m, 4H), 6.97 (d aparente, 1H, J=7.6 Hz),

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6.91 (d aparente, 2H, J=8.7 Hz), 5.34 (dd aparente, 1H, J=4.4, 8.0 Hz), 3.40 (m, 2H), 2.98 (m, 2H), 2.53 (sept aparente, parcialmente oculto, 1H, J=8.1 Hz), 2.44 (m, 1H), 2.30-2.10 (m, 6H), 1.93 (d, 2H) 1.26 (d, 6H, J=6.9 Hz); ESMS m/e: 533.4 $(M + H)^+$.

Ejemplo 79

2-METIL-N-(3-{1-[(3R)-3-(3-NITROFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Una mezcla de N-(3-{1-[(3S)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.20 mg, 0.0137 mmol), 3-nitrofenol (100 mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$] dió el producto deseado (2.80 mg, rendimiento 40.8%) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 7.76 (dm, 1H), 7.71 (t, 1H, J=1.8 Hz), 7.50-7.40 (m, 2H), 7,40-7.25 (m, 7H), 7.17 (dd aparente, 1H, J=2.4, 8.2 Hz), 6.97 (d aparente, 1H, J=7.7 Hz), 5.45 (dd aparente, 1H, J=5.0, 8.1 Hz), 3.45 (m, 2H), 2.89 (m, 2H), 2.53 (sept aparente, parcialmente oculto, 2H, J=8.3 Hz), 2.30-2.10 (m, 6H), 1.92 (m, 2H), 1.25 (d, 6H, J=6.8 Hz); ESMS m/e: 502.3 $(M + H)^+$.

Ejemplo 80

N-(3-{1-[(3S)-3-(2-ETOXIFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.20 mg, 0.0137 mmol), 2-etoxifenol (100 mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$] dió el producto deseado (1.16 mg, rendimiento 15.5%) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) .8.06 (s,1H), 7.52 (s, 1H), 7.40-7.33 (m, 4H), 7.30-7.20 (m, 3H), 6.97 (d aparente, 1H, J=7.7 Hz), 6.88 (m, 2H), 6,68 (m, 2H), 5.21 (m, 1H), 4.11 (q, 2H, J=7.3 Hz), 3.37 (m, 2H), 2.71 (m, 2H), 2.53 (sept aparente, parcialmente oculto, 2H, J=7.6 Hz), 2,30-2.10 (m, 6H), 1.89 (m, 2H), 1,49 (t, 3H, J=7.3 Hz), 1.25 (d, 6H, J=6.8 Hz); ESMS m/e: 501.4 $(M + H)^+$.

Ejemplo 81

2-METIL-N-(3-{1-[(3S)-3-(1-NAFTILOXI)-3-FNILPROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (5.20 mg, 0.0137 mmol), 1-naftol (100 mg), trifenilfosina (30.0 mg, 0.115 mmol) y azodicarboxilato de

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dietilo (7.42 mg, 0.0426 mmol) en THF (0.50 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$] dió el producto deseado (4.30 mg, rendimiento 66.2%) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 8.06 (s, 1H), 7,72 (d, 1H, J=8.5 Hz), 7,59 (d, 1H, J=8,5 Hz), 7.5 (m, 2H), 7.45-7.30 (m, 6H), 7.25 (m, 3H), 7.17 (dd aparente, 1H, J=2.6, 9.0 Hz), 7.01 (d aparente, 1H, J=2.6 Hz), 6.97 (d aparente, 1H, J=7.9 Hz), 5.46 (dd aparente, 1H, J=8.1 Hz), 3,12 (m, 2H), 2.61 (m, 2H), 2.53 (sept aparente, parcialmente oculto, 2H, J=7.9 Hz), 2,30-2.10 (m, 6H), 1.90 (m, 2H), 1.25 (d, 6H, J=7.3 Hz, traslapado); ESMS m/e: 507.2 $(M + H)^+$.

Ejemplo 82

N-(3-{1-[(3S)-3-(1,3-DIOXO-1,3-DIHYDRO-2H-ISOINDOL-2-IL)-3-FENILPROPIL]-4PIPERIDINIL}FENIL)-2-METILPROPANAMIDA

Etapa 1:

2-[(1S)-3-CLORO-1-FENILPROPIL]-1H-ISOINDOL-1,3(2H)-DIONA: De acuerdo al procedimiento general descrito en Srebnik, M.; Ramachandran, P.V.; Brown, H.C. J. Org.Chem. 1988, 53, 2916-2920, una mezcla de (0.147 g, 1.0 mmol), (R)-(+)-3-cloro-fenil-1-propanol (0.171 g, 1.0 mmol), trifenilfosina (0.262 g, 1.0 mmol) y azodicarboxilato de dietilo (0.174 g, 1.0

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mmol) en 5.0 mL de THF, se agitó a temperatura ambiente durante 24 h. La mezcla de reacción se concentró *in vacuo*. El residuo se lavó con pentano (x3) y los extractos combinados de pentano se concentraron y cromatografiaron (sílice con hexanos:EtOAc, como el eluyente) para dar el producto deseado (0.121 g, rendimiento 50.2%) como un sólido amarillo: RMN ^1H (400 MHz, $CDCl_3$) 7.82 (dd aparente, 2H, J=2.9 Hz), 7,70 (dd aparente, 2H, J=2.9 Hz), 7.56 (m, 2H), 7.39-7.27 (m, 3H), 5.64 (dd aparente, 1H, J=7.0, 9.2 Hz), 3.57 (m, 2H), 3.05 (m, 1H), 2.82 (sept aparente, 1H, J=7.0 Hz); ESMS m/e: 300.13 $(M+H)^+$.

Etapa 2:

N-(3-{1-[(3S)-3-(1,3-DIOXO-1,3-DIHIDRO-2H-ISOINDOL-2-IL)-3-FENILPROPIL]-4-PIPERIDIN-2-METILPROPANAMIDA: Una mezcla de carbonato de potasio (29.2 mg, 0.211 mmol), yoduro de sodio (47.5 mg, 0.317 mmol),2-metil-N-[3-(4-piperidinil) fenil]propanamida (51.8 mg, 0.211 mmol), 2-[(1S)-3-cloro-1-fenilpropil]-1H-isoindol-1,3(2H)-diona (63.1 mg, 0.211 mmol) en DMF (5.0 mL), se agitó a 100°C durante 3 hrs, tiempo en el cual la TLC indicó que la reacción estaba completa. La mezcla de reacción se vació en agua (50 mL) y la capa acuosa se extrajo con cloruro de metileno (3x30 mL). Los extractos orgánicos combinados se lavaron con salmuera (30 mL), se secaron sobre $MgSO_4$ y se concentraron bajo presión reducida.

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El producto crudo se purificó por medio de placas de TLC preparatorias [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$] para dar el producto deseado (74.1 mg, rendimiento 77.1%) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 7.83 (dd aparente, 2H, J=2,9 Hz), 7.69 (dd aparente, 2H, J=2.9 Hz), 7,56 (dt aparente, 3H, J=2.9, 7.3 Hz), 7.33 (m, 4H), 7.21 (t, 1H, J=7.8 Hz), 7.09 (s, 1H), 6.81 (d aparente, 1H, J=7.8 Hz), 5.49 (dd aparente, 1H, J=5.5, 9.5 Hz), 2.98 (d, 1H, J=9.5 Hz), 2,87 (m, 2H), 2,50 (sept aparente, 1H, J=6.7 Hz), 2,40-2,35 (m, 4H), 1.94 (m, 2H), 1.70-1.50 (m, 4H), 1.25 (d, 6H, J=7.9 Hz); ESMS m/e: 510.37 $(M + H)^+$.

Ejemplo 83

2-METIL-N-(3-{1-[(3S)-3-(4-FENOXIFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL) PROPANAMIDA

Etapa 1:

4-{[(1S)-3-CLORO-1-FENILPROPIL] OXI}-(4-FENOXI)BENCENO: Una mezcla de 4-fenoxifenol (1.86 g, 10.0 mmol), (R)-(-)-3-cloro-fenil-1-propanol (1.70 g, 10,0 mmol), trifenilfosphina (2.62 g, 10.0 mmol), azodicarboxilato de dietilo (1.57 mL, 10.0 mmol) en 5.0 mL de THF, se agitó a temperatura ambiente durante 24 h. La mezcla de reacción se concentró *in vacuo*. El residuo se lavó con pentano (x3) y los extractos de pentano combinados se concentraron y cromatografiaron

(sílice con hexanos-EtOAc 97:3 como el eluyente)para dar el producto deseado como un aceite espeso que solidificó en reposo (2.51 g, 75.7 %): RMN ^1H (400 MHz, $CDCl_3$) 7.4-7.23 (m, 7H), 7.03 (t aparente, 1H, J=7.3 Hz), 6.91 (dm aparente, 2H, J=7.8 Hz), 6.93 (q aparente, 4H, J=7.8 Hz), 5.31 (dd aparente, 1H, J=4.5, 8.6 Hz), 3.82 (m, 1H), 3,62 (quinteto aparente, 1H, J=5.6 Hz), 2.47 (m, 1H) , 2.20 (m, 1H)

Etapa 2:

2METIL-N-(3-{1-[(3S)-3-(4-FENOXIFENOXI)-3-FENILPROPI]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Una mezcla de 2-metil-N-[3-(4-piperidinil)fenil]propanamida (65.5 mg, 0.266 mmol), 4-{[(1S)-3-cloro-1-fenilpropil]oxi}-(4-fenoxi)benceno (0.100 mg, 0.296 mmol), carbonato de potasio (40.9 mg, 0.296 mmol), y yoduro de sodio (67.0 mg, 0.444 mmol), en DMF (1.0 mL), se calentó a 100°C durante 3 hrs. La mezcla de reacción se vació en agua (50 mL) y la capa acuosa se extrajo con cloruro de metileno (3x30 mL). Los extractos orgánicos combinados se lavaron con salmuera (30 mL), se secaron sobre $MgSO_4$ y se concentraron bajo presión reducida. El producto crudo se purificó por medio de placas de TLC preparatorias [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$] para dar el producto deseado (0.109 g, rendimiento 74.6%) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) 7.48 (s, 1H), 7.40-7.30 (m, 4H), 7.20-7,10 (m, 6 H), 7.09 (s, 1H), 6,99 (d aparente, 1H, J=7.8 Hz),

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6.98 (t aparente, 1H, J=7.8 Hz), 6.93 (t aparente d, 2H, J=8.4 Hz), 6.84 (m, 2H), 5.20 (dd aparente, 1H, J=4.4, 8.5 Hz), 3.03 (m, 2H), 2.51 (m, 4H), 2.24 (sept aparente, 1H, J=7.8 Hz), 2.20-2.10 (m, 3H), 1.90 (m, 4H), 1.25 (d, 6H, J=7.9 Hz); ESMS m/e: 549.41 $(M + H)^+$; Cálc. Anál.para $C_{36}H_{40}N_2O_3$: C, 78.80; H, 7.35; N, 5.11. Encontrado: C, 78.58; H, 7.48; N, 5.09.

Ejemplo 84

N-(4-{1-[(3R)-3-(3,4-DIMETOXIFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA

Etapa 1:

1-[(3R)-3-(3,4-DIMETOXIFENOXI)-3-FENILPROPIL]-4-(4-NITROFENIL)-1,2,3,6-TETRAHIDROPIRIDINA: Una mezcla de carbonato de potasio (24.0 mg, 0.174 mmol), yoduro de sodio (39.0 mg, 0.260 mmol), 2-(4-nitrofenil)-1,2,3,6-tetrahidropiridina (35.4 mg, 0.174 mmol) y 4{[(1R)-3-cloro-1-fenilpropil]oxi}-1,2dimetoxibenceno (53.4 mg, 0.174 mmol) en DMF (5.0 mL), se agitó a 100°C durante 3 hrs, tiempo en el cual la TLC indicó que la reacción estaba completa. La mezcla de reacción se vació en agua (5.0mL) y la capa acuosa se extrajo con cloruro de metileno (3x30 mL). Los extractos orgánicos combinados se lavaron con salmuera (30 mL), se secaron sobre $MgSO_4$ y se concentraron bajo presión reducida.

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El producto crudo se purificó por medio de placas de TLC preparatorias [1:1=hexano:acetato de etilo con NH_3 al 1%] para producir el producto deseado (63.1 mg, rendimiento 76.6%) como un aceite amarillo: El producto se utilizó en la siguiente reacción sin purificación adicional.

Etapa 2:

4-{1[(3R)-3-(3,4-DIMETOXIFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}ANILINA: Un matraz RB de 25 mL, equipado con una bola llena de hidrógeno, se cargó con 1-[(3R)-3-(3,4-dimetoxifenoxi)-3-fenilpropil]-4-(4-nitrofenil)-1,2,3,6-tetrahidropiridina (63.0 mg, 0.133 mmol), paldio sobre carbón (5.0 mol-eq%, 0.00665 mmol, 7,04 mg) y etanol (2.0 mL) a temperatura ambiente. Después de 1 h, se filtró la mezcla de reacción a través de un tampón de Celite 545 y se concentró bajo presión reducida. El producto crudo (54.1 mg, 89.4%), se utilizó en la siguiente reacción sin purificación adicional.

Etapa 3:

N-(4-{1-[(3R)-3-(3,4-DIMETOXIFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de 4-{1-[(3R)-3-(3,4-dimetoxifenoxi)-3-fenilpropil]-4-piperidinil}aniline (5.31 mg, 0.0119 mmol), cloruro de isobutirilo (2.08 mg, 0.019 mmol), N,N-diisopropiletilamina

(8.40 mg, 0.0650 mmol) en cloruro de metileno (1.0 mL), se agitó a temperatura ambiente durante 24 horas. La mezcla de reacción se concentró y cromatografió utilizando una placa preparatoria de TLC [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$] para dar el producto (3.5 mg, 56.5%) como un aceite espeso:RMN ^1H (400 MHz, $CDCl_3$) δ 7.38 (d, 1H, J=8.6 Hz), 7.30-7,20 (m, 4H), 7.20(m, 1H), 7.11 (d, 2H, J=8.6 Hz), 7.04 (s, 1H), 6,57 (d, 1H, J=8.3 Hz), 6.44 (d, 1H, J=2.6 Hz), 6.22 (dd, 1H, J=2.6, 8.3 Hz), 5.09 (dd aparente, 1H, J=4.4, 8.1 Hz), 3.72 (s, 3H), 3.70 (s, 3H), 3,08 (m, 2H), 2.57 (m, 2 H), 2.43 (sept aparente, parcialmente oculto, 2H, J=6.8 Hz), 2.30-2.10 (m, 6H), 1.80 (m, 2H), 1.25 (d, 6H, J=7.9 Hz); ESMS m/e: 517.3 $(M+H)^+$.

Ejemplo 85

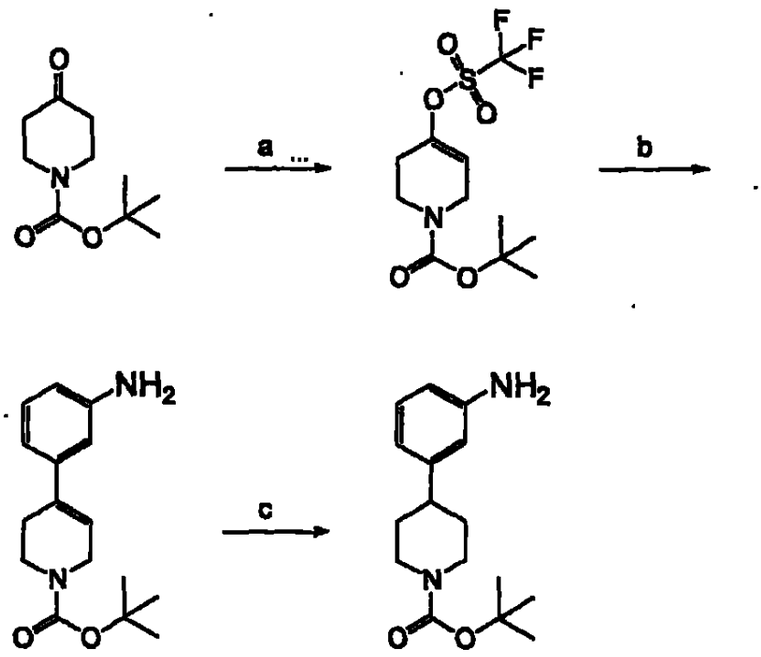
N-(3-{1-[(3S)-3-(3-ACETILFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: En un matraz RB de 25 mL se adicionó trifenilfosfina (9.80 mg, 0.0375 mmol), azodicarboxilato de dietilo (5.22 mg, 0.0300 mmol),N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metil-propanamida (9.53 mg, 0.0250 mmol), 3-hidroxiacetofenona (100 mg) y THF (1.0 mL) a temperatura ambiente. La mezcla de reacción se agitó a temperatura ambiente durante la noche (16 hrs). Se retiró el solvente bajo presión reducida y el residuo se purificó por medio de placas de TLC preparatorias

1933,535

[2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], para producir el producto deseado: RMN ^1H ($CDCl_3$) δ 70-7.64 (m, 2H), 7.54 (m, 2H), 7.49-7.44 (m, 6H), 7.25 (m, 1H), 7.05 (d, 1H, J=8.3 Hz), 6.96 (d aparente, 1H, J=7.7 Hz), 5.34 (dd aparente, 1H, J=4.8, 8.2 Hz), 3.15 (m, 2H), 2.67 (m, 2H), 2.52 (s, 3H), 2.53 (sept aparente, parcialmente oculto, 2H, J=7.6 Hz), 2.30-2.10 (m, 6H), 1.89 (m, 2H), 1.25 (d, 6H, J=6.9 Hz); ESMS m/e: 499.4 $(M + H)^+$.

Esquema A. Síntesis de 4-83-aminofenil)-1-piperidincarboxilato de tert-butilo.

1984 1536



a. n-BuLi, diisopropilamina, THF, $PhN(Tf)_2$, -78°C a temperatura ambiente, 81%.

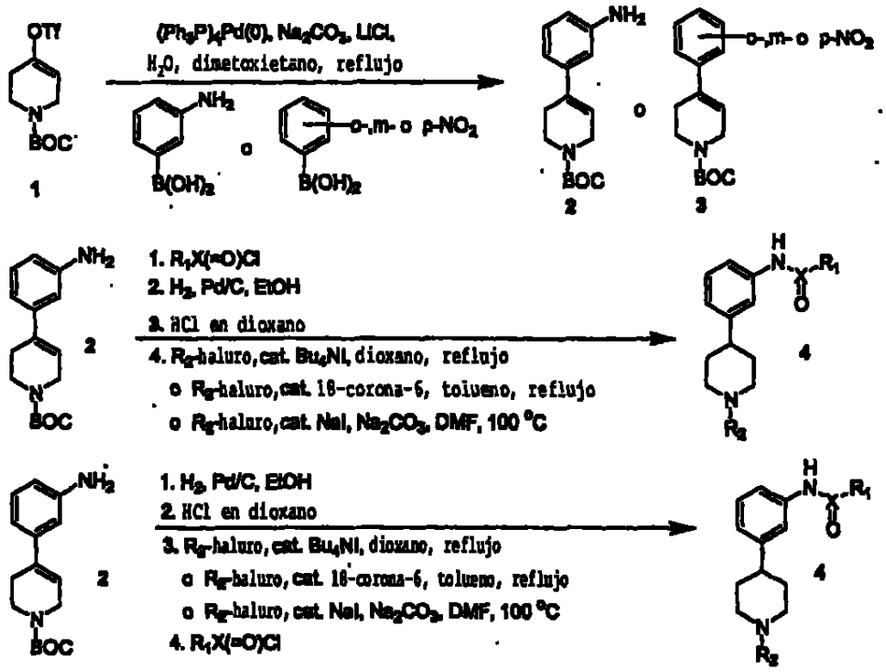
b. Hemisulfato del ácido 3-aminofenilborónico, Lic., tetrakis-trifenilfosfina-paladio (0), Na_2CO_3, DME-H_2O, reflujo, 81%.

c. Pd/C al 10%, etanol, H_2, temperatura ambiente, método del matraz, 84%.

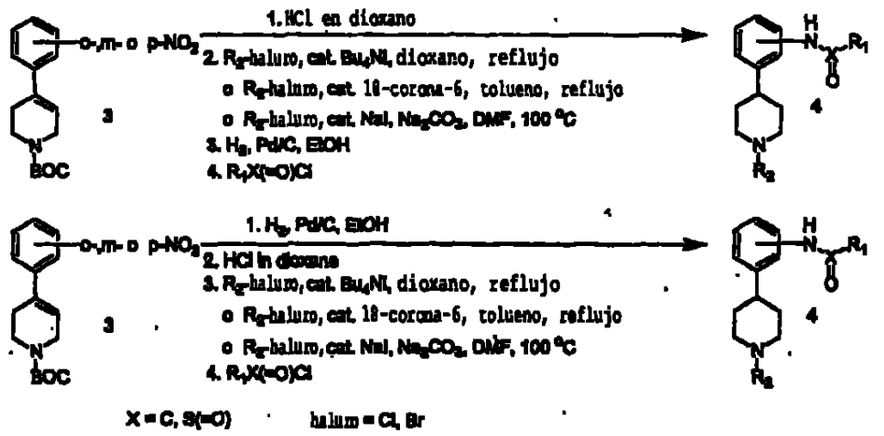
1037

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Esquema B1. Una síntesis general del antagonista de MCH



Esquema B2. Una síntesis general de los antagonistas MCH

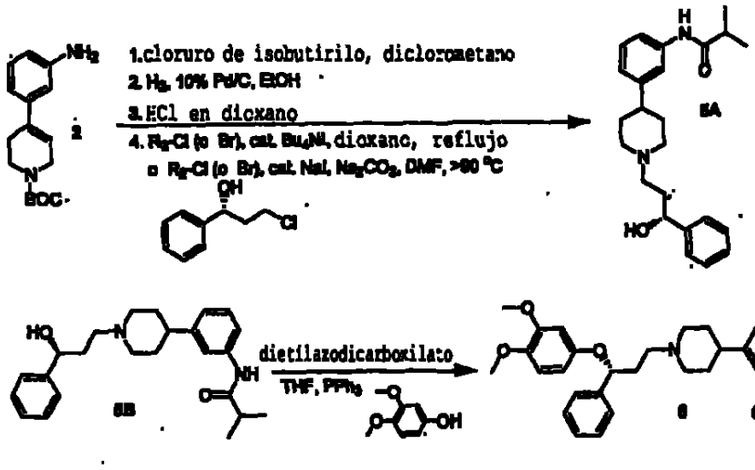


X = C, S(=O) halum = Cl, Br

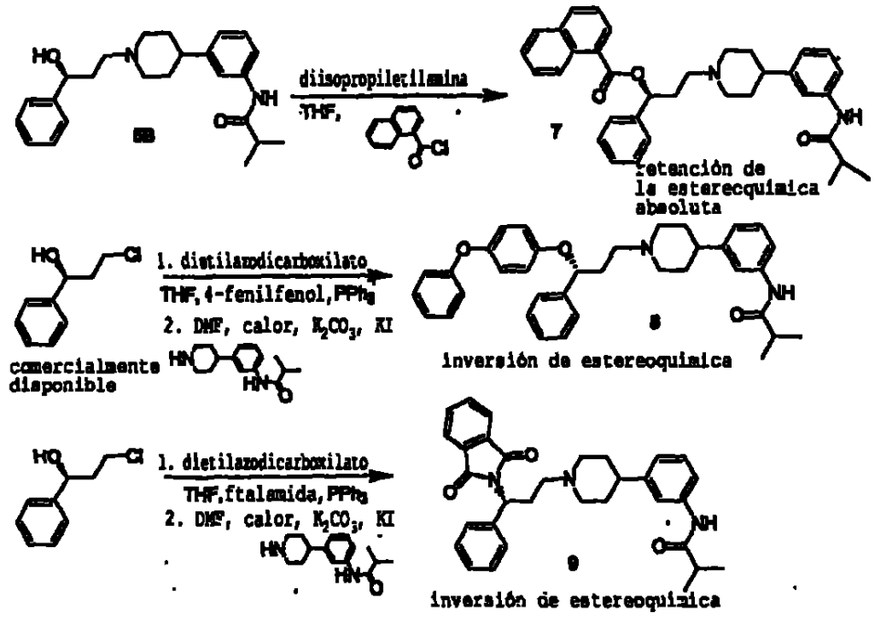
1538

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Esquema C1. Ejemplos específicos de la síntesis de los antagonistas de MCH

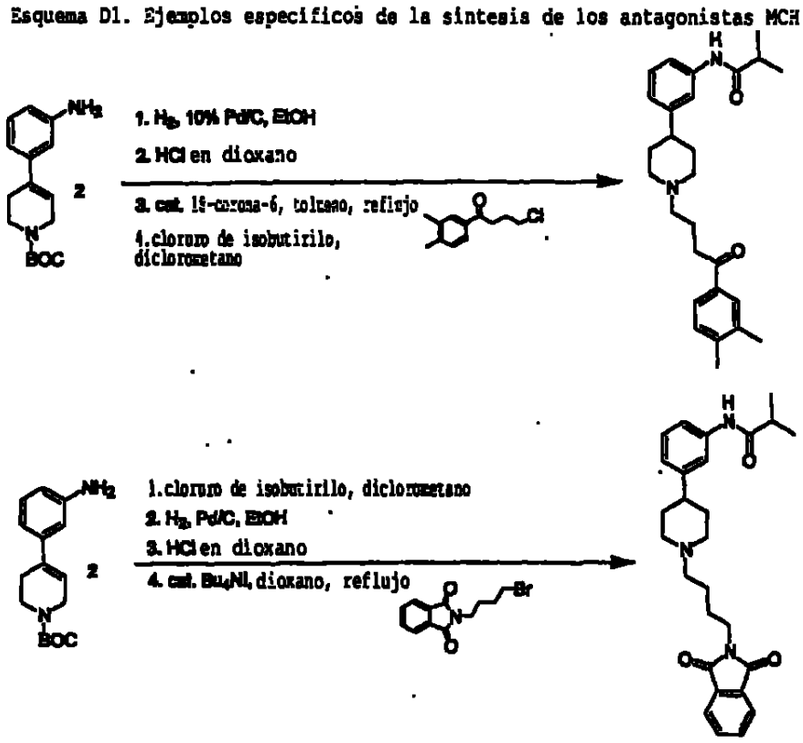


Esquema C2. Ejemplos específicos de la síntesis de los antagonistas de MCH

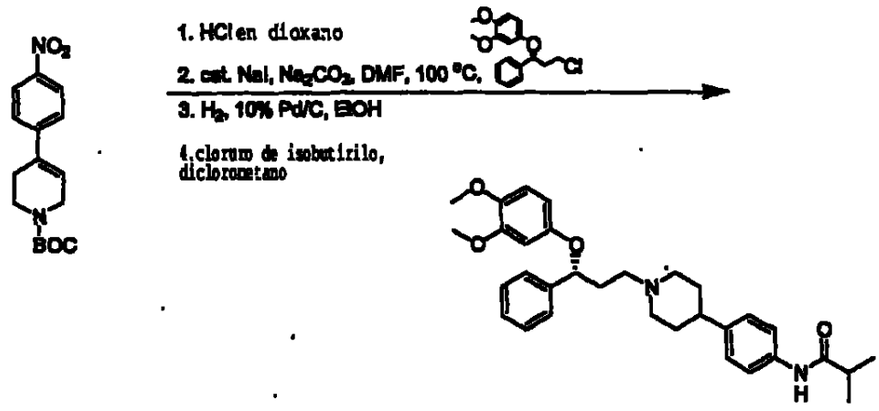


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Esquema D1. Ejemplos específicos de la síntesis de los antagonistas MCH

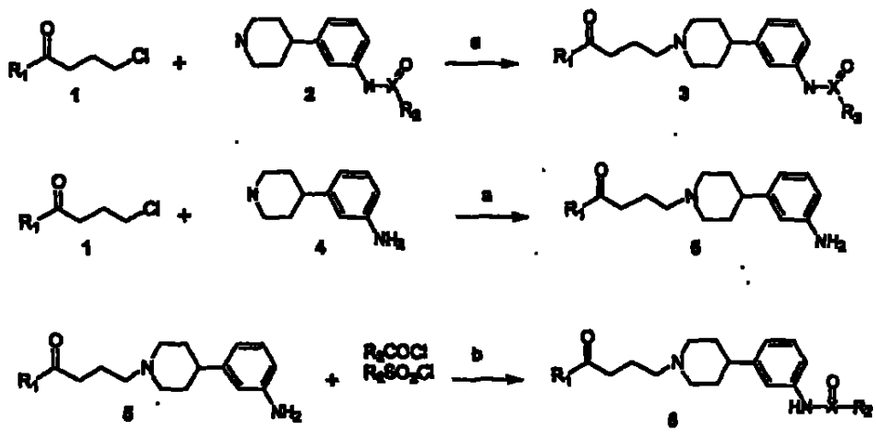


Esquema D2. Ejemplos específicos de la síntesis de los antagonistas MCH



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Esquema E: Síntesis general de los antagonistas MCH



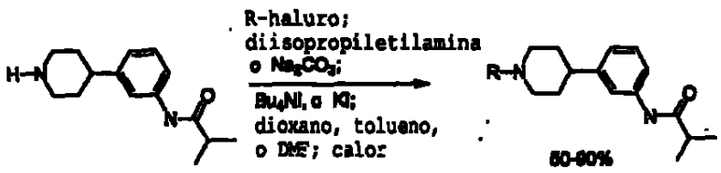
a. dioxano, diisopropiletilamina, Bu_4NI, reflujo
   o DMF, KI, Na_2CO_3, 90-100ºC
   o tolueno, 110ºC, 18-corona-6
b. diisopropiletilamina, diclorometano

X=S(=O),C
R_1=Aromático, heterocíclico o aromático sustituido
R_2=alifático o aromático

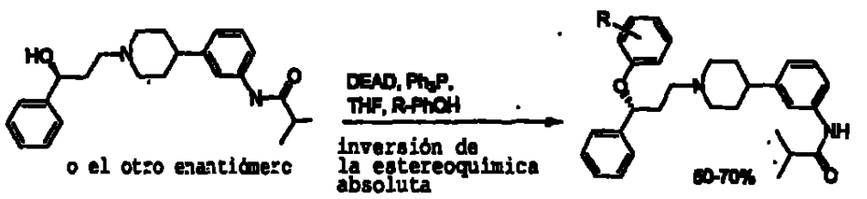
1041

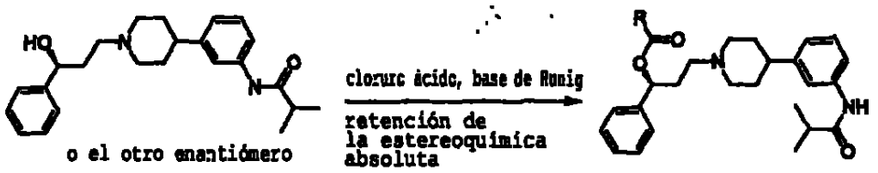
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Esquema F. Síntesis general de los antagonistas MCH



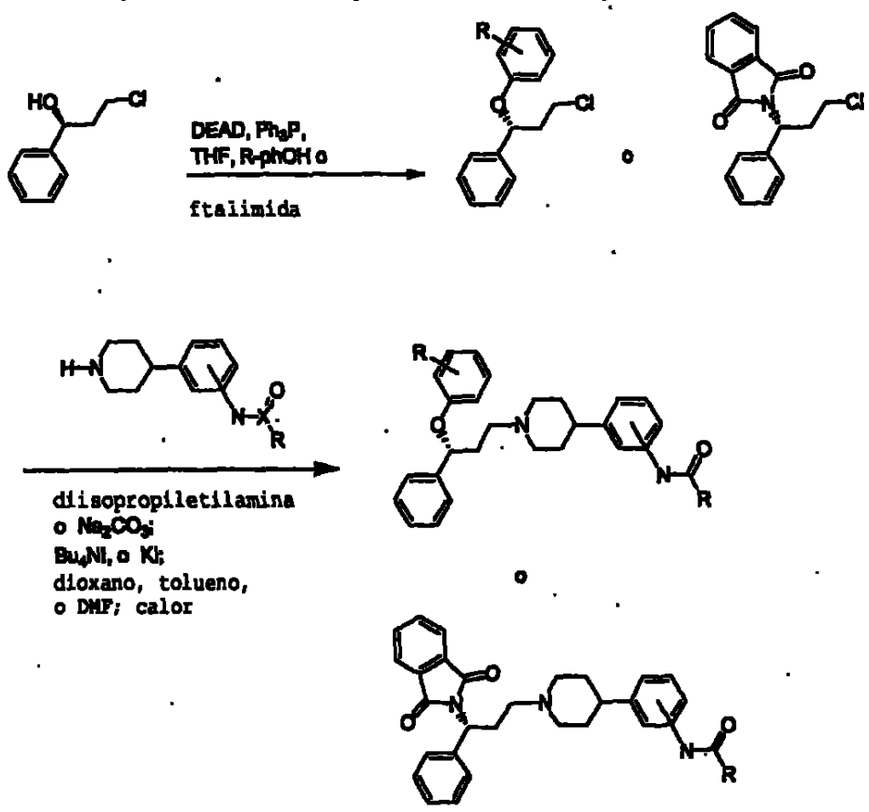
Si R = $(CH_2)_nCHOH$-Ar, entonces,





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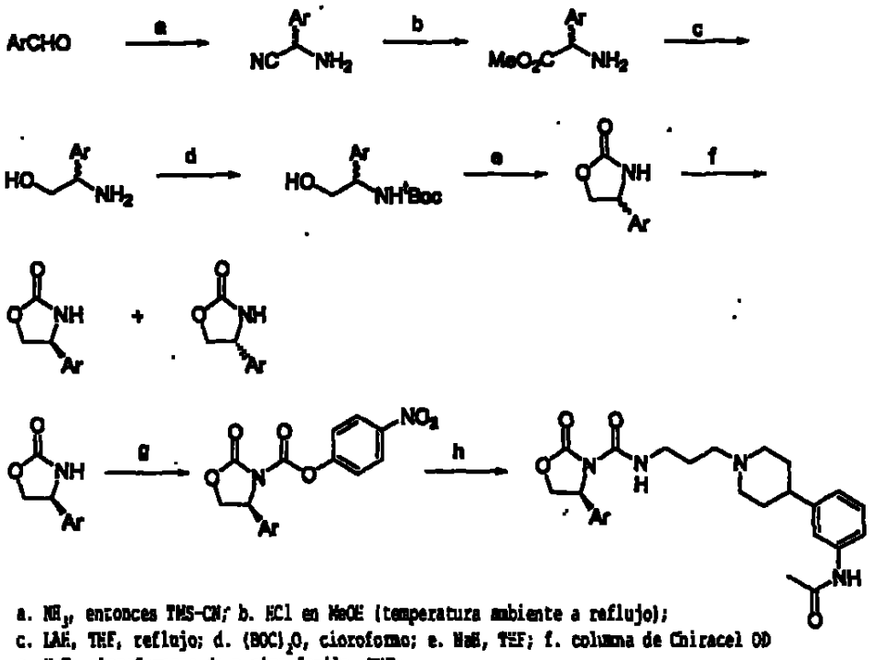
Esquema G. Síntesis general de los antagonistas MCH



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Esquema H. Síntesis de Oxazolidinonas

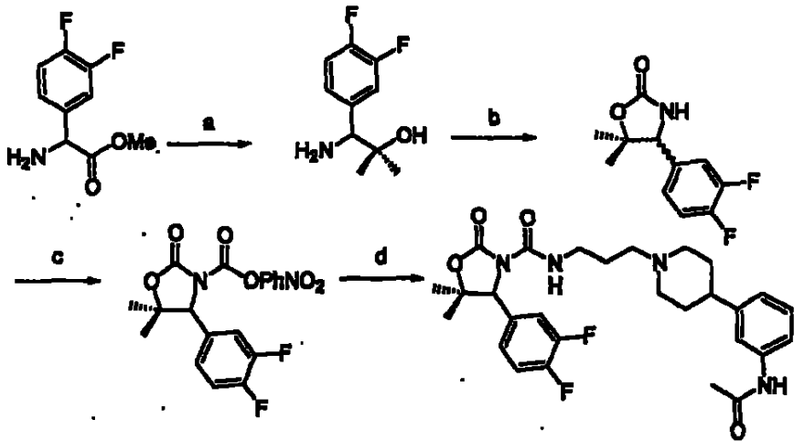


a. NH_3, entonces TMS-CN; b. HCl en MeOH (temperatura ambiente a reflujo);
c. LAH, THF, reflujo; d. $(BOC)_2O$, cloroformo; e. NaH, THF; f. columna de Chiracel OD
g. NaH, cloroformato de p-nitrofenilo, THF;
h. una amina tal como N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}acetamida

Ar=3,4-difluorofenilo, 3,5-difluorofenilo o 3,4,5-trifluorofenilo

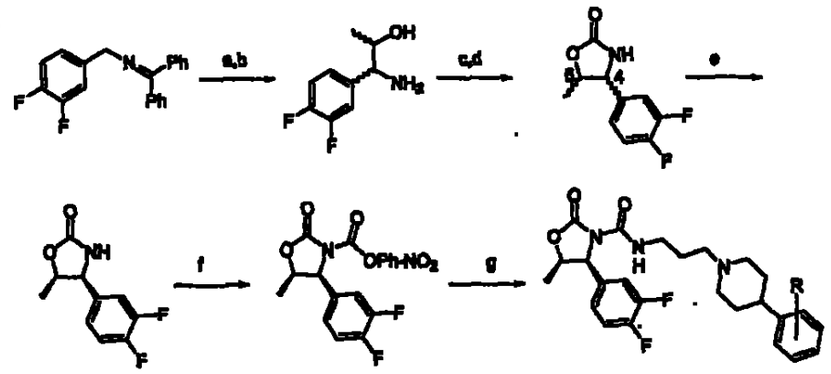
1044
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Esquema I. Síntesis de Oxazolidinonas sustituidas en gem-Dialquilo



a. bromuro de metilmagnesio, THF; b. N, N-carbonildiimidazol, DCM; c. NaH, THF, cloroformato de p-nitrofenilo; d. una amina tal como N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}acetamida

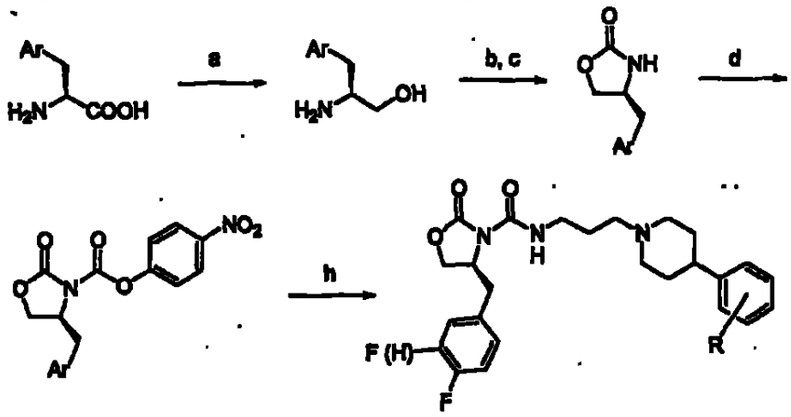
Esquema J. Síntesis y resolución Quiral de Oxazolidinonas



[a](a) t-BuLi, THF, RCHO (b) $CH_3ONH_2.HCl$, MeOH, 50-68% sobre 2 etapas (c) BoC_2O, $CHCl_3$, >90% (d) NaH, THF, 76-92% (e) diastereómeros separados por cromatografía de columna y enantiómeros separados por fase quiral CLAP, 10-16% (f) n-BuLi, THF, cloroformato de 4-nitrofenilo, ~75% (g) THF, >80%, una amina tal como N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}acetamida

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Esquema K. Síntesis de Oxazolidonas a partir de aminoacidos

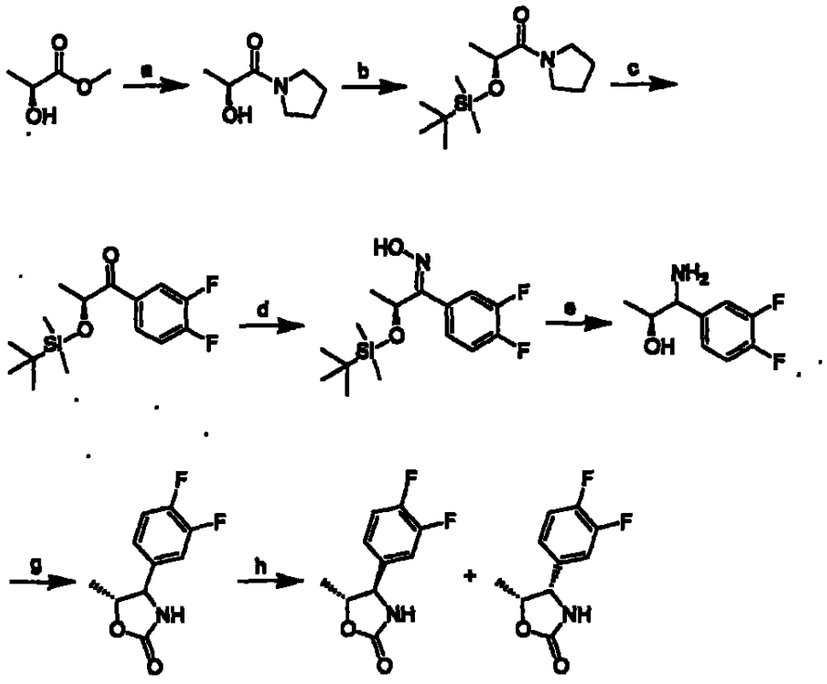


a. LAH, THF; b. $(BOC)_2O$, $CHCl_3$; c. NaH, THF; d. cloroformato de p-nitrofenilo, NaH, THF; h. una amina tal como N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}acetamida

Ar=aromático tal como 4-fluorofenilo o 3,4-difluorofenilo

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Esquema L. Determinación de la estereoquímica absoluta de las Oxazolidinonas Di-sustituidas utilizando derivados del ácido láctico

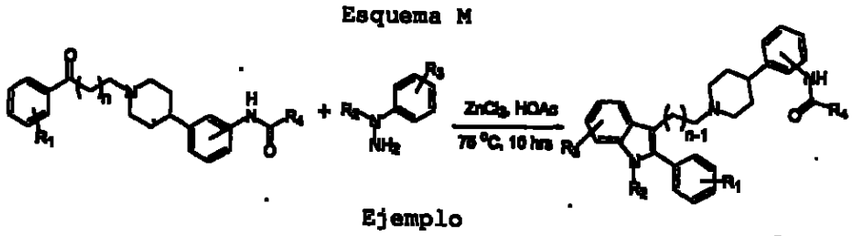


a. pirrolidina, metanol, calor; b. cloruro de t-butildimetilsililo; c. LAH, éter, reflujo d. $(BOC)_2O$, cloroformo; e. NaE, THF; h. cromatografía de gel de silice

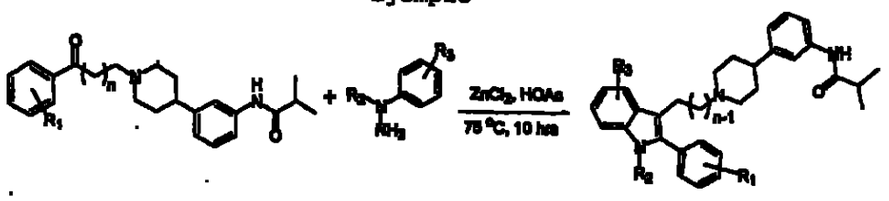
Para mas detalles ver: Lagu, B.; Wetzel, J. M.; Forray, C.; Patane, M. A.; Bock, M. G. "Determination of the Relative and Absolute Stereochemistry of a Potent α1A Selective Adrenoceptor Antagonist" Bioorg. Med. Chem. Lett. 2000, 10, 2705.

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Esquema M

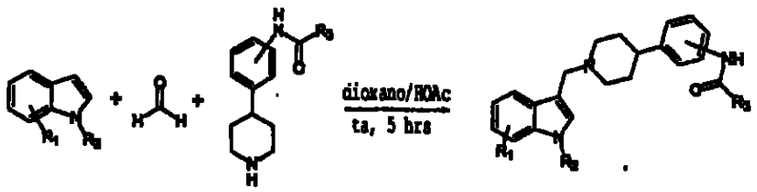


Ejemplo

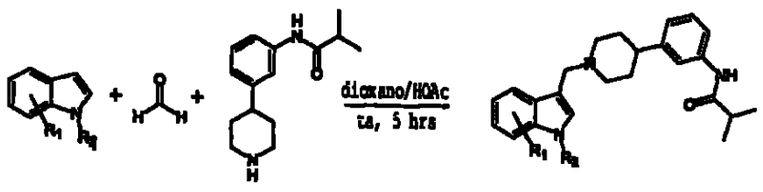


n=2, R1=H, R2=Ph, R3=H
n=2, R1=H, R2=H, R3=6-OMe
n=1, R1=H, R2=Ph, R3=H
n=4, R1=H, R2=H, R3=6-OMe

Esquema N



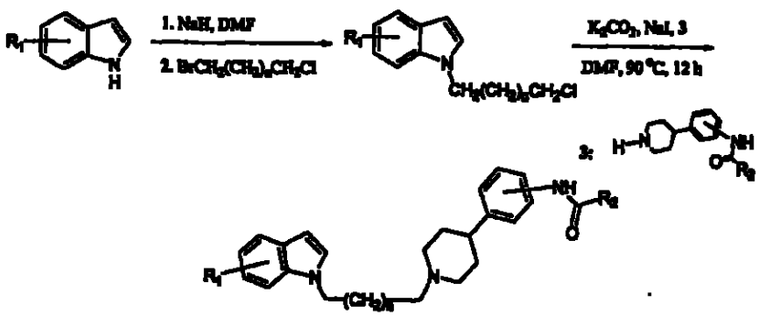
Ejemplo



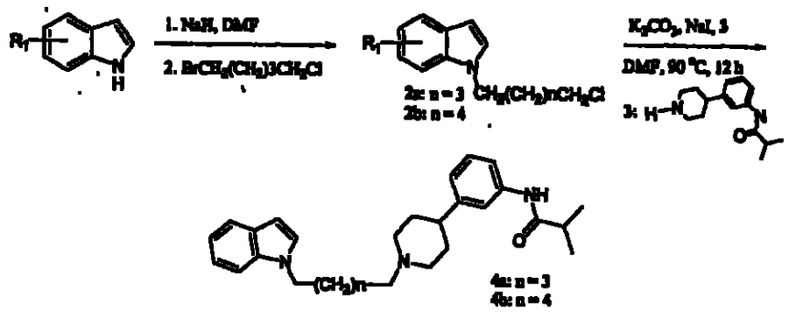
R1=6-Cl, R2=H
R1=H, R2=4-tolilo

1046

Esqema P

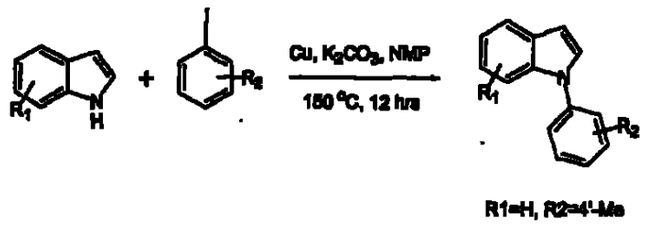


Ejemplo



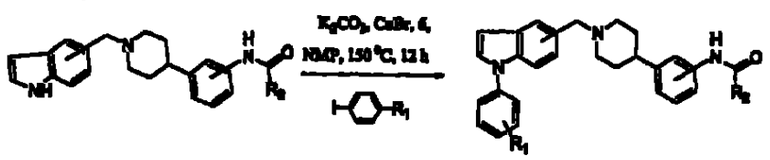
1049
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Esquema O

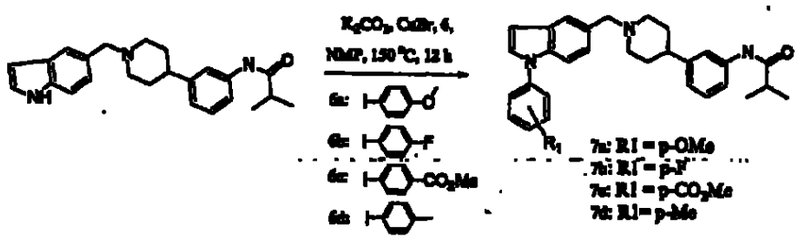


R1=H, R2=4'-Me

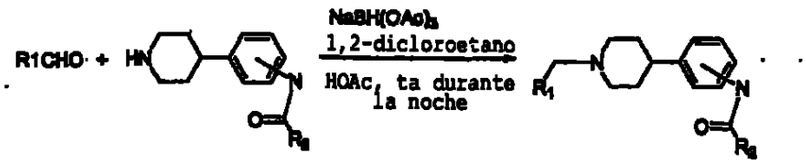
Esquema Q



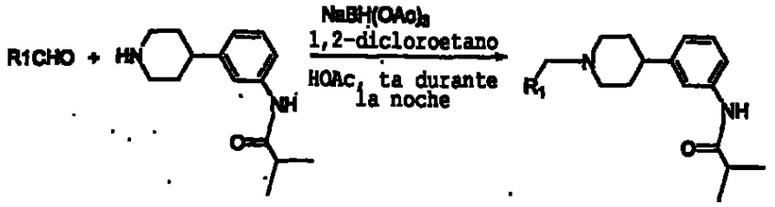
Ejemplo



Esquema R



Ejemplo



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SECCION EXPERIMENTAL

Las siguientes abreviaciones son utilizadas: HOAC, ácido acético; DMF, N,N-dimetilformamida; EtOAc, acetato de etilo; MeOH, metanol; NMP, 1-metil-2-pirrolidinona; TEA, trietilamina; THF, tetrahidrofurano: Todas las proporciones de solvente están en volumen/volumen, a menos de que se establezca lo contrario.

1-(4-METILFENIL)1H-INDOL: Una mezcla de 1-H-indol (58.5 mg, 0.500 mmol), 1—(yodo)-4-metilbenceno (0.218 g, 1.00 mmol), polvo de cobre (32.0 mg, 0.500 mmol), y K_2CO_3 (0.138 g, 1.00 mmol) en 1-metil-2-pirrolidinona (1 mL), se calentó a 150°C durante 12 h bajo argón. La mezcla resultante se diluyó con H_2O (6 mL). La capa acuosa se extrajo con CH_2Cl_2 (3 X 10 mL). Los extractos orgánicos combinados se lavaron con salmuera (10 mL), se secaron sobre $MgSO_4$ y se concentraron *in vacuo*. El residuo se purificó por medio de TLC preparatoria utilizando EtOAc/hexano (1:4), para dar el producto deseado (82 mg, 79%). RMN ^1H (400 MHz, $CDCl_3$) δ 6 7.67 (d, 1H, J = 7.7 Hz), 7.52 (d, 1H, J = 7,4 Hz), 7.38 (d, 2H, J = 8.4 Hz), 7.34—7.29 (m, 3H), 7.21 (t, 1H, J = 7.0 Hz), 7.15 (t, 1H, J = 7.0 Hz), 6.66 (d, 1H, 3.3 Hz), 2.43 (s, 3H); ESMS m/e: 208.0 $(M + H)^+$.

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Ejemplo 86

N-(3-{1-[(6-CLORO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENYL)-2-METILPROPANAMIDA: Una solución de 2-metil-N-[3-(4-piperidil)fenil]propanamida (0.369 g, 1.50 mmol) y 37% en peso de formaldehido acuoso (30.0 mg, 1,50 mmol) en 1 mL de HOAc:dioxano (1:4), se adicionó a 6-cloro-1-H-indol (0.152 g, 1.00 mmol) y la mezcla de reacción se agito durante 12 h a temperatura ambiente. La mezcla resultante se diluyó con H_2O (10 mL). La capa acuosa se extrajo con CH_2Cl_2 (3 X 100 mL). Los extractos orgánicos combinados se lavaron con salmuera (10 mL), se secaron sobre $MgSO_4$ y se concentraron *in vacuo*. El residuo se purificó por medio de TLC preparatoria en sílice utilizando 5% de NH_3 (2.0 M en metanol) en CH_2Cl_2, para dar el producto deseado (79mg, 42%). RMN ^1H (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.04 (s, 1H), 7.52 (t, 2H, J = 8.1 Hz), 7.35 (d, 2H, J = 13.3Hz), 7.18 (t, 1H, J = 7.9 Hz), 7.09 (dd, 1H, J = 1.9, 8.5 Hz), 6.85 (d, 1H, J = 7.4 Hz), 5.18 (s, 1H), 4.01 (s, 2H), 2.55 (septet, 1H, J = 6.8 Hz), 2.48-2.34 (m, 3H), 2.08-1.95 (m, 4H), 1.78 (d, 2H, J = 12.8 Hz), 1.22 (d, 6H, J = 6.8 Hz); ESMS m/e: 410.1 $(M + H)^+$.

Ejemplo 87

2-METIL-N-[3-(1-{1-(4-METILFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: De acuerdo al procedimiento

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utilizado para la síntesis de N-(3-{1-[(6-cloro-1H-indol-3-il)metil]-4-piperidinil}fenil)-2-metilpropanamida, 1-(4-metilfenil)-1H-indol (0.207 g, 1.00 mmol) proporcionó 2-metil-N-[3-(1-{[1-(4-metilfenil)-1H-indol-3-il]metil}-4-piperidinil)fenil]propanamida (0.441 g, 78%). RMN ^{1}H (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.73 (d, 1H, J = 7.2 Hz), 7.58–7.51 (m, 2H), 7.43–7.36 (m, 3H), 7.35-7.29 (m, 3H), 7.26–7.15 (m, 3H), 6.89 (d, 1H, J = 7.7 Hz), 4.07 (s, 2H), 3.36 (d, 2H, J = 11.6 Hz), 2.59–2.39 (m, 6H), 2.55 (sept, 1H, J = 6.7Hz), 2.10–1.98 (m, 2H), 1.83 (d, 2H, J = 12.9 Hz), 1.23 (d, 6H, J = 6.9 Hz); ESMS m/e: 466.2 $(M + H)^+$.

2-[(1S)-3-CLORO-1-FENILPROPIL]-1H-ISOINDOL-1,3(2H)-DIONA: Trifenilfosfina (5.25 g, 20.0 mmol) y azodicarboxilato de dietilo (3.58 g, 20.0 mmol), se adicionaron a una solución de (1R)-3-cloro-1-fenil-1-propanol (3.42 g, 20.0 mmol) y ftalimida (2.94 g, 20.0 mmol) en THF (100 mL). La mezcla de reacción se agitó durante 4 h a temperatura ambiente. Se retiró el solvente bajo presión reducida y el residuo se trituró con pentano (3 X 50 mL). Las fracciones de pentano combinadas se concentraron *in vacuo* y el producto crudo se purificó por cromatografía en sílice utilizando EtOAc/hexano (3:97)para dar el producto deseado (4.40 g, 74%). RMN ^{1}H (400 MHz, $CDCl_3$) δ 7,82 (d, 1H, J = 5.7 Hz), 7.81 (d, 1H, J = 5.5 Hz), 7.70 (d, 1H, J = 5.4 Hz), 7.69 (d, 1H, J = 5.8

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Hz), 7.55 (d, 2H, J = 7.2 Hz), 7.38–7.28 (m, 3H), 5,64 (dd, 1H, J = 6.8, 9.2 Hz), 3.56 (t, 2H, J = 6.4 Hz), 3.11–3.02 (m, 1H), 2.85–2.75 (m, 1H); ESMS m/e: 300.1 $(M + H)^+$.

N-(3-{1-[(3S)-3-(1,3-DIOXO-1,3-DIHIDRO-2H-ISOINDOL-2-IL)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de 2–[(1S)-cloro-1-fenilpropil]-1H-isoindol-1,3(2H)-diona (4.50 g, 15.0 mmol), 2-metil-N-[3–(4–piperidinil)fenil]propanamida (4.26 g, 15.0 mmol), K_2CO_3 (4.16 g, 30.0 mmol), y NaI (3.40 g, 20.0 mmol) en DMF (40 mL), se agitó a 90°C durante 12 hrs. La mezcla de reacción se diluyó con agua (50 mL), se extrajo con CH_2Cl_2 (3 X 50 mL), y los extractos orgánicos combinados se lavaron con salmuera (50 mL), se secó sobre $MgSO_4$, y se concentró bajo presión reducida. El residuo se purificó por cromatografía sobre sílice utilizando 5% de NH_3 (2.0 M en metanol) en CH_2Cl_2 para dar el producto deseado (5.10 g, 74%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.83 (d, 1H, J = 5.5 Hz), 7.82 (d, 1H, J = 5.5 Hz), 7.71 (d, 1H, J = 5.5 Hz), 7.70 (d, 1H, J = 5.4 Hz), 7.56 (d, 2H, J= 7.1 Hz), 7.35–7.27 (m, 5H), 7.22 (t, 1H, J = 7.5 Hz), 7.09 (s, 1H), 6.81 (d, 1H, J = 7.8 Hz), 5,49 (dd, 1H, J = 5.5, 9.6 Hz), 2.97 (d, 1H, J = 10.1 Hz), 2.92–2.82 (m, 2H), 2.44 (sept, 1H, J = 6.7 Hz), 2.40–2.29 (m, 3H), 2.00–1.83 (m, 2H), 1.79–1.39 (m, 5H) , 1.26 (d, 6H, J = 6.9 Hz); ESMS m/e: 510.4 $(M + H)^+$.

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N-(3-{1-[(3S)-3-AMINO-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3S)-3-(1,3-dioxo-1,3-dihidro-2H-isoindol-2-il)-3-fenilpropil]-4-piperidinil}-fenil)-2-metilpropanamida (4.60 g, 9.06 mmol) e hidrazina (3.62 g, 72.4 mmol) en etanol (150 mL), se reflujo durante 12 h. El precipitado blanco resultante se filtró y el filtrado se concentró bajo vacio. El residuo se lavó con CH_2Cl_2/EtOAc (1:1, 3 X 50 mL) y las fracciones orgánicas combinadas se concentraron *in vacuo* para dar el producto deseado (2.90 g, 95 %). RMN ^1H (400 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.39–7.30 (m, 6H), 7.29–7.19 (m, 2H), 6.95 (d, 1H, J = 7.2), 4.01 (t, 1H, J = 6.8 Hz), 3.04 (t, 2H, J = 10.6 Hz), 2.62–2.30 (m, 6H), 2.05–1.70 (m, 8H), 1.24 (d, 6H, J =6.8 Hz); ESMS m/e: 380.4 $(M + H)^+$.

Ejemplo 88

2.METIL-N-(3-{1-[3S)-3-FENIL-3-(PROPIONILAMINO)PROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: De acuerdo al procedimiento utilizado para la síntesis de N-(3-{1-[(3S)-3-(acetilamino)-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamide, N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamide (11.0 mg, 0.0280 mmol) y cloruro de propionilo (3.80 mg, 0.0420 mmol) se proporcionó 2-metil-N-(3-{1-[(3S)-3-fenil-3-(propionilamino)propil]-4-piperidi-

nil}fenil)propanamida (12 mg, rendimiento 97%). RMN ^1H (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.59 (s, 1H), 7.40–7.20 (m, 7H), 6.96 (s, 1H), 5.19-5.12 (m, 1H), 3.18 (d, 1 H, J=12.0 Hz), 2.99 (d, 1H, J= 10.4 Hz), 2.93–2.86 (m, 1H), 2.61–2.40 (m, 3H), 2.38–2.23 (m, 3H), 2.19–1.75 (m, 8H), 1.25 (d, 6H, J= 6.9 Hz), 1.22-1.08 (m, 3H); ESMS m/e: 436.4 $(M + H)^+$.

Ejemplo 89

N-{3-[1-((3S)-3-{[(4-FLUOROFENIL)ACETIL]AMINO}-3-FENILPROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Una mezcla de N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida (11.0 mg, 0.0280 mmol) y cloruro de (4-fluorofenil)acetilo (7.20 mg, 0,0420 mmol) en THF (5 mL), se agitó a temperatura ambiente durante 4 h. Se retiró el solvente bajo presión reducida y se purificó el residuo por medio de TLC preparatoria utilizando hexano:EtOAc (2:1), para dar el producto deseado (13 mg, rendimiento 90%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.89 (d, 1H, J= 8.4 Hz), 7.59 (s, 1H), 7.31–6,93 (m, 13H), 5.13 (q, 1H, J= 6.0 Hz), 3.56 (s, 2H), 3.07 (d, 1H, J=11.7 Hz), 2.91 (d, 1H, J= 11,0 Hz), 2,62–2.42 (m, 2H), 2.40–2.30 (m, 1H), 2.12–1.54 (m, 9H), 1.24 (d, 6H, J= 6.7 Hz); ESMS m/e: 515.3 $(M + H)^+$.

Ejemplo 90

N-(3-{1-[3-(1,2-DIFENIL-1H-INDOL-3-IL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de clorohidrato de 1,1-difenilhidrazina (10.3 mg, 0.0470 mmol), 2-metil-N-{3-[1-(5-oxo-5-fenilpentil)-4-piperidinil]-fenil}propanamida (14.7 mg, 0.0362 mmol), $ZnCl_2$ (14.85 mg, 0.109 mmol), y HOAc (0.5 mL), se calentó durante 4 h a 80°C. La mezcla cruda resultante se diluyó con agua (10 mL), la capa acuosa se neuralizó con K_2CO_3 saturado y se extrajo con CH_2CL_2 (3 X 20 mL). Las capas orgánicas combinadas se concentraron *in vacuo* y el residuo se purificó por TLC preparatoria utilizando 5% de NH_3 (2.0 M en metanol) en CH_2Cl_2 para dar el producto deseado N-(3-{1-[3-(1,2-difenil-1H-indol-3-il)propil]-4-piperidinil}-fenil)-2-metilpropanamida (4.1 mg, 37%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.71–7.65 (m, 1H) 7.42 (d, 1H, J= 7.4 Hz), 7.39 (s, 1H), 7.36–7.15 (m, 15H), 6.94 (d, 1H, J=7,8 Hz), 3.12 (d, 2H, J= 11.2 Hz), 2.90 (t, 2H, J= 7.8 Hz), 2.59–2.45 (m, 3H), 2.19–1.91 (m, 7H), 1.82 (d, 2H, J=13.5 Hz), 1.24 (d, 6H, J= 6.9 Hz); ESMS m/e: 555.3 $(M + H)^+$.

Ejemplo 91

N-(3-{1-[3-(5-METOXI-2-FENIL-1H-INDOL-3-IL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: De acuerdo al procedimiento utilizado para la síntesis de N-(3-{1-[3-(1,2-difenil-1H-indol-3-il)propil]-4-piperidinil}fenil)-2-metil-

propanamida, 2-metil-N-{3-[1-(5-oxo-5-fenilpentil)-4-piperidinil]fenil}propanamida (15.6 mg, 38.2 mmol), y clorohidrato de 1-(4-metoxifenil)hidrazina (8.00 mg, 0.0458 mmol) proporcionan N-(3-{1-[3-(5-metoxi-2-fenil-1H-indol-3-il)propil]-4-piperidinil}fenil)-2-metilpropanamida (3.9mg, 20%). RMN ^{1}H (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.55 (d, 2H, J= 7.4 Hz) 7.43–7.39 (m, 3H), 7.38–7.35 (m, 2H), 7.27–7.19 (m, 3H), 7.08 (d, 1H, J= 7.4 Hz), 6.94 (d, 1H, J= 7.6 Hz), 6.87 (dd, 1H, J= 4.0, 6.6 Hz), 3.88 (s, 3H), 3.80–3.69 (m, 1H), 2.99 (d, 2H, J= 11.7 Hz), 2.89 (t, 2H, J= 7.3), 2.55–2.39 (m, 4H), 2.02–1.88 (m, 3H), 1.82–1.68- (m, 4H), 1.24 (d, 6H, J= 6,9 Hz); ESMS m/e: 510.3 $(M + H)^+$.

Ejemplo 92

N-(3-{1-[4-(5-METOXI-2-FENIL-1H-INDOL-3-IL)BUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: De acuerdo al procedimiento utilizado para la síntesis de N-(3-{1-[3-(1,2-difenil-1H-indol-3-il)propil]-4-piperidinil}fenil)-2-metilpropanamida, 2-metil-N-{3-[1-(6-oxo-6-fenilhexil)-4-piperidinil]fenil}-propanamida (14.3 mg, 0.0339 mmol), y clorohidrato de 1-(4-metoxifenil)hidrazina (7.10 mg, 0.0407 mmol) proporcionan N-(3-{1-[4-(5-metoxi-2-fenil-1H-indol-3-il)butil]-4-piperidinil}fenil)-2-metilpropanamida (5.8 mg, 33%). RMN ^{1}H (400 MHz, $CDCl_3$) δ 7.95 (d, 2H, 5 = 7.8 Hz), 7.61–7.15 (m, 11H), 6.97 (d, 1H, J= 7.0 Hz), 3.88 (s, 3H), 3.09 (d, 2H,J= 11,3

Hz), 2.99 (t, 2H, J= 7.0 Hz), 2.55–2.35 (m, 4H), 2.12–1.70 (m, 6H), 1.68–1.52 (m, 2H), 1.48–1.34 (m, 2H), 1,25 (d, 6H, J= 6.7 Hz); ESMS m/e: 524.3 $(M + H)^+$.

Ejemplo 93

2-METIL-N-(3-{1-[(1-FENIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: De acuerdo al procedimiento utilizado para la síntesis de N-(3-{1-[3-(1,2-difenil-1H-indol-3-il)propil]-4-piperidinil}fenil)-2-metilpropanamida, N-{3-[1-(3,3-dimetoxipropil)-4-piperidinil]fenil}-2-metil-propanamida (15.2 mg, 0.0436 mmol), y clorohidrato de 1,1-difenilhidrazina (11.6 mg, 0.0524 mmol) proporcionan 2-metil-N-(3-{1-[1-fenil-1H-indol-3-il)metil]-4-piperidinil}-fenil)propanamida (11 mg, 56%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.79 (d, 1H, J= 7.8 Hz), 7.57 (d, 1H, J= 7.7 Hz), 7.54-7.47 (m, 4H), 7.43-7.32 (m, 4H), 7.25-7.16 (m, 4H), 6.95 (d, 1H, J= 7.8 Hz), 3.87 (s, 2H), 2.63-2.47 (m, 2H), 2.21 (dt,2H, J= 3,0, 10.5 Hz), 2,12-1.77 (m, 6H), 1.24 (d, 6H, J= 6.9 Hz); ESMS m/e: 451.3 $(M + H)^+$.

Ejemplo 94

2–METIL-N-(3-{1-[(4E)-4-FENIL-4-(2-PIRIDINILHIDRAZONO)BUTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: De acuerdo al procedimiento utilizado para la síntesis de N-(3-{1-[3-(1,2-difenil-1H-indol-3-il)propil]-4-piperidinil}fenil)-2-metil-

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propanamida, 2-metil-N-{3-[1-(4-oxo-4-fenilbutil)-4-piperidinil]fenil}propanamida (8.70 mg, 0.0223 mmol), y 2-hidrazinopiridina (2.92 mg, 0.0268 mmol) proporcionan 2-metil-N-(3-{1-[4E)-4-fenil-4-(2-piridinilhidrazono)butil-4-piridinil}fenil)propanamida (2.5 mg, 24%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.97 (d, 1H, J = 8.6 Hz), 7,85 (d, 1H, J= 7.3 Hz), 7.64-7.27 (m, 9H), 7.09 (d, 1H, J= 8.0 Hz), 6.97 (d, 1H, J= 8.4 Hz), 6.73 (q, 1H, J= 6.6 Hz), 3.52—3.48 (m, 2H), 3.20—3.10 (m, 2H), 2.85—1.75 (m, 13H), 1.26 (d, 6H, J= 6.8 Hz); ESMS m/e: 484.4 $(M + H)^+$.

Ejemplo 95

N-(3-{1-[3-(5-METOXI-1H-INDOL-3-IL) PROPIL]-4-PIPERIDINIL]-2-METILPROPANAMIDA: De acuerdo al procedimiento utilizado para la síntesis de N-(3-{1-[3-(1,2-difenil-1H-indol-3-il)propil]-4-piperidinil}fenil)-2-metil-propanamida, N-(3-{1-[4-(1,3-dioxolan-2-il)butil]-4-piperidinil}fenil}-2-metilpropanamida (23.5 mg, 0.0628 mmol), y clorohidrato de 1-(4-metoxifenil)hidracina (13.2 mg, 0.0774 mmol) proporcionan N-(3-{1-[3(5-metoxi-1H-indol-3-il)propil]-4-piperidinil}-2-metilpropanamida (11 mg, 42%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.45 (s, 1H); 7.32 (d, 1H, J= 8.4 Hz), 7,28—7.21 (m, 2H), 7.10 (s, 1H), 7.05 (d, 1H, J= 2.3 Hz), 7.00—6.91 (m, 2H), 6.85 (dd, 1H, J= 2.7, 9.0 Hz), 3.87 (s, 3H), 3.06 (d, 2H, J= 11.6 Hz), 2.75 (t, 2H, J=7.2 Hz), 2.55—2.42 (m,

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4H), 2.08–1.90 (m, 4H), 1.88–1.74 (m, 4H), 1.25 (d, 6H, J= 6.9 Hz); ESMS m/e: 434.2 $(M + H)^+$.

4-[3-(PROPIONILAMINO)FENIL]-1-PIPERIDINCARBOXILATO DE TERT-BUTILO: Cloruro de propionilo (5.53 g, 0.0597 mol) se adicionó gota a gota a una solución de 4-(3-aminofenil)-1-piperidincarboxilato de tert-butilo (15.0 g, 0.0543 mol) y TEA (16.5 g, 0.163 mol) en THF (200 mL) y la mezcla se agitó a temperatura ambiente durante 3 h. Se adicionó agua (50 mL) a la mezcla de reacción, la capa acuosa se extrajo con CH_2Cl_2 (3 X 100 mL) y los extractos orgánicos combinados se lavaron con salmuera (50 mL), se secaron sobre Na_2SO_4 y se concentraron bajo presión reducida. Se purificó el residuo por cromatografía sobre sílice utilizando hexano/EtOAc (10:1) para producir el producto (18.8 g, 99%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.34–7.21 (m, 3H), 6.93 (d, 1H, J= 7.4 Hz), 2.77 (t, 2H, J= 11.5 Hz), 2.68-2.58 (m, 1H), 2.38 (q, 2H, J= 7.6 Hz), 1.87–1.67 (m, 4H), 1.67-1.54 (m, 2H), 1.48 (s, 9H), 1.25 (t, 3H, J= 7.5 Hz); ESMS m/e: 333.4 $(M+H)^+$.

N-[3-(4-PIPERIDINIL)FENIL]PROPANAMIDA: En una solución agitada de 4-[3(propionilamino)fenil]-1-piperidincarboxilato de tert-butilo (18.8 g, 0.0543 mmol) en dioxano(100 mL) a 5 °C, se burbujeo gas de HCl durante 2 h. El solvente se

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retiró *in vacuo*, después se disolvió en agua (100 mL) y se neutralizó al adicionar una solución acuosa de KOH al 10%. La capa acuosa se extrajo (3 X 200 mL) con una mezcla de $CHCl_3$/alcohol isopropílico (3:1), y las capas orgánicas combinadas se lavaron con salmuera (100 mL), se secaron sobre Na_2SO_4, se filtraron y concentraron *in vacuo*. El residuo se purificó por cromatografía de columna en sílice utilizando 5% de NH_3 (2.0 M en metanol) en CH_2Cl_2 para producir el producto deseado (12.6 g, 99%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.44 (s, 1H), 7.32 (d, 1H, J= 7.2 Hz), 7.28–7,21 (m, 1H), 7.09 (s, 1H), 6,97 (d, 1H, J= 7,6 Hz), 3.18 (d, 2H, J= 12.6 Hz), 2,73 (dt., 2H, J= 2.2, 11.2 Hz), 2.65-2.57 (m, 1H), 2.38 (q, 2H, J= 7.4 Hz), 1,83 (d, 2H, J= 12.1 Hz), 1.70–1.61 (m, 3H) 1.25 (t, 3H, J= 7.5 Hz); ESMS m/e: 233.1 $(M + H)^+$.

4-{3-[(CICLOPROPILCARBONIL) AMINO] FENIL} 1-PIPERIDINCARBOXILATO DE TERT-BUTILO: De conformidad con el procedimiento utilizado para la síntesis de 4-[3-(propionilamino)fenll]-1-piperidincar-boxilato de tert-butilo, 4-(3-aminofenil)-1-piperidincar-boxilato de tert-butilo (16.47 g, 0.0596 mol) y cloruro de ciclopropancarbonilo (6.27 g, 0.0597 mol) proporcionan 4-{3-[(ciclopropilcarbonil) amino] fenil} 1-piperidincarboxilato (18.1 g, 100%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.55–7.46 (m, 2H), 7.29–7.21 (m, 2H), 6.96–6.89(m,

1H), 2.79 (t, 2H, J 12.1 Hz), 2.68-2.58 (m 1H), 1.84 (d, 2H, J = 12.6 Hz), 1.83–1.76 (m, 4H), 1,48 (s, 9H), 1.19–1.12 (m, 1H), 1.09–1,05 (m, 2H), 0.89–0.75 (m, 2H); ESMS m/e: 345.5 $(M+H)^+$.

N-[3-(4-PIPERIDINIL)FENIL]CICLOPROPANCARBOXAMIDA: De conformidad con el procedimiento utilizado para la síntesis de N–[3-(4-piperidinil)fenil]propanamida, 4-{3-[[ciclopropilcarbonil)amino]fenil}-1-piperidincarboxilato de butilo (18.9 g, 0.0543 mol) proporcionaron N[3-(4-piperidinil)-fenil]ciclopropancarboxamida (13.2g, 100 %). RMN ^1H (400 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.36–7.22 (m, 3H), 7.23 (d, 1H, J= 6.9 Hz), 3,17 (d, 2H, J= 11.9 Hz), 2.72 (dt, 2H, J = 2.6, 12.2 Hz), 2,65-2,55 (m, 1H), 1.82 (d, 2H, J = 13.9 Hz), 1.63 (dt, 3H, J = 4.1, 12.5 Hz), 1.53-1.45 (m, 1H), 1.11–1.06 (m, 2H), 0.87–0.81 (m, 2H); ESMS m/e: 245.03 $(M+H)^+$.

1-(6-CLOROHEXIL)-1H-INDOL. A una mezcla de NaH (0.249 g, 10.0 mmol) en DMF (5 mL) a 0°C, se adicionó una solución de 1-H-indol (0.585 g, 5.00 mmol) en DMF (2 mL). La mezcla de reacción se agitó durante 30 minutos y se calentó a temperatura ambiente. Después, 1-bromo-6-clorohexano (0.998 g, 5.00 mmol) se adicionaron gota a gota por medio de jeringa y la mezcla de reacción se agitó durante la noche. La mezcla de reacción se diluyó con EtOAc (30 mL), se lavó

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con agua (3 X 10 mL), se secó sobre $MgSO_4$, se concentró *in vacuo* y se purificó por medio de cromatografía utilizando hexano/EtOAc (97.5:2.5) para dar el producto deseado (0.900 g, 76 %). RMN ^1H ($CDCl_3$) δ 7.76–7.54 (m, 1H), 7.47–6.96 (m, 4H), 6.60–6.34 (m, 1H), 4.13 (t, 2H, J = 6,8 Hz), 3.50 (t, 2H, J = 5.6 Hz), 1.98 1.79 (m, 2H), 1.79 1.64 (m, 2H), 1.54–1.17 (m, 4H).

1-(5-CLOROPENTIL)-1H-INDOL: De acuerdo con el procedimiento utilizado para la síntesis de 1-(6-clorohexil)-1–H-indol, 1-H-indol (0.585 g, 5.00 mmol) y 1-bromo-5-cloropentano (0.928 g, 5.00 mmol) dan el producto deseado (0.890 g, 80%). RMN ^1H ($CDCl_3$) δ 7.76–7.51 (m, 1H), 7,44-6.96 (m, 4H), 6.60–6,38 (m, 1H), 4.11 (t, 2H, J = 6,8 Hz), 3.47 (t, 2H, J = 6.4 Hz), 1.97–1.79 (m, 2H),1.79–1.61 (m, 2H), 1.58–1.32 (m, 2H).

Ejemplo 96

N-(3{1-[6-(1H-INDOL-1-IL)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: 1-(6-Clorohexil)-1H-indol (23.6 mg, 0.100 mmol), 2-metil-N-[3-(4-piperidinil)fenil]propanamida (24.6 mg, 0.100 mmol), K_2CO_3 (27.6 mg, 0.200 mmol), NaI (22.5 mg, 0.150 mmol) y DMF (1.00 mL) se combinaron y agitaron durante la noche a 100°C. La mezcla de reacción se enfrió a temperatura ambiente y el material crudo se purificó por medio de TLC preparatoria utilizando 5 % de NH_3 (2.0 M en

metanol) en CH_2Cl_2, para dar el producto deseado como un sólido amarillo (40 mg, 90%). RMN ^1H (400 MHz, $CDCl_3$) δ 8.08-6.52 (m, 11H), 4.17 (t, 2H, J = 7,2 Hz), 3.26 (d, 2H, J = 11.6 Hz), 2.74-2.52 (m, 4H), 2.44-2,28 (m, 2H), 2.20-2.02 (m, 2H), 1.98-1.82 (m, 4H), 1.78-1.62 (m, 2H), 1.43-1.28 (m, 4H), 1,28 (d, 6H, J = 6.8 Hz); ESMS m/e: 446.5 $(M + H)^+$.

Ejemplo 97

N-(3-{1-[5-(1H-INDOL-1-IL)PENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Se preparó como el ejemplo anterior utilizando 1-(5-cloropentil)-1H-indol (22.2 mg, 0.100 mmol), 2-metil-N-[3-(4-piperidinil)fenil]propanamida (24.6 mg, 0.100 mmol), K_2CO_3 (27.6 mg, 0.200 mmol), NaI (23.0 mg, 0.150 mmol) y DMF (1.00 mL),dando el producto deseado como un aceite amarillo (36 mg, 81%). RMN ^1H (400 MHz, $CDCl_3$) δ 8.08-6 52(m, 11H), 4.19 (t, 2H, J = 7.2 Hz), 3.26-3.10 (m, 2H), 2.71-2.55 (m, 2H), 2.55-2.42 (m, 2H), 2.35-2.12 (m, 2H), 2.12-1.80 (m, 6H), 1.80-1.57 (m, 2H), 1.51-1,34 (m, 2H), 1.31 (d, 6H, J = 6.8 Hz); ESMS m/e: 432.2 $(M + H)^+$.

Ejemplo 98

N-(4-{1[(9-ETIL-9H-CARBAZOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: De acuerdo al procedimiento utilizado para la síntesis de N-(3-{1-[4-(4-clorofenoxi)bencil]-4-piperidinil}fenil)-2-metilpropan-

amida(Ejemplo 108), N-(3-{1-[3-(1,2-difenil-1H-indol-3-il)propil]-4-piperidinil}fe-nil)-2-difenil-1H-indol-3-il)-propil]-4-piperidinil}fenil)-2-metilpropanamida, 9-etil-9H-carbazol-3-carbaldehido (22.3 mg, 0.100 mmol) y 2-metil-N-[4-[4-piperidinil)fenil]propanamida (24.6 mg, 0.100 mmol) proporcionan N-(4-{1[(9-etil-9H-carbazol-3-il)metil]-4-piperidinil}fenil)-2-metilpropanamida. El producto se obtuvó como un producto sólido cristalino blanco (20 mg, 44%). RMN ^1H (400 MHz, $CDCl_3$) δ 8.21-7.09 (m, 12H), 4.38 (q, 2H, J = 7,2 Hz), 3.81 (s, 2H), 3.25-3.03 (m, 2H), 2.60-2.38 (m, 2H), 2.31-2.09 (m, 2H), 1.98-1,69 (m, 4H), 1.44 (t, 3H, J = 7.2 Hz), 1.23 (d, 6H, J = 6.8 Hz); ESMS m/e: 454.3 $(M + H)^+$.

Ejemplo 99

N-(3-{1-[(9-ETIL-9H-CARBAZOL-3-IL)METIL]-4-PIPERIDINIL}FE-NIL)-2-METILPROPANAMIDA: De acuerdo al procedimiento utilizado para la síntesis de N-(3-{1—[4-(4-clorofenoxi)ben-cil]-4-piperidinil}fenil)-2-metilpropanamida (Ejemplo 108), N-(4-{1-[(9-etil-9H-carbazol-3-il)metil]-4-piperidinil}fe-nil)-2-metilpropanamida, 9-etil-9H-carbazol-3-carbaldehido y 2-metil-N-[3-[4-piperidinil)fenil]propanamida proporcionaron N-(3-{1-[(9-etil-9H-carbazol-3-il)metil]-4-piperidinil}fe-nil)-2-metilpropanamida (37 mg, 95%). RMN ^1H (400 MHz, $CDCl_3$) δ 8.24-6.29 (m, 12H), 4.37 (q, 2H, J 7.2 Hz), 3.82 (s, 2H), 3.23-3.06 (m, 2H), 2.65-2.38 (m, 2H), 2.31-2.11 (m, 2H),

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2.01-1.73 (m, 4H), 1.43 (t, 3H, J = 7.2 Hz), 1.25 (d, 6H, J = 4.0 Hz); ESMS m/e: 454.3 $(M + H)^+$.

Ejemplo 100

N-[3-(1-{[1(4-METOXIFENIL)-1H-INDOL-5-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: De acuerdo con el procedimiento utilizado para la síntesis de 1-(4-metilfenil)1H-indol, N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida (37.5 mg, 0.100 mmol) y 1-yodo-4-metoxibenceno (46.8 mg, 0.200 mmol), dieron el producto deseado (27 mg, 56%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.70-6.58 (m, 14H), 3.88 (s, 3H), 3.67 (s, 2H), 3.14-3.01 (m, 2H), 2,57-2.41 (m, 2H), 2.25-2.01 (m, 2H), 1.93-1.69 (m, 4H), 1.24 (d, 6H, J = 7.2 Hz); ESMS m/e: 482.2 $(M + H)^+$.

Ejemplo 101

N-[3-(1-{[1-(4FLUOROFENIL)-1H-INDOL-5-IL]METIL}-4-PIPERIDINIL)FENIL-2-METILPROPANAMIDA: De acuerdo al procedimiento utilzado para la síntesis de 1-(4-metilfenil)1H-indol, N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida (37.5 mg, 0.100 mmol) y 1-fluoro-4-yodobenceno (44.4 mg, 0.200 mmol), dieron el producto deseado (21 mg, 45%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.71-6.60 (m, 14H), 3.69 (s, 2H), 3.19-2.99 (m, 2H), 2.62-

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2.41 (m, 2H), 2.22-2.07 (m, 2H), 1.94-1.70 (m, 4H), 1.24 (d, 6H, J = 6.8 Hz); ESMS m/e: 470.2 $(M + H)^+$.

Ejemplo 102

METIL-4-[5-({4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}METIL)-1H-INDOL-1-IL] BENZOATE: De acuerdo al procedimiento utilizado para la síntesis de 1-(4-metilfenil)1H-indol, N-{3-[1-(1H-indol-5-ilmetil)-4-piperi-dinil]fenil}-2-metilpropanamida (37.5 mg, 0.100 mmol) y 4-yodobenzoato de metilo (52.4 mg, 0.200 mmol), dieron el producto deseado (11 mg, 22%). RMN ^1H (400 MHz, $CDCl_3$) δ 8.31-6.64 (m, 14H), 3.96 (s, 3H), 3.67 (s, 2H), 3.16-2.96 (m, 2H), 2.57-2.41 (m, 2H), 2.18-2.02 (m, 2H), 1.91-1.73 (m, 4H), 1.24 (d, 6H, J = 6.8 Hz), ESMS m/e: 510.2 $(M + H)^+$.

Ejemplo 103

2-METIL-N-[3-(1-{[1-(3-METILFENIL)-1H-INDOL-5-IL] METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: De acuerdo al procedimiento utilizado para la síntesis de 1-(4-metilfenil)1H-indol, N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida (37.5 mg, 0.100 mmol) y 1-yodo-3metilbenceno (43.6 mg, 0.200 mmol), dieron el producto deseado (28 mg, 60%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.68-6.60 (m, 14H), 3.66 (s, 2H), 3,16-2.96 (m, 2H), 2.59-2.44 (m, 2H), 2.44 (s, 3H), 2.18-

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2.01 (m, 2H), 1.91-1.68 (m, 4H), 1.24 (d, 6H, J = 6.8 Hz); ESMS m/e: 466.2 $(M + H)^+$.

Ejemplo 104

N-{3-[1-(3-{[(4-CLORO-3-NITROFENIL)SULFONIL]AMINO}PROPYL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Una mezcla de N-{3[1-(2-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida(10.0 mg, 0.0350 mmol), cloruro de 4-cloro-3-nitrobencen-sulfonilo (9.90 mg, 0.0380 mmol) y TEA (7.00: mg, 0.0700 mmol) en THF (2 mL), se agitó durante 12h a temperatura ambiente. El producto crudo se purificó por medio de TLC preparatoria (CH_2Cl_2/MeOH/isopropilamina = 19:1:0.2), para dar el producto deseado (16 mg, 86%). RMN ^1H (400 MHz, $CDCl_3$) δ 8.45–8.38 (m, 1H), 8.02 (d, 1H, J = 8,4 Hz), 7.72 (d, 1H, J = 8.8 Hz), 7.48–7.40 (m, 3H), 7.29–7,24 (m, 2H), 6.96 (d, 1H, J = 7.5 Hz), 3.17-3.09 (m, 4H), 2.63–2.48 (m, 4H), 2.15 (t, 2H, J = 11,8 Hz), 1.96-1.72 (m, 6H), 1.25 (d, 6H, J = 6.9 Hz); ESMS m/e: 523.2 $(M + H)^+$.

Ejemplo 105

N-[-1-{5-[4-(3,4-DIFLUOROFENIL)-2OXO-1,3-OXAZOLIDIN-3-IL]PENTIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Una mezcla de 3-(5-bromopentil)-4-(3,4-difluorofenil)-1,3-oxazolidin-2-ona (38.0 mg, 0.110 mmol), 2-metil-N-[3-(4-piperidinil)fenil]propanamida (26.0 mg, 0100 mmol), NaI

(23.0 mg, 0,150 mmol), y K_2CO_3 (14.0 mg, 0.100 mmol) en DMF (2 mL), se calentó durante 1 h a 50°C. El producto crudo se purificó por medio de TLC preparatoria utilizando CH_2Cl_2/MeOH/isopropilamina (19:1:0.2) para dar el producto deseado (21 mg, 41%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.39-7.32 (m, 2H), 7.26-7.20 (m, 2H), 7.18-7.11 (m, 1H), 7.10-7.03 (m, 1H), 6.96 (d, 1H, J = 7.6 Hz), 4.80-4.73 (m, 1H), 4.62 (t, 1H, J 7.9 Hz), 4,09-4.04 (m, 1H), 3.51-3.42 (m, 1H) , 3.03 (d, 2H, J= 11.7 Hz), 2.82-2.72 (m, 1H), 2,51-2.42 (m, 2H), 2.32 (t, 2H, J = 7.9 Hz), 2.11 (s, 1H), 2.03-1.97 (m, 2H), 1.85-1.70 (m, 4H), 1.49 (m, 4H), 1.31-1.27 (m, 1H), 1.24 (d, 6H, J = 6.9 Hz); ESMS m/e: 514.4 $(M + H)^+$.

Ejemplo 106

3-(2,6-DICLOROFENIL)-N-(5-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PENTIL)-5-METIL-4-ISOXAZOLCARBOXAMIDA: Una mezcla de cloruro de 3-(2,6-diclorofenil)-4-formil-5-isoxazolcarbonilo (69.0 mg, 0.250 mmol), N-{3-[1-(5-aminopentil)-4-piperidinil]fenil}-2-etilpropanamida(44.0 mg, 0150 mmol), TEA (30.0 mg, 0,300 mmol), en THF (2 mL), se agitó durante 12 h a temperatura ambiente. El producto crudo se purificó por medio de TLC preparatoria utilizando CH_2Cl_2/MeOH/isopropilamina (19:1:0.2) para dar el producto deseado (52 mg, 67%). RMN ^1H (400 MHz, $CDCl_3$) δ .52–7.49 (m, 2H), 7.49–7.41 (m, 2H), 7.39–7.31 (m, 2H), 7.29–7.21 (m,

2H), 6.92 (d, 1H, J = 7.6 Hz), 3.25–3.11 (m, 5H), 2.81–2.74 (m, 4H), 2.58–2.44 (m, 4H), 2.30–2.19 (m, 2H), 1,93–1.78 (m, 4H), 1.56–1.44 (m, 2H), 1.31–1.28 (m, 2H), 1.24 (d, 6H, J = 6.6 Hz); ESMS m/e: 585.2 $(M + H)^+$.

Ejemplo 107

N-[3-(1-{2-[(DIFENILACETIL)AMINO]ETIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Una mezcla de N-{3[1-(2aminoetil)-4-piperidinil]fenil}-2-metilpropanamida (20.0 mg, 0.0700 mmol), cloruro de difenilacetilo (23.0 mg, 0.110 mmol), y TEA (20.0 mg, 0,140 mmol) en THF (2 mL),se agitó durante la noche 23°C. El producto crudo se purificó por medio de TLC preparatoria utilizando CH_2Cl_2/MeOH/isopropilamina (19:1:0.2) para dar el producto deseado (8.0 mg, 47%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.37–7.20 (m, 13H), 6.97–6.92 (m, 1H), 6.67 (s, 1H), 4.98 (s, 1H), 3.43 (q, 2H, J = 5.9 Hz), 2.90 (d, 2H, J = 11.6 Hz), 2.57–2.42 (m, 4H), 2.11 (t, 2H, J = 10.4 Hz), 1.75 (d, 2H, J = 12.4 Hz), 1.70–1.58 (m, 2H), 1,25 (d, 6H, J = 6.7 Hz) ; ESMS m/e: 484.2 $(M + H)^+$.

Ejemplo 108

N-(3-{1-[4-(4-CLOROFENOXI)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: 4-(4-clorofenoxi)benzaldehido (0.119 g, 0.510 mmol) y 2-metil-N-[3-(4-piperidinil)fenil]propanamida

(0.126 g, 0.510 mmol) se mezclaron en 1,2-dicloroetano (5 mL) y después se trataron con triacetoxiborohidruro de sodio (0.424 g, 2.00 mmol) y HOAc (0.03 mL, 0.5 mmol). La mezcla se agitó a temperatura ambiente durante la noche. La mezcla de reacción se neutralizó con una solución acuosa de $NaHCO_3$ saturada y la capa acuosa se extrajo con CH_2Cl_2 (3 X 10 mL). Las capas orgánicas combinadas se lavaron con salmuera, se secaron sobre $MgSO_4$, se concentraron *in vacuo* y se purificaron por medio de TLC preparatoria utilizando 5% de NH_3 (2,0 M en metanol) en CH_2Cl_2, para dar el producto deseado (53 mg, 23%).RMN ^1H (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.34–7.19 (m, 7H), 6.98–6.87 (m, 5H), 3.50 (s, 2H), 2.98 (d, 2H, J= 11.8 Hz), 2.58–2.44 (m, 2H), 2.10–1.98 (m, 2H), 1.83–1.76 (m, 4H), 1.24 (d, 6H, J= 6.8 Hz); ESMS m/e: 463.2 $(M + H)^+$.

Ejemplo 109

N–{3-[1-({2,5-DIMETIL-1-[3-(TRIFLUOROMETIL)FENIL]-1H-PIRROL-IL}METIL-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el procedimiento descrito en el ejemplo 108, sustituyendo 2,5-dimetil-1-[3-(trifluorometil)fenil]-1H-pirrol-3-carbaldehido (0.136 g, 0.510 mmol) por 4-(4-clorofenoxi)benzaldehido. RMN ^1H (400 MHz,. $CDCl_3$) δ 7.69–7.56 (m, 2H), 7,53–7.32 (m, 4H), 7,28–7.18 (m, 2H), 6.99 (s, 1H),

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5.98 (s, 1H), 3.43 (s, 2H), 3.16–3.06 (m, 2H), 2.57–2.42 (m, 2H), 2.07–1.95 (m, 8H), 1.89–1,76 (m, 4H), 1.24 (d, 6H, J = 6.8 Hz); ESMS m/e: 498.2 $(M + H)^+$.

Ejemplo 110

N-(3-{1-[4-(3,4-DIFLUOROFENOXI)BENCIL]-4-PIPERIDINIL}FENIL}-2-METILPROPANAMIDA: Preparada por el procedimiento descrito en el ejemplo 108, sustituyendo 4-(3,4-difluorofenoxi)benzaldehido (0.119 g, 0.510 mmol) por 4-(4-clorofenoxi)benzaldehido. RMN ^1H (400 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.32 (d, 2H, J = 8.4 Hz), 7.28–7.21 (m, 2H), 7,14–7.06 (m, 2H), 6.98–6.94 (m, 3H), 6.86–6.79 (m, 1H), 6.76–6.69 (m, 1H), 3.51 (s, 2H), 2.99 (d, 2H, J = 11.7 Hz), 2.55–2.44 (m, 2H), 2.12–2.02 (m, 2H), 1.86–1.74 (m, 4H), 1.25 (d, 6H, J = 7,0 Hz); ESMS m/e: 465.2 $(M + H)^+$.

Ejemplo 111

N-(3-{1-[(5-CLORO-3-METIL-1-FENIL-1H-PIRAZOL-4-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el procedimiento descrito en el ejemplo 108, sustituyendo 5-cloro-3-metil-1-fenil-1H-pirazol-4-carbaldehido (0.113 g, 0.510 mmol) por 4-(4-clorofenoxi)benzaldehido. RMN ^1H (400 MHz, $CDCl_3$) δ 7.62-7.19 (m, 9H), 6.97 (s, 1H), 3.43 (s, 2H), 3.08–2.98 (m, 2H), 2.58–2.43 (m, 2H), 2.39–2.32 (m, 3H),

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2.18–1.71 (m, 6H), 1.24 (d, 6H, J= 6.9 Hz); ESMS ni/e: 451.2 $(M + H)^+$.

Ejemplo 112

N-(3-{1-[4-(3,4-DICLOROFENOXI)BENCIL]-4-PIPERIDINIL}FENIL-2-METILPROPANAMIDA: Preparada por el procedimiento descrito en el ejemplo 108, sustituyendo 4-(3,4-diclorofenoxi)benzaldehido (0.136 g, 0.510 mmol) por 4-(4-clorofenoxi)benzaldehido. RMN ^1H (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.36–7.18 (m, 6H), 7.08 (d, 1H, J = 1.8 Hz), 6.96 (d, 3H, J= 6.8 Hz), 6.84 (dd, 1H, J= 2.8, 8.9 Hz), 3.51 (s, 2H), 2.99 (d, 2H, J = 11.5 Hz), 2.55–2.42 (m, 2H), 2.12–2.02 (m, 2H), 1.84–1.73 (m, 4H), 1.24 (d, 6H, J = 7.0 Hz); ESMS m/e: 497.1 $(M + H)^+$.

Ejemplo 113

2-METIL-N-(3-{1-[(2-FENIL-1H-IMIDAZOL-4-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparada por el procedimiento descrito en el ejemplo 108, sustituyendo 2-fenil-1H-imidazol-4-carbaldehido (88.0 g, 0.510 mmol) por 4-(4-clorofenoxi)benzaldehido. RMN ^1H (400 MHz, $CDCl_3$) δ 7.92 (d, 2H, J= 7.4 Hz), 7.65–7.31 (m, 6H), 7.28–7.18 (m, 2H), 7,12–7.05 (m, 1H), 6.95–6.88 (m, 1H), 3.69 (s, 2H), 3.17-3.05 (m, 2H), 2.62–2,45 (m, 2H), 2.28–2.18 (m, 2H), 1.88-1.70 (m, 4H), 1.25 (d, 6H, J = 6.8 Hz); ESMS m/e: 403.2 $(M + H)^+$.

Ejemplo 114

N-(3-{1-[4-(DIFENILAMINO)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el procedimiento descrito en el ejemplo 108, sustituyendo 4-(difenilamino)benzaldehido (0.139 g, 0.510 mmol) por 4-(4-clorofenoxi)benzaldehido. RMN ^1H (400 MHz, $CDCl_3$) δ 7.49 (s, 1H), 7.39–6.92 (m, 18H), 3,49 (s, 2H), 3.02–2,99 (m, 2H), 2.59–2.43 (m, 2H), 2.15–2,03 (m, 2H), 1.92–1.76 (m, 4H), 1.23 (d, 6H, J= 6.8 Hz); ESMS m/e: 504,2 $(M + H)^+$.

Ejemplo 115

N-[3-(1-{[4-BROMO-1-(4-CLOROBENCIL)-1H-PIRAZOL-5-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el procedimiento descrito en el ejemplo 108, sustituyendo 4-bromo-1-(4-clorobencil)-1H-pirazol-5-carbaldehido (0.153 g, 0.510 mmol) por 4-(4-clorofenoxi)benzaldehido. RMN ^1H (400 MHz, $CDCl_3$) δ 7.41 (s, 1H), 7.36 (d, 1H, J 8.8 Hz), 7.34–7.30 (m, 3H), 7,29–7.26 (m, 1H), 7.22 (t, 1H, J = 7.8 Hz), 7.16 (d, 2H, J= 8.6 Hz), 6.95 (d, 1H, J = 7.5 Hz), 5.24 (s, 2H), 3.61 (s, 2H), 3.09 (d, 2H, J= 11.9 Hz), 2.55–2.42 (m, 2H), 2.19 (dt, 2H, J = 4.4, 11.4 Hz), 1.89–1.76 (m, 4H), 1.24 (d, 6H, J= 6.7 Hz); ESMS m/e: 529.1 $(M + H)^+$.

1-(3-[{(1R)-3-CLORO-FENILPROPIL]OXI}FENIL)ETANONA: Azodicarboxilato (5.37 g, 0.0310 mol) se adicionaron a una solución de trifenilfosfina (8.09 g, 0.0308 mol), 1S-3-cloro-1-fenil-1-propanol (4.20 g, 0.031 mol) y 1-(3-hidroxifenil)etanona en THF (150 mL). La mezcla de reacción se agitó durante 4 días a 23°C. El solvente se retiró bajo presión reducida y el residuo se trituró con éter/hexano (1:2, (3 X 100 mL). Las fracciones orgánicas combinadas se concentraron *in vacuo* y el producto crudo se purificó por cromatografía utilizando EtOAc/hexano (1:14) para dar el producto deseado (6.55 g, 74%). RMN ^1H (400 MHz, $CDCl_3$) δ 7,48–7.31 (m, 6H), 7.26 (t, 2H, J = 8.2 Hz), 7.04 (d, 1H, J = 8.1 Hz), 5.44 (dd, 1H, J = 4.4, 8.1 Hz), 3.83–3.74 (m, 1H), 3.63–3.56 (m, 1H), 2.51 (s, 3H), 2.51–2.45 (m, 1H), 2.29–2.17 (m, 1H); ESMS m/e: 289.0 $(M + H)^+$.

Ejemplo 116

N-(3-{1-[(3R)-3-(3-ACETILFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de 1-(3-{[(1R)-3-cloro-1-fenilpropil]oxi}fenil)etanona (58.5 mg, 0.200 mmol), 2-metil-N-[3-(4-piperidinil)fenil]propanamida (56.8 mg, 0.200 mmol), NaI (34.0 mg, 0.200 mmol) y K_2CO_3 (55.5 mg, 0.400 mmol) en DMF (1 mL), se agitó a 100°C durante 3 h. El solvente se retiró bajo presión reducida y el residuo se purificó por cromatografía sobre sílice

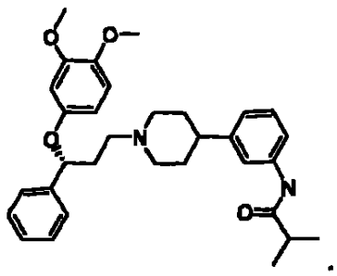
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utilizando 5% de NH_3 (2.0 M en metanol) en CH_2Cl_2 para dar el producto deseado (98 mg, 98%). RMN ^1H (400 MHz, $CDCl_3$) δ 8,01 (s, 1H), 7.49–7.21 (m, 11H), 7.09–7,03 (m, 1H), 6.96 (d, 1H, J = 7.9 Hz), 5.32 (dd, 1H, J = 5.0, 7.9 Hz), 3.08–2.98 (m, 2H), 2.57-2.43 (m, 6H), 2.11–1.72 (m, 9H), 1.25 (d, 6H, J = 6,8 Hz); ESMS m/e: 499.4 $(M + H)^+$.

Procedimiento:

Procedimiento A (ver también ejemplo 48)

N-(3-{1-[(3R)-3-(3,4-DIMETOXIFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA:



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Método A

4-{[(1R)-3-CLORO-1-FENILPROPIL]OXI}-1,2-DIMETOXIBENCENO: Una mezcla de 3,4-dimetoxifenol (4.07 g, 26.4 mmol), (S)-(-)-3-cloro-fenil-1-propanol (4.50 g, 26.4 mmol, 99% ee, Aldrich Chemical Co.), trifenilfosfina (6.92 g, 26.4 mmol) y azodicarboxilato de dietilo (4.59 g, 26.4 mmol) en THF (110 mL), se agitó a temperatura ambiente durante 24 h. La mezcla de reacción se concentró *in vacuo*. En este punto, el residuo puede ser aún ser lavado con pentano y los extractos de pentano combinados se concentraron y cromatografiaron con hexano:EtOAc (8:1) como el eluyente, para dar el producto deseado (como se describe en el procedimiento general de Srebnik, M.; Ramachandran, P,V,; Brown, H.C. J. Org. Chem. 1988, 53, 2916-2920). Este procedimiento se llevó a cabo en una reacción a escala pequeña y solamente un rendimiento de 40% del producto se realizó.

Alternativamente a una escala mayor (26.4 mmol), el producto crudo se trituró con una pequeña cantidad de diclorometano y el óxido de trifenilfosfina precipitado, se filtró. El filtrado se concentró y el producto crudo se cromatografió, para dar el producto deseado como un aceite amarillo espeso (7.30 g, rendimiento 88.9%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.39-7.32 (m, 4H), 7.20 (m, 1H), 6.64 (d, 1H, J = 8.7 Hz), 6.51 (d, 1H, J = 2,7 Hz), 6.30 (dd, 1H, J= 2.7, 8.7 Hz), 5,27 (dd aparente, 1H, J= 4.5, 8,7 Hz), 3.79 (s,

3H), 3.77 (s, 3H), 3.61 (m, 1H), 2.45 (m, 1 H), 2.20 (m, 1H), 1,80 (s, 1H); ESMS m/e: 307.1 $(M + H)^+$.

N-(3-{1-[(3R)-3-(3,4-DIMETOXIFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de carbonato de potasio (321 mg, 2.32 mmol), yoduro de sodio (522 mg, 3.48 mmol), 2-metil-N-[3-(4-piperidinil)fenil]-propanamida (570 mg, 2.32 mmol) y 4-{[(1R)-3-cloro-1-fenilpropil]oxi}-1,2-dimetoxibenceno (712 mg, 2.32 mmol) en DMF (5.0 mL), se agitó a 100°C durante 3 hrs, tiempo en el cual la TLC indicó que la reacción fue completa. La mezcla de reacción se vació en agua (50 mL) y la capa acuosa se extrajo con cloruro de metileno (3 x 30 mL). Los extractos orgánicos combinados se lavaron con salmuera (30 mL), se secaron sobre $MgSO_4$ y se concentraron bajo presión reducida. El producto crudo se purificó por medio de placas de TLC preparatorias [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$] para producir el producto (970 mg, 90.1%) como un aceite espeso.

Método B

En un matraz RB de 25 mL se adicionó trifenilfosfina (9.80 mg, 0.0375 mmol), azodicarboxilato de dietilo (5.22 mg, 0.0300 mmol), N-(3-{1-[(3S)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metil-propanamida (9.53 mg, 0.0250 mmol), 3,4-dimetoxifenol (7.70 mg, 0.0500 mmol) y

THF (1.00 mL) a temperatura ambiente. La mezcla de reacción se agitó a temperatura ambiente durante la noche (16 hrs). Se retiró el solvente bajo presión reducida y el residuo se purificó por medio de placas de TLC preparatorias [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], para producir el producto deseado (4.40 mg, rendimiento 34.1%) como un aceite espeso: RMN ^1H (400 MHz, $CDCl_3$) δ 7.46 (s, 1 H), 7.40-7.30 (m, 4H), 7.25 (m, 3H), 6.97 (d, 1H, J = 7.8 Hz), 6.64 (d, 1H, J = 9.1 Hz), 6.51 (d, 1H, J = 2.6 Hz), 6.29 (d, 1H, J= 2.6, 9.1 Hz), 5.20 (dd aparente, 1H, J= 4.4, 8.5 Hz), 3.80 (s, 3H), 3.77 (s, 3H), 3.23 (m, 2H), 2.77 (m, 2H), 2.5 (m, 2H), 2.3-2,1 (m, 6H), 1.80 (m, 2H), 1.25 (d, 6H, J= 7.9 Hz); ESMS m/e: 517.4 $(M + H)^+$.

Procedimiento B (ver también ejemplo 49)

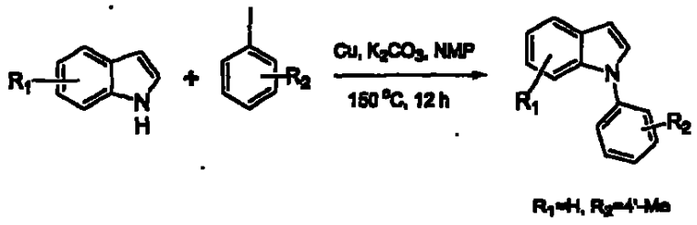
2-METIL-N-(3-{1-[(3S)-3-FENOXI-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Una mezcla de N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil)-4-piperidinil}fenil)-2-metilpropanamida (9.53 mg, 0.0250 mmol), fenol (4.70 mg, 0.050 mmol), trifenilosfina (9.80 mg, 0.0375 mmol) y azodicarboxilato de dietilo (5.22 mg, 0.0300 mmol) en THF (1.0 mL), se agitó a temperatura ambiente durante 3 días. La cromatografia utilizando placas de TLC preparatorias de sílice [2.5% de NH_3 (2.0 M en metanol) en $CHCl_3$], dió el producto deseado (2.70 mg, rendimiento 23.6 %) como un aceite espeso: RMN ^1H

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7.46 (s, 2H), 7.40-7.30 (m, 4H), 7.25 (m, 3H), 7,20 (m, 2H), 6.97 (d aparente, 1H, J = 7.4 Hz), 6.89 (tt aparente, 1H, J= 0.8, 7.6 Hz), 6.84 (dt aparente, 1H, J = 0.8, 8.0 Hz), 5.20 (dd aparente, 1H, J =4.4, 8.5 Hz), 3.35 (m, 2H), 2.91 (m, 2H), 2.60 (m, 2H), 2.30-2.10 (m, 6H), 1.90 (m, 2H), 1.25 (d, 6H, J = 7.9 Hz); ESMS m/e: 457.4 $(M + H)^+$.

Procedimiento C

Esquema O



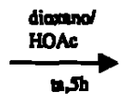
1-(4-METILFENIL)1H-INDOL: Una mezcla de 1-H-indol (58.5 mg, 0.500 mmol), 1—(yodo)-4-metilbenceno (0.218 g, 1.00 mmol), polvo de cobre (32.0 mg, 0.500 mmol), y K_2CO_3 (0.138 g, 1.00 mmol) en 1-metil-2-pirrolidinona (1 mL), se calentó a 150°C durante 12 h bajo argón. La mezcla resultante se diluyó con H_2O (6 mL). La capa acuosa se extrajo con CH_2Cl_2 (3 X 10 mL).

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Los extractos orgánicos combinados se lavaron con salmuera (10 mL), se secaron sobre $MgSO_4$ y se concentraron *in vacuo*. El residuo se purificó por medio de TLC preparatoria utilizando EtOAc/hexano (1:4), para dar el producto deseado (82 mg, 79%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.67 (d, 1H, J = 7.7 Hz), 7.52 (d, 1H, J = 7.4 Hz), 7.38 (d, 2H, J = 8.4 Hz), 7.34–7.29 (m, 3H), 7.21 (t, 1H, J = 7,0 Hz), 7.15 (t, 1H, J = 7.0 Hz), 6,66 (d, 1H, J = 3.3 Hz), 2.43 (s, 3H); ESMS m/e: 208.0 $(M + H)^+$.

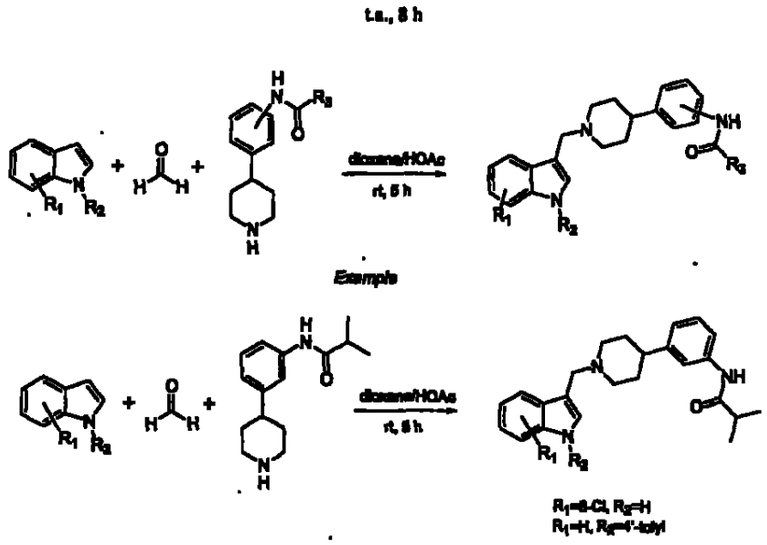
Procedimiento D (ver también ejemplo 86)

Esquema N



Ejemplo





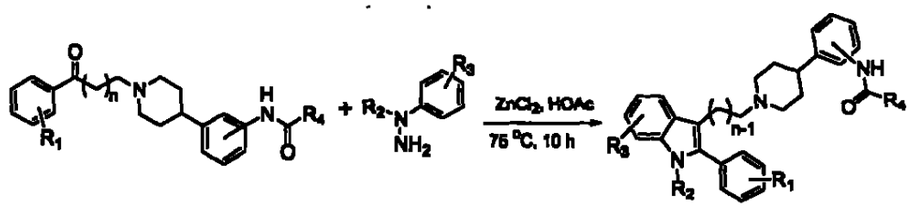
N-(3-{1-[(6-CLORO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENYL)-2-METILPROPANAMIDA: Una solución de 2-metil-N-[3-(4-piperidil)fenil]propanamida (0.369 g, 1.50 mmol) y 37% en peso de formaldehido acuoso (30.0 mg, 1,50 mmol) en 1 mL de HOAc:dioxano (1:4), se adicionó a 6-cloro-1-H-indol (0.152 g, 1.00 mmol) y la mezcla de reacción se agitó durante 12 h a temperatura ambiente. La mezcla resultante se diluyó con H_2O (10 mL). La capa acuosa se extrajo con CH_2Cl_2 (3 X 100 mL). Los extractos orgánicos combinados se lavaron con salmuera (10 mL), se secaron sobre $MgSO_4$ y se concentraron *in vacuo*. El residuo se purificó por medio de placas de TLC preparatoria utilizando 5% de NH_3 (2.0 M en metanol) en CH_2Cl_2, para dar el producto deseado (79mg, 42%). RMN ^1H (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 8.04 (s, 1H), 7.52 (t, 2H, J =

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8.1 Hz), 7.35 (d, 2H, J = 13.3Hz), 7.18 (t, 1H,J = 7.9 Hz), 7.09 (dd, 1H, J = 1.9, 8.5 Hz), 6.85 (d, 1H, J = 7.4 Hz), 5.18 (s, 1H), 4.01 (s, 2H), 2.55 (septet, 1H, J = 6.8 Hz), 2.48-2.34 (m, 3H), 2.08-1.95 (m, 4H), 1.78 (d, 2H, J = 12.8 Hz), 1.22 (d, 6H, J = 6.8 Hz); ESMS m/e: 410.1 $(M + H)^+$.

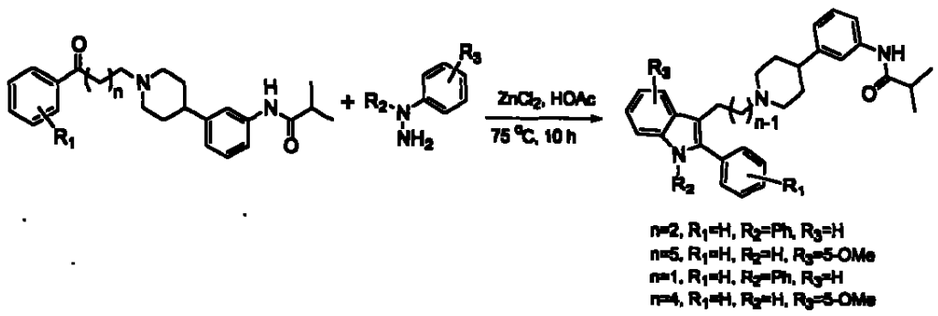
Procedimiento E (ver también ejemplo 90)

Esquema M



Ejemplo

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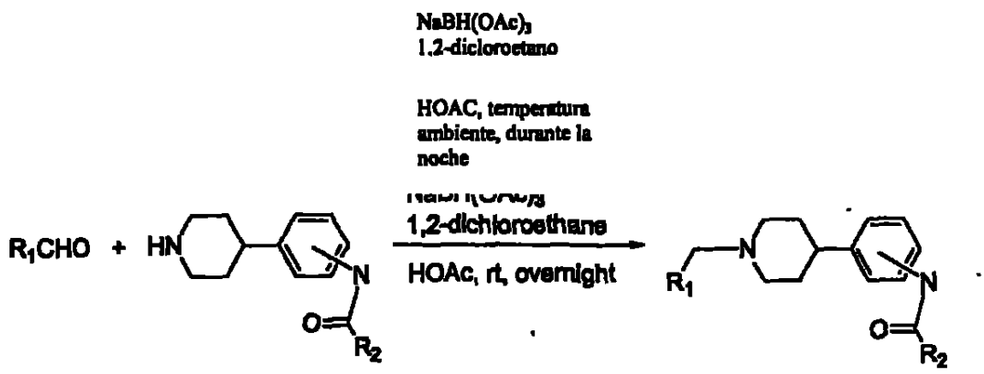


N-(3-{1-[3-(1,2-DIFENIL-1H-INDOL-3-IL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de clorohidrato de 1,1-difenilhidrazina (10.3 mg, 0.0470 mmol), 2-metil-N-{3-[1-(5-oxo-5-fenilpentil)-4-piperidinil]-fenil}propanamida (14.7 mg, 0.0362 mmol), $ZnCl_2$ (14.85 mg, 0.109 mmol), y HOAc (0.500 mL), se calentó durante 4 h a 80°C. La mezcla cruda resultante se diluyó con agua (10 mL), la capa acuosa se neuralizó con K_2CO_3 saturado y se extrajo con CH_2CL_2 (3 X 20 mL). Las capas orgánicas combinadas se concentraron in vacuo y el residuo se purificó por medio de placas de TLC preparatoria utilizando 5% de NH_3 (2.0 M en metanol) en CH_2Cl_2 para dar el producto deseado N-(3-{1-[3-(1,2-difenil-1H-indol-3-il)propil]-4-piperidinil}-fenil)-2-metilpropanamida (4.10 mg, 37.0%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.71–7.65 (m, 1H) 7.42 (d, 1H, J= 7.4 Hz), 7.39 (s, 1H), 7.36–7.15 (m, 15H), 6.94 (d, 1H, J=7,8 Hz), 3.12 (d, 2H, J= 11.2 Hz), 2.90

(t, 2H, J= 7.8 Hz), 2.59–2.45 (m, 3H), 2.19–1.91 (m, 7H), 1.82 (d, 2H, J=13.5 Hz), 1.24 (d, 6H, J= 6.9 Hz); ESMS m/e: 555.3 $(M + H)^+$.

Procedimiento F (ver también ejemplo 108

Esquema R

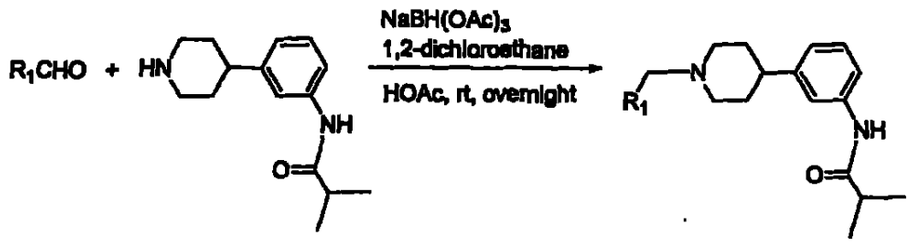


Ejemplo

NaBH(OAc)3
1.2-dicloroetano

HOAC,ta, durante la noche

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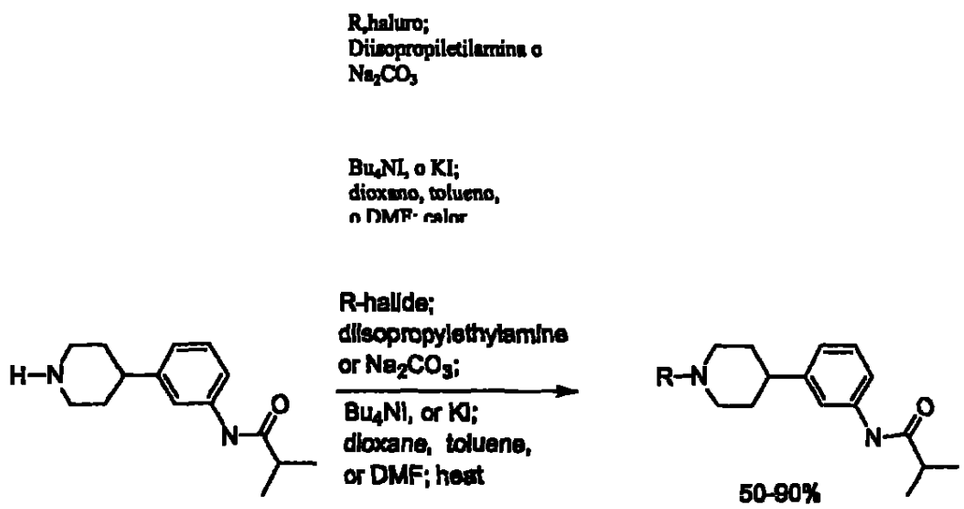


N-(3-{1-[4-(4-CLOROFENOXI)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una solución de 4-(4-clorofenoxi)benzaldehido (0.119 g, 0.510 mmol) y 2-metil-N-[3-(4-piperidinil)fenil]propanamida (0.126 g, 0.510 mmol) en 1,2-dicloroetano (5 mL) se trató con triacetoxiborohidruro de sodio (0.424 g, 2.00 mmol) y HOAc (0.03 mL, 0.500 mmol) a temperatura ambiente. La mezcla se agitó durante la noche a temperatura ambiente. La mezcla de reacción se neutralizó con una solución acuosa de $NaHCO_3$ saturada (10 mL) y la capa acuosa se extrajo con CH_2Cl_2 (3 X 10 mL). Las capas orgánicas combinadas se lavaron con salmuera, se secaron sobre $MgSO_4$, se concentraron *in vacuo* y se purificaron por medio de placas de TLC preparatoria utilizando 5% de NH_3 (2,0 M en metanol) en CH_2Cl_2, para dar el producto deseado (53 mg, 23%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.34–7.19 (m, 7H), 6.98–6.87 (m, 5H), 3.50 (s, 2H), 2.98 (d, 2H, J= 11.8

Hz), 2.58–2.44 (m, 2H), 2.10–1.98 (m, 2H), 1.83–1.76 (m, 4H), 1.24 (d, 6H, J= 6.8 Hz); ESMS m/e: 463.2 $(M + H)^+$.

Procedimiento G (ver también ejemplo 116)

Esquema F

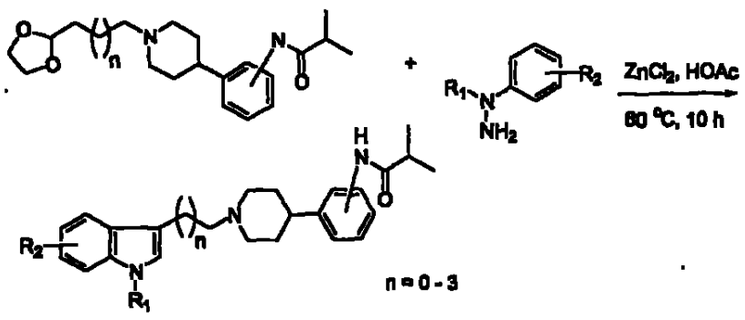


N-(3-{1-[(3R)-3-(3-ACETILFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de 1-(3-{[(1R)-3-cloro-1-fenilpropil]oxi}fenil)etanona (58.5 mg, 0.200 mmol), 2-metil-N-[3-(4-piperidinil)fenil]propanamida (56.8 mg, 0.200 mmol), NaI (34.0 mg, 0.200 mmol) y K_2CO_3 (55.5 mg, 0.400 mmol) en DMF (1 mL), se agitó a 100°C durante 3 h. El

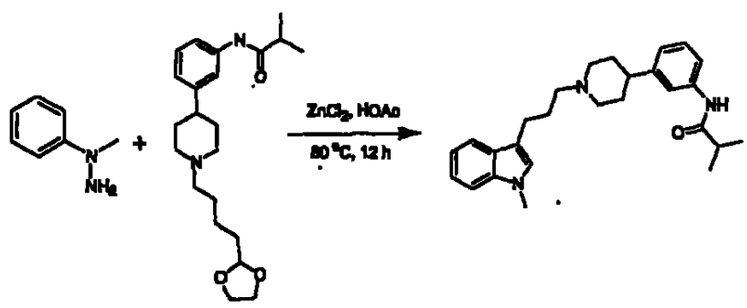
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solvente se retiró bajo presión reducida y el residuo se purificó por cromatografía sobre sílice utilizando 5% de NH_3 (2.0 M en metanol) en CH_2Cl_2 para dar el producto deseado (98 mg, 98%). RMN ^1H (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.49–7.21 (m, 11H), 7.09–7,03 (m, 1H), 6.96 (d, 1H, J = 7.9 Hz), 5.32 (dd, 1H, J = 5.0, 7.9 Hz), 3.08–2.98 (m, 2H), 2.57-2.43 (m, 6H), 2.11–1.72 (m, 9H), 1.25 (d, 6H, J = 6,8 Hz); ESMS m/e: 499.4 $(M + H)^+$.

Esquema S



Procedimiento H

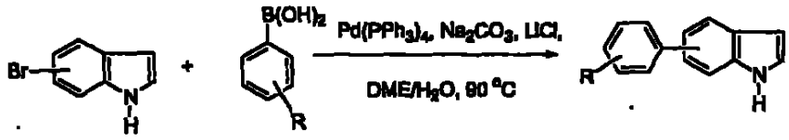


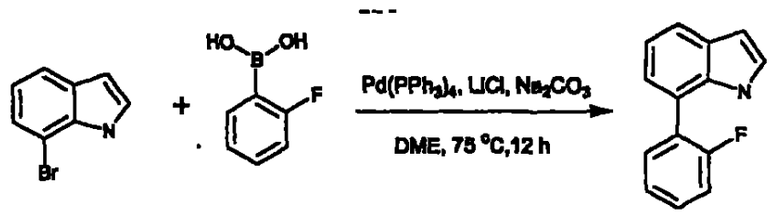
2-METIL-N-(3-{1-[3-(1-METIL-1H-INDOL-3-IL)PROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Un mezcla de N-(3-{1-[4-(1,3-dioxolan-2-il)butil]-4-piperidinil}fenil)-2-metilpropanamida (100 mg, 0.270 mmol), 1-metil-1-fenilhidrazina (106 mg, 0.870 mmol), $ZnCl_2$ (119 mg, 0.870 mmol), y HOAc (1.00 mL), se calentó durante 12 h a 80°C. La mezcla resultante cruda se diluyó con agua (20 mL), la capa acuosa se neutralizó con una solución de K_2CO_3 saturada (10 mL) y se extrajo con CH_2Cl_2 (3 X 20 mL). Las capas orgánicas combinadas se concentraron *in vacuo* y el residuo se purificó por medio de

TLC preparatoria utilizando 3% de NH_3 (2.0 M en metanol) en CH_2Cl_2 para dar el producto deseado 2-metil-N-(3-{1-[3-(1-metil-1H-indol-3-il)propil]-4-piperidinil}fenil)propanamida (20.7 mg, 18.7%): RMN ^1H (400 MHz, $CDCl_3$) δ 7.60 (d, 1H, J= 8.1 Hz), 7.45 (s, 1H), 7.35 (d, 1H, J= 7.4 Hz), 7.26-7.24 (m, 4H), 7.09 (t, 1H, J = 7.3 Hz), 6.97 (d, 1H, J= 7.3 Hz), 6.86 (s, 1H), 3.75 (s, 3H), 3.11 (d, 2H, J = 11.6 Hz), 2.79 (t, 2H, J= 7.3 Hz), 2.51-2.50 (m, 4H), 2.12-1.81 (m, 8H), 1.25 (d, 6H, J= 7.1 Hz); Cál. Anál. para $C_{27}H_{35}N_3O+0.225CHCl_3$: C, 73.57; H, 7.99; N, 9.45. Encontrado: C, 73.93; H, 7.90; N, 9.23; ESMS m/e: 418.2 $(M + H)^+$.

Procedimiento I

Esquema T



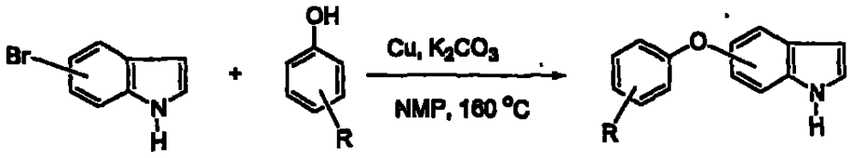


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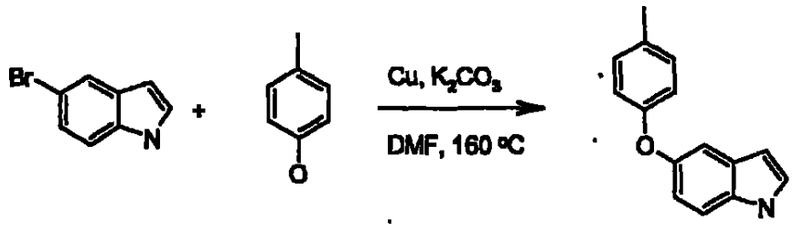
7-(2-FLUOROFENIL)-1H-INDOL: Una mezcla de ácido 2-fluorofenilborónico (83.4 mg, 0.600 mmol), 7-bromo-1H-indol (98.0 mg, 0.500 mmol), LiCl (42.0 mg, 1.00 mmol), Na_2CO_3 (2.0 M, 0.100 mL), $Pd(PPh_3)_4$ (115 mg, 0.100 mmol) y DME (2.0 mL), se calentó a 75°C durante 12 h bajo argón. La mezcla resultante cruda se diluyó con agua (40 mL), la capa acuosa se extrajo con CH_2Cl_2 (3 X 20 mL). Las capas orgánicas combinadas se lavaron con salmuera (30 mL), se secaron sobre Na_2SO_4, se filtraron y concentraron *in vacuo*. El residuo se purificó por medio de TLC preparatoria utilizando hexano:EtOAc (8:1) para dar el producto deseado 7-(2-fluorofenil)-1H-indol (108 mg, 100%): RMN ^1H (400 MHz, $CDCl_3$) δ 8.21 (br s, 1H), 7.71 (dm, 1H, J= 7.3 Hz), 7.55 (dt, 1H, J= 7.3, 1.6 Hz), 7.39 (m, 1H), 7.30-7.19 (m, 5H), 6.62 (dd, 1H, J= 2.1-3.3 Hz); ESMS m/e: 211.9 $(M + H)^+$.

Procedimiento J

Esquema U

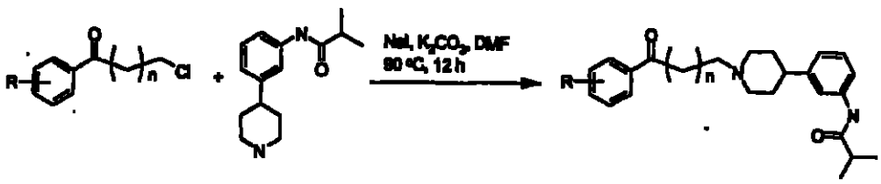


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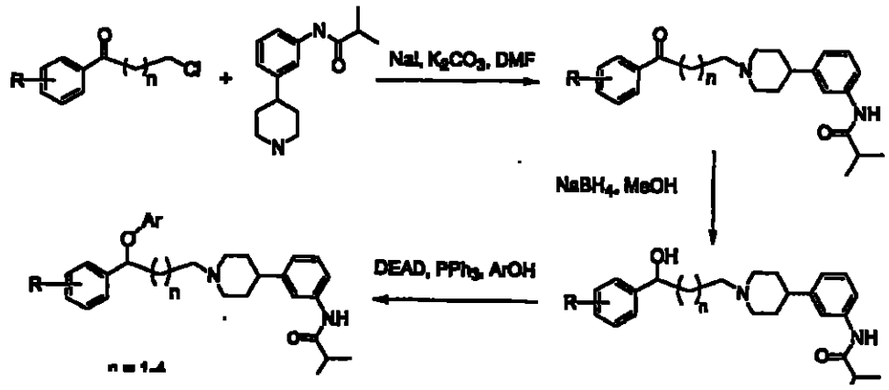


5-(4-METILFENOXI)-1H-INDOL: Una mezcla de 5-bromo-1H-indol (98.0 mg, 0.500 mmol), p-cresol (108 mg, 1.00 mmol), Cu (32.0 mg, 0.500 mmol), K_2CO_3 (138 mg, 1.00 mL) y DMF (1.00 mL), se calentó a 160°C durante 12 h. La mezcla resultante cruda se diluyó con agua (40 mL), la capa acuosa se extrajo con CH_2Cl_2 (3 X 20 mL). Las capas orgánicas combinadas se lavaron con salmuera (30 mL), se secaron sobre Na_2SO_4, se filtraron y concentraron *in vacuo*. El residuo se purificó por medio de TLC preparatoria utilizando hexano:EtOAc (4:1) para dar el producto deseado 5-(4-metilfenoxi)-1H-indol (57.5 mg, 51.5%): ESMS m/e: 224.0 $(M + H)^+$.

Procedimiento K



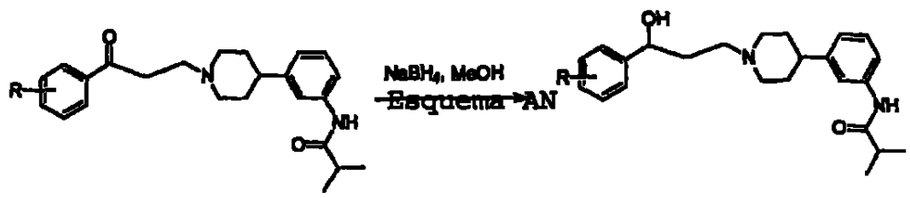
Esquema AN

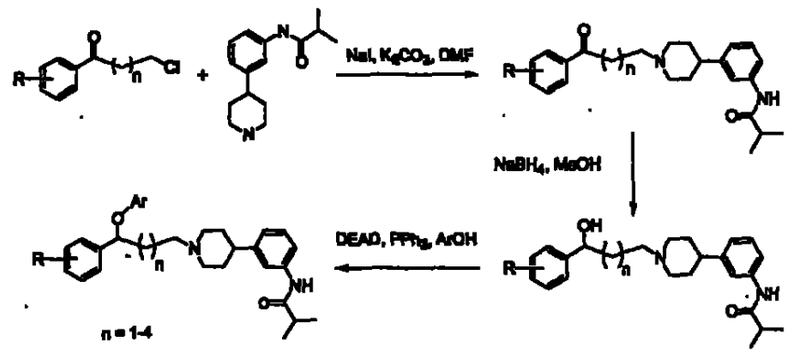


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N-(3-{1-[7-(2-FLUOROFENIL)-7-OXOHEPTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Un matraz de fondo redondo de 50 mL se cargó con una solución de 7-cloro-1-oxo-1(2-fluorofenil)-heptano (2.42 g, 10.0 mmol), 2-metil-N-[3-(4-pi-peridinil)-fenil]propanamida (2.46 g, 10.0 mmol), K_2CO_3 (2.76 g, 20.0 mmol) y NaI (2.25 g, 15.0 mmol) en DMF (25.0 mL). La mezcla fue agitada durante 10 min a 25°C y después se calentó a 100°C durante 12h, enfriada a 25°C y diluida con EtOAc (100 mL). La mezcla resultante se lavó con agua (4 X 50 mL), y la capa acuosa se extrajo con EtOAc (100 mL). Las capas orgánicas se lavaron con salmuera (50 mL), se secaron sobre $MgSO_4$, se concentraron *in vacuo* y el producto crudo se purificó por medio de (EtOAc:MeOH 97:3) para dar el producto deseado (3.70 g, 82.0%).

Procedimiento L





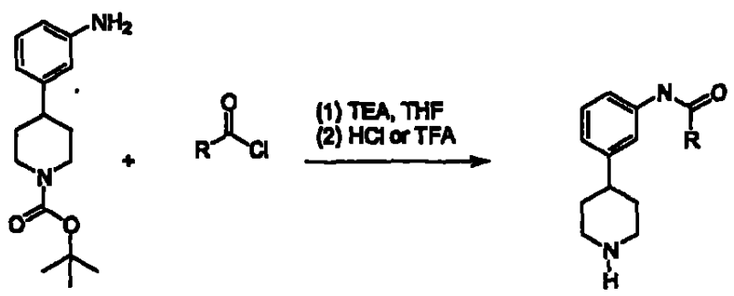
N-(3-{1-[7-(2-FLUOROFENIL)-7-HIDROXIHEPIL]-4-PIPERIDINIL}-FENIL-2-METILPROPANAMIDA: Un matraz de fondo redondo de 50 mL se cargó con N-(3-{1-[7-(2-fluorofenil)-7-oxoheptil]-4-piperidinil}fenil)-2-metilpropanamida (5.0 mmol) y metanol (20 mL), se le adicionó $NaBH_4$ (7.5 mmol) a 0°C en un baño de hielo. La mezcla de reacción fue calentada a 25°C y se agitó durante 2h. La mezcla fue minitoreada por medio de TLC (EtOAc:MeOH 95:5). Sio es necesario, otros 5.0 mmol de $NaBH_4$ se adicionaron a la mezcla de reacción y la mezcla de reacción fue reflujada durante 1 h. La reacción fue enfriada rápidamente con agua (5.0 mL) y se diluyó con EtOAc (10 mL). La capa orgánica fue separada, se lavó con una solución de

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$NaHCO_3$ saturada (10 mL), se secó sobre $MgSO_4$, y se concentró *in vacuo*. El producto crudo se purificó por medio cromatografía (EtOAc:MeOH 97:3) para dar el producto deseado (90%).

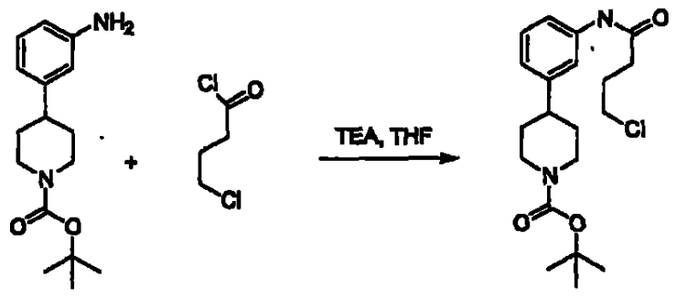
Procedimiento M

Esquema A



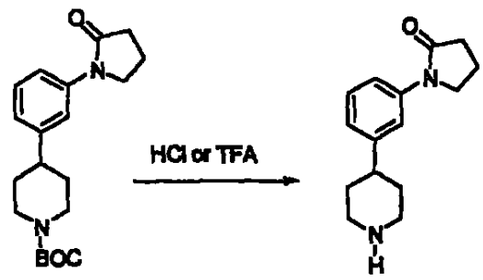
Etapa 1: Si la reacción es individual, una solución de la amina o anilina (1.00 eq), diisopropiletilamina o TEA (2.00 eq) y un electrófilo (1.50 eq) en CH_2Cl_2, se agitó durante 24 h a 23°C. Se retiró el solvente *in vacuo* y el producto crudo se cromatografió (sílice) para dar el producto final.

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4-{[(3-CLOROBUTANOIL)AMINO]FENIL}-1-PIPERIDINILCARBOXILATO DE TERT-BUTILO (3.32 g, 87.4%) se sintetizó de acuerdo al esquema A y procedimiento M: RMN ^{1}H (400 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.47 (s, 1H), 7.37 (m, 1H), 7.28 (m, 1H), 6.97 (d, 1H, J= 7.6 Hz), 3.89 (t, 1H, J= 6.4 Hz), 3.74 (m, 2H), 2.79-2.75 (m, 4H), 2.64 (m, 2H), 1.88-1.77 (m, 4H), 1.60-1.59 (m, 4H), 1.48 (s, 9H).

* HCl o TFA

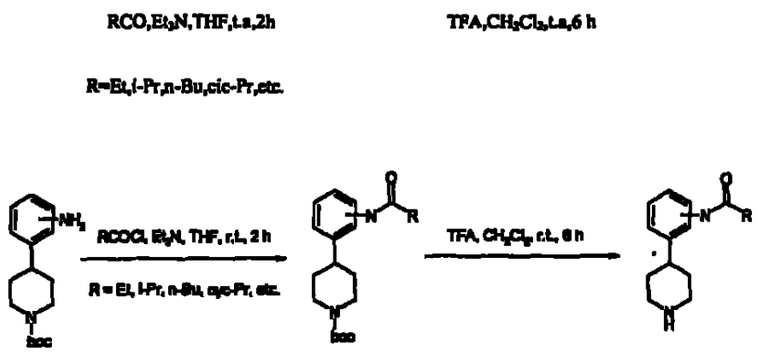


Etapa B:

4-[3-(2-OXO-1-PIRROLIDINIL)FENIL]-1-PIPERIDINCARBOXILATO DE TERT-BUTILO: A una solución de 4-[3-(2-oxo-1-pirrolidinil)-fenil]-1-piperidincarboxilato de tert-butilo (0.429 g, 16.9 mmol) en dioxano (100 mL), se burbujeó gas de HCl durante 1 h a 25°C. La mezcla cruda resultante se basificó con una solución de KOH al 10% (100 mL), la capa acuosa se extrajo con 3:1 $CHCl_3$:alcohol isopropílico (3 X 150 mL). Las capas orgánicas combinadas se lavaron con salmuera (100 mL), se secaron sobre Na_2SO_4, se filtraron, y se concentraron *in vacuo*. El residuo se purificó por medio de TLC preparatoria utilizando NH_3 al 20% (2.0 M en MeOH) en una solución de CH_2CL_2 para dar el rpoducto deseado 4-[3-(2-oxo-1-pirrolidinil)fenil]-1-piperidincarboxilato de tert-butilo (245 mg, 78.7 %): RMN ^1H (400 MHz, $CDCl_3$) δ 7.52 (t, 1H, J= 1.8 Hz), 7.41 (ddd, 1H, J= 8.1, 2.3, 0.9 Hz), 7.30 (t, 1H, J= 7.9 Hz), 7.02 (d, 1H, J= 7.9 Hz), 3.86 (t, 2H, J= 7.3

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Hz), 3.21 (dt, 2H, J= 11.9, 2.9 Hz), 2.76 (dt, 2H, J= 12.1, 2.4 Hz), 2.65 (tt, 1H, J= 11.9, 3.5 Hz), 2.61 (t, 2H, J= 8.3 Hz), 2.22 (br s, 1H), 2.16 (qt, 2H, J= 7.5 Hz), 1.85 (d, 2H, J= 12.4 Hz), 1.67 (dq, 2H, J= 12.5, 4.0 Hz).



4-(4-AMINOFENIL)-1-PIPERIDINCARBOXILATO DE TERT-BUTILI: Disponible de Arch Chemical Company, NJ.

2-metil-N-[4-(4-PIPERIDINIL)FENIL]PROPANAMIDA: A una solución de 4-(4-aminofenil)-1-piperidincarboxilato de tert-butilo (8.20 g, 29.7 mmol) y trietilamina (8.4 mL, 60 mmol) en THF seco (100 mL) a 0°C, se adicionó lentamente una solución de cloruro de 2-metilpropanoilo (3.84 g, 36.0 mmol) en THF (50 mL). Después la mezcla de reacción se calentó a temperatura ambiente y se agitó durante 2 h. Después de retirar el solvente *in vacuo*, el producto crudo se purificó

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por recristalización (hexano/THF), produciendo la amida deseada 4-[4-(isobutirilamino)fenil]-1-piperidincarboxilato de tert-butilo, como un sólido blanco (8.60 g, 84%). El 4-[4-(isobutirilamino)fenil]-1-piperidincarboxilato de tert-butilo se disolvió en CH_2Cl_2 (50 mL) a temperatura ambiente, TFA (13.68 g, 120 mmol, 5 equiv.) se adicionó por medio de una jeringa. La mezcla de reacción se agitó durante 3 o 4 h y otros 5 equivalentes de TFA se adicionaron y la mezcla se agitó durante 2 o 3 h más. La solución de reacción se basificó entonces a pH > 14 por KOH (ac, 2 M). La solución se extrajo con CH_2Cl_2 (8 X 200 mL). La capa orgánica combinada se secó sobre K_2CO_3. El solvente se retiró bajo presión reducida para dar la amina libre, 2-metil-N-[4-(4-piperidinil)fenil]propanamida, como un sólido pardusco (5.99 g, 98%). RMN ^1H (400 MHz, $CDCl_3$) δ 7.55-7.35 (m, 2H), 7.35-6.9 (m, 3H), 3.26-2.98 (m, 2H), 2.84-2.64 (m, 2H), 2.64-2.53 (m, 1H), 2.53-2.32 (m, 1H), 1.90-1.68 (m, 2H), 1.68-1.36 (m, 3H), 1.22 (d, 6H, J=6.0 Hz); ESMS m/e : 247.1 $(M + H)^+$.

N-[4-(4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el procedimiento para 2-metil-N-[4-(4-piperidinil)fenil]propanamida utilizando 4-(4-aminofenil)-1-piperidincarboxilato de tert-butilo y cloruro de propanoilo: ESMS m/e : 233.1 $(M + H)^+$.

N-[4-(4-PIPERIDNIL)FENIL]BUTANAMIDA: Preparada por el procedimiento para 2-metil-N-[4-(4-piperidinil)fenil]propanamida utilizando 4-(4-aminofenil)-1-piperidincarboxilato de tert-butilo y cloruro de butanoilo: ESMS m/e : 247.2 $(M + H)^+$.

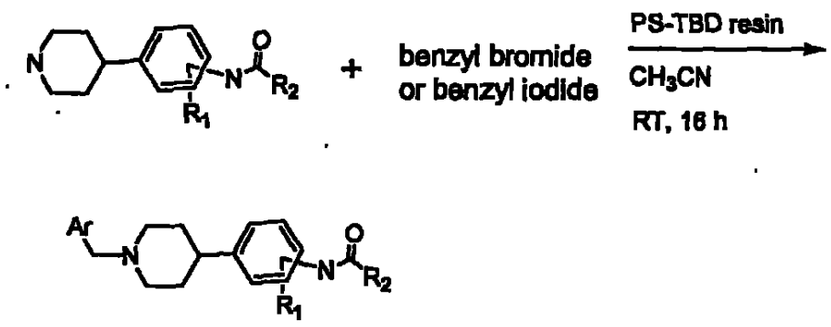
N-[3-(4-PIPERIDNIL)FENIL]CICLOPROPANCARBOXAMIDA: Preparada por el procedimiento para 2-metil-N-[4-(4-piperidinil)fenil]propanamida utilizando 4-(3-aminofenil)-1-piperidincarboxilato de tert-butilo y cloruro de ciclopropancarbonilo: Cálc. Anál. para $C_{15}H_{20}N_2O+0.15CH_2Cl_2$: C, 7.8; H, 7.87; N, 10.9. Encontrado: C, 70.9; H, 7.68; N, 11.1; ESMS m/e : 245.0 $(M + H)^+$.

N-[3-(4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el procedimiento para 2-metil-N-[4-(4-piperidinil)fenil]propanamida utilizando 4-(3-aminofenil)-1-piperidincarboxilato de tert-butilo y cloruro de propanoilo: Cálc. Anál. para $C_{14}H_{20}N_2O$: C, 72.2; H, 8.63; N, 12.1. Encontrado: C, 72.4; H, 8.68; N, 12.1; ESMS m/e : 233.1.

Procedimiento N

Esquema AV

Resina de PS-TBD



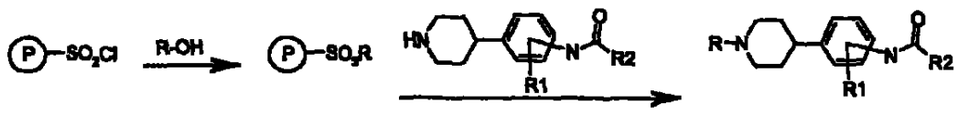
La biblioteca fue construida en Bloques de Reactor de placas Robbins de 46 pozos de polipropileno. En el período de incubación inicial, cada pozo se cargó con resina PS-TBD (Argonaut Technologies, 0.280 mmol, 2.50 eq, 200 mg) y piperidina (0.120 mmol, 1.10 eq) en acetonitrilo (0.500 mL) y se agitó durante 1 h. Una solución de bromuro o yoduro de bencilo (0.110 mmol, 1.00 eq) en acetonitrilo (0.500 mL) se adicionó a cada pozo seguida por la adición de acetonitrilo (1.00 mL) para producir un volumen total de 2.00 mL y la mezcla se giró en un horno rotatorio Robbins a temperatura ambiente durante 16 h. Después, se adicionó resina de AP-isocianato (Argonaut Technologies, 250 mg, 0.430 mmol, 4.00 eq) a cada pozo y se hizo reaccionar además

a temperatura ambiente durante otras 12 h. La mezcla se filtró y el filtrado se concentró *in vacuo* para obtener el producto deseado que se caracterizó vía LC-MS.

Procedimiento O

La alquilación de piperidinas utilizando alcoholes y resinas PS-TSC1 en "Bloques de Reactor" Robbins de 48 pozos.

Esquema W



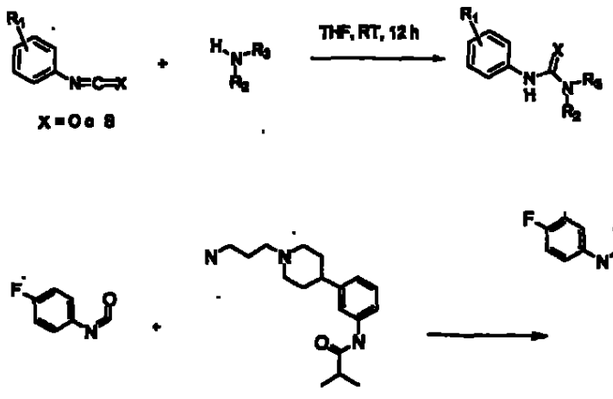
La biblioteca se construyó en "Bloques de Reactor" Robbins de placas de 46 pozos, de polipropileno. Resina PS-TSC1 (100 mg, 1.00 eq, comprado de Argonaut Technologies) se colocó en cada pozo de las placas de 46 pozos de los "Bloques de Reactor". A cada pozo se le adicionó un alcohol (1.50 mmol) en 3.00 mL de CH_2Cl_2 y piridina (1:1). La mezcla se agitó durante 5 h. y la resina se lavó con CH_2Cl_2 (3 X 4 mL), DMF (5 x 4.0 mL), DMF/H_2O (3:1, 5 X 4.0 mL), THF (3 x

4.0 mL), CH_2Cl_2 (3 x 4.0 mL), acetonitrilo (2 x 4.0 mL), y se secó bajo presión reducida. Una solución de una amina (0.0750 mmol, 0.500 eq) y N, N-diisopropiletilamina (19.0 mg, 0.150 mmol, 1.00 eq), en acetonitrilo (3.00 mL), se adicionó al pozo que contiene la resina derivatizada y la mezcla se hizó reaccionar a 70°C durante 16 h. Finalmente, la resina de AP-isocianato (120 mg, 0.150 mmol), 1.00 eq) y THF (2.00 mL), se adicionó al recipiente de reacción y se hizó reaccionar atemperatura ambiente durante otras 3 h. La solución se filtró en las placas de recepción Robbins y se concentró *in vacuo* para dar la amina terciaria deseada, la cual se analizó vía LC-MS.

Procedimiento P

Esquema AB

THF,T.A.,12h



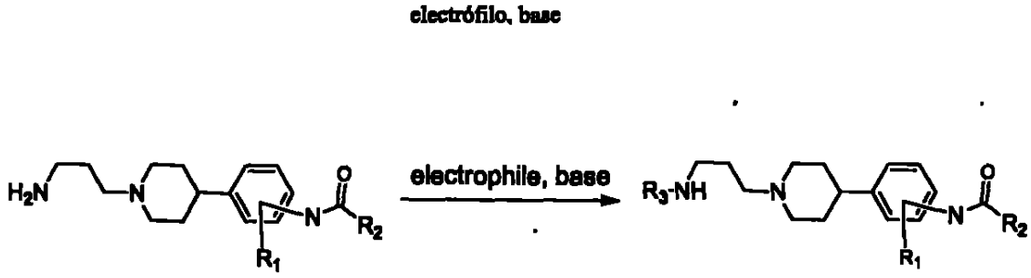
N-{3-[1-(3-{[(4-FLUOROANILINO)CARBONIL]AMINO}PROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Una solución de N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida (26.4 mg, 0.0870 mol), 1-fluoro-4-isocianatobenceno (11.9 mg, 0.0870 mmol), en THF (1.00 mL), se agitó durante 12 h a 25°C. La mezcla cruda resultante se diluyó con agua (10 mL), la capa acuosa se extrajo con CH_2Cl_2 (3 X 20 mL). Las capas orgánicas combinadas se concentraron in vacuo y el residuo se purificó por medio de TLC preparatoria utilizando 2.5 % de NH_3 (2.0 M en metanol) en CH_2Cl_2 para dar el producto deseado N-{3-[1-(3-{[(4-fluoroanilino)carbonil]amino}propil)-4-piperidinil]fenil}-2-metilpropanamida (4.18 mg, 10.9%): RMN ^1H (400 MHz, $CDCl_3$) δ 7.45 (q, 2H, J= 4.7 Hz), 7.23-7.21 (m, 4H), 7.05 (t, 4H, J= 7.8 Hz), 6.75 (m, 1H), 4.05 (m, 1H9, 3.19 (s, 1H), 2.71 (m, 1H), 2.53 (m, 1H),

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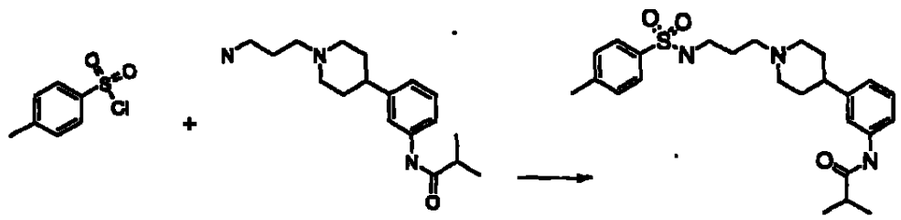
2.26-2.21 (m, 3H), 1.80-1.60 (m, 9H), 1.25 (d, 6H, J=6.4 Hz); ESMS m/e : 439.4 $(m + H)^+$.

Procedimiento Q_1

Esquema AT



Si la reacción es individual, una solución de la amina (1.0 eq), un electrófilo (1.5 eq), diisopropiletilamina (2.0 eq), en CH_2Cl_2 se agitó durante 1 día. El solvente se retiró *in vacuo* y el producto crudo se cromatografió para dar el producto final.



2-METIL-N-{3-[1-(3-{[(4-METILFENIL)SULFONIL]AMINO}PROPIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Una solución de cloruro de 4-metilbencensulfonilo (16.6 mg, 0.0870 mmol), N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida (26.4 mg, 0.870 mmol), TEA (10.0 mg, 0.174 mmol) en THF (1.00 mL), se agitó durante 12 h a 25°C. La mezcla resultante cruda se diluyó con agua (20 mL), la capa acuosa se extrajo con CH_2Cl_2 (2 x 20 mL). Las capas orgánicas combinadas se concentraron *in vacuo* y el residuo se purificó por TLC preparatoria utilizando 2.5% de NH_3 (2.0 M en metanol) en CH_2Cl_2 para dar el producto deseado 2-metil-N-{3-[1-(3-{[(4-metilfenil)-sulfonil]amino}propil)-4-piperidinil]fenil}propanamida (17.3 mg, 43.6%): RMN ^1H (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.53 (s, 1H), 7.41 (s, 1H), 7.32-7.21 (m, 4H), 7.16 (s, 1H), 6.97 (d, 1H, J= 7.9 Hz), 3.44 (t, 2H, J= 6.3 Hz), 3.15 (d, 2H, J= 9.8 Hz), 2.62-2.45 (m, 4H), 2.15 (m, 3H), 2.05 (s, 3H), 1.95-1.71 (m, 5H), 1.26 (d, 6H, J= 6.6 Hz),; ESMS m/e : 458.2 $(M + H)^+$.

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Procedimiento Q_2

La Captura y Método de Liberación para la Síntesis y Purificación de la Biblioteca de Piperidina.

La resina de intercambio Amberlyst 15 obtenida comercialmente (Aldrich) se activó utilizando el siguiente procedimiento:

1. La resina se agitó en metanol durante 24 hr.
2. La resina se filtró y lavó con metanol en un embudo de sinterizado.
3. La resina se neutralizó con NH_3 2N en MeOH (pH verificado) - agitar o menear durante 1 h.
4. La resina neutralizada se acidificó con HCl 3M en MeOH (pH verificado) - se agitó o meneo durante 1 hr.
5. La resina se capturó en un embudo de sinterizado y se lavó con MeOH.
6. La resina se secó *in vacuo* y se almacenó.

Síntesis (Acilación de las Aminas):

La biblioteca se construyó en "Bloques de Reactor" Robbins, de placas con 46 pozos, de polipropileno. En cada placa un arreglo de 5 aminas (0.10 mmol) y 8 electrófilos (cloruros de ácido, cloruros de sulfonilo, 1. eq.) en presencia de trietilamina (2.0 eq) en THF/DCM 3:1 (2.0 mL), se hicieron reaccionar durante la noche para dar 40

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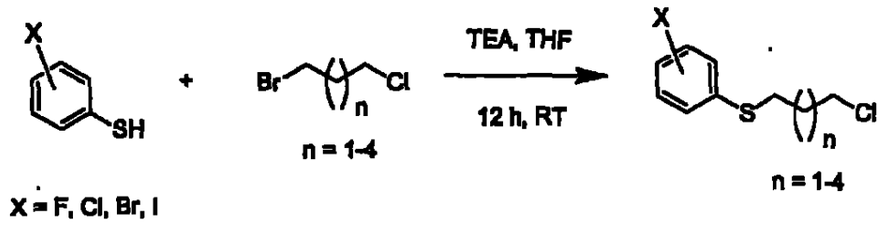
compuestos/placa. Las reacciones fueron rigurosamente monitoreadas vía TLC hasta el agotamiento de la amina de partida debido a siguiente metodología de purificación vía la resina de Amberlyst 15 acídica. Seguido de la desaparición de la amina de partida, los productos deseados se capturaron y después se liberaron utilizando el proceso bosquejado enseguida.

Purificación de los Productos de Piperidina: La resina de intercambio Amberlyst 15 activada (0.90 g, Aldrich), se adicionó a cada pozo, y las placas se giraron durante 2 horas en un horno rotatorio Robbins para capturar el producto final deseado de la mezcla de reacción. El solvente se filtró y la resina se lavó con CH_3OH y CH_2Cl_2 (x 3) alternativamente con cada uno de los solventes (durante 10 minutos en cada ocasión). Después de la última filtración, amonio 2 N en metanol se adicionó a la resina (2 mL a cada pozo) y los bloques de reacción se giraron durante 2 horas para liberar los compuestos deseados de la resina. Los compuestos finales se filtraron en "Bloques de Recepción" de Robbins, el solvente se retiró y los compuestos se analizaron vía LC-MS.

Procedimiento R

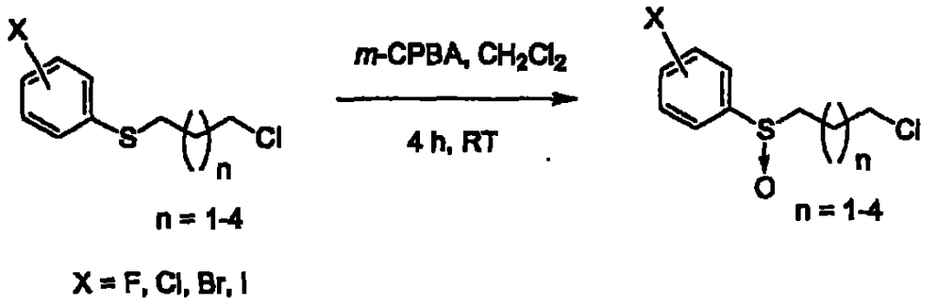
Esquema Z

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[(3-CLOROPROPIL)SULFANIL]BENCENO: Una mezcla de bencenotiol (0.550 g, 5.00 mmol), 1-bromo-3-cloropropano (106 mg, 5.50 mol), TEA (1.01 g, 10.0 mmol) y THF (10.0 mL), se agitó durante 12 h a 25°C. La mezcla cruda resultante se diluyó con agua (40 mL), la capa acuosa acuosa se extrajo con CH_2Cl_2 (3 X 30 mL). Las capas orgánicas combinadas se concentraron *in vacuo* y el rersiduo se purificó por medio de TLC preparatoria utilizando hexano:EtOAc (10:1) para dar el producto deseado [(3-cloropropil)sulfanil]benceno (1.05 g, 100%).

Esquema AA



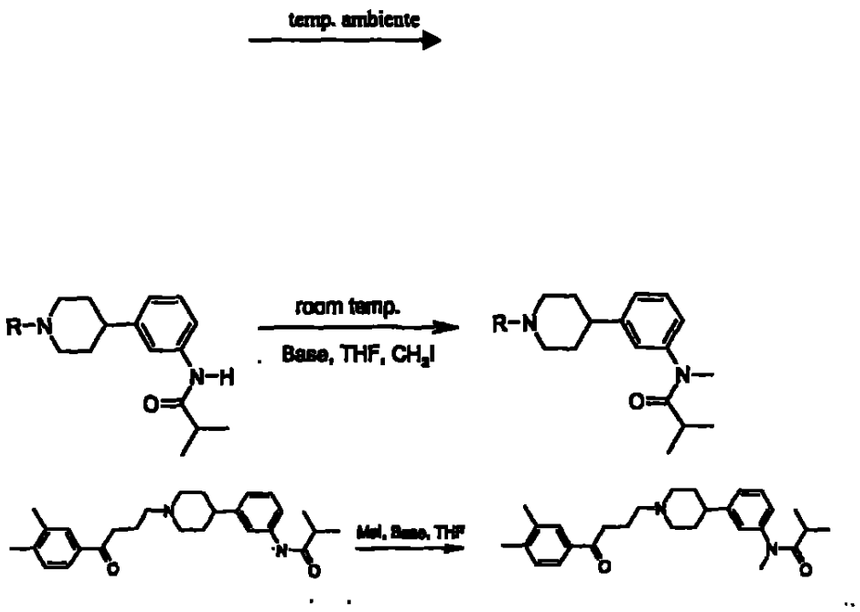
Procedimiento S

4-FLUOROFENIL SULFOXIDO DE 3-CLOROPROPILO: Una solución de 3-4-fluorofenil sulfuro de cloropropil (77.5 mg, 0.380 mmol) en CH_2Cl_2 (2.00 mL), se enfrió a 0°C. A esta solución se adicionó m-CPBA (78.7 mg, 0.460 mmol). La mezcla de reacción se agitó a 0°C durante 30 min, después a 23°C durante 4 h. La mezcla cruda resultante se diluyó con Na_2SO_3 al 10% (10 mL), la capa acuosa se extrajo con CH_2Cl_2 (2 X 15 mL). Las capas orgánicas combinadas se lavaron con salmuera (10 mL), se secaron sobre Na_2SO_4, se filtraron y concentraron

in vacuo. El residuo se purificó por medio de TLC preparatoria utilizando 2.5% de NH_3 (2.0 M en metanol) en CH_2Cl_2 para dar el producto deseado 4-fluorofenil sulfóxido de 3-cloropropilo (47.8 mg, 57.0%).

Procedimiento T

Esquema AD

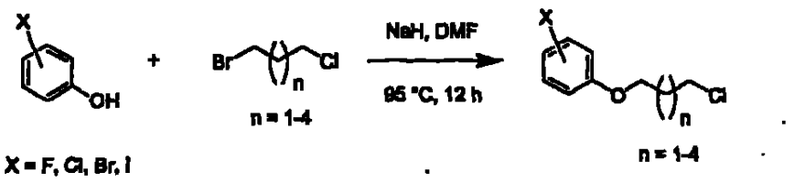


N-(3-{1-[4-(3,4-DIMETILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)-N-2-DIMETILPROPANAMIDA: Una mezcla de N-(3-{1-[4-(3,4-dimetilfenil)-4-oxobutil]-4-piperidinil}fenil)-2-metilpropanamida (15.0 mg, 0.0357 mmol), MeI (5.07 mg, 0.0357 mmol), NaOtBu (6.86 mg, 0.0714 mmol) y THF (1.00 mL), se agitó

durante 5 h a 25°C. La mezcla cruda resultante se diluyó con agua (10 mL), la capa acuosa se extrajo con CH_2Cl_2 (3 X 20 mL). Las capas orgánicas combinadas se concentraron *in vacuo* y el residuo se purificó por medio de TLC preparatoria utilizando 4.0% de NH_3 (2.0 M en metanol) en CH_2Cl_2 para producir el producto deseado N-(3-{1-[4-(3,4-dimetilfenil)-4-oxobutil]-4-piperidinil}fenil)-N-2-dimetilpropanamida(13.8 mg, 89.1%): RMN ^1H (400 MHz, $CDCl_3$)δ 7.76 (s, 1H), 7.72 (dd, 1H, J= 1.8, 7.7 Hz), 7.33 (t, 1H, J= 8.8 Hz), 7.22 (d, 1H, J= 7.8 Hz), 7.18 (d, 1H, J= 8.8 Hz), 7.01 (m, 2H), 3.24 (s, 3H), 3.10 (d, 1H, J= 10.6 Hz), 3.00 (t, 1H, J= 7.6 Hz), 2.49-2.44 (m, 4H), 2.33 (s, 6H), 2.11-2.10 (m, 2H), 1.99 (m, 1H), 1.79-1.177 (m, 4H), 1.26 (t, 2H, J= 7.6 Hz), 1.02 (d, 6H, J= 7.6 Hz),; ESMS m/e : 435.2 $(M + H)^+$.

Procedimiento U

Esquema AK

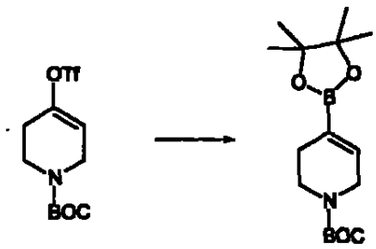


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1-[3-(3-CLOROPROPOXI)FENIL]ETANONA: A una suspensión de NaH (50.5 mg, 2.00 mmol) en DMF (1.00 mL), se le adicionó 1-(3-hidroxifenil)etanona (136 mg, 1.00 mmol) a 0°C. La mezcla de reacción se agitó a temperatura ambiente durante 1 h. A esta mezcla se le adicionó una solución de 1-bromo-3-cloropropano (188 mg, 1.20 mmol), en DMF (0.500 mL). La mezcla de reacción se agitó a temperatura ambiente durante 5 h. La mezcla cruda resultante se diluyó con agua (20 mL), la capa acuosa se extrajo con CH_2Cl_2 (3 X 20 mL). La capa orgánica combinada se lavó con salmuera (20 mL), se secó sobre Na_2SO_4, se filtró y se concentró *in vacuo*. El residuo se purificó por medio de TLC preparatoria utilizando hexano:EtOAc (4:1) para producir el producto deseado 1-[3-(3-cloropropoxi)-fenil]etanona (235 mg, 55.2%): RMN ^1H (400 MHz, $CDCl_3$) δ 7.7 (d, 1H, J= 6.6 Hz), 7.52 (s, 1H), 7.25 (t, 1H, J= 6.6 Hz), 7.01 (m, 1H), 4.11 (t, 2H, J= 7.9 Hz), 3.69 (t, 2H, J= 7.9 Hz), 2.61 (s, 3H), 1.95-1.92 (m, 2H).

Procedimiento V

Esquema AE

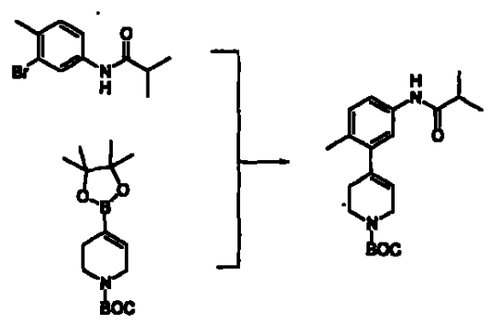


1-[(2,2-DIMETILPROPANOIL)OXI]-4-(4,4,5,5-TETRAMETIL-1,3,2-DIOXOBOROLAN-2-IL)-1,2,3,6-TETRAHIDROPIRIDINA: Un matraz RB (fondo redondo) de 50 mL, se cargó con bis(pinacolato)diboro (422 mg, 1.66 mmol), KOAc (444 mg, 4.53 mmol) y $PdCl_2$dppf (37.0 mg, 3.00 mol %), dppf (25.0 mg, 3.00 mol%), se le adicionó una solución de trifluorometansulfonato de 1-[(2,2-dimetilpropanoil)oxi]-1,2,3,6-tetrahidro-4-piridinilo (500 mg, 1.51 mmol) en 1,4-dioxano (10.0 mL) a temperatura ambiente bajo argón. La mezcla se calentó a 80°C durante la noche. Después de que se enfrió a temperatura ambiente, la mezcla se filtró a través de celita y la celita se lavó con EtOAc (3 X 20 mL). Los filtrados se concentraron *in vacuo*. El residuo resultante se disolvió en EtOAc y se lavó con H_2O y salmuera, se secó sobre $MgSO_4$, se filtró y concentró *in vacuo*. El material crudo se purificó por medio de cromatografía instantanea (1:9 EtOAc:hexano) para dar 1-[(2,2-dimetilpropanoil)oxi]-4-(4,4,5,5-tetrametil-1,3,2-

dioxaborolan-2-il]-1,2,3,6-tetrahidropiridina (355 mg, 76.0%).

Procedimiento W

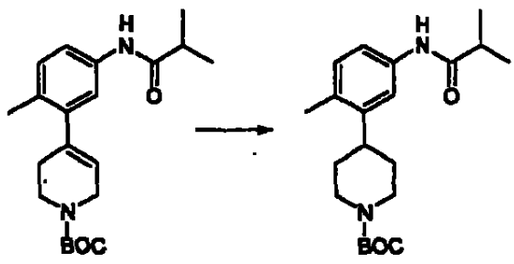
Esquema AF



4-[5-(ISOBUTIRILAMINO)-2-METILFENIL]-3,6-DIHIDRO-1(2H)-PIRIDINCARBOXILATO DE TERT-BUTILO: A un matraz RB (fondo redondo) de 50 mL que contiene 1-[(2,2-dimetilpropanoil)-oxi]-4-(4,4,5,5-tetrametil-1,3,2-dioxoborolan-2-il)-1,2,3,6-tetrahidropiridina (500 mg, 1.62 mmol), K_2CO_3 (670 mg, 4.86 mmol) y $PdCl_2dppf$ (155 mg), se le adicionó una solución de N-(3-bromo-4-metilfenil)-2-metilpropanamida (415 mg, 1.62

mmol) en DMF (10.0 mL) a temperatura ambiente bajo argón. La mezcla se calentó a 80°C bajo argón durante la noche. Después de que se enfrió a temperatura ambiente, la mezcla se filtró a través de celita y la celita se lavó con EtOAc (3 x 20 mL). Los filtrados se lavaron con H_2O (20 mL), salmuera (20 mL), se secaron sobre $MgSO_4$, se filtró y concentró *in vacuo*. El material crudo se purificó por cromatografía instantánea (EtOAc/hexano al 20%) para dar 4-[5-(isobutirilamino)-2-metilfenil]-3,6-dihidro-1(2H)-piridincarboxilato de tert-butilo (360 mg, 62.0 %).

Esquema AG

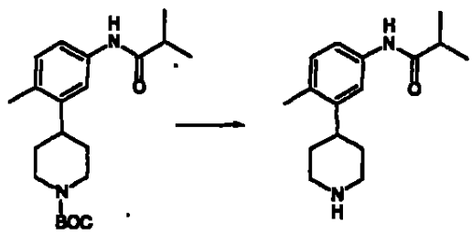


Procedimiento X

4-[5-(ISOBUTIRILAMINO)-2-METILFENIL]-1-PIPERIDINILCARBOXILATO DE TERT-BUTILO: Una solución de 4-[5-(isobutirilamino)-2-metilfenil]-3,6-dihidro-1(2H)-piridin-carboxilato de tert-butilo (335 mg, 0.93 mmol) y Pd/C al 10% (350 mg) en EtOH (20.0 mL), se hidrogenó a temperatura ambiente durante la noche utilizando el método del matraz de hidrógeno. La mezcla de reacción se filtró a través de celita y se lavó con etanol (3 x 10 mL). Los extractos combinados se concentraron *in vacuo* para producir 4-[5-(isobutirilamino)-2-metilfenil]-1-piperidincarboxilato de tert-butilo (335 mg, 100%).

Procedimiento Y

Esquema AH

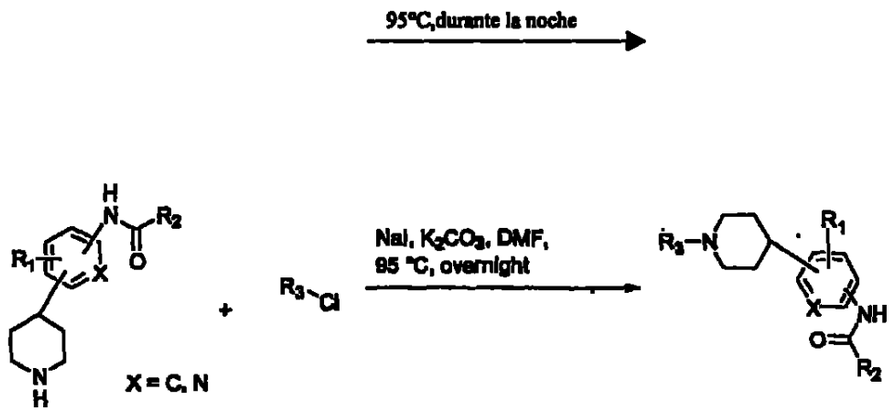


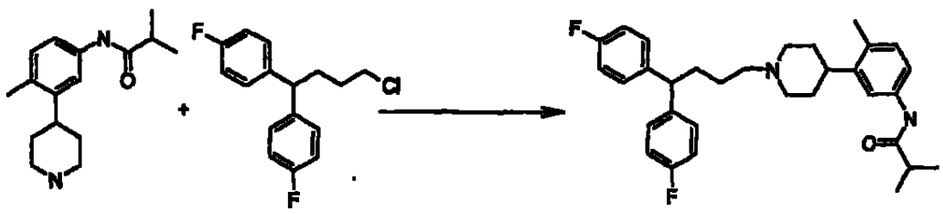
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2-METIL-N-[4-METIL-3-(4-PIPERIDINIL)FENIL]PROPANAMIDA: En una solución de 4-[5-(isobutilamino)-2-metilfenil]-1-piperidincarboxilato de tert-butilo (335 mg, 0.030 mmol) en CH_2Cl_2 (10.0 mL), se adicionó a TFA (10.0 mL)a temperatura ambiente. La mezcla de reacción se agitó durante 2 h y se concentró *in vacuo*. El residuo se disolvió en 20 mL de $CHCl_3$/i-PrOH (3:1) y se basificó con solución de KOH al 5% (10 mL). La capa acuosa se extrajo con $CHCl_3$/i-PrOH (3:1, 3 x 10 mL). Los extracto orgánicos combinados se lavaron con salmuera, se secaron sobre $MgSO_4$, se filtraron y concentraron *in vacuo* para dar 2-metil-N-[4-metil-3-(4-piperidinil)fenil]propanamida (190 mg, 78.0%).

Procedimiento Z

Esquema AI



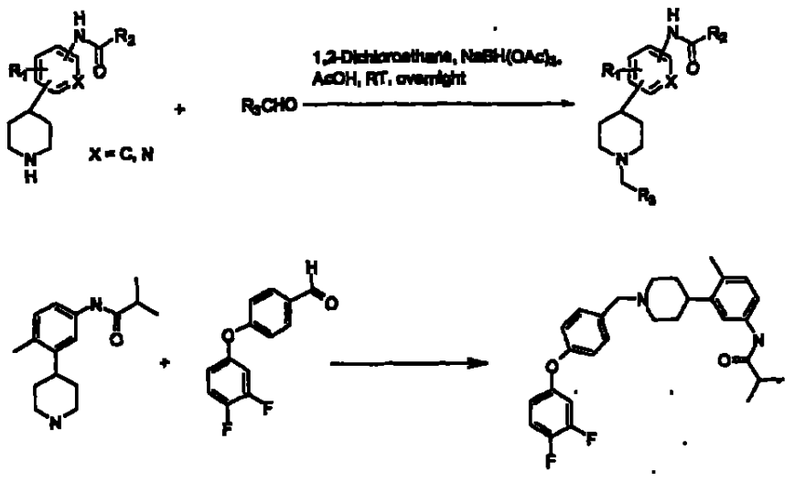


N-(3-{1-[4,4-BIS(4-FLUOROFENIL)BUTIL]-4-PIPERIDINIL}-4-METILFFENIL)-2-METILPROPANAMIDA: Una solución de 2-metil-N-[4-metil-3-(4-piperidinil)fenil]propanamida 49.0 mg, 0.190 mmol), 1-[4-cloro-1-(4-fluorofenil)butil]-4-fluorobenceno (58.0 mg, 0.210 mmol), NaI (42.0 mg, 0.280 mmol), y K_2CO_3 (52 mg, 0.380 mmol) en DMF (10 mL),se calentó a 95°C durante la noche. La mezcla se diluyó con agua (20 mL), y la capa acuosa se extrajo con EtOAc (3 x 20 mL). Las capas orgánicas combinadas se lavaron con salmuera, se secaron sobre $MgSO_4$, y se concentraron *in vacuo*. El producto crudo se purificó por cromatagrafía instantánea [NH_3 al 5% (2.0 M en MeOH) en CH_2Cl_2] para producir N-(3-{1-[4,4-bis(4-fluorofenil)butil]-4-piperidnil}-4-metilfenil)-2-metilpropanamida (37.0 mg, 38.0%).

Procedimiento AA

Esquema AJ

1,2-dicloroetano,NaBH(OAc)$_3$,
AcOH,T.A.,durante la noche



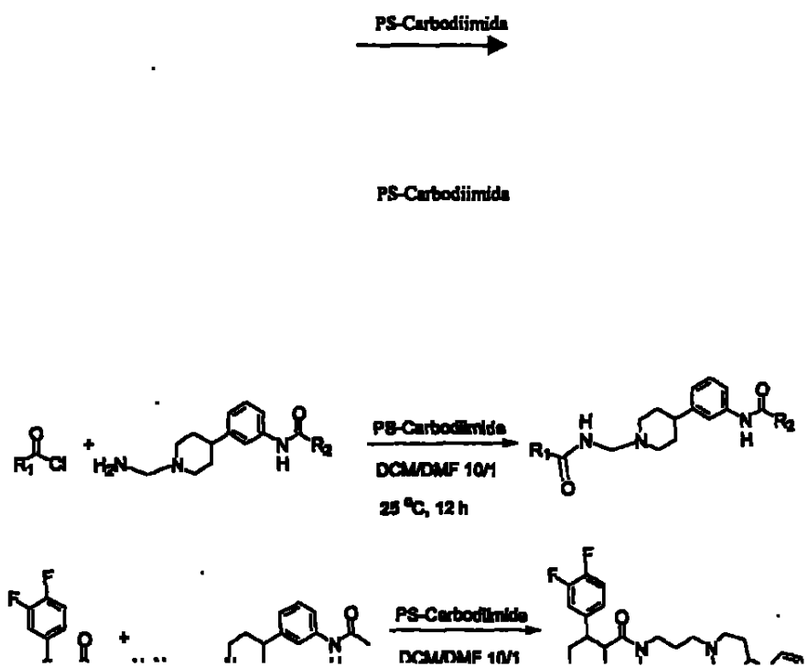
N-(3-{1-[4-(3,4-DIFLUOROFENOXI)BENCIL]-4-PIPERIDNIL}-4-METILFENIL-2-METILPROPANAMIDA: A una solución de 4-(,4-difluorofenoxi)benzaldehido (41.0 mg, 0.170 mmol) y 2-metil-N-[4-metil-3-(4-piperidinil)fenil]propanamida (45.0 mg, 0.170 mmol) en 1,2-dicloroetano (5.00 mL), se le adicionó triacetoxiborohidruro de sodio (110 mg, 0.520 mmol), y AcOH

1122 1119

(10.0 L, 0.170 mmol) a temperatura ambiente. La mezcla se agitó durante la noche. La mezcla de reacción fue rápidamente enfriada por medio de una solución de $NaHCO_3$ saturada (10 mL) y se extrajo con CH_2Cl_2 (3 x 10 mL). Las capas orgánicas combinadas se lavaron con salmuera, se secaron sobre $MgSO_4$, se concentraron *in vacuo*. El producto crudo se purificó por medio de TLC preparatoria utilizando NH_3 al 5% (2.0 M en MeOH) en CH_2Cl_2 para dar el producto deseado N-(3-{1-[4-(3,4-difluorofenoxi)bencil]-4-piperidinil}-4-metilfenil)-2-metilpropanamida (44.0 mg, 54.0%).

Procedimiento AC

Esquema AT: síntesis de Amidas utilizando resina de PS-carbodiimida.

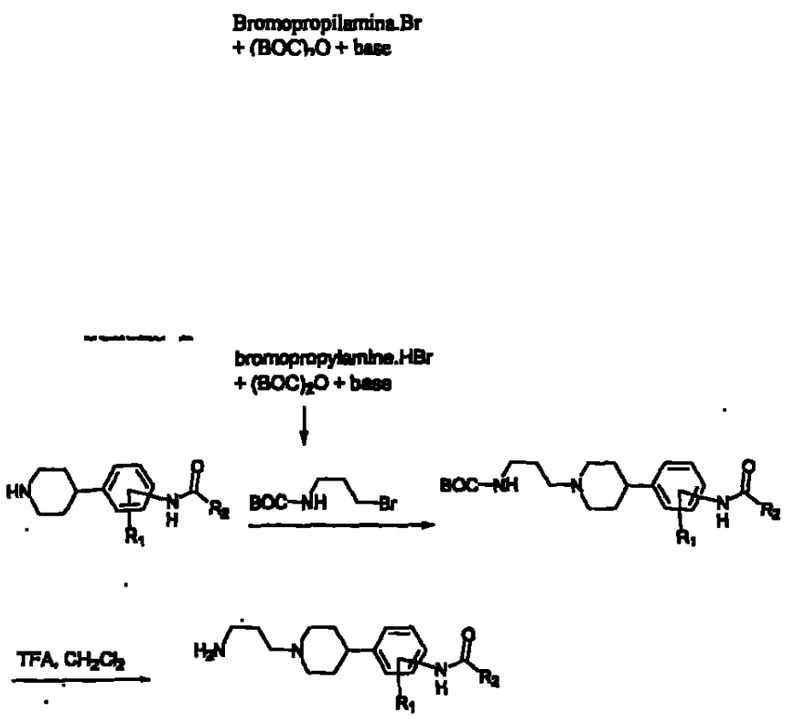


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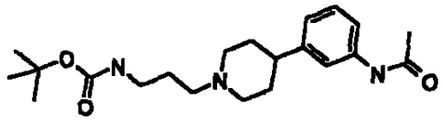
Una mezcla de ácido carboxílico (0.0800 mmol) y resina de PS-carbodiimida (2.00 eq, 80.0 mg, 1.34 mmol/g) en DCM:DMF (10:1, 3.00 mL), se agitó o meneo durante 30 minutos. A la mezcla resultante se le adicionó amina (0.0540 mmol) y la mezcla resultante se agitó durante 12 h a temperatura ambiente. La mezcla de reacción se filtró y la resina se lavó con CH_2Cl_2. Los extractos orgánicos combinados se concentraron hasta un pequeño volumen, se le aplicó una placa de TLC preparatoria y se eluyó con NH_3 al 6% (2.0 M en MeOH) en CH_2Cl_2 para dar el producto deseado.

Procedimiento AD

Esquema X



N-(3-BROMOPROPIL)CARBAMATO DE TERT-BUTILO: Se preparó a partir de bromohidrato de 3-bromopropilamina y BOC_2O en presencia de una base en CH_2Cl_2: RMN ^1H (300 MHz) δ 5.07 (br, 1H), 3.31 (t, 2H, J= 6.6 Hz), 3.12 (br q aparente, 2H, J= 6.0 Hz), 1.92 (p, 2H, J= 6.6 Hz), 1.30 (s, 9H).



Etapa 1: A una solución de piperidina (19.3 mmol) en dioxano (20.0 mL), se le adicionó N-(tert-butoxicarbonil)-3-bromopropilamina (21.2 mmol) y carbonato de potasio (38.7 mmol) a temperatura ambiente y la mezcla se calentó a temperatura de reflujo durante 24 h. La mezcla de reacción se enfrió a temperatura ambiente, se concentró *in vacuo* y se dividió entre $CHCl_3$ (40 mL) y agua (5.0 mL). La capa orgánica se lavó con salmuera, se secó sobre sulfato de sodio, se filtró y se concentró *in vacuo*. El producto crudo se purificó por medio de cromatografía de columna (acetato de etilo:metanol 9:1) para rendir el producto requerido 3-

{4-[3-(acetilamino)fenil]-1-piperidinil}propil-carbamato, como un aceite incoloro: ESMS m/e : 376.2 $[M + H]^+$.

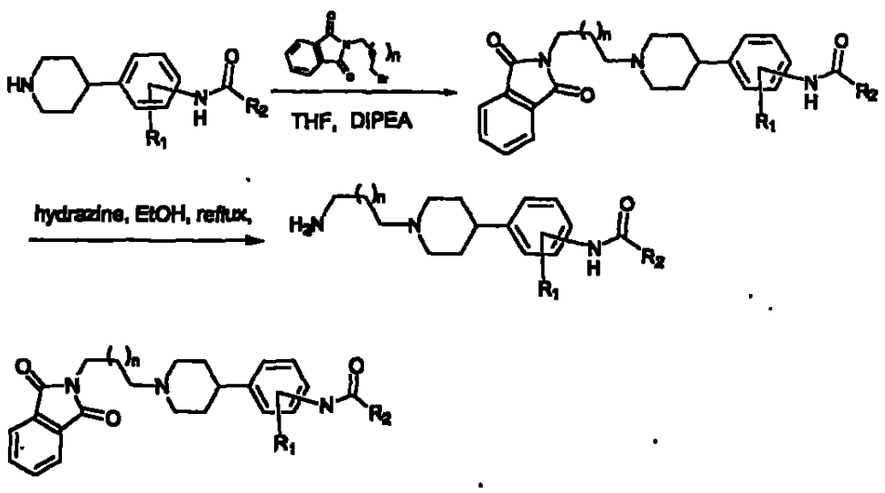
Etapa 2. Se burbujeó gas de HCl en la solución de amina protegida (12.1 mmol) en dioxano (5.00 mL) durante 10-20 minutos a 0-5°C. La solución resultante se agitó a 0-5°C durante 1 h, se concentró, se neutralizó con solución de KOH al 10% (10 mL) y se extrajo en CH_2Cl_2 (25 mL). El extracto orgánico se lavó con salmuera, se secó sobre sulfato de sodio y se concentró *in vacuo*. El producto crudo se cromatografió para dar el producto deseado N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}acetamida: ESMS m/e : 276.1 $[M + H]^+$.

Procedimiento AE

Esquema Y

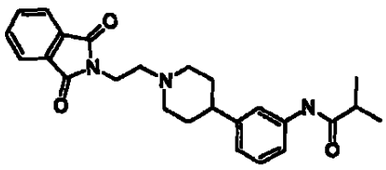
hidrazina,EtOH,reflujo

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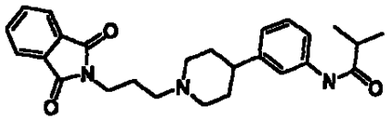


Etapa 1: Una mezcla de piperidina (1.00 eq, 0.0226 mmol), N-(bromoalquil)ftalamida (1.50 eq, 0.0338 mmol), Bu_4NI (200mg) y diisopropiletilamina (5.00 eq, 0113 mmol) en dioxano (200 mL), se calentó a 99°C durante 24 h. La reacción fue seguida por análisis de TLC (95:5 CH_2Cl_2:metanol). Si es necesario, se adicionó 0.0113 mmol de las bromoalquilftalamidas apropiadas a cada mezcla de reacción y se continuó el calentamiento durante 48 h adicionales. La mezcla de reacción se enfrió a temperatura ambiente, las sales de amonio se filtraron y el solvente se retiró bajo presión reducida. El producto crudo se cromatografió para dar el producto deseado.

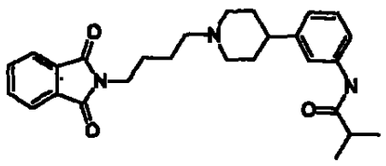
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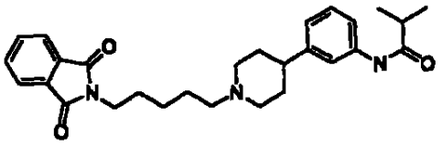
ESMS m/e: 420.2
$[M+H]^+$



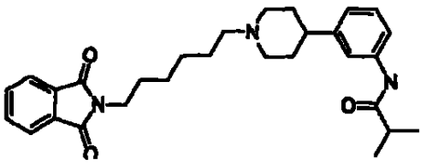
ESMS m/e: 434.4
$[M+H]^+$



ESMS m/e: 448.4
$[M+H]^+$



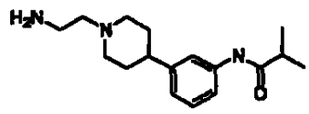
ESMS m/e: 462.4
$[M+H]^+$



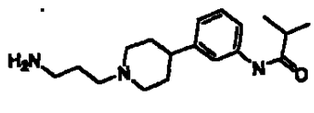
17:5 1128

Etapa 2: La desprotección de las ftalamidas resultantes se realizó por medio de calentamiento de una solución de aminas protegidas con ftalamida con exceso de hidrato de hidrazina (10 eq) en etanol (0.5-1.0 M) a 90°C durante 4 h. La mezcla de reacción se monitoreo por medio de TLC hasta la complementación. Hasta que la reacción se complemento, la mezcla se enfrió a temperatura ambiente, los subproductos insolubles se filtraron a través de celita y el solvente se retiró *in* vacuo. El producto crudo se cromatografió (diclorometano-metanol-isopropilamina) para dar los productos deseados.

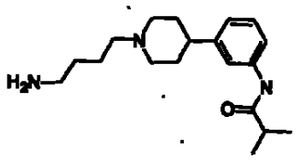
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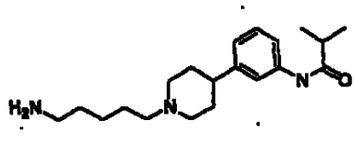
ESMS m/e: 290.2 $[M+H]^+$



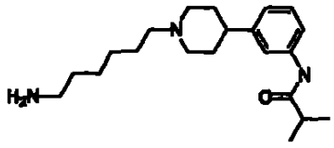
ESMS m/e: 304.1 $[M+H]^+$



ESMS m/e: 318.2 $[M+H]^+$



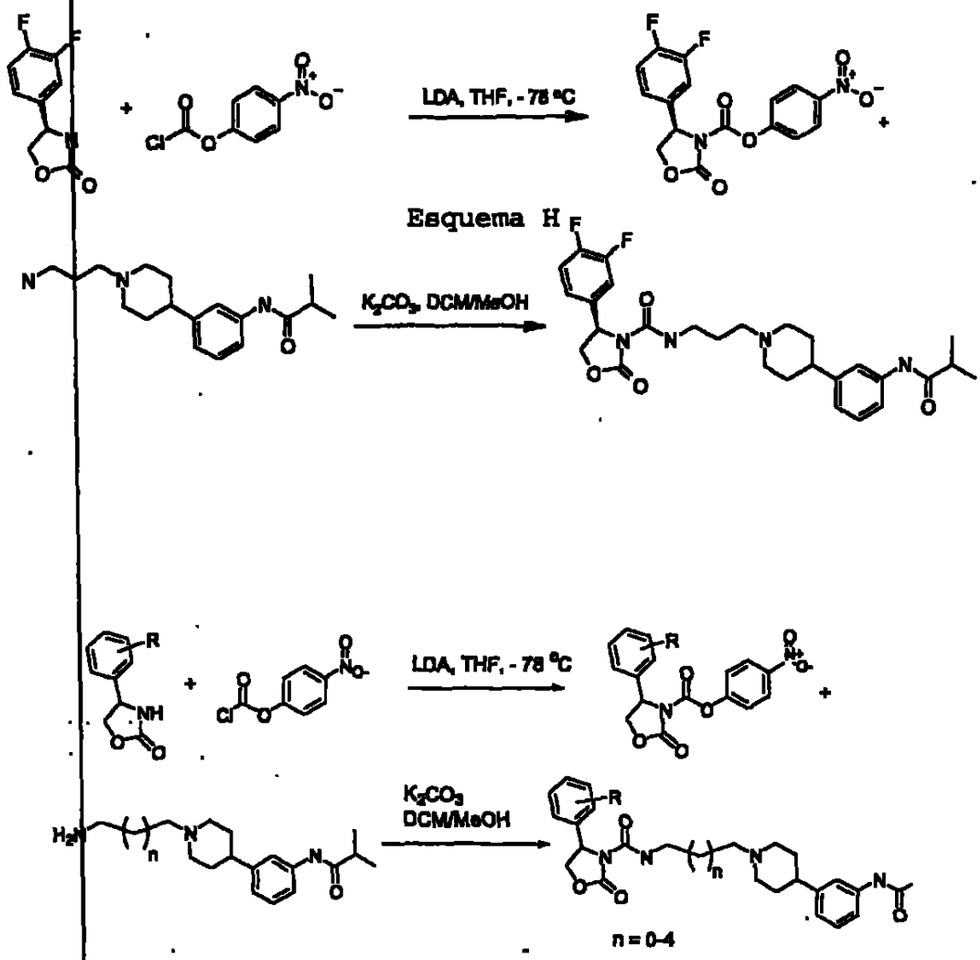
ESMS m/e: 332.2 $[M+H]^+$



ESMS m/e: 346.3 $[M+H]^+$

Procedimiento AF

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(4R)-4-(3,4-DIFLUOROFENIL)-N-(3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-2-OXO-1,3-OXAZOLIDIN-3-CARBOXAMIDA se sintetizó de acuerdo con el esquema H y procedimiento AF: A una solución de (4R)-4-(3,4-difluorfenil)-1,3-oxazolidin-2-ona (este compuesto y análogos se prepararon de acuerdo a J. Med. Chem 2000, 43, 2775) (0.300 mol, 60.0 mg) en THF (5.00 mL), se le adicionó LDA (2.0 M en

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THF, 0.390 mmol, 0.200 mL) a -78°C bajo argón. Después de 30 minutos a -78°C, se le adicionó a la mezcla de reacción una solución de cloroformato de 4-nitrofenilo (0.330 mmol, 51.2 mg) en THF (0.500 mL) a -78°C. Después de agitar durante 30 minutos a -78°C, se diluyó la mezcla de reacción con una solución de Na_2CO_3 (5.0 mL) y la capa acuosa se extrajo con CH_2Cl_2 (3 x 10 mL). Las capas orgánicas combinadas se lavaron con salmuera (10 mL), se secaron sobre Na_2SO_4 y se concentraron *in vacuo*. El residuo se purificó por medio de placas de TLC preparatorias (10:1 hexano:acetato de etilo) para producir (4R)-4-(3,4-difluorofenil)-2-oxo-1,3-oxazolidin-3-carboxilato de 4-nitrofenilo (51.5 mg, 54.0 %).

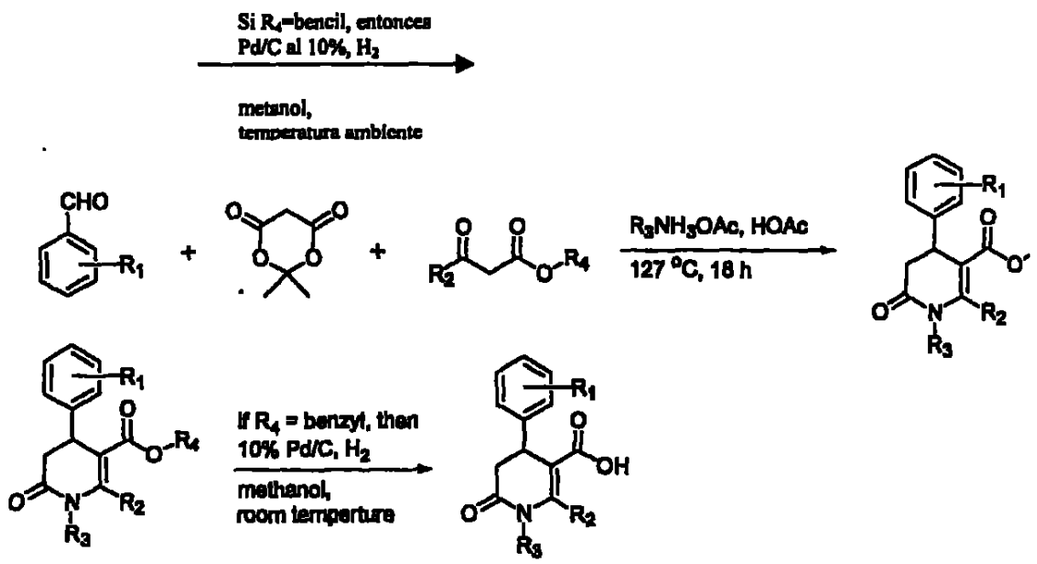
(4R)-4-(3,4-difluorofenil)-2-oxo-1,3-oxazolidin-3-carboxilato de 4-nitrofenilo (169 mg, 0.465 mmol), N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida (141 mg, 0.465 mmol), K_2CO_3 (0.193 g, 1.39 mmol), CH_2Cl_2 (10 mL), y metanol (0.1 mL), se combinaron en un matraz. La mezcla se agitó durante la noche a temperatura ambiente, el solvente se retiró *in vacuo*, y el residuo se purificó por cromatografía [2.5% de NH_3 (2.0 M en metanol) en CH_2Cl_2] para producir el producto deseado (26.1 mg, 10.6 %): RMN ^1H (400 MHz, $CDCl_3$) δ 8.08(t, 1H, J= 5.5 Hz), 7.45 (s, 2H), 7.38 (d, 1H, J= 8.6 Hz), 7.24-7.12 (m, 3H), 7.06 (m, 1H), 6.97 (d, 1H, J= 8.6 Hz), 5.40 (dd, 1H, J= 3.9-8.8 Hz), 4.71 (t, 1H,

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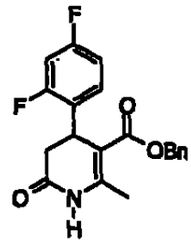
J= 8.8 Hz), 4.23 (dd, 1H, J= 4.4, 9.1 Hz), 3.32 (qt, 2H, J= 6.1 Hz), 2.99 (d, 2H, J= 11.0 Hz), 2.49 (qt, 2H, J= 7.0 Hz), 2.41 (t, 2H, J= 7.0 Hz), 1.99-1.97 (m, 2H), 1.82-1.68 (m, 6H), 1.23 (d, 6H, J= 7.3 Hz); Calc. Anál. para $C_{28}H_{34}F_2N4O_4$+HCl+0.185 $CHCl_3$: C, 57.6; H, 6.04; N, 9.54. Encontrado: C, 58.5; H, 6.8; N, 9.47; ESMS m/e : 529.1 $(M + H)^+$.

Procedimiento AG

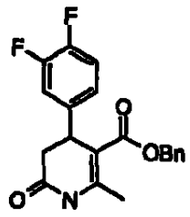
Esquema AR



Etapa 1: Una solución de cetoéster (10 mmol), ácido de Meldrum (10 mmol), aldehido (10 mmol) y un acetato de amonio (1 mmol) en HOAc (10 mL), se calentó a temperatura de reflujo durante 18 h.[1] La mezcla de reacción enfriada se vació sobre hielo (100 g). Los aceites precipitados se recolectaron y se secaron sobre presión reducida. Los análogos protegidos de bencil éster se solidificaron hasta trituración con una mezcla de éter/hexano.

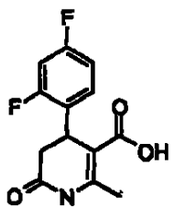


1.05 g, 29.0 %



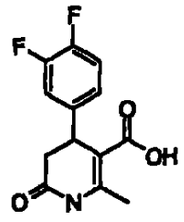
523 mg, 15.0%

[1]Etapa 2: una mezcla de bencil éster y Pd/C al 10% en metanol se hidrogenó utilizando el método del matraz a temperatura ambiente. La mezcla de reacción se monitoreo (TLC) hasta que se complementó, se filtro a través de Celite 545 y la torta de filtro de Celite se lavó con metanol (3 X 10 mL). Los extractos de metanol combinados se concentraron *in vacuo* para dar el ácido carboxílico deseado que fue utilizado en la siguiente etapa sin ninguna purificación adicional.



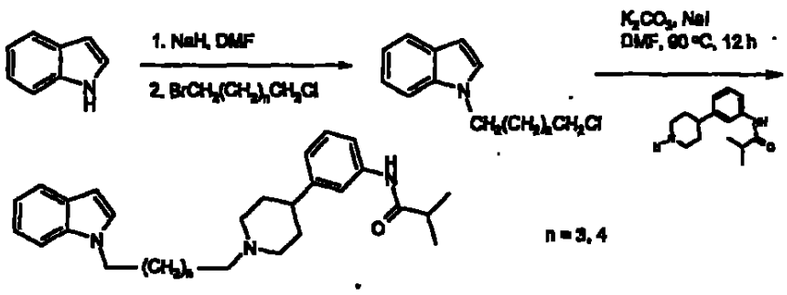
[1] MORALES, A.; OCHOA, E.; SUAREZ, M.; VERDECIA, Y.; GONZALEZ, L.; MARTIN,N.; QUINTEIRO, M.; SEOANE, C.; SOTO, J.L.; Heterocycl. Chem. [JHTCAD] 1996, 33 (1), 103-107.

ACIDO DE 4-(2,4-DIFLUOROFENIL)-2-METIL-6-OXO-1,4,5,6-TETRA-HIDRO-3-PIRIDINCARBOXILICO se sintetizó de acuerdo al procedimiento AG y el Esquema AR: RMN ^1H ($CDCl_3$, 400 MHz) δ 7.82 (s,1H), 7.00-6.72 (m, 3H), 4.51 (d, 1H, J= 8.4 Hz), 2.90 (dd, 1H, J= 8.4, 16.3 Hz), 2.68 (d, 1H, J= 16.3 Hz), 2.46 (s, 3H).



ACIDO 4-(3,4-DIFLUOROFENIL)-2-METIL-6-OXO-1,4,5,6-TETRA-HIDRO-3-PIRIDINCARBOXILICO se sintetizó de acuerdo al procedimiento AG y el Esquema R: RMN ^1H ($CDCl_3$, 300 MHz) δ 7.40-6.80 (m, 4H), 4.23 (d, 1H, J= 7.5 promedio Hz), 2.93 (dd, 1H, J= 16.8, 7.5 promedio Hz), 2.68 8d, 1H, J= 16.5 promedio Hz), 2.45 (s, 3H).

Procedimiento AH



1-(6-CLOROHEXIL)-1H-INDOL: A una mezcla de NaH (0.249g, 10.0 mmol) en DMF (5.00 mL) seadicionó a una solución de 1-H-indol (0.585 g, 5.00 mmol) en DMF (2.00 mL), a 0°C. La mezcla de reacción se agitó durante 30 minutos a 0°C y se calentó hasta temperatura ambiente. A la mezcla de reacción se adicionó 1-bromo-6-clorohexano (0.998 g, 5.00 mmol) gota a gota vía jeringa y la mezcla de reacción se agitó durante la noche. La mezcla de reacción se diluyó con EtOAc (30 mL), se lavó con agua (3 x 10 mL), salmuera (10 mL), se secó sobre $MgSO_4$, se concentró *in vacuo* y se purificó por cromatografía utilizando hexano:EtOAc (95.5:2.5) para dar el producto deseado (0.900 g, 76.0%): RMN ^1H (400 MHz, $CDCl_3$)

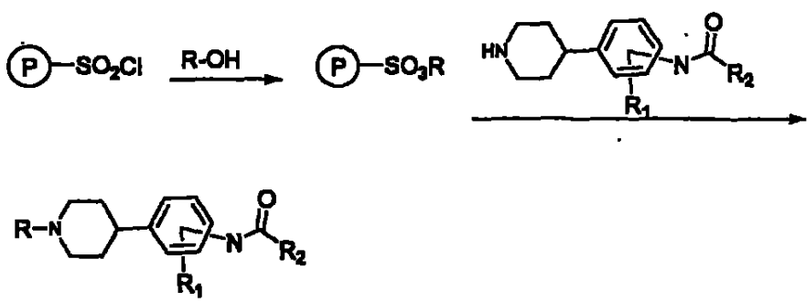
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7.76-7.54 (m, 1H), 7.47-6.96 (m, 4H), 6.60-6.34 (m, 1H), 4.13 (t, 2H, J= 6.8 Hz), 3.50 (t, 2H, J= 5.6 Hz), 1.98-1.79 (m, 2H), 1.79-1.64 (m, 2H), 1.54-1.17 (m, 4H).

N-(3-{1-[6-(1H-INDOL-1-IL)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Una mezcla de 1-(6-clorohexil)-1H-indol (23.6 mg, 0.100 mmol), 2-metil-N-[3-(4-piperidinil)fenil]-propanamida (24.6 mg, 0.100 mmol), K_2CO_3 (27.6 mg, 0.200 mmol), NaI (22.5 mg, 0.150 mmol) y DMF (1.00 mL), se calentó a 100°C durante 12 h. La mezcla de reacción se enfrió a temperatura ambiente y el material crudo se purificó por medio de TLC preparatoria utilizando 5% de NH_3 (2.0 M en metanol) en CH_2Cl_2 para dar el producto deseado como un sólido amarillo (40 mg, 90%): RMN ^1H (400 MHz, $CDCl_3$) δ 8.08-6.52 (m, 11H), 4.17 (t, 2H, J= 7.2 Hz), 3.26 (d, 2H, J= 11.6 Hz), 2.74-2.52 (m, 4H), 2.44-2.28 (m, 2H), 2.20-2.02 (m, 2H), 1.98-1.82 (m, 4H), 1.78-1.62 (m, 2H), 1.43-1.28 (m, 4H), 1.28 (d, 6H, J= 6.8 Hz); ESMS m/e : 446.5 $(M + H)^+$.

Procedimiento AI:

Esquema AU: Preparación de tert-Piperidinas utilizando Resina PS-SO2C1.

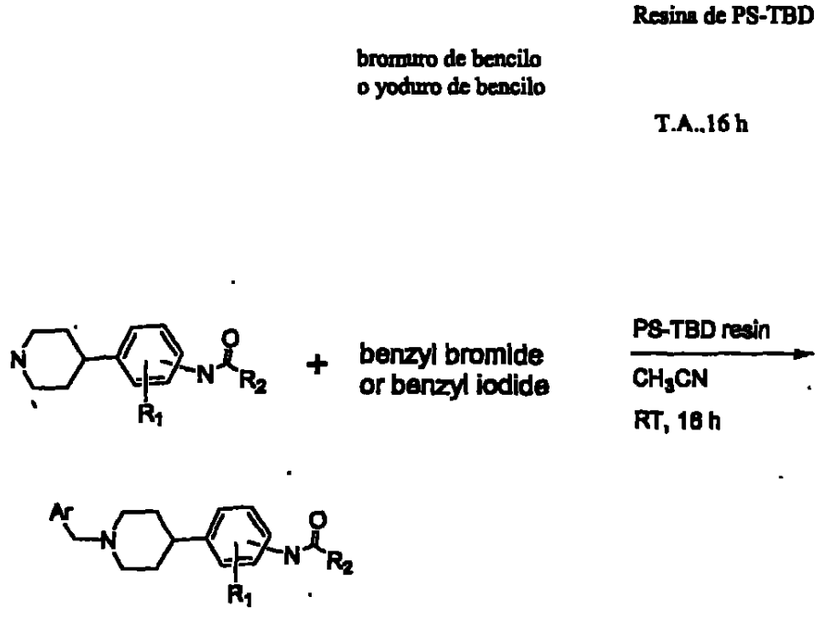


La biblioteca se construyó en "Bloques de Reactor" Robbins, placas de 48 pozos, de polipropileno. La resina PS-TSC1 (100 mg, 1.0 eq, vendido por Argonaut Technologies), se colocó en cada pozo de las placas de 48 pozos de "Bloques de Reactor". A cada pozo se adicionó 2-10 eq de un alcohol en diclorometano:piridina (1:1, 3.00 mL). La mezcla de reacción se agitó a temperatura ambiente durante 5 h y la resina se lavó con diclorometano (3 x 4.00 mL), DMF (5 x 4.00 mL), DMF/H_2O (3:1, 5 x 4.00 mL), THF (3 x 4.00 mL), diclorometano (3 x 4.00 mL), acetonitrilo (2 x 4.00 mL) y se secó bajo presión reducida. Una solución de una amina (0.0750 mmol, 0.500 eq) y N,N-diisopropietilamina (19.0 mg, 0.150 mmol, 1.00 eq) en acetonitrilo (3.00 mL), se adicionó al pozo que contiene la resina derivatizada y la mezcla se

hizó reaccionar a 70°C durante 16 h en el horno rotatorio de Robbins. Después del enfriamiento la resina de AP-isocianato (120 mg, 0.150 mmol, 1.00 eq) y THF (2.00 mL), se adicionaron a cada recipiente de reacción y se hicieron reaccionar a temperatura ambiente durante 3h adicionales. La solución se filtró en las placas de recepción Robbins® y se concentró *in vacuo* para dar las aminas terciarias deseadas, las cuales fueron analizadas vía LC-MS.

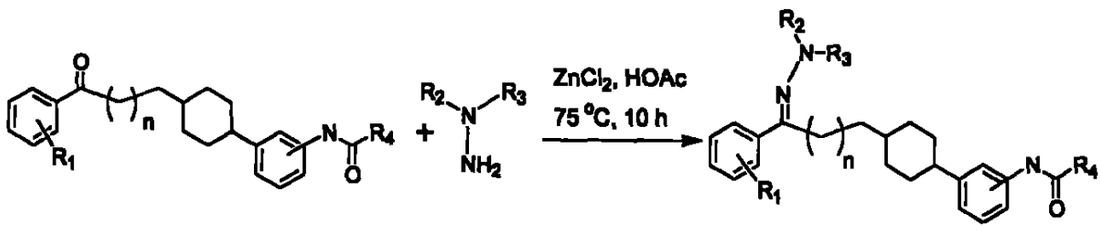
Procedimiento AJ:

Esquema AV: Preparación de tert-Piperidinas utilizando Piperidinas,



La biblioteca se construyó en Bloques de Reactor de placas de 48 pozos Robbins® de polipropileno. En el periodo de incubación inicial, cada pozo se cargó con resina de PS-TBD (de Argonaut Technologies, 200 mg, 0.280 mmol, 250 eq) y piperidina (0.120 mmol, 1.10 eq) en acetonitrilo (0.500 mL) y se agitó durante 1 h. Una solución de yoduro de bencilo o bromuro (0.110 mmol, 1.00 eq) en acetonitrilo (0.500 mL) se adicionó a cada pozo siguiente mediante acetonitrilo (1.00 mL) para hacer un volumen total de 2 mL y la mezcla se hizo girar en un horno rotatorio Robbins a temperatura ambiente durante 16 h. Después se adicionó resina de AP-isocianato (Argonaut technologies, 250 mg (0.430 mmol, 4.00 eq) a cada pozo y se hizo reaccionar además a temperatura ambiente durante otras 12 h. La mezcla se filtró y el filtrado se concentró *in vacuo* para obtener el producto deseado que se caracterizó vía LC-MS.

Esquema AX



Ejemplo 117

N-(3-{1-[3-(4-BROMOFENIL)-3-OXOPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Procedimiento K (KI) y Esquema E (K_2CO_3) utilizando 1-(4-bromofenil)-3-cloro-1-propanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e : 457.1 $(M + H)^+$.

Ejemplo 118

N-(3-{1-[3-(4-CLOROFENIL)-3-OXOPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Procedimiento K (KI) y Esquema E (K_2CO_3) utilizando 3-cloro-1-(4-clorofenil)-1-propanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e : 413.1 $(M + H)^+$.

Ejemplo 119

N-(3-{1-[3-(4-METOXIFENIL)-3-OXOPROPIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Procedimiento K (KI) y Esquema E (K_2CO_3) utilizando 3-cloro-1-(4-metoxifenil)-1-propanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e : $(M + H)^+$

Ejemplo 120

N-(3-{1-[3-(2,3-DIHIDRO-1H-INDEN-5-IL)-3-OXOPROPIL]-4-PI-PERIDINIL}FENIL)-2-METILPROPANAMIDA: Procedimiento K (KI) y Esquema E (K_2CO_3) utilizando 3-cloro-1-(2,3-dihidro-1H-inden-

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5-il)-1-propanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e 419.2 $(M + H)^+$.

Ejemplo 121

2-METIL-N-{3-{1-(3-OXO-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Procedimiento K (KI) y Esquema E (K_2CO_3) utilizando 3-cloro-1-fenil-1-propanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e 379.2 $(M + H)^+$.

Ejemplo 122

2-METIL-N-(3-{1-[3-(4-METILFENIL)-3-OXOPROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Procedimiento K (KI) y Esquema E (K_2CO_3) utilizando 3-cloro-1-(4-metilfenil)-1-propanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e : 393.2 $(M + H)^+$.

Ejemplo 123

N-(3-{1-[3-(4-FLUOROFENIL)-3-OXOPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Procedimiento K (KI) y Esquema E (K_2CO_3) utilizando 3-cloro-1-(4-fluorofenil)-1-propanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 397.2 $(M + H)^+$.

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Ejemplo 124

N-(3-{1-[3-(4-CLOFOFENIL)-3-HIDROXIPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento L y esquema AN utilizando N-(3-{1-[3-(4-clorofenil)-3-oxopropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 415.1 $(M + H)^+$.

Ejemplo 125

N(3-{1-[3-(4-CLOFOFENIL)-3-(3,4-DIFLUOROFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento L y esquema AN utilizando N-(3-{1-[3-(4-clorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 3,4-difluorofenol: ESMS m/e: 526.8 $(M + H)^+$.

Ejemplo 126

N-(3-{1-[3-(4-CLOROFENIL)-3-(2-METILFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento L y esquema AN utilizando N-(3-{1-[3-(4-clorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metilpropanamida y o-cresol: ESMS m/e: 504.4 $(M + H)^+$.

Ejemplo 127

N-(3-{1-[3-(4-FLUOROFENIL)-3-HIDROXIPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el

procedimiento L y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-oxopropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 399.2 $(M + H)^+$.

Ejemplo 128

N-(3-{1-[3-HIDROXI-3-(4-METOXIFENIL)PROPIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento L y esquema AN utilizando N-(3-{1-[3-(4-metoxifenil)-3-oxopropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 411.2 $(M + H)^+$.

Ejemplo 129

N-(3-{1-[3-(4-BROMOFENIL)-3-HIDROXIPROPIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento L y esquema AN utilizando N-(3-{1-[3-(4-bromofenil)-3-oxopropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 459.1 $(M + H)^+$.

Ejemplo130

N-(3-{1-[3-(4-CLOROFENIL)-3-(4-METOXIFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-clorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metilpropanamida y 4-metoxifenol: ESMS m/e: 520.8 $(M + H)^+$.

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Ejemplo 131

N-(3-{1-[3-(4-CLOROFENIL)-3-(4-FLUOROFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 4-clorofenol: ESMS m/e: 509.1 $(M + H)^+$.

Ejemplo 132

N-(3-{1-[3-(4-FLUOROFENIL)-3-(2,3,4,5,6-PENTAFLUOROFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metilpropanamida y 2,3,4,5,6-pentafluorofenol: ESMS m/e: 564.7 $(M + H)^+$.

Ejemplo 133

N-(3-{1-[3-(4-BROMOFENIL)-3-(2-METILFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-bromofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 2-metilfenol: ESMS m/e: 548.8 $(M + H)^+$.

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Ejemplo 134

N-(3-{1-[3-(3,4-DIFLUOROFENOXI)-3-(4-FLUOROFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 3,4-difluorofenol: ESMS m/e: 511.1 $(M + H)^+$.

Ejemplo 135

N-(3-{1-[3-(4-BROMOFENOXI)-3-(4-FLUOROFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 4-bromofenol: ESMS m/e: 553.0 $(M + H)^+$.

Ejemplo 136

N-(3-{1-[3-(3,4-DICLOROFENOXI)-3-(4-FLUOROFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 3,4-diclorofenol: ESMS m/e: 542.7 $(M + H)^+$.

Ejemplo 137

N-[3-(1-{3-(4-FLUOROFENIL)-3-[4-(TRIFLUOROMETIL)-FENOXI]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por

el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 4-(trifluorometil)fenol: ESMS m/e: 543.1 $(M + H)^+$.

Ejemplo 138

N-(3-{1-[3-(3-BROMOFENOXI)-3-(4-FLUOROFENIL)PROPIL}-4-PIPERIDINIL}FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 3-bromofenil: ESMS m/e: 552.7 $(M + H)^+$.

Ejemplo 139

N-(3-{1-[3-(4-FLUOROFENOXI)-3-(4-FLUOROFENIL)PROPIL]-4-PIPERIDINIL}FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 4-fluorofenol: ESMS m/e: 493.2 $(M + H)^+$.

Ejemplo 140

N-(3-{1-[3-(3-FLUOROFENOXI)-3-(4-FLUOROFENIL)PROPIL]-4-PIPERIDINIL}FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-

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fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 3-fluorofenol: ESMS m/e: 492.9 $(M + H)^+$.

Ejemplo 141

N-(3-{1-[3-(2,6-DICLOROFENOXI)-3-(4-FLUOROFENIL)PROPIL]-4-PIPERIDINIL}FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 2,6-diclorofenol: ESMS m/e: 543.0 $(M + H)^+$.

Ejemplo 142

N-(3-{1-[3-(2,5-DIFLUOROFENOXI)-3-(4-FLUOROFENIL)PROPIL]-4-PIPERIDINIL}FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 2,5-difluorofenol: ESMS m/e: 511.5 $(M + H)^+$.

Ejemplo 143

N-(3-{1-[3-(3-CLOROFENOXI)-3-(4-FLUOROFENIL)PROPIL]-4-PIPERIDINIL}FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 3-clorofenol: ESMS m/e: 509.1 $(M + H)^+$.

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Ejemplo 144

N-(3-{1-[3-(4-BROMOFENIL)-3-(3-METILFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-bromofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 3-metilfenol: ESMS m/e: 549.1 $(M + H)^+$.

Ejemplo 145

N-(3-{1-[3-([1,1'-BIFENIL]-4-ILOXI)-3-(4-BROMOFENIL)PROPIL]-4-PIPERIDINIL}FEMNIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-bromofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 4-fenilfenol: ESMS m/e: 611.2 $(M + H)^+$.

Ejemplo 146

N-(3-{1-[3-(2,4-DIFLUOROFENOXI)-3-(4-FLUOROFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 2,4-difluorofenol: ESMS m/e: 511.1 $(M + H)^+$.

Ejemplo 147

N-(3-{1-[3-(4-BROMOFENIL)-3-(3-METOXIFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-

bromofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 3-metoxifenol: ESMS m/e: 564.6 $(M + H)^+$.

Ejemplo 148

4-(1-(4-BROMOFENIL)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPOXI)BENZOATO DE METILO: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-bromofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 4-hidroxibenzoato de metilo: ESMS m/e: 593.0 $(M + H)^+$.

Ejemplo 149

N-(3-{1-[3-(4-BROMOFENIL)-3-(4-FENOXIFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-bromofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 4-metoxifenol: ESMS m/e: 626.6 $(M + H)^+$.

Ejemplo 150

N-(3-{1-[3-(4-BROMOFENIL)-3-(2-CLORO-4-METILFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-bromofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 2-cloro-4-metilfenol: ESMS m/e 583.0 $(M + H)^+$.

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Ejemplo 151

N-(3-{1-[3-(4-BROMOFENIL)-3-FENOXIPROPIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-bromofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metilpropanamida y fenol: ESMS m/e: 535.0 $(M + H)^+$.

Ejemplo 152

N-[3-(1-{3-(4-BROMOFENIL)-3-[4-(TRIFLUOROMETIL)FENOXI]-PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-bromofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 4-(trifluorometil)fenol: ESMS m/e: 603.1 $(M + H)^+$.

Ejemplo 153

N-(3-{1-[3-(2-ACETILFENOXI)-3-(4-BROMOFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-bromofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metilpropanamida y 2-acetilfenol: ESMS m/e: 576.6 $(M + H)^+$.

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Ejemplo 154

N-(3-{1-[3-(3-ACETILFENOXI)-3-(4-BROMOFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-bromofenil)-3-hidroxipropil}-4-piperidinil}fenil)-2-metilpropanamida y 3-acetilfenol: ESMS m/e: 576.9 $(M + H)^+$.

Ejemplo 155

N-(3-{1-[3-(3-ACETILFENOXI)-3-(2,3-DIHIDRO-1H-INDEN-5-IL)-PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(2,3-dihidro-1H-inden-5-il)-3-hidroxipropil]-4-piperidinil}-fenil)-2-metilpropanamida y 3-acetilfenol: ESMS m/e: 532.9 $(M + H)^+$.

Ejemplo 156

N-(3-{1-[3-(2,3-DIHIDRO-1H-IDEN-5-IL)-3-FENOXIPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(2,3-dihidro-1H-inden-5-il)-3-hidroxipropil]-4-piperidinil}fenil)-2-metilpropanamida y fenol: ESMS m/e: 479.2 $(M + H)^+$.

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Ejemplo 157

N-(3-{1-[3-(2-ACETILFENOXI)-3-(2,3-DIHIDRO-1H-INDEN-5-IL)-PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(2,3-dihidro-1H-inden-5-il)-3-hidroxipropil]-4-piperidinil}-fenil)-2-metilpropanamida 2-acetilfenol: ESMS m/e: 539.1 $(M + H)^+$.

Ejemplo 158

N-(3-{1-[3-(4-BROMOFENOXI)-3-(4-BROMOFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-bromofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 4-bromofenol: ESMS m/e: 612.7 $(M + H)^+$.

Ejemplo 159

N-(3-{1-[3-(4-BROMOFENIL)-3-(4-CLOROFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-bromofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 4-clorofenol: ESMS m/e: 568.7 $(M + H)^+$.

Ejemplo 160

N-(3-{1-[3-(4-BROMOFENIL)-3-(4-FLUOROFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-bromofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metilpropanamida y 4-fluorofenil: ESMS m/e: 552.8 $(M + H)^+$.

Ejemplo 161

N-(3-{1-[3-(2,3-DIHIDRO-1H-INDEN-5-IL)-3-(4-METILFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(2,3-dihidro-1H-inden-5-il)-3-hidroxipropil]-4-piperidinil}fenil)-2-metilpropanamida y 4-metoxifenol: ESMS m/e: 527.3 $(M + H)^+$.

Ejemplo 162

N-(3-{1-[3-(2,3-DIHIDRO-1H-INDEN-5-IL)-3-(4-FLUOROFENOXI)-PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(2,3-dihidro-1H-inden-5-il)-3-hidroxipropil]-4-piperidinil}-fenil)-2-metilpropanamida y 4-fluorofenol: ESMS m/e: 515.2 $(M + H)^+$.

Ejemplo 163

N-(3-{1-[3-(2,3-DIHIDRO-1H-INDEN-5-IL)-3-HIDROXIPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento L y esquema AN utilizando N-(3-{1-[3-(2,3-dihidro-1H-inden-5-il)-3-oxopropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 421.2 $(M + H)^+$.

Ejemplo 164

N-[3-(1-{3-(2,3-DIHIDRO-1H-INDEN-5-IL)-3-[4-(TRIFLUOROMETIL)FENOXI]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(2,3-dihidro-1H-inden-5-il)-3-hidroxipropil]-4-piperidinil}fenil)-2-metilpropanamida y 4-trifluorometilfenol: ESMS m/e: 565.0 $(M + H)^+$.

Ejemplo 165

N-(3-{1-[3-(4-BROMOFENOXI)-3-(2,3-DIHIDRO-1H-INDEN-5-IL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(2,3-dihidro-1H-inden-5-il)-3-hidroxipropil]-4-piperidinil}fenil)-2-metilpropanamida y 4-bromofenol: ESMS m/e: 577.4 $(M + H)^+$.

Ejemplo 166

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N-(3-{1-[3-(3-ACETILFENOXI)-3-(4-CLOROFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-clorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metilpropanamida y 3-acetilfenol: SMS m/e: 533.1 $(M + H)^+$.

Ejemplo 167

N-(3-{1-[3-(4-METOXIFENOXI)-3-(4-METOXIFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMID: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-hidroxi-3-(4-metoxifenil)propil]-3-piperidinil}fenil)-2-metilpropanamida y 4-metoxifenol: ESMS m/e: 517.4 $(M + H)^+$.

Ejemplo 168

N-(3-{1-[3-(4-CLOROFENOXI)-3-(2,3-DIHIDRO-1-INDEN-5-IL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(2,3-dihidro-1H-inden-5-il)-3-hidroxipropil]-4-piperidinil}fenil)-2-metilpropanamida y 4-clorofenol: ESMS m/e: 531.1 $(M + H)^+$.

Ejemplo 169

N-(3-{1-[3-(2-ACETILFENOXI)-3-(4-CLOROFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el

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procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-clorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 2-acetilfenol: ESMS m/e: 533.4 $(M + H)^+$.

Ejemplo 170

N-(3-{1-[3-(4-BROMOFENIL)-3-(4-METOXIFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-bromofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 4-metoxifenol: ESMS m/e: 565.0 $(M + H)^+$.

Ejemplo 171

N-(3-{1-[3-(4-BROMOFENOXI)-3-(4-CLOROFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-clorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 4-bromofenol: ESMS m/e: 568.8 $(M + H)^+$.

Ejemplo 172

N-(3-{1-[3-(4-CLOROFENOXI)-3-(4-CLOROFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-clorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 4-clorofenol:; ESMS m/e: 525.0 $(M + H)^+$.

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Ejemplo 173

N-(3-{1-[3-(4-METOXIFENIL)-3-FENOXIPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-hidroxi-3-(4-metoxifenil)propil]-4-piperidinil}fenil)-2-metilpropanamida y fenol: ESMS m/e: 487.4 $(M + H)^+$.

Ejemplo 174

N-(3-{1-[3-(4-FLUOROFENIL)-3-FENOXIPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metilpropanamida y fenol: ESMS m/e: 475.6 $(M + H)^+$.

Ejemplo 175

N-(3-{1-[3-(2-ACETILFENOXI)-3-(FLUOROFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metilpropanamida y 2-acetilfenol: ESMS m/e: 517.1 $(M + H)^+$.

Ejemplo 176

N-(3-{1-[3-(3-ACETILFENOXI)-3-(4-FLUOROFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el

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procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 3-acetilfenol: ESMS m/e: 516.9 $(M + H)^+$.

Ejemplo 177

N-(3-{1-[3-(4-FLUOROFENIL)-3-(4-METOXIFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-fluorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 4-metoxifenol: ESMS m/e: 505.2 $(M + H)^+$.

Ejemplo 178

N-(3-{1-[3-(4-CLOROFENOXI)-3-(4-METILFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-hidroxi-3-(4-metoxifenil)propil]-4-piperidinil}fenil)-2-metil-propanamida y 4-clorofenol: ESMS m/e: 521.5 $(M + H)^+$.

Ejemplo 179

N-(3-{1-[3-(3-ACETILFENOXI)-3-(4-METOXIFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-hidroxi-3-(4-metoxifenil)propil]-4-piperidinil}fenil)-2-metil-propanamida y 3-acetilfenol: ESMS m/e: 529.0 $(M + H)^+$.

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Ejemplo 180

N-(3-{1-[3-(4-CLOROFENIL)-3-FENOXIPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-clorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metilpropanamida y fenol. ESMS m/e: 490.9 $(M + H)^+$.

Ejemplo 181

N-(3-{1-[3-(4-BROMOFENOXI)-3-(4-METOXIFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-hidroxi-3-(4-metoxifenil)propil]-4-piperidinil}fenil)-2-metilpropanamida y 4-bromofenol: ESMS m/e: 564.9 $(M + H)^+$.

Ejemplo 182

N-[3-(1-{3-(4-METOXIFENIL)-3-[4-(TRIFLUOROMETIL)FENOXI]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-hidroxi-3-(4-metoxifenil)propil]-4-piperidinil}fenil)-2-metilpropanamida y 4-trifluorometilfenol: ESMS m/e: 555.1 $(M + H)^+$.

Ejemplo 183

N-(3-{1-[3-(4-CLOROFENIL)-3-(FLUOROFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-(4-clorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metil-propanamida y 4-fluorofenol: ESMS m/e: 509.1 $(M + H)^+$.

Ejemplo 184

N-(3-{1-[3-(4-FLUIOROFENOXI)-3-(4-METOXIFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-hidroxi-3-(4-metoxifenil)propil]-4-piperidinil{fenil)-2-metil-propanamida y 4-fluorofenol: ESMS m/e: 505.5 $(M + H)^+$.

Ejemplo 185

N-(3-{1-[3-(2-ACETILFENOXI)-3-(4-METOXIFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento A y esquema AN utilizando N-(3-{1-[3-hidroxi-3-(4-metoxifenil)propil]-4-piperidinil}fenil)-2-metil-propanamida y 2-acetilfenol: ESMS m/e: 529.2 $(M + H)^+$.

Ejemplo 186

N-[3-(1-{3-(4-CLOROFENIL)-3-[4-(TRIFLUOROMETIL)FENOXI]PROPIL}-4-PIPERIDINIL)FENIL]-2-METIL-PROPANAMIDA: Preparado por el procedimiento A y esquema AN

utilizando N-(3-{1-[3-(4-clorofenil)-3-hidroxipropil]-4-piperidinil}fenil)-2-metilpropanamida y 4-trifluorometilfenol: SMS m/e: 559.1 $(M + H)^+$.

Ejemplo 187

N-(3-{1-[(3S)-3-(3-ACETILFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}-4-METILFENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema AI utilizando 1-(3-{[(1s)-3-cloro-1-fenilpropil]oxi}fenil)etanona y 2-metil-N-[4-metil-3-(4-piperidinil)fenil]propanamida: ESMS m/e: 513.0 $(M + H)^+$.

2-(ISOPENTILOXI)-1-NAFTALDEHÍDO: Se combinan en un matraz 2-hidroxi-1-naftaldehído (1.72 g, 10.0 mmol) y THF (50 ml). Se agrega NaH (312 mg, 13 mmol) seguido por 1-bromo-3-metilbutano (1.20 mL, 10.0 mmol). La solución se agita a temperatura ambiente durante la noche, el solvente se elimina *in vacuo* y el residuo se purifica por cromatografía (5-10 % acetato de etilo/hexano): RMN ^1H (400 MHz, $CDCl_3$) 10.9 (s, 1H), 9.28 (dd, 1H, J = 0.7 Hz, 8.6 Hz), 8.02 (d, 1h, j = 9.1 Hz)), 7.75 (d, 1H, J = 8.1 Hz), 7.63-7.59 (m, 1H), 7.43-7.39 (m, 1H), 7.27 (d, 1H, J = 9.2 Hz), 4.25 (t, 2H, J = 6.5 Hz), 1.98-1.84 (m, 1H), 1.80-1.75 (m, 2H), 0.99 (d, 6H, J = 6.6 Hz); ESMS m/e: 242.8 $(M + H)^+$.

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Ejemplo 188

N-[3-(1-{[2-(ISOPENTILOXI)-1-NAFTIL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento F y el esquema R utilizando 2-(isopentiloxi)-1-naftaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 473.3 $(M + H)^+$.

2-PROPOXI-1-NAFTALDEHÍDO: Preparado de acuerdo al procedimiento para 2-(isopentiloxi)-1-naftaldehído utilizando 2-hidroxi-1-naftaldehído y 1-bromopropano.

Ejemplo 189

2-METIL-N-(3-{1-[(2-PROPOXI-1-NAFTIL)METIL]-4-PIPERIDINIL}-FENIL)PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 2-propoxi-1-naftaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 445.2 $(M + H)^+$.

4-{[(1-FORMIL-2-NAFTIL)OXI]METIL}BENZONITRILO: Preparado de acuerdo con el procedimiento para 2-(isopentiloxi)-1-naftaldehído utilizando 2-hidroxi-1-naftaldehído y 4-(bromometil)benzonitrilo.

Ejemplo 190

N-{3-[1-({2-[(4-CIANOBENCIL)OXI]-1-NAFTIL}METIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-{[(1-formil-2-naftil)oxi]metil}benzonitrilo y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 518.2 $(M + H)^+$.

[(1-FORMIL-2-NAFTIL)OXI]ACETONITRILO: Preparado de acuerdo con el procedimiento para 2-(isopentiloxi)-1-naftaldehído utilizando 2-hidroxi-1-naftaldehído y bromoacetonitrilo.

Ejemplo 191

N-[3-(1-{[2-(CIANOMETOXI)-1-NAFTIL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando [(1-formil-2-naftil)oxi]acetonitrilo y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 442.2 $(M + H)^+$.

2-[(3-CLOROBENCIL)OXI]-1-NAFTALDEHÍDO: Preparado de acuerdo con el procedimiento para 2-(isopentiloxi)-1-naftaldehído utilizando 2-hidroxi-1-naftaldehído y 1-(bromometil)-3-clorobenceno.

Ejemplo 192

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N-{3-[1-({2-[(3-CLOROBENCIL)OXI]-1-NAFTIL}METIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 2-[(3-clorobencil)oxi]-1-naftaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 527.2 $(M + H)^+$.

Ejemplo 193

N-(3-{1-[4-(4-CLOROFENOXI)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-(4-clorofenoxi)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: RMN ^1H (400 MHz, $CDCl_3$) 7.50 (s, 1H), 7.34-7.19 (m, 7H)(, 6.98-6.87 (m, 5H), 3.50 (s, 2H), 2.98 (d, 2H, J = 11.8 Hz), 2.58-2.44 (m, 2H), 2.10-1.98 m(m, 2H), 1.83-1.76 (m, 4H), 1.24 (d, 6H, J = 6.8 Hz); ESMS m/e: 463.2 $(M + H)^+$.

Ejemplo 194

N-(3-{1-[4-(3,4-DIFLUOROFENOXI)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-(3,4-difluorofenoxi)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 465.2 $(M + H)^+$.

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4-(ISOPENTILOXI)-1-NAFTALDEHÍDO: Preparado de acuerdo con el procedimiento para 2-(isopentiloxi)-1-naftaldehído utilizando 4-hidroxi-1-naftaldehído y 1-bromo-3-metilbutano.

Ejemplo 195

N-[3-(1-{[4-(ISOPENTILOXI)-1-NAFTIL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-(isopentiloxi)-1-naftaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 473.3 $(M + H)^+$.

Ejemplo 196

N-(3-{1-[4-METOXIFENOXI)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-(4-metoxifenoxi)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 459.2 $(M + H)^+$.

4-PROPOXI-1-NAFTALEDEHÍDO: Preparado de acuerdo con el procedimiento para 2-(isopentiloxi)-1-naftaldehído utilizando 4-hidroxi-1-naftaldehído y 1-bromopropano.

Ejemplo 197

2-METIL-N-(3-{1-[(4-PROPOXI-1-NAFTIL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento F y

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esquema R utilizando 4-propoxi-1-naftaldehído y 2-metil-N-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 445.2 $(M + H)^+$.

Ejemplo 198

N-(3-{1-[4-(3,4-DICLOFOFENOXI)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-(3,4-diclorofenoxi)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 497.1 $(M + H)^+$.

Ejemplo 199

N-(3-{1-[4-(DIFENILAMINO)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-(difenilamino)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 504.2 $(M + H)^+$.

Ejemplo 200

N-{3-[1-({2,5-DIMETIL-1-[3-(TRIFLUOROMETIL)FENIL]-1H-PIRROL-3-IL}METIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 2,5-dimetil-1-[3-(trifluorometil)fenil]-1H-pirrol-3-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 498.2 $(M + H)^+$.

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Ejemplo 201

2-METIL-N-(3-{1-[1-(2-FENIL-1,3-TIAZOL-4-IL)ETIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA : Preparado por el procedimiento F y esquema R utilizando 1-(2-fenil-1,3-tiazol-4-il)etanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 434.2 $(M + H)^+$.

Ejemplo 202

N-(3-{1-[(5-CLORO-3-METIL-1-FENIL-1H-PIRAZOL-4-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 5-cloro-3-metil-1-fenil-1H-pirazol-4-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 451.2 $(M + H)^+$.

Ejemplo 203

2-METIL-N-(3-{1-[(2-FENIL-1H-IMIDAZOL-4-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 2-fenil-1H-imidazol-4-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 403.2 $(M + H)^+$.

Ejemplo 204

N-[3-(1-{[4-BROMO-1-(4-CLOROBENCIL)-1H-PIRAZOL-5-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA; Preparado por el

procedimiento F y esquema R utilizando 4-bromo-1-(4-clorobencil)-1H-pirazol-5-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 529.1 $(M + H)^+$.

Ejemplo 205

2-METIL-N-{3-[1-(3-FENOXIBENCIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 3-fenoxibenzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 429.2 $(M + H)^+$.

Ejemplo 206

N-(3-{1-[3-(3,4-DICLOROFENOXI)BENCIL]-4-PIPERIDINIL}FENIL)-2-METOXIPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 3-(3,4-diclorofenoxi)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 497.15 $(M + H)^+$.

Ejemplo 207

N-(3-{1-[3-(3,5-DICLOROFENOXI)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 3-(3,5-diclorofenoxi)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 497.2 $(M + H)^+$.

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Ejemplo 208

2-METIL-N-(3-{1-[3-(4-METILFENOXI)BENCIL]-4-PIPERIDINIL}-FENIL)PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 3-(4-metilfenoxi)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 443.2 $(M + H)^+$.

Ejemplo 209

2-METIL-N-[3-(1-{3-[3-(TRIFLUOROMETIL)FENOXI]BENCIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 3-[3-(trifluorometil)fenoxi]-benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 497.2 $(M + H)^+$.

Ejemplo 210

N-(3-{1-[3-(4-CLOROFENOXI)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 3-(4-clorofenoxi)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 463.2 $(M + H)^+$.

Ejemplo 211

N-(3-{1-[3-(DIMETILAMINO)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema

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R utilizando 3-(dimetilamino)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 380.2 $(M + H)^+$.

Ejemplo 212

N-(3-{1-[3-(4-METOXIFENOXI)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 3-(4-metoxifenoxi)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 459.2 $(M + H)^+$.

Ejemplo 213

N-(3-{1-[3-(4-TERBUTILFENOXI)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 3-(4-terbutilfenoxi)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 485.3 $(M + H)^+$.

Ejemplo 214

2-METIL-N-(3-{1-[3-NITRO-4-(1-PIPERIDINIL)BENCIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 3-nitro-4-(1-piperidinil)benzaldehído y 2-metil-N-[3-(4-piperidinil)-fenil]propanamida: ESMS m/e: 465.2 $(M + H)^+$.

Ejemplo 215

(N-(3-{1-[(3,4-DIMETILTIENO[2,3-B]TIEN-2-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 3,4-dimetiltieno[2,3-b]tiofen-2-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 427.1 $(M + H)^+$.

Ejemplo 216

2-METIL-N-{3-[1-({3-[4-TRIFLUOROMETIL)FENIL]-1H-PIRAZOL-4-IL}METIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 3-[4-(trifluorometil)fenil]-1H-pirazol-4-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 471.1 $(M + H)^+$.

Ejemplo 217

2-METIL-N-(3-{1-[4-(1H-1,2,4-TRIAZOL-1-IL)BENCIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-(1H-1,2,4-triazol-1-il)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 404.1 $(M + H)^+$.

Ejemplo 218

2-METIL-N-(3-{1-[(5-METIL-1-FENIL-1H-PIRAZOL-4-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el

procedimiento F y esquema R utilizando 5-metil-1-fenil-1H-pirazol-4-carbaldehído y 2-metil-N-[3-(4-piperidinol)fenil]propanamida: ESMS m/e: 417.1 $(M + H)^+$.

Ejemplo 219

2-METIL-N-(3-{1-[4-(4-MORFOLINIL)-3-NITROBENCIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-(4-morfolinil)-3-nitrobenzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 467.1 $(M + H)^+$.

Ejemplo 220

N-{3-[1-({5-[2-CLORO-4-(TRIFLUOROMETIL)FENIL]-2-FURIL}METIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 5-[2-cloro-4-(trifluorometil)fenil]-2-furaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 505.0 $(m + h)^+$.

Ejemplo 221

4-({4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}METIL)-2,5-DIMETIL-1-FENIL-1H-PIRROL-3-CARBOXILATO DE ETILO: Preparado por el procedimiento F y esquema R utilizando 4-formil-2,5-dimetil-1-fenil-1H-pirrol-3-carboxilato de etilo y 2-metil-

N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 502.2 (M + H)$^+$.

Ejemplo 222

5-(4-CLOROFENIL)-2-({4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}METIL)-3-FUROATO DE ETILO: Preparado por el procedimiento F y esquema R utilizando 5-(4-clorofenil)-2-formil-3-furoato de etilo y 2-metil-N-[3-(4-piperidinil)-fenil]propanamida: ESMS m/e: 509.0 (M + H)$^+$.

Ejemplo 223

N-{3-[1-(2,3-DIHIDRO-1,4-BENZODIOXI-6-ILMETIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 2,3-dihidro-benzodioxin-6-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 395.1 (M + H)$^+$.

Ejemplo 224

2-METIL-N-(3-{1-[(6-FENOXI-3-PIPERIDINIL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 6-fenoxinicotinaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 430.1 (M + H)$^+$.

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Ejemplo 225

2-METIL-N-[3-(1-{[5-(2-PIRIDINIL)-2-TIENIL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 5-(2-piridinil)-2-tiofencarbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 420.1 $(M + H)^+$.

Ejemplo 226

2-METIL-N-{3-[1-({5-[1-METIL-3-(TRIFLUOROMETIL)-1H-PIRAZOL-5-IL]-2-TIENIL}METIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 5-[1-metil-3-(trifluorometil)-1H-pirazol-5-il]-2-tiofencarbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 491.0 $(M + H)^+$.

Ejemplo 227

2-METIL-N-[3-(1-{[1-(FENILSULFONIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 1-(fenilsulfonil)-1H-indol-3-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 516.1 $(M + H)^+$.

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Ejemplo 228

N-(3-{1-[(1,5-DIMETIL-3-OXO-2-FENIL-2,3-DIHIDRO-1H-PIRAZOL-4-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA:

Preparado por el procedimiento F y esquema R utilizando 1,5-dimetil-3-oxo-2-fenil-2,3-dihidro-1H-pirazol-4-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 447.2 $(M + H)^+$.

Ejemplo 229

N-(3-{1-[4-(4-TERBUTIL-1,3-TIAZOL-2-IL)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-(4-terbutil-1,3-tiazol-2-il)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida.

Ejemplo 230

N-{3-[1-(2,3-DIHIDRO-1-BENZOFURAN-5-ILMETIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 2,3-dihidro-1-benzofuran-5-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 379.1 $(M + H)^+$.

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Ejemplo 231

2-METIL-N-(3-{1-[(4-METIL-2-FENIL-5-PIRIMIDINIL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-metil-2-fenil-5-pirimidincarbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 429.2 $(M + H)^+$.

Ejemplo 232

N-{3-[1-(2,1,3-BENZOTIADIAZOL-5-ILMETIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 2,1,3-benzotiadiazol-5-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 395.1 $(M + H)^+$.

Ejemplo 233

2-METIL-N-(3-{1-[(5-FENIL-2-TIENIL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 5-fenil-2-tiofencarbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 419.1 $(M + H)^+$.

Ejemplo 234

N-{3-[1-(3,4-DIHIDRO-2H-1,5-BENZODIOXEPIN-7-ILMETIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el

procedimiento F y esquema R utilizando 3,4-dihidro-2H-1,5-benzodioxepin-7-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 409.2 $(M + H)^+$.

Ejemplo 235

2.METIL-N-[3-(1-{[3-(2-TIENIL)-1H-PIRAZOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 3-(2-tienil)-1H-pirazol-4-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 409.1 $(M + H)^+$.

Ejemplo 236

N-{3-[1-([1,1'-BITIENIL-4-ILMETIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA_ Preparado por el procedimiento F y esquema R utilizando 2,2'-bitiofen-5-carboxaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 425.0 $(M + H)^+$.

Ejemplo 237

N-(3-{1-[(2,2-DIMETIL-3,4-DIHIDRO-2H-CROMEN-6-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 2,2-dimetil-6-cromancarbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 421.2 $(M + H)^+$.

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Ejemplo 238

2-METIL-N-{3-[1-({5-[1-METIL-5-(TRIFLUOROMETIL)-1H-PIRAZOL-3-IL]-2-TIENIL}METIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 5-[1-metil-5-(trifluorometil)-1H-pirazol-3-il]-2-tiofencarbaldehído y 2-metil-n-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 491.1 $(M + H)^+$.

Ejemplo 239

2-METIL-N-(3-{1-[(2-FENIL-1,3-TIAZOL-4-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 2-fenil-1,3-tiazol-4-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 420.0 $(M + H)^+$.

Ejemplo 240

2-METIL-N-(3-{1-[(3-FENOXI-2-TIENIL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 3-fenoxi-2-tiofencarbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 435.0 $(M + H)^+$.

Ejemplo 241

N-{3-[1-({-[(4-CLOROFENIL)SULFANIL]-3-TIENIL}METIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 2-[(4-clorofenil)sulfanil]-3-tiofencarbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 485.0 $(M + H)^+$.

Ejemplo 242

N-[3-(1-{[1-(4-CLOROFENIL)-1H-PIRROL-2-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 1-(4-clorofenil)-1H-pirrol-2-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 436.0 $(M + H)^+$.

Ejemplo 243

2-METIL-N-{3-[1-({5-[2-(TRIFLUOROMETOXI)FENIL]-2-FURIL}METIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 5-[2-(trifluorometoxi)fenil]-2-furaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 487.1 $(M + H)^+$.

Ejemplo 244

2-METIL-N-(3-{1-[2-(4-MORFOLINIL)BENCIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el

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procedimiento F y esquema R utilizando 2-(4-morfolinil)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 422.2 $(M + H)^+$.

Ejemplo 245

N-[3-(1-{[3-(4-METOXIFENIL)-1H-PIRAZOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 3-(4-metoxifenil)-1H-pirazol-4-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 4343.1 $(M + H)^+$.

Ejemplo 246

2-METIL-N-(3-{1-[4-(1H-PIRAZOL-1-IL)BENCIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-(1H-pirazol-1-il)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 402.8 $(M + H)^+$.

Ejemplo 247

2-METIL-N-{3-[1-(4-QUINOLINILMETIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-quinolincarbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 388.1 $(M + H)^+$.

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Ejemplo 248

2-METIL-N-(3-{1-[4-(4-MORFOLINIL)BENCIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-(4-morfolinil)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 422.5 $(M + H)^+$.

Ejemplo 249

2-METIL-N-(3-{1-[4-(2-TIENIL)BENCIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-(2-tienil)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 419.1 $(M + H)^+$.

Ejemplo 250

2-METIL-N-(3-{1-[(2-METIL-5-FENIL-3-FURIL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 2-metil-5-fenil-3-furaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 417.2 $(M + H)^+$.

Ejemplo 251

N-(3-{1-[3-(CICLOPENTILOXI)-4-METOXIBENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 3-(ciclopentiloxi)-4-metilbenzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 451.1 $(M + H)^+$.

Ejemplo 252

2-METIL-N-{3-[1-({5-[4-(TRIFLUOROMETOXI)FENIL]-2-FURIL}METIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 5-[4-(trifluorometoxi)fenil]-2-furaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 487.1 $(M + H)^+$.

Ejemplo 253

N-{3-[1-(1-BENZOTIEN-2-ILMETIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 1-benzotiofen-2-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 393.2 $(M + H)^+$.

Ejemplo 254

2-METIL-N-{3-[1-({5-[3-(TRIFLUOROMETOXI)FENIL]-2-FURIL}METIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 5-[3-

(trifluorometoxi)fenil]-2-furaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 487.2 $(M + H)^+$.

Ejemplo 255

2-METIL-N-{3-[1-(2-QUINOLINILMETIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 2-quinolincarbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 388.1 $(M + H)^+$.

Ejemplo 256

N-(3-{1-[4-(1H-IMIDAZOL-1-IL)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-(1H-imidazol-1-il)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 403.2 $(M + H)^+$.

Ejemplo 257

N-{3-[1-(9H-FLUOREN-2-ILMETIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 9H-fluoren-2-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 425.1 $(M + H)^+$.

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Ejemplo 258

3-[5-({4-[3-ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}METIL)-2-FURIL]-2-TIOFENCARBOXILATO DE METILO: Preparado por el procedimiento F y esquema R utilizando 3-(5-formil-2-furil)-2-tiofencarboxilato de metilo y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 467.1 $(M + H)^+$.

Ejemplo 259

2-METIL-N-{3-[1-(4-FENOXIBENCIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-fenoxibenzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida; EMS m/e: 429.2 $(M + H)^+$.

Ejemplo 260

N-{3-[1-([1,1'-BIFENIL]-4-ILMETIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando [1,1'-bifenil]-4-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 413.2 $(M + H)^+$.

Ejemplo 261

N-(3-{1-[4-(DIBUTILAMINO)BENCIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento F y esquema

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R utilizando 4-(dibutilamino)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 464.6 $(M + H)^+$.

Ejemplo 262

2-METIL-N-[3-(1-{4-[(4-METILFENIL)SULFANIL]-3-NITROBENCIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento F y esquema R utilizando 4-[(4-metilfenil)sulfanil]-3-nitrobenzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 504.2 $(M + H)^+$.

Ejemplo 263

2-METIL-N-(3-{1-[4-(1,2,3-TIADIAZOL-4-IL)BENCIL]-4-PIPERIDINIL}FENIL)PROPANAMID: Preparado por el procedimiento F y esquema R utilizando 4-(1,2,3-tiadiazol-4-il)benzaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 421.1 $(M + H)^+$.

1-(3-{[1S)-3-CLORO-1-FENILPROPIL]OXI}FENIL]ETANONA: (1R)-3-cloro-1-fenil-1-propanol (1.000 g, 5.86 mmoles), 1-(3-hidroxifenil)etanona (0.797 g, 5.86 mmoles), trifenilfosfina (1.54 g, 5.86 mmoles) y dietilazodicarboxilato (1.53 g, 8.79 mmoles) se combinan en un matraz,

RMN ^1H (400 MHz, $CDCl_3$) 7.49-7.46 (m, 2H), 7.40-7.26 (m, 6H), 7.07-7.04 (m, 1H), 5.46-5.43 (dd, 1H, J = 4.4 Hz, 8.8

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Hz), 3.84-3.78 (m, 1H), 3.64-3.59 (m, 1H), 2.52 (s, 3H), 2.51-2.46 (m, 1H), 2.29-2.22 (m, 1H).

4-(3,4-DIFLUOROFENOXI)BENZALDEHÍDO:

RMN ^1H (400 MHz, $CDCl_3$) 9.95 (s, 1H), 7.88 (dd, 2H), J = 0.8 Hz, 8.8 Hz), 7.24-7.17 (m, 1H), 7.07 (d, 2H, J = 8.8 Hz), 6.97-6.92 (m, 1H), 6.86-6.82 (m, 1H); ESMS m/e: 235.0 $(M + H)^+$.

4-(4,4,5,5-TETRAMETIL-1,3,2-DIOXABOROLAN-2-IL)-3,6-DIHIDRO-1(2H)-PIRIDICARBOXILATO DE TERBUTILO

RMN ^1H (400 MHz, $CDCl_3$) 6.44 (s amplio, 1H), 3.93 (s amplio, 2H), 3.42 (s amplio, 2H), 2.21 (s amplio, 2H), 1.45 (s, 9H), 1.25 (s, 12H); ESMS m/e: 310.4 $(M + H)^+$.

N-(6-BROMO-2-PIRIDINIL)-2-METILPROPANAMIDA: Preparado por el procedimiento Q1 utilizando cloruro de 2-metilpropanoilo y 6-bromo-2-piridinamida: ESMS m/e: 242.8 $(M + H)^+$.

4-[[6-(ISOBUTIRILAMINO)-2-PIRIDINIL]-3,6-DIHIDRO-1(2H)-PIRIDINCARBOXILATO DE TERBUTILO: Preparado por el procedimiento W y esquema AF utilizando N-(6-bromo-2-piridinil)-2-metilpropanamida y 4-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-3,6-dihidro-1(2H)-piridincarboxilato de terbutilo: ESMS m/e: 245.8 $(M - 100)^+$.

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2-METIL-N-{6-(4-PIPERIDINIL)-2-PIRIDINIL)PROPANAMIDA: Preparado por los procedimientos X e Y, esquema AG y AH, respectivamente utilizando 4-[6-(isobutirilamino)-2-piridinil]-3,6-dihidro-1(2H)-piridinilcarboxilato de terbutilo: ESMS m/e: 248.1 $(M + H)^+$.

Ejemplo 264

N-(6-{1-[4-(3,4-DIMETILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-2-PIRIDINIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema AI utilizando 4-cloro-1-(3,4-dimetilfenil)-1-butanona y 2-metil-N-[6-(4-piperidinil)-1-butanona y 2-metil-N-[6-(4-piperidinil)-2-piridinil]propanamida: ESMS m/e: 422.1 $(M + H)^+$.

Ejemplo 265

N-(6-{1-[4,4-BIS(4-FLUOROFENIL)BUTIL]-4-PIPERIDINIL}-2-PIRIDINIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema AI utilizando 1-[4-cloro-1-(4-fluorofenil)butil]-4-fluorobenceno y 2-metil-N-[6-(4-piperidinil)-2-piridinil]propanamida: ESMS m/e: 492.2 $(M + H)^+$.

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Ejemplo 266

N-(6-{1-[4-3,4-DIFLUOROFENOXI)BENCIL]-4-PIPERIDINIL}-2-PIRIDINIL)-2-METILPROPANAMIDA: Preparado por el procedimiento AA y esquema AJ utilizando 4-(3,4-difluorofenoxi)benzaldehído y 2-metil-N-[6-(4-piperidinil)-2-piridinil}propanamida: ESMS m/e: 466.0 $(M + H)^+$.

N-(3-BROMO-4-METILFENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento Q1 utilizando cloruro de 2-metilpropanoilo y 3-bromo-4-metilanilina: ESMS m/e: 255.9 $(M + H)^+$.

4-[5-(ISOBUTIRILAMINO)-2-METILFENIL]-3,6-DIHIDRO-1(2H)-PIRIDINCARBOXILATO DE TERBUTILO: Preparado por el procedimiento W y esquema AF utilizando N-(3-bromo-4-metilfenil)-2-metilpropanamida y 4-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-3,6-dihidro-1(2H)-piridincarboxilato de terbutilo: ESMS m/e: 259.1 $(M - 100)^+$.

2-METIL-N-[4-METIL-3-(4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por los procedimientos X E y, esquemas AG y AH, respectivamente utilizando 4-[5-(isobutirilamino)-2-metilfenil]-3,6-dihidro-1(2H)-piridincarboxilato de terbutilo: ESMS m/e: 261.0 $(M + H)^+$.

Ejemplo 267

N-(3-{1-[4-(3,4-DIFLUOROFENOXI)BENCIL]-4-PIPERIDINIL}-4-METILFENIL)-2-METILPROPANAMIDA: Preparado por el

procedimiento AA y esquema AJ utilizando 4-(3,4-difluorofenoxi)benzaldehído y utilizando 2-metil-N-[4-metil-3-(4-piperidinil)fenil]propanamida: ESMS m/e: 479.1 $(M + H)^+$.

N-(5-BROMO-2-METILFENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento Q1 utilizando cloruro de 2-metilpropanoilo y 5-bromo-2-metilanilina: ESMS m/e: 255.9 $(M + H)^+$.

4-(3-(ISOBUTIRILAMINO)-4-METILFENIL]-3,6-DIHIDRO-1(2H)-PIRIDINCARBOXILATO DE TERBUTILO: Preparado por el procedimiento W y esquema AF utilizando N-(5-bromo-2-metilfenil)-2-metilpropanamida y 4-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-3,6-dihidro-1(2H)-piridincarboxilato de terbutilo: ESMS m/e: 259.1 $(M - 100)^+$.

2-METIL-N-[2-METIL-5-(4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por los procedimientos X e Y, esquemas AG y AH, respectivamente utilizando 4-[3-(isobutirilamino)-4-metilfenil]-3,6-dihidro-1(2H)-piridincarboxilato de terbutilo: ESMS m/e: 261.0 $(M + H)^+$.

Ejemplo 268

N-(5-{1-[(9-ETIL-9H-CARBAZOL-3-IL)METIL]-4-PIPERIDINIL}-2-METILFENIL)-2-METILPROPANAMIDA: Preparado por el

procedimiento AA y esquema AJ utilizando 9-etil-9H-carbazol-3-carbaldehído y 2-metil-N-[2-metil-5-(4-piperidinil)fenil]propanamida: ESMS m/e: 468.1 $(M + H)^+$.

Ejemplo 269

N-(5-{1-[4-(3,4-DIFLUOROFENOXI)BENCIL]-4-PIPERIDINIL}-2-METILFENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento AA y esquema AJ utilizando 4-(3,4-difluorofenoxi)benzaldehído y 2-metil-N-[2-metil-5-(4-piperidinil)fenil]propanamida: ESMS m/e: 479.2 $(M + H)^+$.

Ejemplo 270

N-(3-{1-[(9-ETIL-9H-CARBAZOL-3-IL)METIL]-4-PIPERIDINIOL}-4-METILFENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento AA y esquema AJ utilizando 9-etil-9H-carbazol-3-carbaldehído y 2-metil-N-[4-metil-3-(4-piperidinil)fenil]propanamida: ESMS m/e: 468.1 $(M + H)^+$.

Ejemplo 271

2-METIL-N-[2-METIL-5-(4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento G y esquema AI utilizando 1-[4-cloro-1-(4-fluorofenil)butil]-4-fluorobenceno y 2-metil-N-[2-metil-5-(4-piperidinil)fenil]propanamida: ESMS m/e: 505.1 $(M + H)^+$.

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Ejemplo 272

N-(3-{1-[(3S)-3-(3-ACETILFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}-4-METILFENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema AI utilizando 1-(3-{[(1S)-3-cloro-1-fenilpropil]oxi}fenil)etanona y 2-metil-N-[4-metil-3-(4-piperidinil)fenil]propanamida: ESMS m/e: 513.0 $(M + H)^+$.

Ejemplo 273

N-(5-{1-[(3S)-3-(3-ACETILFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}-2-METILFENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema AI utilizando 1-(3-{[(1S)-3-cloro-1-fenilpropil]oxi}fenil)etanona y 2-metil-N-[2-metil-5-(4-piperidinil)fenil]propanamida: ESMS m/e: 512.9 $(M + H)^+$.

N-(2-YODOFENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento Q1 utilizando cloruro de 2-metilpropanoilo y 2-yodoanilina: ESMS m/e: 289.9 $(M + H)^+$.

4-[2-(ISOBUTIRILAMINO)FENIL]-3,6-DIHIDRO-1(2H)-PIRIDINCARBOXILATO DE TERBUTILO: Preparado por el procedimiento W y esquema AF utilizando N-(2-yodofenil)-2-

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metilpropanamida y 4-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-3,6-dihidro-1(2H)-piridincarboxilato de terbutilo: ESMS m/e: 245.1 $(M - 100)^+$.

2-METIL-N-[2-(4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por los procedimientos X e Y, esquema AG y AH, respectivamente utilizando 4-[2-(isobutirilamino)fenil]-3,6-dihidro-1(2H)-piridincarboxilato de terbutilo: ESMS m/e: 247.1 $(M + H)^+$.

Ejemplo 274

N-(2-{1-[(9-ETIL-9H-CARBAZOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento AA y esquema AJ utilizando 9-etil-9H-carbazol-3-carbaldehído y 2-metil-N-[2-(4-piperidinil)fenil]propanamida: ESMS m/e: 454.1 $(M + H)^+$.

Ejemplo 275

N-(3-{1-[4,4-BIS(4-FLUOROFENIL)BUTIL]-4-PIPERIDINIL}-4-METILFENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema AI utilizando 1-[4-cloro-1-(4-fluorofenil)butil]-4-fluorobenceno y 2-metil-N-[4-metil-3-(4-piperidinil)fenil]propanamida: ESMS m/e: 505.0 $(M + H)^+$.

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Ejemplo 276

N-(2-{1-[4,4-BIS(4-FLUOROFENIL)BUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema AI utilizando 1-[4-CLORO-1-(4-fluorofenil)butil]-4-fluorobenceno y 2-metil-N-[2-(4-piperidinil)fenil]propanamida: ESMS m/e: 490.9 $(M + H)^+$.

N-[2-BROMO-4-(TRIFLUOROMETOXI)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento Q1 utilizando cloruro de 2-metilpropanoilo y 2-bromo-4-(trifluorometoxi)anilina: ESMS m/e: 325.9 $(M + H)^+$.

4-[2-(ISOBUTIRILAMINO)-5-(TRIFLUOROMETOXI)FENIL]-3,6-DIHIDRO-1(2H)-PIRIDINCARBOXILATO DE TERBUTILO: Preparado por el procedimiento W y esquema AF utilizando N-[2-bromo-4-(trifluorometoxi)fenil]-2-metilpropanamida y 4-(4,4,5,5-tetrametil-1,3,2-dioxaborolan-2-il)-3,6-dihidro-1(2H)-piridincarboxilato de terbutilo: ESMS m/e: 329.0 $(M - 100)^+$.

2-METIL-N-[2-(4-PIPERIDINIL)-4-(TRIFLUOROMETOXI)FENIL]-PROPANAMIDA: Preparado por los procedimientos X e Y, esquemas AG y AH, respectivamente utilizando 4-[2-(isobutirilamino)-5-(trifluorometoxi)fenil]-3,6-dihidro-1(2H)-piridincarboxilato de terbutilo: ESMS m/e: 330.9 $(M + H)^+$.

Ejemplo 277

N-[2-{1-[4,4-BIS(4-FLUOROFENIL)BUTIL]-4-PIPERIDINIL}-4-(TRIFLUOROMETOXI)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema AI utilizando 1-[4-CLORO-1-(4-fluorofenil)butil]-4-fluorobenceno y 2-metil-N-[2-(4-piperidinil)-4-(trifluorometoxi)fenil]propanamida: ESMS m/e: 574.8 $(M + H)^+$.

N-{3-[1-(4-HIDROXIBUTIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema BI utilizando 4-cloro-1-butanol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 319.3 $(M + H)^+$.

N-{3-[1-(5-HIDOXIPENTIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema BI utilizando 5-cloro-1-pentanol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 333.3 $(M + H)^+$.

N-{3-[1-(6-HIDROXIHEXIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema BI utilizando 6-cloro-1-hexanol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 347.3 $(M + H)^+$.

N-{3-[1-(3-HIDROXIPROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema

BI utilizando 3-cloro-1-propanol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 305.3 $(M + H)^+$.

N-(3-{1-[(2S)-2-HIDROXI-2-FENILETIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema BI utilizando (1s)-2-cloro-1-feniletanol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 367.2 $(M + H)^+$.

N-(3-{1-[(2R)-2-HIDROXI-2-FENILETIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema BI utilizando (1R)-2-cloro-1-feniletanol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 367.2 $(M + H)^+$.

N-(3-{1-[(2S)-3-HIDROXI-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema BI utilizando (2R)-3-cloro-2-metil-1-propanol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 319.2 $(M + H)^+$.

N-(3-{1-[(2R)-3-HIDROXI-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema BI utilizando (2S)-3-cloro-2-metil-1-propanol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 319.2 $(M + H)^+$.

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Ejemplo 278

N-(3-{1-[(3R)-3-HIDROXI-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCRBOXAMIDA: Preparado por el procedimiento G y esquema B1 utilizando (1R)-3-cloro-1-fenil-1-propanol y N-[3-(4-piperidinil)fenil]ciclopropan-carboxamida: ESMS m/e: 379.2 $(M + H)^+$.

Ejemplo 279

N-{3-[1-(4-HIDROXI-4-FENILBUTIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento L y esquema AN, etapa 1 utilizando 2-metil-N-{3-[1-(4-oxo-4-fenilbutil)-4-piperidinil]fenil}propanamida: Análisis calculado para $C25H34N2O2+0.08CHCl_3$: C, 74.5; H, 8.50; N, 6.93. Encontrado: C, 74.5; H, 8.63; N, 6.81; ESMS m/e: 395.2 $(M + H)^+$.

Ejemplo 280

N-{3-[1-(5-HIDROXI-5-FENILPENTIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento L y esquema AN, etapa 1 utilizando 2-metil-N-{3-[1-(5-oxo-5-fenilpentil)-4-piperidinil]fenil}propanamida: Análisis calculado para $C26H36N2O2+0.25CHCl_3$: C, 71.9; H, 8.33; N, 6.39. Encontrado: C, 71.3; H, 8.96; N, 6.86; ESMS M/E: 409.2 $(M + H)^+$.

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Ejemplo 281

N-{3-[1-(6-HIDROXI-6-FENILHEXIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento L y esquema AN, etapa 1 utilizando 2-metil-N-{3-[1-(6-oxo-6-fenilhexil)-4-piperidinil]fenil}propanamida: Análisis calculado para: $C_{27}H_{38}N_2O_2+0.1CHCl_3$: C, 75.5; H, 8.93; N, 6.50. Encontrado: C, 75,3; H, 8.52; N, 6.00; ESMS m/e: 423.2 $(M + H)^+$.

Ejemplo 282

N-{3-[1-(7-HIDROXI-7-FENILHEPTIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento L y esquema AN, etapa 1 utilizando 2-metil-N-{3-[1-(7-oxo-7-fenilheptil)-4-piperidinil]fenil}propanamida: Análisis calculado para: $C_{28}H_{40}N_2O_2+0.1CHCl_3$: C, 75.8; H, 9.10; N, 6.29. Encontrado: C, 75.1; H, 9.24; N, 6.51; ESMS m/e: 437.1 $(M + H)^+$.

Ejemplo 283

N-(3-{1-[4-(4-FLUOROFENIL)-4-HIDROXIBUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento L y esquema AN, etapa 1 utilizando N-(3-{1-[4-(4-fluorofenil)-4-oxobutil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 413.1 $(M + H)^+$.

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Ejemplo 284

3-(2,6-DICLOROFENIL)-5-METIL-4-ISOXAZOLCARBOXILATO DE 4-{4-[3-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILBUTILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-{3-[1-(4-hidroxi-4-fenilbutil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-(2,6-diclorofenil)-5-metil-4-isoxazolcarbonilo: RMN ^1H (400 MHz, $CDCl_3$) 7.56 (m, 1H), 7.47 (m, 2H), 7.44-7.39 (m, 3H), 7.25 (m, 2H), 7.09 (s, 1H), 7.03 (m, 2H), 6.95 (m, 1H); 6.83 (m, 1H), 5.75 (t, 1H, J = 7.1 Hz), 3.03 (t, 2H, J = 7.2 Hz), 2.93 (m, 2H), 2.78 (s, 3H), 2.48 (m, 3H), 2.25 (m, 2H), 1.48 (m, 3H), 1.77 (m, 2H), 1.54 (m, 2H), 1.25 (d, 6H, J = 7.3 Hz); ESMS m/e: 647.7 $(M + H)^+$.

Ejemplo 285

(4-FLUOROFENIL)ACETATO DE 4-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILBUTILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-{3-[1-(4-hidroxi-4-fenilbutil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de (4-fluorofenil)acetilo: RMN ^1H (400 MHz, $CDCl_3$) 7.45 (s, 1H), 7.34-7.19 (m, 8H), 7.11 (m, 1H), 6.98 (m, 3H), 5.75 (t, 1H, J = 6.8 Hz), 3.61 (s, 2H), 2.92 (d, 2H, J = 8.1 Hz), 2.48 (m, 2H), 2.31 (m, 2H), 1.99-1.84 (m, 4H), 1.84-

1.67 (m, 5H), 1.55-1.35 (m, 2H), 1.25 (d, 6H, J = 6.9 Hz); ESMS m/e: 531.1 $(M + H)^+$.

Ejemplo 286

(4-FLUOROFENIL)ACETATO DE 3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-{3-[1-(3-hidroxipropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de (4-fluorofenil)acetilo: ESMS m/e: 441.3 $(M + H)^+$.

Ejemplo 287

3-(2-CLORO-6-FLUOROFENIL)-5-METIL-4-ISOXAZOLCARBOXILATO DE 3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-{3-[1-(3-hidroxipropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-(2-cloro-6-fluorofenil)-5-metil-4-isoxazolcarbonilo: ESMS m/e: 542.2 $(M + H)^+$.

Ejemplo 288

3-(2,6-DICLOROFENIL)-5-METIL-4-ISOXAZOLCARBOXILATO DE 3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-{3-[1-(3-hidroxipropil)-4-piperidinil]fenil}-2-metilpropanamida

y cloruro de 3-(2,6-diclorofenil)-5-metil-4-isoxazolcarbonilo: ESMS m/e: 558.2 $(M + H)^+$.

Ejemplo 289

3-(2-CLOROFENIL)-5-METIL-4-ISOXAZOLCARBOXILATO DE 3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-{3-[1-(3-hidroxipropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-(2-clorofenil)-5-metil-4-isoxazolcarbonilo: ESMS m/e: 254.2 $(M + H)^+$.

Ejemplo 290

3-(2,6-DICLOROFENIL)-5-METIL-4-ISOXAZOLCARBOXILATO DE (1S)-3-{4-[3-ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-(3-{1-[(3S)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 3-(2,6-diclorofenil)-5-metil-4-isoxazolcarbonilo: ESMS m/e: 633.6 $(M + H)^+$.

Ejemplo 291

3-(2-CLORO-6-FLUOROFENIL)-5-METIL-4-ISOXAZOLCARBOXILATO DE 4-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}BUTILO: Preparado por el procedimiento Q1 y esquema C2 (TEA)

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utilizando N-{3-[1-(4-hidroxibutil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-(2-cloro-6-fluorofenil)-5-metil-4-isoxazolcarbonilo: Análisis calculado para: $C_{30}H_{35}ClFN_3O_4+CH_2Cl_2$: C, 63.3; H, 6.23; N, 7.33. Encontrado: C, 63.0; H, 6.39; N, 7.03; ESMS m/e: 556.2 $(M + H)^+$.

Ejemplo 392

3-(2-CLOROFENIL)-5-METIL-4-ISOXAZOLCARBOXILATO DE 4-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}BUTILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-{3-[1-(4-hidroxibutil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-(2-clorofenil)-5-metil-4-isoxazolcarbonilo: ESMS m/e: 538.2 $(M + H)^+$.

Ejemplo 293

5-METIL-3-FENIL-4-ISOXAZOLCARBOXILATO DE 3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-{3-[1-(3-hidroxipropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 5-metil-3-fenil-4-isoxazolcarbonilo: ESMS m/e: 490.3 $(M + H)^+$.

Ejemplo 294

3-(2,6-DICLOROFENIL)-5-METIL-4-ISOXAZOLCARBOXILATO DE 4-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}BUTILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-{3-[1-(4-hidroxibutil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-(2,6-diclorofenil)-5-metil-4-isoxazolcarbonilo: ESMS m/e: 572.2 $(M + H)^+$.

Ejemplo 295

3-(2-CLORO-6-FLUOROFENIL)-5-METIL-4-ISOXAZOLCARBOXILATO DE 4-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILBUTILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-{3-[1-(4-hidroxi-4-fenilbutil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-(2-cloro-6-fluorofenil)-5-metil-4-isoxazolcarbonilo: Análisis calculado para $C36H39ClFN3O4+0.54CHCl_3$: C, 63.0; H, 5.72; N, 6.03. Encontrado: C, 63.0; H, 5.54; N, 6.05; ESMS m/e: 632.2 $(M + H)^+$.

Ejemplo 296

5-METIL-3-FENIL-4-ISOXAZOLCARBOXILATO DE 4-{3-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}BUTILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-{3-[1-(4-hidroxibutil)-4-piperidinil]fenil}-2-metilpropanamida y

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cloruro de 5-metil-3-fenil-4-isoxazolcarbonilo: ESMS m/e: 504.3 $(M + H)^+$.

Ejemplo 297

3-(2,6-DICLOROFENIL)-5-METIL-4-ISOXAZOLCARBOXILATO DE 6-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}HEXILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-{3-[1-(6-hidroxihexil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-(2,6-diclorofenil)-5-metil-4-isoxazolcarbonilo: ESMS m/e: 600.0 $(M + H)^+$.

Ejemplo 298

5-METIL-3-FENIL-4-ISOXAZOLCARBOXILATO DE 6-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}HEXILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-{3-[1-(6-hidroxihexil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 5-metil-3-fenil-4-isoxazolcarbonilo: ESMS m/e: 532.1 $(M + H)^+$.

Ejemplo 299

(4-FLUOROFENIL)ACETATO DE 4-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}BUTILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-{3-[1-(4-hidroxibutil)-4-

piperidinil]fenil}-2-metilpropanamida y cloruro de (4-fluorofenil)acetilo: ESMS m/e: 455.3 $(M + H)^+$.

Ejemplo 300

3-(2-CLOROFENIL)-5-METIL-4-ISOXAZOLCARBOXILATO DE 4-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILBUTILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-{3-[1-(4-hidroxi-4-fenilbutil)-4-piperidinil}fenil}-2-metilpropanamida y cloruro de 3-(2-clorofenil)-5-metil-4-isoxazolcarbonilo: ESMS m/e: 614.2 $(M + H)^+$.

Ejemplo 301

5-METIL-3-FENIL-4-ISOXAZOLCARBOXILATO DE 4-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILBUTILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-{3-[1-(4-hidroxi-4-fenilbutil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 5-metil-3-fenil-4-isoxazolcarbonilo: ESMS m/e: 580.0 $(M + H)^+$.

Ejemplo 302

(4-FLUOROFENIL)ACETATO DE (1S)-3-{4-[3-(ISOBUTIRILAMINO)-FENIL]-1-PIPERIDINIL}-1-FENILPROPILO: Preparado por el procedimiento Q1 y esquema C2 (TEA) utilizando N-(3-{1-

[(3s)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de (4-fluorofenil)acetilo: Análisis calculado para: $C_{32}H_{37}FN_2O_3+0.07CHCl_3$: C, 73.4; H, 7.12; N, 5.34. Encontrado: C, 73.4; H, 6.96; N, 5.14; ESMS m/e 517.1 $(M + H)^+$.

Ejemplo 303

N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)BENZAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de benzoilo: Análisis calculado para: $C_{31}H_{37}N_3O_2+0.55CHCl_3$: C, 69.0; H, 6.89; N, 7.65. Encontrado: C, 69.7; H, 6.73; N, 6.03; ESMS m/e: 484.4 $(M + H)^+$.

Ejemplo 304

N-[3-(1-{(3S)-3-[(DIFENILACETIL)AMINO]-3-FENILPROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de difenilacetilo: ESMS m/e: 574.3 $(M + H)^+$.

Ejemplo 305

3-CLORO-N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)BENZAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 3-clorobenzoilo: ESMS m/e: 518.3 $(M + H)^+$.

Ejemplo 306

3,5-DICLORO-N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)BENZAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 3,5-diclorobenzoilo: ESMS m/e: 552.3 $(M + H)^+$.

Ejemplo 307

2-(ETILSULFANIL)-N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)NICOTINAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 2-(etilsulfanil)nicotinilo: ESMS m/e: 545.3 $(M + H)^+$.

Ejemplo 308

N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)[1,1'-BIFENIL]-4-CARBOXAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de [1,1'-bifenil]-4-carbonilo: ESMS m/e: 560.3 $(M + H)^+$.

Ejemplo 309

N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)-2-PIRIDINCARBOXAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando n-(3-{1-[(3s)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 2-piridincarbonilo: ESMS m/e: 484.6 $(M + H)^+$.

Ejemplo 310

N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)-2-METOXIBENZAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-metilpropanamida y cloruro de 2-metoxibenzoilo: ESMS m/e: 514.1 $(M + H)^+$.

Ejemplo 311

N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)-1-NAFTAMIDA: Preparado por el procedimiento Q1

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y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 1-naftoilo: ESMS m/e: 533.7 $(M + H)^+$.

Ejemplo 312

2,4-DIFLUORO-N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)BENZAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 2,4-difluorobenzoilo: ESMS m/e: 520.2 $(M + H)^+$.

Ejemplo 313

3-(2-CLORO-6-FLUOROFENIL)-N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)-5-METIL-4-ISOXAZOLCARBOXAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 3-(2-cloro-6-fluorofenil)-5-metil-4-isoxazolcarbonilo: ESMS M/E: 617.2 $(M + H)^+$.

Ejemplo 314

3-CLORO-N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)-2-TIOFENCARBOXAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-

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[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 3-cloro-2-tiofencarbonilo: ESMS m/e: 524.2 $(M + H)^+$.

Ejemplo 315

N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)-2-FENOXINICOTINAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 2-fenoxinicotinoilo: ESMS m/e: 577.3 $(M + H)^+$.

Ejemplo 316

1-(4-CLOROFENIL)-N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)-3-PROPIL-1H-PIRAZOL-4-CARBOXAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 1-(4-clorofenil)-3-propil-1H-pirazol-4-carbonilo: ESMS m/e: 626.3 $(M + H)^+$.

Ejemplo 317

4-CLORO-N-((1S)-3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)-1,3-DIMETIL-1H-PIRAZOLO[3,4-B]PIRIDINA-5-CARBOXAMIDA: Preparado por el procedimiento Q1 y esquema AC

utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 4-cloro-1,3-dimetil-1H-pirazolo[3,4-b]piridin-5-carbonilo: ESMS m/e: 587.3 $(M + H)^+$.

Ejemplo 318

5-(3,5-DICLOROFENOXI)-N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)-1H-PIRROL-2-CARBOXAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 5-(3,5-diclorofenoxi)-1H-pirrol-2-carbonilo: ESMS m/e: 634.2 $(M + H)^+$.

Ejemplo 319

N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)NICOTINAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de nicotinoilo: ESMS m/e: 485.3 $(M + H)^+$.

Ejemplo 320

3,4-DIFLUORO-N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)BENZAMIDA: Preparado por el

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procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 3,4-difluorobenzoilo: ESMS m/e: 520.3 $(M + H)^+$.

Ejemplo 321

N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)-1-FENIL-3-PROPIL-1H-PIRAZOL-4-CARBOXAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 1-fenil-3-propil-1H-pirazol-4-carbonilo: ESMS m/e: 592.2 $(M + H)^+$.

Ejemplo 322

4-(DIMETILAMINO)-N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)BENZAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 4-(dimetilamino)benzoilo: ESMS m/e: 527.3 $(M + H)^+$.

Ejemplo 323

N-(81S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)-2-TIOFENCARBOXAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-

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amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 2-tiofencarbonilo: ESMS m/e: 490.2 $(M + H)^+$.

Ejemplo 324

N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)-5-NITRO-2-FURAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 5-nitro-2-furoilo: ESMS m/e: 519.2 $(M + H)^+$.

Ejemplo 325

N-(3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-5-METIL-3-FENIL-4-ISOXAZOLCARBOXAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 5-metil-3-fenil-4-isoxazolcarbonilo: ESMS m/e: 489.1 $(M + H)^+$.

Ejemplo 326

N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)-2-FURAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-{3-[1-(3-aminopropil)-4-piperidinil)fenil}-2-metilpropanamida y cloruro de 2-furoilo: ESMS m/e: 474.2 $(M + H)^+$.

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Ejemplo 327

N-((1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-1-FENILPROPIL)-1-(4-NITROFENIL)-5-(TRIFLUOROMETIL)-1H-PIRAZOL-4-CARBOXAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y cloruro de 1-(4-nitrofenil)-5-(trifluorometil)-1H-pirazol-4-carbonilo: ESMS m/e: 663.2 $(M + H)^+$.

Ejemplo 328

3-(2-CLORO-6-FLUOROFENIL)-N-(3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-5-METIL-4-ISOXAZOLCARBOXAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-(3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-(2-cloro-6-fluorofenil)-5-metil-4-isoxazolcarbonilo: ESMS m/e: 541.2 $(M + H)^+$.

Ejemplo 329

N-[3-(1-{3-[(DIFENILACETIL)AMINO]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida y

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cloruro de difenilacetilo: RMN ^1H (400 MHz, $CDCl_3$) 7.51 (s, 1H), 7.33-7.21 (m, 13H), 6.94 (m, 2H), 4.88 (s, 1H), 3.30 (t, 2H, J = 5.6 Hz), 2.93 (d, 2H, J = 11.3 Hz), 2.52-2.36 (m, 4H), 1.97 (t, 2H, J = 11.3 Hz), 1.83-1.58 (m, 6H), 1.24 (d, 6H, J = 7.6 Hz); Análisis calculado para $C_{32}H_{39}N_3O_2+HCl+0.19CHCl_3$: C, 69.44; H, 7.27; N, 7.55. Encontrado: C, 69.44; H, 7.43; N, 7.43; ESMS m/e: 498.4 $(M + H)^+$.

Ejemplo 330

N-(3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-1-BENZOTIOFEN-3-CARBOXAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 1-benzotiofen-3-carbonilo: ESMS m/e: 464.2 $(M + H)^+$.

Ejemplo 331

3-(2-CLOROFENIL)-N-(3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-5-METIL-4-ISOXAZOLCARBOXAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-(2-clorofenil)-5-metil-4-isoxazolcarbonilo: ESMS m/e: 523.1 $(M + H)^+$.

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Ejemplo 332

3-(2,6-DICLOROFENIL)-N-(3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-5-METIL-4-ISOXAZOLCARBOXAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-(2,6-diclorofenil)-5-metil-4-isoxazolcarbonilo: RMN ^{1}H (400 MHz, $CDCl_3$) 7.50 (d, 1H, J = 2.3 Hz), 7.48 (s, 1H), 7.39 (s, 1H), 7.37 (m, 2H), 7.24 (t, 1H, J = 7.2 Hz), 6.92 (d, 1H, J = 7.9 Hz), 6.06 (s, 1H), 3.31 (q, 2H, J = 6.4 Hz), 2.94 (d, 2H, J = 10.8 Hz), 2.79 (s, 3H), 2.53 (q, 1H, J = 6.1), 2.47 (tt, 1H, J = 4.2, 11.4 Hz), 2.29 (t, 2H, J = 7.2 Hz), 1.99 (t, 2H, J = 11.4 Hz), 1.81 (m, 2H), 1.69 (dt, 2H, J = 2.4, 11.6), 1.59 (q, 2H, J = 6.6 Hz), 1.24 (d, 6H, J = 6.5 Hz); ESMS m/e: 557.0 $(M + H)^+$.

1-[3-(3-CLOROPROPOXI)FENIL]ETANONA: Preparado por el procedimiento U y esquema AK utilizando 1-(3-hidroxifenil)etanona y 1-bromo-3-cloropropano.

1-(3-CLOROPROPOXI)-2-FLUOROBENCENO: Preparado por el procedimiento U y esquema AK utilizando 2-fluorofenol y 1-bromo-3-cloropropano.

1-CLORO-3-(3-CLOROPROPOXI)BENCENO: Preparado por el procedimiento U y esquema AK utilizando 2-clorofenol y 1-bromo-3-cloropropano.

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1-CLORO-4-(3-CLOROPROPOXI)BENCENO: Preparado por el procedimiento U y esquema AK utilizando 4-clorofenol y 1-bromo-3-cloropropano.

1-(3-CLOROPROPOXI)-3-FLUOROBENCENO: Preparado por el procedimiento U y esquema AK utilizando 3-fluorofenol y 1-bromo-3-cloropropano.

1-(3-CLOROPROPOXI)-4-FLUOROBENCENO: Preparado por el procedimiento U y esquema AK utilizando 4-fluorofenol y 1-bromo-3-cloropropano.

1-CLORO-2-(3-CLOROPROPOXI)BENCENO: Preparado por el procedimiento U y esquema AK utilizando 2-clorofenol y 1-bromo-3-cloropropano.

4-(3-CLOROPROPOXI)-1,2-DIMETILBENCENO: Preparado por el procedimiento U y esquema AK utilizando 3,4-dimetilfenol y 1-bromo-3-cloropropano.

1-BROMO-2-(3-CLOROPROPOXI)BENCENO: Preparado por el procedimiento U y esquema AK utilizando 2-bromofenol y 1-bromo-3-cloropropano.

1-BROMO-3-(3-CLOROPROPOXI)BENCENO: Preparado por el procedimiento U y esquema AK utilizando 3-bromofenol y 1-bromo-3-cloropropano.

1-BROMO-4-(3-CLOROPROPOXI)BENCENO: Preparado por el procedimiento U y esquema AK utilizando 4-bromofenol y 1-bromo-3-cloropropano.

1-(3-CLOROPROPOXI)-4-METILBENCENO: Preparado por el procedimiento U y esquema AK utilizando p-cresol y 1-bromo-3-cloropropano.

(2R)-3-CLORO-2-METILPROPILÉTER DE 4-BROMOFENILO: Preparado por el procedimiento U y esquema AK utilizando 4-bromofenol y (2S)-1-bromo-3-cloro-2-metilpropano.

1-{[(2R)-3-CLORO-2-METILPROPIL]OXI}-2,4,5-TRIFLUOROBENCENO: Preparado por el procedimiento U y esquema AK utilizando 2,4,5-trifluorofenol y (2S)-1-bromo-3-cloro-2-metilpropano.

1-CLORO-3-{[(2R)-3-CLORO-2-METILPROPIL]OXI}BENCENO: Preparado por el procedimiento U y esquema AK utilizando 3-clorofenol y (2S)-1-bromo-3-cloro-2-metilpropano.

1-{[(2R)-3-CLORO-2-METILPROPIL]OXI}-4-FLUOROBENCENO: Preparado por el procedimiento U y esquema AK utilizando 4-fluorofenol y (2S)-1-bromo-3-cloro-2-metilpropano.

1-{[(2R)-3-CLORO-2-METILPROPIL]OXI}-3-FLUOROBENCENO: Preparado por el procedimiento U y esquema AK utilizando 3-fluorofenol y (2S)-1-bromo-3-cloro-2-metilpropano.

1-CLORO-2-{[(2R)-3-CLORO-2-METILPROPIL]OXI}BENCENO: Preparado por el procedimiento U y esquema AK utilizando 2-clorofenol y (2S)-1-bromo-3-cloro-2-metilpropano.

1-{[(2R)-3-CLORO-2-METILPROPIL]OXI}-2-FLUOROBENCENO: Preparado por el procedimiento U y esquema AK utilizando 2-fluorofenol y (2S)-1-bromo-3-cloro-2-metilpropano.

1-CLORO-4-{[(2R)-3-CLORO-2-METILPROPIL]OXI}BENCENO: Preparado por el procedimiento U y esquema AK utilizando 4-clorofenol y (2S)-1-bromo-3-cloro-2-metilpropano.

(2R)-3-CLORO-2-METILPROPILÉTER DE 3-BROMOFENILO: Preparado por el procedimiento U y esquema AK utilizando 3-bromofenol y (2S)-1-bromo-3-cloro-2-metilpropano.

(2R)-3-CLORO-2-METILPROPILÉTER DE 2-BROMOFENILO: Preparado por el procedimiento U y esquema AK utilizando 2-bromofenol y (2S)-1-bromo-3-cloro-2-metilpropano.

1-{[(2S)-3-CLORO-2-METILPROPIL]OXI}-3-FLUOROBENCENO: Preparado por el procedimiento U y esquema AK utilizando 3-fluorofenol y (2R)-1-bromo-3-cloro-2-metilpropano.

1-{[(2S)-3-CLORO-2-METILPROPIL]OXI}-4-FLUOROBENCENO: Preparado por el procedimiento U y esquema AK utilizando 4-fluorofenol y (2R)-1-bromo-3-cloro-2-metilpropano.

1-{[(2S)-3-CLORO-2-METILPROPILO]OXI}-2-FLUOROBENCENO: Preparado por el procedimiento U y esquema AK utilizando 2-fluorofenol y (2R)-1-bromo-3-cloro-2-metilpropano.

1-CLORO-2-{[(2S)-3-CLORO-2-METILPROPIL]OXI}BENCENO: Preparado por el procedimiento U y esquema AK utilizando 2-clorofenol y (2R)-1-bromo-3-cloro-2-metilpropano.

1-CLORO-4-{[(2S)-3-CLORO-2-METILPROPIL]OXI}BENCENO: Preparado por el procedimiento U y esquema AK utilizando 4-clorofenol y (2R)-1-bromo-3-cloro-2-metilpropano.

(2S)-3-CLORO-2-METILPROPILÉTER DE 4-BROMOFENILO: Preparado por el procedimiento U y esquema AK utilizando 4-bromofenol y (2R)-1-bromo-3-cloro-2-metilpropano.

(2S)-3-CLORO-2-METILPROPILÉTERT DE 3-BROMOFENILO: Preparado por el procedimiento U y esquema AK utilizando 3-fluorofenol y (2R)-1-bromo-3-cloro-2-metilpropano.

(2S)-3-CLORO-2-METILPROPILÉTER de 2-BROMOFENILO: Preparado por el procedimiento U y esquema AK utilizando 2-bromofenol y (2R)-1-bromo-3-cloro-2-metilpropano.

1-CLORO-3-{[(2S)-3-CLORO-2-METILPROPIL]OXI}BENCENO: Preparado por el procedimiento U y esquema AK utilizando 3-clorofenol y (2R)-1-bromo-3-cloro-2-metilpropano.

1-[3-(4-CLOROBUTOXI)FENIL]ETANONA: Preparado por el procedimiento U y esquema AK utilizando 1-(3-hidroxifenil)etanona y 1-bromo-4-clorobutano.

1-[3-(4-CLOROBUTOXI)FENIL]ETANONA: Preparado por el procedimiento U y esquema AK utilizando 1-(3-hidroxifenil)etanona y 1-bromo-4-clorobutano.

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1-(4-CLOROBUTOXI)-3-METOXIBENCENO: Preparado por el procedimiento U y esquema AK utilizando 3-metoxifenil y 1-bromo-4-clorobutano.

1-(4-CLOROBUTOXI)-4-METILBENCENO: Preparado por el procedimiento U y esquema AK utilizando 4-metoxifenil y 1-bromo-4-clorobutano.

1-(4-CLOROBUTOXI)-2-METOXIBENCENO: Preparado por el procedimiento U y esquema AK utilizando 2-metoxifenol y 1-bromo-4-clorobutano.

4-(CLOROBUTOXI)-1,2-DIMETILBENCENO: Preparado por el procedimiento U y esquema AK utilizando 3,4-dimetilfenol y 1-bromo-4-clorobutano.

1-{3-[(5-CLOROPENTIL)OXI]FENIL}ETANONA: Preparado por el procedimiento U y esquema AK utilizando 1-(3-hidroxifenil)etanona y 1-bromo-5-cloropentano.

1-{3-[(5-CLOROPENTIL)OXI}FENIL}ETANONA: Preparado por el procedimiento U y esquema AK utilizando 1-(3-hidroxifenil)etanona y 1-bromo-5-clorobutano.

1-[3-[(6-CLOROHEXIL)OXI]FENIL}ETANONA: Preparado por el procedimiento U y esquema AK utilizando 1-(3-hidroxifenil)etanona y 1-bromo-5-clorohexano.

1-{3-[(6-CLOROHEXIL)OZI]FENIL}ETANONA: Preparado por el procedimiento U y esquema AK utilizando 1-(3-hidroxifenil)etanona y 1-bromo-6-clorohexano.

Ejemplo 333

N-(3-{1-[(2S)-2-(3-ACETILFENOXI)-2-FENILETIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento B y esquema B1 utilizando 1-(3-hidroxifenil)etanona y N-(3-{1-[(2R)-2-hidroxi-2-feniletil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 485.0 (M + H)$^+$.

Ejemplo 334

N-(3-{1-[(2S)-2-(2-ACETILFENOXI)-2-FENILETIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento B y esquema B1 utilizando 1-(2-hidroxifenil)etanona y N-(3-{1-[(2R)-2-hidroxi-2-feniletil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 485.2 (M + H)$^+$.

Ejemplo 335

N-(3-{1-[(2S)-2-(3-CLOROFENOXI)-2-FENILETIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento B y esquema B1 utilizando 3-clorofenol y N-(3-{1-[(2R)-2-hidroxi-2-feniletil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 477.1 $(M + H)^+$.

Ejemplo 336

N-(3-{1-[(2S)-2-(3,4-DIMETOXIFENOXI)-2-FENILETIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento B y esquema B1 utilizando 3,4-dimetoxifenol y N-(3-{1-[(2R)-2-hidroxi-2-feniletil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 503.2 $(M + H)^+$.

Ejemplo 337

N-(3-{1-[(2R)-2-(4-FLUOROFENOXI)-2-FENILETIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento B y esquema B1 utilizando 4-fluorofenol y N-(3-{1-[(2S)-2-hidroxi-2-feniletil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 461.2 $(M + H)^+$.

Ejemplo 338

N-(3-{1-[(2R)-2-(3-METOXIFENOXI)-2-FENILETIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el

procedimiento B y esquema B1 utilizando 3-metoxifenol y N-(3-{1-[(2S)-2-hidroxi-2-feniletil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 472.9 $(M + H)^+$.

Ejemplo 339

N-(3-{1-[(2R)-2-(3-CLOROFENOXI)-2-FENILETIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento B y esquema B1 utilizando 3-clorofenol y N-(3-{1-[(2S)-2-hidroxi-2-feniletil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 478.5 $(M + H)^+$.

N-{3-[1-(3,3-DIMETOXIPROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 3-bromo-1,1-dimetoxipropano y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 349.2 $(M + H)^+$.

Ejemplo 340

N-(3-{1-[(3S)-3-(3-ACETILFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento B y esquema B1 utilizando 1-(3-hidroxifenil)etanona y N-(3-{1-[(3R)-3-hidroxi-3-fenilpropil]-4-piperidinil}fenil)ciclopropancarboxamida: ESMS m/e: 497.1 $(M + H)^+$.

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Ejemplo 341

N-(3-{1-[3-(3-ACETILFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-[3-(3-cloropropoxi)fenil]etanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 423.2 (M + H)$^+$.

Ejemplo 342

N-(3-{1-[3-(3-ACETILFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-PROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-[3-(3-cloropropoxi)fenil]etanona y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 421.2 (M + H)$^+$.

Ejemplo 343

N-(3-{1-[3-(2-FLUOROFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-(3-cloropropoxi)-2-fluorobenceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 399.2 (M + H)$^+$.

Ejemplo 344

N-(3-{1-[3-(3-CLOROFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema

B1 utilizando 1-cloro-3-(3-cloropropoxi)benceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 415.2 $(M + H)^+$.

Ejemplo 345

N-(3-{1-[3-(4-CLOROFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-cloro-4-(3-cloropropoxi)benceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: RMN ^1H (400 MHz, $CDCl_3$) 7.71 (dd, 1H, J = 3.2, 5.7 Hz), 7.53 (dd, 1H, J = 3.2, 5.7 Hz), 7.50 (m, 1H), 7.31 (m, 1H), 7.24-7.20 (m, 2H), 6.94 (d, 1H, J = 7.9 Hz), 6.85-6.82 (m, 2H), 4.00 (t, 2H, J = 6.1 Hz), 3.07 (d, 2H, J = 10.9 Hz), 2.55 (m, 3H), 2.50 (sept, 1H, J = 6.2 Hz), 2.08 (dt, 2H, J = 3.1, 10.9 Hz), 2.00 (m, 2H), 1.83 (m, 3H), 1.59 (qt, 1H, J = 6.2 Hz), 1.24 (d, 6H, J = 6.8 Hz); Análisis calculado para: $C_{24}H_{31}ClN_2O_2$+HCl: C, 63.8; H, 7.09; N, 6.21. Encontrado: C, 63.3; H, 7.05; N, 6.27; ESMS m/e: 415.2 $(M + H)^+$.

Ejemplo 346

N-(3-{1-[3-(3-FLUOROFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-(3-cloropropoxi)-3-fluorobenceno y 2-metil-

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N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 399.2 (M + H)$^+$.

Ejemplo 347

N-(3-{1-[3-(4-FLUOROFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-(3-cloropropoxi)-4-fluorobenceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 399.2 (M + H)$^+$.

Ejemplo 348

N-(3-{1-[3-(2-CLOROFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-cloro-2-(3-cloropropoxi)benceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 415.2 (M + H)$^+$.

Ejemplo 349

N-(3-{1-[3-(3,4-DIMETILFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 4-(3-cloropropoxi)-1,2-dimetilbenceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 409.2 (M + H)$^+$.

Ejemplo 350

N-(3-{1-[3-(2-BROMOFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-bromo-2-(3-cloropropoxi)benceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: RMN ^1H (400 MHz, $CDCl_3$) 7.53 (dd, 1H, J = 1.6, 7.9 Hz), 7.48 (s, 1H), 7.32 (m, 1H), 7.28-7.22 (m, 3H), 7.17 (s, 1H), 6.98 (d, 1H, J = 7.7 Hz), 6.93 (dd, 1H, J = 1.4, 8.4 Hz), 6.82 (dt, 1H, J = 7.7 Hz),. 6.93 (dd, 1H, J = 1.4, 8.4 Hz), 6.82 (dt, 1H, J = 7.6, 1.4 Hz), 4.11 (t, 2H, J = 6.3 Hz), 3.07 (d, 2H, J = 11.3 Hz), 2.61 (t, 2H, J = 6.9 Hz), 2.50 (m, 3H), 2.07 (m, 1H), 1.8-1.75 (m, 5H), 1.25 (d, 6H, J = 6.7 Hz); Análisis calculado para $C_{24}H_{31}BrN_2O_2.HCl+0.2\ CHCl_3$: C, 55.9; H, 6.24; N, 5.39. Encontrado: C, 55.8; H, 6.23; N, 5.47; ESMS m/e: 459.1 $(M + H)^+$.

Ejemplo 351

N-(3-{1-[3-(3-BROMOFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-bromo-3-(3-cloropropoxi)benceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 459.1 $(M + H)^+$.

Ejemplo 352

N-(3-{1-[3-(4-BROMOFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-bromo-4-(3-cloropropoxi)benceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: RMN ^1H (400 MHz, $CDCl_3$) 7.51 (s, 1H), 7.37 (d, 2H, J = 7.6 Hz), 7.26 (m, 3H), 6.97 (d, 1H, J = 7.7 Hz), 6.79 (d, 2H, J = 7.7 Hz), 4.01 (t, 2H, J = 5.6 Hz), 3.08 (d, 2H, J = 9.4 Hz), 2.53 (m, 4H), 2.05 (m, 4H), 1.84 (m, 4H), 1.24 (d, 6H, J = 5.9 Hz); Análisis calculado para: $C_{24}H_{31}BeN_2O_2.HCl+0.34CHCl_3$: C, 54.5; H, 6.08; N, 5.22. Encontrado: C, 54.5; H, 6.22; N, 5.22; ESMS m/e: 459.1 $(M + H)^+$.

Ejemplo 353

N-(3-{1-[(3R)-3-(3,4-DIMETOXIFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-N,2-DIMETILPROPANAMIDA: Preparado por el procedimiento T y esquema AD utilizando N-(3-{1-[(3R)-3-(3,4-dimetoxifenil)-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y yoduro de metilo: ESMS M/E: 531.2 $(M + H)^+$.

Ejemplo 354

N-(3-}1-[(3R)-3-(3-ACETILFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-N,2-DIMETILPROPANMIDA: Preparado por el

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procedimiento T y esquema AD utilizando N-(3-}1-[(3R)-3-(3-acetilfenoxi)-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y yoduro de metilo: ESMS m/e: 513.2 (M + H)$^+$.

Ejemplo 355

N-(3-{1-[(1S)-3-(ACETILFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-N,2-DIMETILPROPANAMIDA: Preparado por el procedimiento T y esquema AD utilizando N-(3-{1-[(3S)-3-(3-acetilfenoxi)-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida y yoduro de metilo: ESMS m/e: 513.2 (M + H)$^+$.

Ejemplo 356

N-(3-{1-[(2S)-3-(4-BROMOFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando (2R)-3-cloro-2-metilpropiléter de 4-bromofenilo y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 473.0 (M + H)$^+$.

Ejemplo 357

2-METIL-N-(3-{1-[(2S)-2-METIL-3-(2,4,5-TRIFLUOROFENOXI)PROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-

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{(2R)-3-cloro-2-metilpropil]oxi}-2,4,5-trifluorobenceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 449.2 $(M + H)^+$.

Ejemplo 358

N-(3-{1-[(2S)-3-(3-CLOROFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-cloro-3-{[(2R)-3-cloro-2-metilpropil]oxi}benceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 429.2 $(M + H)^+$.

Ejemplo 359

N-(3-{1-[(2S)-3-(4-FLUOROFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-{[(2R)-3-cloro-2-metilpropil]oxi}-4-fluorobenceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 413.2 $(M + H)^+$.

Ejemplo 360

N-(3-{1-[(2S)-3-(FLUOROFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-{[(2R)-3-cloro-2-metilpropil]oxi}3-fluorobenceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 413.2 $(M + H)^+$.

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Ejemplo 361

N-(3-{1-[(2S)-3-(2-CLOROFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-cloro-2-{[(2R)-3-cloro-2-metilpropil]oxi}benceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 429.1 $(M + H)^+$.

Ejemplo 362

N-(3-{1-[(2S)-3-(2-FLUOROFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-{[(2R)-3-cloro-2-metilpropil]oxi}-2-fluorobenceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 413.2 $(M + H)^+$.

Ejemplo 363

N-(3-{1-[(2S)-3-(4-CLOROFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-cloro-4-{[(2R)-3-cloro-2-metilpropil]oxi}benceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 429.2 $(M + H)^+$.

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Ejemplo 364

N-(3-{1-[(2S)-3-(3-BROMOFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando (2R)-3-cloro-2-metilpropiléter de 3-bromofenilo y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 474.0 $(M + H)^+$.

Ejemplo 365

N-(3-{1-[(2S)-3-(2-BROMOFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando (2R)-3-cloro-2-metilpropiléter de 2-bromofenilo y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 473.0 $(M + H)^+$.

Ejemplo 366

N-(3-{1-[(2R)-3-(3-FLUOROFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-{[(2R)-3-cloro-2-metilpropil]oxi}-3-fluorobenceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 413.2 $(M + H)^+$.

Ejemplo 367

N-(3-{1-[(2R)-3-(4-FLUOROFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el

procedimiento G y esquema B1 utilizando 1-{[(2R)-3-cloro-2-metilpropil]oxi}-4-fluorobenceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 413.8 $(M + H)^+$.

Ejemplo 368

N-(3-{1-[(2R)-3-(2-CLOROFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-cloro-3-{[(2S)-3-cloro-2-metilpropil]oxi}benceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 429.1 $(M + H)^+$.

Ejemplo 369

N-(3-{1-[(2R)-3-(4-CLOROFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-cloro-3-{[(2S)-3-cloro-2-metilpropil]oxi}benceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 429.1 $(M + H)^+$.

Ejemplo 370

N-(3-{1-[(2R)-3-(4-BROMOFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando (2S)-3-cloro-2-metilpropiléter de 4-bromofenilo y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 473.0 $(M + H)^+$.

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Ejemplo 371

N-(3-{1-[(2R)-3-(3-BROMOFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando (2S)-3-cloro-2-metilpropiléter de 3-bromofenilo y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 473.0 $(M + H)^+$.

Ejemplo 372

N-(3-{1-[(2R)-3-(2-BROMOFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando (2S)-3-cloro-2-metilpropiléter de 2-bromofenilo y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 473.0 $(M + H)^+$.

Ejemplo 373

N-(3-{1-[(2R)-3-(CLOROFENOXI)-2-METILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-cloro-3-{[(2S)-3-cloro-2-metilpropil]oxi}benceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 429.1 $(M + H)^+$.

Ejemplo 74

N-(3-{1-[3-(5,5-DIMETIL-1,3-DIOXAN-2-IL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 2-(3-bromopropil)-5,5-dimetil-1,3-dioxano y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 403.2 $(M + H)^+$.

Ejemplo 375

N-(3-{1-[4-(3-ACETILFENOXI)BUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-[3-(4-clorobutoxi)fenil]etanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 437.2 $(M + H)^+$.

Ejemplo 376

N-(3-{1-[4-(3-METOXIFENOXI)BUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-(4-clorobutoxi)-3-metoxibenceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 425.2 $(M + H)^+$.

Ejemplo 377

N-(3-{1-[4-(4-METOXIFENOXI)BUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema

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B1 utilizando 1-(4-clorobutoxi)-4-metoxibenceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 425.2 $(M + H)^+$.

Ejemplo 378

N-(3-{1-[4-(2-METOXIFENOXI)BUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-(4-clorobutoxi)-2-metoxibenceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 425.2 $(M + H)^+$.

Ejemplo 379

N-(3-{1-[4-(3,4-DIMETILFENOXI)BUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 4-(4-clorobutoxi)-1,2-dimetilbenceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 423.2 $(M + H)^+$.

Ejemplo 380

N-(3-{1-[4-(1,3-DIOXOLAN-2-IL)BUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 2-(4-clorobutil)-1,3-dioxolano y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 375.2 $(M + H)^+$.

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Ejemplo 381

N-(3-{1-[5-(3-ACETILFENOXI)PENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-{3-[(5-cloropentil)oxi]fenil}etanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 451.3 $(M + H)^+$.

Ejemplo 382

N-(3-{1-[5-(3-ACETILFENOXI)PENTIL]-4-PIPERIDINIL}FENIL)-ICLOPROPANCARBOXAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-(3-[(5-cloropentil)oxi]fenil}etanona y n-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 449.2 $(M + H)^+$.

Ejemplo 383

N-(3-{1-[6-(3-ACETILFENOXI)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 1-{3-[(6-clorohexil)oxi]fenil}etanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 465.3 $(M + H)^+$.

Ejemplo 384

N-(3-{1-[6-(3-ACETILFENOXI)HEXIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el

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procedimiento G y esquema B1 utilizando 1-{3-[(6-clorohexil)oxi]fenil}etanona y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 463.3 (M + H)$^+$.

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Ejemplo 385

N-(3-{1-[4-(4-CLOROFENOXI)-4-(4-CLOROFENIL)BUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento B y esquema AN utilizando 4-clorofenol y N-(3-{1-[4-(4-clorofenil)-4-hidroxibutil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 562.9 $(M + 23)^+$.

Ejemplo 386

2-METIL-N-(3-{1-[2-(1-METIL-2-FENIL-1H-INDOL-3-IL)ETIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(4-oxo-4-fenilbutil)-4-piperidinil]fenil}propanamida y 1-metil-1-fenilhidrazina: ESMS m/e: 480.3 $(M + H)^+$.

Ejemplo 387

2-METIL-N-(3-{1-[2-(2-FENIL-1H-BENZO[G]INDOL-3-IL)ETIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(4-oxo-4-fenilbutil)-4-piperidinil]fenil}propanamida y clorhidrato de 1-(1-naftil)hidrazina: ESMS m/e: 516.4 $(M + H)^+$.

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Ejemplo 388

2-METIL-N-(3-{1-[3-(2-FENIL-1H-BENZO[G]INDOL-3-IL)PROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(5-oxo-4-fenilbutil)-4-piperidinil]fenil}propanamida y clorhidrato de 1-(1-naftil)hidrazina: ESMS m/e: 530.216.4 $(M + H)^+$.

Ejemplo 389

2-METIL-N-[3-(1-{3-[2-FENIL-5-(TRIFLUOROMETOXI)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(5-oxo-4-fenilpentil)-4-piperidinil]fenil}propanamida y clorhidrato de 1-[4-(trifluorometoxi)fenil]hidrazina: ESMS m/e: 564.2 $(M + H)^+$.

Ejemplo 390

2-METIL-N-[3-(1-{4-[2-FENIL-5-(TRIFLUOROMETOXI)-1H-INDOL-3-IL]BUTIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(6-oxo-6-fenilhexil)-4-piperidinil]fenil}propanamida y clorhidrato de 1-[4-(trifluorometoxi)fenil]hidrazina: ESMS m/e: 578.2 $(M + H)^+$.

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Ejemplo 391

2-METIL-N-(3-{1-[3-(1-METIL-2-FENIL-1H-INDOL-3-IL)PROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(5-oxo-5-fenilpentil)-4-piperidinil]fenil}propanamida y 1-metil-1-fenilhidrazina: ESMS m/e: 495.3 $(M + H)^+$.

Ejemplo 392

N-(3-{1-[4-(1,2-DIFENIL-1H-INDOL-3-IL)BUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(6-oxo-6-fenilhexil)-4-piperidinil]fenil}propanamida y clorhidrato de 1,1-difenilhidrazina: ESMS m/e: $(M + H)^+$. 570.3.

Ejemplo 393

2-METIL-N-[3-(1-{5-[2-FENIL-5-(TRIFLUOROMETOXI)-1H-INDOL-3-IL]PENTIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(7-oxo-7-fenilheptil)-4-piperidinil]fenil}propanamida y clorhidrato de 1-[4-(trifluorometoxi)fenil]hidrazina: ESMS m/e: 592.3 $(M + H)^+$.

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Ejemplo 394

N-(3-{1-[5-(1,2-DIFENIL-1H-INDOL-3-IL)PENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(7-oxo-7-fenilheptil)-4-piperidinil]fenil}propanamida y clorhidrato de 1,1-difenilhidrazina: ESMS m/e: 584.3 $(M + H)^+$.

Ejemplo 395

N-2-METIL-N-(3-{1-[5-(1-METIL-2-FENIL-1H-INDOL-3-IL)PENTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(7-oxo-7-fenilheptil)-4-piperazinil]fenil}propanamida y 1-metil-1-fenilhidrazina: ESMS m/e: $(M + H)^+$.

Ejemplo 396

2-METIL-N-(3-{1-[4-(2-FENIL-1H-BENZO[G]INDOL-3-IL)BUTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(6-oxo-6-fenilhexil)-4-piperidinil]fenil}propanamida y clorhidrato de 1-(1-naftil)hidrazina: ESMS m/e: 544.3 $(M + H)^+$.

Ejemplo 397

2-METIL-N-(3-{1-[4-(1-METIL-2-FENIL-1H-INDOL-3-IL)BUTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(6-oxo-6-fenilhexil)-4-piperidinil]fenil}propanamida y 1-metil-1-fenilhidrazina: ESMS m/e: 508.3 $(M + H)^+$.

Ejemplo 398

2-METIL-N-(3-{1-[5-FENIL-1H-BENZO[G]INDOL-3-IL)PENTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(7-oxo-7-fenilheptil)-4-piperidinil]fenil}propanamida e hidrazina de 1-(1-naftil)hidrazina: ESMS m/e: 558.2 $(M + H)^+$.

Ejemplo 399

2-METIL-N-(3-{1-[2-(5-METIL-2-FENIL-1H-INDOL-3-IL)ETIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(4-oxo-4-fenilbutil)-4-piperidinil]fenil}propanamida y clorhidrato de 1-(4-metilfenil)hidrazina: ESMS m/e: 480.2 $(M + H)^+$.

Ejemplo 400

N-(3-{1-[2-(7-METOXI-2-FENIL-1H-INDOL-3-IL)ETIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(4-oxo-4-fenilbutil)-4-piperidinil]fenil}propanamida y clorhidrato de 1-(2-metoxifenil)hidrazina: ESMS m/e: 496.2 $(M + H)^+$.

Ejemplo 401

2-METIL-N-(3-{1-[2-(7-METIL-2-FENIL-1H-INDOL-3-IL)ETIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(4-oxo-4-fenilbutil)-4-piperidinil]fenil}propanamida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS m/e: 480.2 $(M + H)^+$.

Ejemplo 402

N-(3-{1-[3-(7-METOXI-2-FENIL-1H-INDOL-3-IL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(5-oxo-5-fenilpentil)-4-piperidinil]fenil}propanamida y 1-5-fenilpentil)-4-piperidinil]fenil}propanamida y clorhidrato de 1-(2-metoxifenil)hidrazina: ESMS m/e: 510.2 $(M + H)^+$.

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Ejemplo 403

2-METIL-N-(3-{1-[4-(7-METIL-2-FENIL-1H-INDOL-3-IL)BUTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(6-oxo-6-fenilhexil)-4-piperidinil]fenil}propanamida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS m/e: 508.3 $(M + H)^+$.

Ejemplo 404

N-(3-{1-[2-(5-METOXI-2-FENIL-1H-INDOL-3-IL)ETIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(4-oxo-4-fenilbutil)-4-piperidinil]fenil}propanamida y clorhidrato de 1-(4-metoxifenil)hidrazina: ESMS m/e: 496.2 $(M + H)^+$.

Ejemplo 405

2-METIL-N-(3-{1-[3-(5-METIL-2-FENIL-1H-INDOL-3-IL)PROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(5-oxo-5-fenilpentil)-4-piperidinil]fenil}propanamida y clorhidrato de 1-(4-metilfenil)hidrazina: ESMS m/e: 494.3 $(M + H)^+$.

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Ejemplo 406

N-(3-{1-[4-(7-METOXI-2-FENIL-1H-INDOL-3-IL)BUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(6-oxo-6-fenilhexil)-4-piperidinil]fenil}propanamida y clorhidrato de 1-(2-metoxifenil)hidrazina: ESMS m/e: 524.3 $(M + H)^+$.

Ejemplo 407

2-METIL-N-(3-{1-[3-(1-FENIL-1H-INDOL-3-IL)PROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento H y esquema S utilizando N-(3-{1-[4-(1,3-dioxolan-2-il)butil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1,1-difenilhidrazina: ESMS m/e: 480.2 $(M + H)^+$.

Ejemplo 408

2-METIL-N-(3-{1-[3-(1-FENIL-1H-INDOL-3-IL)ETIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento H y esquema S utilizando N-(3-{1-[4-(1,3-dioxolan-2-il)propil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1,1-difenilhidrazina: ESMS m/e: 466.2 $(M + H)^+$.

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Ejemplo 409

2-METIL-N-(3-{1-[2-(7-METIL-1H-INDOL-3-IL)ETIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento H y esquema S utilizando N-(3-{1-[3-(1,3-dioxolan-2-il)propil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS m/e: 404.2 (M + H).

Ejemplo 410

2-METIL-N-(3-{1-[2-(1-METIL-1H-INDOL-3-IL)ETIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento H y esquema S utilizando N-(3-{1-[3-(1,3-dioxolan-2-il)propil]-4-piperidinil}fenil)-2-metilpropanamida y 1-metil-1-fenilhidrazina: ESMS m/e: 404.2 $(M + H)^+$.

Ejemplo 411

2-METIL-N-(3-{1-[2-(5-METIL-1H-INDOL-3-IL)ETIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento H y esquema S utilizando N-(3-{1-[3-(1,3-dioxolan-2-il)propil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-(4-metilfenil)hidrazina: ESMS m/e: 404.2 $(M + H)^+$.

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Ejemplo 412

2-METIL-N-[3-(1-{2-[5-(TRIFLUOROMETOXI)-1H-INDOL-3-IL]ETIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento H y esquema S utilizando N-(3-{1-[3-(1,3-dioxolan-2-il)propil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-[4-(trifluorometoxi)fenil]hidrazina: ESMS m/e: 474.2 $(M + H)^+$.

Ejemplo 413

N-(3-{1-[3-(1H-BENZO[G]INDOL-3-IL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento H y esquema S utilizando N-(3-{1-[4-(1,3-dioxolan-2-il)propil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-(1-naftil)hidrazina: ESMS m/e: 454.2 $(M + H)^+$.

Ejemplo 414

2-METIL-N-(3-{1-[3-METIL-1H-INDOL-3-IL)PROPIL]-4-PIPERIDNIL}FENIL)PROPANAMIDA: Preparado por el procedimiento H y esquema S. Una mezcla de N-(3-{1-[4-(1,3-dioxolan-2-il)butil]-4-piperidinil}fenil)-2-metilpropanamida (100 mg, 0.270 mmoles) 1-metil-1-fenilhidrazina (106 mg, 0.870 mmoles), $ZnCl_2$ (119 mg, 0.870 mmoles) y HOAc (1.00 ml) se calienta durante 12 hors a 80°C. La mezcla cruda resultante

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se diluye con agua (20 ml), la capa acuosa se neutraliza con K_2CO_3 saturado (10 ml) y extracto con CH_2Cl_2 (3 x 20 ml). Las capas orgánicas combinadas se concentran in vacuo y el residuo se purifica por TLC preparativa utilizando 3% de NH_3 (2.0 M en metanol) en CH_2Cl_2 para proporcionar el producto deseado 2-metil-N-(3-{1-[3-(1-metil-1H-indol-3-il)propil]-4-piperidinil}fenil)propanamida (20.7 mg, 18.7%): RMN ^1H (400 MHz, $CDCl_3$) 7.60 (d, 1H, J = 8.1 Hz), 7.45 (s, 1H), 7.35 (d, 1H, J = 7.4 Hz), 7.25 (m, 4H), 7.09 (t, 1H, J = 7.3 Hz), 6.97 (d, 1H, J = 7.3 Hz), 6.86 (s, 1H), 3.75 (s, 3H), 3.11 (d, 2H, J = 11.6 Hz), 2.79 (t, 2H, J = 7.3 Hz), 2.51 (m, 4H), 2.12-1.81 (m, 8H), 1.25 (d, 6H, J = 7.1 Hz); Análisis calculado para $C_{27}H_{35}N_3O$+0.225 $CHCl_3$: C, 73.57; H, 7.99; N, 9.45. Encontrado: C, 73.93; H, 7.90; N, 9.23; ESMS m/e: 418.2 $(M + H)^+$.

Ejemplo 415

2-METIL-N-(3-{1-[3-(5-METIL-1H-INDOL-3-IL)PROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento H y esquema S utilizando N-(3-{1-[4-(1,3-dioxolan-2-il)butil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-(4-metilfenil)hidrazina: ESMS m/e: 418.2 $(M + H)^+$.

Ejemplo 416

2-METIL-N-[3-(1-{3-[5-(TRIFLUOROMETIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento H y esquema S utilizando N-(3-{1-[4-(1,3-dioxolan-2-il)butil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de (trifluorometoxi)fenil]hidrazina: ESMS m/e: 488.2 $(M + H)^+$.

Ejemplo 417

2-METIL-N-(3-{1-[3-(7-METIL-1H-INDOL-3-IL)PROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento H y esquema S utilizando N-(3-{1-[4-(1,3-dioxolan-2-il)butil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS m/e: 418.2 $(M + H)^+$.

Ejemplo 418

N-(3-{1-[3-(7-METOXI-1H-INDOL-3-IL)PROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento H y esquema S utilizando N-(3-{1-[4-(1,3-dioxolan-2-il)butil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-(2-metoxifenil)hidrazina: ESMS m/e: 434.0 $(M + H)^+$.

Ejemplo 419

N-(3-{1-[2-(7-METOXI-1H-INDOL-3-IL)ETIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento H y esquema S utilizando N-(3-{1-[3-(1,3-dioxolan-2-il)propil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-(2-metoxifenil)hidrazina: ESMS m/e: 420.2 $(M + H)^+$.

Ejemplo 420

N-(3-{1-[2-(5-METOXI-1H-INDOL-3-IL)ETIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento H y esquema S utilizando N-(3-{1-[3-(1,3-dioxolan-2-il)propil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-(4-metoxifenil)hidrazina: ESMS m/e: 420.2 $(M + H)^+$.

Ejemplo 421

2-METIL-N-(3-{1-[4-(5-METIL-2-FENIL-1H-INDOL-3-IL)BUTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento E y esquema M utilizando 2-metil-N-{3-[1-(6-oxo-6-fenilhexil)-4-piperidinil]fenil}propanamida y clorhidrato de 1-(4-metilfenil)hidrazina: ESMS m/e: 508.3 $(M + H)^+$.

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Ejemplo 422

2-METIL-N-[4-(1-{(1-(4-METILFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[4-(4-piperidinil)fenil]propanamida y 1-(4-metilfenil)-1H-indol: ESMS m/e: 466.2 $(M + H)^+$.

Ejemplo 423

N-[4-(1-{[1-(4-METILFENIL)-1H-INDOL-3.-IL]METIL}-4-PIPERIDINIL)FENIL]BUTANAMID: Preparado por el procedimiento D y esquema N utilizando N-[4-(4-piperidinil)fenil]butanamida y 1-(4-metilfenil)-1H-indol: ESMS m/e: 466.2 $(M + H)^+$.

Ejemplo 424

N-[3-(1-{[2-(2-AMINOFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 2-(1H-indol-2-il)anilina: ESMS m/e: 467.2 $(M + H)^+$.

Ejemplo 425

3-({4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}METIL)-1H-INDOL-2-CARBOXILATO DE ETILO: Preparado por el procedimiento

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D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 1H-indol-2-carboxilato de etilo: ESMS m/e: 448.2 $(M + H)^+$.

Ejemplo 426

2-METIL-N-(3-{1-[(1-METIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 1-metil-1H-indol: ESMS m/e: 390.2 $(M + H)^+$.

Ejemplo 427

N-(3-{1-[(5-METOXI-2-METIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 5-metoxi-2-metil-1H-indol: ESMS m/e: 420.2 $(M + H)^+$.

Ejemplo 428

2-METIL-N-(3-{1-[(1-METIL-2-FENIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 1-metil-2-fenil-1H-indol: ESMS m/e: 46.2 $(M + H)^+$.

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Ejemplo 429

2-METIL-N-(3-{1-[(5-NITRO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 5-nitro-1H-indol: ESMS m/e: 421.1 $(M + H)^+$.

Ejemplo 430

2-METIL-N-(3-{1-[(2-METIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 2-metil-1H-indol: ESMS m/e: 390.2 $(M + H)^+$.

Ejemplo 431

N-(3-{1-[(4-BROMO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 4-bromo-1H-indol: ESMS m/e: 455.0 $(M + H)^+$.

Ejemplo 432

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N-[3-(1-{[2-(4-FLUOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 2-(4-fluorofenil)-1H-indol: ESMS m/e: 470.0 $(M + H)^+$.

Ejemplo 433

N-(3-{1-[(1,2-DIFENIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 1,2-difenil-1H-indol: ESMS m/e: 528.2 $(M + H)^+$.

Ejemplo 434

N-[3-(1-{[2-(4-CLOROFENIL)-1-ETIL-1H-INDOL-3-IL]METIL}-3-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 2-(4-clorofenil)-1-etil-1H-indol: ESMS m/e: 514.1 $(M + H)^+$.

Ejemplo 435

N-(3-{1-[(5-CLORO-2-METIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-

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piperidinil)fenil]propanamida y 5-cloro-2-metil-1H-indol: ESMS m/e: 424.1 $(M + H)^+$.

Ejemplo 436

N-(3-{1-[(5-CIANO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 1H-indol-5-carbonitrilo: ESMS m/e: 401.1 $(M + H)^+$.

Ejemplo 437

2-METIL-N-(3-{1-[(5-METIL-2-FENIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 5-metil-2-fenil-1H-indol: ESMS m/e: 466.2 $(M + H)^+$.

Ejemplo 438

2-METIL-N-[3-(1-{[1-(4-NITROFENIL)-1H-INDOL-3-IL)METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 1-(4-nitrofenil)-1H-indol: ESMS m/e: 497.2 $(M + H)^+$.

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Ejemplo 439

N-[3-(1-{[1-(2-FLUOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 1-(2-fluorofenil)-1H-indol: ESMS m/e: 470.1 $(M + H)^+$.

Ejemplo 440

N-(3-{1-[(5,6-DIMETOXI-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 5,6-dimetoxi-1H-indol: ESMS m/e: 436.2 $(M + H)^+$.

Ejemplo 441

2-METIL-N-[3-(1-{[1-(3-METILFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 1-(3-metilfenil)-1H-indol: ESMS m/e: 466.2 $(M + H)^+$.

Ejemplo 442

2-METIL-N-{3-[1-({1-[3-(TRIFLUOROMETIL)FENIL]-1H-INDOL-3-IL}METIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el

procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 1-[3-(trifluorometil)fenil]-1H-indol: ESMS m/e: 520.2 $(M + H)^+$.

Ejemplo 443

N-[3-(1-{[1-(4-METOXIFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 5-metoxi-2-fenil-1H-indol: ESMS m/e: 482.2 $(M + H)^+$.

Ejemplo 445

2-METIL-N-(3-{1-[(5-METIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 5-metil-1H-indol: ESMS m/e: 390.2 $(M + H)^+$.

Ejemplo 446

N-[3-(1-{[1-(2-NITROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-(2-nitrofenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 497.2 $(M + H)^+$.

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Ejemplo 447

N-[3-(1-{[1-(2-METOXIFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-(2-metoxifenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 482.2 $(M + H)^+$.

Ejemplo 448

2-METIL-N-{3-[1-({1-[2-TRIFLUOROMETIL)FENIL]-1H-INDOL-3-IL}METIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-[2-(trifluorometil)fenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 520.2 $(M + H)^+$.

Ejemplo 449

N-(3-{1-[(5-METOXI-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1H-indol-5-ilmetiléster y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 406.2 $(M + H)^+$.

Ejemplo 450

N-[3-(1-{[1-(4-FLUOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-(4-fluorofenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 470.2 $(M + H)^+$.

Ejemplo 451

N-[3-(1-{[1-(3-METOXIFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-(3-metoxifenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 482.2 $(M + H)^+$.

Ejemplo 452

2-METIL-N-[3-(1-{[1-(2-METILFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-(2-metilfenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 46.2 $(M + H)^+$.

Ejemplo 453

3-({4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}METIL)-5-METOXI-1H-INDOL-2-CARBOXILATO DE ETILO: Preparado por el procedimiento D y esquema N utilizando 5-metoxi-1H-indol-2-

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carboxilato de etilo y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 478.2 $(M + H)^+$.

Ejemplo 454

N-(3-{1-[(5-FLUORO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 5-fluoro-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 394.2 $(M + H)^+$.

1-FENIL-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 1H-indol y yodobenceno: ESMS m/e: 193.9 $(M + H)^+$.

1-(4-CLOROFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 1H-indol y 1-cloro-4-yodobenceno: ESMS m/e: 227.9 $(M + H)^+$.

1-(3-CLOROFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 1H-indol y 1-cloro-2-yodobenceno: ESMS m/e: 227.9 $(M + H)^+$.

1-(2-CLOROFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 1H-indol y 1-cloro-2-yodobenceno: ESMS m/e: 227.9 $(M + H)^+$.

1-[2-(TRIFLUOROMETIL)FENIL]-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 1H-indol y 1-yodo-2-(trifluorometil)benceno: ESMS m/e: 262.0 $(M + H)^+$.

4-(1H-1-IL)BENZONITRILO: Preparado por el procedimiento C y esquema O utilizando 1H-indol y 4-yodobenzonitrilo: ESMS m/e: 219.0 $(M + H)^+$.

1-(4-NITROFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 1H-indol y 1-yodo-4-nitrobenceno: ESMS m/e: 238.2 $(M + H)^+$.

1-(2-NITROFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 1H-indol y 1-yodo-2-nitrobenceno: ESMS m/e: 238.2 $(M + H)^+$.

Ejemplo 455

N-[3-(1-{[1-(4-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-(4-clorofenil)-1H-

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indol y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 472.1 $(M + H)^+$.

Ejemplo 456

N-[3-(1-{[1-(3-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-(3-clorofenil)-1H-indol y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 472.1 $(M + H)^+$.

Ejemplo 457

N-[3-(1-{[1-(2-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]CICLOPROPANANCARBOXAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-(2-clorofenil)-1H-indol y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 484.1 $(M + H)^+$.

Ejemplo 458

N-[3-(1-{[1-(3-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-(3-clorofenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 468.1 $(M + H)^+$.

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Ejemplo 459

N-[3-(1-{[1-(4-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-(4-clorofenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 486.2 $(M + H)^+$.

Ejemplo 460

N-[3-(1-{[1-(2-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-(4-clorofenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 486.2 $(M + H)^+$.

Ejemplo 461

N-[3-(1-{[1-(2-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-(2-clorofenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 472.1 $(M + H)^+$.

Ejemplo 462

N-[3-(1-{[1-(4-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]CICLOPROPANCARBOXAMIDA: Preparado por el

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procedimiento D y esquema N utilizando 1-(4-clorofenil)-1H-indol y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 484.1 $(M + H)^+$.

Ejemplo 463

N-[3-(1-{[1-(3-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-(3-clorofenil)-1H-indol y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 484.1 $(M + H)^+$.

Ejemplo 464

N-(3-{1-[(1-FENIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-fenil)-1H-indol y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 438.2 $(M + H)^+$.

Ejemplo 465

N-(3-{1-[(1-FENIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-fenil)-1H-indol y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 450.2 $(M + H)^+$.

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6-CLORO-1-(4-NITROFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 6-cloro-1H-indol y 1-yodo-4-nitrobenceno: ESMS m/e: 272.6 $(M + H)^+$.

6-CLORO-1-(2,3-DICLOROFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 6-cloro-1H-indol y 1,2-dicloro-3-yodobenceno: ESMS m/e: 296.5 $(M + H)^+$.

6-CLORO-1-(3-METILFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 6-cloro-1H-indol y 1-yodo-3-metilbenceno: ESMS m/e: 241.9 $(M + H)^+$.

6-CLORO-1-(2-METILFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 6-cloro-1H-indol y 1-yodo-2-metilbenceno: ESMS m/e: 241.9 $(M + H)^+$.

2-(6-CLORO-1H-INDOL-1-IL)FENILMETILÉTER: Preparado por el procedimiento C y esquema O utilizando 6-cloro-1H-indol y 1-yodo-2-metoxibenceno: ESMS m/e: 257.9 $(M + H)^+$.

6-CLORO-1-[3-(TRIFLUOROMETIL)FENIL]-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 6-cloro-1H-indol y 1-yodo-3-(trifluorometil)benceno: ESMS m/e: 295.6 $(M + H)^+$.

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6-CLORO-1-(2-FLUOROFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 6-cloro-1H-indol y 1-fluoro-2-yodobenceno: ESMS m/e: 245.9 $(M + H)^+$.

6-CLORO-1-(3-CLOROFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 6-cloro-1H-indol y 1-cloro-3-yodobenceno: ESMS m/e: 261.9 $(M + H)^+$.

6-CLORO-1-(4-CLOROFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 6-cloro-1H-indol y 1-cloro-4-yodobenceno: ESMS m/e: 262.9 $(M + H)^+$.

6-CLORO-1-(2-CLOROFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 6-cloro-1H-indol y 1-yodo-3-yodobenceno: ESMS m/e: 262.972.6 $(M + H)^+$.

3-(6-CLORO-1H-INDOL-1-IL)FENILMETILÉTER: Preparado por el procedimiento C y esquema O utilizando 6-cloro-1H-indol y 1-yodo-3-metoxibenceno: ESMS m/e: 257.9 $(M + H)^+$.

6-CLORO-1-[4-(TRIFLUOROMETIL)FENIL]-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 6-cloro-1H-indol y 1-yodo-4-(trifluorometil)benceno: ESMS m/e: 295.6 $(M + H)^+$.

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6-CLORO-1-(4-METILFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 6-cloro-1H-indol y 1-yodo-4-metilbenceno: ESMS m/e: 241.9 $(M + H)^+$.

6-CLORO-1-(4-FLUOROFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 6-cloro-1H-indol y 1-fluoro-4-yodobenceno: ESMS m/e: 245.9 $(M + H)^+$.

Ejemplo 466

N-[3-(1-{[6-CLORO-1-(4-FLUOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-(4-fluorofenil)-1H-indol y N-[3-(4-piperidinil)fenil] ciclopropancarboxamida: ESMS m/e: 502.1 $(M + H)^+$.

Ejemplo 467

N-[3-(1-{[6-CLORO-1-(4-FLUOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-(4-fluorofenil)-1H-indol y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 490.1 $(M + H)^+$.

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Ejemplo 468

N-(3-{1-[(6-FLUORO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-(4-fluorofenil)-1H-indol y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 380.1 $(M + H)^+$.

Ejemplo 469

N-(3-{1-[(6-FLUORO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-fluoro-1H-indol y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 392.1 $(M + H)^+$.

Ejemplo 470

N-(3-{1-[(6-FLUORO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-fluoro-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 394.1 $(M + H)^+$.

Ejemplo 471

N-[3-(1-{[6-CLORO-1-(4-FLUOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el

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procedimiento D y esquema N utilizando 6-cloro-1-(4-fluorofenil)1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 504.1 $(M + H)^+$.

Ejemplo 472

N-[3-(1-{[6-CLORO-1-(2-FLUOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-(2-fluorofenil)1H-indol y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 490.1 $(M + H)^+$.

Ejemplo 473

N-[3-(1-{[6-CLORO-1-(2-FLUOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-(2-fluorofenil)1H-indol y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 502.1 $(M + H)^+$.

Ejemplo 474

N-[3-(1-{[6-CLORO-1-(2-FLUOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-(4-

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fluorofenil)1H-indol y 2-metil-N-[3-(2-piperidinil)fenil]propanamida: ESMS m/e: 504.1 $(M + H)^+$.

Ejemplo 475

N-[3-(1-{[6-CLORO-1-(4-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-(4-clorofenil)1H-indol y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 506.1 $(M + H)^+$.

Ejemplo 476

N-[3-(1-{[6-CLORO-1-(4-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL}CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-(4-clorofenil)1H-indol y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 518.1 $(M + H)^+$.

Ejemplo 477

N-[3-(1-{[6-CLORO-1-(4-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-(4-clorofenil)1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 520.1 $(M + H)^+$.

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Ejemplo 478

N-[3-(1-{[6-CLORO-1-(3-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-(4-clorofenil)1H-indol y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 506.1 $(M + H)^+$.

Ejemplo 479

N-[3-(1-{[6-CLORO-1-(3-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-(3-clorofenil)1H-indol y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: RMN ^1H: (400 MHz, $CDCl_3$) 7.72 (d, 1H, J = 8.4 Hz), 7.68 (s, 1H), 7.49 (m, 2H), 7.44 (d, 2H, J = 7.9 Hz), 7.49-7.25 (m, 4H), 7.21 (d, 1H, J = 7.9 Hz), 7.17 (d, 1H, J = 7.9 Hz), 6.93 (d, 1H, J = 7.9 Hz), 3.79 (s, 2H), 3.13 (d, 2H, J = 9.4 Hz), 2.48 (sept, 1H, J = 7.5 Hz), 2.16 (m, 2H), 1.80 (m, 4H), 1.51 (s, 1H), 1.06 (m, 2H), 0.806 (m, 2H); Análisis calculado para: $C_{30}H_{29}Cl_2N_3O+HCl+1.4H_2O$: C, 62.11; H, 5.70; N, 7.24. Encontrado: C, 62.19; H, 6.21; N, 7.06; ESMS m/e: 519.2 $(M + H)^+$.

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Ejemplo 480

N-[3-(1-{[6-CLORO-1-(3-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-(3-clorofenil)1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 520.1 $(M + H)^+$.

Ejemplo 481

N-(3-{1-[(5-FLUORO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento D y esquema N utilizando 5-fluoro-1H-indol y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 392.1 $(M + H)^+$.

Ejemplo 482

N-[3-(1-{[6-CLORO-1-(2-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-(2-clorofenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: *ESMS m/e:* 520.2 $(M + H)^+$.

Ejemplo 483

N-[3-(1-{[6-CLORO-1-(3-METOXIFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el

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procedimiento D y esquema N utilizando 3-(6-cloro-1H-indol-1-il)fenilmetiléter y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: *ESMS m/e:* 516.2 $(M + H)^+$.

Ejemplo 484

N-[3-(1-{[6-CLORO-1-(2-METOXIFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 2-(6-cloro-1H-indol-1-il)fenilmetiléter y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: *ESMS m/e:* 516.2 $(M + H)^+$.

Ejemplo 485

N-[3-(1-{[6-CLORO-1-(2,3-DICLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-(2,3-diclorofenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: *ESMS m/e: 555.1* $(M + H)^+$.

Ejemplo 486

N-[3-(1-{[6-CLORO-1-(4-METILFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1(4-

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metilfenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 500.2 $(M + H)^+$.

Ejemplo 487

N-{3-[1-({6-CLORO-1-[3-(TRIFLUOROMETIL)FENIL]-1H-INDOL-3-IL}METIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-[3-(trifluorometil)fenil]-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: *MS m/e:* 554.2 $(M + H)^+$.

Ejemplo 488

N-{3-[1-({6-CLORO-1-[4-(TRIFLUOROMETIL)FENIL]-1H-INDOL-3-IL}METIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-[4-(trifluorometil)fenil]-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 554.2 $(M + H)^+$.

Ejemplo 489

N-[3-(1-{[6-CLORO-1-(2-METILFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-(2-metilfenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 500.2 $(M + H)^+$.

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Ejemplo 490

N-[3-(1-{[6-CLORO-1-(3-METILFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA:

Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-(3-metilfenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 500.2 $(M + H)^+$.

Ejemplo 491

N-(3-{1-[(7-CLORO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento D y esquema N utilizando 7-cloro-H-1-indol y N[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 408. $(M + H)^+$.

Ejemplo 492

N-(3-{1-[(7-CLORO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 7-cloro-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 410.1 $(M + H)^+$.

Ejemplo 493

N-(3-{1-[(4-FLUORO-1H-INDOL-3-IL)METIL]-4-

PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 4-fluoro-1H-indol y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 380.2 (M + H)$^+$.

Ejemplo 494

N-(3-{1-[(7-CLORO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 7-cloro-1H-indol y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 396.1 (M + H)$^+$.

Ejemplo 495

2-METIL-N-(3-{1-[(6-METIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-metil-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 390.2 (M + H)$^+$.

Ejemplo 496

N-[3-(1-{[6-(BENCILOXI)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-(benciloxi)-1H-

indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 482.2 $(M + H)^+$.

Ejemplo 497

N-(3-{1-[(6-METOXI-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1H-indol-6-ilmetiléter y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 406.2 $(M + H)^+$.

Ejemplo 498

3-({4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}METIL)-1H-INDOL-6-CARBOXILATO DE METILO: Preparado por el procedimiento D y esquema N utilizando 1H-indol-6-carboxilato de metilo y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 434.2 $(M + H)^+$.

Ejemplo 499

2-METIL-N-[3-(1-{[6-(TRIFLUOROMETIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-(trifluorometil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: RMN ^1H (400 MHz, $CDCl_3$)

8.11 (s, 1H), 7.66 (s, 1H), 7.63 (s, 2H), 7.44 (d, 1H, J = 8.4 Hz) 7.39 (s, 2H), 7.32 (d, 1H, J = 8.4 Hz), 7.16 (t, 1H, J = 8.4 Hz), 6.84 (d, 1H, J = 8.4 Hz), 4.06 (s, 2H), 3.27 (d, 2H, J = 11.6 Hz), 2.56 (sept, 1H, J = 6.8 Hz), 2.37 (m, 3H), 1.93 (m, 2H), 1.75 (m, 2H), 1.22 (d, 6H, J = 6.8 Hz); Análisis calculado para: $C_{25}H_{28}F_3O$+2HCl+0.5EtOAc: C, 57.8; H, 6. 11; N, 7. 50. Encontrado: C, 56.5; H, 6.46; N, 7.77; ESMS m/e: 444.2 $(M + H)^+$.

1-(2-PIRIDINIL)-1H-INDOL: Preparado por el procedimiento C y esquema 0 utilizando 2-yodopiridina y 1H-indol: ESMS m/e: 195.0 $(M + H)^+$.

1-(3-PIRIDINIL)-1H-INDOL: Preparado por el procedimiento C y esquema 0 utilizando 3-yodopiridina y 1H-indol: ESMS m/e: 195.0 $(M + H)^+$.

Ejemplo 500

2-METIL-N-[3-(1-{[1-(3-PIRIDINIL)-1H-INDOL-3-IL]METIL}-4-PIPEPIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-(3-piridinil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 453.2 $(M + E)^+$.

Ejemplo 501

2-METIL-N-[3-(1-{[1-(2-PIRIDINIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-(2-piridinil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 453.2 $(M + H)^+$.

Ejemplo 502

N-(3-{1-[(6-FLUORO-1-FENIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-fluoro-1-fenil-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 470.2 $(M + H)^+$.

Ejemplo 503

N-(3-{1-[(6-CLORO-1-FENIL-1H-INDOL-3-IL)METIL]-4-PIPEPIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-cloro-1-fenil-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 486.2 $(M + H)^+$.

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7-METIL-1-FENIL-1H-INDOL: Preparado por el procedimiento C y esquema 0 utilizando 7-metil-1H-indol y yodobenceno: *ESMS m/e:* 208.1 (M + H)+.

1-FENIL-1H-INDOL-6-CARBOXILATO DE METILO: Preparado por el procedimiento C y esquema 0 utilizando metil-1H-indol-6-carboxilato y yodobenceno: ESMS m/e: 252.0 $(M + H)^+$.

6-METIL-1-FENIL-1H-INDOL: Preparado por el procedimiento C y esquema 0 utilizando 6-metil-1H-indol y yodobenceno:

7-CLORO-1-FENIL-1H-INDOL: Preparado por el procedimiento C y esquema 0 utilizando 7-cloro-1H-indol y yodobenceno: ESMS m/e: 22 8.0 $(M + H)^+$

6-NITRO-1-FENIL-INDOL: Preparado por el procedimiento C y esquema 0 utilizando 6-nitro-1H-indol y yodobenceno: ESMS m/e: 238.2 $(M + H)^+$.

6-METOXI-1-FENIL-1H-INDOL: Preparado por el procedimiento C y esquema 0 utilizando 1H-indol-6-ilmetiléter y yodobenceno: ESMS m/e: 224.0 $(M + H)^+$.

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BENCIL-1-FENIL-1H-INDOL-6-ILETER: Preparado por el procedimiento C y esquema 0 utilizando 6-(benciloxi-1H-indol y yodobenceno: ESMS *m/e:* 300.0 $(M + H)^+$

1-FENIL-1H-INDOL-6-ILTRIFLUOROMETILETER: Preparado por el procedimiento C y esquema 0 utilizando 6-(trifluorometoxi)-1H-indol y yodobenceno: ESMS m/e: 278.0 $(M + H)^+$.

7-METOXI-1-FENIL-1H-INDOL: Preparado por el procedimiento C y esquema 0 utilizando 1H-indol-7-ilmetiléter y yodobenceno: ESMS m/e: 224.0 $(M + H)^+$.

1-FENIL-6-(TRIFLUOROMETIL)-1H-INDOL: Preparado por el procedimiento C y esquema 0 utilizando 6-(trifluorometil)-1H-indol y yodobenceno: ESMS m/e: 262.0 $(M + H)^+$.

1-(4-PIRIDINIL)-1H-INDOL: Preparado por el procedimiento C y esquema 0 utilizando 1H-indol y 4-yodopiridina: ESMS m/e: 195 $(M + H)^+$.

Ejemplo 504

N-[3-(1-{[6-(BENCILOXI)-1-FENIL-1H-INDOL-3-IL]METIL}-

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4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-fenil-1H-indol-6-iléter bencílico y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 558.0 $(M + H)^+$.

Ejemplo 505

2-METIL-N-(3-{1-[(6-METIL-1-FENIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-metil-1-fenil-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: RMN ^1H (400 MHz, $CDCl_3$) 7.66 (s, 1H), 7.64 (d, 1H, J = 7.8 Hz), 7.51 (d, 1H, J = 3.9 Hz), 7.50 (m, 3H), 7.4 (m, 2H), 7.36-7.32 (m, 2H), 7,31 (s, 1H), 7.19 (t, 1H, J = 7.8 Hz), 7.04 (d, 1H, J = 7.8 Hz), 6.91 (d, 1H, J = 7.8 Hz), 3.94 (s, 2H), 3.25 (d, 2H, J = 9.2 Hz), 2.52 (sept, 1H, J = 6.4 Hz), 2.46 (s, 3H), 2.28 (dt, 2H, J = 11.8, 2.6 Hz), 1.89 (dq, 2H, J = 2.9 Hz), 1.80 (m, 3H), 1.22 (d, 6H, J = 6.9 Hz); Análisis calculado para: C, 72.2; H, 7.41; N, 7.57. Encontrado: C, 71.0; H, 7.40; N, 7.66; ESMS m/e: 466 $(M + H)^+$.

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Ejemplo 506

3-({4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}METIL)-1-FENIL-1H-INDOL-6-CARBOXILATO DE METILO: Preparado por el procedimiento D y esquema N utilizando 1-fenil-1H-indol-6-carboxilato de metilo y 2-metil-il-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 510.0 $(M + H)^+$.

Ejemplo 507

2-METIL-N-(3-{1-[(6-NITRO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-nitro-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 421.0 $(M + H)^+$.

Ejemplo 508

2-METIL-N-[3-(1-{[1-FENIL-6-(TRIFLUOROMETIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-fenil-6(trifluorometil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 520.0 $(M + H)^+$.

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Ejemplo 509

2-METIL-N-(3-{1-[(7-METIL-1-FENIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 7-metil-1-fenil-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 466.0 $(M + H)^+$.

Ejemplo 510

N-(3-{1-[(7-METOXI-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1H-indol-7-ilmetiléter y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 406.0 $(M + H)^+$.

Ejemplo 511

N-(3-{1-[(7-METOXI-1-FENIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 7-metoxi-1-fenil-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 482.0 $(M + H)^+$.

Ejemplo 512

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N-(3-{1-[(7-CLORO-1-FENIL-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 7-cloro-1-fenil-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 488.6 $(M + H)^+$.

Ejemplo 513

2-METIL-N-(3-{1-[(7-NITRO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 7-nitro-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 421.1 $(M + H)^+$.

Ejemplo 514

N-(3-{1-[(7-NITRO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento D y esquema N utilizando 7-nitro-1H-indol y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 419.5 $(M + H)^+$.

Ejemplo 515

N-(3-{1-[(7-NITRO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el

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procedimiento D y esquema N utilizando 7-nitro-1H-indol y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 407.3 (M + H)+.

7-(2-FLUOROFENIL)-1H-INDOL: Preparado por el procedimiento I y esquema T utilizando 7-bromo-1H-indol y ácido 2-fluorofenilborónico: ESMS m/e: 211.9 $(M + H)^+$.

Ejemplo 516

N-[3-(1-{[7-(2-FLUOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)PI-IENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N. Una solución de 2-metil-N-[3(4-piperidinil)fenil]propanamida (23.3 mg, 0.0948 mmoles) y 37% en peso de formaldehído acuoso (11.4 mg, 0.142 mmoles) en 1.00 ml de HOAc:dioxano (1:4) se agrega a 7-(2-fluorofenil)-1H-indol (20.0 mg, 0.0948 mmoles) y la mezcla de reacción se agita durante 12 horas a temperatura ambiente. La mezcla resultante se diluye con H_2O (10 ml). La capa acuosa se extrae con CH_2Cl_2 (3 x 10 ml). Los extractos combinados se lavan con salmuera (10 ml), se secan sobre $MgSO_4$ y se concentran in *vacuo*. El residuo se purifica por TLC preparativa en sílice utilizando 4% de NH_3 (2.0 M en metanol) en CH_2Cl_2 para proporcionar el producto deseado

(56.1 mg, 100%): RMN ^{1}H (400 MHz, $CDCl_3$) 8.58 *(s, 1H)*, 7.73 (dd, 1H, *J* = 2.8, 6.3 Hz), 7.69 *(s, 1H)*, 7.53 (dt, IH, J = 1.8, 7.6 Hz), 7.44 (d, 1H, J = 8.1 Hz), 7.38 (m, 2H), 7.32 (s, 1H), 7.27-7.21 (m, 4H), 7.17 (t, 1H, J = 7.6 Hz), 6.88 (d, 1H, J = 7.6 Hz), 3.92 (s, 2H); 3.20 (d, 1H, J = 11.6 Hz), 2.51 (qt, 1H, *J* = 6.7 Hz), 2.42 (m, 1H), 2.25 (dt, 2H, *J* = 2.2, 11.6 Hz), 1.89-1.72 (m, 5H), 1.22 (d, 6H, J = 7.3 Hz); ESMS m/e: 470.1 $(M + H)^+$.

7-(4-ETILFENIL)-1H-INDOL: Preparado por el procedimiento I y esquema T utilizando 7-bromo-1H-indol y ácido 4-etilfenilborónico: ESMS m/e: 222.0 $(M + H)^+$.

7-(2-NAFTIL)-1H-INDOL: Preparado por el procedimiento T y esquema T utilizando 7-bromo-1H-indol y ácido 2-naftilborónico: ESMS m/e: 244.0 $(M + H)^+$.

7-(3-CLOROFENIL)-1H-INDOL: Preparado por el procedimiento I y esquema T utilizando 7-bromo-1H-indol y ácido 3-clorofenilborónico: ESMS m/e: 227.9 $(M + H)^+$.

6-(2-FLUOROFENIL)-1H-INDOL: Preparado por el procedimiento I y esquema T utilizando 6-bromo-1H-indol y ácido 2-fluorofenilborónico: ESMS *m/e:* 211.9 $(M + H)^+$.

7-(3-NITROFENIL)-1H-INDOL: Preparado por el procedimiento I y

Esquema T utilizando 7-bromo-1H-indol y ácido 3-nitrofenilborónico: ESMS *m/e:* 238.9 (M + H)+.

1-[4-(1H-INDOL-7-IL)FENIL]ETANONA: Preparado por el procedimiento I y esquema T utilizando 7-bromo-1H-indol y ácido 4-acetilfenilborónico: ESMS m/e: 235.2 $(M + H)^+$.

6-(2-METILFENIL)-1H-INDOL: Preparado por el procedimiento I

y esquema T utilizando 6-bromo-1H-indol y ácido 2-metilfenilborónico: ESMS m/e: 207.9 $(M + H)^+$.

6-(3-CLOROFENIL)-1H-INDOL: Preparado por el procedimiento I

y esquema T utilizando 6-bromo-1H-indol y ácido 3-clorofenilborónico: ESMS m/e: 227.9 $(M + H)^+$.

1-[4-(1H-INDOL-6-IL)FENIL]ETANONA: Preparado por el procedimiento I y esquema T utilizando 6-bromo-1H-indol y ácido 4-acetilfenilborónico: ESMS m/e: 235.8 $(M + H)^+$

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7-(2-METILFENIL)-1H-INDOL: Preparado por el procedimiento I y Esquema T utilizando 7-bromo-1H-indol y ácido 2-metilfenilborónico: ESMS m/e: 208 $(M + H)^+$.

6-(4-ETILFENIL)-1H-INDOL: Preparado por el procedimiento I y Esquema T utilizando 6-bromo-1H-indol y ácido 4-etilfenilborónico: ESMS *m/e*: 221.9 $(M + H)^+$.

Ejemplo 517

2-METIL-N-[3-(1-{[7-(2-NAFTIL)-1H-INDOL-3-IL]METIL}4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 7-(2-naftil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 502.2 $(M + H)^+$.

Ejemplo 518

N-[3-(1-{[7-(4-ETILFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 7-(4-etilfenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 480.2 $(M + H)^+$.

Ejemplo 519

2-METIL-N-[3-(1-{[6-(2-METILFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-(2-metilfenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: RMN ^1H (400 MHz, $CDCl_3$) 8.2 (s, 1H), 7.53 (m, 4H), 7.41 (d, 1H, J 8.4 Hz), 7.34 (m, 2H), 7.27-7.12 (m, 5H), 6.81 (d, 1H, J = 8.4 Hz), 4.09 (s, 2H), 3.32 (d, 2H, J = 11.4 Hz), 2.57 (q, 2H, J = 7.6 Hz), 2.43 (m, 3H), 2.08 (s, 3H), 1.98 (m, 1H), 1.75 (m, 2H), 1.22 (d, 6H, J = 6.3 Hz); Análisis calculado para: C, 57.0; H, 6.09; N, 8.06. Encontrado: C, 56.5; H, 5.94; N, 7.76; ESMS m/e: 466.2 $(M + H)^+$.

Ejemplo 520

N-[3-(1-{[7-(3-CLOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 7-(3-clorofenil)-1H-indol y 2-metil-N-(3-(4-piperidinil)fenil]propanamida: ESMS m/e: 486.1 $(M + H)^+$.

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Ejemplo 521

2-METIL-N-[3-(1-{[7-(3-NITROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 7-(3-nitrofenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 497.0 $(M + H)^+$.

Ejemplo 522

N-[3-(1-{[7-(4-ACETILFENIL)-1H-INDOL-3-IL]METIL)-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 1-[4-(1H-indol-7il)fenil]etanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 493.6 $(M + H)^+$.

Ejemplo 523

N-[3-(1-{[6-(4-ETYLFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-(4-etilfenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 480.1 $(M + H)^+$.

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Ejemplo 524

2-METIL-N-[3-(1-{[7-(2-METILFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 7-(2-metilfenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 466.1 $(M + H)^+$.

Ejemplo 525

N-[3-(1-{[6-(2-FLUOROFENIL)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 6-(2-fluorofenil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 470.2 $(M + H)^+$.

5-(4-METILFENOXI)-1H-INDOL: Preparado por el procedimiento I y esquema U utilizando 5-bromo-1H-indol y p-cresol: ESMS *m/e*. 224.0 $(M + H)^+$.

Ejemplo 526

N-(3-{1-[(5-BROMO-1H-INDOL-3-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 5-bromo-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 454.0 $(M + H)^+$.

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1-(4-PIRIDINIL)-6-(TRIFLUOROMETIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 6-(trifluorometil)-1H-indol y 4-yodopiridina: ESMS m/e 262.9 $(M + H)^+$.

Ejemplo 527

2-METIL-N-[3-(1-{[5-(4-METILPEENOXY)-1H-INDOL-3-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento D y esquema N utilizando 5-(4-metilfenoxi)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 481.9 $(M + H)^+$.

1-(4-METILFENL)-1H-INDOL: Preparado por el procedimiento C y esquema 0 utilizando 1H-indol y 1-yodo-4-metilbenceno: ESMS m/e: 208.0 $(M + H)^+$.

1-(3-METILFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema 0 utilizando 1H-indol y 1-yodo-3-metilbenceno: *ESMS m/e:* 208.0 $(M + H)^+$.

1-[3-(TRIFLUOROMETIL)FENIL]-1H-INDOL: Preparado por el procedimiento C y esquema 0 utilizando 1H-indol y 1-yodo-3(trifluorometil)benceno: ESMS m/e: 262.0 $(M + H)^+$.

1-(4-METOXIFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 1H-indol y 1-yodo-4-metoxibenceno: ESMS *m/e*: 224.0 $(M + H)^+$.

1-(2-METOXIFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 1H-indol y 1-yodo-2-metoxibenceno: ESMS m/e: 224.0 $(M + H)^+$.

1-(3-METOXIFENIL)-1H-INDOL: Preparado por el procedimiento C y Esquema O utilizando 1H-indol y 1-yodo-3-metoxibenceno: ESMS m/e: 224.0 $(M + H)^+$.

1-(2-METILFENIL)-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 1H-indol y 1-yodo-2-metilbenceno: ESMS m/e: 208.0 $(M + H)^+$.

6-FLUORO-1-FENIL-1H-INDOL: Preparado por el procedimiento C y esquema O utilizando 6-fluoro-1H-indol y yodobenceno: ESMS m/e: 212.0 $(M + H)^+$.

6-CLORO-1-FENIL-1H-INDOL: Preparado por el procedimiento C y esquema 0 utilizando 6-cloro-1H-indol y yodobenceno: ESMS *m/e*: 212.0 $(M + H)^+$.

7-CLORO-1-FENIL-1H-INDOL: Preparado por el procedimiento C y esquema 0 utilizando 7-cloro-1H-indol y yodobenceno: ESMS m/e: 228.0 $(M + H)^+$.

6-(2-FLUOROFENIL)-1H-INDOL: Preparado por el procedimiento I y esquema T utilizando 6-bromo-1H-indol y ácido 2-fluorofenilborónico: ESMS *m/e*: 211.9 $(M + H)^+$.

Ejemplo 528

2-METIL-N-{3-[1-(7-OXO-7-FENILHEPTIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 7-cloro-1-fenil-1-heptanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 435.1$(M + 1)^+$.

Ejemplo 529

2-METIL-N-{3-[1-(6-OXO-6-FENILHEXIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 6-cloro-1-fenil-1-

hexanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: Análisis calculado para: $C_{27}H_{36}N_2O_2+0.1CHCl_3$: C, 75.3; H, 8.39; N, 6.46. Encontrado: C, 75.4; H, 7.89; N, 6.18; ESMS *m/e*: 421.1 $(M + H)^+$.

Ejemplo 530

2-METIL-N-{3-[1-(5-OXO-5-FENILPENTIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 5-cloro-1-fenil-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 407.1 $(M + H)^+$.

Ejemplo 531

N-(3-{1-[4-(4-METOXIFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento K y Esquema B1 utilizando 4-cloro-1-(4-metoxifenil)-1-butanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 409-2 $(M + H)^+$.

Ejemplo 532

N-(3-{1-[4-(4-CLOROFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 4-cloro-1-(4-

clorofenil)-1-butanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 413.1 $(M + H)^+$.

Ejemplo 533

N-(3-{1-[4-(4-BROMOFENIL)-4-OXOBUTIL]-4-PIPEPIDINIL}FENIL) PROPANAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 1-(4-bromofenil)-4-cloro-1-butanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 457.1 $(M + H)^+$.

Ejemplo 534

N-(3-{1-[4-(4-TERBUTILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL) PROPANAMIDA. Preparado por el procedimiento K y Esquema B1 utilizando 1-(4-ter-butilfenil)-4-cloro-1-butanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 435.2 $(M + H)^+$.

Ejemplo 535

N-(3-{1-[4-(4-FLUOROFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 4-cloro-1-(4-fluorofenil)-1-butanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 397.2 $(M + H)^+$.

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Ejemplo 536

N-(3-{1-[4-OXO-4-(4-FENOXIFENIL)BUTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento K y esquema Bl utilizando 4-cloro-1-(4-fenoxifenil)-1-butanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 471.2 $(M + H)^+$.

Ejemplo 537

N-(3-{1-[4-(4-ISOPROPILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento K y esquema Bl utilizando 4-cloro-1-(4-isopropilfenil)-1-butanona y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 433.2 $(M + H)^+$.

Ejemplo 538

N-(3-{1-[4-(4-METOXIFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento K y Esquema Bl utilizando 4-cloro-1-(4-metoxifenil)-1-butanona y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 421.2 $(M + H)^+$.

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Ejemplo 539

N-(3-{1-[4-OXO-4-(4-FENOXIFENIL)BUTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento K y Esquema Bl utilizando 4-cloro-1-(4-fenoxifenil)-1-butanona y *N*-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 483:2 $(M + H)^+$.

Ejemplo 540

N-(3-{1-14-(4-ISOPROPILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento K y Esquema Bl utilizando 4-cloro-1-(4-isopropilfenil)-1-butanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 421.3 $(M + H)^+$.

Ejemplo 541

N-(3-{1-[4-(4-TER-BUTILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL)FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento K y esquema Bl utilizando 1-(4-ter-butilfenil)-4-cloro-1-butanona y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 447.2 $(M + H)^+$.

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Ejemplo 542

N-(3-{1-[4-(4-METILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento K y esquema Bl utilizando 4-cloro-1-(4-metilfenil)-1-butanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 393.2 $(M + H)^+$.

Ejemplo 543

N-(3-{1-[4-(3,4-DIMETILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento K y Esquema Bl utilizando 4-cloro-1-(3,4-dimetilfenil)-1-butanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 407.2 $(M + H)^+$.

Ejemplo 544

N-(3-{1-[4-(4-BRMOFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento K y esquema Bl utilizando 1-(4-bromofenil) -4-cloro-1-butanona y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 469.1 $(M + H)^+$.

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Ejemplo 545

N-(3-{1-[5-(4-FLUOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento K y esquema Bl utilizando 5-cloro-1-(4-fluorofenil)-1-pentanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 411.2 $(M + H)^+$.

Ejemplo 546

N-(3-{1-[4-(3,4-DIMETILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el Procedimiento K y esquema Bl utilizando 4-cloro-1-(3,4--dimetilfenil)-1-butanona y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 419.2 $(M + H)^+$.

Ejemplo 547

N-(3-{1-[4-(4-METILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento K y esquema Bl utilizando 4-cloro-1-(4-metilfenil)-1-butanona y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 405.2 $(M + H)^+$.

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Ejemplo 548

N-(3-{1-[4-(4-FLUOROFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 4-cloro-1-(4-fluorofenil)-1-butanona y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 409.2 $(M + H)^+$.

Ejemplo 549

N-(3-{1-[5-(3-FLUOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por Procedimiento K y esquema B1 utilizando 5-cloro-1-(3-fluorofenil)-1-pentanona y *N-[3-(4-*piperidinil)fenil]ciclopropancarboxamida: ESMS *m/e:* 423.2 $(M + H)^+$.

Ejemplo 550

N-[3-(1-{5-OXO-5-[4-(TRIFLUOROMETIL)FENIL]PENTIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 5-cloro-1-[4-(trifluorometil)fenil]-1-pentanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 461.2 $(M + H)^+$.

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Ejemplo 551

N-(3-{1-[5-(4-FLUOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 5-cloro-1-(4-fluorofenil)-1-pentanona y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS *m/e:* 423.2 $(M + H)^+$.

Ejemplo 552

N-(3-{1-[5-(3-NITROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 5-cloro-1-(3-nitrofenil)-1-pentanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 438.2 $(M + H)^+$.

Ejemplo 553

N-(3-{1-[5-(3-NITROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento *K* y esquema B1 utilizando 5-cloro-1-(3-nitrofenil)-1-pentanona y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 450.2 $(M + H)^+$.

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Ejemplo 554

N-(3-{1-[5-(2-FLUOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento K y esquema B 1 utilizando 5-cloro-1-(2-fluorofenil)-1-pentanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 411.2 $(M + H)^+$.

Ejemplo 555

N-(3-{1-[5-(3-FLUOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento K y esquema Bl utilizando 5-cloro-1-(3-fluorofenil)-1-pentanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 411.2 $(M + H)^+$.

Ejemplo 556

N-(3-{1-[5-(4-NITROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento K y esquema Bl utilizando 5-cloro-1-(4-nitrofenil)-1-pentanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 438.1 $(M + H)^+$.

Ejemplo 557

N-(3-{1-[5-(4-NITROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 5-cloro-1-(4-nitrofenil)-1-pentanona y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS *m/e:* 450.1 $(M + H)^+$.

Ejemplo 558

N-(3-{1-[5-(4-CLOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 5-cloro-1-(4-clorofenil)-1-pentanona y *N-[3-(4-*piperidinil)fenil]ciclopropancarboxamida: ESME m/e: 439.1 $(M + H)^+$.

Ejemplo 559

N-[3-(1-{5-OXO-5-[2-(TRIFLUOROMETIL)FENIL]PENTIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 5-cloro-1-[2-(trifluorometil)fenil]-1-pentanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e:* 461.2 $(M + H)^+$.

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Ejemplo 560

N-[3-(1-{5-OXO-5-[2-(TRIFLUOROMETIL)FENIL]PENTIL}-4-PIPERIDINIL)FENIL]CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 5-cloro-1-[2(trifluorometil)fenil]-1-pentanona y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS *m/e:* 473.2 (M + H)$^+$.

Ejemplo 561

N-(3-{1-[5-(4-CLOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 5-cloro-1-(4-clorofenil)-1-pentanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 427.1 (M + H)$^+$.

Ejemplo 562

N-(3-{1-[5-(3-CLOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL) PROPANAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 5-cloro-1-(3-clorofenil)-1-pentanona y N-[3-(4-piperinil)fenil]propanamida: ESMS m/e: 427.1 (M + H)$^+$.

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Ejemplo 563

N-(3-{1-[5-(2-FLUOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por procedimiento *K* y esquema B1 utilizando 5-cloro-1-(2-fluorofenil)-1-pentanona y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 423.1 (M + H)$^+$.

Ejemplo 564

N-(3-{1-[5-(3-CLOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por procedimiento *K* y esquema B1 utilizando 5-cloro-1-(3-clorofenil)-1-pentanona y *N*-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 439.1 (M + H)$^+$.

Ejemplo 565

N-[3-(1-{5-OXO-5-[4-(TRIFLUOROMETIL)FENIL]PENTIL}-4-PIPERIDINIL)FENIL]CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 5-cloro-1-[4(trifluorometil)fenil]-1-pentanona y *N*-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS *m/e:* 473.2 (M + H)$^+$.

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Ejemplo 566

N-(3-{1-15-(2-CLOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento K y esquema Bl utilizando 5-cloro-1-(2-clorofenil)-1-pentanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 427.1 $(M + H)^+$.

Ejemplo 567

N-(3-{1-5-(2-CLOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento K y esquema Bl utilizando 5-cloro-1-(2-clorofenil)-1-pentanona y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 439.1 $(M + H)^+$.

Ejemplo 568

N-[3-(1-{5-OXO-5-[3-(TRIFLUOROMETIL)FENIL]PENTIL}-4-PIPERIDINIL)FENIL]CICLOPROPANCARBOXAMIDA: Preparado por el procedimiento K y esquema Bl utilizando 5-cloro-1-[3(trifluorometil)fenil]-1-pentanona y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS *m/e*: 473.2 $(M + H)^+$.

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Ejemplo 569

N-(3-{1-[4-(3,4-DIMETILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)-N,2-DIMETILPROPANAMIDA: Preparado por el procedimiento T y esquema AD utilizando N-(3-{1-[4-(3,4-dimetilfenil)-4-oxobutil]-4-piperidinil}fenil)-2-etilpropanamida y yoduro de metilo. RMN ^{1}H (400 MHz, $CDCl_3$) 7.76 (s, 1H), 7.72 (dd, 1H, J = 1.8, 7.7 Hz), 7.33 (t, 1H, J = 8.8 Hz), 7.22 (d, 1H, J = 7.8 Hz), 7.18 (d, 1H, J = 8.8 Hz), 7.01 (m, 2H), 3.24 (s, 3H), 3.10 (d, 1H, J = 10.6 Hz), 3.00 (t, 1H, J = 7.6 Hz), 2.49 (m, 4H), 2.33 (s, 6H), 2.11 (m, 3H), 1.99 (m, 1H), 1.79 (m, 1H), 1.26 (t, 2H, J = 7.6 Hz), 1.02 (d, 6H, J = 7.6 Hz); ESMS m/e: 435.2 $(M + H)^+$.

Ejemplo 570

2-METIL-N-{3-[1-(1-METIL-4-OXO-4-FENILBUTIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 4-cloro-1-fenil-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 407.2 $(M + H)^+$.

Ejemplo 571

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N-1[-(1-{5-OXO-5-[3-(TRIFLUOROMETIL)FENIL]PENTIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento K y esquema B1 utilizando 5-cloro-1-[3-(trifluorometil)fenil]-1-pentanona y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 461.2 $(M + H)^+$.

3-(5-CLOROPENTANOIL)-4-(3,4-DIFLUOROFENIL)-1,3-OXAZOLIDIN-2-ONA: Preparado por el procedimiento AF y esquema H utilizando 4-(3,4-difluorofenil)-1,3-oxazolidin-2-ona y cloruro de cloropentanoilo.

3-(5-CLOROPENTIL)-4-(3,4-DIFLUOROFENIL)-1,3-OXAZOLIDIN-2-ONA: Preparado por el procedimiento G y Esquema C1 utilizando 4-(3,4-difluorofenil)-1,3-oxazolidin-2-ona y 1-bromo-5-cloropentano.

Ejemplo 572

N-[3-(1-{5-[(4R)-4-(3,4-DIFLUOROFENIL)-2-OXO-1,3-OZAZOLIDIN-3-IL]-5-OXOPENTIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento G y Esquema B1 utilizando (4R)-3-(5-cloropentanoil)-4-(3,4-difluorofenil)-1,3-oxazolidin-2-ona y 2-metil-N-[3(4-piperidinil)fenil]propanamida: *ESMS m/e* 528.2 $(M + H)^+$.

Ejemplo 573

(4R)-4-(3,4-DIFLUOROFENIL)-N-(3-{4-3(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-2-OXO-1,3-OXAZOLIDIN-3-CARBOXAMIDA: Preparado por el procedimiento AF y esquema H utilizando 4-nitrofenil (4R)-4(3,4-difluorofenil)-2-oxo-1,3-oxazolidin-3-carboxilato y N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida: RMN ^{1}H (400 MHz, $CDCl_3$) 8.08 (t, 1H, J = 5.5 Hz), 7.45 (s, 2H), 7.38 (d, 1H, *J* = 8.6 Hz), 7.24-7.12 (m, 3H), 7.06 (m, 1H), 6.97 (d, 1H, *J* = 8.6 Hz), 5.40 (dd, 1H, *J* = 3.9,8.8 Hz), 4.71 (t, 1H, *J* = 8.8 Hz), 4.23 (dd, 1H, *J* = 4.4, 9.1 Hz), 3.32 (qt, 2H, J = 6.1 Hz), 2.99 (d, 1H, *J* = 11.0 Hz), 2.49 (qt, 2H, J = 7.0 Hz), 2.41 (t, 2H, J = 7.0 Hz), 1.99 (m, 2H), 1.82-1.68 (m, 6H), 1.23 (d, 6H, *J* = 7.3 Hz); ESMS m/e: 529.1 $(M + H)^+$.

(4S)-3-(5-CLOROPENTIL)-4-(3,4-DIFLUOROFENIL)-1,3-OXAZOLIDIN-2-ONA: Preparado por el procedimiento G y esquema C1 utilizando (4S)-4-(3,4-difluorofenil)-1,3-oxazolidin-2-ona y 1-bromo-5-cloropentano.

Ejemplo 574

H-[3-(1-{5-[(4S)-4-(3,4-DIFLUOROFENIL)-2-OXO-1,3-OXAZOLIDIN-3-IL]PENTIL}-4-PIPERIDINIL)FENIL]-2-

METILPROPANAMIDA: Preparado por el procedimiento G y Esquema Bl utilizando (4S)-3-(5-cloropentil)-4-(3,4-difluorofenil)-1,3-oxazolidin 2-ona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: RMN ^1H (400 MHz, $CDCl_3$) 7.48 (s, 1H), 7.32 (d, 1H, J = 8.6 Hz), 7.26-7.21 (m, 2H), 7.20-7.12 (m, 2H), 7.06 (m, 1H), 6.97 (d, 1H, J = 6.96 Hz), 4.76 (dd, 1H, J = 6.3, 8.3 Hz), 4.62 (t, 1H, J = 9.0 Hz), 4.06 (dd, 1H, J 6.4, 8.7 Hz), 3.46 (m, 1H), 3.0 (d, 2H, J = 9.0 Hz), 2.77 (q, 1H, J = 6.8 Hz), 2.50 (q, 2H, J = 6.8 Hz), 2.31 (t, 2H, J = 6. 8 Hz), 2.01 (m, 4H), 1.81 (m, 4H), 1.48 (m, 4H), 1.26 (d, 6H, J = 7.3 Hz); Análisis calculado para $C_{28}H_{37}F_2N_3O_3$+HCl+0.25$CHCl_3$: C, 60.6; H, 6.65; N, 7.25. Encontrado: C, 60.7; H, 6.91; N, 7.05: ESMS m/e: 514.2 $(M + H)^+$.

Ejemplo 575

N-[3-(1-{5-[(4S)-4-(3,4-DIFLUOROFENIL)-2-OXO-1,3-OXAZOLIDIN-3-IL]-5-OXOPENTIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento G y Esquema Bl utilizando (4S)-3-(5-cloropentanoil)-4-(3,4-difluorofenil)-1,3-oxazolidin-2-ona y 2-metil-N-[3(4-piperidinil)fenil]propanamida: ESMS m/e: 528.1 $(M + H)^+$.

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Ejemplo 576

(4S)-4-(3,4-DIFLUOROFENIL)-N-(3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-2-OXO-1,3-OXAZOLIDIN-3-CARBOXAMIDA: Preparado por el procedimiento AF y esquema H utilizando 4-nitrofenil (4S)-4-(3,4-difluorofenil)-2-oxo-1,3-oxazolidin-3-carboxilato y N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS m/e: 529.1 $(M + H)^+$.

Ejemplo 577

(4S)-N-(3-{4-[3-(ISOBUTIRILAMINO)FENIL]-PIPERIDINIL}PROPIL)-2-OXO-4-(3,4,5-TRIFLUOROFENIL)-1,3-OXAZOLIDIN-3-CARBOXAMIDA: Preparado por el procedimiento AF y Esquema H utilizando (4S)-4-(3,4-difluorofenil)-2-oxo-1,3-oxazolidin-3-carboxilato de 4-nitrofenilo y N-3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e:* 547.1 $(M + H)^+$.

Ejemplo 578

(4S)-4-(3,5-DIFLUOROFENIL)-N-(3-{4-3(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-2-OXO-1,3-OXAZOLIDIN-3-CARBOXAMIDA: Procedimiento AF y esquema H utilizando (4S)-4(3,4-difluorofenil)-2-oxo-1,3-oxazolidin-

3-carboxilato de 4-nitrofenilo y N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e:* 529.2 $(M + H)^+$.

Ejemplo 579

N-(3-{1-[3-(FENILSULPANIL)PROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento G y esquema Bl utilizando [(3-cloropropil)sulfanil]benceno y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 382.9 $(M + H)^+$.

Ejemplo 580

N-(3-{1-[3-(FENILSULFANIL)PROPIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por Procedimiento G y esquema Bl utilizando [(3cloropropil)sulfanil]benceno y *N-[3-(4-*piperidinil)fenil]ciclopropancarboxamida: ESMS m/e: 395.1 $(M + H)^+$.

Ejemplo 581

2-METIL-N-(3-{1-[3-(FENILSULFANIL)PROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento G y esquema Bl utilizando [(3-

cloropropil)sulfanil]benceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: RMN ^{1}H (400 MHz, CDCl3) 7.63 (s, 1H), 7.4 8 (s, 1H) 7.33 (m, 3H), 7.27 (t, 2H, J = 7.5 Hz), 7.20 (t, 1H, J = 7.9 Hz), 7.15 (tt, 1H, J = 7.2, 1.4 Hz) , 6.95. (d, 1H, J = 7.6 Hz), 2.97 (t, 4H, J = 7.3 Hz), 2.46 (m, 4H) , 1. 99 (dt, 2H, *J* = 11.4, 3.0 Hz), 1.64 (qt, 2H, J = 7.3 Hz), 1.77 (m, 4H), 1.21 (d, 6H, *J* = 6. 8 Hz); ESMS m/e: 396.8 $(M + H)^+$.

Ejemplo 582

N-(3-{1-[6-(FENILSULFANIL)HEXIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por el Procedimiento G y esquema Bl utilizando [(6-clorohexil)sulfanil]benceno y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS *m/e*: 437.4 $(M + H)^+$.

Ejemplo 583

N-(3-{1-[4-(FENILSULFANIL)BUTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento G y esquema Bl utilizando [(4-clorobutil)sulfanil]benceno y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 396.8 $(M + H)^+$.

Ejemplo 584

N-(3-{1-[4-(FENILSULFANIL)BUTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por Procedimiento G y esquema Bl utilizando [(4-clorobutil)sulfanil]benceno y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS *m/e:* 409.5 $(M + H)^+$.

Ejemplo 585

2-METIL-N-(3-{1-[4-(FENILSULFANIL)BUTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento G y esquema Bl utilizando [(4-clorobutil)sulfanil]benceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 410.6 $(M + H)^+$.

Ejemplo 586

2-METIL-N-(3-{1-[5-(FENILSULFANIL)PENTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento G y esquema Bl utilizando [(5-cloropentil)sulfanil]benceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 425.1 $(M + H)^+$.

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Ejemplo 587

N-(3-{1-[5-(FENILSULFANIL)PENTIL]-4-PIPERIDINIL}FENIL)CICLOPROPANCARBOXAMIDA: Preparado por Procedimiento G y esquema B1 utilizando [(5-cloropentil)sulfanil]benceno y N-[3-(4-piperidinil)fenil]ciclopropancarboxamida: ESMS *m/e:* 423.1 $(M + H)^+$.

[(6-CLOROHEXIL)SULFANIL]BENCENO: Preparado por el procedimiento R y esquema Z utilizando bencentiol y 1-bromo-6-clorohexano.

[(4-CLOROBUTIL)SULFANIL]BENCENO: Preparado por el procedimiento R y esquema Z utilizando bencentiol y 1-bromo-4-clorobutano.

Ejemplo 588

N-(3-{1-[6-(FENILSULFANIL)HEXIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando [(6-clorohexil)sulfanil]benceno y N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 425.4 $(M + H)^+$.

[(5-CLOROPENTIL)SULFANIL]BENCENO: Preparado por el procedimiento R y esquema Z utilizando bencentiol y 1-bromo-5-cloropentano.

[(3-CLOROPROPIL)SULFANIL]BENCENO: Preparado por el procedimiento R y esquema Z utilizando bencentiol y 1-bromo-3-cloropropano: RMN ^{1}H (400 MHz, $CDCl_3$) 7.37- 7.34 (m, 2H), 7.32-7.26 (m, 2H) , 7.19 (tt, 1H, J = 1.4, 7.3 Hz), 3. 67 (t, 2H, *J* = 6.6 Hz), 3.08 (t, 2H, *J* = *6.6* Hz), 2.06 (qt, 2H, J = 6.6 Hz).

Ejemplo 589

N-(3-{1-[5-(FENILSULFANIL)PENTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando [(5-cloropentil)sulfanil]benceno y N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e:* 411.1 (M + H)+.

4-FLUOROFENILSULFURO DE 3-CLOROPROPILO: Preparado por el procedimiento R y esquema Z utilizando 4-fluorobencentiol y 1-bromo-3-cloropropano.

1-BROMO-2-[(3-CLOROPROPIL)SULFANIL]BENCENO: Preparado por el procedimiento R y esquema Z utilizando 2-bromobencentiol y 1-bromo-3-cloropropano.

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4-FLUOROFENILSULFOXIDO DE 3-CLOROPROPILO: Preparado por el procedimiento S y esquema AA utilizando 3-cloropropilo 4-fluorofenil sulfuro y 1 eq M-CPBA: RMN ^{1}H (400 MHz, $CDCl_3$) 7.65-7.62 (m, 2H), 7.28-7.21 (m, 2H), 3.65 (m, 2H), 2.94 (m, 2H), 2.28 (m, 1H), 2.06 (m, 1H); ESMS m/e: 220.9 $(M + H)^+$.

FLUOROFENILSULFURO DE 3-CLOROPROPILO: Preparado por el procedimiento R y esquema Z utilizando 3-fluorobencentiol y 1-bromo-3-cloropropano.

2-FLUOROFENILSULFURO DE 3-CLOROPROPILO: Preparado por el procedimiento R y esquema Z utilizando 2-fluorobencentiol y 1-bromo-3-cloropropano.

1-BROMO-2-[(3-CLOROPROPIL)SULFINIL]BENCENO: Preparado por el Procedimiento S y esquema AA utilizando 1-bromo-2-[(3cloropropil)sulfanil]benceno y 1 eq *M-CPBA*: ESMS m/e: 282.8 $(M + H)^+$.

1-CLORO-2-[(3-CLOROPROPIL)SULFANIL]BENCENO: Preparado por el procedimiento R y esquema Z utilizando 2-clorobencentiol y 1-bromo-3-cloropropano.

1-CLORO-3-[(3-CLOROPROPIL)SULFANIL]BENCENO: Preparado por el procedimiento R y esquema Z utilizando 3-clorobencentiol y 1-bromo-3-cloropropano.

1-CLORO-4-[(3-CLOROPROPIL)SULFANIL]BENCENO: Preparado por el procedimiento R y esquema Z utilizando 4-clorobencentiol y 1-bromo-3-cloropropano.

1-BROMO-3-[(3-CICLOROPROPIL)SULFANIL]BENCENO: Preparado por el procedimiento R y esquema Z utilizando 3-bromobencentiol y 1-bromo-3-cloropropano.

1-BROMO-4-[(3-CLOROPROPIL)SULFANIL]BENCENO: Preparado por el procedimiento R y esquema Z utilizando 4-bromobencentiol y 1-bromo-3-cloropropano.

3,4-DIMETILFENILSULFURO DE 3-CLOROPROPILO: Preparado por el procedimiento R y esquema Z utilizando 3,4-dimetilbencentiol y 1-bromo-3-cloropropano.

Ejemplo 590

N-[3-(1-{3-[(4-FLUOROFENIL)SULFINIL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento G y esquema B1 utilizando 3-cloropropil 4-fluorofenilsulfóxido de 3-cloropropilo y pipridinil)fenil]propanamida: RMN ^{1}H (400 MHz, $CDCl_3$) 7.64 (m, 2H), 7.53 (s, 1H), 7.24 (m, 5H), 6.94 (d, 1H, J = 7.7 Hz), 2.89 (m, 4H), 2.45 (m, 4H), 1.99 (m, 3H), 1.77 (m, 5H), 1.24 (d, 6H, *J* = 6.8 Hz); Análisis calculado para

$C_{24}H_{31}FN_2O_2S+0.6EtOAc$: C, 65.5: H, 7.45; N, 5.79. Encontrado: C, 65.4; H, 7.30; N, 5.73; ESMS m/e: 431.1 $(M + H)^+$.

Ejemplo 591

N-[3-(1-{3-[(2-BROMOFENIL)SULINIL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparado por el procedimiento *G* y esquema Bl utilizando 1-bromo-2-[(3-cloropropil)sulfinil]benceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: Análisis calculado para $C_{24}H_{31}BrN_2O_2S+0.3HCl_3$: ESMS *m/e:* 491.0 $(M + H)^+$.

Ejemplo 592

N-{3-[1-(3S)-3-{[(3,4-DIFLUOROFENIL)SULFONIL]AMINO}-FENILPROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento Ql y esquema AC utilizando cloruro de 3,4-difluorobencensulfonilo y N-(3-{1-[(3S)-3-amino-3-fenilpropil-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e:* 556.2 $(M + H)^+$.

Ejemplo 593

3-CLORO-N-(1S)-3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-I-FENILPROPIL)-2-TIOFENCARBOXAMIDA: Preparado por el procedimiento Ql y esquema AC utilizando cloruro de

3-cloro-2-tiofencarbonilo y N-(3-{1-[(3S)-3-amino-3-fenil]propil-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e:* 524.2 $(M + H)^+$.

Ejemplo 594

N-(3-{1-[*(3S)*-3,5-(DIMETILAMINO)NAFTIL]SULFONIL}AMINO)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando cloruro de 5-(dimetilamino)-1-naftalensulfonilo y N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e:* 613.3 $(M + H)^+$.

Ejemplo 595

2-METIL-N-{3-[1-(*(3S)*-3-(4-METILFENIL)SULFONIL]AMINO}-3-FENILPROPIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando cloruro de 4-metilbencensulfonilo y N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e:* 534.2 $(M + H)^+$.

Ejemplo 596

N-{3-[1-(3S)-3-{[(3,5-DICLORO-2-HYDROXIFENIL)SULFONIL]AMINO}-3-FENILPROPIL)-4-

PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando cloruro de 3,5-dicloro-2-hidroxibencensulfonilo y *N-(3-{1(3S)*-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: *ESMS m/e:* 605.4 $(M + H)^+$.

Ejemplo 597

2-METIL-N-[3-(1-{(3S)-3-[(METILSULFONIL)AMINO]-3-FENILPROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando cloruro de metansulfonilo y N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: *ESMS m/e:* 458.6 $(M + H)^+$.

Ejemplo 598

N-{3-[1-(3S)-3-{[(4-FLUOROFENIL)SULFONIL]AMINO}-3-FENILPROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando cloruro de 4-fluorobencensulfonilo y *N-(3-{1-[(3S)*-3amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e:* 538.1 $(M + H)^+$.

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Ejemplo 599

N-{3-[1-(3S)-3-{[(4-TERBUTILFENIL)SULFONIL]AMINO}-FENILPROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA:

Preparado por el procedimiento Q1 y esquema AC utilizando cloruro de 4-ter-butilbencensulfonilo y N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 576.2 $(M + H)^+$.

Ejemplo 600

N-{3-[1-(3S)-3-{[(2,5-DICLOROFENIL)SULFONIL]AMINO}-3-FENILPROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA:

Preparado por el procedimiento Q1 y esquema AC utilizando cloruro de 2,5-diclorobencensulfonilo y N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 588.0 $(M + H)^+$.

Ejemplo 601

2-METIL-N-[3-(1-{(3S)-3-FENIL-3[(PROPILSULFONIL)AMINO]-PROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando cloruro de 1-propansulfonilo y N(3-{1-[(3S)-3-amino-3-fenilpropil1-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 486.2 $(M + H)^+$.

Ejemplo 602

N-{3-[1-(3S)-3-{[(3,5-DIMETIL-4-ISOXAZOLIL)SULFONIL]AMINO}-3-FENILPROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Procedimiento Q1 y esquema AC utilizando cloruro de 3,5-dimetil-4-isoxazolsulfonilo y N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$) 7.53 (s, 2H), 7.3-7.1 (m, 5H), 7.05 (t, 2H, J = 6.5 Hz), 6.81 (d, 1H, J = 7.1 Hz), 4.65 (dd, 1H, J = 6.3, 2.2 Hz), 3.11 (t, 2H, J = 7.2 Hz), 2.4 (m, 4H), 2.2 (s, 3H), 2.05 (m, 2H), 2.01 (s, 3H), 2.01.8 (m, 7H), 1.21 (d, 6H, *J* = 7.1 Hz); ESMS m/e: 539.5 $(M + H)^+$.

Ejemplo 603

3-{[(3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)AMINOSULFONIL}-2-TIOFENCARBOXILATO DE METILO: Preparado por el procedimiento Q1 y Esquema AC utilizando 3-(clorosulfonil)-2-tiofencarboxilato de metilo y N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-etilpropanamida: Análisis calculado para $C_{24}H_{33}N_3O_5S.HCl$: C, 6.00; H, 5.30; N, 7.72. Encontrado: C, 52.9; H, 6.04; N, 7.59; ESMS *m/e*: 508.2 $(M + H)^+$.

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Ejemplo 604

2-METIL-N-{3-[1-(3S)-3-{[(4-FENOXIANILINO)CARBONIL]AMINO}-3-FENILPROPIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparado por el procedimiento P y esquema AB utilizando 1-isocianato-4-fenoxibenceno y N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: *ESMS m/e: 591.3* $(M + H)^+$.

PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparado por el procedimiento Q1 y esquema AC utilizando cloruro de 3,5-dimetil-4-isoxazolsulfonilo y N-(3-{1-[(3S)3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$) 7.53 (s, 2H), 7.3-7.1 (m, 5H), 7.05 (t, 2H, J = 6.5 Hz), 6.81 (d, 1H, J = 7.1 Hz), 4.65 (dd, 1H, J = 6.3, 2.2 Hz), 3.11 (t, 2H, J = 7.2 Hz), 2.4.(m, 4H), 2.2 (s, 3H), 2.05 (m, 2H), 2.01 (s, 3H), 2.0-1.8 (m, 7H), 1.21 (d, 6H, J = 7.1 Hz) ; *ESMS m/e:* 539.5 $(M + H)^+$.

Ejemplo 605

N-[3-(1-{(3S)-3-[(ANILINOCARBONIL)AMINO]-3-FENILPROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento P y Esquema AB utilizando isocianatobenceno y N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 499.2 $(M + H)^+$.

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Ejemplo 606

N-{3-[1-((3S)-3-{[(TER-BUTILAMINO)CARBOTIOIL]AMINO}-3-FENILPROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento P y Esquema AB utilizando 2-isotiocianato-2-metilpropano y N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 495.1 $(M + H)^+$.

Ejemplo 607

N-{3-[1-((3S)-3-{[(2-FLUOROANILINO)CARBONIL]AMINO}-3-FENILPROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento P y Esquema AB utilizando 1-fluoro-2-isocianatobenceno y N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 517.0 $(M + H)^+$.

Ejemplo 608

1-METIL-N-[3-(1-{(3S)-3-FENIL-3-[(2-TOLUIDINOCARBOTIOIL)-AMINO]PROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento P y Esquema AB utilizando 1-isotiocianato-2-metilbenceno y N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 529.1 (M +

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H)$^+$.

Ejemplo 609

N-{3-[1-((3S)-3-{[(BENCILAMINO)CARBONIL]AMINO}-3-FENIL-PROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA:

fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: RMN ^{1}H (400 MHz, $CDCl_3$) Γ 8.44 (s, 1H), 7.67 (d, 1H, J = 7.9 Hz), 7.31-7.13 (m, 13H), 6.38 (s, 1H), 6.80 (d, 1H, J = 7.9 Hz), 5.54 (m, 1H), 4.81 (m, 1H), 4.41 (dd, 1H, J = 14.8, 6.2 Hz), 4.29 (dd, 1H, J = 14.9, 5.4 Hz), 2.99 (d, 1H, J = 11.2 Hz), 2.87 (d, 1H, J = 11.2 Hz), 2.67 (q, 1H, J = 6.2 Hz), 2.3 (m, 3H), 2.0-1.5 (m, 7H), 1.23 (d, 6H, J = 6.7 Hz); ESMS *m/e*: 513.2 (M + H)$^+$.

Ejemplo 610

2-METIL-N-{3-[1-((3S)-3-{[(2-NITROANILINO)CARBONIL]AMINO}-3-FENILPROPIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el Procedimiento P y Esquema AB utilizando 1-isocianato-2-nitrobenceno y N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 543.6 (M + H)$^+$.

Ejemplo 611

N-{3-[1-((3S)-3-{[(3,4-DICLOROANILINO)CARONIL]AMINO}-3-

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FENILPR PIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento P y Esquema AB utilizando 1,2-dicloro-4-isocianatobenceno y N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 567.1 $(M + H)^+$.

Ejemplo 612

2-METIL-N-(3-{1-[(3S)-3-({[2-(METILSULFANIL)ANILINO]CARBONIL}AMINO)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparada por el Procedimiento P y Esquema AB utilizando 1-isocianato-2-(metilsulfanil)benceno y N-(3-{1-[(3S)-3-amino-3-fenilpropil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 545.0 $(M + H)^+$.

Ejemplo 613

N-{3-[1-(3-{[(4-FLUOROANILINO)CARBONIL]AMINO}PROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento P y Esquema AB utilizando 1-fluoro-4-isocianatobenceno y N-{3-[1-(3-aminopropil)-4-piperidinil]-fenil}-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$) Γ 7.45 (q, 2H, J = 4.7 Hz), 7.23 (m, 4H), 7.05 (t, 4H, J = 7.8 Hz), 6.75 (m, 1H), 4.05 (m, 1H), 3.19 (s, 1H), 2.71 (m, 1H), 2.53 (m, 1H), 2.25 (m, 3H), 1.8 (m, 9H), 1.25 (d, 6H, J = 6.4 Hz); ESMS *m/e*: 441.1 $(M + H)^+$.

Ejemplo 614

N-{3-[1-(3-{[(3,4-DICLOROANILINO)CARBONIL]AMINO}PROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento P y Esquema AB utilizando 1,2-dicloro-4-isocianatobenceno y N-{3-[1-(3-aminopropil)-4-piperidinil]-fenil}-2-metilpropanamida: ESMS *m/e*: 493.2 $(M + H)^+$.

Ejemplo 615

2-METIL-N-[3-(1-{3-[(2-TOLUIDINOCARBOTIOL)AMINO]PROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento P y Esquema AB utilizando 1-isotiocianato-2-metilbenceno y N-{3-[1-(3-aminopropil)-4-piperidinil]-fenil}-2-metilpropanamida: ESMS *m/e*: 453.2 $(M + H)^+$.

Ejemplo 616

N-{3-[1-(3-{[(BENCILAMINO)CARBONIL]AMINO}PROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento P y Esquema AB utilizando (isocianatometil)-benceno y N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 437.2 $(M + H)^+$.

Ejemplo 617

N-{3-[1-(3-{[(4-ETOXIANILINO)CARBONIL]AMINO}PROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el

Procedimiento P y Esquema AB utilizando 1-etoxi-4-isocianatobenceno y N-{3-[1-(3-aminopropil)-4-piperidinil]-fenil}-2-metilpropanamida: ESMS *m/e*: 467.2 $(M + H)^+$.

Ejemplo 618

N-[3-(1-{3-[(ANILINOCARBONIL)AMINO]PROPIL}-4-PIPERIDINIL)-FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento P y Esquema AB utilizando isocianatobenceno y N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 422.9 $(M + H)^+$.

Ejemplo 619

2-METIL-N-(3-{1-[3-({[2-(METILSULFANIL)ANILINO]CARBONIL}-AMINO)PROPIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparada por el Procedimiento P y Esquema AB utilizando 1-isocianato-2-(metilsulfanil)benceno y N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 469.1 $(M + H)^+$.

Ejemplo 620

N-{3-[1-(3-{[(TER-BUTILAMINO)CARBOTIOIL]AMINO}PROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento P y Esquema AB utilizando 2-isotiocianato-2-metilpropano y N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 419.0 $(M + H)^+$.

Ejemplo 621

2-METIL-N-{3-[1-(3-{[(4-FENOXIANILINO)CARBONIL]AMINO}-PROPIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el Procedimiento P y Esquema AB utilizando 1-isocianato-4-fenoxibenceno y N-{3-[1-(3-aminopropil)-4-piperidinil]-fenil}-2-metilpropanamida: ESMS *m/e*: 515.5 $(M + H)^+$.

Ejemplo 622

N-(3-{4-[3-(ACETILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-4-(2,4-DIFLUOROFENIL)-2-METIL-6-OXO-1,4,5,6-TETRAHIDRO-3-PIPERIDIN-CARBOXAMIDA: Preparada por el Procedimiento AC y Esquema AM utilizando N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-acetamida y ácido 4-(2,4-difluorofenil)-2-metil-6-oxo-1,4,5,6-tetrahidro-3-piridincarboxílico: ESMS *m/e*: 525.2 $(M + H)^+$.

Ejemplo 623

N-(3-{4-[3-(ACETILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-4-(3,4-DIFLUOROFENIL)-2-METIL-6-OXO-1,4,5,6-TETRAHIDRO-3-PIPERIDIN-CARBOXAMIDA: Preparada por el Procedimiento AC y Esquema AM utilizando N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-acetamida y ácido 4-(3,4-difluorofenil)-2-metil-6-oxo-1,4,5,6-tetrahidro-3-piridincarboxílico: ESMS *m/e*: 525.2 $(M + H)^+$.

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Ejemplo 624

N-(6-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}HEXIL)-1-(4-NITROFENIL)-5-(TRIFLUOROMETIL)-1H-PIRAZOL-4-CARBOXAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(6-aminohexil)-4-piperidinil]fenil}-2-metil-propanamida y cloruro de 1-(4-nitrofenil)-5-(trifluorometil)-1H-pirazol-4-carbonilo: ESMS *m/e*: 629.2 (M + H)$^+$.

Ejemplo 625

N-[3-(1-{6-[(DIFENILACETIL)AMINO]HEXIL}-4-PIPERIDINIL)-FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(6-aminohexil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de difenilacetilo: ESMS *m/e*: 540.3 (M + H)$^+$.

Ejemplo 626

5-(3,5-DICLOROFENOXI)-N-(6-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}HEXIL)-2-FURAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(6-aminohexil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 5-(3,5-diclorofenoxi)-2-furoilo: ESMS *m/e*: 600.2 (M + H)$^+$.

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Ejemplo 627

N-(6-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}HEXIL)-2-FENOXINICOTINAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(6-aminohexil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 2-fenoxinicotinoilo: ESMS *m/e*: 543.3 $(M + H)^+$.

Ejemplo 628

N-(6-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}HEXIL)-2-NAFTAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(6-aminohexil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 2-naftoilo: ESMS *m/e*: 500.3 $(M + H)^+$.

Ejemplo 629

1-BENCIL-3-TER-BUTIL-N-(6-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}HEXIL)-1H-PIRAZOL-5-CARBOXAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(6-aminohexil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 1-bencil-3-ter-butil-1H-pirazol-5-carbonilo: ESMS *m/e*: 586.3 $(M + H)^+$.

Ejemplo 630

3-CLORO-N-(6-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-HEXIL)-4-(ISOPROPILSULFONIL)-2-TIOFENCARBOXAMIDA: Preparada

por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(6-aminohexil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-cloro-4-(isopropilsulfonil)-2-tiofenocarbonilo: ESMS *m/e*: 596.2 $(M + H)^+$.

Ejemplo 631

N-[3-(1-{6-[(ANILINOCARBONIL)AMINO]HEXIL}-4-PIPERIDINIL)-FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(6-aminohexil)-4-piperidinil]fenil}-2-metilpropanamida e isocianato de fenilo: ESMS *m/e*: 465.2 $(M + H)^+$.

Ejemplo 632

N-{3-[1-(6-{[(2,4-DICLOROANILINO)CARBONIL]AMINO}HEXIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(6-aminohexil)-4-piperidinil]fenil}-2-metilpropanamida e isocianato de 2,4-diclorofenilo: ESMS *m/e*: 533.2 $(M + H)^+$.

Ejemplo 633

N-(6-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}HEXIL)-1-FENIL-5-PROPIL-1H-PIRAZOL-4-CARBOXAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(6-aminohexil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 1-fenil-5-propil-1H-pirazol-4-carbonilo: ESMS *m/e*: 558.3

$(M + H)^+$.

Ejemplo 634

2-METIL-N-{3-[1-(6-{[(1-NAFTILAMINO)CARBONIL]AMINO}HEXIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(6-aminohexil)-4-piperidinil]fenil}-2-metilpropanamida e isocianato de 1-naftilo: ESMS *m/e*: 515.3 $(M + H)^+$.

Ejemplo 635

N-{3-[1-(6-{[([1,1'-BIFENIL]-4-ILAMINO)CARBONIL]AMINO}-HEXIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(6-aminohexil)-4-piperidinil]fenil}-2-metilpropanamida e isocianato de 4-bifenilo: ESMS *m/e*: 541.3 $(M + H)^+$.

Ejemplo 636

2-METIL-N-{3-[1-(6-{[(2-NAFTILAMINO)CARBONIL]AMINO}HEXIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(6-aminohexil)-4-piperidinil]fenil}-2-metilpropanamida e isocianato de 2-naftilo: ESMS *m/e*: 515.3 $(M + H)^+$.

Ejemplo 637

N-{3-[1-(6-{[(3,4-DIMETOXIFENIL)SULFONIL]AMINO}PROPIL)-4-

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PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3,4-dimetoxibencensulfonilo: ESMS *m/e*: 504.2 $(M + H)^+$.

Ejemplo 638

N-(3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-5-METIL-3-FENIL-4-ISOXAZOLCARBOXAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 5-metil-3-fenil-4-isoxazolcarbonilo: ESMS *m/e*: 489.3 $(M + H)^+$.

Ejemplo 639

N-{3-[1-(3-{[(4-FLUOROFENIL)ACETIL]AMINO}PROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de (4-fluorofenil)acetilo: ESMS *m/e*: 440.3 $(M + H)^+$.

Ejemplo 640

N-{3-[1-(3-{[(4-CLORO-3-NITROFENIL)SULFONIL]AMINO}PROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(3-

aminopropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 4-cloro-3-nitrobencensulfonilo: ESMS *m/e*: 523.1 $(M + H)^+$.

Ejemplo 641

2-(4-CLOROFENOXI)-N-(3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)NICOTINAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 2-(4-clorofenoxi)nicotinoilo: ESMS *m/e*: 535.2 $(M + H)^+$.

Ejemplo 642

5-(3,5-DICLOROFENOXI)-N-(3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-2-FURAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 5-(3,5-diclorofenoxi)-2-furoilo: ESMS *m/e*: 558.2 $(M + H)^+$.

Ejemplo 643

N-{3-[1-(3-{[(2-FLUOROFENIL)SULFONIL]AMINO}PROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida y

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cloruro de 2-fluorobencensulfonilo: ESMS *m/e*: 462.2 (M + H)$^+$.

Ejemplo 644

N-{3-[1-(3-{[(3,5-DIMETIL-4-ISOXAZOLIL)SULFONIL]AMINO}-PROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3,5-dimetil-4-isoxazolsulfonilo: ESMS *m/e*: 463.2 (M + H)$^+$.

Ejemplo 645

N-{3-[1-(3-{[(4-TER-BUTILFENIL)SULFONIL]AMINO}PROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 4-ter-butilbencensulfonilo: ESMS *m/e*: 500.3 (M + H)$^+$.

Ejemplo 646

N-{3-[1-(6-AMINOHEXIL)-4-PIPERIDINIL]FENIL}-2-METILPROPAN-AMIDA: Preparada por el Procedimiento AE y Esquema Y utilizando N-(3-{1-[6-(1,3-dioxo-1,3-dihidro-2H-isoindol-2-il)hexil]-4-piperidinil}fenil)-2-metilpropanamida e hidrato de hidrazina: ESMS *m/e*: 346.2 (M + H)$^+$.

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Ejemplo 647

N-{3-[1-(2-{[([1,1'-BIFENIL]-4-ILAMINO)CARBONIL]AMINO}ETIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(2-aminoetil)-4-piperidinil]fenil}-2-metilpropanamida e isocianato de 4-bifenilo: ESMS *m/e*: 485.2 $(M + H)^+$.

Ejemplo 648

5-(3,5-DICLOFOFENOXI)-N-(2-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}ETIL)-3-FURAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(2-aminoetil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 5-(3,5-diclorofenoxi)-3-furoilo: ESMS *m/e*: 544.1 $(M + H)^+$.

Ejemplo 649

N-[3-(1-{2-[(DIFENILACETIL)AMINO]ETIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(2-aminoetil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de difenilacetilo: ESMS *m/e*: 484.2 $(M + H)^+$.

Ejemplo 650

N-(2-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}ETIL)-2-NAFTAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema

AT utilizando N-{3-[1-(2-aminoetil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 2-naftoilo: ESMS m/e: 444.2 (M + H)$^+$.

Ejemplo 651

3-(2,6-DICLOROFENIL)-N-(4-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}BUTIL)-5-METIL-4-ISOXAZOLCARBOXAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(4-aminobutil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-(2,6-diclorofenil)-5-metil-4-isoxazolcarbonilo: ESMS *m/e*: 571.2 (M + H)$^+$.

Ejemplo 652

3-(2,6-DICLOROFENIL)-N-(5-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PENTIL)-5-METIL-4-ISOXAZOLCARBOXAMIDA: Preparada por el Procedimiento Q1 (THF) y Esquema AT utilizando N-{3-[1-(5-aminopentil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-(2,6-diclorofenil)-5-metil-4-isoxazolcarbonilo: ESMS *m/e*: 585.2 (M + H)$^+$.

Ejemplo 653

N-[3-(1-{4-[(DIFENILACETIL)AMINO]BUTIL}-4-PIPERIDINIL)-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento Q2 (THF/DCM, 1:3)) y Esquema AT utilizando N-{3-[1-(4-aminobutil)-4-piperidinil]fenil}-2-metilpropanamida y

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cloruro de difenilacetilo: ESMS *m/e*: 512.0 $(M + H)^+$.

Ejemplo 654

N-[3-(1-{5-[(DIFENILACETIL)AMINO]PENTIL}-4-PIPERIDINIL)-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento Q2 (THF/DCM, 1:3)) y Esquema AT utilizando N-{3-[1-(5-aminopentil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de difenilacetilo: ESMS *m/e*: 526.0 $(M + H)^+$.

Ejemplo 655

3,5-DICLORO-N-(4-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-BUTIL)BENZAMIDA: Preparada por el Procedimiento Q2 (THF/DCM, 1:3) y Esquema AT utilizando N-{3-[1-(4-aminobutil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3,5-diclorobenzoilo: ESMS *m/e*: 490.0 $(M + H)^+$.

Ejemplo 656

5-(3,5-DICLOROFENOXI)-N-(4-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}BUTIL)FURAMIDA: Preparada por el Procedimiento Q2 (THF/DCM, 1:3) y Esquema AT utilizando N-{3-[1-(4-aminobutil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 5-(3,5-diclorofenoxi)-2-furoilo: ESMS *m/e*: 572.0 $(M + H)^+$.

Ejemplo 657

3-CLORO-N-(4-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}-BUTIL)BENZAMIDA: Preparada por el Procedimiento Q2 (THF/DCM, 1:3) y Esquema AT utilizando N-{3-[1-(4-aminobutil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-clorobenzoilo: ESMS *m/e*: 456.0 $(M + H)^+$.

Ejemplo 658

3,4-DIFLUORO-N-(4-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}BUTIL)BENZAMIDA: Preparada por el Procedimiento Q2 (THF/DCM, 1:3) y Esquema AT utilizando N-{3-[1-(4-aminobutil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3,4-difluorobenzoilo: ESMS *m/e*: 458.0 $(M + H)^+$.

Ejemplo 659

N-{3-[1-(4-{[(3,5-DICLOROANILINO)CARBONIL]AMINO}BUTIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento Q2 (THF/DCM, 1:3) y Esquema AT utilizando N-(3-{1-[4-(formilamino)butil]-4-piperidinil}fenil)-2-metil-propanamida e isocianato de 3,5-diclorofenilo: ESMS *m/e*: 505.0 $(M + H)^+$.

Ejemplo 660

N-{3-[1-(4-{[([1,1'-BIFENIL]-4-ILAMINO)CARBONIL]AMINO}-BUTIL)-4-PIPERIDINI]FENIL}-2-METILPROPANAMIDA: Preparada por

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el Procedimiento Q2 (THF/DCM, 1:3) y Esquema AT utilizando N-{3-[1-(4-aminobutil)-4-piperidinil]fenil}-2-metilpropanamida e isocianato de 4-bifenilo: ESMS *m/e*: 513.0 $(M + H)^+$.

Ejemplo 661

2-METIL-N-(3-{1-[5-(4-NITROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 5-cloro-1-(4-nitrofenil)-1-pentanona y 2-metil-N-[3-(4-piperidinil)-fenil]propanamida: ESMS *m/e*: 452.2 $(M + H)^+$.

Ejemplo 662

N-(3-{1-[5-(4-FLUOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 5-cloro-1-(4-fluorofenil)-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 425.2 $(M + H)^+$.

Ejemplo 663

2-METIL-N-[3-(1-{5-OXO-5-[2-(TRIFLUOROMETIL)FENIL]PENTIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 5-cloro-1-[2-(trifluorometil)fenil]-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 475.2 $(M + H)^+$.

Ejemplo 664

N-(3-{1-[5-(3-BROMOFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 1-(3-brofenil)-5-cloro-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 485.1 $(M + H)^+$.

Ejemplo 665

2-METIL-N-(3-{1-[5-(3-NITROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 5-cloro-1-(3-nitrofenil)-1-pentanona y 2-metil-N-[3-(4-piperidinil)-fenil]propanamida: ESMS *m/e*: 452.2 $(M + H)^+$.

Ejemplo 666

N-(3-{1-[5-(3-CLOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 1-(3-clorofenil)-5-cloro-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 441.1 $(M + H)^+$.

Ejemplo 667

N-(3-{1-[5-(3-BROMOFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 1-(4-bromofenil)-5-cloro-1-

pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 485.1 $(M + H)^+$.

Ejemplo 668

N-(3-{1-[5-(2-YODOFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 1-(2-yodofenil)-5-cloro-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 533.0 $(M + H)^+$.

Ejemplo 669

N-(3-{1-[5-(3-FLUOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 1-(3-fluorofenil)-5-cloro-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 425.2 $(M + H)^+$.

Ejemplo 670

2-METIL-N-[3-(1-{5-OXO-5-[3-(TRIFLUOROMETIL)FENIL]PENTIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 1-[3-(trifluorometil)fenil]-5-cloro-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 475.2 $(M + H)^+$.

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Ejemplo 671

N-(3-{1-[5-(2-FLUOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 1-(2-fluorofenil)-5-cloro-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 425.2 $(M + H)^+$.

Ejemplo 672

N-(3-{1-[5-(3-YODOFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 1-(3-yodofenil)-5-cloro-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 533.0 $(M + H)^+$.

Ejemplo 673

N-(3-{1-[5-(2-CLOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 1-(2-clorofenil)-5-cloro-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 441.1 $(M + H)^+$.

Ejemplo 674

2-METIL-N-[3-(1-{5-OXO-5-[4-(TRIFLUOROMETIL)FENIL]PENTIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 1-[4-

(trifluorometil)fenil]-5-cloro-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 475.2 $(M + H)^+$.

Ejemplo 675

N-(3-{1-[5-(4-CLOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 1-(4-clorofenil)-5-cloro-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 441.1 $(M + H)^+$.

Ejemplo 676

N-(3-{1-[5-(4-YODOFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 1-(4-yodofenil)-5-cloro-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 533 $(M + H)^+$.

Ejemplo 677

N-(3-{1-[5-(2-BROMOFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema B1 (K_2CO_3) utilizando 1-(2-bromofenil)-5-cloro-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 485.1 $(M + H)^+$.

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Ejemplo 678

2-(4-CLOROFENOXI)-N-(4-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}BUTIL)NICOTINAMIDA: Preparada por el Procedimiento Q2 (THF/DCM, 1:3) y Esquema AT utilizando N-{3-[1-(4-aminobutil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 2-(4-clorofenoxi)nicotinoilo: ESMS *m/e*: 549.0 $(M + H)^+$.

Ejemplo 679

N-(4-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}BUTIL)-3,4-DIMETOXIBENZAMIDA: Preparada por el Procedimiento Q2 (THF/DCM, 1:3) y Esquema AT utilizando N-{3-[1-(4-aminobutil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3,4-dimetoxibenzoilo: ESMS *m/e*: 482.0 $(M + H)^+$.

Ejemplo 680

3-(2-CLOROFENILO)-N-(4-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}BUTIL)-5-METIL-4-ISOXAZOLCARBOXAMIDA: Preparada por el Procedimiento Q2 (THF/DCM, 1:3) y Esquema AT utilizando N-{3-[1-(4-aminobutil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-(2-clorofenil)-5-metil-4-isoxazolcarbonilo: ESMS *m/e*: 537.0 $(M + H)^+$.

Ejemplo 681

3-(2-CLOROFENILO)-N-(5-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-

PIPERIDINIL}PENTIL)-5-METIL-4-ISOXAZOLCARBOXAMIDA: Preparada por el Procedimiento Q2 (THF/DCM, 1:3) y Esquema AT utilizando N-{3-[1-(5-aminopentil)-4-piperidinil]fenil}-2-metilpropanamida y cloruro de 3-(2-clorofenil)-5-metil-4-isoxazolcarbonilo: ESMS *m/e*: 551.0 $(M + H)^+$.

Ejemplo 682

2-METIL-N-{3-[1-(3-{1-METIL-2-[4-(TRIFLUOROMETIL)FENIL]-1H-INDOL-3-IL}PROPIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-[3-(1-{5-oxo-5-[4-(trifluorometil)fenil]pentil}-4-piperidinil)-fenil]propanamida y 1-metil-1-fenilhidrazina: ESMS *m/e*: 562.0 $(M + H)^+$.

Ejemplo 683

2-METIL-N-{3-[1-(3-{1-METIL-2-[4-(TRIFLUOROMETIL)FENIL]-1H-INDOL-3-IL}PROPIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-[3-(1-{5-oxo-5-[4-(trifluorometil)fenil]pentil}-4-piperidinil)-fenil]propanamida y clorhidrato de 4-(trifluorometoxi)-fenilhidrazina: ESMS *m/e*: 632.2 $(M + H)^+$.

Ejemplo 684

2-METIL-N-{3-[1-(3-{2-[4-(TRIFLUOROMETIL)FENIL]-1H-INDOL-3-IL}PROPIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el

Procedimiento E y Esquema M utilizando 2-metil-N-[3-(1-{5-oxo-5-[4-(trifluorometil)fenil]pentil}-4-piperidinil)fenil]-propanamida y fenilhidrazina: ESMS *m/e*: 548.0 $(M + H)^+$.

Ejemplo 685

2-METIL-N-{3-[1-(3-{1-FENIL-2-[4-(TRIFLUOROMETIL)FENIL]-1H-INDOL-3-IL}PROPIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-[3-(1-{5-oxo-5-[4-(trifluorometil)fenil]pentil}-4-piperidinil)-fenil]propanamida y clorhidrato de 1,1-difenilhidrazina: ESMS *m/e*: 624.2 $(M + H)^+$.

Ejemplo 686

2-METIL-N-{3-[1-(3-{2-[4-(TRIFLUOROMETIL)FENIL]-1H-BENZO[G]-INDOL-3-IL}PROPIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-[3-(1-{5-oxo-5-[4-(trifluorometil)fenil]pentil}-4-piperidinil)-fenil]propanamida y clorhidrato de 1-naftilhidrazina: ESMS *m/e*: 598.2 $(M + H)^+$.

Ejemplo 687

2-METIL-N-{3-[1-(3-{7-METIL-2-[4-(TRIFLUOROMETIL)FENIL]-1H-INDOL-3-IL}PROPIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-[3-(1-{5-oxo-5-[4-(trifluorometil)fenil]pentil}-4-

piperidinil)-fenil]propanamida y clorhidrato de 1-(2-metilfenil)-hidrazina: ESMS *m/e*: 562.2 $(M + H)^+$.

Ejemplo 688

2-METIL-N-{3-[1-(3-{5-METIL-2-[4-(TRIFLUOROMETIL)FENIL]-1H-INDOL-3-IL}PROPIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-[3-(1-{5-oxo-5-[4-(trifluorometil)fenil]pentil}-4-piperidinil)-fenil]propanamida y clorhidrato de 4-metilfenilhidrazina: ESMS *m/e*: 562.2 $(M + H)^+$.

Ejemplo 689

N-{3-[1-(3-{5-METOXI-2-[4-(TRIFLUOROMETIL)FENIL]-1H-INDOL-3-IL}PROPIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-[3-(1-{5-oxo-5-[4-(trifluorometil)fenil]pentil}-4-piperidinil)-fenil]propanamida y clorhidrato de 4-metoxifenilhidrazina: ESMS *m/e*: 578.2 $(M + H)^+$.

Ejemplo 690

N-[3-(1-{3-[2-(3-FLUOROFENIL)-7-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS *m/e*:

512.2 $(M + H)^+$.

Ejemplo 691

N-[3-(1-{3-[2-(4-CLOROFENIL)-1-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y 1-metil-1-fenilhidrazina: ESMS *m/e*: 528.2 $(M + H)^+$.

Ejemplo 692

N-[3-(1-{3-[2-(4-FLUOROFENIL)-5-METOXI-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-metoxifenilhidrazina: ESMS *m/e*: 528.2 $(M + H)^+$.

Ejemplo 693

N-[3-(1-{3-[2-(2-FLUOROFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y fenilhidrazina: ESMS *m/e*: 498.2 $(M + H)^+$.

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Ejemplo 694

N-[3-(1-{3-[2-(3-FLUOROFENIL)-5-(TRIFLUOROMETOXI)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-(trifluorometoxi)fenilhidrazina: ESMS *m/e*: 582.2 $(M + H)^+$.

Ejemplo 695

N-[3-(1-{3-[2-(2-FLUOROFENIL)-5-(TRIFLUOROMETOXI)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-(trifluorometoxi)fenilhidrazina: ESMS *m/e*: 582.2 $(M + H)^+$.

Ejemplo 696

N-[3-(1-{3-[2-(4-FLUOROFENIL)-1-FENIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1,1-difenilhidrazina: ESMS *m/e*: 548.2 $(M + H)^+$.

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Ejemplo 697

N-[3-(1-{3-[2-(2-FLUOROFENIL)-1H-BENZO[G]INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1-naftilhidrazina: ESMS *m/e*: 547.7 $(M + H)^+$.

Ejemplo 698

N-[3-(1-{3-[2-(2-FLUOROFENIL)-5-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-metilfenilhidrazina: ESMS *m/e*: 512.2 $(M + H)^+$.

Ejemplo 699

N-[3-(1-{3-[2-(3-FLUOROFENIL)-1H-BENZO[G]-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1-naftilhidrazina: ESMS *m/e*: 548.2 $(M + H)^+$.

Ejemplo 700

N-[3-(1-{3-[2-(4-FLUOROFENIL)-1-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y 1-metil-1-fenilhidrazina: ESMS *m/e*: 512.2 $(M + H)^+$.

Ejemplo 701

N-[3-(1-{3-[2-(3-FLUOROFENIL)-5-METOXI-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-metoxifenilhidrazina: ESMS *m/e*: 528.2 $(M + H)^+$.

Ejemplo 702

N-[3-(1-{3-[2-(3-FLUOROFENIL)-1-FENIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1,1-difenilhidrazina: ESMS *m/e*: 574.2 $(M + H)^+$.

Ejemplo 703

N-[3-(1-{3-[2-(4-CLOROFENIL)-5-(TRIFLUOROMETOXI)-1H-INDOL-3-

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IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-(trifluorometoxi)fenilhidrazina: ESMS *m/e*: 598.2 $(M + H)^+$.

Ejemplo 704

N-[3-(1-{3-[2-(3-FLUOROFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y fenilhidrazina: ESMS *m/e*: 498.2 $(M + H)^+$.

Ejemplo 705

N-[3-(1-{3-[2-(3-FLUOROFENIL)-1-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y 1-metil-1-fenilhidrazina: ESMS *m/e*: 512.2 $(M + H)^+$.

Ejemplo 706

N-[3-(1-{3-[2-(3-FLUOROFENIL)-5-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-

amida y clorhidrato de 4-metilfenilhidrazina: ESMS *m/e*: 512.2 $(M + H)^+$.

Ejemplo 707

N-[3-(1-{3-[2-(4-CLOROFENIL)-1H-BENZO[G]INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1-naftilhidrazina: ESMS *m/e*: 564.2 $(M + H)^+$.

Ejemplo 708

N-[3-(1-{3-[2-(4-CLOROFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1-fenilhidrazina: ESMS *m/e*: 514.2 $(M + H)^+$.

Ejemplo 709

N-[3-(1-{3-[2-(2-FLUOROFENIL)-1-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y 1-metil-1-fenilhidrazina: ESMS *m/e*:

512.2 $(M + H)^+$.

Ejemplo 710

N-[3-(1-{3-[2-(2-FLUOROFENIL)-7-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS *m/e*: 512.2 $(M + H)^+$.

Ejemplo 711

N-[3-(1-{3-[2-(2-FLUOROFENIL)-1-FENIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1,1-difenilhidrazina: ESMS *m/e*: 574.2 $(M + H)^+$.

Ejemplo 712

N-[3-(1-{3-[2-(2-FLUOROFENIL)-5-METOXI-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-metoxifenilhidrazina: ESMS *m/e*: 528.2 $(M + H)^+$.

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Ejemplo 713

N-[3-(1-{3-[2-(4-CLOROFENIL)-5-METOXI-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-metoxifenilhidrazina: ESMS *m/e*: 544.2 $(M + H)^+$.

Ejemplo 714

N-[3-(1-{3-[2-(2-FLUOROFENIL)-1-FENIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1-naftilhidrazina: ESMS *m/e*: 548.2 $(M + H)^+$.

Ejemplo 715

N-[3-(1-{3-[2-(4-FLUOROFENIL)-5-(TRIFLUOROMETOXI)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-(trifluorometoxi)fenilhidrazina: ESMS *m/e*: 582.9 $(M + H)^+$.

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Ejemplo 716

N-[3-(1-{3-[2-(4-FLUOROFENIL)-7-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS *m/e*: 512.2 $(M + H)^+$.

Ejemplo 717

N-[3-(1-{3-[2-(4-FLUOROFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y fenilhidrazina: ESMS *m/e*: 498.2 $(M + H)^+$.

Ejemplo 718

N-[3-(1-{3-[2-(4-FLUOROFENIL)-5-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-metilfenilhidrazina: ESMS *m/e*: 512.2 $(M + H)^+$.

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Ejemplo 719

N-[3-(1-{3-[2-(4-CLOROFENIL)-7-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS *m/e*: 528.2 $(M + H)^+$.

Ejemplo 720

N-[3-(1-{3-[2-(4-CLOROFENIL)-5-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 4-metilfenilhidrazina: ESMS *m/e*: 528.2 $(M + H)^+$.

Ejemplo 721

N-[3-(1-{3-[2-(4-CLOROFENIL)-1-FENIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1,1-difenilhidrazina: ESMS *m/e*: 590.2 $(M + H)^+$.

Ejemplo 722

N-[3-(1-{3-[2-(3-CLOROFENIL)-7-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS *m/e*: 528.1 $(M + H)^+$.

Ejemplo 723

N-[3-(1-{3-[2-(3-CLOROFENIL)-5-(TRIFLUOROMETOXI)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-(trifluorometoxi)fenilhidrazina: ESMS *m/e*: 598.2 $(M + H)^+$.

Ejemplo 724

N-[3-(1-{3-[2-(3-CLOROFENIL)-1-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y 1-metil-fenilhidrazina: ESMS *m/e*: 528.2 $(M + H)^+$.

Ejemplo 725

N-[3-(1-{3-[2-(3-CLOROFENIL)-1-FENIL-1H-INDOL-3-IL]PROPIL}-

4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1,1-difenilhidrazina: ESMS *m/e*: 590.3 $(M + H)^+$.

Ejemplo 726

N-[3-(1-{3-[2-(3-CLOROFENIL)-5-METOXI-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 4-metoxifenilhidrazina: ESMS *m/e*: 544.3 $(M + H)^+$.

Ejemplo 727

N-[3-(1-{3-[2-(3-CLOROFENIL)-5-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 4-metilfenilhidrazina: ESMS *m/e*: 528.2 $(M + H)^+$.

Ejemplo 728

N-[3-(1-{3-[2-(3-CLOROFENIL)-1H-BENZO[G]-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el

Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1-naftilhidrazina: ESMS *m/e*: 564.2 (M + H)$^+$.

Ejemplo 729

N-[3-(1-{3-[2-(3-CLOROFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y fenilhidrazina: ESMS *m/e*: 514.2 (M + H)$^+$.

Ejemplo 730

N-[3-(1-{3-[2-(2-CLOROFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y fenilhidrazina: ESMS *m/e*: 514.2 (M + H)$^+$.

Ejemplo 731

N-[3-(1-{3-[2-(2-CLOROFENIL)-5-(TRIFLUOROMETOXI)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-

(trifluorometoxi)fenilhidrazina: ESMS *m/e*: 598.2 $(M + H)^+$.

Ejemplo 732

N-[3-(1-{3-[2-(2-CLOROFENIL)-1H-BENZO[G]INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-naftilhidrazina: ESMS *m/e*: 564.2 $(M + H)^+$.

Ejemplo 733

N-[3-(1-{3-[2-(2-CLOROFENIL)-7-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS *m/e*: 528.2 $(M + H)^+$.

Ejemplo 734

N-[3-(1-{3-[2-(2-CLOROFENIL)-1-FENIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1,1-difenilhidrazina: ESMS *m/e*: 590.2 $(M + H)^+$.

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Ejemplo 735

N-[3-(1-{3-[2-(2-CLOROFENIL)-1-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y 1-metil-1-fenilhidrazina: ESMS *m/e*: 528.2 $(M + H)^+$.

Ejemplo 736

N-[3-(1-{3-[2-(2-CLOROFENIL)-5-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 4-metilfenilhidrazina: ESMS *m/e*: 528.2 $(M + H)^+$.

Ejemplo 737

N-[3-(1-{3-[2-(3-YODOFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y fenilhidrazina: ESMS *m/e*: 606.2 $(M + H)^+$.

Ejemplo 738

N-[3-(1-{3-[2-(3-YODOFENIL)-1-METIL-1H-INDOL-3-IL]PROPIL}-4-

PIPERIDINIL)FENIL]-2-METILPR PANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y 1-metil-1-fenilhidrazina: ESMS *m/e*: 620.2 $(M + H)^+$.

Ejemplo 739

N-[3-(1-{3-[2-(3-YODOFENIL)-1-FENIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1,1-difenilhidrazina: ESMS *m/e*: 682.2 $(M + H)^+$.

Ejemplo 740

N-[3-(1-{3-[2-(3-YODOFENIL)-1H-BENZO[G]INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-naftilhidrazina: ESMS *m/e*: 656.2 $(M + H)^+$.

Ejemplo 741

N-[3-(1-{3-[2-(3-YODOFENIL)-5-(TRIFLUOROMETOXI)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-

(3-{1-[5-(3-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-(trifluorometoxi)fenilhidrazina: ESMS *m/e*: 690.2 $(M + H)^+$.

Ejemplo 742

N-[3-(1-{3-[2-(3-YODOFENIL)-5-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-metilfenilhidrazina: ESMS *m/e*: 620.2 $(M + H)^+$.

Ejemplo 743

N-[3-(1-{3-[2-(3-YODOFENIL)-7-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS *m/e*: 620.2 $(M + H)^+$.

Ejemplo 744

N-[3-(1-{3-[2-(4-YODOFENIL)-5-(TRIFLUOROMETOXI)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-

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metilpropan-amida y clorhidrato de 4-(trifluorometoxi)fenilhidrazina: ESMS *m/e*: 690.1 $(M + H)^+$.

Ejemplo 745

N-[3-(1-{3-[2-(4-YODOFENIL)-5-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-metilfenilhidrazina: ESMS *m/e*: 620.1 $(M + H)^+$.

Ejemplo 746

N-[3-(1-{3-[2-(4-YODOFENIL)-7-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS *m/e*: 620.1 $(M + H)^+$.

Ejemplo 747

N-[3-(1-{3-[2-(4-YODOFENIL)-1-FENIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1,1-difenilhidrazina: ESMS *m/e*: 682.1

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$(M + H)^+$.

Ejemplo 748

N-[3-(1-{3-[2-(4-YODOFENIL)-1-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y 1-metil-1-fenilhidrazina: ESMS *m/e*: 620.1 $(M + H)^+$.

Ejemplo 749

N-[3-(1-{3-[2-(4-YODOFENIL)-1H-BENZO[G]INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-naftilhidrazina: ESMS *m/e*: 656.1 $(M + H)^+$.

Ejemplo 750

N-[3-(1-{3-[2-(4-YODOFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y fenilhidrazina: ESMS *m/e*: 606.1 $(M + H)^+$.

Ejemplo 751

N-[3-(1-{3-[2-(3-BROMOFENIL)-5-(TRIFLUOROMETOXI)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-(trifluorometoxi)fenilhidrazina: ESMS *m/e*: 642.0 $(M + H)^+$.

Ejemplo 752

N-[3-(1-{3-[2-(4-BROMOFENIL)-1H-BENZO[G]INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1-naftilhidrazina: ESMS *m/e*: 608.0 $(M + H)^+$.

Ejemplo 753

N-[3-(1-{3-[2-(4-BROMOFENIL)-7-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS *m/e*: 572 $(M + H)^+$.

Ejemplo 754

N-[3-(1-{3-[2-(4-BROMOFENIL)-5-(TRIFLUOROMETOXI)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-(trifluorometoxi)fenilhidrazina: ESMS *m/e*: 642 $(M + H)^+$.

Ejemplo 755

N-[3-(1-{3-[2-(3-BROMOFENIL)-1H-BENZO[G]INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1-naftilhidrazina: ESMS *m/e*: 608.0 $(M + H)^+$.

Ejemplo 756

N-[3-(1-{3-[2-(4-BROMOFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y fenilhidrazina: ESMS *m/e*: 558.1 $(M + H)^+$.

Ejemplo 757

N-[3-(1-{3-[2-(3-BROMOFENIL)-1-FENIL-1H-INDOL-3-IL]PROPIL}-

4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1,1-difenilhidrazina: ESMS *m/e*: 634.0 $(M + H)^+$.

Ejemplo 758

N-[3-(1-{3-[2-(3-BROMOFENIL)-1-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y 1-metil-1-fenilhidrazina: ESMS *m/e*: 572.0 $(M + H)^+$.

Ejemplo 759

N-[3-(1-{3-[2-(4-BROMOFENIL)-1-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y 1-metil-1-fenilhidrazina: ESMS *m/e*: 572.0 $(M + H)^+$.

Ejemplo 760

N-[3-(1-{3-[2-(4-BROMOFENIL)-1-FENIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-

amida y clorhidrato de 1,1-difenilhidrazina: ESMS *m/e*: 634.0 $(M + H)^+$.

Ejemplo 761

N-[3-(1-{3-[2-(4-BROMOFENIL)-5-METOXI-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 4-metoxifenilhidrazina: ESMS *m/e*: 588.1 $(M + H)^+$.

Ejemplo 762

N-[3-(1-{3-[2-(3-BROMOFENIL)-7-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS *m/e*: 572 $(M + H)^+$.

Ejemplo 763

N-[3-(1-{3-[2-(3-BROMOFENIL)-5-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 4-metilfenilhidrazina: ESMS *m/e*: 572

$(M + H)^+$.

Ejemplo 764

N-[3-(1-{3-[2-(4-BROMOFENIL)-5-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(4-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 4-metilfenilhidrazina: ESMS *m/e*: 572.0 $(M + H)^+$.

Ejemplo 765

N-[3-(1-{3-[2-(3-BROMOFENIL)-5-METOXI-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(3-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 4-metoxifenilhidrazina: ESMS *m/e*: 588.0 $(M + H)^+$.

Ejemplo 766

2-METIL-N-[3-(1-{3-[2-(3-NITROFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-(3-{1-[5-(3-nitrofenil)-5-oxopentil]-4-piperidinil}fenil)propanamida y fenilhidrazina: ESMS *m/e*: 525.2 $(M + H)^+$.

Ejemplo 767

2-METIL-N-[3-(1-{3-[2-(3-NITROFENIL)-1H-BENZO[G]INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-(3-{1-[5-(3-nitrofenil)-5-oxopentil]-4-piperidinil}fenil)propanamida y clorhidrato de 1-naftilhidrazina: ESMS *m/e*: 575.1 $(M + H)^+$.

Ejemplo 768

2-METIL-N-[3-(1-{3-[2-(3-NITROFENIL)-5-(TRIFLUOROMETOXI)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-(3-{1-[5-(3-nitrofenil)-5-oxopentil]-4-piperidinil}-fenil)-propanamida y clorhidrato de 4-(trifluorometoxi)-fenilhidrazina: ESMS *m/e*: 609.1 $(M + H)^+$.

Ejemplo 769

2-METIL-N-[3-(1-{3-[5-METIL-2-(3-NITROFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-(3-{1-[5-(3-nitrofenil)-5-oxopentil]-4-piperidinil}fenil)propanamida y clorhidrato de 4-metilfenilhidrazina: ESMS *m/e*: 539.2 $(M + H)^+$.

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Ejemplo 770

N-[3-(1-{3-[5-METOXI-2-(3-NITROFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-(3-{1-[5-(3-nitrofenil)-5-oxopentil]-4-piperidinil}fenil)propanamida y clorhidrato de 4-metoxifenilhidrazina: ESMS *m/e*: 555.2 (M + H)$^+$.

Ejemplo 771

2-METIL-N-[3-(1-{3-[2-(3-NITROFENIL)-1-FENIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-(3-{1-[5-(3-nitrofenil)-5-oxopentil]-4-piperidinil}fenil)propanamida y clorhidrato de 1,1-difenilhidrazina: ESMS *m/e*: 601.1 (M + H)$^+$.

Ejemplo 772

2-METIL-N-[3-(1-{3-[1-METIL-2-(3-NITROFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-(3-{1-[5-(3-nitrofenil)-5-oxopentil]-4-piperidinil}fenil)propanamida y 1-metil-1-fenilhidrazina: ESMS *m/e*: 539.2 (M + H)$^+$.

Ejemplo 773

2-METIL-N-[3-(1-{3-[7-METIL-2-(3-NITROFENIL)-1H-INDOL-3-

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IL]PROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-(3-{1-[5-(3-nitrofenil)-5-oxopentil]-4-piperidinil}fenil)propanamida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS *m/e*: 539.2 $(M + H)^+$.

Ejemplo 774

N-[3-(1-{3-[5-METOXI-2-(4-NITROFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-(3-{1-[5-(4-nitrofenil)-5-oxopentil]-4-piperidinil}fenil)propanamida y clorhidrato de 4-metoxifenilhidrazina: ESMS *m/e*: 555.6 $(M + H)^+$.

Ejemplo 775

N-[3-(1-{3-[2-BROMOFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y fenilhidrazina: ESMS *m/e*: 557.9 $(M + H)^+$.

Ejemplo 776

2-METIL-N-[3-(1-{3-[5-METIL-2-(4-NITROFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-(3-{1-[5-

(4-nitrofenil)-5-oxopentil]-4-piperidinil}fenil)propanamida y clorhidrato de 4-metilfenilhidrazina: ESMS *m/e*: 539.1 (M + H)$^+$.

Ejemplo 777

2-METIL-N-[3-(1-{3-[2-(4-NITROFENIL)-1H-BENZO[G]INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-(3-{1-[5-(4-nitrofenil)-5-oxopentil]-4-piperidinil}fenil)propanamida y clorhidrato de 1-naftilhidrazina: ESMS *m/e*: 574.7 (M + H)$^+$.

Ejemplo 778

2-METIL-N-(3-{1-[(5E)-5-(4-NITROFENIL)-5-(FENILHIDRAZONO)-PENTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparada por el Procedimiento E y Esquema AX utilizando 2-metil-N-(3-{1-[5-(4-nitrofenil)-5-oxopentil]-4-piperidinil}fenil)propanamida y fenilhidrazina: ESMS *m/e*: 542.4 (M + H)$^+$.

Ejemplo 779

2-METIL-N-[3-(1-{3-[7-METIL-2-(4-NITROFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-(3-{1-[5-(4-nitrofenil)-5-oxopentil]-4-piperidinil}fenil)propanamida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS *m/e*: 538.8

$(M + H)^+$.

Ejemplo 780

2-METIL-N-(3-{1-[(5E)-5-(4-NITROFENIL)-5-{[4-(TRIFLUORO-METOXI)FENIL]HIDRAZONO}PENTIL)-4-PIPERIDINIL]FENIL}-PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-(3-{1-[5-(4-nitrofenil)-5-oxopentil]-4-piperidinil}fenil)propanamida y clorhidrato de 4-(trifluorometoxi)fenilhidrazina: ESMS *m/e*: 626.2 $(M + H)^+$.

Ejemplo 781

N-[3-(1-{3-[2-(2-BROMOFENIL)-1H-BENZO[G]INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 1-naftilhidrazina: ESMS m/e: 608.0 $(M + H)^+$.

Ejemplo 782

N-[3-(1-{3-[2-(2-BROMOFENIL)-5-(TRIFLUOROMETOXI)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-(trifluorometoxi)fenilhidrazina: ESMS *m/e*: 641.9 $(M + H)^+$.

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Ejemplo 783

N-[3-(1-{3-[2-(2-BROMOFENIL)-7-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS *m/e*: 572.0 $(M + H)^+$.

Ejemplo 784

N-[3-(1-{3-[2-(2-BROMOFENIL)-1-FENIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1,1-difenilhidrazina: ESMS *m/e*: 634 $(M + H)^+$.

Ejemplo 785

N-[3-(1-{3-[2-(2-BROMOFENIL)-5-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 4-metilfenilhidrazina: ESMS *m/e*: 572.0 $(M + H)^+$.

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Ejemplo 786

N-[3-(1-{3-[2-(2-YODOFENIL)-5-(TRIFLUOROMETOXI)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-(trifluorometoxi)fenilhidrazina: ESMS *m/e*: 690.0 $(M + H)^+$.

Ejemplo 787

N-[3-(1-{3-[2-(2-YODOFENIL)-5-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropan-amida y clorhidrato de 4-metilfenilhidrazina: ESMS *m/e*: 620.2 $(M + H)^+$.

Ejemplo 788

2-METIL-N-[3-(1-{3-[1-METIL-2-(4-NITROFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-(3-{1-[5-(4-nitrofenil)-5-oxopentil]-4-piperidinil}fenil)propanamida y 1-metil-1-fenilhidrazina: ESMS *m/e*: 539.6 $(M + H)^+$.

Ejemplo 789

2-METIL-N-[3-(1-{3-[2-(4-NITROFENIL)-1-FENIL-1H-INDOL-3-

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IL]PROPIL}-4-PIPERIDINIL)FENIL]PR PANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando 2-metil-N-(3-{1-[5-(4-nitrofenil)-5-oxopentil]-4-piperidinil}fenil)propanamida y clorhidrato de 1,1-difenilhidrazina: ESMS *m/e*: 601.6 (M + H)$^+$.

Ejemplo 790

N-[3-(1-{3-[2-(2-YODOFENIL)-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y fenilhidrazina: ESMS *m/e*: 606.1 (M + H)$^+$.

Ejemplo 791

N-[3-(1-{3-[2-(2-YODOFENIL)-1H-BENZO[G]INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-naftilhidrazina: ESMS *m/e*: 656.1 (M + H)$^+$.

Ejemplo 792

N-[3-(1-{3-[2-(2-YODOFENIL)-1-FENIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-

yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1,1-difenilhidrazina: ESMS *m/e*: 682.1 $(M + H)^+$.

Ejemplo 793

N-[3-(1-{3-[2-(2-YODOFENIL)-7-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-yodofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y clorhidrato de 1-(2-metilfenil)hidrazina: ESMS *m/e*: 619.6 $(M + H)^+$.

Ejemplo 794

N-[3-(1-{3-[2-(2-BROMOFENIL)-1-METIL-1H-INDOL-3-IL]PROPIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento E y Esquema M utilizando N-(3-{1-[5-(2-bromofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida y 1-metil-1-fenilhidrazina: ESMS *m/e*: 572 $(M + H)^+$.

Ejemplo 795

4-(3,4-DIFLUOROFENIL)-N-(3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-2-METIL-6-OXO-1,4,5,6-TETRAHIDRO-3-PIRIDINCARBOXAMIDA: Preparada por el Procedimiento AC y Esquema AM utilizando ácido 4-(3,4-difluorofenil)-2-metil-6-oxo-1,4,5,6-tetrahidro-3-piridincarboxílico y N-{3-[1-(3-

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aminopropil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 553.0 $(M + H)^+$.

Ejemplo 796

4-(2,4-DIFLUOROFENIL)-N-(3-{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}PROPIL)-2-METIL-6-OXO-1,4,5,6-TETRAHIDRO-3-PIRIDINCARBOXAMIDA: Preparada por el Procedimiento AC y Esquema AM utilizando ácido 4-(2,4-difluorofenil)-2-metil-6-oxo-1,4,5,6-tetrahidro-3-piridincarboxílico y N-{3-[1-(3-aminopropil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 553.0 $(M + H)^+$.

Ejemplo 797

N-(3-{1-[4-(4-METOXIFENIL)BUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento O y Esquema W utilizando 4-(4-metoxifenil)-1-butanol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 409 $(M + H)^+$.

Ejemplo 798

N-(4-{1-[3-(1,2-DIFENIL-1H-INDOL-3-IL)PROPIL]-4-PIPERIDINIL}-FENIL)PROPANAMIDA: Preparada por el Procedimiento O y Esquema W utilizando 3-(1,2-difenil-1H-indol-3-il)-1-propanol y N-[4-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 542.0 $(M + H)^+$.

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Ejemplo 799

N-{4-[1-(3,3-DIFENILPROPIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el Procedimiento O y Esquema W utilizando 3,3-difenil-1-propanol y N-[4-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 427.0 $(M + H)^+$.

Ejemplo 800

2-METIL-N-(3-{1-[4-(4-NITROFENIL)BUTIL]-4-PIPERIDINIL}-FENIL)PROPANAMIDA: Preparada por el Procedimiento O y Esquema W utilizando 4-(4-nitrofenil)-1-butanol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 424.2 $(M + H)^+$.

Ejemplo 801

2-METIL-N-(3-{1-[2-(1-NAFTIL)ETIL]-4-PIPERIDINIL}FENIL)-PROPANAMIDA: Preparada por el Procedimiento O y Esquema W utilizando 2-(1-naftil)etanol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 401.2 $(M + H)^+$.

Ejemplo 802

N-{3-[1-(3,3-DIFENILPROPIL)-4-PIPERIDINIL]FENIL}-2-METIL-PROPANAMIDA: Preparada por el Procedimiento O y Esquema W utilizando 3,3-difenil-1-propanol y 2-metil-N-[3-(4-piperidinil)fenil]propànamida: ESMS *m/e*: 441.2 $(M + H)^+$.

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Ejemplo 803

N-(3-{1-[3-(3,4-DIMETOXIFENIL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento O y Esquema W utilizando 3-(3,4-dimetoxifenil)-1-propanol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 425.2 $(M + H)^+$.

Ejemplo 804

2-METIL-N-{3-[1-(3-FENILPROPIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el Procedimiento O y Esquema W utilizando 3-fenil-1-propanol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 365.2 $(M + H)^+$.

Ejemplo 805

2-METIL-N-(3-{1-[3-(4-PIRIDINIL)PROPIL]-4-PIPERIDINIL}-FENIL)PROPANAMIDA: Preparada por el Procedimiento O y Esquema W utilizando 3-(4-piridinil)-1-propanol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 366.2 $(M + H)^+$.

Ejemplo 806

N-{3-[1-(4-TER-BUTILBENCIL)-4-PIPERIDINIL]FENIL}-2-METIL-PROPANAMIDA: Preparada por el Procedimiento AJ y Esquema AV utilizando 1-bromometil)-4-ter-butilbenceno y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 393.0 $(M + H)^+$.

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Ejemplo 807

N-{3-[1-(4-BENZOILBENCIL)-4-PIPERIDINIL]FENIL}-2-METIL-PROPANAMIDA: Preparada por el Procedimiento AJ y Esquema AV utilizando [4-bromometil)fenil](fenil)metanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 441.0 $(M + H)^+$.

1,2-DICLORO-4-{[(1S)-3-CLORO-1-FENILPROPIL]OXI}BENCENO: Preparado por el Procedimiento A utilizando 3,4-diclorofenol y (1R)-3-cloro-1-fenil-1-propanol.

Ejemplo 808

N-(3-{1-[(3S)-3-(3,4-DICLOROFENOXI)-3-FENILPROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A utilizando 1,2-dicloro-4-{[(1S)-3-cloro-1-fenilpropil]oxi}benceno y 2-metil-N-[3-(4-piperidinil)-fenil]propanamida: ESMS *m/e*: 525.3 $(M + H)^+$.

Ejemplo 809

N-(3-{1-[6-(2-FLUOROFENIL)-6-HIDROXIHEXIL]-PIPERIDINIL}-4-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento L y Esquema AN utilizando N-(3-{1-[6-(2-fluorofenil)-6-oxohexil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 441.3 $(M + H)^+$.

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Ejemplo 810

N-[3-(1-{5-HIDROXI-5-[4-(TRIFLUOROMETIL)FENIL]PENTIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento L y Esquema AN utilizando 2-metil-N-[3-(1-{5-oxo-5-[4-(trifluorometil)fenil]pentil}-4-piperidinil)fenil]-propanamida: ESMS *m/e*: 477.2 $(M + H)^+$.

Ejemplo 811

N-(3-{1-[5-(4-FLUOROFENIL)-5-HIDROXIPENTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento L y Esquema AN utilizando N-(3-{1-[5-(4-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 427.2 $(M + H)^+$.

Ejemplo 812

N-(3-{1-[7-(2-FLUOROFENIL)-7-HIDROXIHEPTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento L y Esquema AN utilizando N-(3-{1-[7-(2-fluorofenil)-7-oxoheptil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 455.2 $(M + H)^+$.

Ejemplo 813

N-(3-{1-[6-(3-FLUOROFENIL)-6-HIDROXIHEXIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento L y Esquema AN utilizando N-(3-{1-[6-(3-fluorofenil)-6-

oxohexil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 441.2 $(M + H)^+$.

Ejemplo 814

N-(3-{1-[5-(2-FLUOROFENIL)-5-HIDROXIPENTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento L y Esquema AN utilizando N-(3-{1-[5-(2-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 427.2 $(M + H)^+$.

Ejemplo 815

N-(3-{1-[5-(3-FLUOROFENIL)-5-HIDROXIPENTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento L y Esquema AN utilizando N-(3-{1-[5-(3-fluorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 427.2 $(M + H)^+$.

Ejemplo 816

N-(3-{1-[5-(3-CLOROFENIL)-5-HIDROXIPENTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento L y Esquema AN utilizando N-(3-{1-[5-(3-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 443.1 $(M + H)^+$.

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Ejemplo 817

N-(3-{1-[6-(4-FLUOROFENIL)-6-HIDROXIHEXIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento L y Esquema AN utilizando N-(3-{1-[6-(4-fluorofenil)-6-oxohexil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 441.2 $(M + H)^+$.

Ejemplo 818

N-(3-{1-[6-(4-CLOROFENIL)-6-HIDROXIHEXIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento L y Esquema AN utilizando N-(3-{1-[6-(4-clorofenil)-6-oxohexil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 456.9 $(M + H)^+$.

Ejemplo 819

N-(3-{1-[5-(4-CLOROFENIL)-5-HIDROXIPENTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento L y Esquema AN utilizando N-(3-{1-[5-(4-clorofenil)-5-oxopentil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS *m/e*: 443.0 $(M + H)^+$.

Ejemplo 820

N-(4-{1-[(9-ETIL-9H-CARBAZOL-3-IL)METIL]-4-PIPERIDINIL}-FENIL)BUTANAMIDA: Preparada por el Procedimiento F y Esquema R, sin HOAc, utilizando 9-etil-9H-carbazol-3-carbaldehído y

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N-[4-(4-piperidinil)fenil]butanamida: ESMS *m/e*: 454.2 (M + H)$^+$.

Ejemplo 821

N-(3-{1-[(9-ETIL-9H-CARBAZOL-3-IL)METIL]-4-PIPERIDINIL}-FENIL)PROPANAMIDA: Preparada por el Procedimiento F y Esquema R, sin HOAc, utilizando 9-etil-9H-carbazol-3-carbaldehído y N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 440.5 (M + H)$^+$.

Ejemplo 822

N-(3-{1-[(1,9-DIMETIL-9H-CARBAZOL-3-IL)METIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento F y Esquema R, sin HOAc, utilizando 1,9-dimetil-9H-carbazol-3-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: RMN ^{1}H (400 MHz, $CDCl_3$) Γ 8.05-6.77 (m, 10H), 5.20-5.12 (m, 1H), 4.04 (s, 3H), 3.93 (s, 2H), 3.34-3.24 (m, 2H), 2.79 (s, 3H), 2.56-2.38 (m, 2H), 2.38-2.26 (m, 2H), 2.08-1.88 (m, 2H), 1.82-1.70 (m, 2H), 1.16 (d, 6H, J= 6.8 Hz); ESMS *m/e*: 454.2 (M + H)$^+$.

Ejemplo 823

N-(3-{1-[(9-ETIL-9H-CARBAZOL-3-IL)METIL]-4-PIPERIDINIL}-FENIL)CICLOPROPANCARBOXAMIDA: Preparada por el Procedimiento F y Esquema R, sin HOAc, utilizando 9-etil-9H-carbazol-3-

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carbaldehído y N-[3-(4-piperidinil)fenil]ciclopropan-carboxamida: ESMS *m/e*: 452.6 $(M + H)^+$.

Ejemplo 824

1-(3-{1-[(9-ETIL-9H-CARBAZOL-3-IL)METIL]-4-PIPERIDINIL}-FENIL)-2-PIRROLIDINONA: Preparada por el Esquema R y Procedimiento F. Una solución de 1-(9-etil-9H-carbazol-3-il)etanona (22.3 mg, 0.100 mmol) y 1-[3-(4-piperidinil)-fenil]-2-pirrolidinona (27.2 mg, 0.100 mmol) en 1,2-dicloro-etano (1.00 mL) se trató con triacetoxiborohidruro de sodio (63.6 mg, 0.300 mmol) y HOAc (5.70 uL, 0.100 mmol). La mezcla se agitó durante la noche a temperatura ambiente. La mezcla de reacción se trató con solución de $NaHCO_3$ acuoso, saturado (10 mL). La capa acuosa se extrajo con CH_2Cl_2 (3 X 10 mL) y las capas orgánicas combinadas se lavaron con salmuera (10 mL), se secaron sobre $MgSO_4$ y se concentraron *in vacuo*. El residuo se purificó por CCF preparativa utilizando 5% de NH_3 (2.0 M en metanol) en CH_2Cl_2 para dar el producto deseado 1-(3-{1-[(9-etil-9H-carbazol-3-il)metil]-4-piperidinil}fenil)-2-pirrolidinona (4.60 mg, 9.43 %): RMN ^1H (400 MHz, $CDCl_3$) Γ 8.04 (d, 1H, J = 7.4 Hz), 7.99 (s, 1H), 7.43-7.28 (m, 5H), 5.96 (d, 1H, J = 7.4 Hz), 4.31 (q, 2H, J = 6.8 Hz), 3.77 (t, 2H, J = 7.3 Hz), 3.70 (s, 2H), 3.06 (d, 2H, J = 10.6 Hz), 2.56-2.42 (m, 3H), 2.07 (m, 4H), 1.77 (m, 4H), 1.36 (m, 3H); ESMS *m/e*: 452.5 $(M + H)^+$.

N-{3-[1-(1H-INDOL-5-ILMETIL)-4-PIPERIDINIL]FENIL}-2-METIL-PROPANAMIDA: Preparada por el Procedimiento F y Esquema R, sin HOAc, utilizando 1H-indol-5-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 376.2 $(M + H)^+$.

1-(4-CLOROBUTIL)-1H-INDOL: Preparado por el Procedimiento AH, y Esquema P utilizando 1H-indol y 1-bromo-4-clorobutano: RMN ^1H (400 MHz, $CDCl_3$) Γ 7.72-7.02 (m, 5H), 6.49 (d, 1H, J = 2.8 Hz), .4.13 (t, 2H, J = 6.8 Hz), 3.48 (t, 2H, J = 6.8 Hz), 2.06-1.92 (m, 2H), 1.80-1.70 (m, 2H).

1-(3-CLOROPROPIL)-1H-INDOL: Preparado por el Procedimiento AH, y Esquema P utilizando 1H-indol y 1-bromo-3-cloro-propano: RMN ^1H (400 MHz, $CDCl_3$) Γ 7.70-7.04 (m, 5H), 6.50 (d, 1H, J = 2.8 Hz), 4.31 (t, 2H, J = 6.8 Hz), 3.42 (t, 2H, J = 6.4 Hz), 2.28-2.20 (m, 2H).

Ejemplo 825

N-(4-{1-[5-(1H-INDOL-1-IL)PENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento AH y Esquema P utilizando 1-(5-cloropentil)-1H-indol y 2-metil-N-[4-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 432.3 $(M + H)^+$.

Ejemplo 826

N-(4-{1-[5-(1H-INDOL-1-IL)PENTIL]-4-PIPERIDINIL}FENIL)-BUTANAMIDA: Preparada por el Procedimiento AH y Esquema P

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utilizando 1-(5-cloropentil)-1H-indol y N-[4-(4-piperidinil)fenil]butanamida: ESMS *m/e*: 432.3 $(M + H)^+$.

Ejemplo 827

N-(4-{1-[5-(1H-INDOL-1-IL)PENTIL]-4-PIPERIDINIL}FENIL)-PROPANAMIDA: Preparada por el Procedimiento AH y Esquema P utilizando 1-(5-cloropentil)-1H-indol y N-[4-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 418.2 $(M + H)^+$.

Ejemplo 828

N-(4-{1-[6-(1H-INDOL-1-IL)HEXIL]-4-PIPERIDINIL}FENIL)-PROPANAMIDA: Preparada por el Procedimiento AH y Esquema P utilizando 1-(6-clorohexil)-1H-indol y N-[4-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 432.3 $(M + H)^+$.

Ejemplo 829

2-METIL-N-(3-{1-[(1-METIL-1H-INDOL-2-IL)METIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparada por el Procedimiento F y Esquema R, sin HOAc, utilizando 1-metil-1H-indol-2-carbaldehído y 2-metil-N-[3-(4-piperidinil)-fenil]propanamida: ESMS *m/e*: 390.3 $(M + H)^+$.

Ejemplo 830

N-{3-[1-(1H-INDOL-4-ILMETIL)-4-PIPERIDINIL]FENIL}-2-METIL-PROPANAMIDA: Preparada por el Procedimiento F y Esquema R,

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sin HOAc, utilizando 1H-indol-4-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 376.2 $(M + H)^+$.

Ejemplo 831

N-(4-{1-[6-(1H-INDOL-1-IL)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento AH y Esquema P utilizando 1-(6-clorohexil)-1H-indol y 2-metil-N-[4-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 446.3 $(M + H)^+$.

Ejemplo 832

N-{3-[1-(1H-INDOL-7-ILMETIL)-4-PIPERIDINIL]FENIL}-2-METIL-PROPANAMIDA: Preparada por el Procedimiento F y Esquema R, sin HOAc, utilizando 1H-indol-7-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 376.2 $(M + H)^+$.

Ejemplo 833

N-[3-(1-{[1-(4-METOXIFENIL)-1H-INDOL-5-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-yodo-4-metoxibenceno y N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 482.0 $(M + H)^+$.

Ejemplo 834

4-[4-({4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}METIL)-1H-INDOL-1-IL]BENZOATO DE METILO: Preparado por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 4-yodobenzoato de metilo y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 510.3 $(M + H)^+$.

Ejemplo 835

2-METIL-N-[3-(1-{[1-(3-METILFENIL)-1H-INDOL-5-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-yodo-3-metilbenceno y N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 466.3 $(M + H)^+$.

Ejemplo 836

N-[3-(1-{[1-(4-FLUOROFENIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-fluoro-4-yodobenceno y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$) Γ 7.66-6.92 (m, 12H), 6.65 (d, 1H, J = 3.2 Hz), 3.69 (s, 2H), 3.15-3.02 (m, 2H), 2.58-2.40 (m, 2H), 2.20-2.04 (m, 2H), 1.94-1.76 (m, 4H), 1.25 (d, 6H, J = 6.8

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Hz); ESMS *m/e*: 470.6 $(M + H)^+$.

Ejemplo 837

N-(3-{1-[4-(1H-INDOL-1-IL)BUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento AH y Esquema P utilizando 1-(4-clorobutil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 418.3 $(M + H)^+$.

Ejemplo 838

N-[3-(1-{[1-(4-CLOROFENIL)-1H-INDOL-5-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-cloro-4-yodobenceno y N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 486.2 $(M + H)^+$.

Ejemplo 839

N-[3-(1-{[1-(3-METOXIFENIL)-1H-INDOL-5-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-yodo-3-metoxibenceno y N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 482.2 $(M + H)^+$.

Ejemplo 840

N-(4-{1-[4-(1H-INDOL-1-IL)BUTIL]-4-PIPERIDINIL}FENIL)BUTANAMIDA: Preparada por el Procedimiento AH y Esquema P utilizando 1-(4-clorobutil)-1H-indol y N-[4-(4-piperidinil)-fenil]butanamida: ESMS *m/e*: 418.2 $(M + H)^+$.

Ejemplo 841

N-[3-(1-{[1-(2-METOXIFENIL)-1H-INDOL-5-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-yodo-2-metoxibenceno y N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 482.2 $(M + H)^+$.

Ejemplo 842

N-[3-(1-{[1-(3-CLOROFENIL)-1H-INDOL-5-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-cloro-4-yodobenceno y N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 486.2 $(M + H)^+$.

Ejemplo 843

2-[5-{{4-[3-(ISOBUTIRILAMINO)FENIL]-1-PIPERIDINIL}METIL)-1H-INDOL-1-IL]BENZOATO DE METILO: Preparado por el

Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 2-yodobenzoato de metilo y N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 510.2 $(M + H)^+$.

Ejemplo 844

N-(3-{1-[3-(1H-INDOL-1-IL)PROPIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento AH y Esquema P utilizando 1-(3-cloropropil)-1H-indol y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 404.2 $(M + H)^+$.

Ejemplo 845

2-METIL-N-{3-[1-({1-[4-(TRIFLUOROMETIL)FENIL]-1H-INDOL-5-IL}METIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-yodo-4-(trifluorometil)benceno y N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 520.2 $(M + H)^+$.

Ejemplo 846

N-(3-{1-[(1-[1,1'-BIFENIL]-2-IL-1H-INDOL-5-IL)METIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 2-yodo-1,1'-bifenilo y N-{3-[1-(1H-indol-5-

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ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 528.3 $(M + H)^+$.

Ejemplo 847

2-METIL-N-[3-(1-{[1-(2-METILFENIL)-1H-INDOL-5-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-yodo-2-metilbenceno y N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 466.2 $(M + H)^+$.

Ejemplo 848

2-METIL-N-[3-(1-{[1-(4-METILFENIL)-1H-INDOL-5-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-yodo-4-metilbenceno y N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 466.3 $(M + H)^+$.

Ejemplo 849

N-[3-(1-{[1-(2-CLOROFENIL)-1H-INDOL-5-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-cloro-2-yodobenceno y N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*:

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486.2 $(M + H)^+$.

Ejemplo 850

2-METIL-N-{3-[1-({1-[3-(TRIFLUOROMETIL)FENIL]-1H-INDOL-5-IL}METIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-yodo-3-(trifluorometil)benceno y N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$) Γ 7.80-6.94 (m, 12H), 6.69 (d, 1H, J = 3.6 Hz), 3.36 (s, 2H), 3.10-3.00 (m, 2H), 2.58-2.42 (m, 2H), 2.16-2.02 (m, 2H), 1.85-1.75 (m, 4H), 1.25 (d, 6H, J = 7.2 Hz); ESMS m/e: 520.2 $(M + H)^+$.

Ejemplo 851

2-METIL-N-[3-(1-{[1-(2-NITROFENIL)-1H-INDOL-5-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-yodo-2-nitrobenceno y N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 497.2 $(M + H)^+$.

Ejemplo 852

N-[3-(1-{[1-(2-FLUOROFENIL)-1H-INDOL-5-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu,

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utilizando 1-fluoro-2-yodobenceno y N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 470.2 $(M + H)^+$.

Ejemplo 853

2-METIL-N-[3-(1-{[1-(1-NAFTIL)-1H-INDOL-5-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-yodonaftaleno y N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 502.2 $(M + H)^+$.

Ejemplo 854

N-[3-(1-{[1-(2,3-DICLOROFENIL)-1H-INDOL-5-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1,2-dicloro-3-yodobenceno y N-{3-[1-(1H-indol-5-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$) Γ 7.68-6.94 (m, 12H), 6.68 (d, 1H, J = 2.8 Hz), 3.69 (s, 2H), 3.15-3.02 (m, 2H), 2.54-2.42 (m, 2H), 2.18-2.02 (m, 2H), 1.88-1.76 (m, 4H), 1.25 (d, 6H, J = 6.8 Hz); ESMS *m/e*: 520.1 $(M + H)^+$.

Ejemplo 855

N-[3-(1-{[1-(2,3-DICLOROFENIL)-1H-INDOL-7-IL]METIL}-4-

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PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1,2-dicloro-3-yodobenceno y N-{3-[1-(1H-indol-7-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 520.2 $(M + H)^+$.

Ejemplo 856

N-[3-(1-{[1-(3-METOXIFENIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-yodo-3-metoxibenceno y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 482.3 $(M + H)^+$.

Ejemplo 857

N-[3-(1-{[1-(2,3-DICLOROFENIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1,2-dicloro-3-yodobenceno y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 520.2 $(M + H)^+$.

Ejemplo 858

N-[3-(1-{[1-(3-CLOROFENIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el

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Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-cloro-3-yodobenceno y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 486.2 $(M + H)^+$.

Ejemplo 859

2-METIL-N-[3-(1-{[1-(3-METILFENIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-yodo-3-metilbenceno y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 466.3 $(M + H)^+$.

Ejemplo 860

N-[3-(1-{[1-(3-METOXIFENIL)-1H-INDOL-7-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-yodo-3-metoxibenceno y N-{3-[1-(1H-indol-7-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 482.3 $(M + H)^+$.

Ejemplo 861

2-METIL-n-{3-[1-({1-[3-(TRIFLUOROMETIL)FENIL]-1H-INDOL-4-IL}METIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu,

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utilizando 1-yodo-3-(trifluorometil)benceno y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 520.2 $(M + H)^+$.

Ejemplo 862

N-[3-(1-{[1-(3,4-DIMETILFENIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]-fenil}-2-metilpropanamida y 4-yodo-1,2-dimetilbenceno: ESMS *m/e*: 480.0 $(M + H)^+$.

Ejemplo 863

N-[3-(1-{[1-(3,4-DIFLUOROFENIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1,3-dicloro-5-yodobenceno y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 520.3 $(M + H)^+$.

Ejemplo 864

N-[3-(1-{[1-(3,4-DICLOROFENIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1,2-dicloro-4-yodobenceno y N-{3-[1-(1H-indol-4-

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ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 520.0 $(M + H)^+$.

Ejemplo 865

N-[3-(1-{[1-(2-CLORO-4-FUOROFENIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 2-cloro-4-fluoro-1-yodobenceno y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 504.0 $(M + H)^+$.

Ejemplo 866

N-[3-(1-{[1-(2,4-DIFLUOROFENIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 2,4-difluoro-1-yodobenceno y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 488.0 $(M + H)^+$.

Ejemplo 867

2-METIL-N-[3-(1-{[1-(3-PIRIDINIL)-1H-INDOL-7-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 3-yodopiridina y N-{3-[1-(1H-indol-7-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 453.1 (M +

H)$^+$.

Ejemplo 868

N-{3-[1-(1H-INDOL-6-ILMETIL)-4-PIPERIDINIL]FENIL}-2-METILPROPANAMIDA: Preparada por el Procedimiento F y Esquema R utilizando 1H-indol-6-carbaldehído y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS *m/e*: 376.2 (M + H)$^+$.

Ejemplo 869

2-METIL-N-[3-(1-{[1-(4-PIRIDINIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 4-yodopiridina y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 453.2 (M + H)$^+$.

Ejemplo 870

2-METIL-N-[3-(1-{[1-(2-PIRIDINIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 2-yodopiridina y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 453.2 (M + H)$^+$.

Ejemplo 871

N-[3-(1-{[1-(2-FLUOROFENIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-fluoro-2-yodobenceno y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 470.1 $(M + H)^+$.

Ejemplo 872

N-[3-(1-{[1-(4-CLOROFENIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-cloro-4-yodobenceno y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 486.1 $(M + H)^+$.

Ejemplo 873

2-METIL-N-[3-(1-{[1-(3-PIRIDINIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 3-yodopiridina y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 453.2 $(M + H)^+$.

Ejemplo 874

N-[3-(1-{[1-(2,3-DIMETILFENIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-yodo-2,3-dimetilbenceno y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 480.1 $(M + H)^+$.

Ejemplo 875

N-[3-(1-{[1-(3-FLUOROFENIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-fluoro-3-yodobenceno y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 470.1 $(M + H)^+$.

Ejemplo 876

2-METIL-N-{3-[1-({1-[2-(TRIFLUOROMETIL)FENIL]-1H-INDOL-4-IL}METIL)-4-PIPERIDINIL]FENIL}PROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-yodo-2-(trifluorometil)benceno y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 520.1 $(M + H)^+$.

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Ejemplo 877

N-[3-(1-{[1-(2-CLOROFENIL)-1H-INDOL-4-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-cloro-2-yodobenceno y N-{3-[1-(1H-indol-4-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 486.1 $(M + H)^+$.

Ejemplo 878

N-[3-(1-{[1-(2,3-DIMETILFENIL)-1H-INDOL-7-IL]METIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento C y Esquema Q1, con CuBr en lugar de Cu, utilizando 1-yodo-2,3-dimetilbenceno y N-{3-[1-(1H-indol-7-ilmetil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS *m/e*: 480.0 $(M + H)^+$.

2-METIL-N-[3-(1-{5-OXO-5-(TRIFLUOROMETIL)FENIL]PENTIL}-4-PIPERIDINIL)FENIL]PROPANAMIDA: Preparada por el Procedimiento K y Esquema E utilizando 5-cloro-1-[4-(trifluormetil)fenil]-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e : 475.1 $(M + H)^+$.

N-[3-{1-[5-(4-FLUOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema E utilizando 5-cloro-1-(4-fluorofenil)-1-pentanona y

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2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e : 425.2 $(M + H)^+$.

N-(3-{1-[5-(3-FLUOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema E utilizando 5-cloro-1-(3-fluorofenil)-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e : 425.2 $(M + H)^+$.

N-(3-{1-[5-(3-CLOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema E utilizando 5-cloro-1-(3-clorofenil)-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e : 441.1 $(M + H)^+$.

N-(3-{1-[5-(4-CLOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema E utilizando 5-cloro-1-(4-clorofenil)-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e : 441.1 $(M + H)^+$.

Ejemplo 879

2-METIL-N-{3-[1-(3-OXO-3-FENILPROPIL)-4-PIPERIDINIL]FENIL}-PROPANAMIDA: Preparada por el Procedimiento K y Esquema E utilizando K_2CO_3 en vez de Na_2CO_3 y NaI en lugar de KI y 3-

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cloro-1-fenil-1-propanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e : 379.3 $(M + H)^+$.

Ejemplo 880

N-(3-{1-[7-(2-FLUOROFENIL)-7-OXOHEPTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema E utilizando K_2CO_3 en vez de Na_2CO_3 y NaI en lugar de KI y 7-cloro-1-(2-fluorofenil)-1-heptanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: RMN ^1H (400 MHz, $CDCl_3$), 8.17 (s, br, 1H), 8.06-6.88 (m, 8H), 3.08-2.94 (m, 4H), 2.62-2.48 (m, 1H), 2.48-2.38 (m, 1H), 2.38-2.15 (m, 2H), 2.02-1.92 (m, 2H), 1.84-1.777 (m, 4H), 1.77-.166 (m, 2H), 1.62-1.46 (m, 2H), 1.46-1.29 (m, 4H), 1.21 (d, 6H, J= 6.8 Hz); ESMS m/e : 453.2 $(M + H)^+$.

Ejemplo 881

N-(3-{1-[5-(2-FLUOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema E utilizando K_2CO_3 en vez de Na_2CO_3 y NaI en lugar de KI y 5-cloro-1-(2-fluorofenil)-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 425.2 $(M + H)^+$.

Ejemplo 882

N-(3-{1-[6-(3-FLUOROFENIL)-6-OXOHEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y

Esquema E utilizando K_2CO_3 en vez de Na_2CO_3 y NaI en lugar de KI y 6-cloro-1-(3-fluorofenil)-1-hexanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 439.2 $(M + H)^+$.

Ejemplo 883

N-(3-{1-[6-(2-FLUOROFENIL)-6-OXOHEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema E utilizando K_2CO_3 en vez de Na_2CO_3 y NaI en lugar de KI y 6-cloro-1-(2-fluorofenil)-1-hexanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 439.2 $(M + H)^+$.

Ejemplo 884

N-(3-{1-[7-(4-FLUOROFENIL)-7-OXOHEPTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema E utilizando K_2CO_3 en vez de Na_2CO_3 y NaI en lugar de KI y 7-cloro-1-(4-fluorofenil)-1-heptanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 453.2 $(M + H)^+$.

N-(3-{1-[5-(2-FLUOROFENIL)-5-OXOPENTIL]-4-PIPERIDINIL}FENIL)2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema E utilizando K_2CO_3 en vez de Na_2CO_3 y NaI en lugar de KI y 5-cloro-1-(2-fluorofenil)-1-pentanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 425.2 $(M + H)^+$.

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Ejemplo 885

N-(3-{1-[6-(4-CLOROFENIL)-6-OXOHEXIL]-4-PIPERIDINIL}FE-NIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema E utilizando K_2CO_3 en vez de Na_2CO_3 y NaI en lugar de KI y 6-cloro-1-(4-clorofenil)-1-hexanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 455.1 $(M + H)^+$.

Ejemplo 886

N-(3-{1-[7-(4-CLOROFENIL)-7-OXOHEPTIL]-4-PIPERIDINIL}FE-NIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema E utilizando K_2CO_3 en vez de Na_2CO_3 y NaI en lugar de KI y 7-cloro-1-(4-clorofenil)-1-hepatanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 469.1 $(M + H)^+$.

Ejemplo 887

N-(3-{1-[6-(4-FLUOROFENIL)-6-OXOHEXIL]-4-PIPERIDINIL}FE-NIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K y Esquema E utilizando K_2CO_3 en vez de Na_2CO_3 y NaI en lugar de KI y 6-cloro-1-(4-fluorofenil)-1-hexanona y 2-metil-N-[3-(4-piperidinil)fenil]propanamida: ESMS m/e: 439.1 $(M + H)^+$.

Ejemplo 888

N-(3-{1-[6-(3-ACETILFENOXI)-6-(2-FLUORFENIL)HEXIL]-4-PIPE-RIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 1-(3-

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hidroxifenil)etanona y N-(3-{1-[6-(2-fluorofenil)-6-hidroxihexil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 559.5 $(M + H)^+$.

Ejemplo 889

N-(3-{1-[6-(2-FLUOROFENOXI)-6-(2-FLUOROFENIL)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 2-fluorofenol y N-(3-{1-[6-(2-fluorofenil)-6-hidroxihexil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 535.1 $(M + H)^+$.

Ejemplo 890

N-(3-{1-[6-(4-FLUOROFENOXI)-6-(2-FLUOROFENIL)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-fluorofenol y N-(3-{1-[6-(2-fluorofenil)-6-hidroxihexil]-4-piperidinil}fenil)-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$), sal de HCl 7.72-6.72 (m, 12H), 5.42-5.34 (m, 1H); 3.68-3.58 (m, br 2H), 3.02-2.92 (m, 2H), 2.80-2.46 (m, 6H), 2.05-1.78 (m, 6H9, 1.68-1.56 (m, 1H), 1.56-1.38 (m, 3H), 1.25 (d, 6H, J= 6.8 Hz); ESMS m/e: 535.1 $(M + H)^+$.

Ejemplo 891

N-(3-{1-[6-(2-FLUOROFENIL)-6-(2-METOXIFENOXI)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el

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Procedimiento A y Esquema AN utilizando 2-metoxifenol y N-(3-{1-[6-(2-fluorofenil)-6-hidroxihexil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 547.0 $(M + H)^+$.

Ejemplo 892

N-(3-{1-[6-(2-FLUOROFENIL)-6-(4-METOXIFENOXI)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-metoxifenol y N-(3-{1-[6-(2-fluorofenil)-6-hidroxihexil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 547.1 $(M + H)^+$.

Ejemplo 893

N-(3-{1-[6-(4-ACETILFENOXI)-6-(2-FLUOROFENIL)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 1-(4-hidroxifenil)etanona y N-(3-{1-[6-(2-fluorofenil)-6-hidroxihexil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 559.2 $(M + H)^+$.

Ejemplo 894

N-(3-{1-[6-(3,4-DIMETOXIFENOXI)-6-(2-FLUOROFENIL)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 3,4-dimetoxifenol y N-(3-{1-[6-(2-fluorofenil)-6-hidroxihexil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 577.6 $(M + H)^+$.

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Ejemplo 895

N-(3-{1-[6-(2-ETOXIFENOXI)-6-(2-FLUOROFENIL)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 2-etoxifenol y N-(3-{1-[6-(2-fluorofenil)-6-hidrohexil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 561.1 $(M + H)^+$.

Ejemplo 896

N-(3-{1-[6-(4-BROMOFENOXI)-6-FENILHEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-bromofenol y N-(3-{1-[6-(hidroxi-6-fenilhexil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS m/e: 577.0 $(M + H)^+$.

Ejemplo 897

N-(3-{1-[6-(4-FLUOROFENOXI)-6-(4-FLUOROFENIL)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-fluorofenol y N-(3-{1-[6-(4-fluorofenil)-6-hidrohexil]-4-piperidinil}fenil)-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$), sal de HCl 8.22 (s, br, 1H), 7.74-6.70 (m, 12H), 5.05-4.94 (m, 1H), 3.66-3.52 (m, br, 2H), 3.02-2.83 (m, br, 2H), 2.81-2.58 (m, br, 4H), 2.58-2.36 (m, br, 2H), 2.02-1.66 (m, br, 6H), 1.66-

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1.46 (m, br, 1H), 1.46.1.35 (m, br, 3H), 1.26 (d, 6H, J= 6.0 Hz); ESMS m/e: 535.1 $(M + H)^+$.

Ejemplo 898

N-(3-{1-[6-(4-METOXIFENOXI)-6-FENILHEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-metoxifenol y N-{3-[1-(6-hidroxi-6-fenilhexil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS m/e: 529.6 $(M + H)^+$.

Ejemplo 899

N-(3-{1-[6-(4-CLOROFENOXI)-6-(4-CLOROFENIL)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-clorofenol y N-(3-{1-[6-(4-clorofenil)-6-hidroxihexil]-4-piperidinil]fenil)-2-metilpropanamida: ESMS m/e: 566.9 $(M + H)^+$.

Ejemplo 900

N-(3-{1-[6-(4-BROMOFENOXI)-6-(4-FLUOROFENIL)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-bromofenol y N-(3-{1-[6-(4-fluorofenil)-6-hidroxihexil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 595.0 $(M + H)^+$.

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Ejemplo 901

N-(3-{1-[6-(4-CLOROFENOXI)-6-(4-FLUOROFENIL)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-clorofenol y N-(3-{1-[6-(4-fluorofenil)-6-hidroxihexil]-4-piperidinil}fenil)-2-metilpropanamida: RMN ^{1}H (400 MHz, $CDCl_3$), sal de HCl 7.93 (s, 1H), 7.72-6.68 (m, 12H), 5.06-4.98 (m, 1H), 3.66-3.50 (m, br, 2H), 3.02-2.82 (m, br, 2H), 2.80-2.57 (m, br, 4H), 2.57-2.38 (m, br, 2H), 2.02-1.76 (m, br, 6H), 1.64-1.48 (m, br, 1H), 1.48-1.36 (m, br, 3H), 1.25 (d, 6H, J= 6.8 Hz); Cálc. Anál. para $C_{33}H_{41}Cl_2FN_2O_2$ 0.5EtOAc: C, 66.55; H, 7.18; N, 4.43. Encontrado: C, 66.35; H, 6.86; N, 4.46. ESMS m/e: 550.8 $(M + H)^+$.

Ejemplo 902

N-(3-{1-[6-(4-CLOROFENIL)-6-(4-FLUOROFENOXI)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-fluorofenol y N-(3-{1-[6-(4-clorofenil)-6-hidroxihexil]-4-piperidinil}fenil)-2-metilpropanamida: RMN ^{1}H (400 MHz, $CDCl_3$), sal de HCl 8.22 (s, br, 1H), 7.74-6.68 (m, 12H), 5.04-4.92 (m, 1H), 3.66-3.50 (m, br, 2H), 3.00-2.82 (br, 2H), 2.80-2.58 (m, br, 4H), 2.58-2.40 (m, br, 2H), 2.00-1.68 (m, br, 6H), 1.66-1.46 (m, br, 1H), 1.46-1.36 (br, 3H), 1.25 (d, 6H, J= 7.2 Hz); ESMS m/e: 551.1 $(M + H)^+$.

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Ejemplo 903

N-(3-{1-[6-(3-ACETILFENOXI)-6-FENILHEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 1-(3-hidroxifenil)etanona y N-{3-[1-(6-hidroxi-6-fenilhexil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS m/e: 541.2 $(M + H)^+$.

Ejemplo 904

N-(3-{1-[6-(4-CLOROFENOXI)-6-FENILHEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-clorofenol y N-{3-[1-(6-hidroxi-6-fenilhexil)-4-piperidinil]fenil}-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$), sal de HCl 8.28 (s, 1H), 7.78-6.70 (m, 13 H), 5.08-4.98 (m, 1H), 3.64-3.46 (m, br, 2H), 3.02-2.82 (br, 2H), 2.82-2.56 (m, br, 4H), 2.56-2.34 (m, br, 2H), 2.05-1.75 (m, br, 6H), 1.64-1.48 (m, br, 1H), 1.48-1.34 (br, 3H), 1.25 (d, 6H), J= 6.8 Hz); ESMS m/e: 533.1 $(M + H)^+$.

Ejemplo 905

N-(3-{1-[6-(4-BROMOFENOXI)-6-(4-CLOROFENIL)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-bromofenol y N-(3-{1-[6-(4-clorofenil)-6-hidrohexil]-4-piperidinil]fenil}-2-metilpropanamida: ESMS m/e : 611.0 $(M + H)^+$.

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Ejemplo 906

N-(3-{1-[6-(4-CLOROFENIL)-6-(4-METOXIFENOXI)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-metoxifenol y N-(3-{1-[6-(4-clorofenil)-6-hidrohexil]-4-piperidinil]fenil}-2-metilpropanamida: ESMS m/e : 563.1 $(M + H)^+$.

Ejemplo 907

N-(3-{1-[6-(4-FLUOROFENIL)-6-(4-METOXIFENOXI)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-metoxifenol y N-(3-{1-[6-(4-fluorofenil)-6-hidrohexil]-4-piperidinil}fenil)-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$), sal de HCl 8.11 (s, 1H), 7.65-7.84 (m, 12H), 5.21-5.10 (m, 1H), 3.66-3.56 (m, br, 2H), 3.02-2.82 (br, 2H), 2.82-2.56 (m, br, 4H),2.54 (s, 3H), 2.53-2.32 (m, br, 2H), 2.02-1.70(m, br, 6H), 1.64-1.48 (m, br, 1H), 1.48-1.34 (br, 3H), 1.25 (d, 6H, J= 6.8 Hz); ESMS m/e : 547.1 $(M + H)^+$.

Ejemplo 911

N-[3-(1-{6-(4-FLUOROFENIL)-6-[2-FLUORO-5-TRIFLUOROMETIL)FENOXI]HEXIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 2-fluoro-5-(trifluorometil)fenol y N-(3-{1-[6-(4-fluorofenil)-

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6-hidrohexil]-4-piperidinil}fenil)-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$), sal de HCl 8.23 (s, br, 1H), 7.74-6.88 (m, 11H), 5.20-5.12 (m, 1H), 3.68-3.52 (m, br, 2H), 3.02-2.82 (m, br, 2H), 2.82-2.60 (m, 4H), 2.58-2.38 (m, br, 2H), 2.12-2.02 (m, br, 1H), 2.02-1.80 (m, br, 5H), 1.68-1.52 (m, br, 1H), 1.52-1.36 (br, 3H), 1.25 (d, 6H, J= 7.2 Hz); ESMS m/e : 603.3 $(M + H)^+$.

Ejemplo 912

N-(3-{1-[6-(3-ACETILFENOXI)-6-(4-CLOROFENIL)HEXIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 1-(3-hidroxifenil)etanona y N-(3-{1-[6-(4-clorofenil)-6-hidrohexil]-4-piperidinil}fenil)-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$), sal de HCl 8.41 (s, 1H), 7.72-6.84 (m, 12H), 5.18-5.10 (m, 1H), 3.62-3.50 (br, 2H), 3.00 (2.92 (m, 2H), 2.90-2.58 (m, 4H), 2.54 (s, 3H), 2.50-2.12 (m, 2H), 2.02-1.70 (m. Br, 6H), 1.64-1.50 (m, br, 1H), 1.50-1.114 (m, br, 3H), 1.25 (d, 6H, J= 6.8 Hz); ESMS m/e : 575.3 $(M + H)^+$.

Ejemplo 913

N-[3-(1-{6-(2-FLUOROFENIL)-6-[2-FLUORO-5-(TRIFLUOROMETIL)FENOXI]HEXIL}-4-PIPERIDINIL)FENIL]-2-METIL-PROPANAMIDA: Preparada por el Procedimiento A y Esquema AN

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utilizando 2-fluoro-5-(trifluorometil)fenol y N-(3-{1-[6-(2-fluorofenil)-6-hidrohexil]-4-piperidinil}fenil)-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$), sal de HCl 8.35 (s, 1H), 7.68-6.82 (m, 11H), 5.58-5.48 (m, 1H), 3.64-3.50 (m, 2H), 3.01-2.94 (m, br, 2H), 2.92-2.54 (m, 4H), 2.48-2.32 (m, br, 2H), 2.20-2.04 (m, 1H), 2.01-1.80 (m, 5H), 1.70-1.54 (m, 1H), 1.54-1.36 (m, 3H), 1.25 (d, 6H, J= 7.2 Hz), Cálc. Anál. para $C_{34}H_{40}ClF_5N_2O_2$ 0.6 MeOH: C, 63.12; H, 6.49; n, 4.25;. Encontrado: C, 63.38; H, 6.61; N, 3.95. (s, 1H), 7.65-7.84 (m, 12H), 5.21-5.10 (m, 1H), 3.66-3.56 (m, br, 2H), 3.02-2.82 (br, 2H), 2.82-2.56 (m, br, 4H),2.54 (s, 3H), 2.53-2.32 (m, br, 2H), 2.02-1.70(m, br, 6H), 1.64-1.48 (m, br, 1H), 1.48-1.34 (br, 3H), 1.25 (d, 6H, J= 6.8 Hz); ESMS m/e : 603.3 $(M + H)^+$.

Ejemplo 914

N-[3-(1-{6-(4-CLOROFENIL)-6-[2-FLUORO-5-(TRIFLUOROMETIL)FENOXI]HEXIL}-4-PIPERIDINIL}FENIL)-2-METIL-PROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 2-fluoro-5-(trifluorometil)fenol y N-(3-{1-[6-(4-clorofenill)-6-hidrohexil]-4-piperidinil}fenil)-2-metil-propanamida: ESMS m/e : 619.2 $(M + H)^+$.

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Ejemplo 915

N-[3-(1-{6-(3-FLUOROFENIL)-6-[2-FLUORO-5-TRIFLUOROMETIL)-FENOXI]HEXIL}-4-PIPERIDINIL}FENIL]-2-METIL-PROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 2-fluoro-5-(trifluorometil)fenol y N-(3-{1-[6-(3-fluorofenil)-6-hidrohexil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e : 603.3 $(M + H)^+$.

Ejemplo 916

N-[3-(1-{6-[2-FLUORO-5-(TRIFLUOROMETIL)FENOXI]-6-FENIL-HEXIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 2-fluoro-5-(trifluorometil)fenol y N-{3-[1-(6-hidroxi-6-fenilhexil-4-piperidinil]fenil}-2-metilpropanamida: ESMS m/e : 585.3 $(M + H)^+$.

Ejemplo 917

N-[3-(1-{7-[2-FLUOROFENIL)-7-[2-FLUORO-5-(TRIFLUOROMETIL)FE-NOXI]HEPTIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 2-fluoro-5-(trifluorometil)fenol y N-{3-[7-(2-fluorofenil)-7-hidroxiheptil]-4-piperidinil]fenil}-2-metilpropanamida: ESMS m/e : 617.3 $(M + H)^+$.

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Ejemplo 918

N-(3-{1-[5-(4-FLUOROFENIL)-5-(4-METOXIFENOXI)FENIL]-4-PENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-metoxifenol y N-(3-{1-[5-(4-fluorofenil)-5-hidroxipentil]-4-piperidinil]fenil)-2-metilpropanamida: ESMS m/e : 533.1 $(M + H)^+$.

Ejemplo 919

N-(3-{1-[5-(4-BROMOFENOXI)-5-(4-FLUOROFENIL)PENTIL]-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-bromofenol y N-(3-{1-[5-(4-fluorofenil)-5-hidroxipentil]-4-piperidinil]fenil}-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$), sal de HCl 7.94 (s, br, 1H), 7.68-6.64 (m, 12H), 5.12-5.04 (m, 1H), 3.68-3.52 (m, br, 2H), 3.01-2.82 (br, 2H), 2.78-2.58 (m, br, 4H), 2.57-2.38 (m, br, 2H), 2.05-1.80 (m, br, 6H), 1.64-1.38 (m, br, 2H), 1.25 (d, 6H, J= 7.2 Hz); ESMS m/e : 581.0 $(M + H)^+$.

Ejemplo 920

N-(3-{1-[5-(4-CLOROFENOXI)-5-(4-CLOROFENIL)PENTIL]-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-clorofenol y N-(3-{1-[5-(4-clorofenil)-5-hidroxipentil]-4-piperidinil]fenil}-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$), sal de HCl

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7.86 (s, br, 1H), 7.62-6.72 (m, 12H), 5.12-5.02 (m, 1H), 3.68-3.52 (m, br, 2H), 3.02-2082 (br, 2H), 2.82-2.56 (m, br, 4H), 2.56-2.40 (m, br, 2H), 2.06-1.80 (m, br, 6H), 1.64-1.40 (m, br, 2H), 1.25 (d, 6H, J= 6.8 Hz). Cálc. Anál. para $C_{32}H_{39}Cl_3N_2O_2$ 1.3MeOH: C, 63.25; H, 7.07; N, 4.42. Encontrado: C, 63.41; H, 6.99; N, 4.17. ESMS m/e: 553.0 $(M + H)^+$.

Ejemplo 921

N-(3-{1-[5-(4-CLOROFENOXI)-5-FENILPENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el procedimiento A y esquema AN utilizando 4-clorofenol y N-{3-[1-(5-hidroxi-5-fenilpentil)-4-piperidinil]fenil}-2-metilpropananamida: RMN ^1H (400 MHz, $CDCl_3$), sal de HCl 7.72-6.72 (m, 13H), 5.12-5.04 (m, 1H), 3.66-3.52 (m, br, 2H), 3.01-2.83 (br, 2H), 2.68-2.62 (m, br, 2H), 2.62-2.48 (m, br, 4H), 2.04-1.82 (m, br, 6H), 1.62-1.40 (m, br, 2H), 1.25 (d, 6H, J = 7.2 Hz); ESMS m/e: 519.1 $(M + H)^+$.

Ejemplo 922

N-(3-{1-[5-(3-ACETILFENOXI)-5-(4-FLUOROFENIL)PENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el procedimiento A y Esquema AN utilizando 1-(3-hidroxifenil)etanona y N-(3-{1-[5-(4-fluorofenil)-5-hidroxipentil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 545.1 $(M + H)^+$.

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Ejemplo 923

N-(3-{1-[5-(4-CLOROFENIL)-5-(4-FLUOROFENOXI)PENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el procedimiento A y Esquema AN utilizando 4-fluorofenol y N-(3-{1-[5-(4-clorofenil)-5-hidroxipentil]-4-piperidinil}-fenil)-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$), sal de HCl 8.05 (s, br, 1H), 7.74-6.68 (m, 12H), 5.08-4.99 (m, 1H), 3.67-3.56 (m, br, 2H), 3.02-2.82 (br, 2H), 2.80-2.57 (m, br, 4H), 2.57-2.38 (m, br, 2H), 2.05—1.80 (m, br, 6H), 1.64-1.40 (m, br, 2H), 1.25 (d, 6H, J = 7.2 Hz).Cálc. Anál. para $C_{32}H_{39}Cl_2FN_2O_2 \cdot 1.3EtOAc$: C, 64.93; H, 7.24; N, 4.07. Encontrado: C, 65.01; H 6.97; N, 3.85. ESMS m/e: 537.1 $(M + H)^+$.

Ejemplo 924

N-(3-{1-[5-(4-BROMOFENOXI)-5-FENILPENTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el procedimiento A y Esquema AN utilizando 4—bromofenol y N-{3-[1-(5-hidroxi-5-fenilpentil)-4-piperidinil]fenil}-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$), sal de HCl 7.74-6.66 (m, 13H), 5.13-5.02 (m, 1H), 3.73-3.51 (m, br, 2H), 3.05-2.83 (br, 2H), 2.83-2,62 (br, 4H), 2.62-2.42 (m, br, 2H), 2.10-1.8 (m, br, 6H), 1.65-1.37 (m, br, 2H), 1.25 (d, 6H, J = 6.8 Hz); ESMS m/e: 562.9 $(M + H)^+$.

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Ejemplo 925

N-(3-{1-[5-(4-CLOROFENIL)-5-(4-METOXIFENOXI)PENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN 4-metoxifenol y N-(3-{1-[5-(4-clorofenil)-5-hidroxipentil]-4-piperidinil}fenil)-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$), sal de HCl 8.13 (s, br, 1H), 7.72-6.70 (m, 12H), 5.08-4.97 (m, 1H). 3.72 (s, 3H), 3.66-3.50 (m, br, 2H), 3.03-2.82 (br, 2H), 2.80-2.54 (m, br, 4H), 2.53-2.17 (m, br, 2H), 2.08-1.78 (m, br, 6H), 1.65-1.38 (m, br, 2H), 1.25 (d, 6H, J = 6.8 Hz). Cálc. Anál. para $C_{33}H_{42}Cl_2N_2O_3 \cdot 0.54CH_2Cl_2$: C, 63.80; H, 6.8; N, 4,44. Encontrado: C, 63.84; H, 7.18; N, 4.00. ESMS m/e : 549.1 $(M + H)^+$.

Ejemplo 926

N-(3-{1-[5-(4-FLUOROFENOXI)-5-(4-FLUROFENIL)PENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por procedimiento A y Esquema AN utilizando 4-fluorofenol y N-(3-{1-[5-(4-fluorofenil)-5-hidroxipentil]-4-piperidinil}-fenil)-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$), sal de HCl 7.62-6.70 (m, 12H), 5.10-5.00 (m, 1H), 3.71-3.56 (m, br, 2H), 3.04-2.82 (br, 2H), 2.78-2.64 (m, br, 3H), 2.64-2.48 (m, br, 3H), 2.05-1.82 (m, br, 6H), 1.62-1.42 (m, br, 2H), 1.25 (d, 6H, J = 6.0 Hz); ESMS m/e: 521.2 $(M + H)^+$.

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Ejemplo 927

N-(3-{1-[5-(3-ACETILFENOXI)-5-FENILPENTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparad por Procedimiento A y esquema AN utilizando1-(3-hidroxifenil)etanona y N-(3-[1-(5-hidroxi-5-fenilpentil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS m/e: 526.9 $(M + H)^+$.

Ejemplo 928

N-(3-{1-[5-(4-METOXIFENOXI)-5-FENILPENTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y esquema AN utilizando 4-metoxifenol y N-{3-[1-(5-hidroxi-5-fenilpentil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS m/e: 515.6 $(M + H)^+$.

Ejemplo 929

N-[3-(1-{5-[2-FLUORO-5-(TRIFLUOROMETIL)FENOXI]-5-[4-(TRIFLUOROMETIL)FENIL]PENTIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimento A y esquema AN utilizando 2-fluoro-5-(trifluorometil)fenol y N-[3-(1-{5-hidroxi-5-[4-(trifluorometil)fenil]pentil}-4-piperidinil)-fenil]—2-metilpropanamida: ESMS m/e: 639.2 $(M + H)^+$.

Ejemplo 930

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N-[3-(1-{5-(3-CLOROFENIL)-5-[2-FLUORO-5-(TRIFLUOROMETIL)FENOXI]PENTIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 2-fluoro-5-(trifluorometil)fenol y N-(3-{1-[5-(3-clorofenil)-5-hidroxipentil]-4-piperidinil}fenil)-2-metilpropanamida: RMN ^{1}H (400 MHz, $CDCl_3$), sal de HCl 8.17 (s, br, 1H), 7.75-6.88 (m, 11H), 5,26-5.14 (m, 1H), 3.68-3.56 (m, br, 2H), 3.05-2.90 (br, 2H), 2.90-2.60 (m, br, 4H), 2,56-2.36 (m, br, 2H), 2.18-1.84 (m, br, 6H), 1.70-1.44 (m, br, 2H), 1.25 (d, 6H, J = 7.2 Hz). Cálc. Anál. Para $C_{33}H_{38}Cl_2F_4N_2O_2 \cdot 0.9$ EtOAc: C, 60.98; H, 6.32; N, 3.89. Encontrado: C, 60.99; H, 6.17; N, 3.81. ESMS m/e: 605.2 $(M + H)^+$.

Ejemplo 931

N-[3-(1-{5-(2-FLUORFENIL)-5-[2-FLUORO-5-(TRIFLUOROMETIL-FENOXI]PENTIL}-4-PIPERIDINIL)FENLL]-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema A utilizando 2-fluoro-5-(trifluorometil)fenol y N—(3-{1-[5-(2-fluorofenil)-5-hidroxipentil]-4-piperidinil}fenil)-2-metilpropanamida. RMN ^{1}H (400 MHz, $CDCl_3$), sal de HCl 7.89 (s, br, 1H), 7.72-6.88 (m, 11H), 5.59-5.48 (m, 1H), 3.70-3.48 (br, 2H), 3.05-2.84 (br, 2H), 2.82-2,58 (m, br, 4H), 2.58-2.40 (m, br, 2H), 2,22-1.82 (m, br, 6H), 1.71-1.42 (m, br, 2H), 1.25 (d, 6H, J= 6.4 Hz); ESMS m/e: 589.3 $(M + H)^+$

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Ejemplo 932

N-[3-(1-{5-(3-FLUOROFENIL)-5-[2-FLUORO-5-(TRIFLUOROMETIL)-FENOXI]PENTIL}-4-PIPERIDINIL)FENIL]-2-METIL-PROPANAMIDA:

Preparada por el Procedimiento A y Esquema AN utilizando 2-fluoro-5-(trifluorometil)fenol y N-(3-{1-[5-(3-fluorofenil)-5-hidroxipentil]-4-piperidinil}fenil)-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$), sal de HCl 7.79 (s, br, 1H), 7.63-6.82 (m, 11H), 5.24-5.15 (m, 1H), 3.70-3.56 (br, 2H), 3,04-2.84 (br, 2H), 2.82-2.60 (m, br, 4H), 2.60-2.42 (m, br, 2H), 2.20-1.83 (m br, 6H), 1.70-1.44 (m, br, 2H), 1.25 (d, 6H, J = 6.4 Hz); ESMS m/e: 589.3 $(M + H)^+$.

Ejemplo 933

N-(3-{1-[5-(3-ACETILFENOXI)-5-(4-CLOROFENIL)PENTIL]-4-PIPERIDINIL}FENIL)-2-METILPRPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 1-(3-hidroxifenil)etanona y N-(3-{1-[5-(4-clorofenil)-5-hidroxipentil]-4-piperidinil}fenil)-2-metilpropanamida: RMN ^1H (400 MHz, $CDCl_3$), sal de HCl 8.05 (s, br, 1H), 7.74-6.88 (m, 12H), 5.27-5.16 (m, 1H), 3.69-3.52 (m, br, 2H), 3.10-2.81 (br, 2H), 2.81-2.57 (m, br, 4H), 2.54 (s, 3H), 2.52-2.40 (m, br, 2H), 2.05-1.80 (m, br, 6H), 1.66-1,42 (m, br, 2H), 1.25 (d, 6H, J = 6.8 Hz); Cálc. Anál. para $C_{34}H_{42}Cl_2N_2O_3 \cdot 0.5CH_2Cl_2 \cdot 1.0H_2O$: C, 63.46; H, 6.91; N, 4.30.

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Encontrado: C, 63.46; H, 7.09; N, 4.00. ESMS m/e: 561.1 (M + H)$^+$.

Ejemplo 934

N-{3-(1-{5-(4-CLOROFENIL)-5-[2-FLUORO-5-(TRIFLUOROMETIL)-FENOXI]PENTIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 2-fluoro-5-(trifluorometil)fenol y N-(3-{1-[5-(4-clorofenil)-5-hidroxipentil)-4-piperidinil}fenil)-2--metilpropanamida: RMN ^{1}H (400 MHz, $CDCl_3$), sal de HCl 7.61–6.92 (m, 11H), 5.24-5.16 (m, 1H), 3.70-3.58 (m, 2H), 3.02-2.91 (br, 2H), 2.80-2.64 (m, br,3H), 2.64-2.50 (m, 3H), 2.18-1.94 (m, br, 6H), 1.62-1.44 (m, br, 2H), 1.25 (d, 6H, J= 7.2 Hz); ESMS m/e: 605.3 (M + H)$^+$.

Ejemplo 935

N-[3-(1-{5-(4-FLUOROFENIL)-5-[2-FLUORO-5-(TRIFLUOROMETIL)-FENOXI]PENTIL}-4-PIPERIDINIL)FENIL]-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 2-fluoro-5-(trifluorometil)fenol N-(3-{1-[5-(4-fluorofenil)-5-hidroxipentil]-4-piperidinil]fenil)-2-metilpropanamida: ESMS m/e: 589.3 (M + H)$^+$.

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Ejemplo 936

N-(3-{1-[5-(4-BROMOFENOXI)-5-(4-CLOROFENIL)PENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y el Esquema AN utilizando 4-bromofenol y N-(3-{1[5-(4-clorofenil)-5-hidroxipentil]-4-piperidinil}-fenil)-2-metilpropanamida: ESMS m/e: 597.2 $(M + H)^+$.

Ejemplo 937

N-(3-{[5-(4-CLOROFENOXI)-5-(4-FLUOROFENILPENTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: preparado por el Procedimiento A y Esquema AN utilizando 4-clorofenol y N-(3-{1-[5-(4fluórofenil)-5-hidroxipentil]-4-piperidinil}fenil)-2-metilpropanamida: ESMS m/e: 537.3 $(M + H)^+$.

Ejemplo 938

N-(3-{1[5-(2-ACETILFENOXI)-5-FENILPENTIL]-4-PIPERIDINIL]-FENIL)-2-METILPROPANAMIDA: Preparada por el procedimiento A y esquema AN utilizando 1-(2-hidroxifenil)etanona y N-{3-[1-(5-hidroxi-5-fenilpentil)-4-piperidinil]fenil}-2-metil-propanamida: ESMS m/e: 527.0 $(M + H)^+$.

Ejemplo 939

N-(3-{1-[5-(2-ETOXIFENOXI)-5-FENILPENTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el procedimiento A y el Esquema AN utilizando 2-etoxifenol y N-{3-[1-(5-

hidroxi-5-fenilpentil)-4-piperidinil]fenil}-2-metipropanamida: ESMS ra/e: 529.2 $(M + H)^+$.

Ejemplo 940

N-(3-{1-[5-(4-FLUOROFENOXI)-5-FENILPENTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento A y Esquema AN utilizando 4-fluorofenol y N-{3-[1-(5-hidroxi-5-fenilpentil)-4-piperidinil]fenil}-2-metilpropanamida: ESMS m/e: 503.2 $(M + H)^+$.

Ejemplo 941

N-(3-{1-[4-(4-FLUOROFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA:Preparada por el Procedimiento K (KI) y Esquema E (K_2CO_3) utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 4-cloro1-(4-fluorofenil)-1-butanona: ESM m/e: 411.2 $(M + H)^+$.

Ejemplo 942

2-METIL-N-(3-{1-[3-(1H-PIRROL-3-IL)PROPIL]-4-PIPERIDINIL}-FENIL)PROPANAMIDA: Preparada por el Procedimiento K (KI) y Esquema E (K_2CO_3) utilizando 2-metil-N-[3-(4-piperidinil)-fenil]propanamida y 3-(3-bromopropil)-1H-pirrol: ESMS m/e: 354.2 $(M + H)^+$.

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Ejemplo 943

N-(3-[1-[4(4-ISOPROPILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K (KI) y Esquema E (K_2CO_3) utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 4-cloro-1-(4-isopropilfenil)-1-butanona: ESMS m/e: 435.2 $(M + H)^+$.

Ejemplo 944

N-(3-{1-[4-(4-METOXIFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K (KI) y Esquema E (K_2CO_3) utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 4-cloro-1-(4-metoxifenil)-1-butanona: ESMS m/e:423.2 $(M + H)^+$.

Ejemplo 945

2-METIL-N-(3-{1-[4-(4-METILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)PROPANAMIDA: Preparada por el Procedimiento K (KI) y Esquema E (K_2CO_3) utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 4-cloro-1-(4-metilfenil)-1-butanona: ESMS m/e: 407.2 $(M + H)^+$.

Ejemplo 946

N-(3-{1-[4-(4-TERT-BUTILFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}-FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K (KI) y Esquema E (K_2CO_3) utilizando 2-metil-N-[3-(4-

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piperidinil)fenil]propanamida y 1-(4-tert-butilfenil)-4-cloro-1-butanona: ESMS m/e: 449.2 $(M + H)^+$.

Ejemplo 947

N-(3-{1[4-(4-BROMOFENIL)-4-OXOBUTIL]-4-PIPERIDINIL}FENIL)-2-METILPROPANAMIDA: Preparada por el Procedimiento K (KI) y Esquema E (K_2CO_3) utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 1-(4-bromofenil)-4-cloro-1-butanona: ESMS m/e: 471.3 $(M + H)^+$.

Ejemplo 948

2-METIL-N-(3-{1-[4-OXO-4-(2-TIENIL)BUTIL]-4-PIPERIDINIL}-FENIL)PROPANAMIDA: Preparada por el Procedimiento K (KI) y Esquema E (K_2CO_3) utilizando 2-metil-N-[3-(4-piperidinil)fenil]propanamida y 4-cloro-1-(2-tienil)-1-butanona: ESME m/e: 399.1 $(M + H)^+$.

II. Métodos Sintéticos para Estructuras Generales

Los ejemplos descritos en la Sección I son meramente ilustrativos de los métodos utilizados para sintetizar los antagonistas de MCH1 de los métodos sintéticos utilizados para la síntesis de los ejemplos.

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Puede ser necesario incorporar estrategias de protección y desprotección para los sustituyentes tal como amino, amido, ácido carboxílico, y grupos hidroxilo en los métodos sintéticos generalizados para formar derivados adicionales. Los métodos de protección y desprotección de tales grupos son bien conocidos en la técnica, y se pueden encontrar, por ejemplo en Green, T.W. and Wuts, P.G.M. (1991) Protection Groups in Organic Síntesis, 2nd Edition John Wiley & Sons, New York.

III. Composiciones Orales

Como una modalidad específica de una composición oral de un compuesto de está invención, 100 mg de uno de los compuestos descritos en la presente se formularon con suficiente lactosa finamente dividida para proporcionar una cantidad total de 580 a 590 mg para llenar un tamaño de cápsula de gel dura en O.

IV. Evaluación Farmacológica de Compuestos en Receptor de MCH1 de rata clonada.

Las propiedades farmacológicas de los compuestos de la presente invención se evaluaron en el receptor de MCH1 de rata clonada utilizando los protocolos descritos enseguida.

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Células hospederas

Una amplia variedad de células hospederos pueden ser utilizadas para estudiar las proteínas expresadas heterólogamente. Estas células incluyen pero no están restringidas a líneas de mamíferos clasificados tal como: Cos-7, CHO, LM (tk-), HEK293, Peak rapid 293, etc.; líneas de célula de insecto tal como: Sf9, sf21, etc.; células de anfibio tal como oocitos de xenopus; y otros.

Células COS 7 se hacen crecer en placas de 150 mm en DMEM con suplementos de (Medio de Aguila Modificado Dulbecco con 10% suero de ternero fetal, glutamina 4mM, 100 unidades/ml de penicilina/100 Fg/ml estreptomicina) a 37°C, 5% CO_2. Placas en almacenamiento de células COS-7 se tripsinizaron y se dividieron 1:6 cada 3-4 días.

Células 293 de riñon embriónico humano se hicieron crecer en placas de 150 mm en DMEM con suplementos (10% suero de ternera, glutamina 4mM, 100 unidades/ml de penicilina/100 Fg/ml estreptomicina) a 37°C, 5% CO_2. Placas en almacenamiento de células 293 se tripsinizaron y dividieron 1:6 cada 3-4 días.

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Células Peak rapid 293 de riñon embriónico humano (Peakr293) se hacen crecer en placas de 150 mm en DMEM con suplementos (10% suero fetal de ternero fetal, 10% L-glutamina, 50 Fg/ml de gentamicina) a 37°C, 5% CO_2. Placas en almacenamiento de células Peak rapid 293 se tripsinizaron y dividieron 1:12 cada 3-4 días.

Células LM(tk-) de fibroblasto de ratón se hacen crecer en placas de 150 mm en DMEM con suplementos (Medio de Aguila Modificado de Dulbecco con 10% suero de ternero fetal, 4 mM glutamina, 100 unidades/ml de penicilina/100 Fg/ml estreptomicina) a 37°C, 5% CO_2. Placas de almacenamiento de células LM(tk-) se tripsinizaron y dividieron 1:10 cada 3-4 días.

Células de ovario de hámster Chino (CHO) se hacen crecer en placas de 150 mm en medio de HAM=s F-12 con suplementos (10% suero de ternero fetal, 4mM L-glutamina y 100 unidades/ml de penicilina/100 Fg/ml estreptomicina) a 37°C, 5% CO_2. Placas de almacenamiento de células CHO se tripsinizaron y dividieron 1:8 cada 3-4 días.

Células NIH-3T3 de fibroblasto embriónico de ratón se hacen crecer en placas de 150 mm en Medio de Aguila Modificado de Dulbecco (DMEM) con suplementos (10% suero de

ternero fetal, 4mM L-glutamina, 100 unidades/ml de penicilina/100 Fg/ml estreptomicina) a 37°C, 5% CO_2. Placas de almacenamiento de células NHI-3T3 se tripsinizaron y dividieron 1:15 cada 3-4 días.

Células Sf9 y Sf21 se hacen crecer en monocapas en platos de cultivo de tejido de 150 mm en un medio de TMN-FH suplementado con 10% suero de ternero fetal, a 27°C, sin CO_2. Células de insecto High_Five se hacen crecer en platos de cultivo de tejido de 150 mm, en un medio Ex-Cell 400™ suplementado con L-glutamina, también a 27°C, sin CO_2.

En algunos casos, las líneas celulares que crecen como monocapas adherentes, se pueden convertir a cultivo de suspensión para incrementar la producción celular y proporcionar grandes lotes de material de ensayo uniforme para los proyectos de protección del receptor de rutina.

Expresiones transientes

Las proteínas que codifican el ADN a ser estudiadas pueden ser expresadas en forma transiente en una variedad de mamíferos, insectos, anfibios, y otras líneas celulares, por diferentes métodos que incluyen pero no están restringidos a; mediado por fosfato de calcio, mediado por DEAE-dextrano, mediado Liposomal, mediado viral, mediado por

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electroporación y suministrado por microinyección. Cada uno de éstos métodos puede requerir optimización de parámetros experimentales clasificados que dependen del ADN, línea celular, y del tipo de ensayo a ser subsecuentemente empleado.

Un protocolo típico par el método del fosfato de calcio como se aplica a las células Peak rapid 293, se describe enseguida.

Células adherentes se cosechan aproximadamente veinticuatro horas antes de la transfección y replacado a una densidad de 3.5 x 10^6 células/placa en una placa de cultivo de tejido de 150 mm y se le permitió incubar durante al noche a 37°C en 5% CO_2. 250 Fl de una mezcla de $CaCl_2$ y ADN (15 Fg ADN en 250 mM de $CaCl_2$) se adicionó a un tubo de plástico de 5 ml y 500 Fl de 2X HBS (280 mM de NaCl, 10 mM de KCl, 1.5 mM de Na_2HPO_4, 12 mM de dextrosa, 50 mM de HEPES), se adicioná lentamente con un mezclado generoso. Se deja que la mezcla incube durante 20 minutos a temperatura ambiente para dejar un precipitado de ADN en forma. La mezcla de precipitado de ADN después es adiconada al medio de cultivo en cada placa y se incuba durante 5 horas a 37°C, 5% CO_2. Después de la incubación, 5 ml del medio de cultivo (DMEM, 10% FBS, 10 % L-glut, y 50 g/ml de gentamicina) se

adicona a cada placa. Las células son después incubadas durante 24 a 48 horas a 37°C, 5% CO_2.

Un protocolo típico para el método de DEAE-dextrano como se aplica para las células COS-7 se describe enseguida; las células a ser utilizadas para transfección se dividen 24 horas antes de la transfección, para proporcionar matraces que son 70-80% confluentes al tiempo de la transfección. En forma breve, 8 Fg de ADN receptor más 8 Fg de cualquier ADN adicional necesitado (e.g., vector de expresión de la proteína G , constructor reportero.marcador de resistencia al antibiótico, vector simulado, etc.), se adicionan a 9 ml del DMEM completo más la mezcla de DEAE-dextrano (10 mg/ml en PBS). Las células Cos-7 plaqueadas en un frasco T225 (sub-confluente), se lavaron una vez con PBS y la mezcla de ADN se adicionó a cada frasco. Se dejaron incubar las células durante 30 minutos a 37°C, 5% CO_2. seguido de la incubación, 36 ml de DMEM completo con cloroquinona 80 FM, se adicionaron a cada frasco y se les dejó incubar unas tres horas adiconales. Después el medio se aspiró y 24 ml del medio completo conteniendo 10% DMSO durante exactamente 2 minutos y después se aspiró. Después las células se lavaron 2 veces con PBS y 30 ml de DMEM completo se adicionaron a cada frasco. Después las células se dejaron incubar durante la noche. Al siguiente día las

células se cosecharon por medio de tripsinación y se volvieron a sembrar como se necesitava dependiendo del tipo de ensayo a ser realizado.

Un protocolo típico para transfección mediada por liposoma como se aplica a las células CHO esta descritó como sigue células a ser utilizadas para transfección se dividen 24 horas antes de la transfección para proporcionar frascos que son 70-80% confluentes al tiempo de la transfección. Un total de 10 Fg de ADN que pueden incluir proporciones variantes del receptor de ADN más cualquier ADN adicional necesitado (e.g., vector de expresión de proteína G, constructo reportero, marcador de resistencia a antiobiótico, vector de simulación, etc) se utiliza para transfectar cada frasco de 75 cm^2 de células. La transfección mediado por liposoma se lleva a cabo de acuerdo a las recomendaciones del proveedor (LipofectAMINE, GibcoBRL, Bethesda, MD). Las células transfectadas se cosechan 24 horas después de la transfección y se utilizan o se vuelven a sembrar de acuerdo a los requerimientos del ensayo a ser empleado.

Un protocolo típico para el método de electroporación como se aplica a las células Cos-7 se describe como se sigue; Células a ser utilizadas para

transfección se dividen 24 horas previas a la transfección para proporcionar frascos que son subconfluentes al mismo tiempo de la transfección. Las células se cosechan por medio de tripsinación resuspendidas en su medio de crecimiento y se cuentan. 4 x 10^6 células se suspenden en 300 F1 de DMEM y se colocan en un recipiente d electroporación. 8 Fg de DNA receptor más 8 Fg de cualquier DNA adicional necesitado (e.g., vector de expresión de proteína G , constructo reportero, marcador de resistencia a antiobiótico, vector de simulación, etc) se adicionan a la suspensión de la célula, el recipiente se coloca en un BioRad gene Pulser y se somete a un impulso eléctrico (ajuste Gene pulser: voltaje de 0.25 kV, capacitancia de 950 FF). El siguiente pulso, 800 F1 de DMEM completo, se adicona a cada recipiente y la suspensión se transfiere a un tubo estéril. El medio completo se adiciona a cada tubo para llevar a la concentración de célula final a 1x 10^5 células/100 F1. Las células son después plaqueadas como se necesiten dependiendo del tipo de ensayo a ser reslizado.

Un protocolo típico para expresión mediada viral de las proteínas heterólogas, se decribe como sigue para infección de baculovirus de células Sf9 de insecto. La región de codificación de ADN que codifica el receptor descrito en la presente puede ser subclonada en pBlueBacIII

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en sitios de restricción existentes o sitios con ingenieria en secuencias 5' y 3' para la región de codificación de los polipéptidos. Para generar los baculovirus, 0.5 Fg de DNA viral (BaculoGold) y 3 Fg de constructo de ADN que codifica un polipéptido pueden ser co-transfectados en 2 x 10^6 células Sf9 de insecto *Spodoptera frugiperda* por el método de co.precipitación de fosfato de calcio como se bosqueja en Pharmingen (en "Baculovirus Expresión Vector System: Procedures and Methods manual"). Después las células se incuban durante 5 días a 27°C: EL sobrenadante de la placa de co-transfección puede ser recolectado por centrifugación y la placa de virus recombinante purificada. El procedimiento para infectar células con virus, para existencias de virus y para titular las existencias de virus son como el descrito en el manual de Pharmingen. Principios similares podrían en general ser aplicados a la expresión de células de mamíferos vía retro-viruses. Virus de bosque Simliki y viruses de ADN con doble hebra tal como viruses de adeno-, herpes-, y vaccinia, y similares.

Expresión estable

DNA heterólogo puede ser incorporado en forma estable en células hospederas, causando que la célula exprese en forma perpétua una proteína extraña. Los métodos para el suministro del DNA en la célula son similares a

aquellos descritos anteriormente para la expresión transiente, pero requieren la co-transfección de un gen anciliar para conferir resistencia a fármaco en la célula hospedera con objetivo. La resistencia al fármaco resultante puede ser explotada al seleccionar y mantener células que se han captado del DNA heterólogo. Una clasificación de genes de resistencia que esta disponible incluye, pero no esta restringida a Neomicina, Kanamicina y higromicina. Para los propósitos de estudios del receptor, la expresión estable de una proteína de receptor heterologa se lleva a cabo en, pero no necesariamente restringida a, células de mamífero incluyendo, CHO, HEK293, (LM(tk-), etc.

Preparación de membrana celular

Para ensayos de enlace, pelotillas (pellets) de células transfectadas se suspenden en una solución amortiguadora enfriada con hielo (20 mM de Tris.HCl, 5 mM de EDTA, pH 7.4) y se homogeniza por sonificación durante 7 seg. Los lizatos celulares se centrifugan a 200 x g durante 5 minutos a 4°C. Los sobrenadantes son después centrifugados a 40,000 x g durante 20 minutos a 4°C. Las pelotillas resultantes se lavaron una vez en la solución amortiguadora de homogenización y se suspendieron en una solución de amortiguamiento de enlace (ver métodos para enlaces de radioligandos).Las concentraciones de la proteína son

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determinadas por el método de Bradford (1976) utilizando albumina de suero bovino como el estándar. Los ensayos de enlace se llevan usualmente inmediatamente, sin embargo, es posible preparar membranas en lotes y congelar para almacenamiento en nitrógeno líquido para futuro uso.

Ensayos de enlace de radioligando

Los ensayos de nelace de radioligando para el receptor de MCH1 de rata se llevan a cabo utilizando plásmido pcADN.1-rMCH1 (ATCC Designación de Depósito de Patente No. PTA-3505).El plásmido pcADN3.1-rMCH1 comprende los elementos regulatorios necesarios para la expresión de DNA en una célula de mamífero operativamente enlazada a ADN que codifica al receptor de MCH1 de rata de manera que permita la expresión del mismo. El plásmido pcDNA3.1-rMCH1 se depositó el 5 de julio del 2001, ante la American Type Cultura Collection (ETCC), 1230 Parklawn Drive, Rockville, Maryland 20852, E.U.A. bajo las condiciones del Tratado de Budapest para el Reconocimiento del Depósito de Microorganismos para el Propósito de Procedimientos de Patente y se acordó como la Designación de Depósito de Patente ATCC No. PTA-3505.

Los ensayos de enlace pueden también ser realizados como se describe posteriormente utilizando

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plásmido pEXJ.HR-TL231 (No. de Acceso de ATCC 203197). El plásmido pEXJ.HR-TL231 codifica el receptor MCH1 humano y se depositó el 17 de septiembre de 1998 ante la American Type Culture Collection (ATCC), 12301 Parklawn Drive, Rockville, Maryland 20852, E.U.A. bajo las condiciones del Tratado de Budapest para el Reconocimiento Internacional del Depósito de Microorganismos para el Propósito del Procedimiento de Patentes y se acordó como el No. de Acceso ATCC 203197.

Células Peak rapid 293 de riñon embriónico de humano (células Peakr293) se transfectaron en forma transitoria con ADN que codifica al receptor MCH1, utilizando el método del fosfato de calcio y membranas celulares se prepararon como se describió anteriormente. Los experimentos de enlace con membranas de células Peakr293 transfectadas con receptor MCH1 de rata se realizaron con 0.08 nM de Compuesto A [^{3}H] (la síntesis del compuesto A esta descrita en detalle enseguida) utilizando una solución amortiguadora de incubación que consiste de 50 mM de Tris pH 7.4, 10 mM de $MgCl_2$, 0.16 mM de PMSF, 1 mM de 1,10-fenantrolina y 0.2% de BSA. El enlace se realizó a 25°C durante 90 minutos. Las incubaciones se terminaron por medio de filtración a vacio rápida sobre filtros de fibra de vidrio GF/C, se presacudieron en 5% de PEI utilizando 50 nM de Tris pH 7.4 conforme se lavó con la solución

amortiguadora. En todos los experimentos, ningún enlace específico esta definido utilizando 10pM del compuesto A.

Ensayos funcionales

Las células pueden ser protegidas para la presencia del receptor de mamífero endógeno utilizando ensayos funcionales. Las células con o sin un nivel bajo de receptor endógeno presente, pueden ser transfectadas con el receptor endógeno para utilizarse en ensayos funcionales.

Un amplio espectro de ensayos se pueden emplear para proteger la activación del receptor. Estos se extienden desde mediciones tradicionales de fosfatidil inositol, cAMP, Ca^{++}, y K^{+}, por ejemplo; hasta mediciones de sistemas de éstos mismos segundos mensajeros sin que hayan sido modificados o adaptados para ser mayores a su través, más genéricos, y más sensibles; a célula a base de plataformas que reportan más eventos celulares generales que resultan de la activación del receptor tal como cambios metabólicos, diferenciación y división/proliferación de células, por ejemplo, ensayos con niveles altos de organismo, los cuales monitorean los cambios de comportamiento o psicológicos complejos, se piensa están implicados en la activación del receptor, incluyendo efectos cardiovasculares, analgésicos orexigénicos, anxiolíticos y de sedación, por ejemplo.

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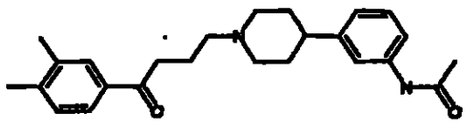
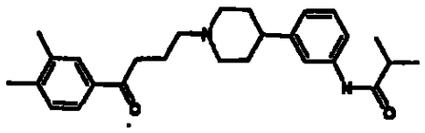
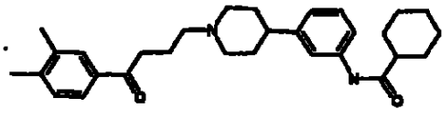
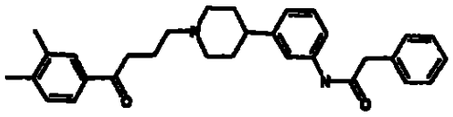
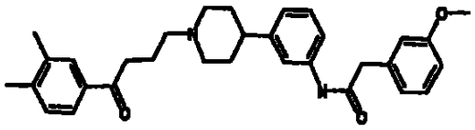
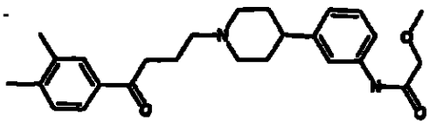
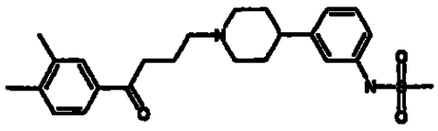
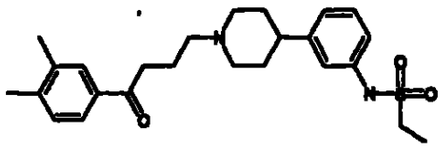
Resultados de Ensayo de Enlace de Radioligando

Los compuestos descritos anteriormente se ensayaron utilizando MCH1 de rata clonada. Las afinidades de enlace de los compuestos se muestran en la Tabla I.

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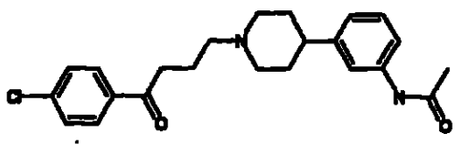
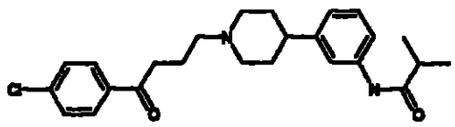
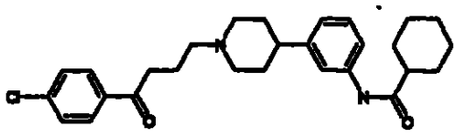
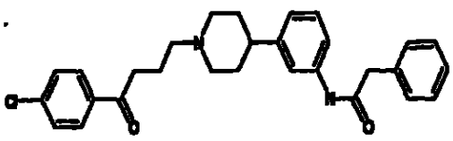
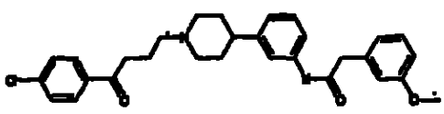
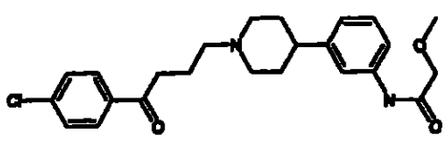
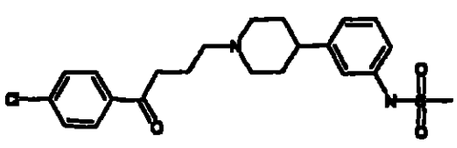
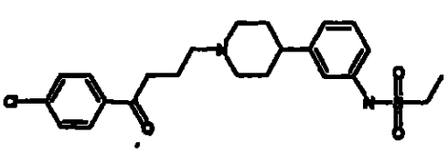
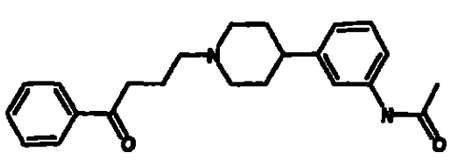
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EJEMPLO No.	ESTRUCTURA	Ki (nM) rMCH1
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2		3.9
3		788
4		357
5		14.2
6		274
7		1000
8		627

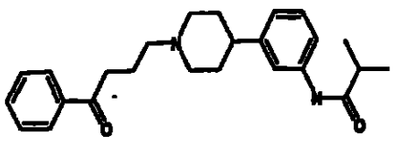
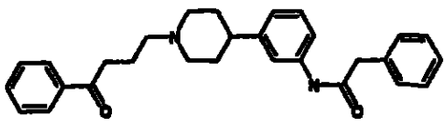
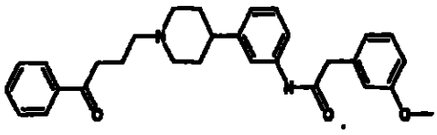
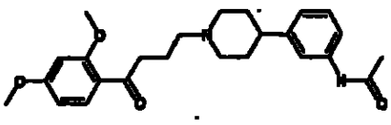
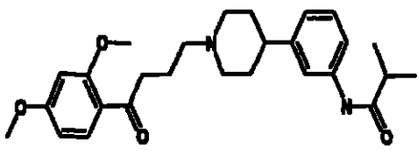
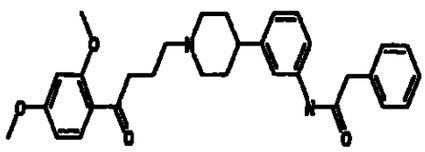
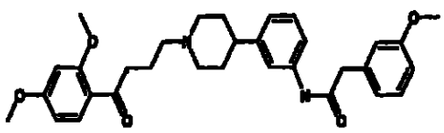
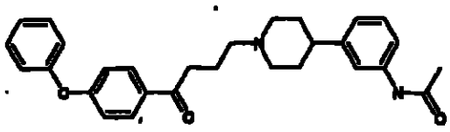
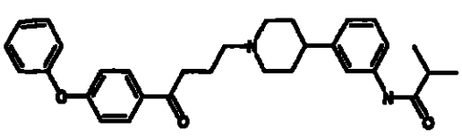
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9		69
10		2.8
11		197
12		84
13		11.9
14		167
15		720
16		272
17		342

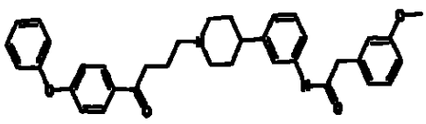
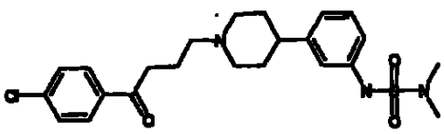
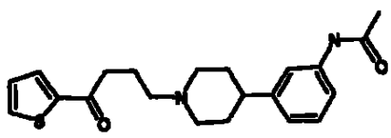
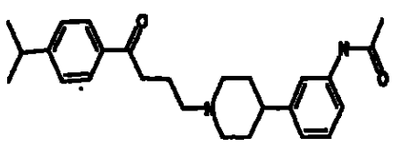
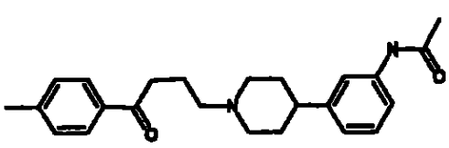
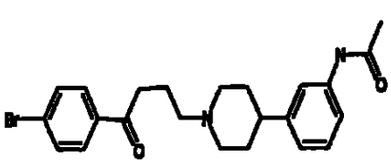
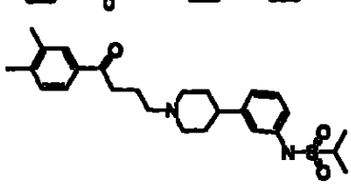
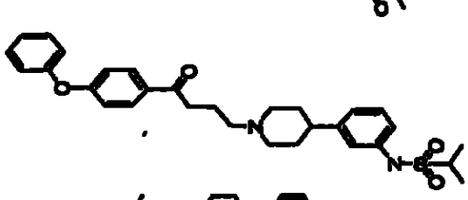
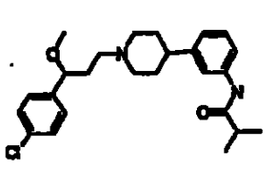
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18		29.5
19		506
20		21
21		630
22		.52
23		1036
24		67
25		483
26		192

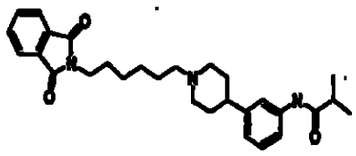
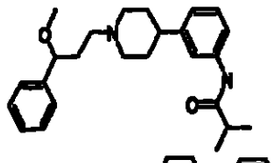
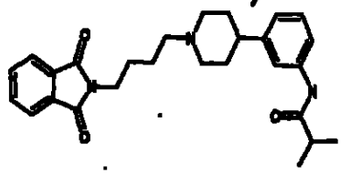
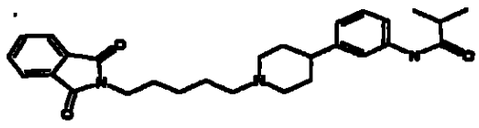
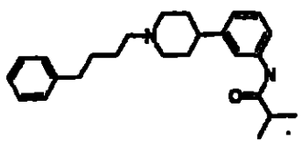
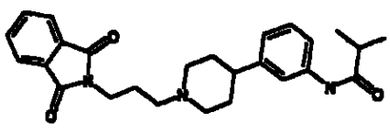
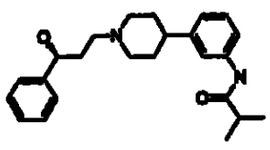
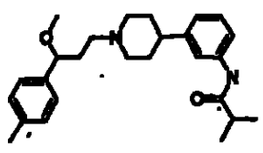
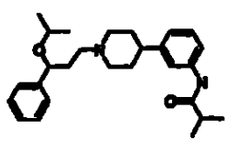
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27		91
28		511
29		654
30		382
31		362
32		160
33		615
34		651
35		11.5

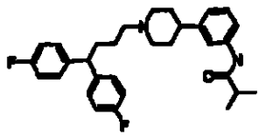
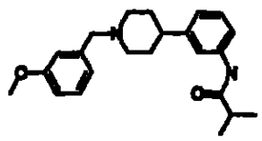
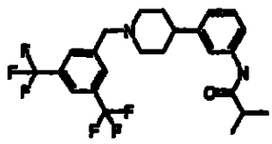
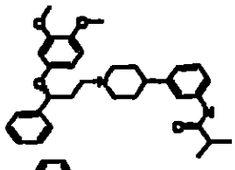
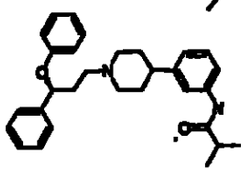
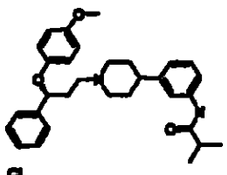
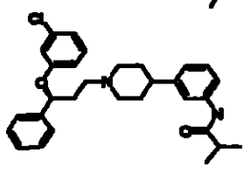
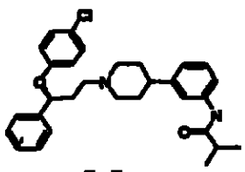
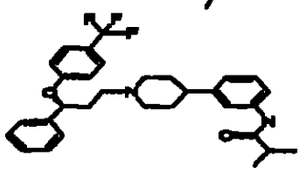
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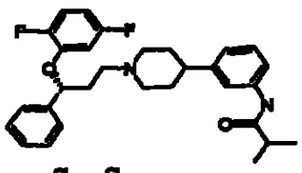
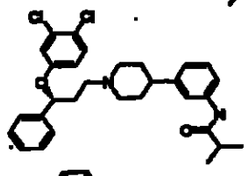
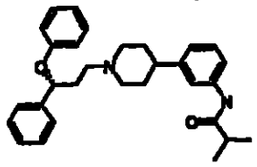
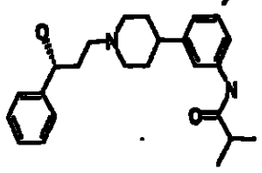
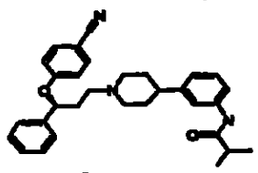
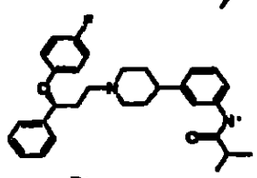
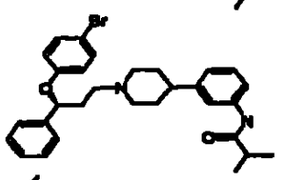
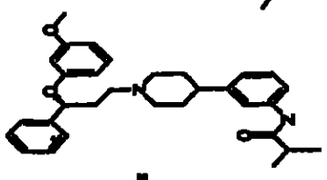
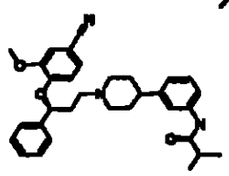
1157

36		62
37		29.1
38		18.2
39		11.8
40		.50
41		946
42		118
43		12
44		11.5

1461

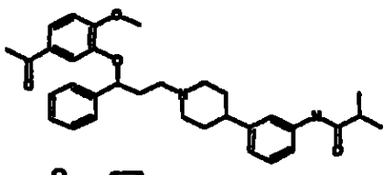
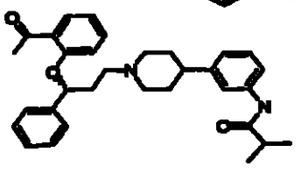
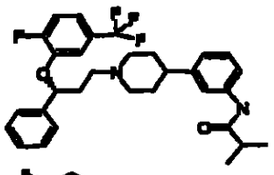
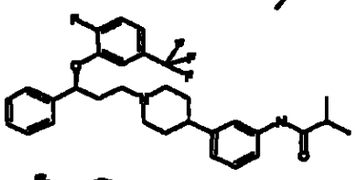
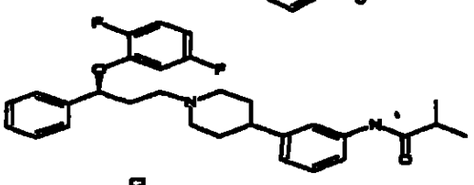
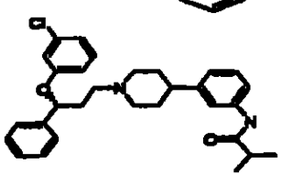
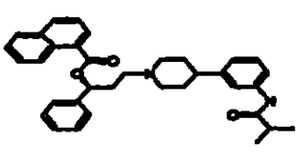
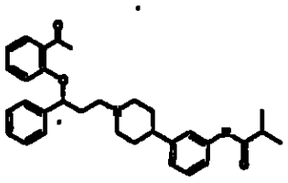
1458

46		1.6
48		167
47		62
48		6.7
49		7.1
50		3.9
51		3.1
52		3.8
53		7.1

54		4.9
55		5
56		22.3
57		16.8
58		2.01
59		12.9
60		0.923
61		13.6
62		12.8

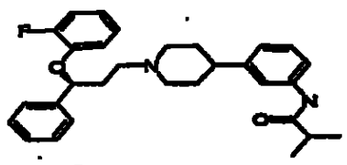
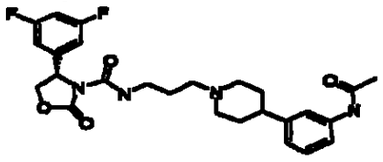
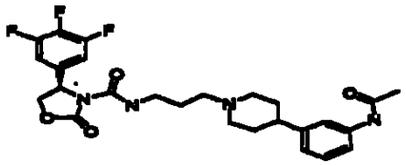
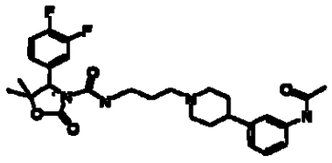
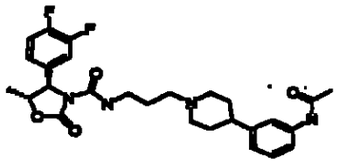
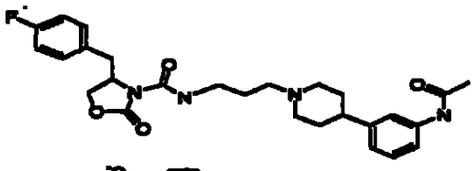
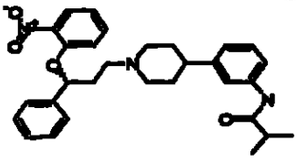
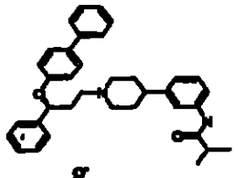
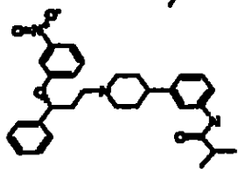
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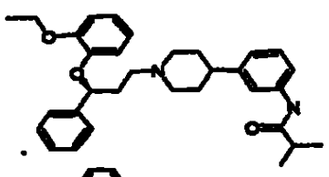
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64		14.8
65		17
66		3.3
67		5.9
68		9.3
69		32.5
70		50

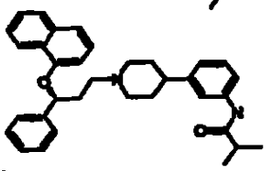
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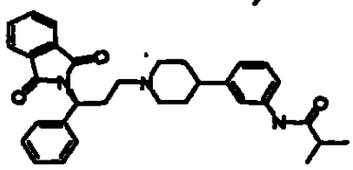
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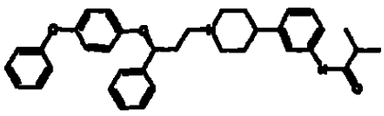
71		6.6
72		31.4
73		22.3
74		48.6
75		11.8
76		44.6
77		25.7
78		22.2
79		19.4

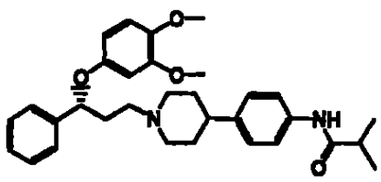
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1/62

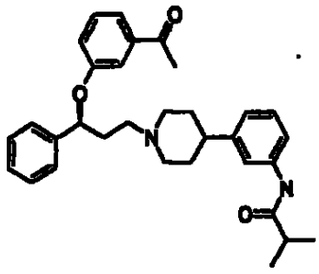
80  14.3

81  377

82  11.2

83  48.1

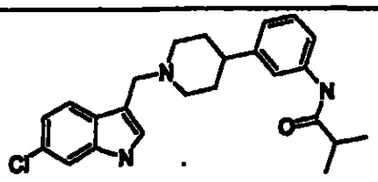
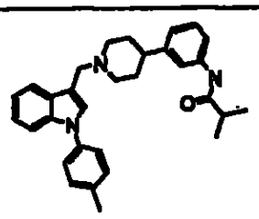
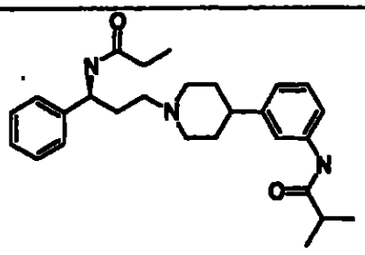
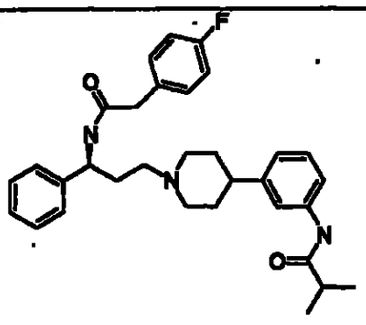
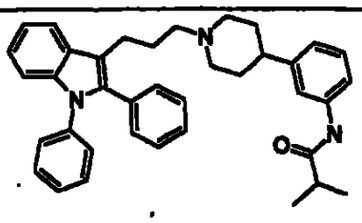
84  721

85  3.2

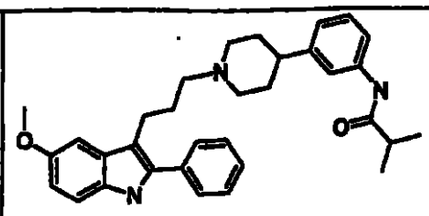
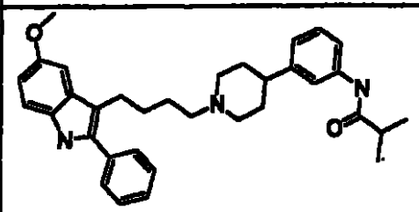
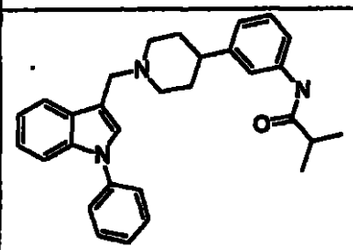
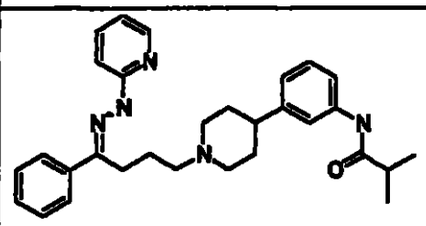
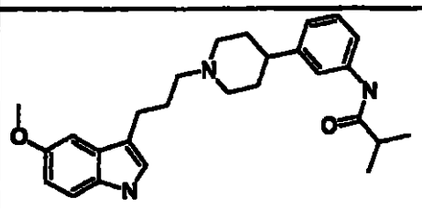
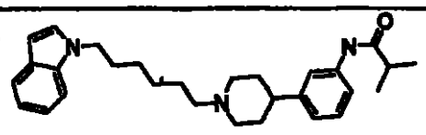
EJEMPLO	ESTRUCTURA	Ki (nM) rMCH1

1466

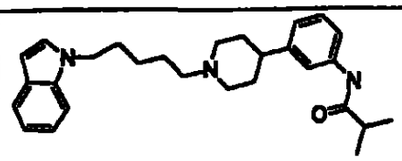
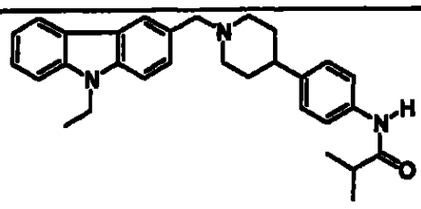
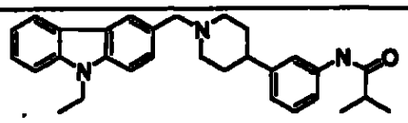
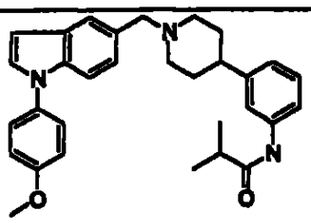
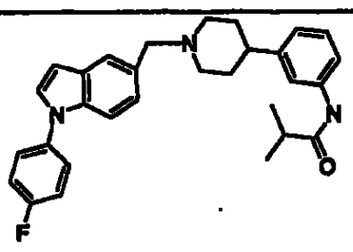
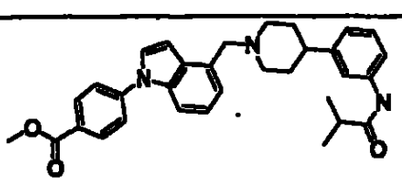
1463

86		20.6
87		14.9
88		16.0
89		3.0
90		3.0

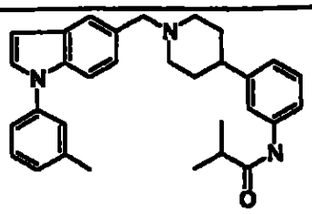
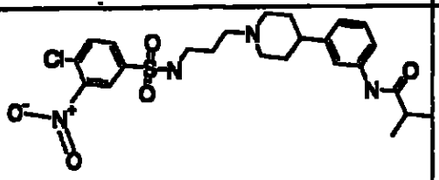
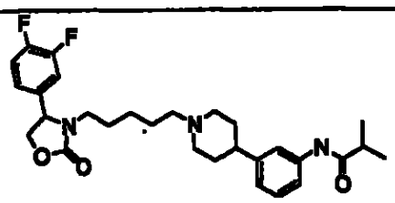
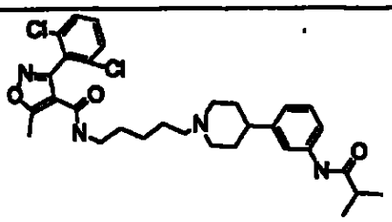
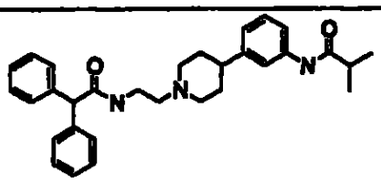
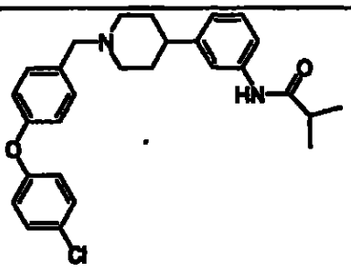
1404 1467

91		2.3
92		8.0
93		4.2
94		2.3
95		5.4
96		15.9

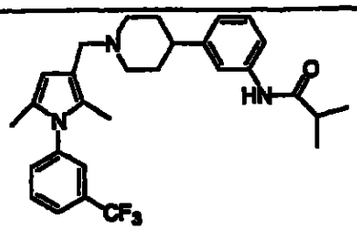
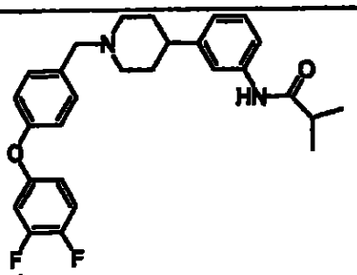
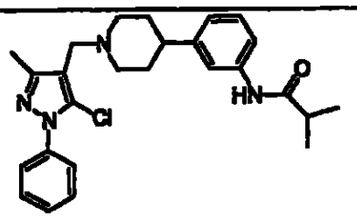
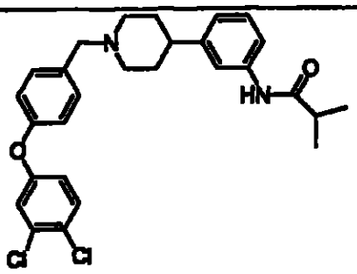
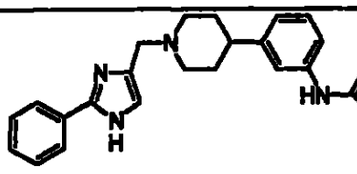
1468
1465

97		27.3
98		37.9
99		1.7
100		27.5
101		7.8
102		38.4

1466 1469

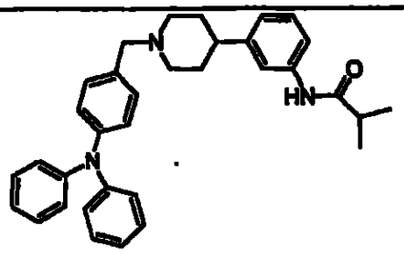
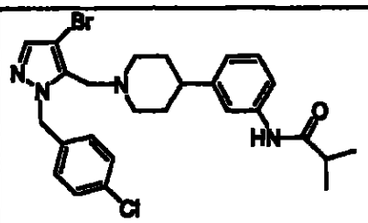
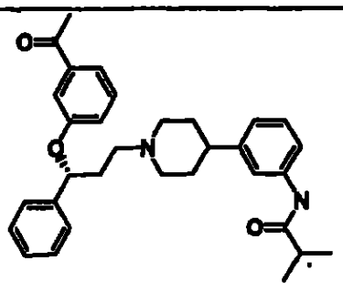
103		21.3
104		11.2
105		4.6
106		7.1
107		1.7
108		5.2

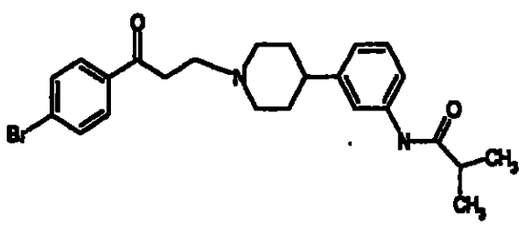
1167 1472

109		20.9
110		1.8
111		ND
112		6.1
113		ND

1471

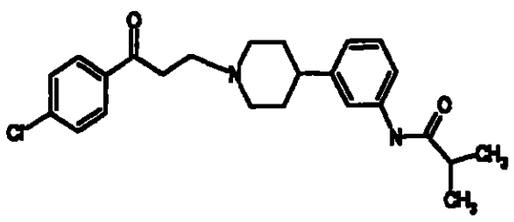
1168

114		3.6
115		ND
116		3.8

117  19.0

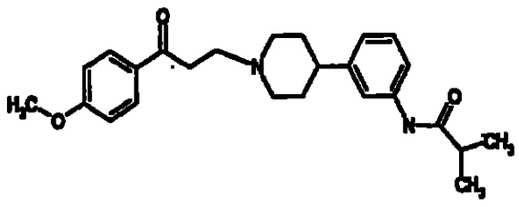
1469 1472

118



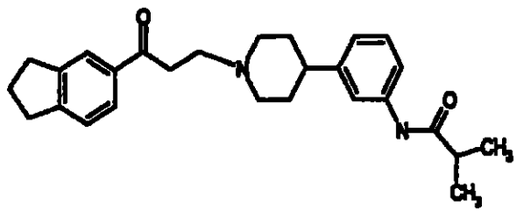
43.6

119



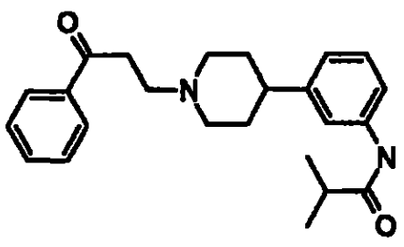
75.7

120



31.1

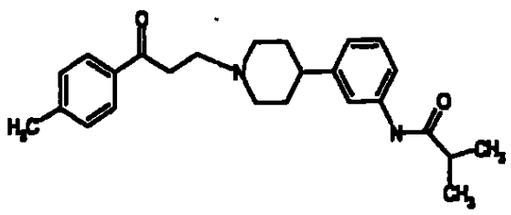
121



183.7

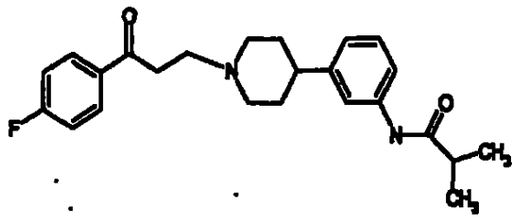
1470
1473

122

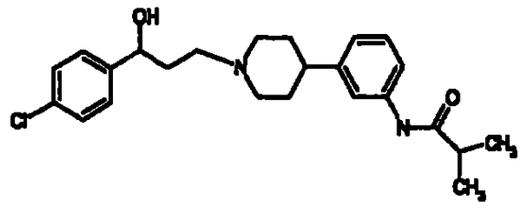
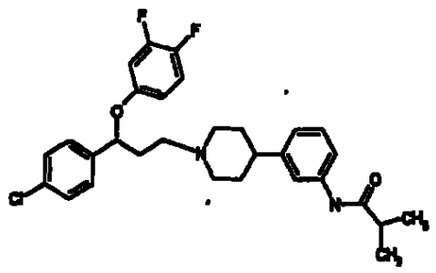


85.1

123



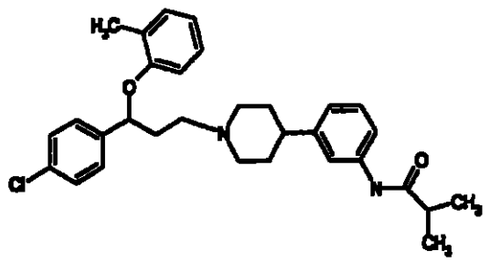
449.8

EJEMPLO	ESTRUCTURA	rMCH1 Ki (nM)
124		33.0
125		5.4

1474

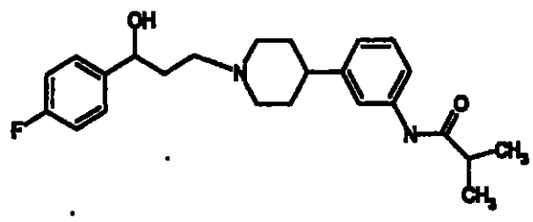
1171

126



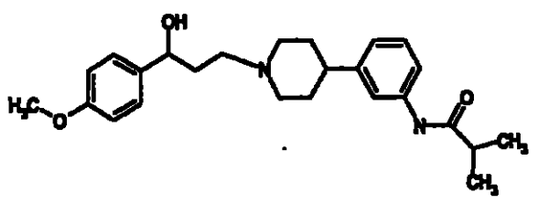
13.8

127



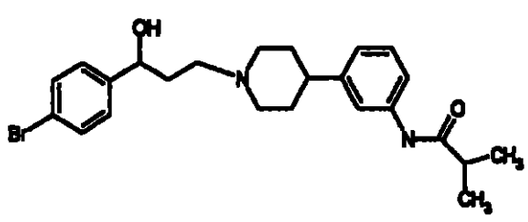
166.5

128



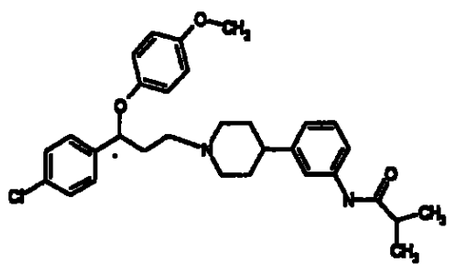
326.6

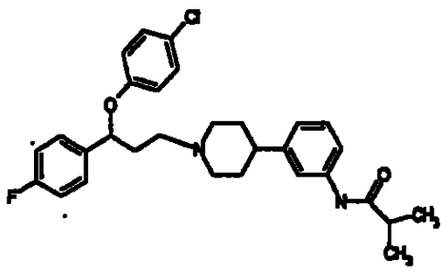
129

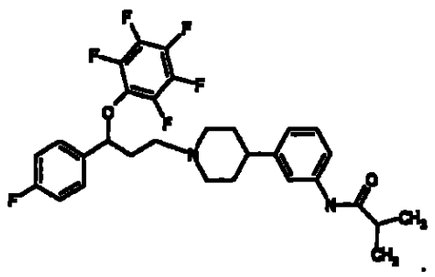


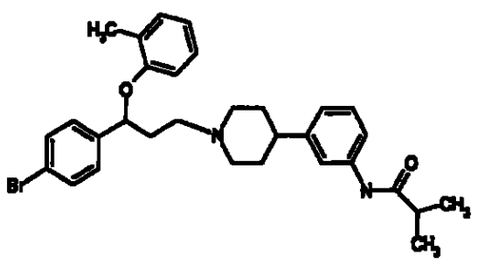
38.8

1475
1472

130  6.0

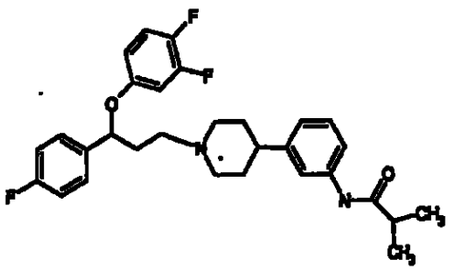
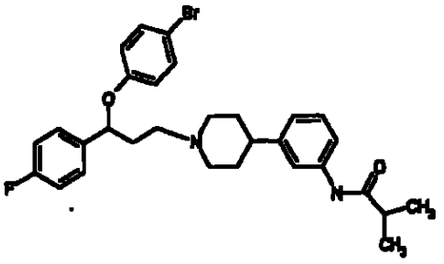
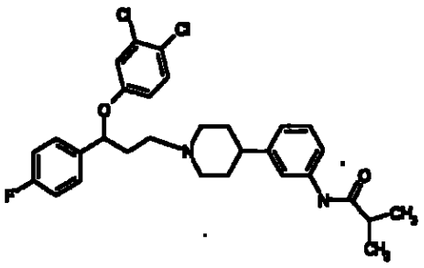
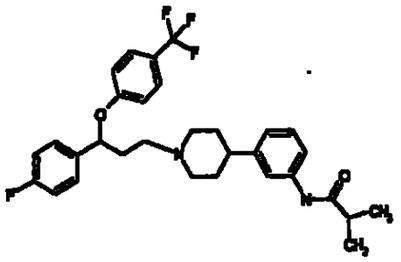
131  11.9

132  41.7

133  14.1

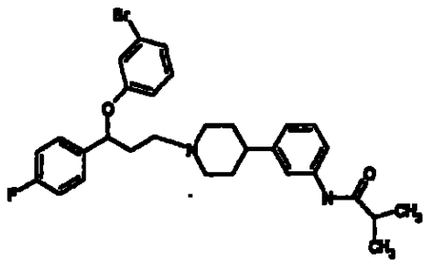
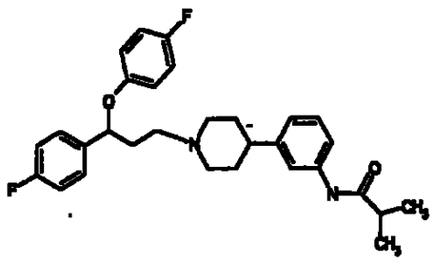
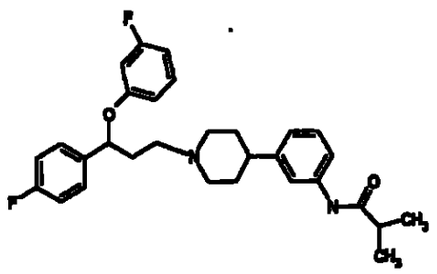
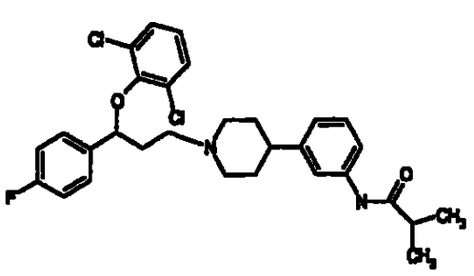
1476

1473

134		36.6
135		10.9
136		15.9
137		25.2

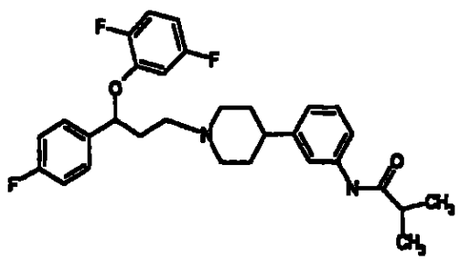
1477

1474

138		9.3
139		38.7
140		27.4
141		61.0

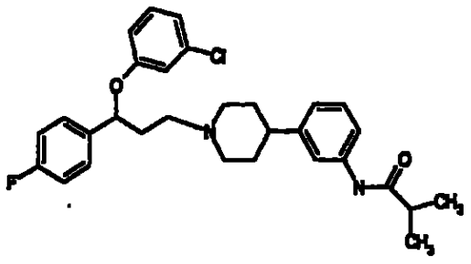
1478
1475

142



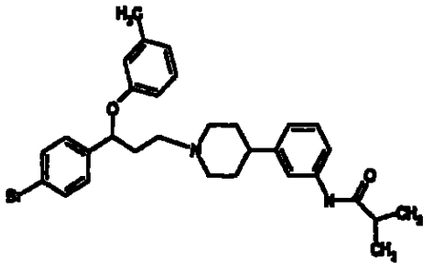
18.3

143



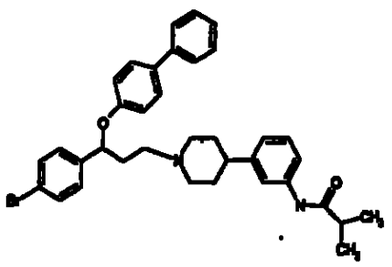
8.7

144



13.4

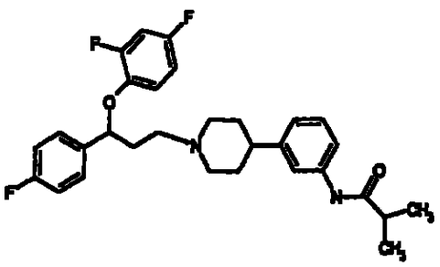
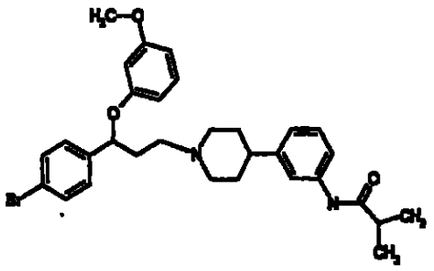
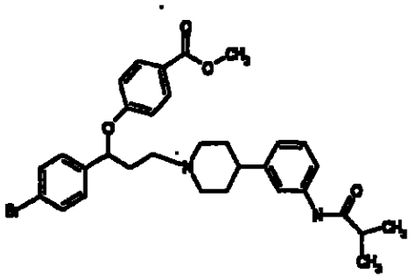
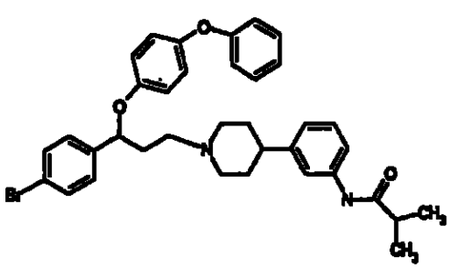
145



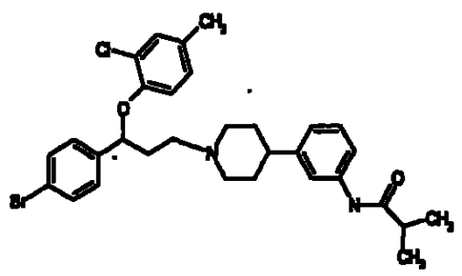
196.8

1479

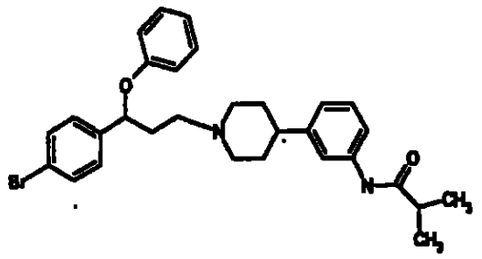
1476

146		19.2
147		8.7
148		24.7
149		148.9

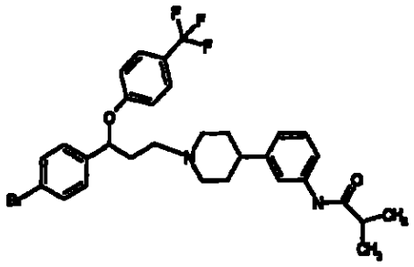
1477 1480

150 

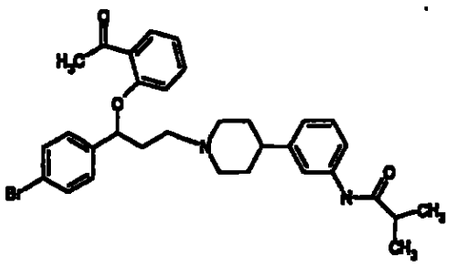
8.0

151 

14.2

152 

13.3

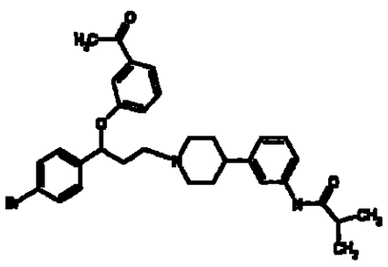
153 

8.1

1481

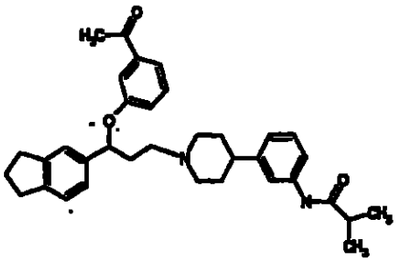
1478

154



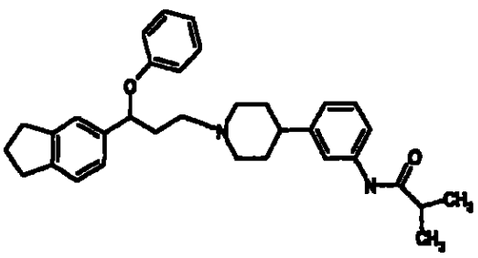
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155



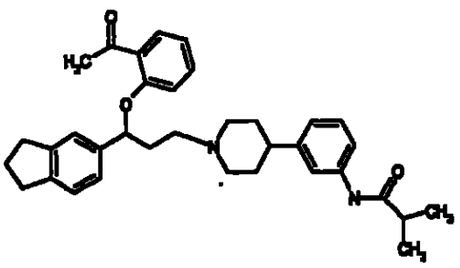
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156



8.8

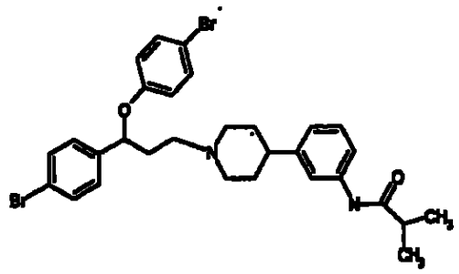
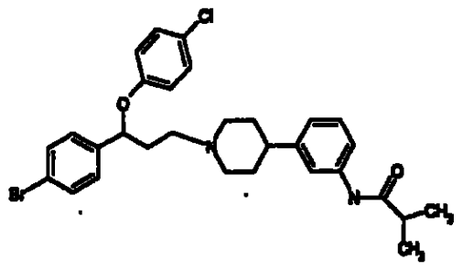
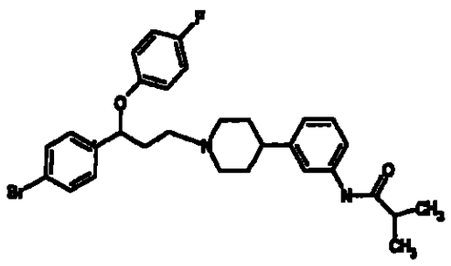
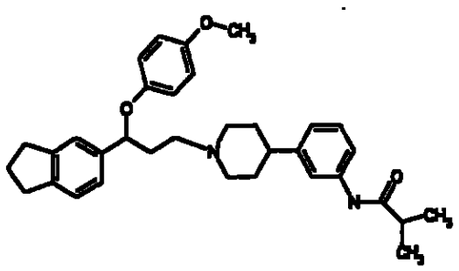
157



15.4

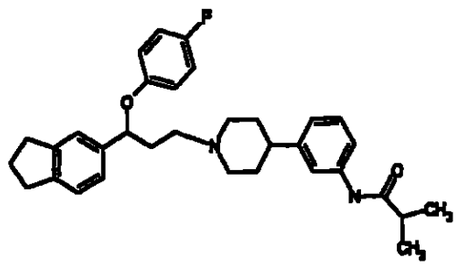
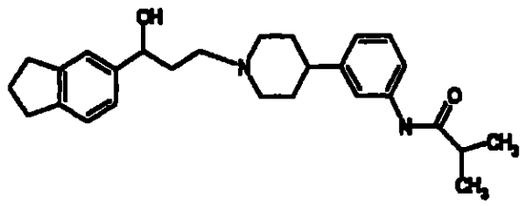
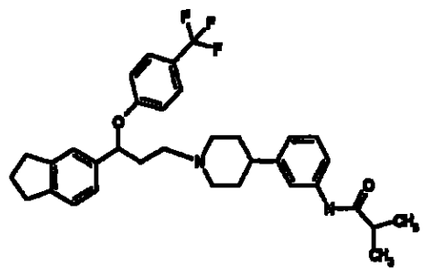
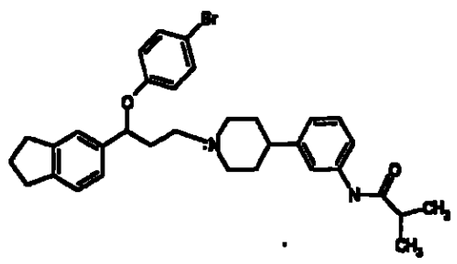
1482

1479

158		7.8
159		4.5
160		6.2
161		7.9

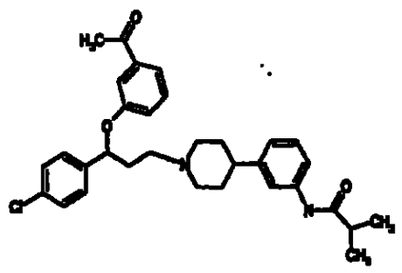
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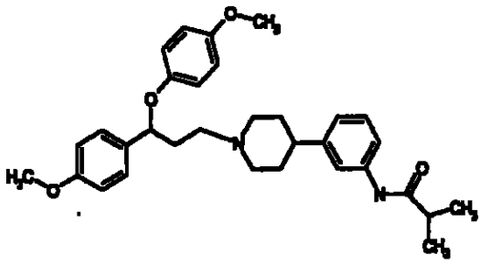
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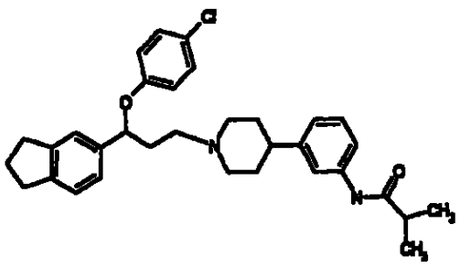
162		7.2
163		58.3
164		16.3
165		6.2

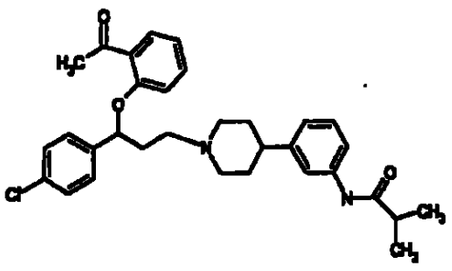
1484

1151

166  7.7

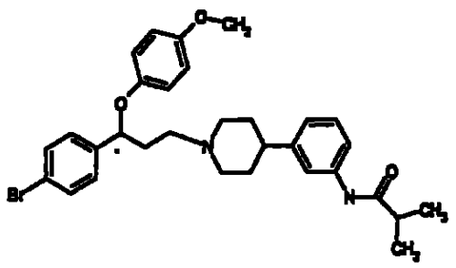
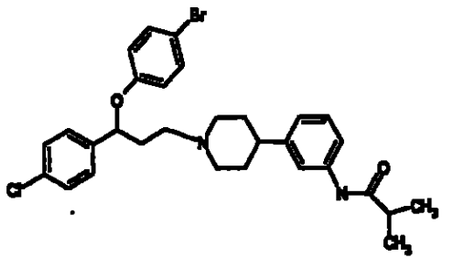
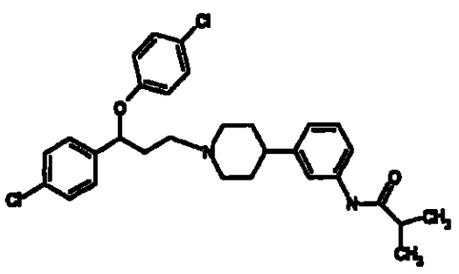
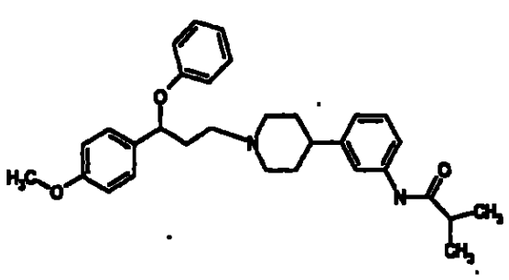
167  80.4

168  7.0

169  7.7

1485

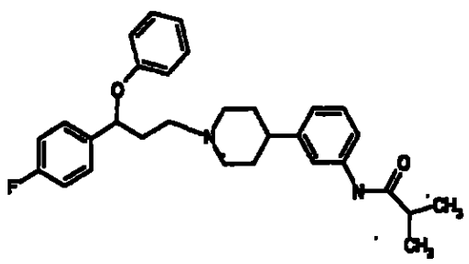
1432

170		3.0
171		3.7
172		3.0
173		112.3

1486

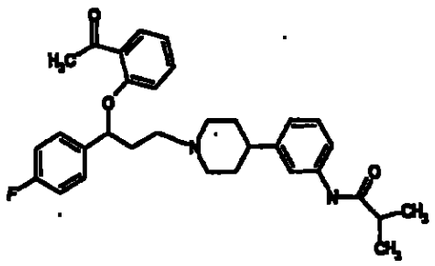
1193

174



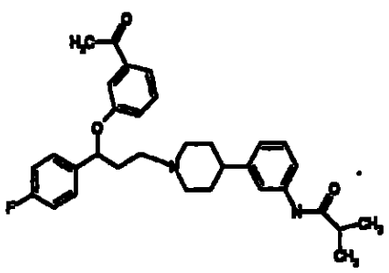
17.0

175



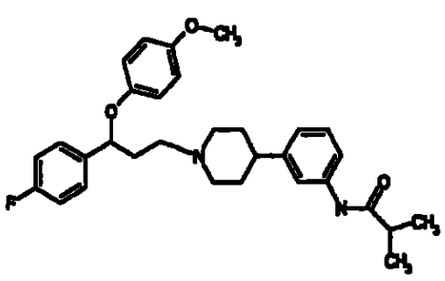
16.2

176



11.8

177

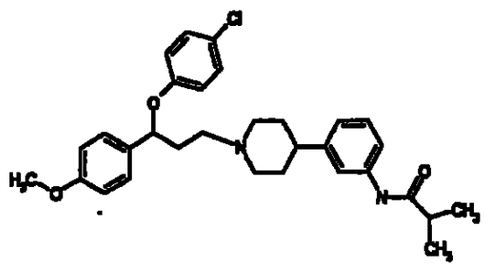


6.8

1487

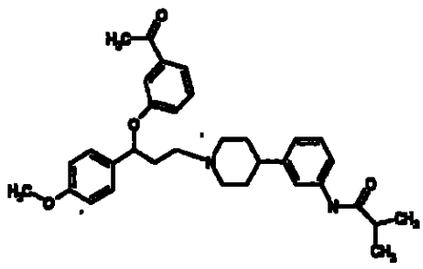
1454

178



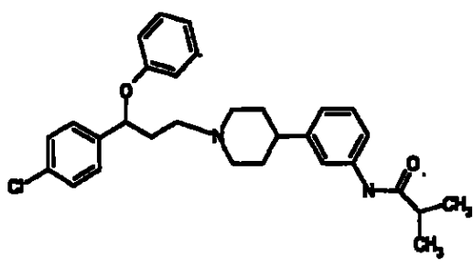
119.2

179



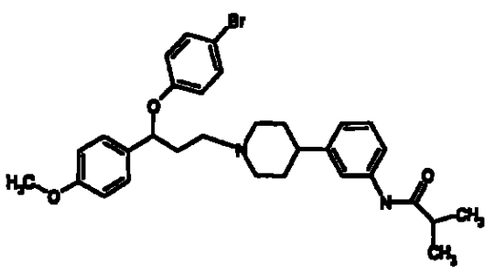
82.3

180



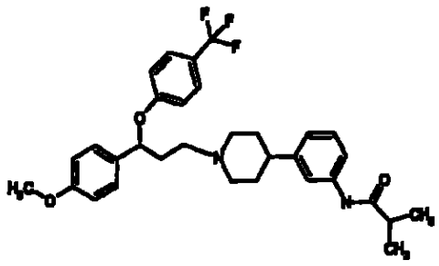
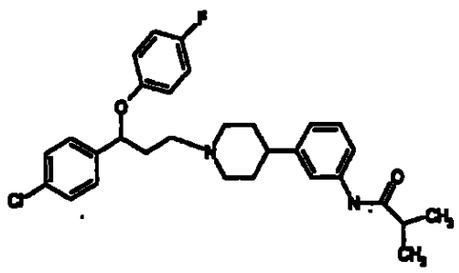
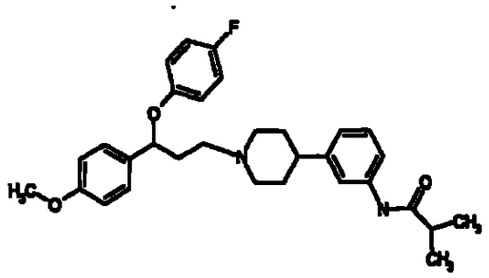
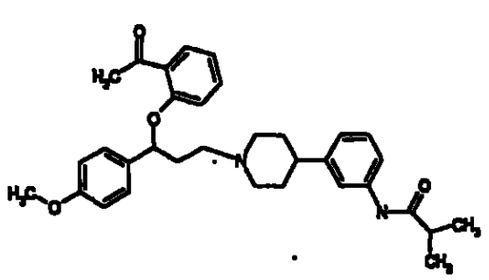
9.7

181

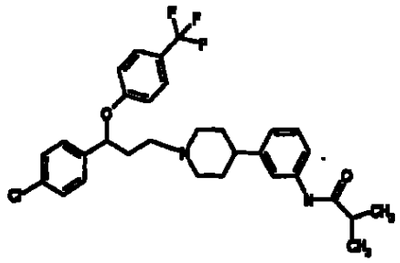
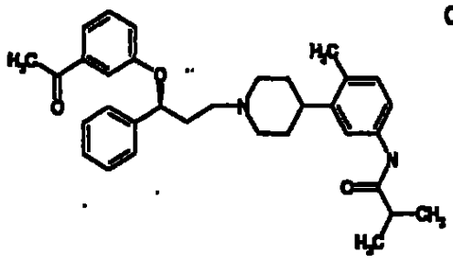


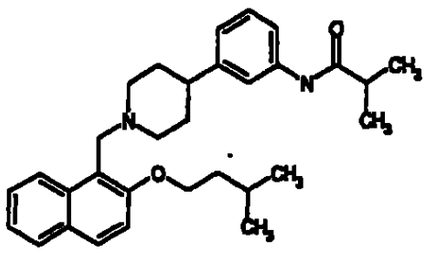
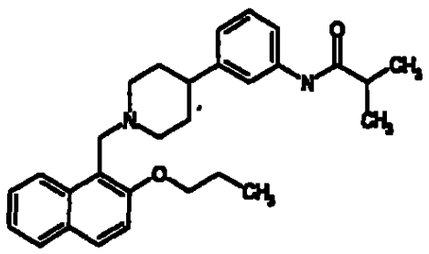
91.9

1488

182		101.3
183		4.0
184		105.2
185		20.6

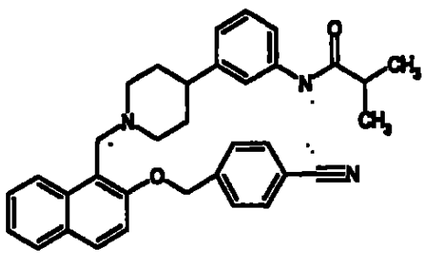
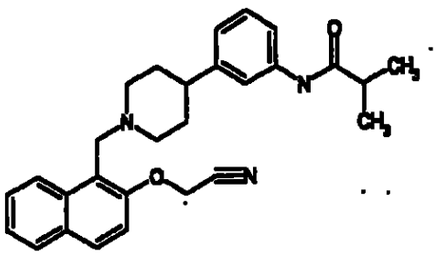
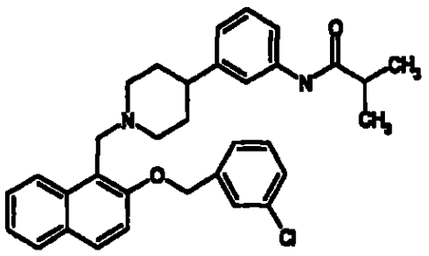
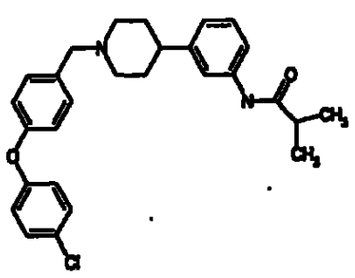
1436 1489

186		4.9
187	 Chiral	15.6

EJEMPLO	ESTRUCTURA	rMCH1 Ki (nM)
188		531.5
189		438.3

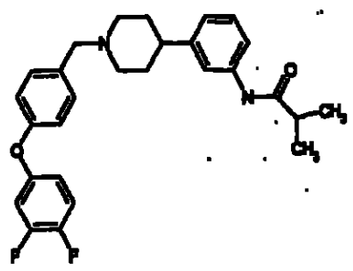
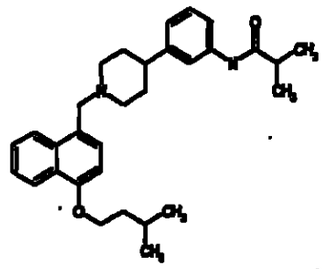
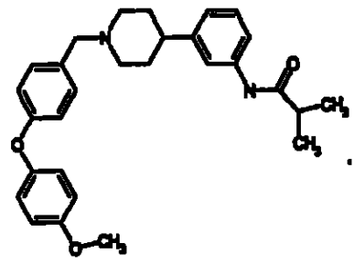
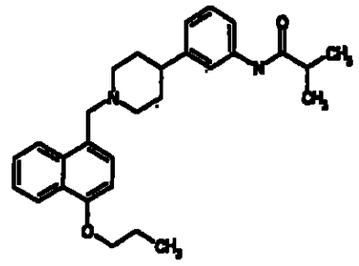
1490

1457

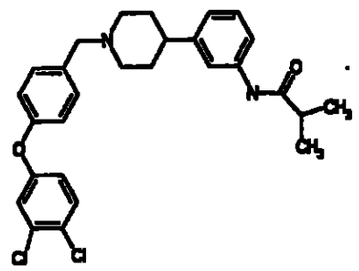
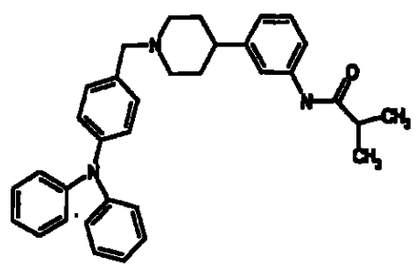
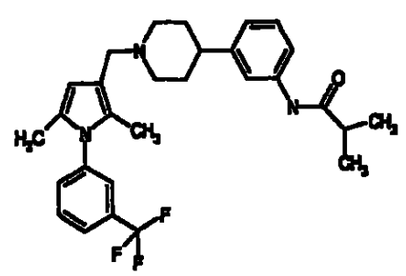
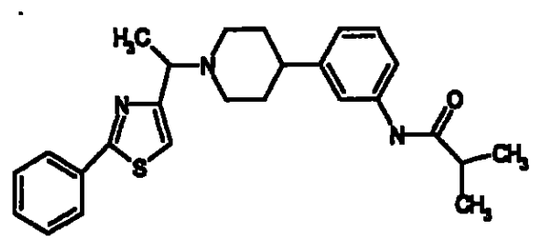
190		435.6
191		648.7
192		80.5
193		5.2

1491

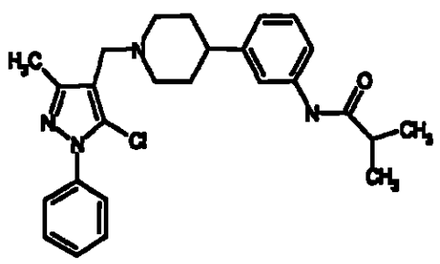
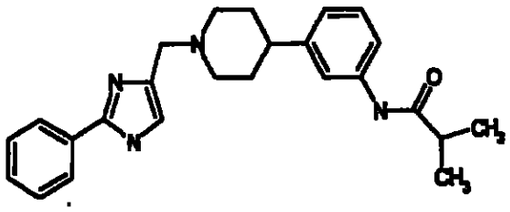
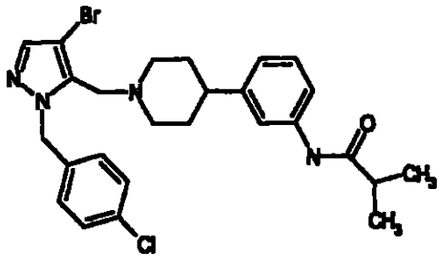
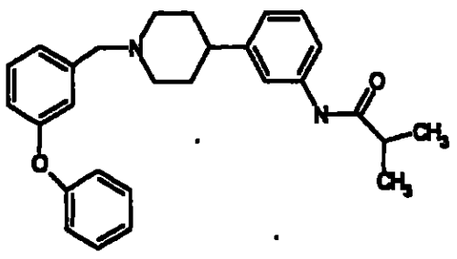
1458

194		1.8
195		106.0
196		35.2
197		63.1

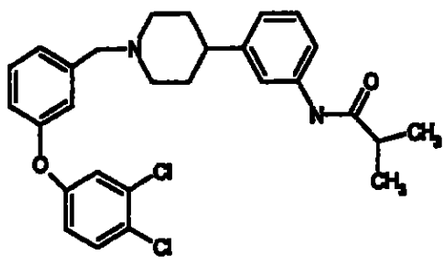
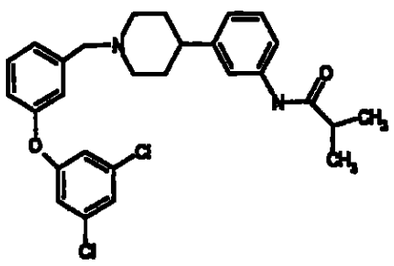
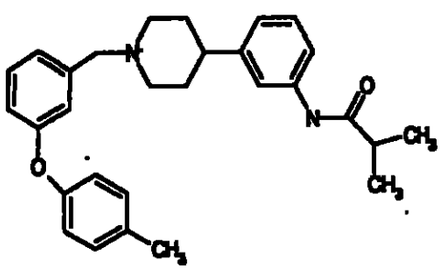
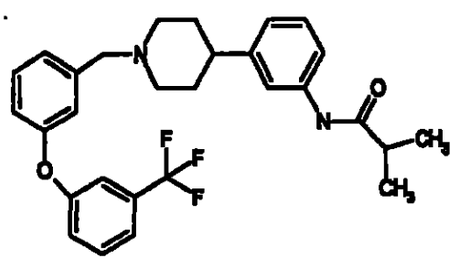
1459 1492

198		6.1
199		3.6
200		20.9
201		998.1

1493
1/30

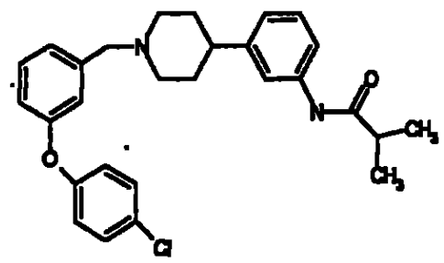
202		154.7
203		79.6
204		39.8
205		26.0

1497

206		17.7
207		138.8
208		30.8
209		64.8

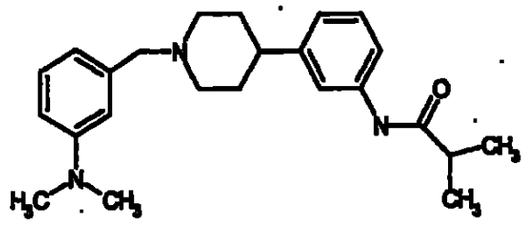
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210



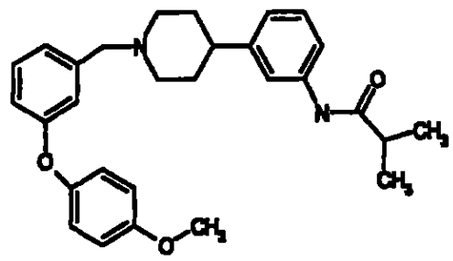
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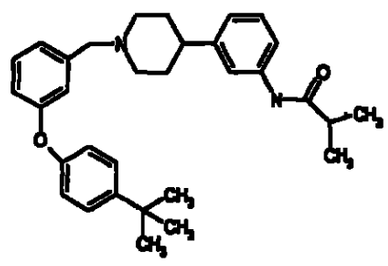
111.3

212



43.0

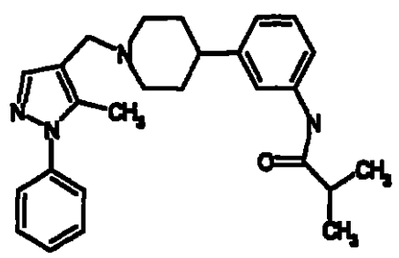
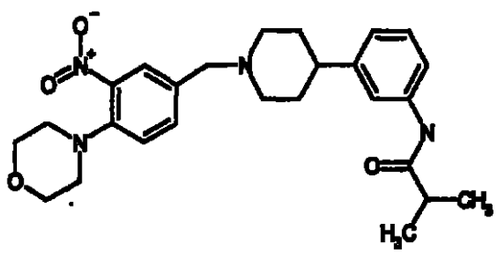
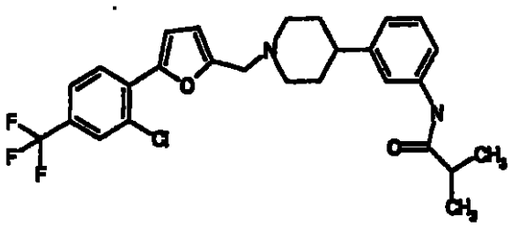
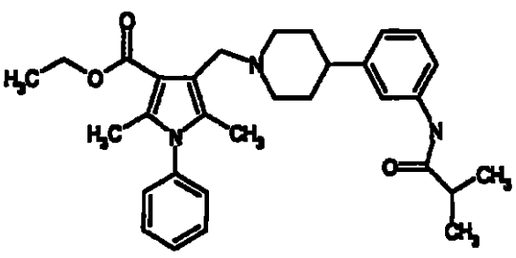
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519.1

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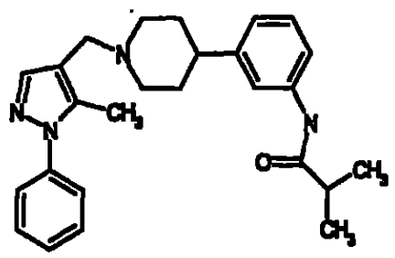
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218		125.6
219		68.8
220		158.6
221		645.7

1497

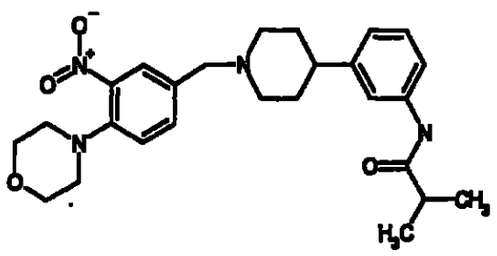
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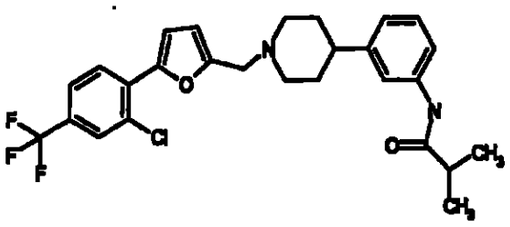
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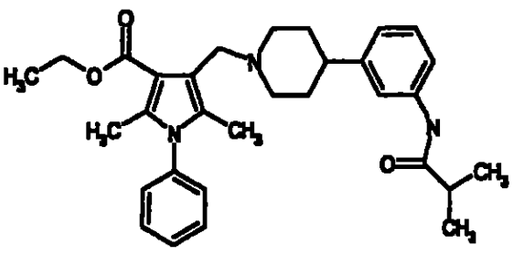
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220



158.6

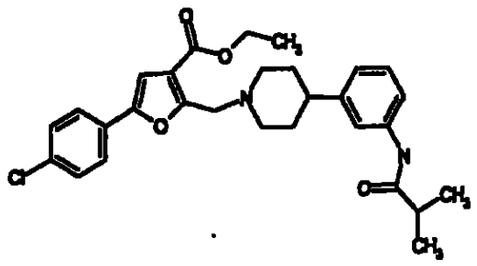
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545.7

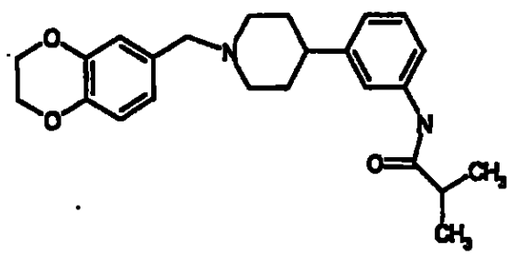
1125 1498

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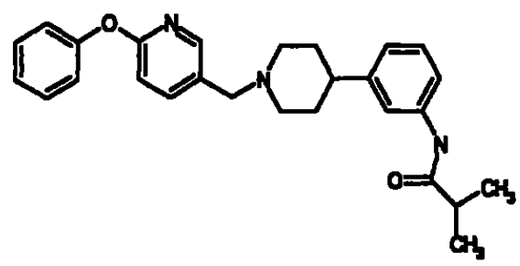
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223



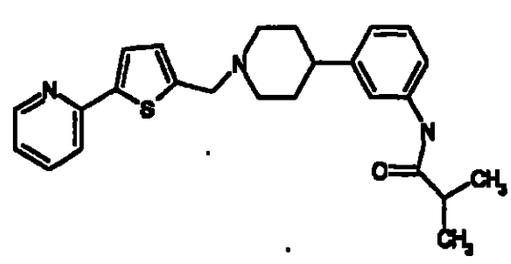
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224



48.0

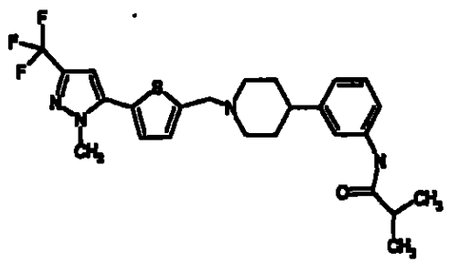
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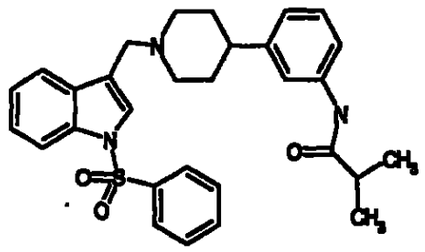
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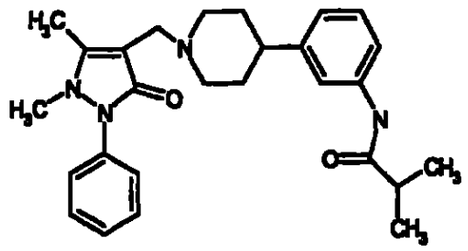
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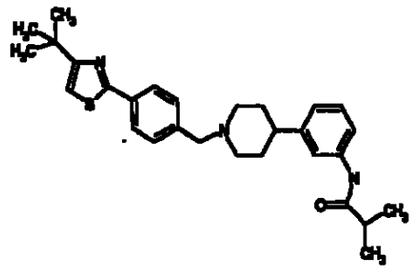
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841.1

229

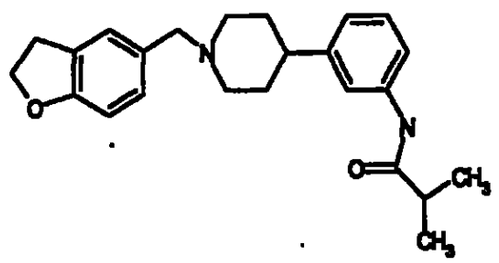


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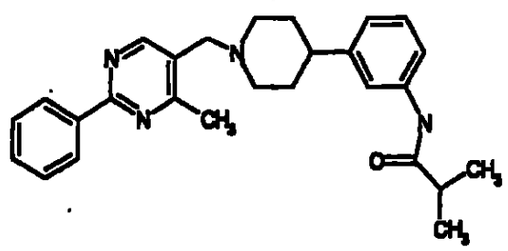
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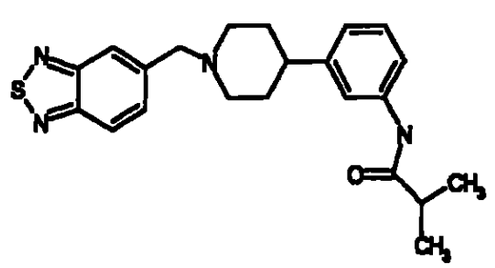
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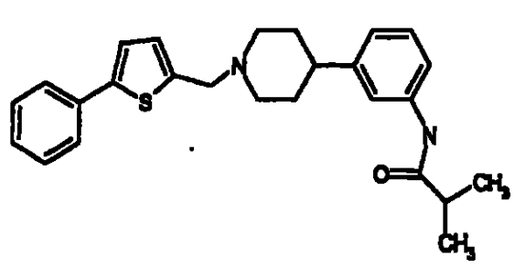
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232 431.2



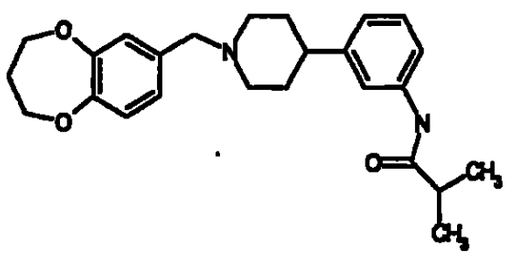
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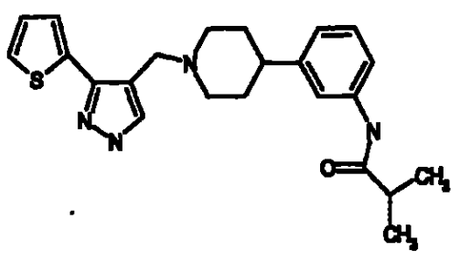
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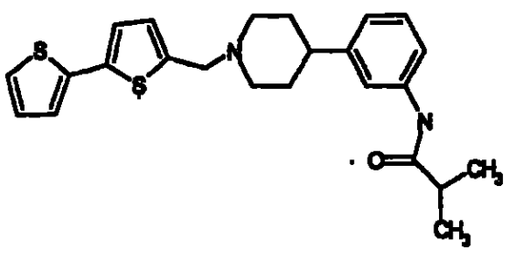
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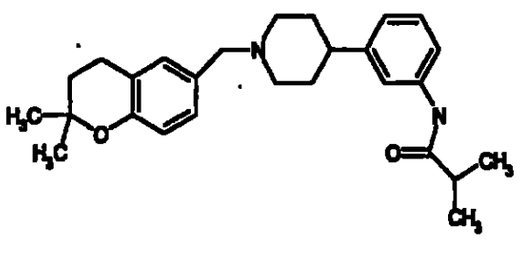
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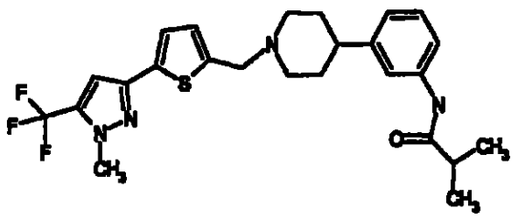
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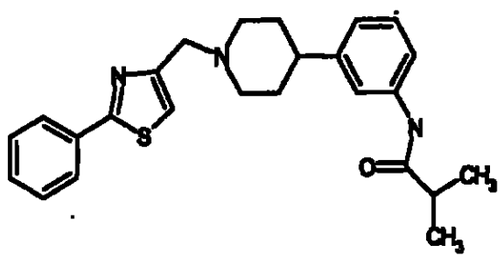
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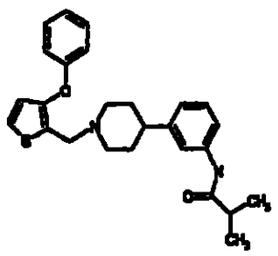


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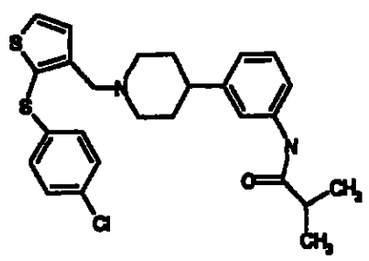
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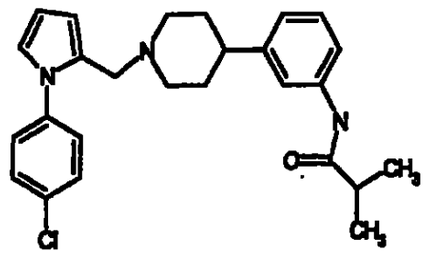
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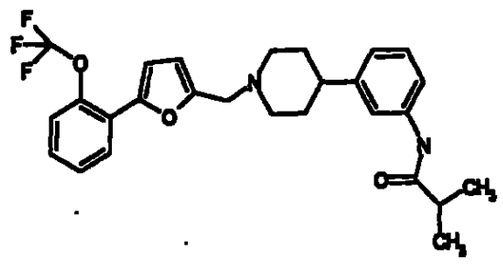
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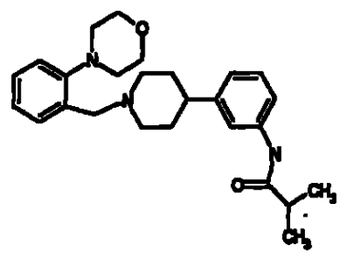
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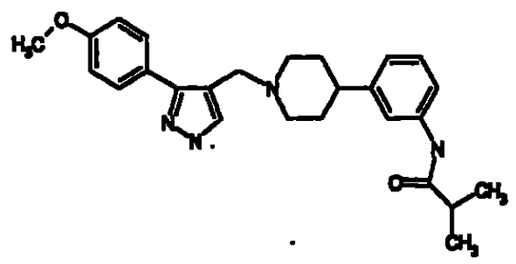
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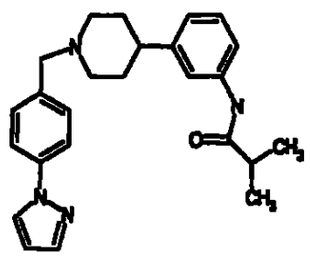


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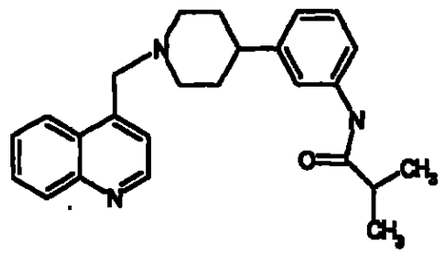


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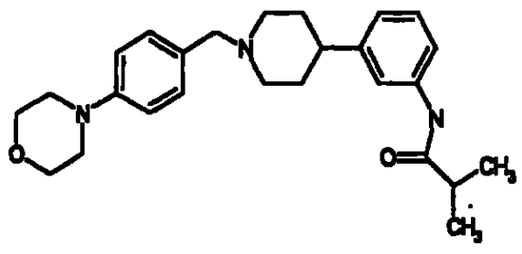
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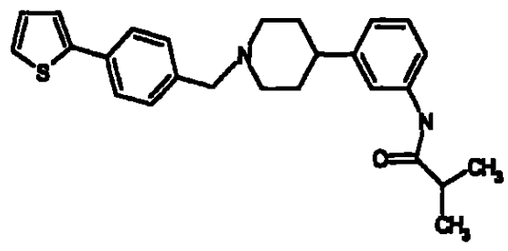
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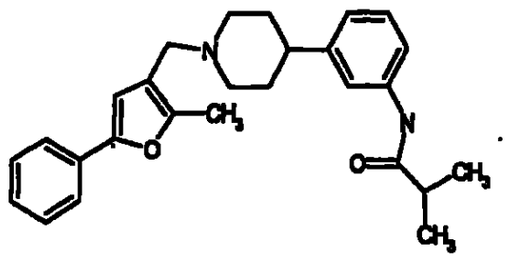
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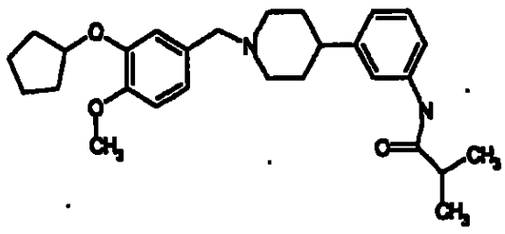
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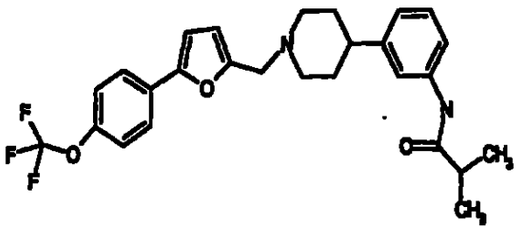
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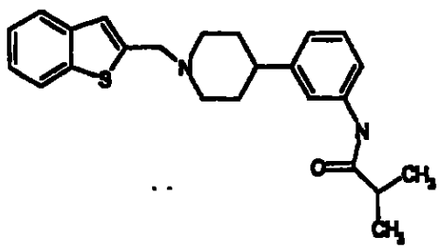
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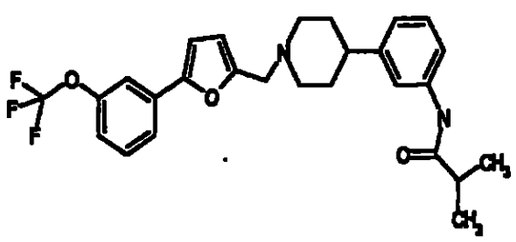


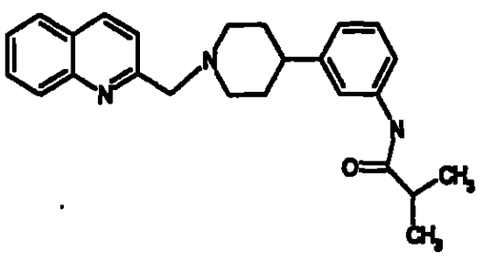
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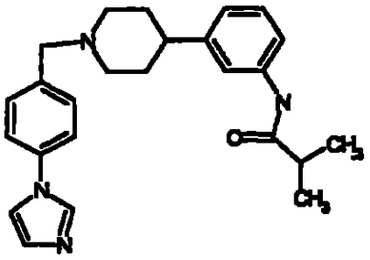


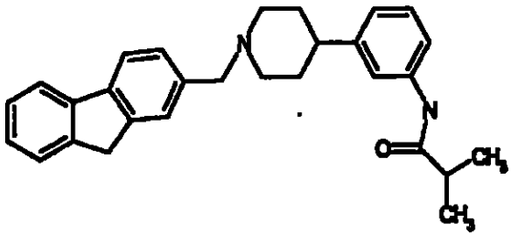
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15/13 1506

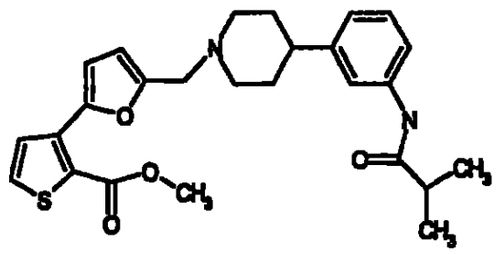
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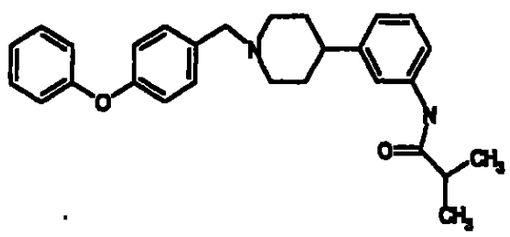
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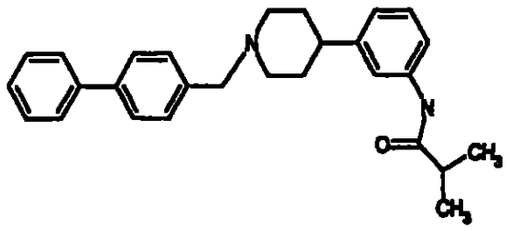
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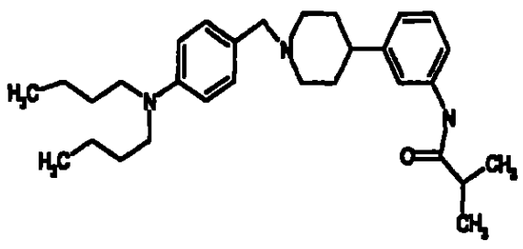
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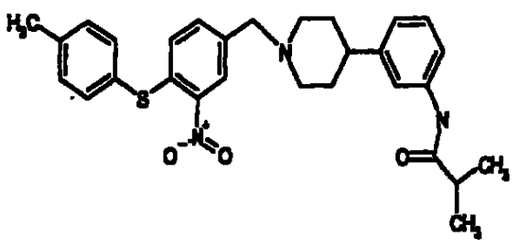
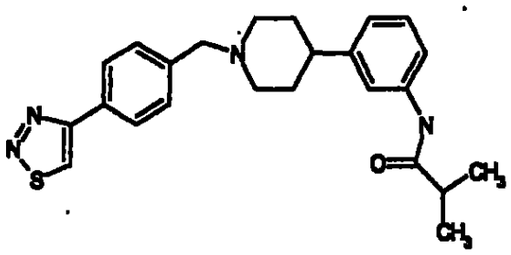
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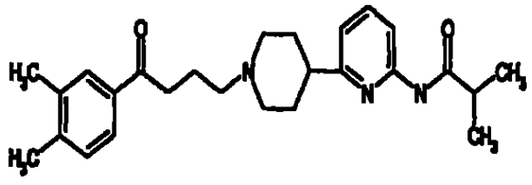
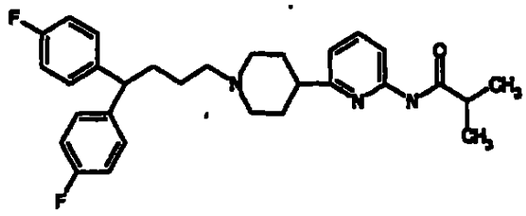
259  16.4

260  77.7

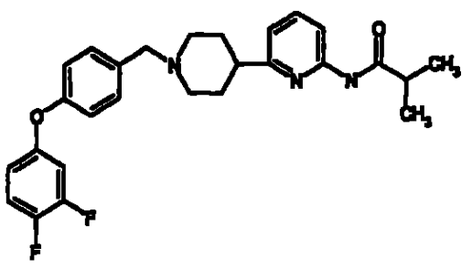
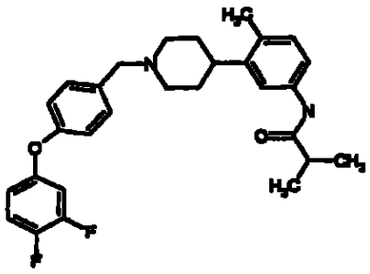
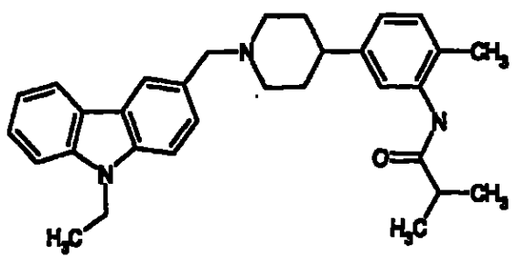
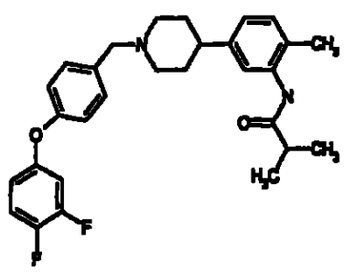
261  6.5

1505/503

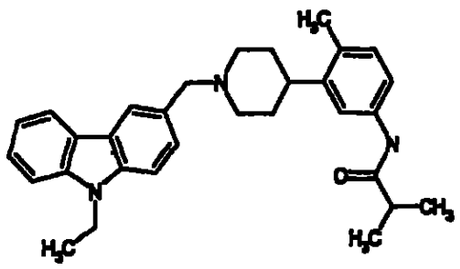
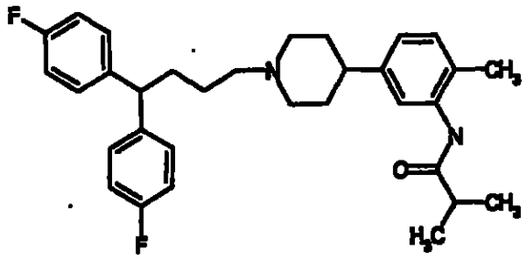
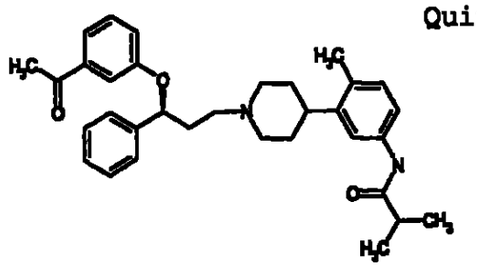
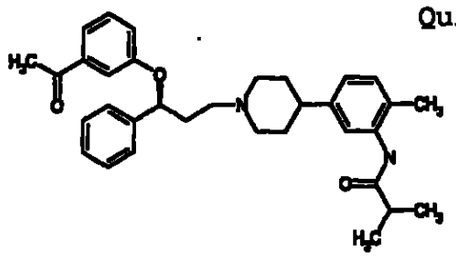
282		64.1
283		156.0

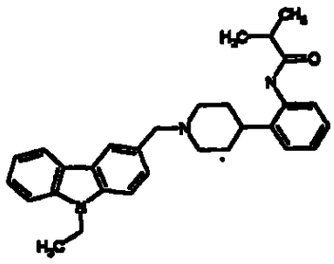
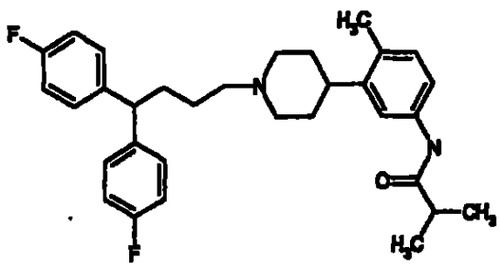
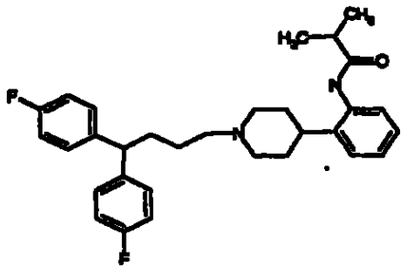
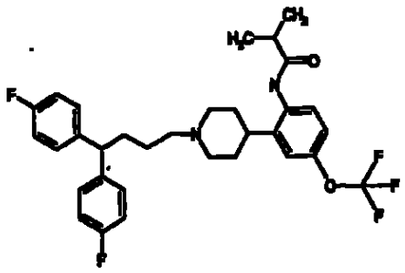
EJEMPLO	ESTRUCTURA	rMCH1 Ki (nM)
284		54.7
285		13.5

1506
159

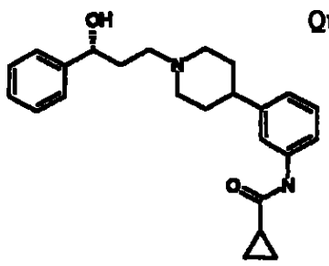
266		6.4
267		2.2
268		20.3
269		27.4

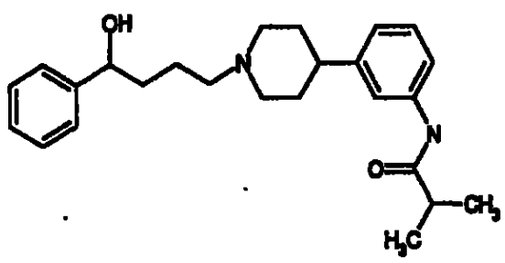
1507
1510

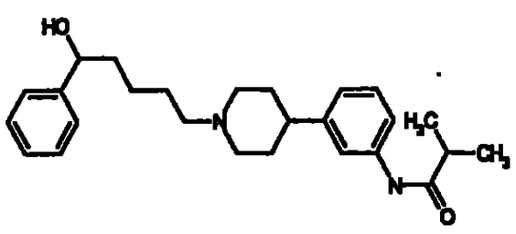
270			3.4
271			40.1
272		Quiral	15.6
273		Quiral	198.4

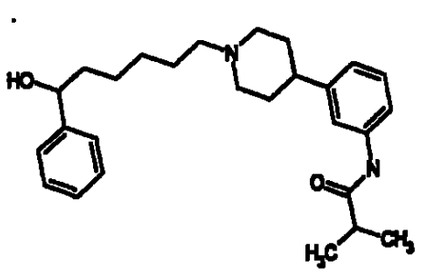
EJEMPLO	ESTRUCTURA	rMCH1 Ki (nM)
274		843.5
275		3.1
276		734.4
277		117.8

1512
1519

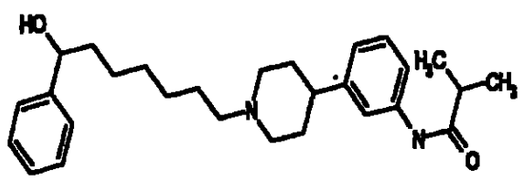
278  Quiral 85.8

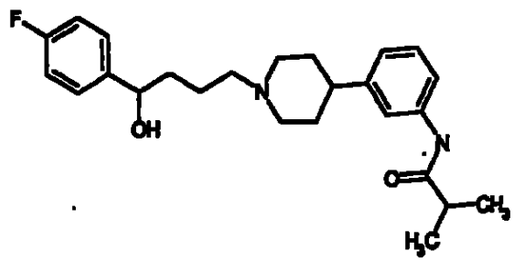
279  74.5

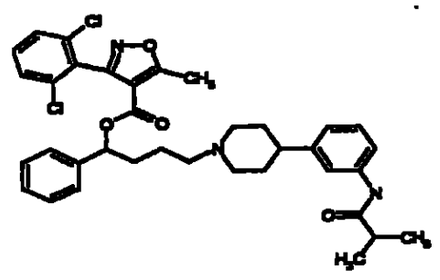
280  27.6

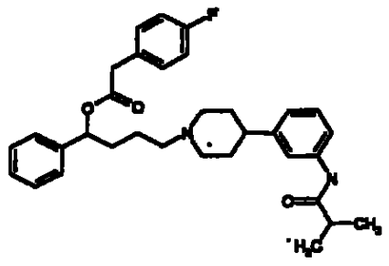
281  7.9

15x10 1513

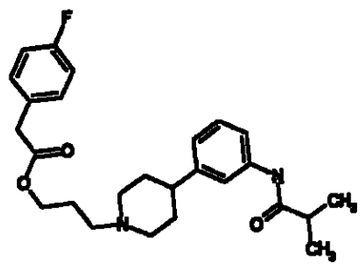
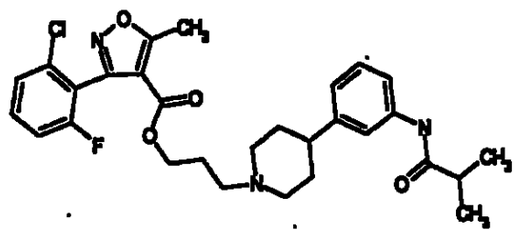
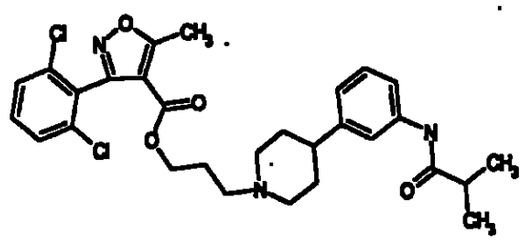
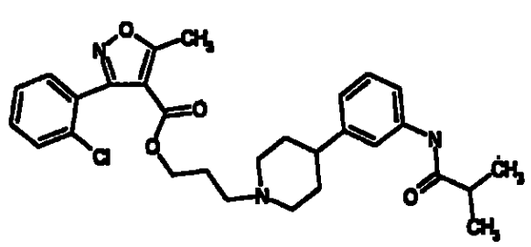
282  23.5

283 

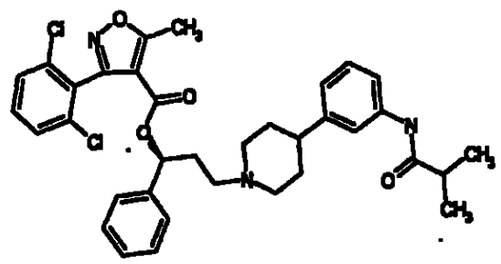
284  16.3

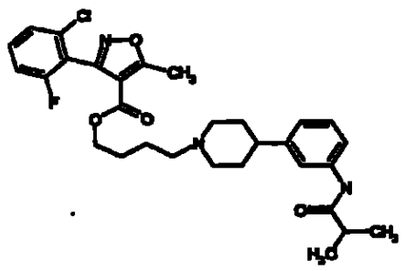
285  10.3

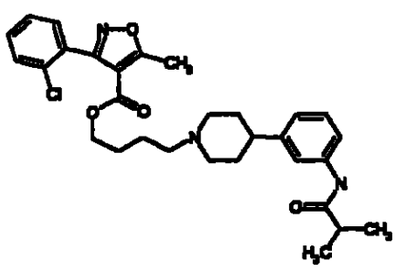
1514
15/11

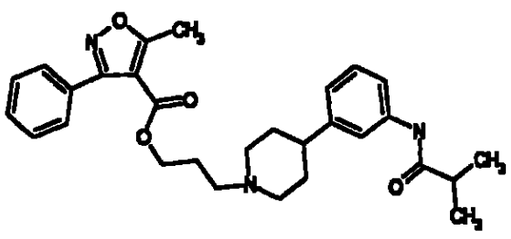
266		67.8
267		34.3
268		30.2
269		31.8

1512
1515

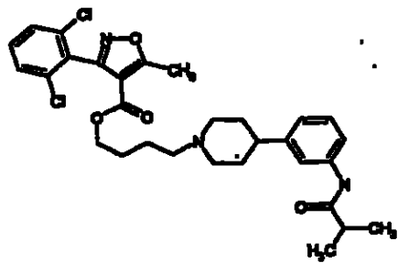
290  61.9

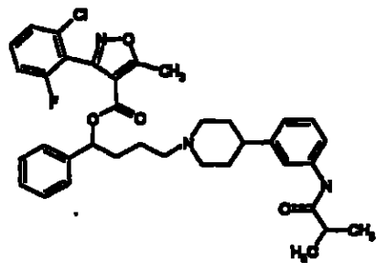
291  24.3

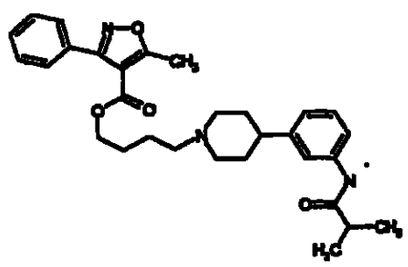
292  18.4

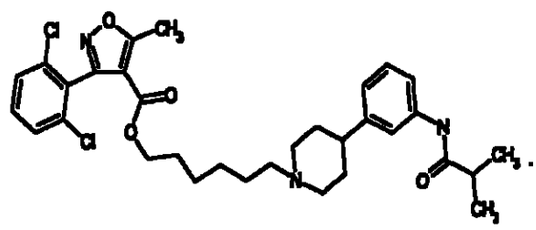
293  39.9

15/13 15/16

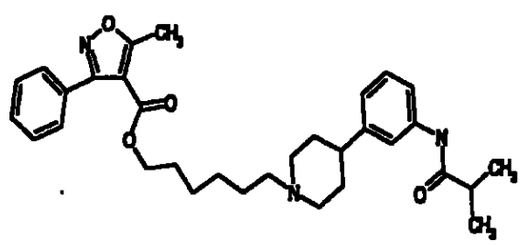
294  15.8

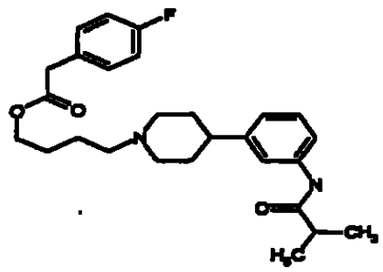
295  8.7

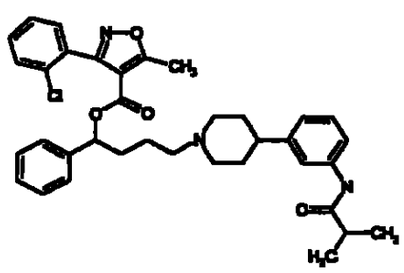
296  20.0

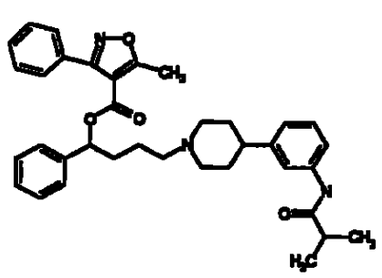
297  11.9

15/14 1512

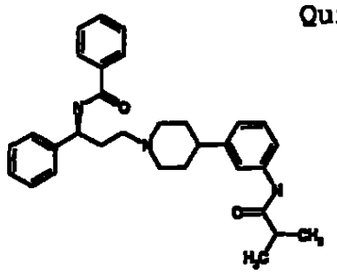
298  40.1

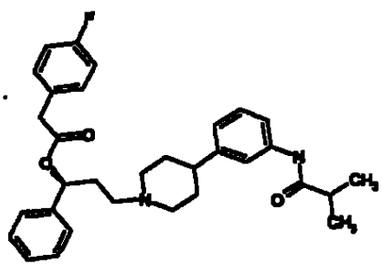
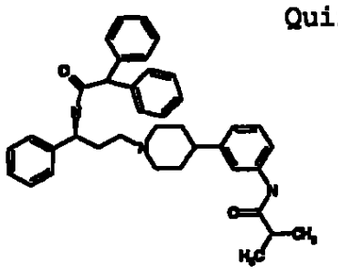
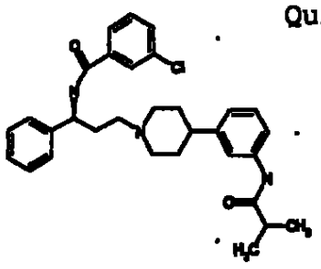
299  37.5

300  7.6

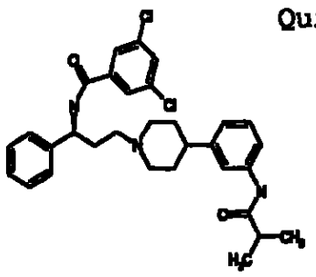
301 

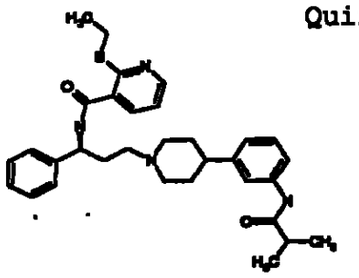
17/1518

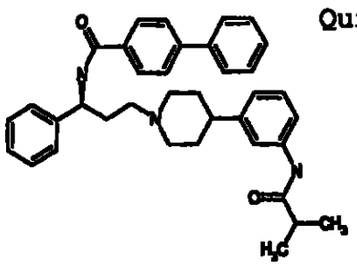
302		Quiral	20.5

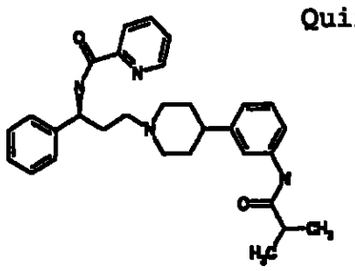
EJEMPLO	ESTRUCTURA		rMCH1 Ki (nM)
303			9.5
304		Quiral	4.0
305		Quiral	177.2

1519
15/16

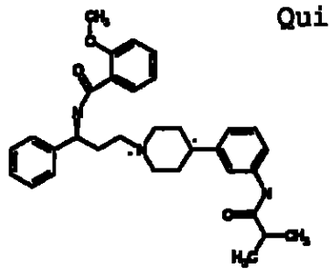
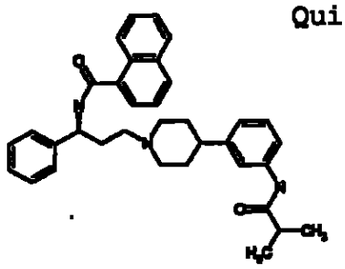
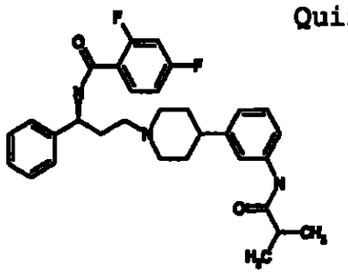
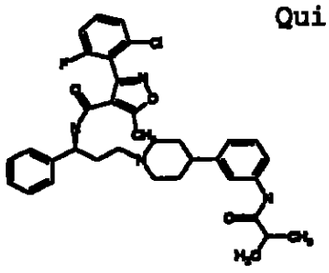
306  Quiral 167.9

307  Quiral 97.4

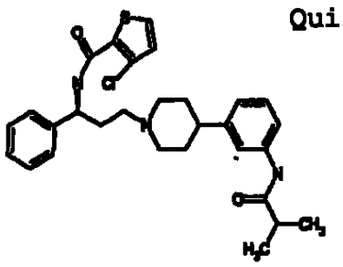
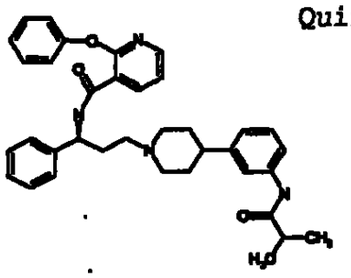
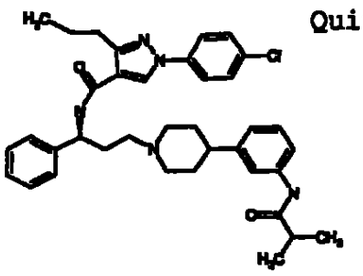
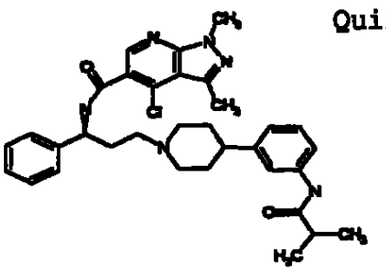
308  Quiral 401.6

309  Quiral 310.1

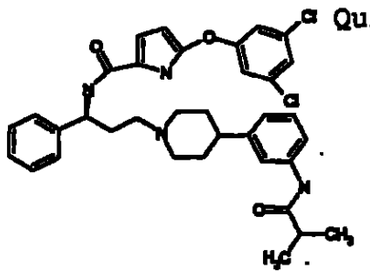
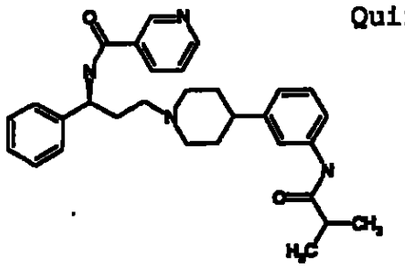
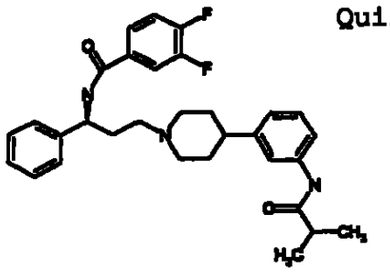
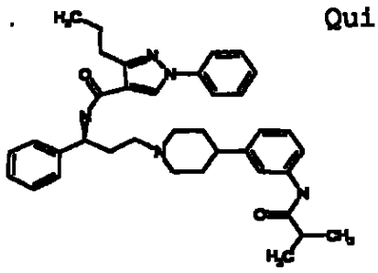
1717 1520

310		Quiral	162.2
311		Quiral	43.0
312		Quiral	61.5
313		Quiral	249.3

1521
15/16

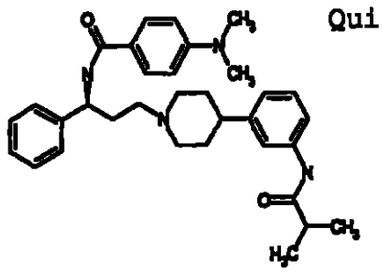
314		Quiral	7.6
315		Quiral	11.4
316		Quiral	8.3
317		Quiral	110.2

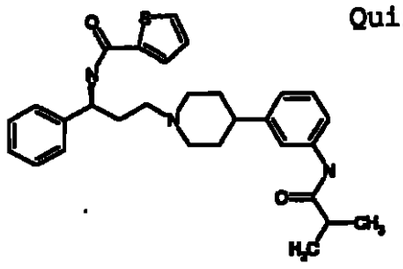
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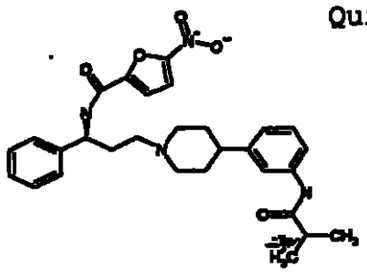
318		Quiral	251.2
319		Quiral	89.6
320		Quiral	10.6
321		Quiral	50.9

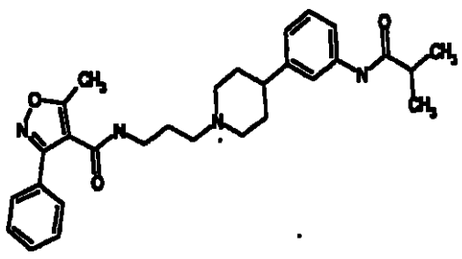
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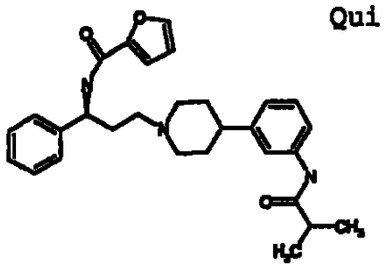
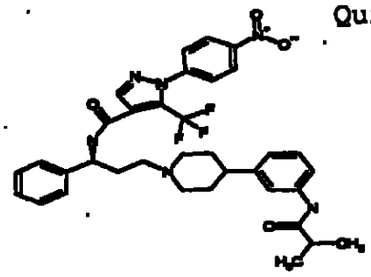
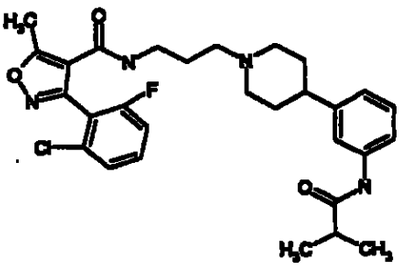
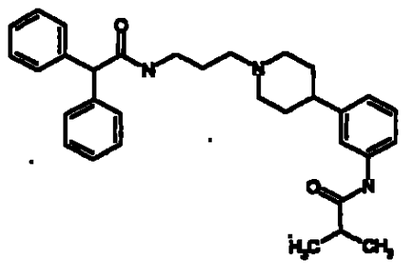
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322  Quiral 99.9

323  Quiral 37.0

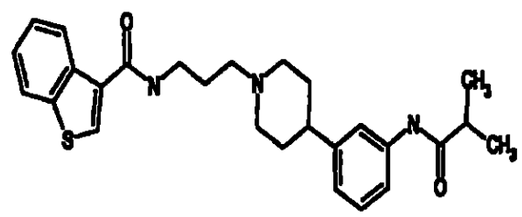
324  Quiral 76.8

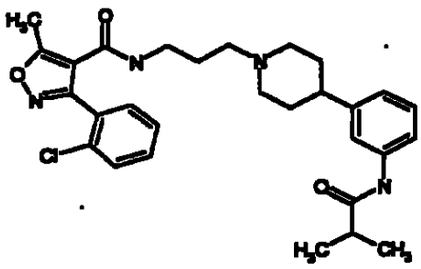
325  29.8

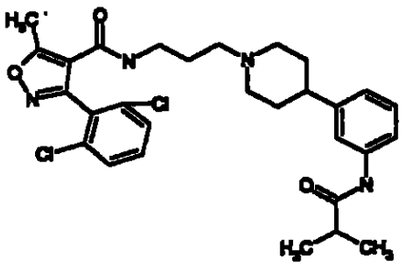
326		Quiral	19.2
327		Quiral	7.7
328			47.6
329			2.9

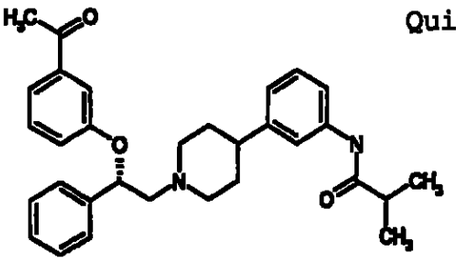
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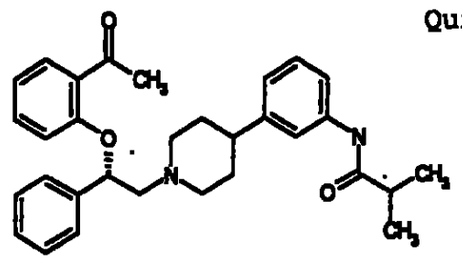
330  215.0

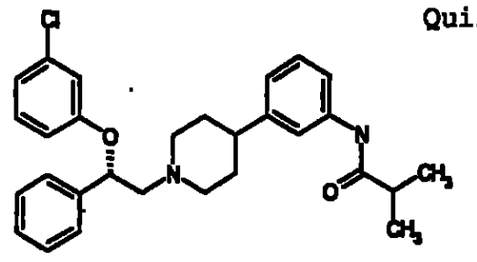
331  51.3

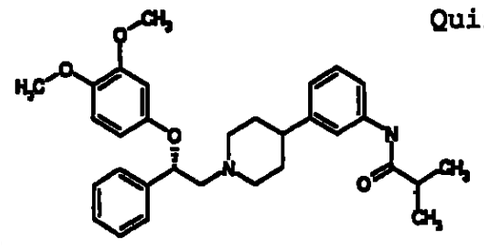
332  29.0

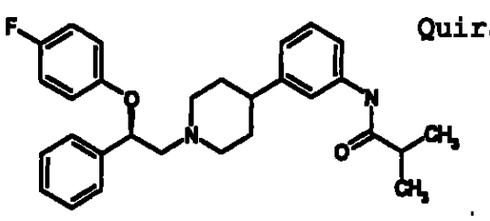
EJEMPLO	ESTRUCTURA	rMCH1 Ki (nM)
333	 Quiral	567.8

15/23 1526

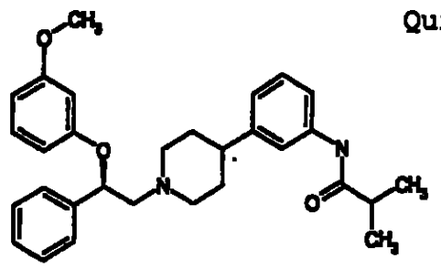
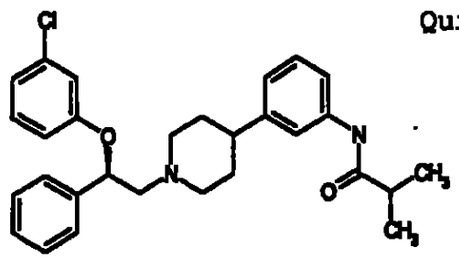
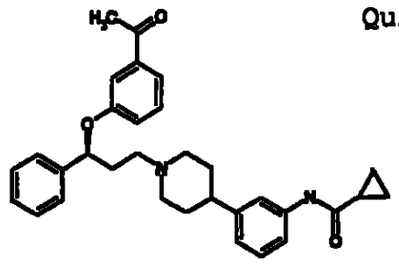
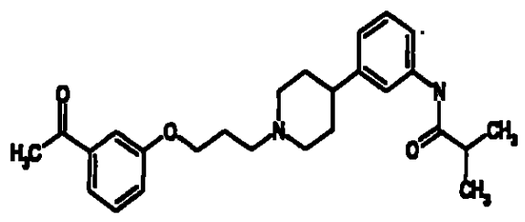
334  Quiral 602.8

335  Quiral 887.7

336  Quiral 693.0

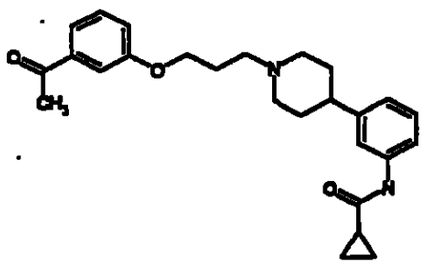
337  Quiral 907.4

1524 1527

338		Quiral	843.9
339		Quiral	889.9
340		Quiral	15.6
341			255.6

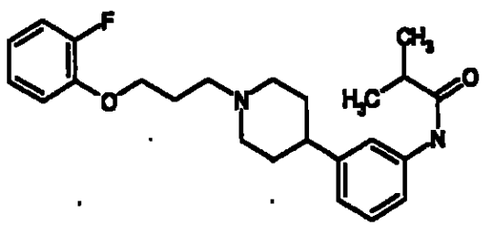
1528
1725

342



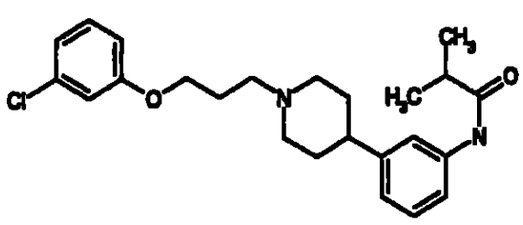
183.0

343



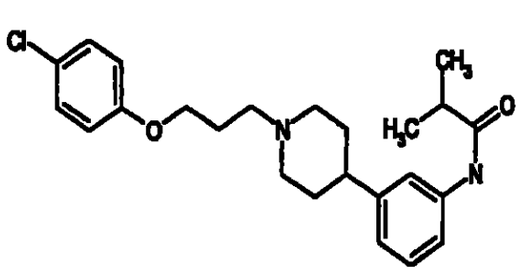
194.7

344

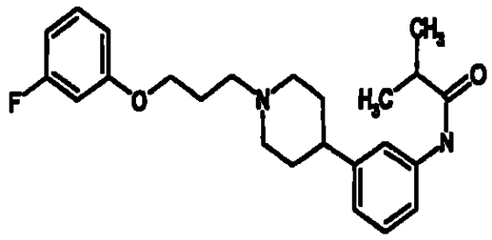


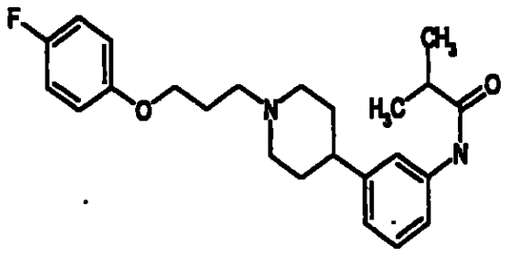
44.6

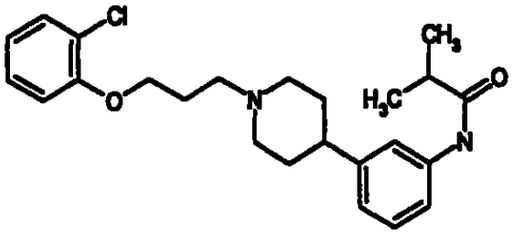
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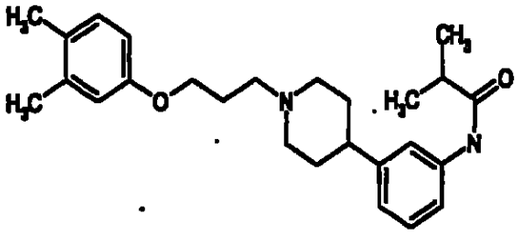


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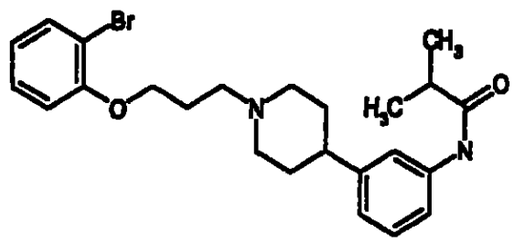
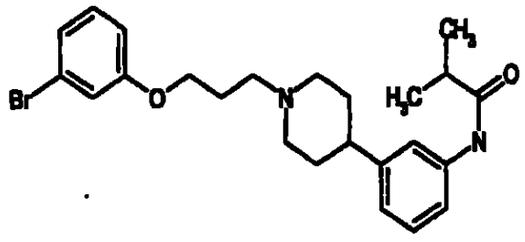
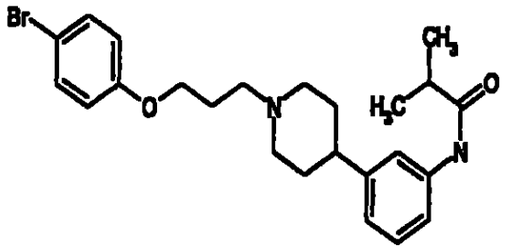
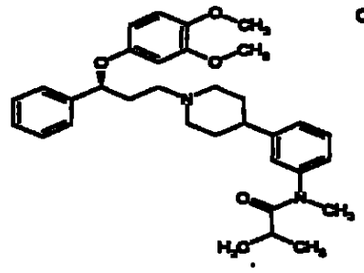
348  106.9

347  64.8

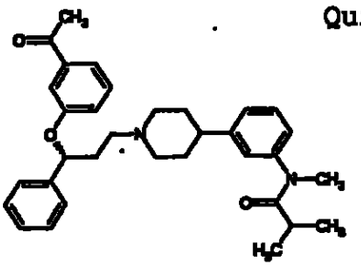
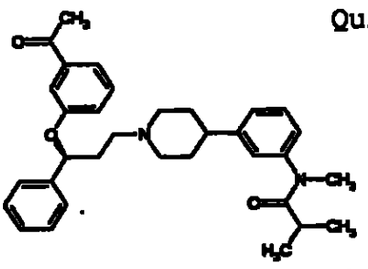
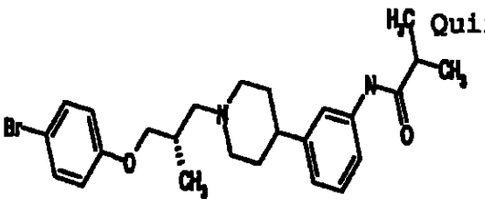
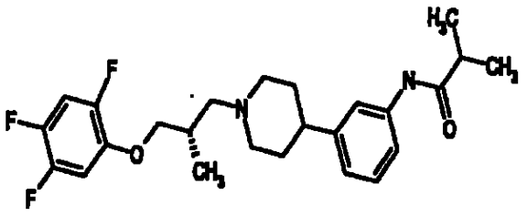
348  84.0

349  20.4

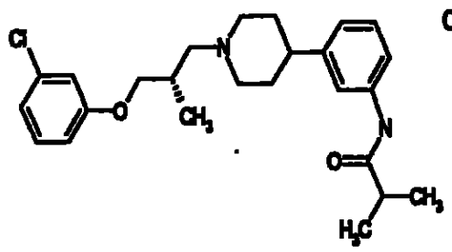
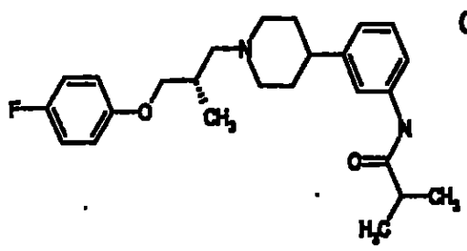
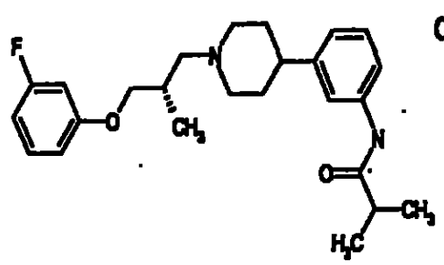
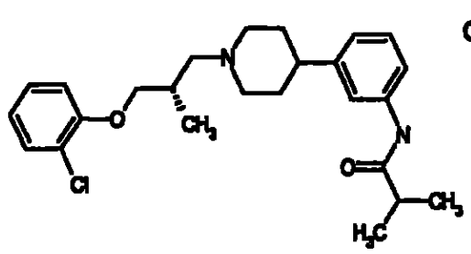
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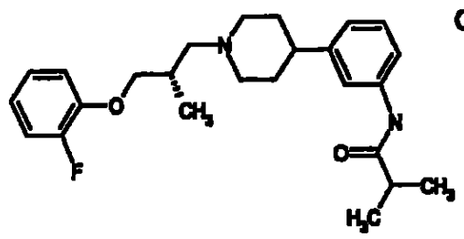
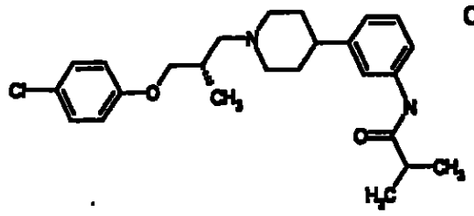
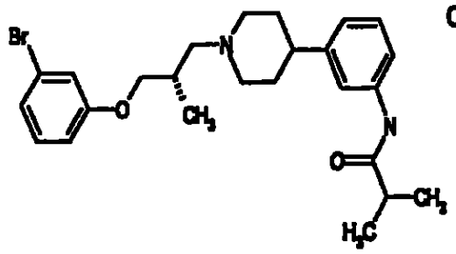
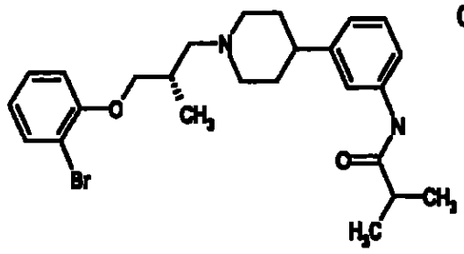
350		12.1
351		61.8
352		13.3
353	 Chiral	41.8

15/28 (53)

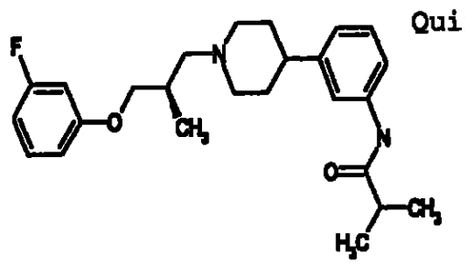
354		Quiral	81.6
355		Quiral	116.6
356		Quiral	64.5
357			115.4

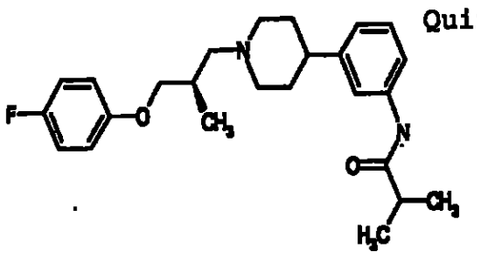
1529 1532

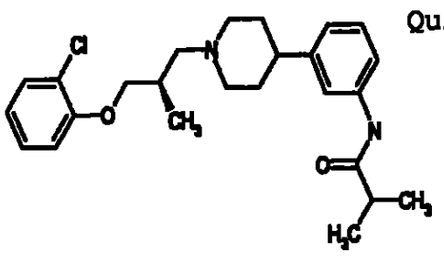
358		Chiral	135.7
359		Chiral	83.2
360		Chiral	163.0
361		Chiral	311.2

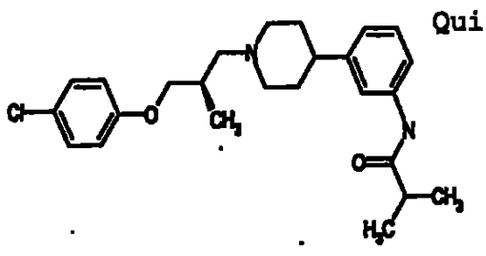
362		Chiral	281.2
363		Chiral	31.6
364		Chiral	144.4
365		Chiral	42.9

1534 1531

366  Quiral 645.5

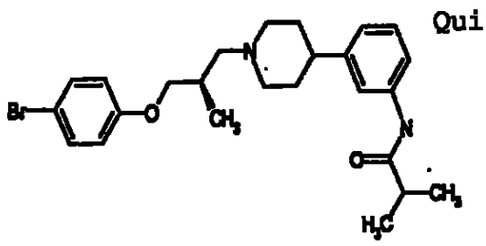
367  Quiral 235.7

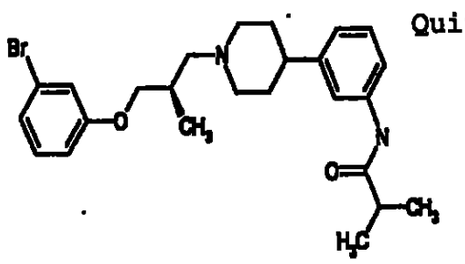
368  Quiral 313.0

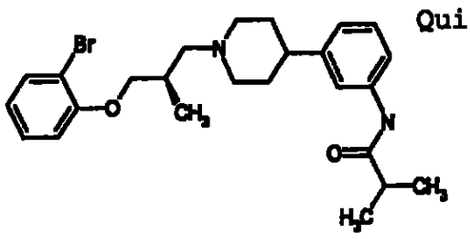
369  Quiral 146.0

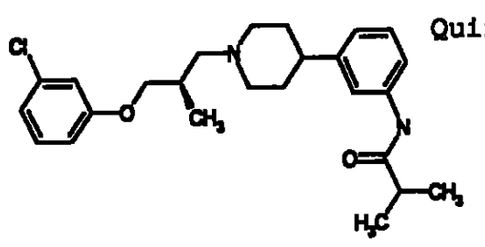
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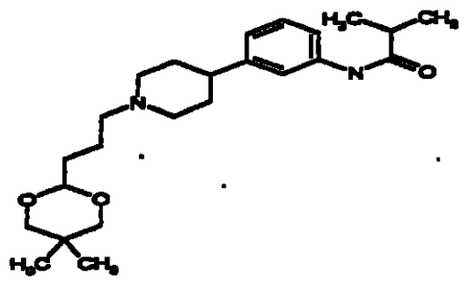
370  Quiral

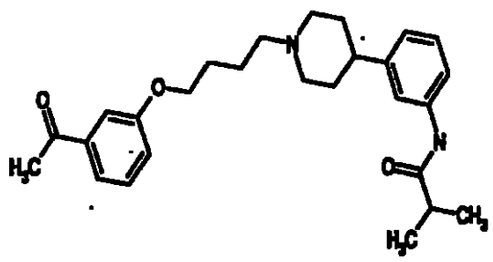
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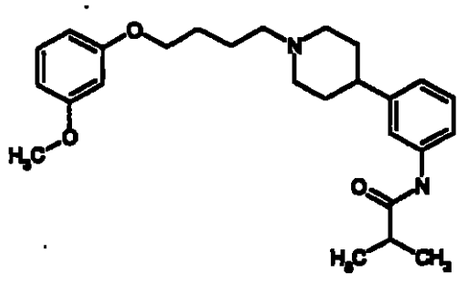
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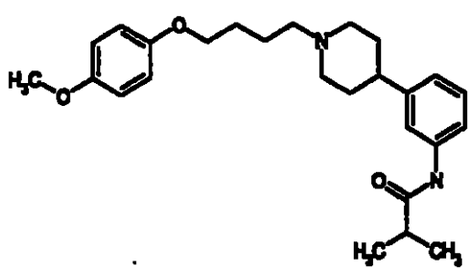
373  Quiral 428.5

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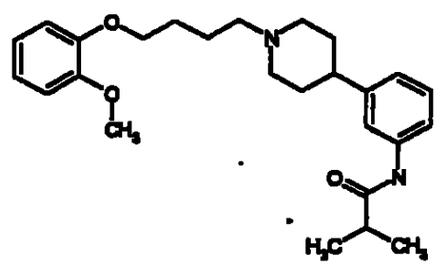
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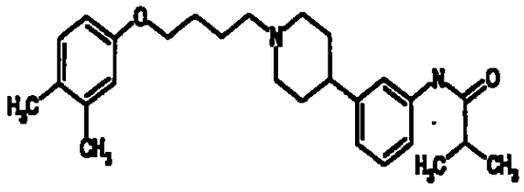
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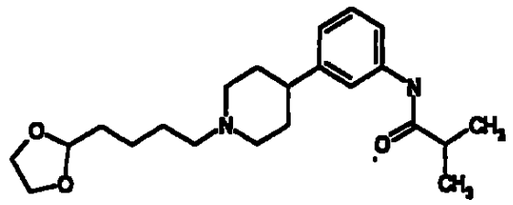
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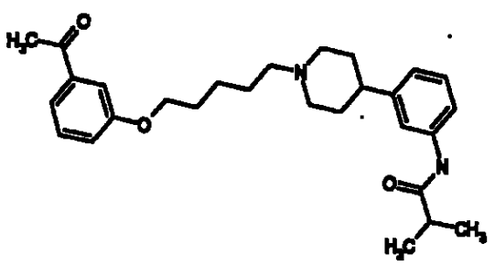
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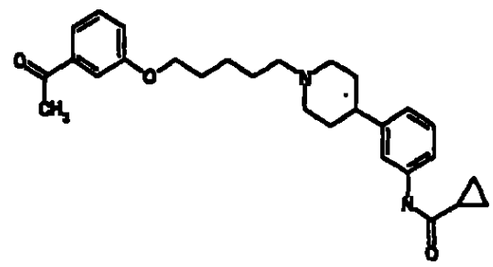
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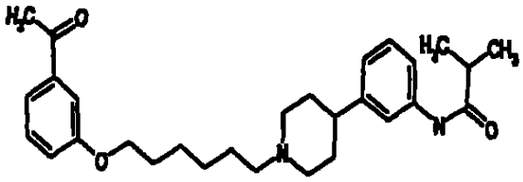
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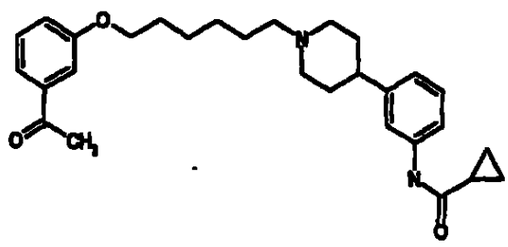
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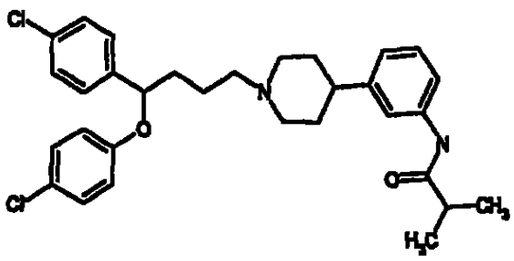
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384  69.0

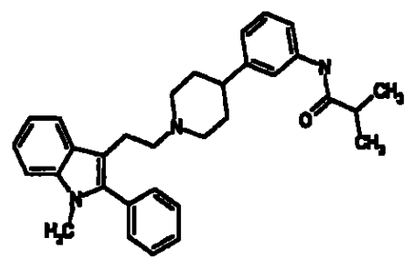
385  324.6

EJEMPLO	ESTRUCTURA	rMCH1 Ki (nM)

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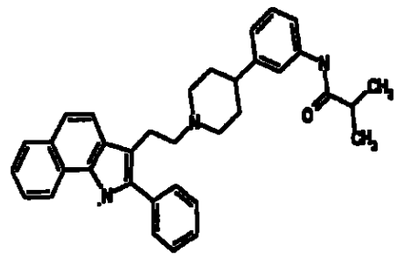
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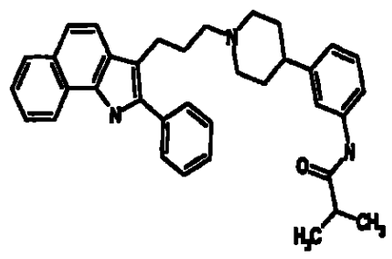
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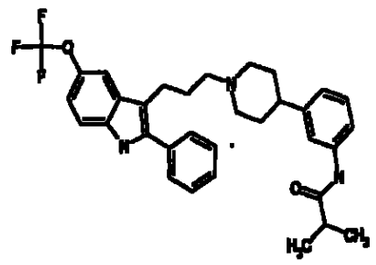
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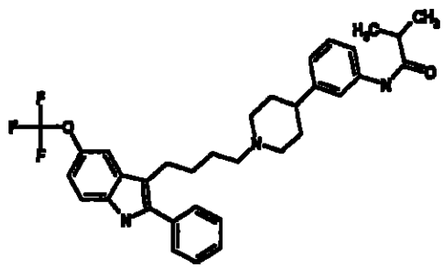
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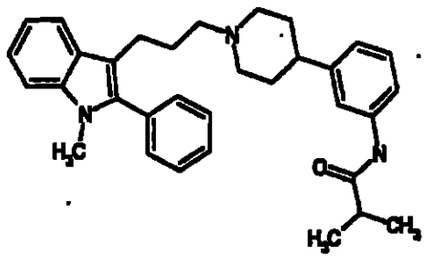
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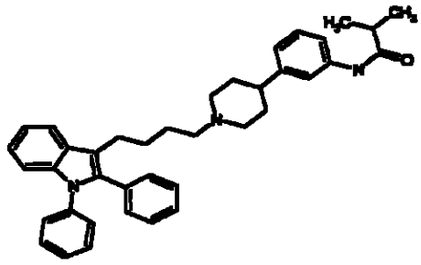


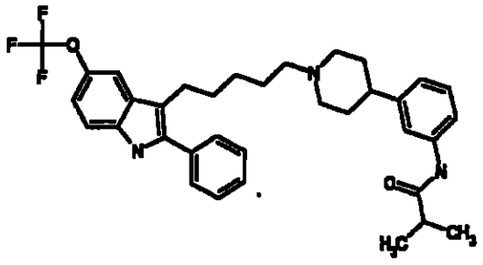
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15377SP

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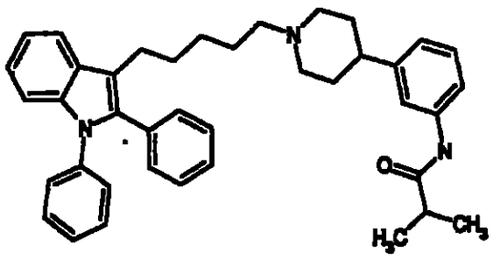
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392  16.1

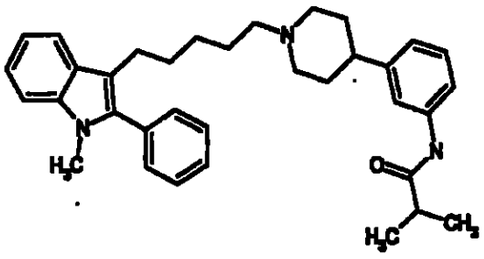
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1538,541

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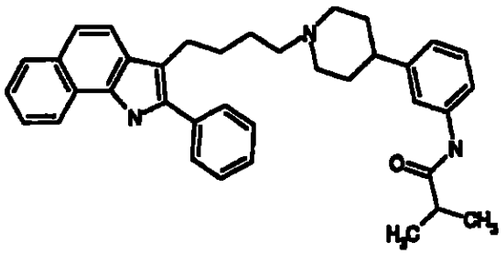


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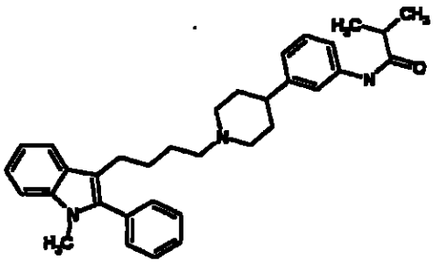


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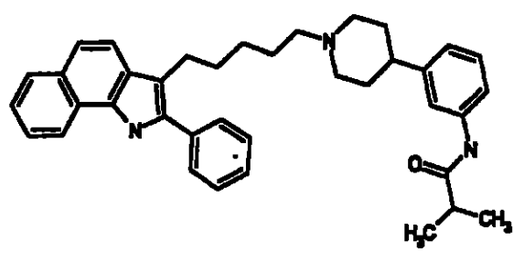
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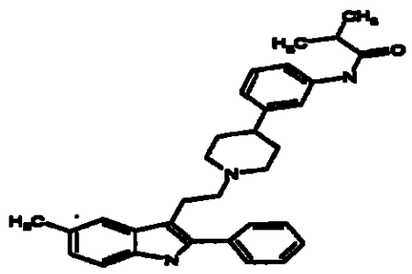


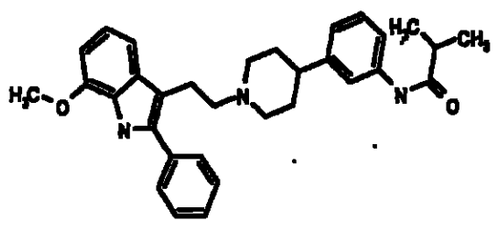
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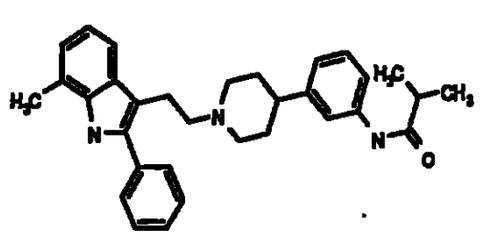


1539 1542

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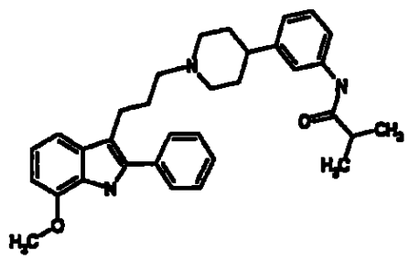
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400  43.9

401  44.6

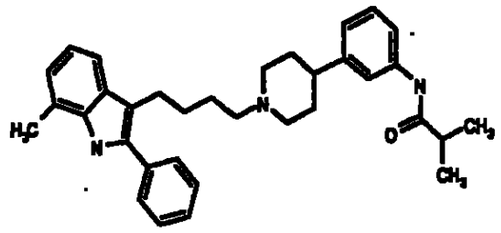
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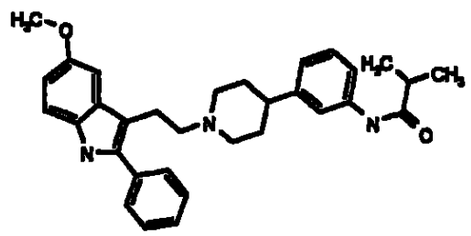


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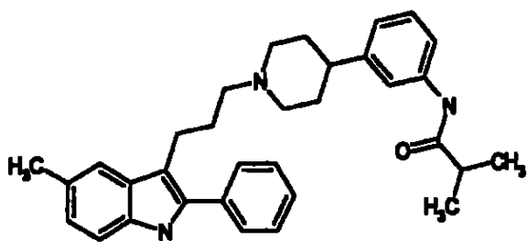
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404

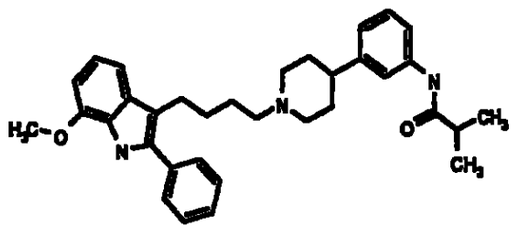


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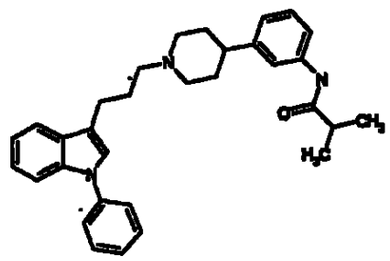
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406



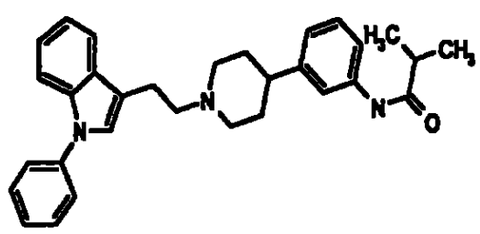
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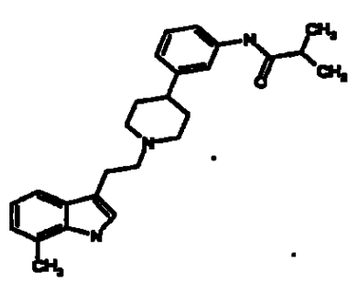
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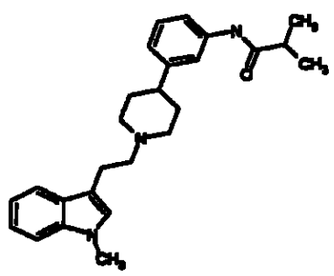
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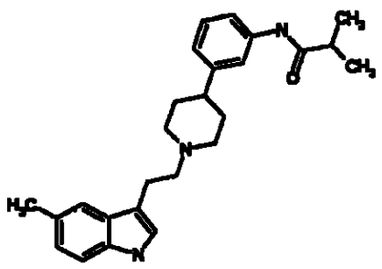
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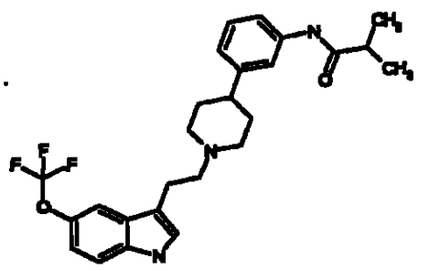


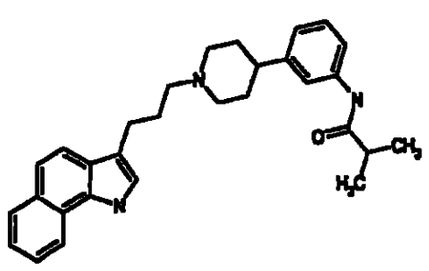
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1545
1542

410  262.7

411  82.3

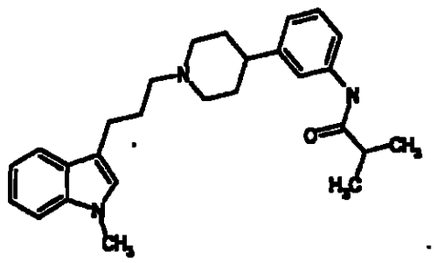
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413  76.8

1546

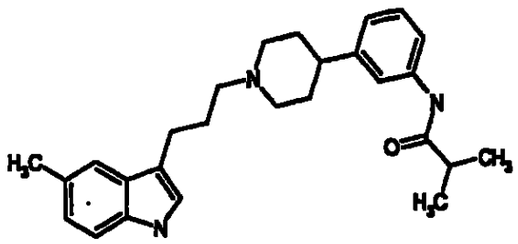
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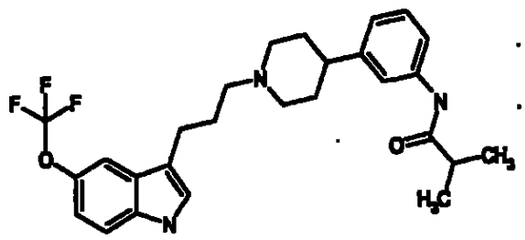
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415



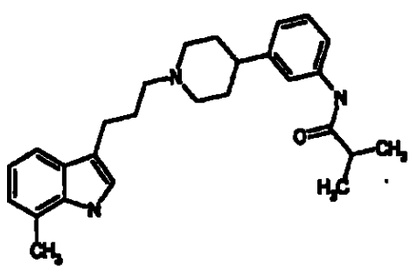
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416



12.6

417

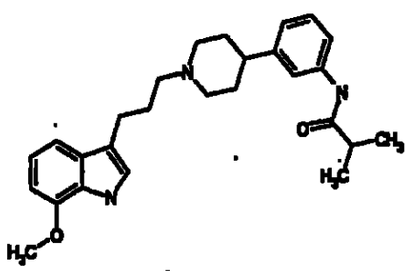


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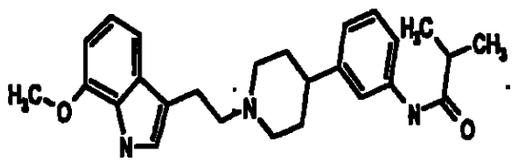
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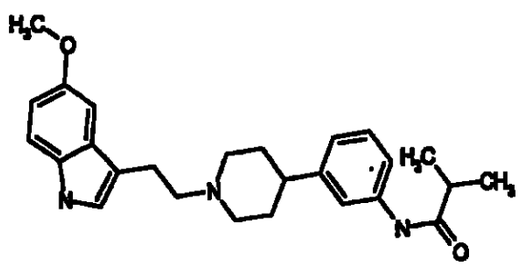
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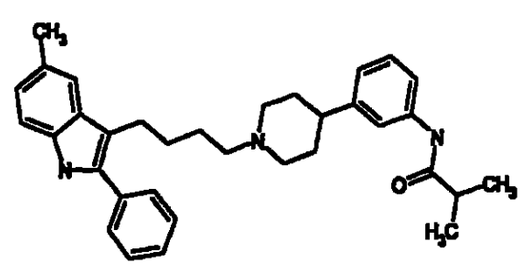


89.9

420



421

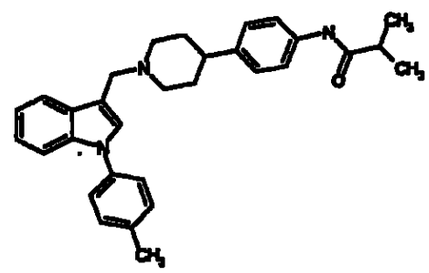


1.8

1548

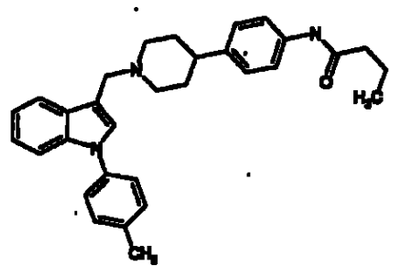
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422



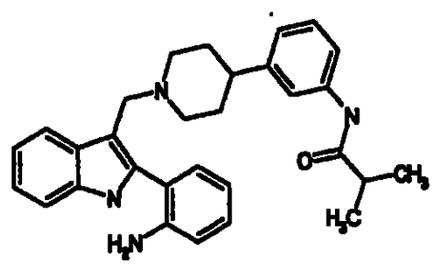
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423



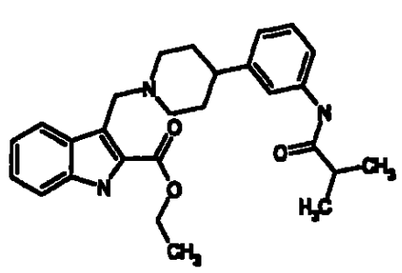
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424



114.2

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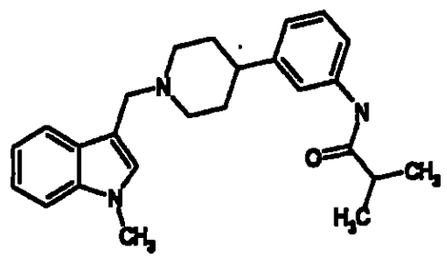


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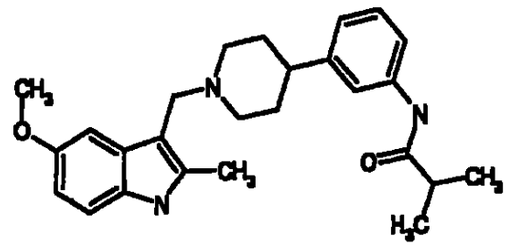
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426



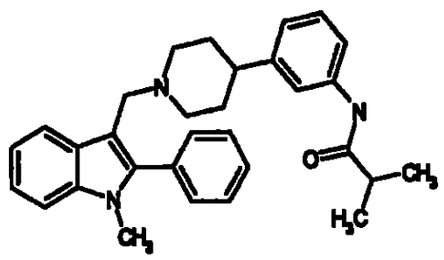
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427



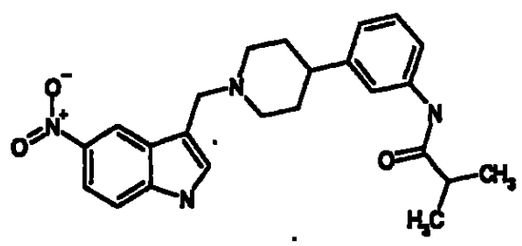
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428



132.4

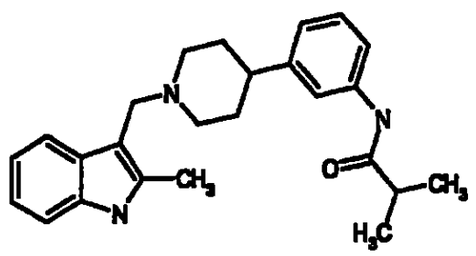
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121.4

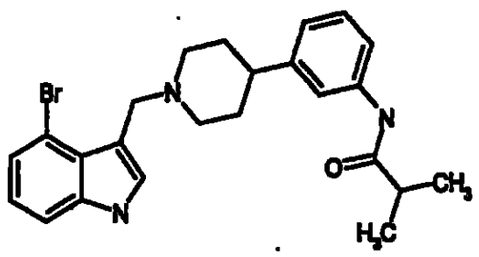
15/17 1550

430



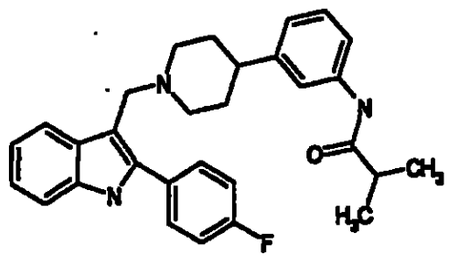
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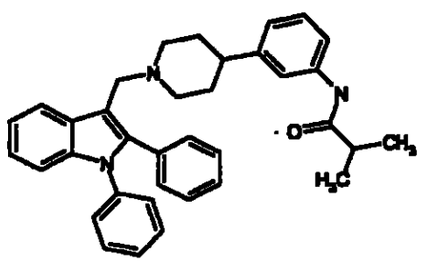
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198.2

433

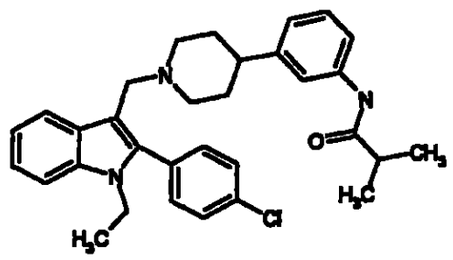


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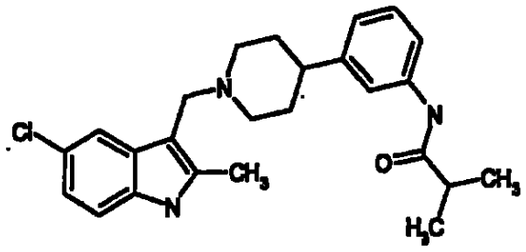
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434



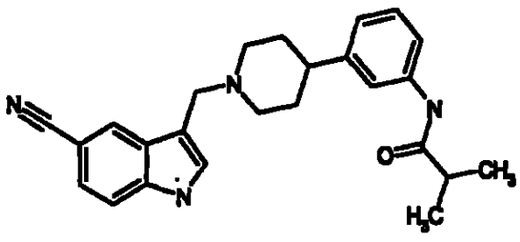
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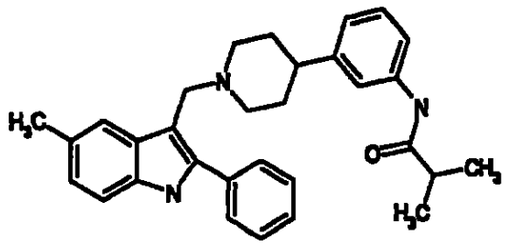
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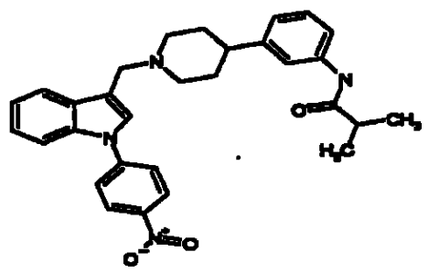
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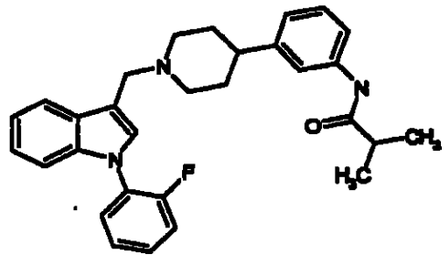
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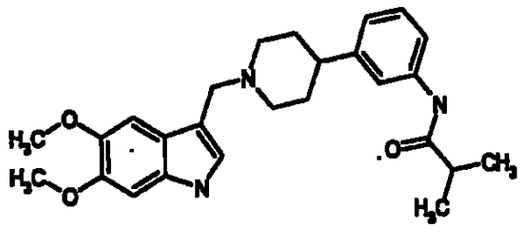


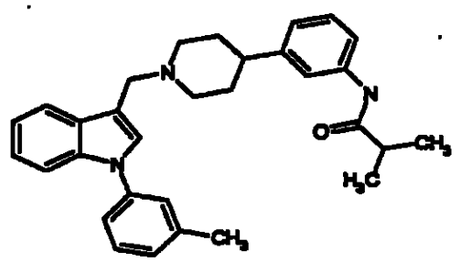
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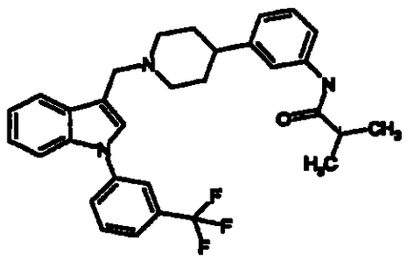
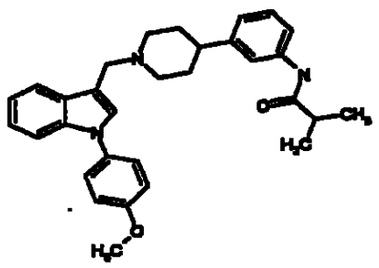
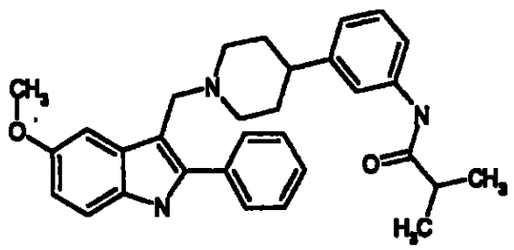
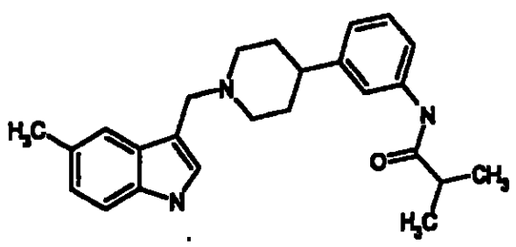
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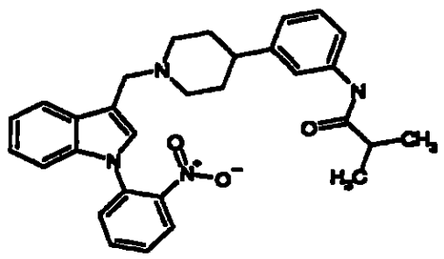
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1554

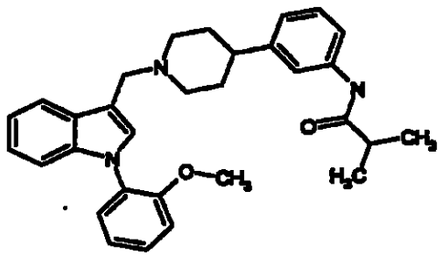
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446



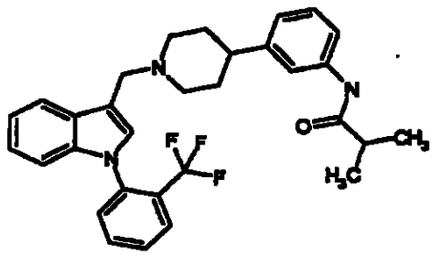
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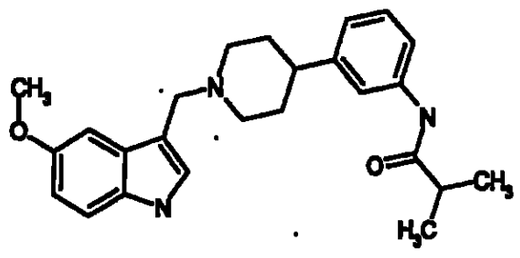
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448



61.0

449

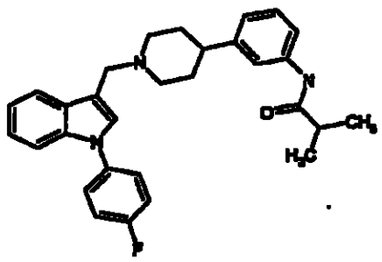


623.4

1555

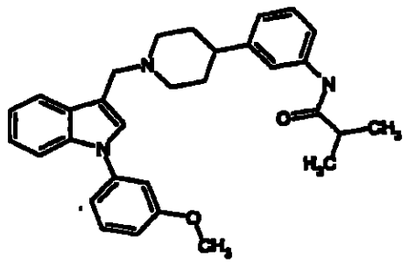
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450



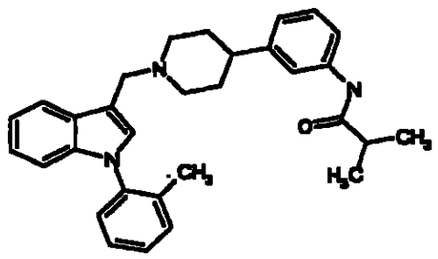
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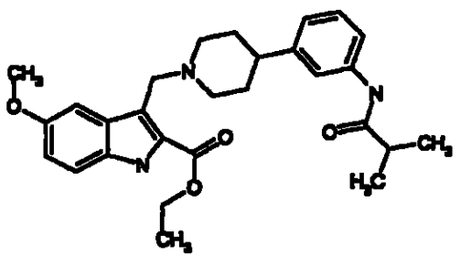
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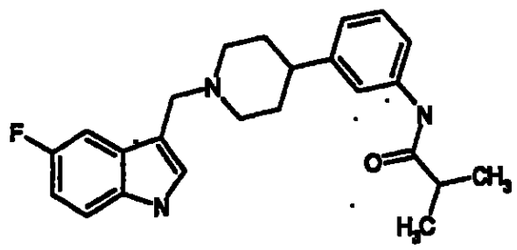
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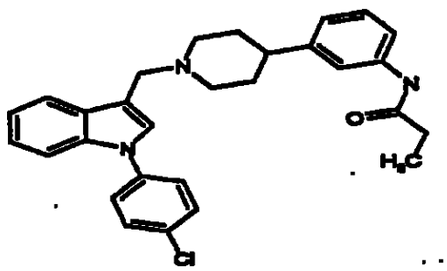
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454



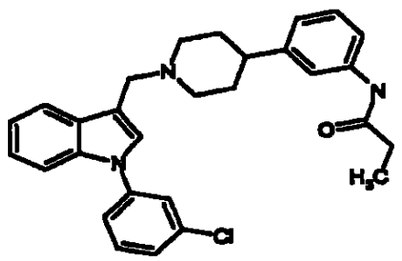
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455



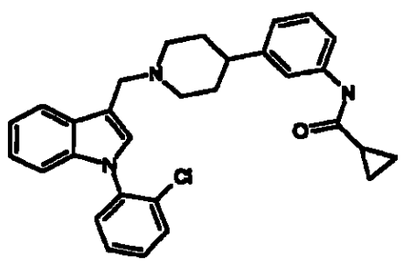
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456



28.0

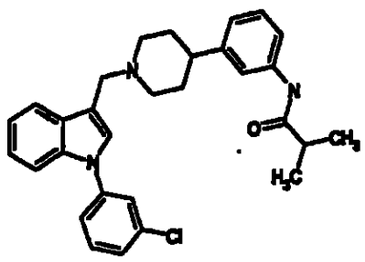
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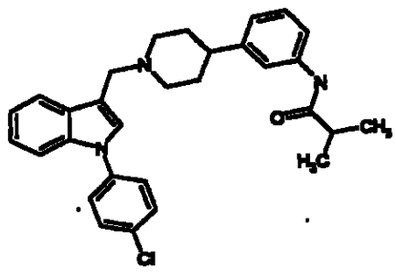
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458



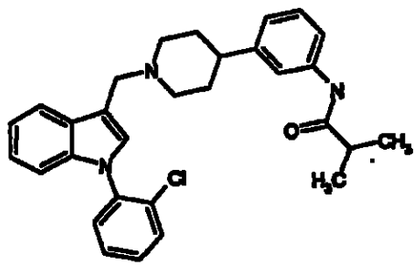
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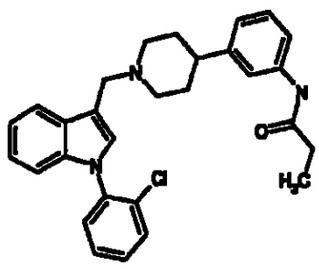
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460



9.1

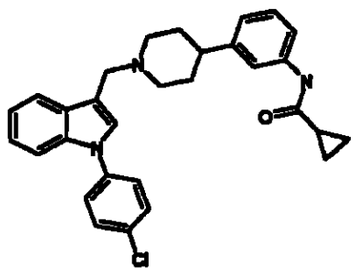
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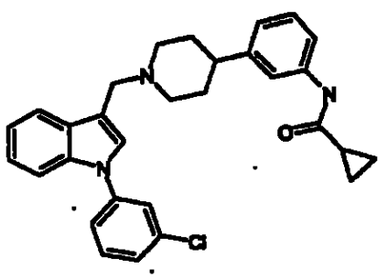
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462



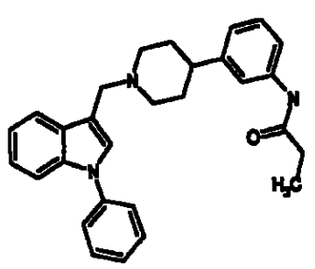
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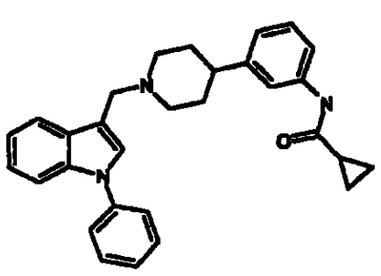
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464



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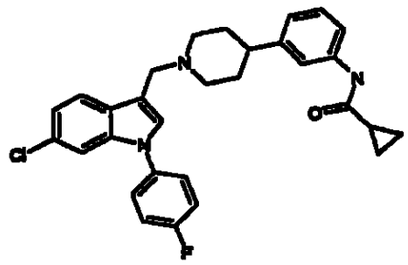
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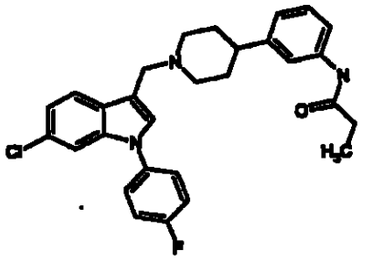
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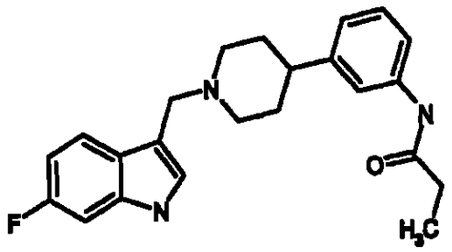


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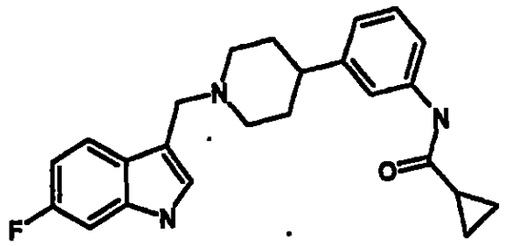
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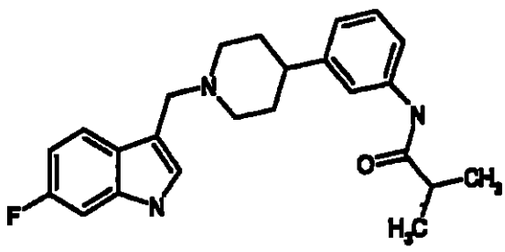
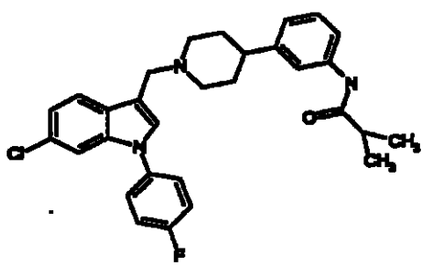
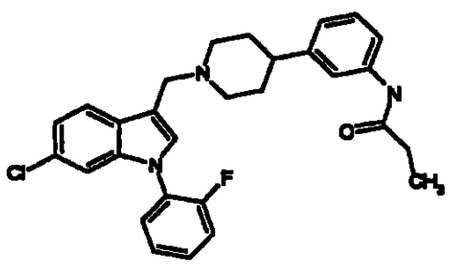
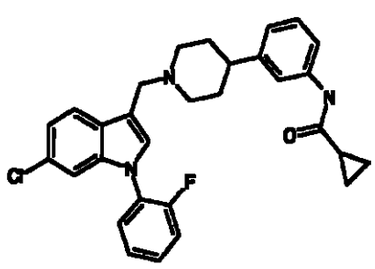


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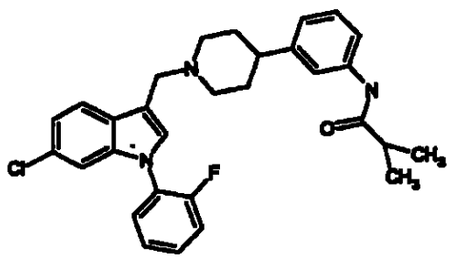
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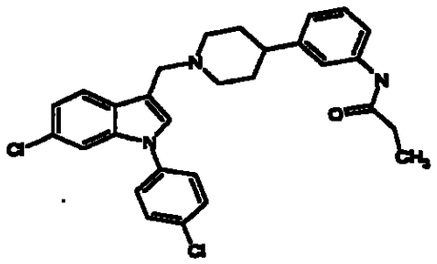


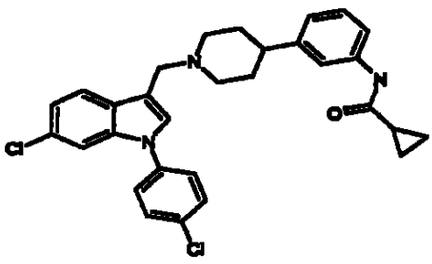
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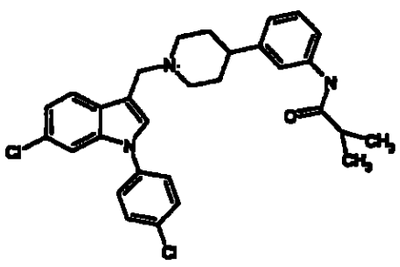
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473		11.3

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474  13.3

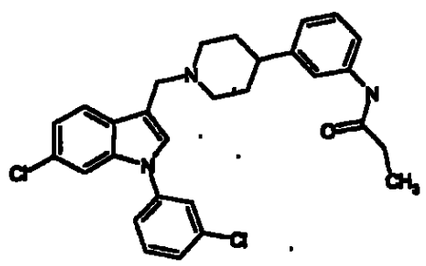
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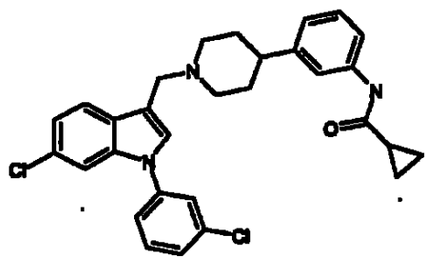
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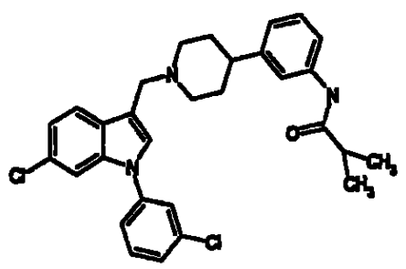
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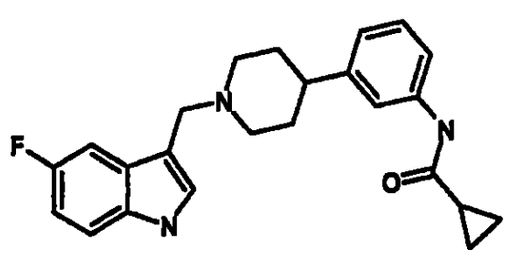
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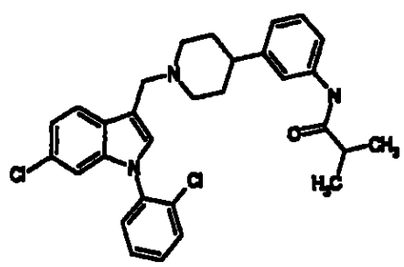
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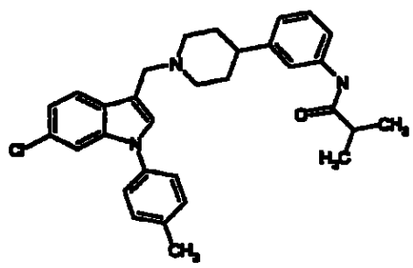
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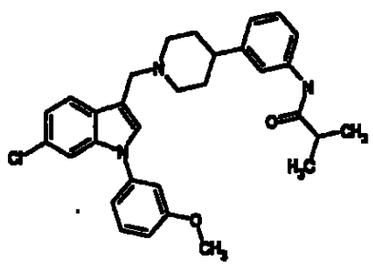
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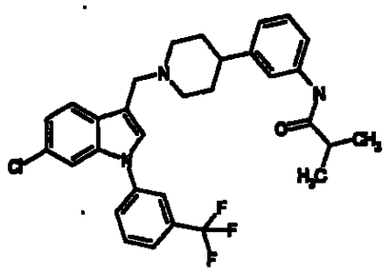
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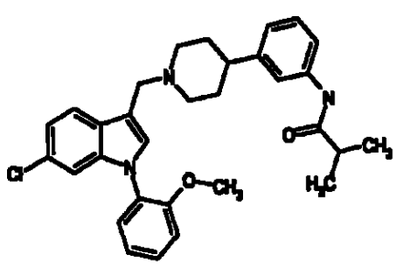
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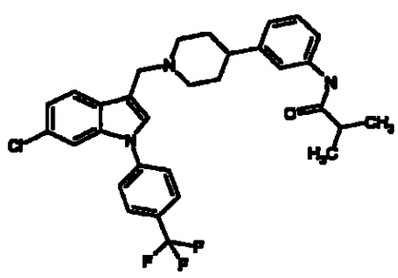
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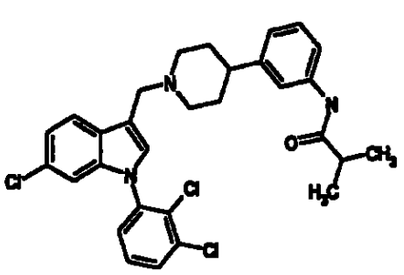
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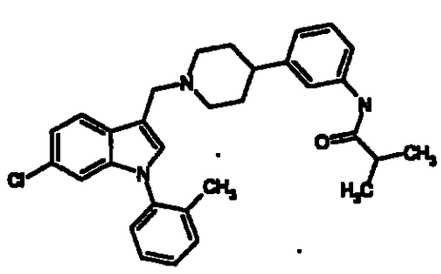
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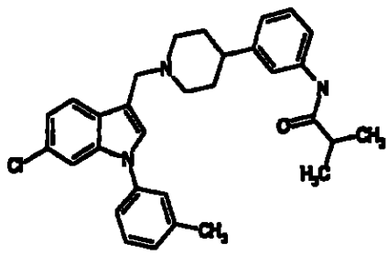
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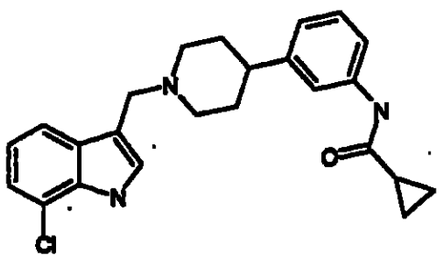
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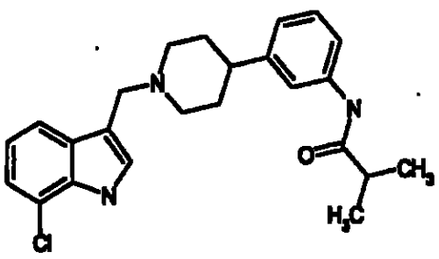
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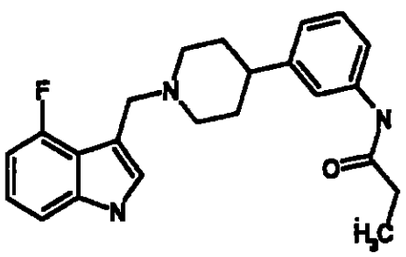
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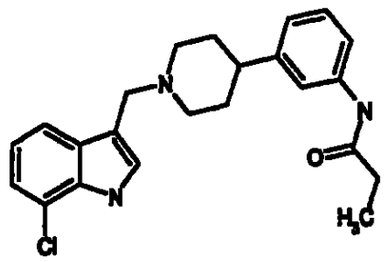


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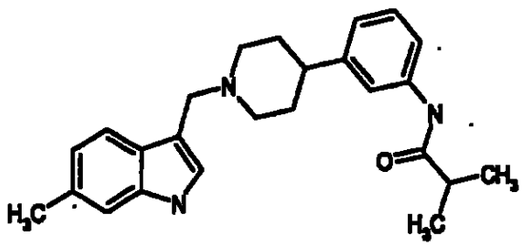


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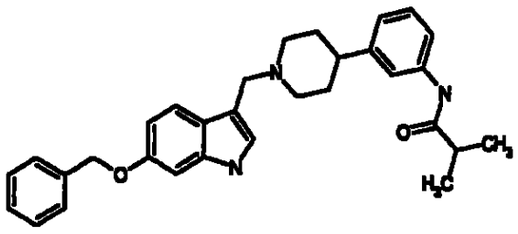
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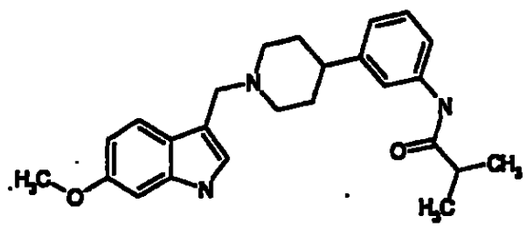
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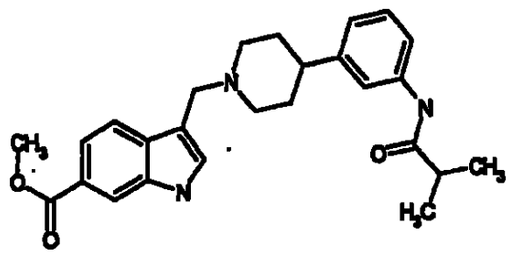
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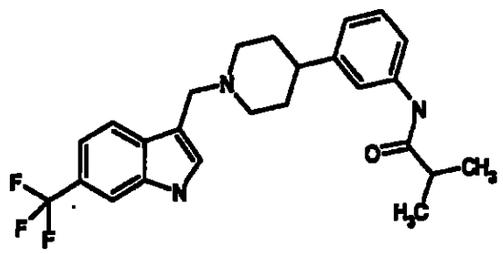
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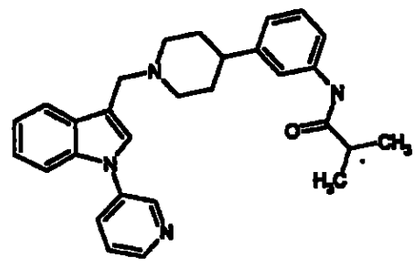
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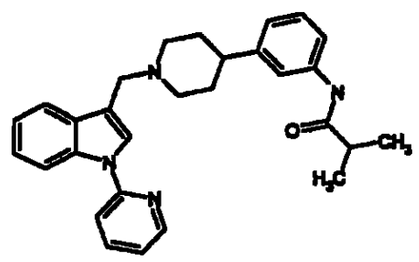
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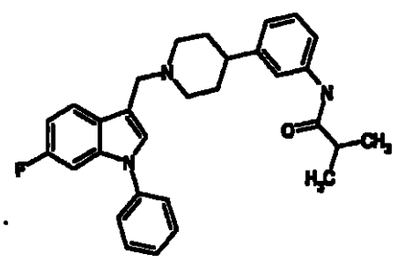
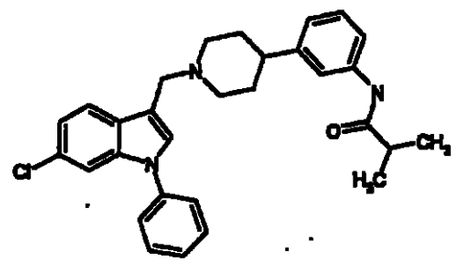
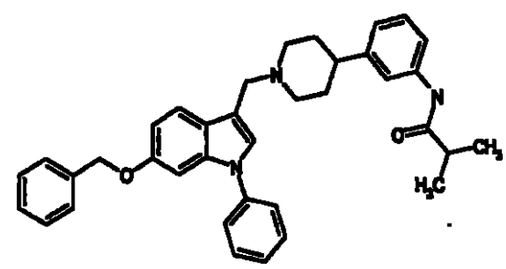
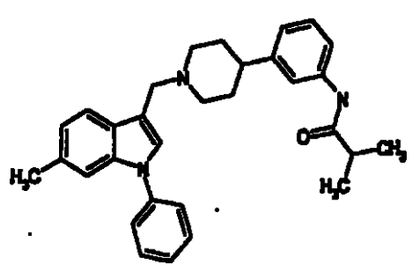
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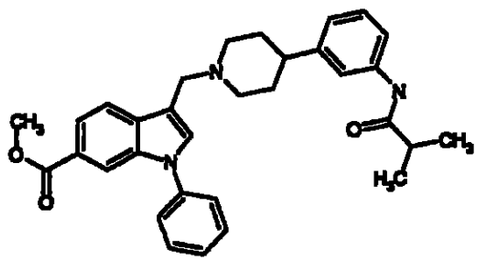


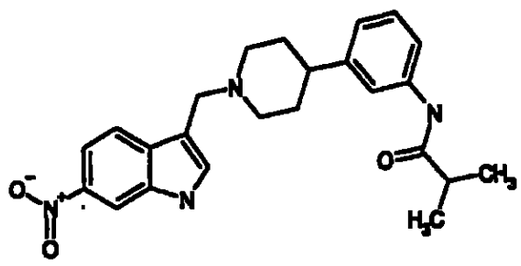
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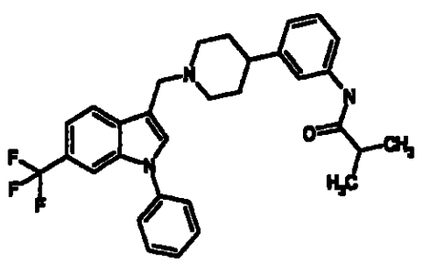
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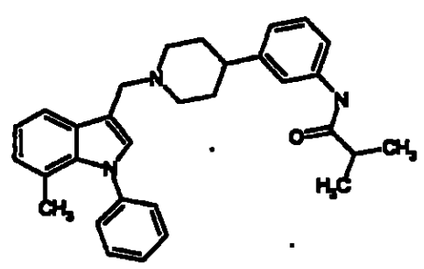
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506  2.5

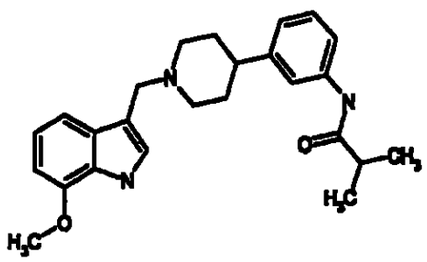
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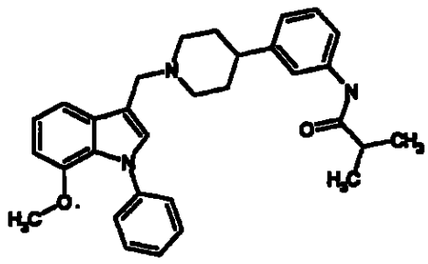
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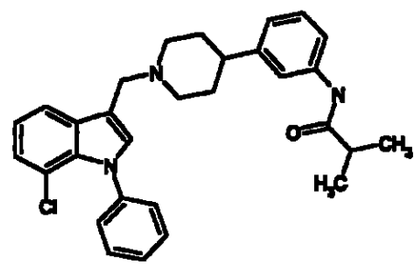
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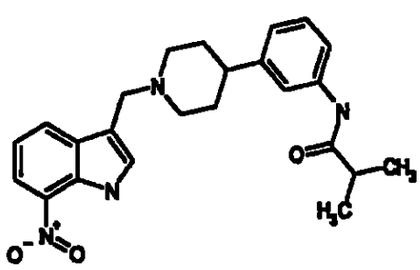
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42.7

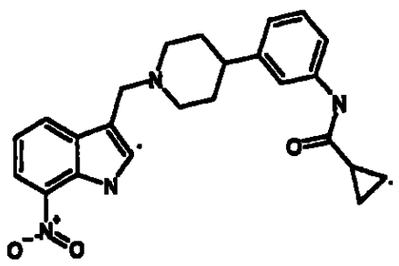
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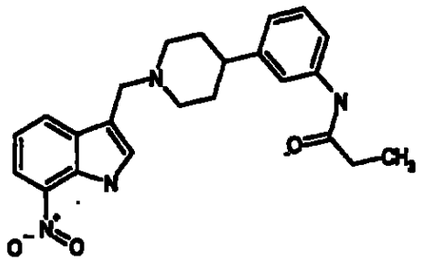
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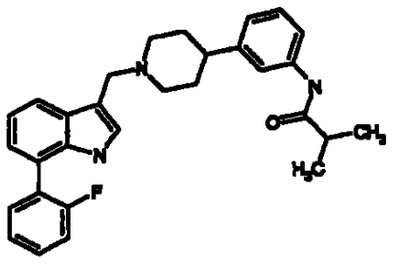
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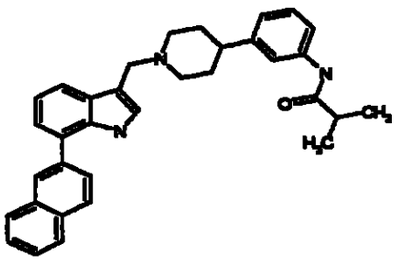
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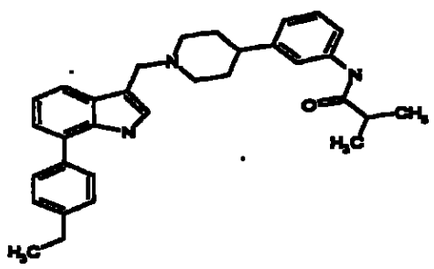
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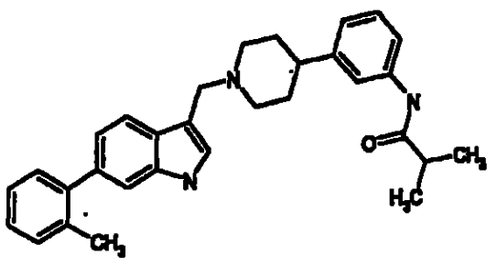
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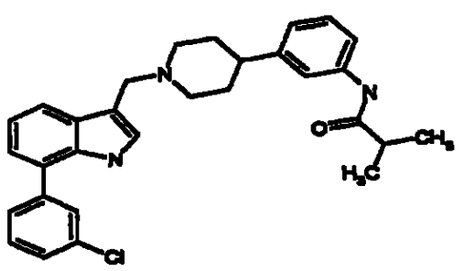


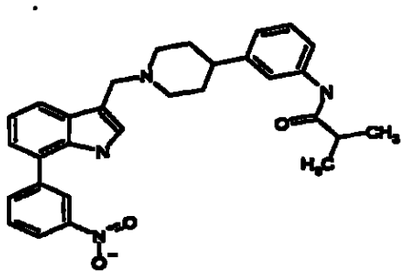
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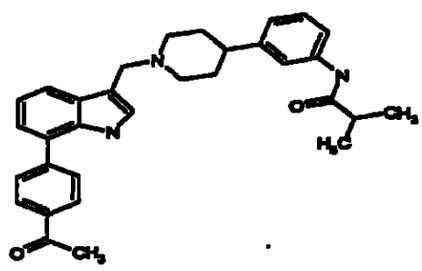
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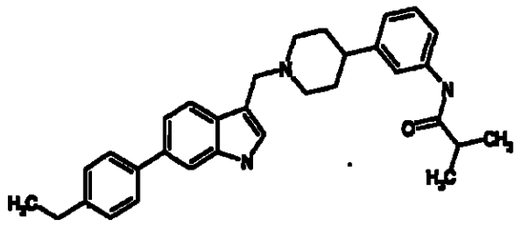
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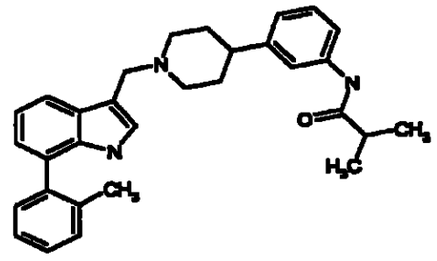
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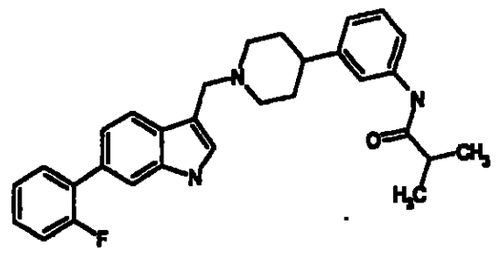
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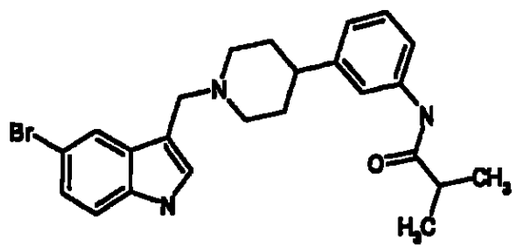
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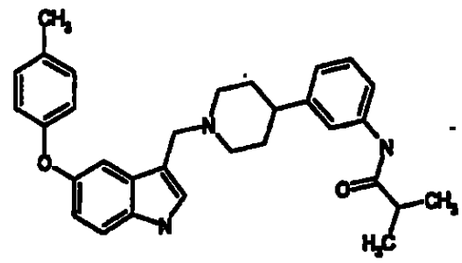
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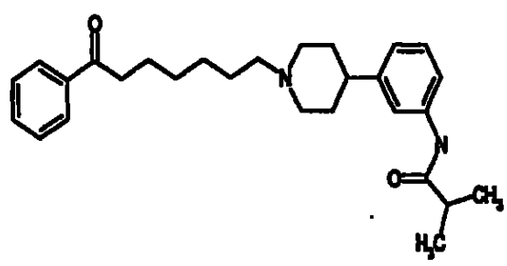
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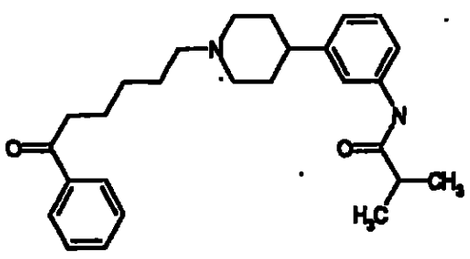
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573
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526  410.6

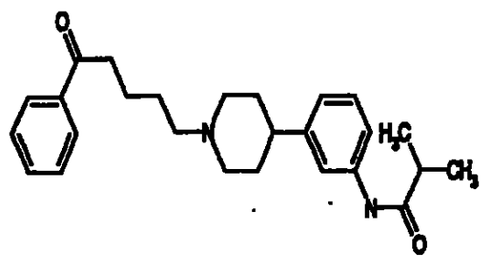
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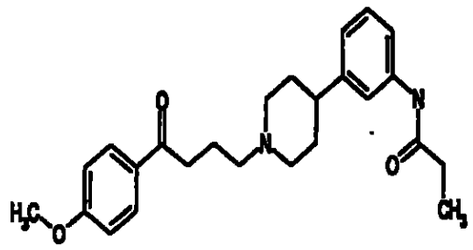
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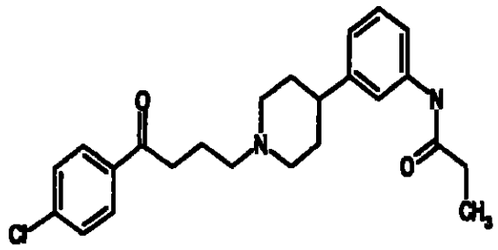
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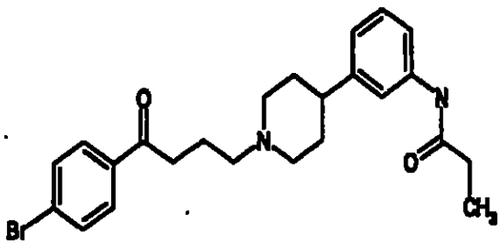
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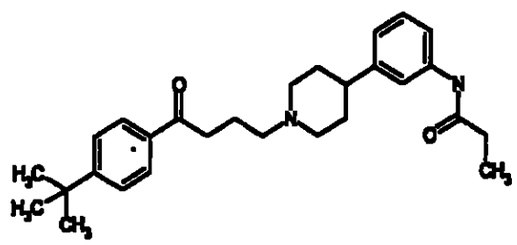


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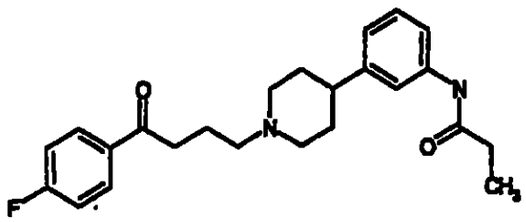
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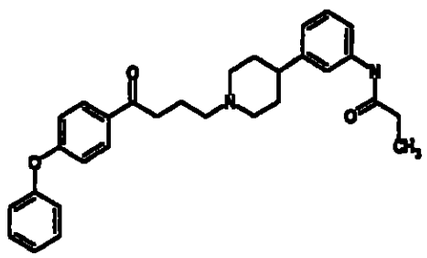
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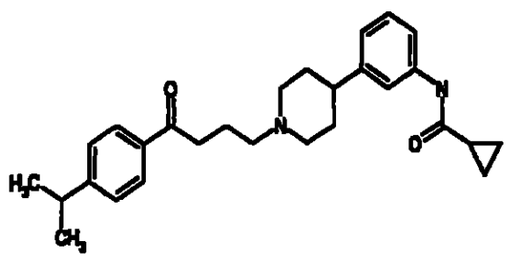
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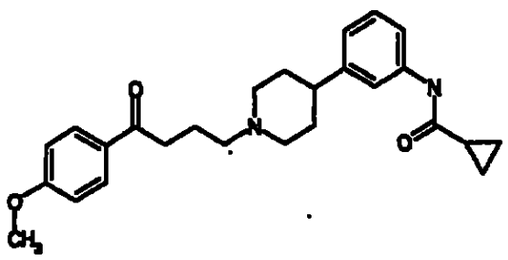
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67.7

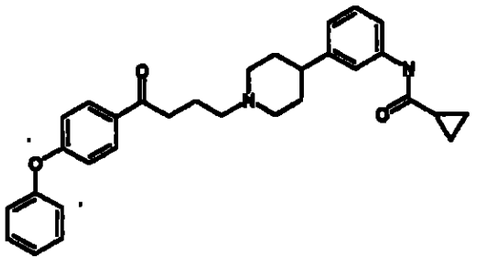
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538



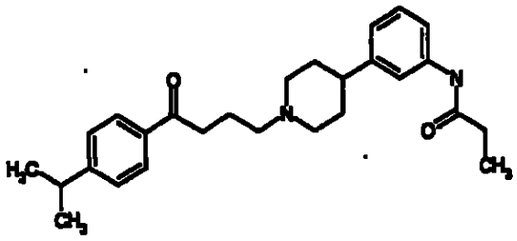
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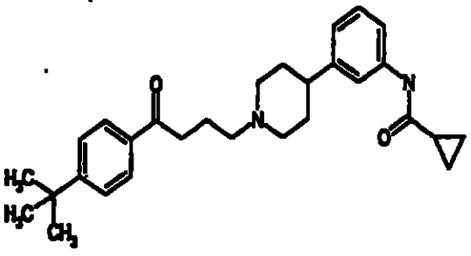
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172.3

541

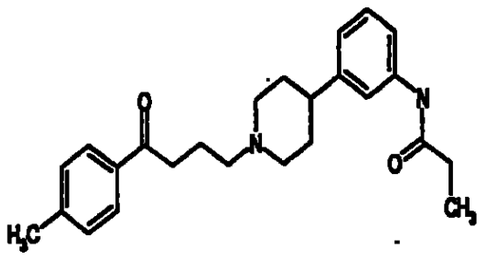


318.6

1577

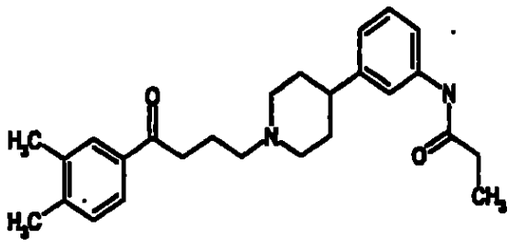
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542



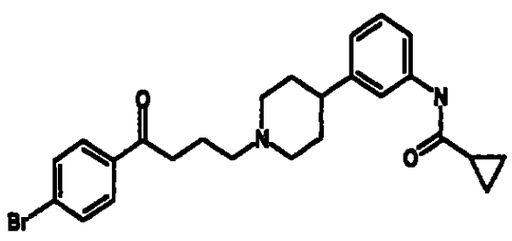
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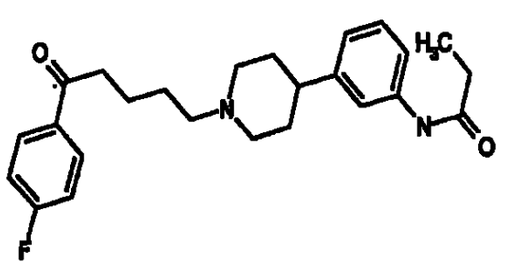
27.6

544



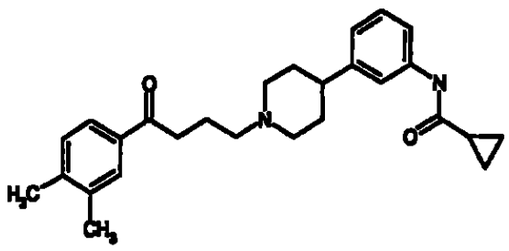
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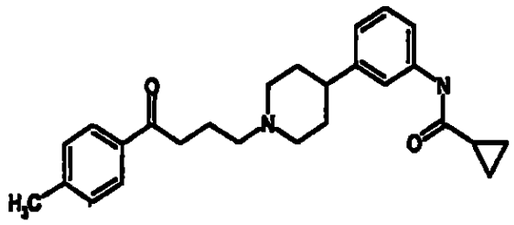
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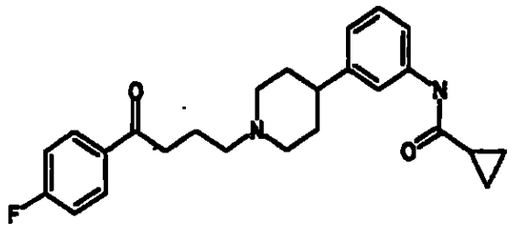


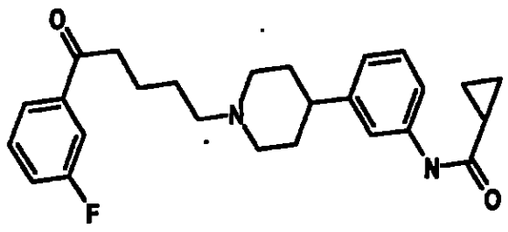
52.0

1575 1578

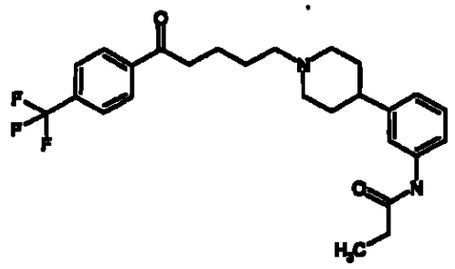
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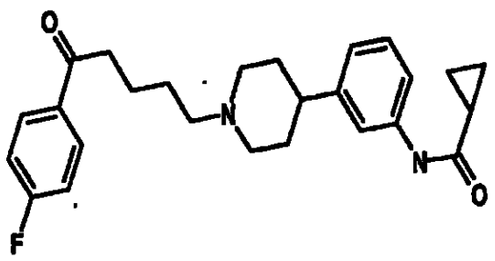
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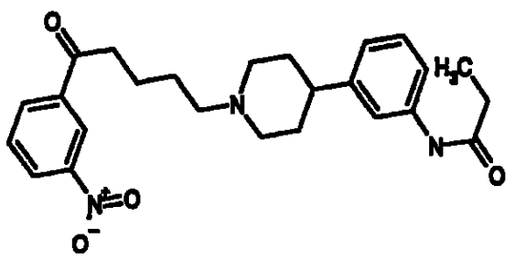
548  125.6

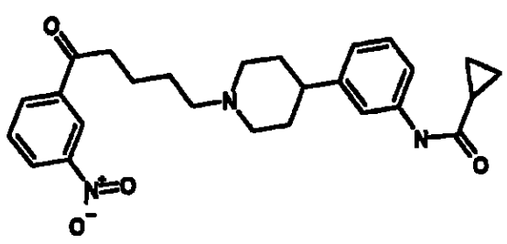
549  39.7

1576 1579

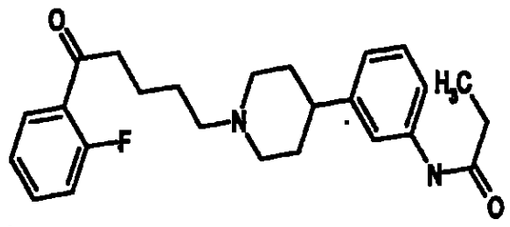
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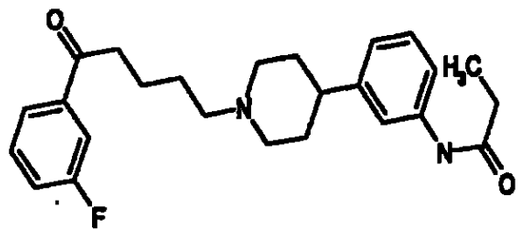
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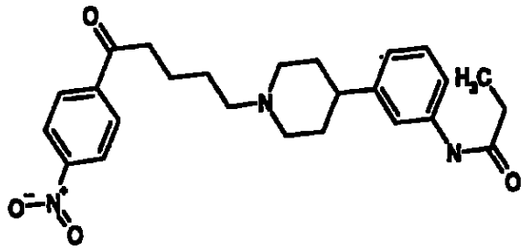
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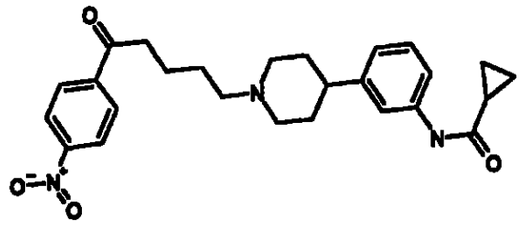
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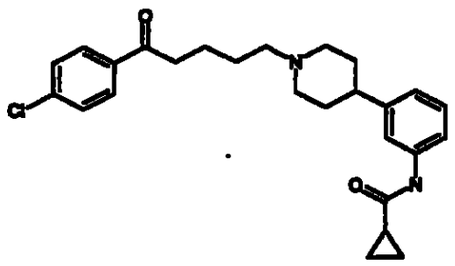
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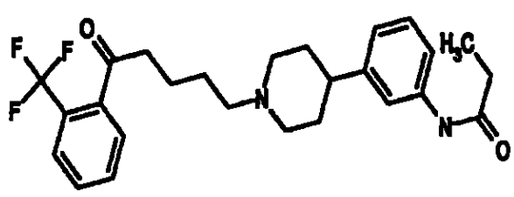
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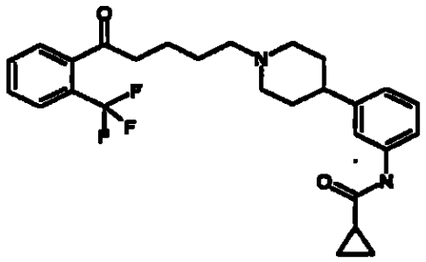
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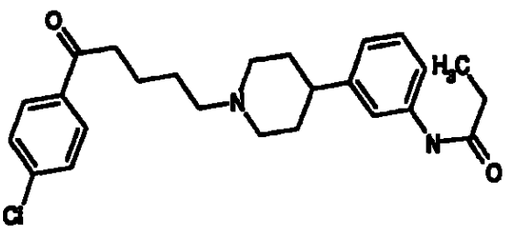
557  25.6

1578 1581

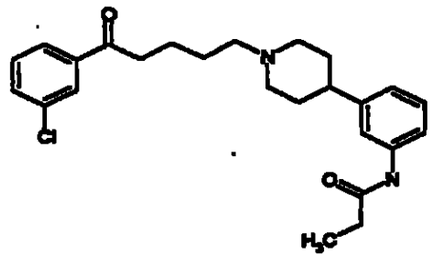
558  20.2

559  62.3

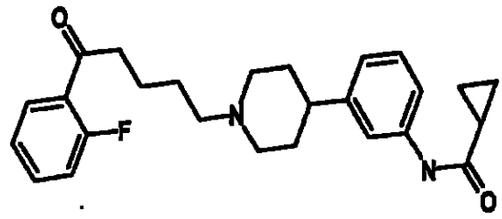
560  55.7

561  92.9

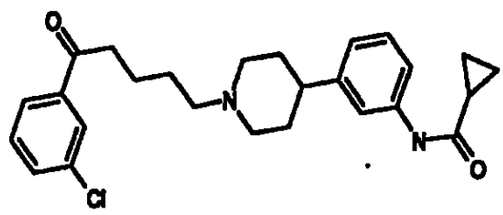
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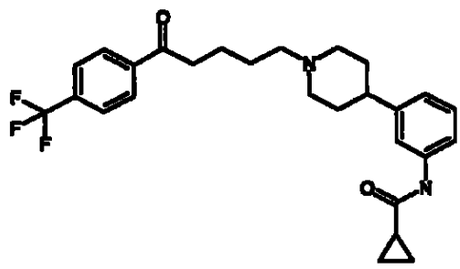
48.1

563 

50.2

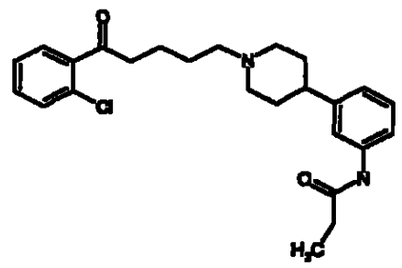
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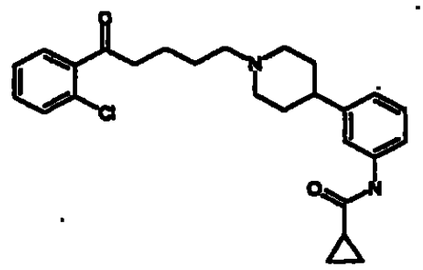
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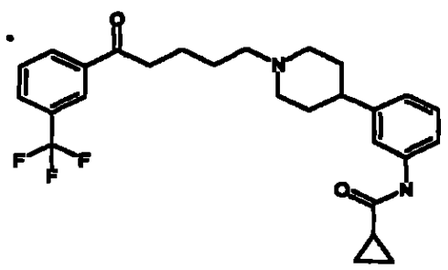
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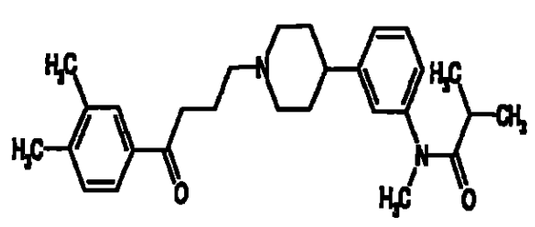
49.2

1583 1580

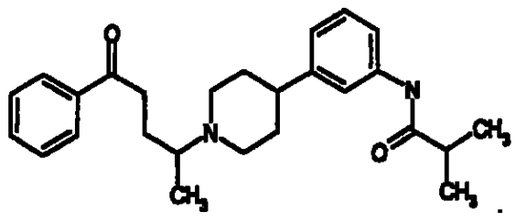
566  77.8

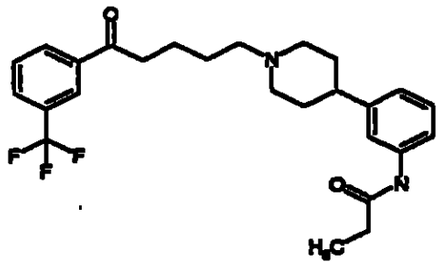
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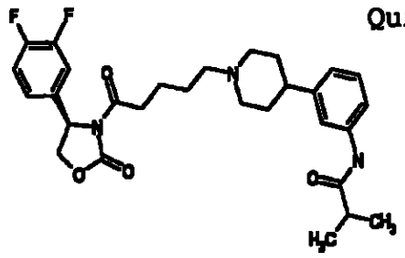
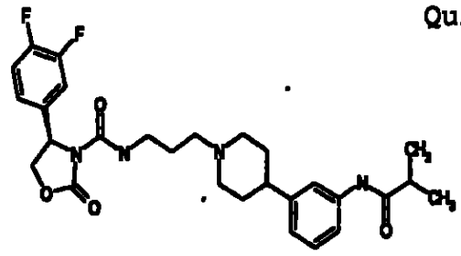
568  68.8

569  549.3

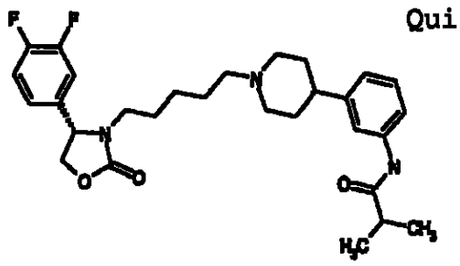
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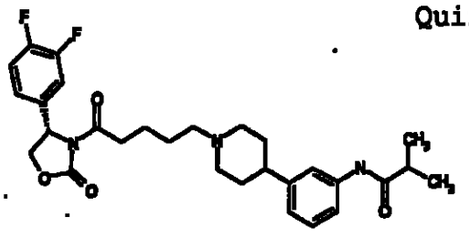
570  136.3

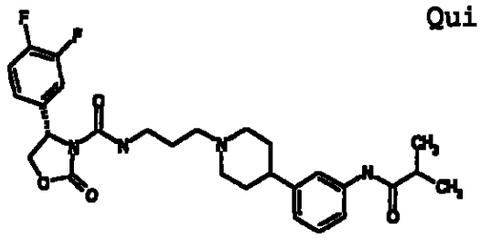
571  88.3

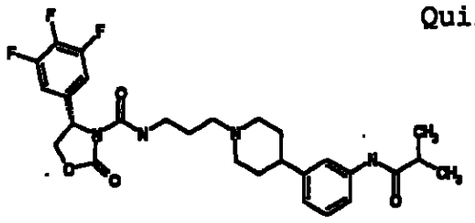
EJEMPLO	ESTRUCTURA	rMCH1 Ki (nM)
572	 Quiral	181.5
573	 Quiral	114.3

1582 1585

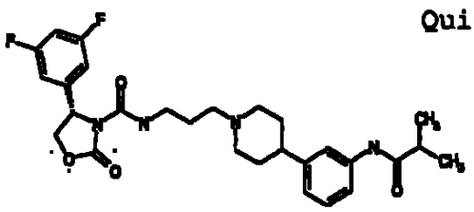
574  Quiral 87.1

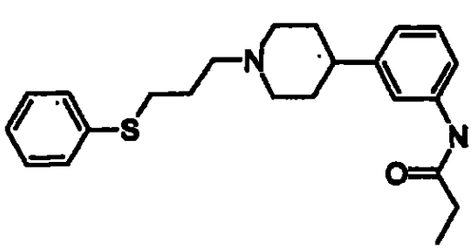
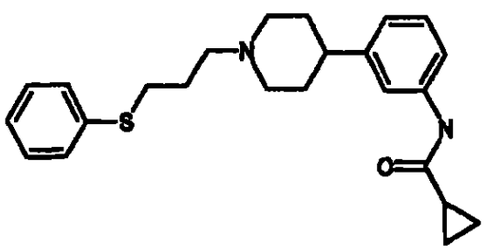
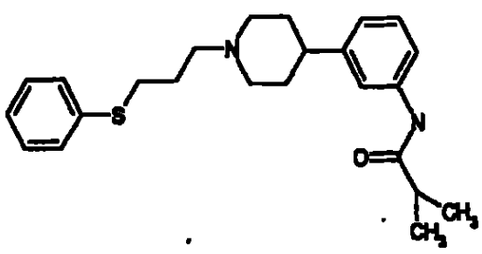
575  Quiral 192.6

576  Quiral 74.3

577  Quiral 64.7

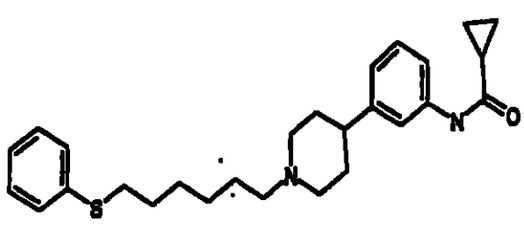
1583
1586

578		Quiral	98.8

EJEMPLO	ESTRUCTURA	rMCH1 Ki (nM)
579		131.1
580		54.0
581		88.4

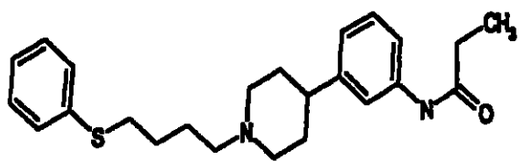
1554 1587

582



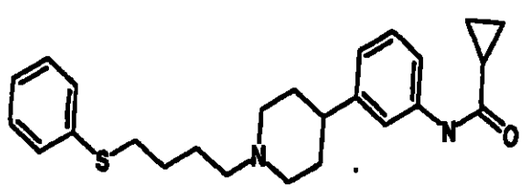
58.3

583



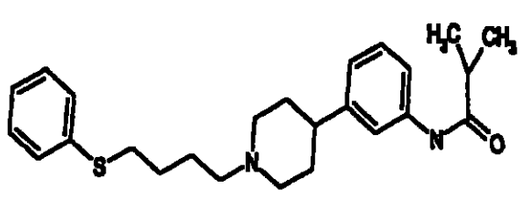
55.5

584



51.8

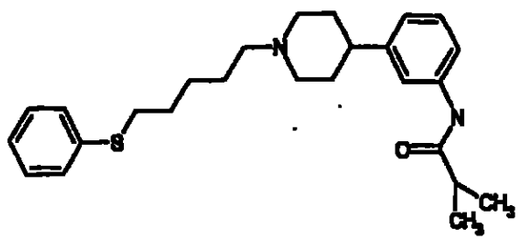
585



37.2

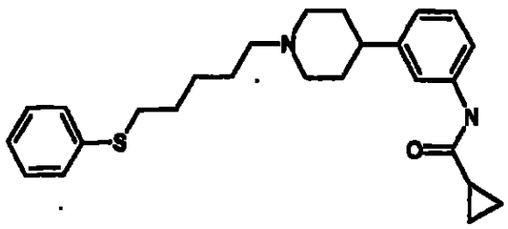
1535
1588

586



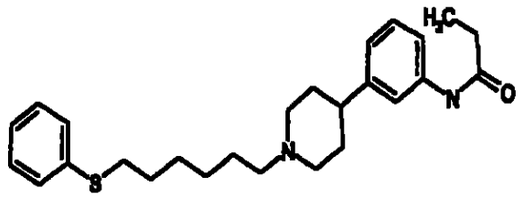
42.9

587



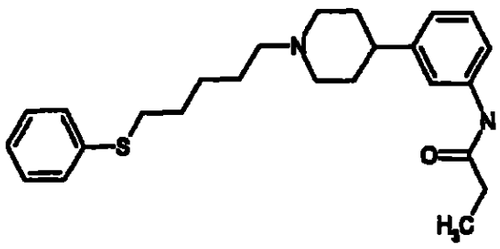
46.9

588



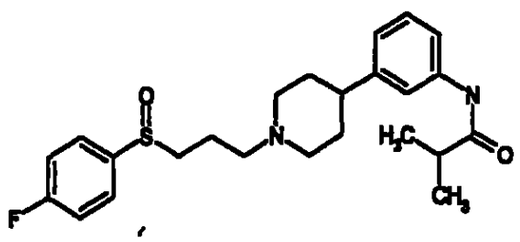
283.9

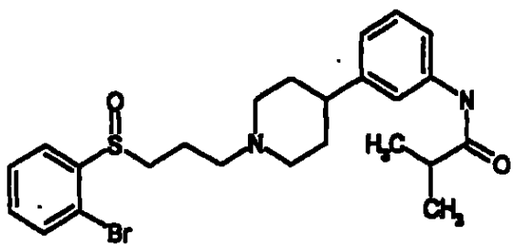
589

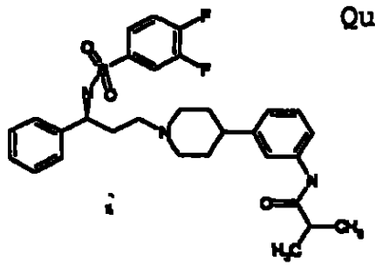
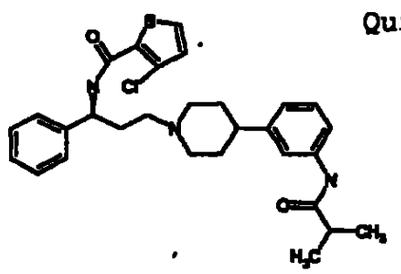


66.6

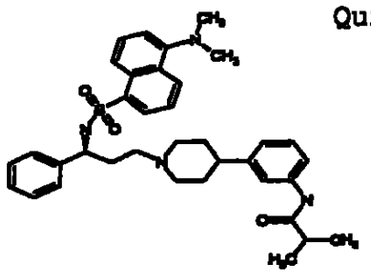
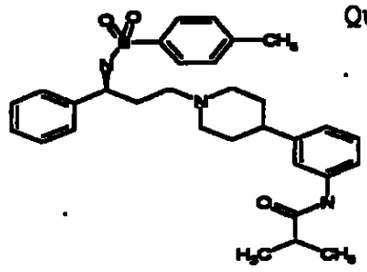
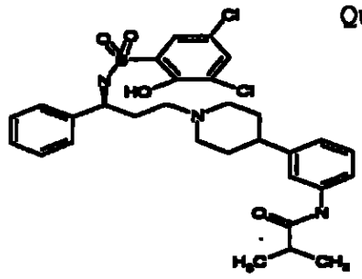
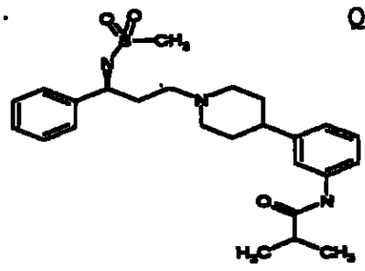
1536 1589

590  157.1

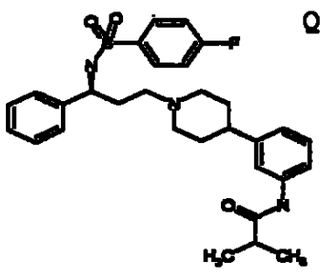
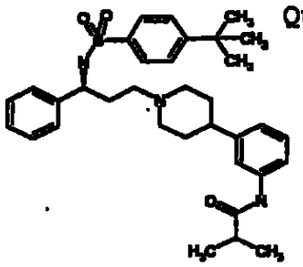
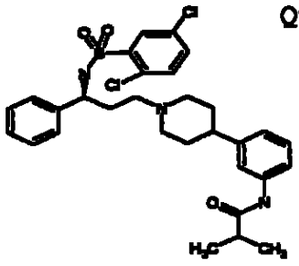
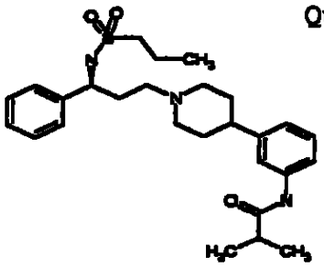
591  137.5

EJEMPLO	ESTRUCTURA	rMCH1 Ki (nM)
592	 Quiral	185.6
593	 Quiral	7.8

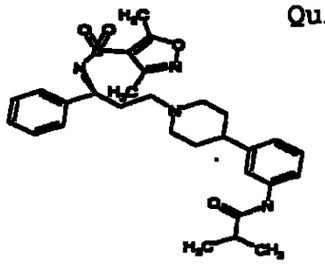
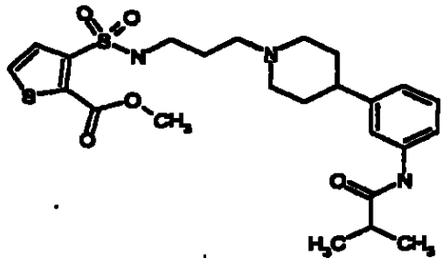
1557 1590

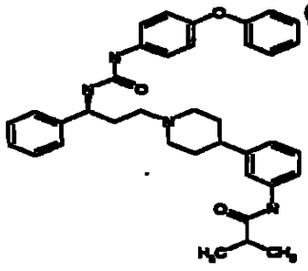
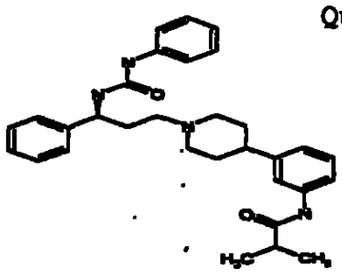
594		Quiral	67.0
595		Quiral	36.3
596		Quiral	596.7
597		Quiral	222.7

1591
1588

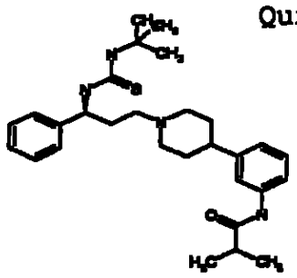
598		Quiral	25.3
599		Quiral	60.0
600		Quiral	41.3
601		Quiral	144.2

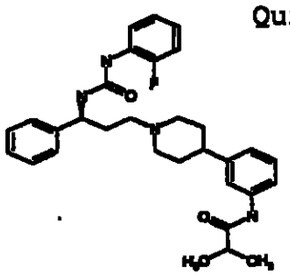
1592 1589

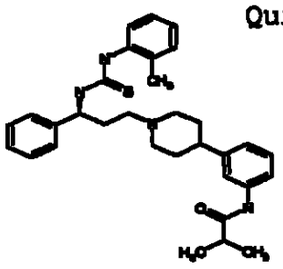
602		Quiral	44.8
603			286.8

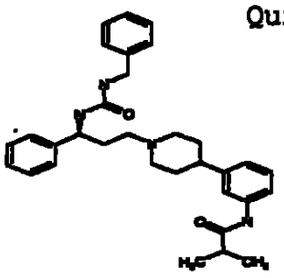
EJEMPLO	MOLESTRUCTURA		rMCH1 Ki (nM)
604		Quiral	36.8
605		Quiral	94.5

1593 1596

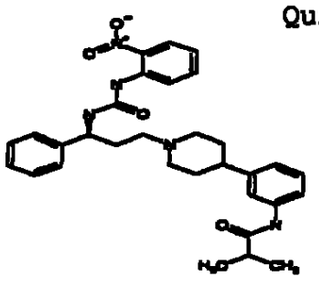
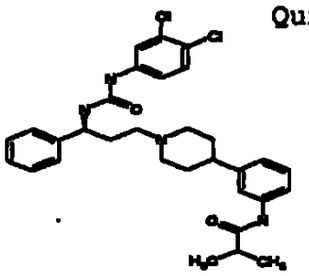
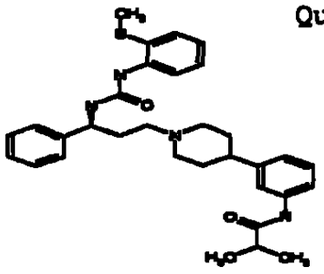
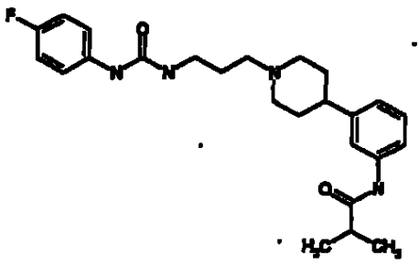
606  Quiral 40.4

607  Quiral 142.1

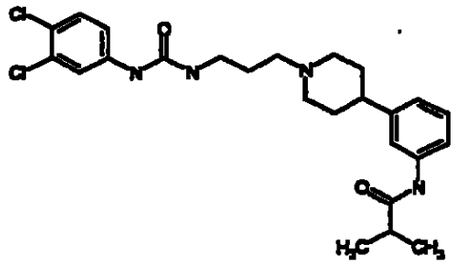
608  Quiral 34.9

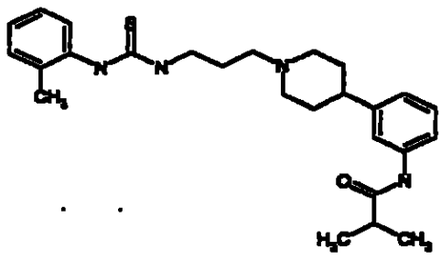
609  Quiral 35.4

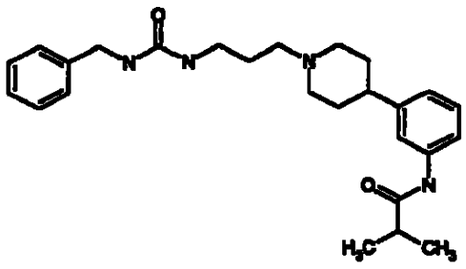
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1591

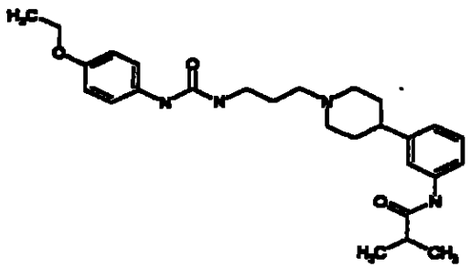
610		Quiral	629.6
611		Quiral	65.1
612		Quiral	121.0
613			34.9

1595 1792

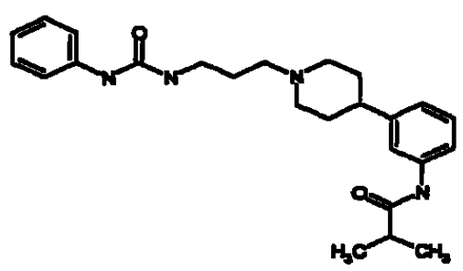
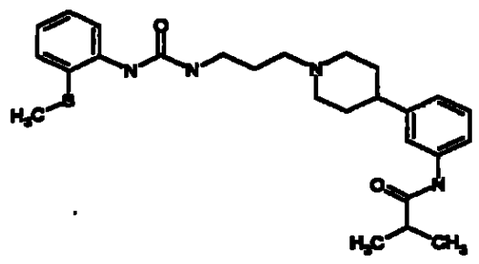
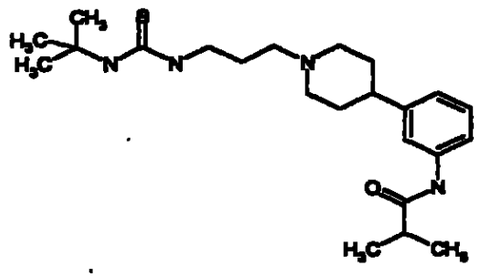
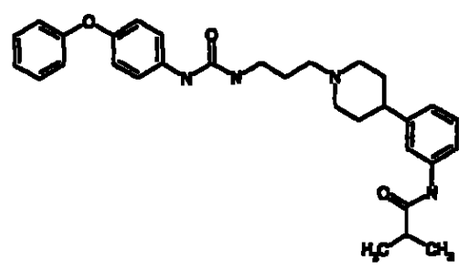
614  84.8

615  210.5

616  405.6

617  608.9

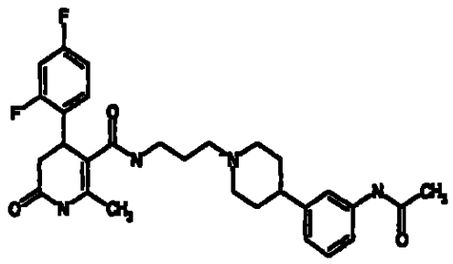
1596
1593

618		399.5
619		177.5
620		223.3
621		204.6

EJEMPLO	ESTRUCTURA	rMCH1 Ki (nM)

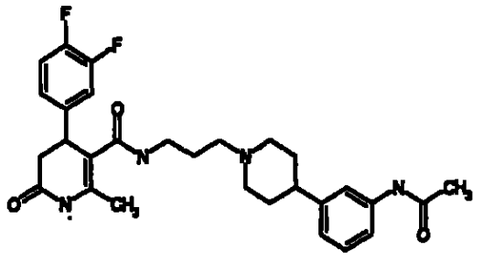
1534 1597

622



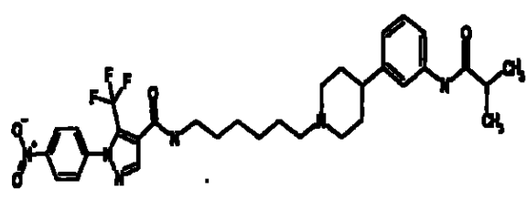
162.4

623



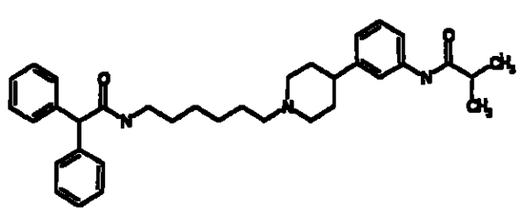
23.1

624



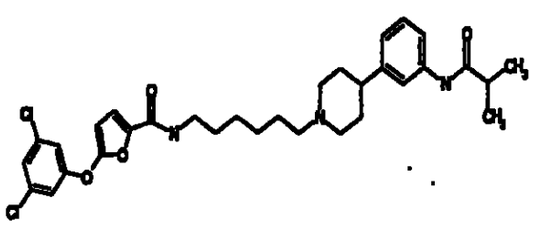
47.8

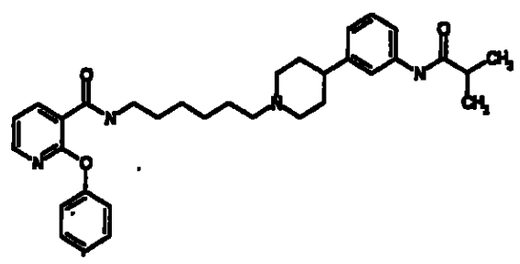
625

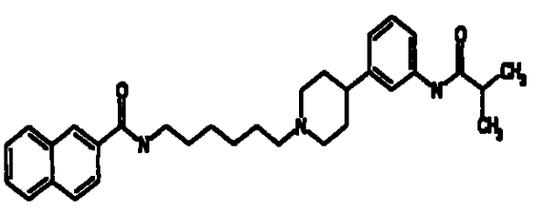


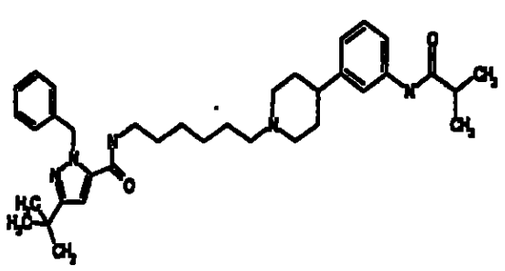
29.5

5PB 15/95

626  20.9

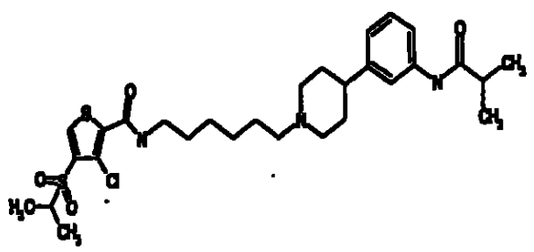
627  109.1

628  160.6

629  42.9

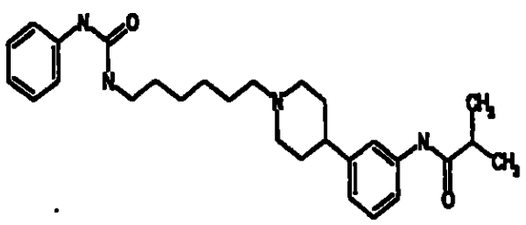
1596
599

630



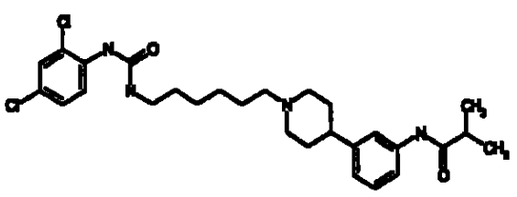
201.8

631



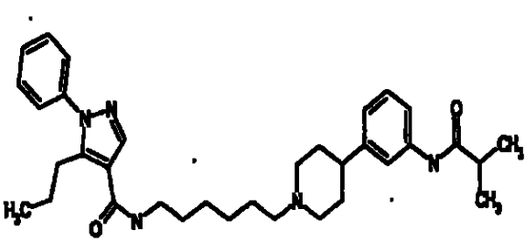
258.8

632



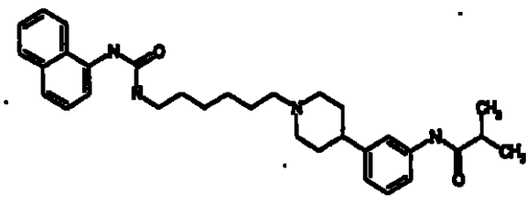
76.6

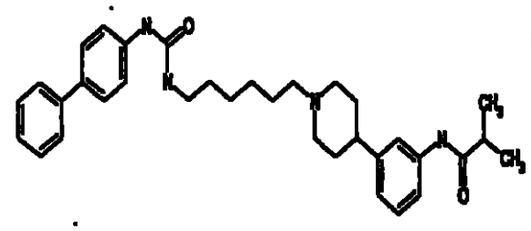
633

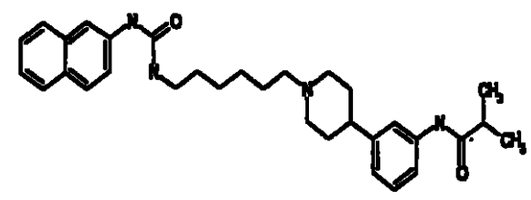


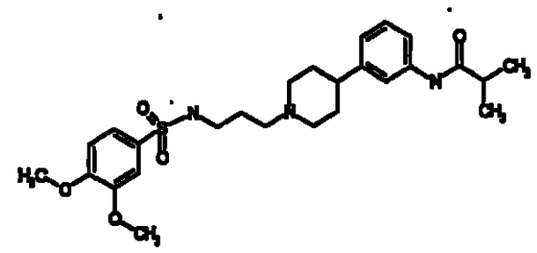
107.9

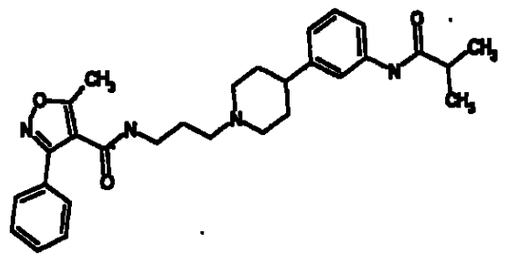
168
1507

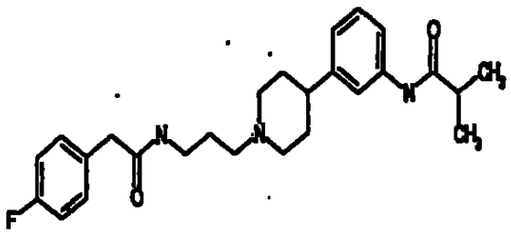
634  116.1

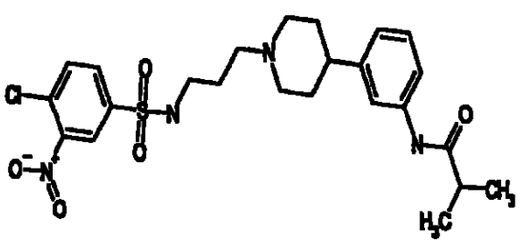
635  73.6

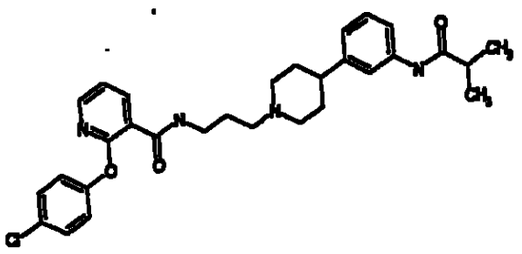
636  40.8

637  105.6

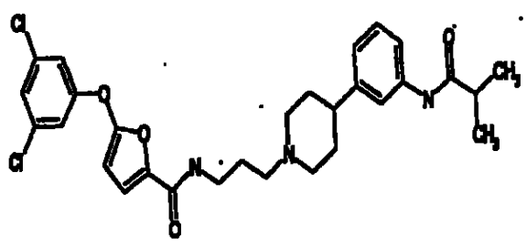
638  29.8

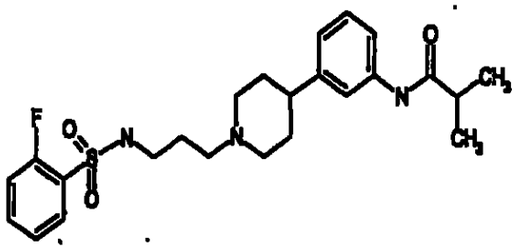
639  36.3

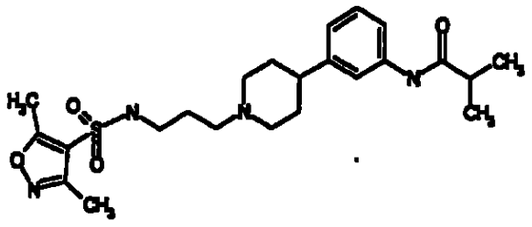
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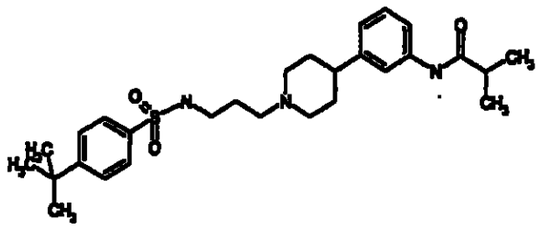
641  14.2

1602
1708

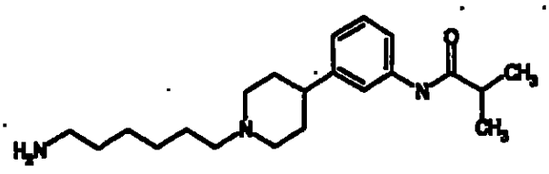
642  8.3

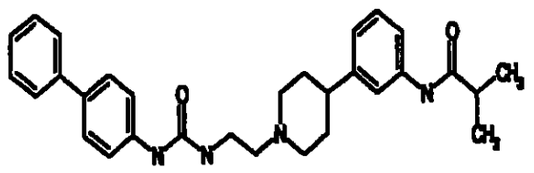
643  129.9

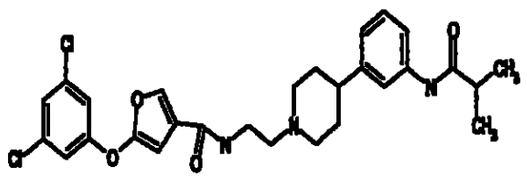
644  196.1

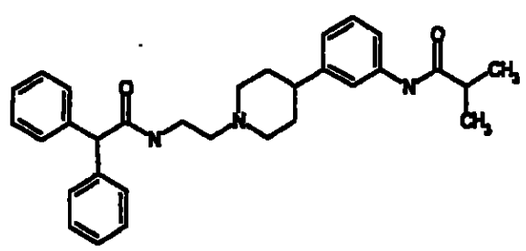
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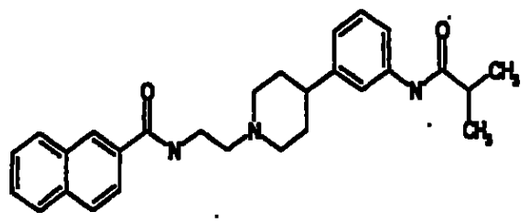
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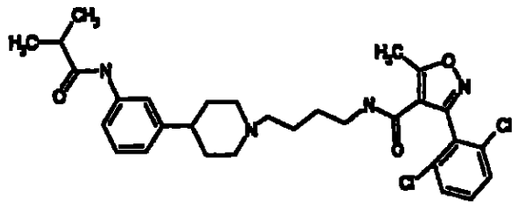
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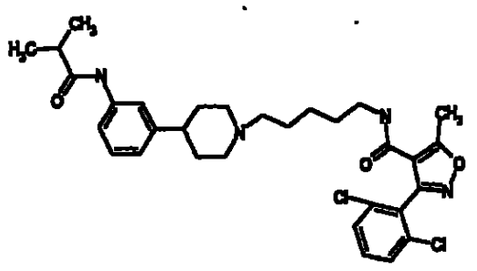
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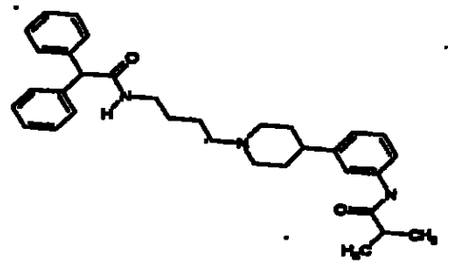
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7.1

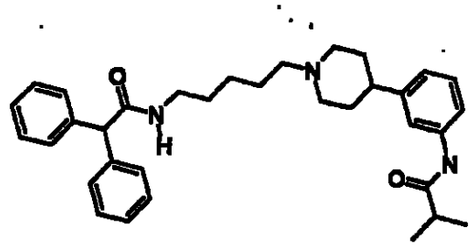
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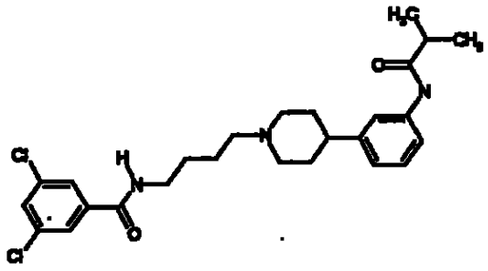
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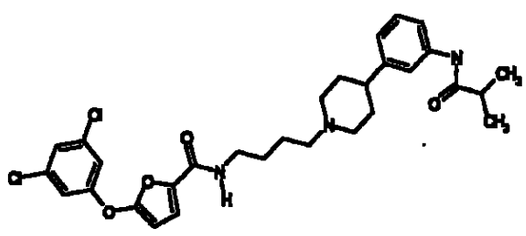
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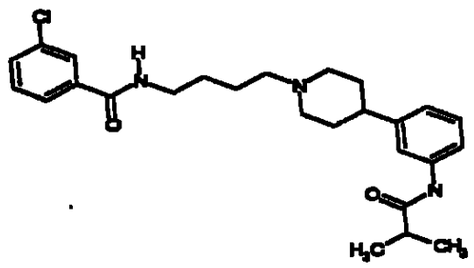
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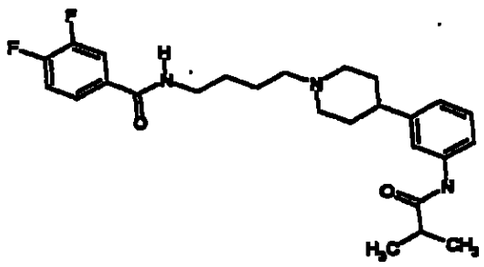
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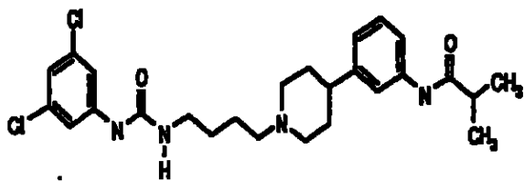
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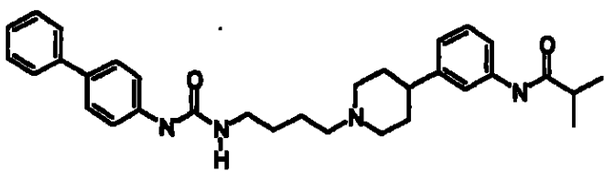


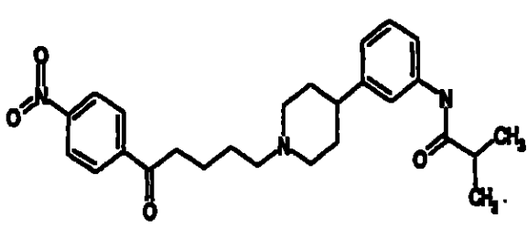
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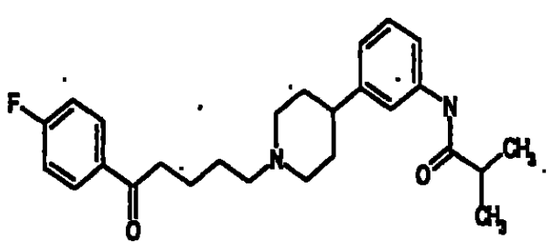
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1606

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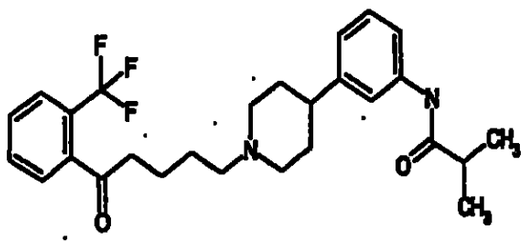
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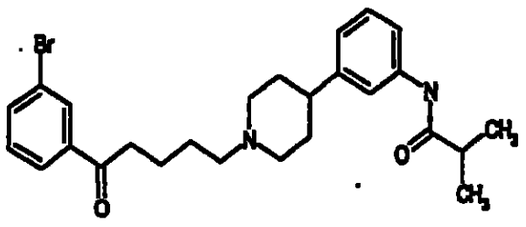
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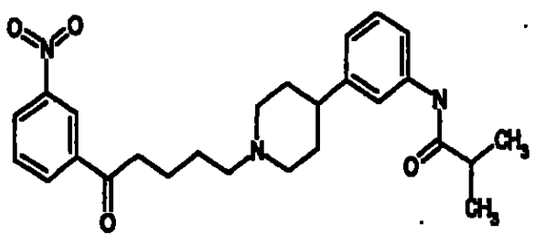
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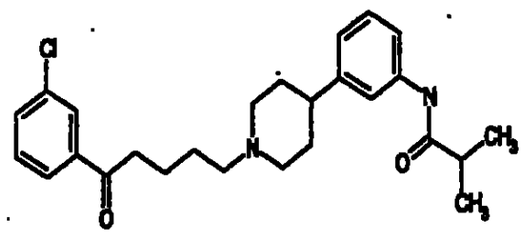
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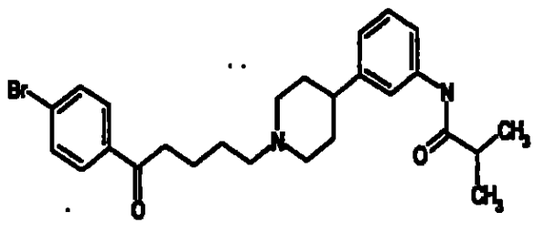
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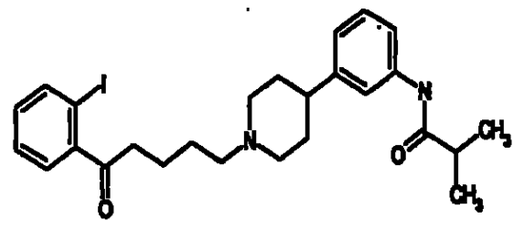
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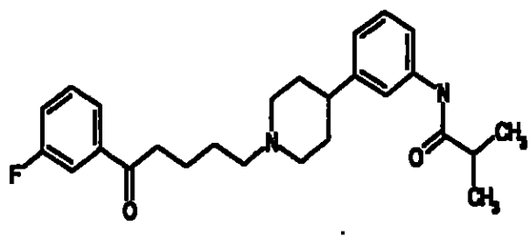
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16/14 168

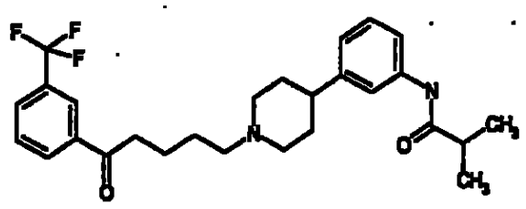
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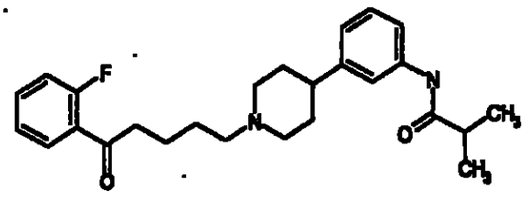
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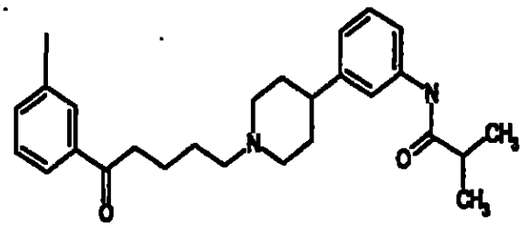
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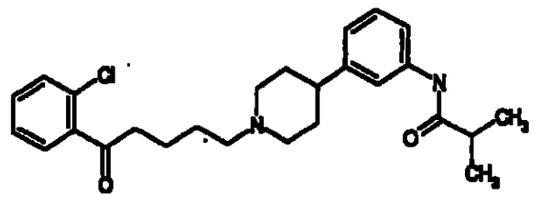
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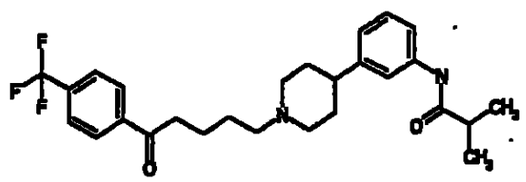
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673  32.5

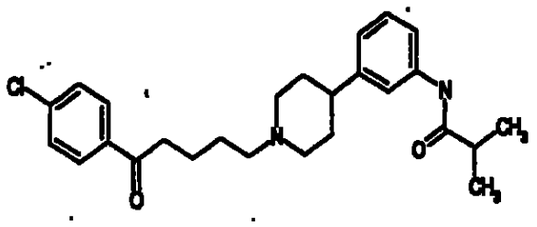
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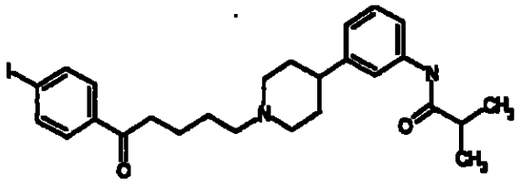
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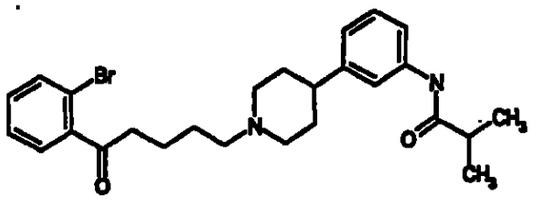
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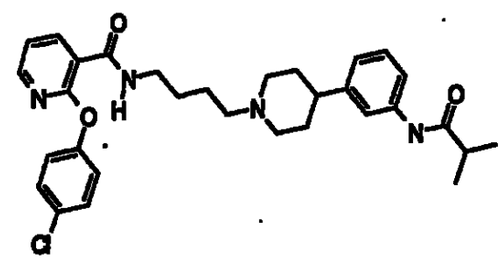
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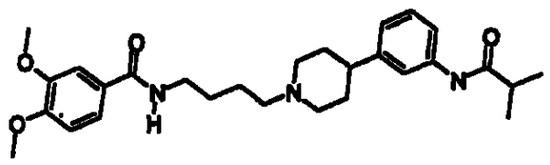
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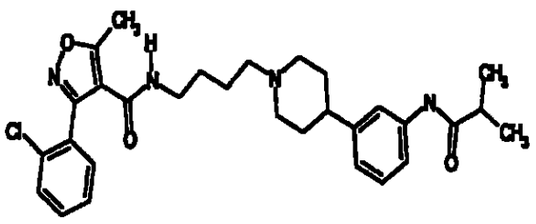
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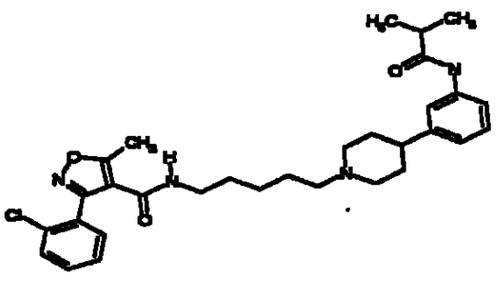
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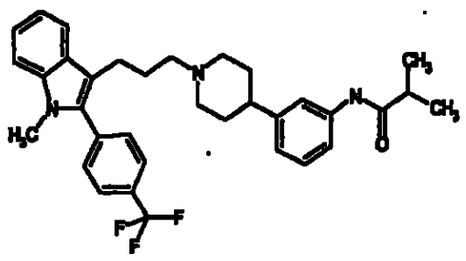
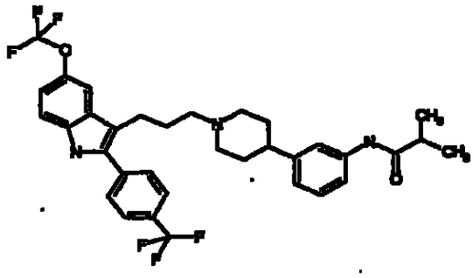
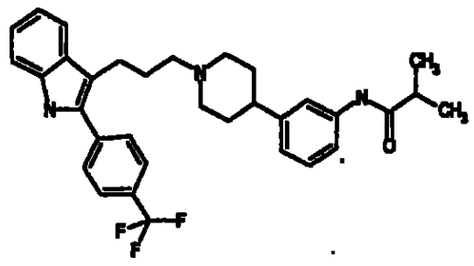
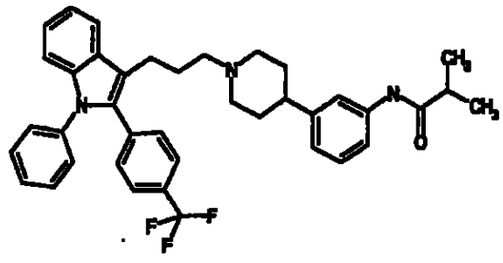
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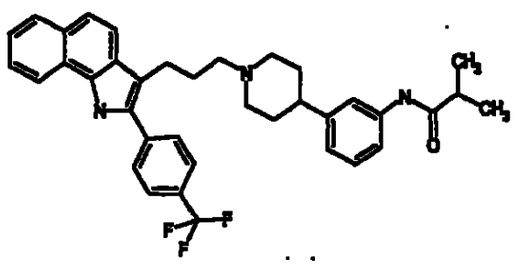
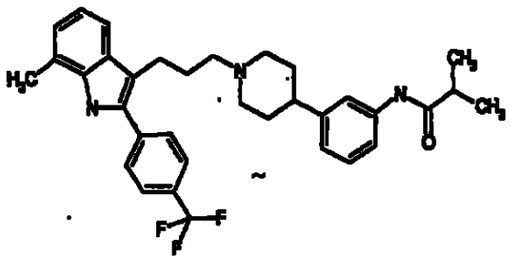
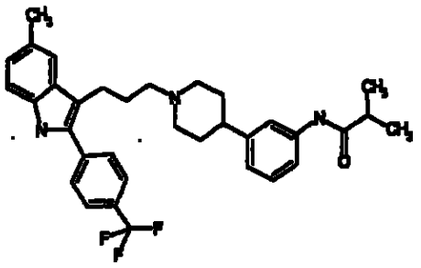
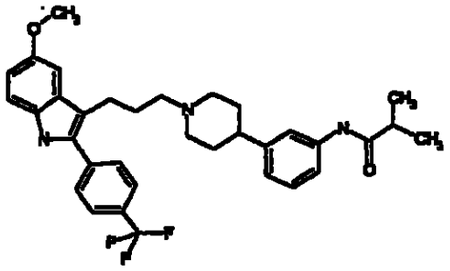


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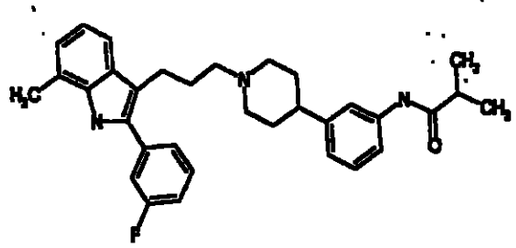
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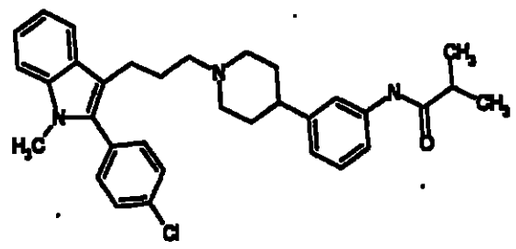
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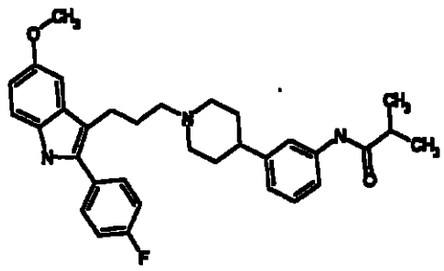
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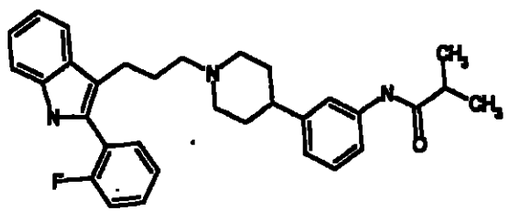
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667		20.6
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669		11.3

16/4 16/10

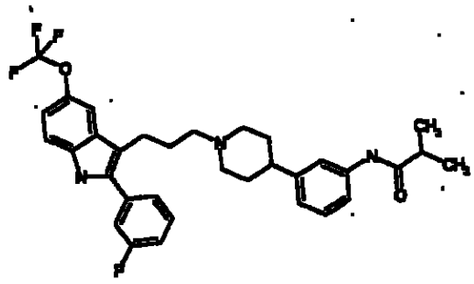
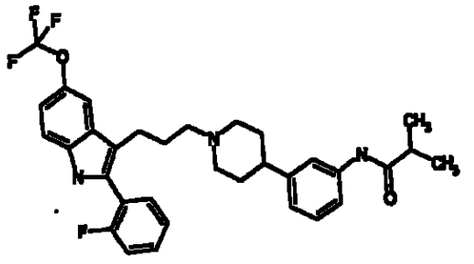
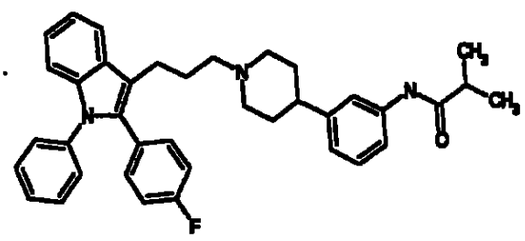
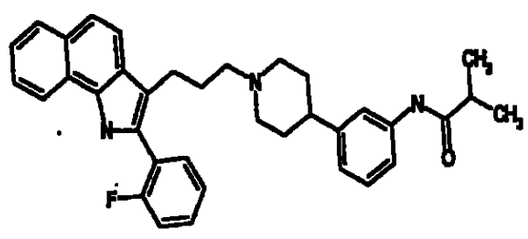
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691  16.3

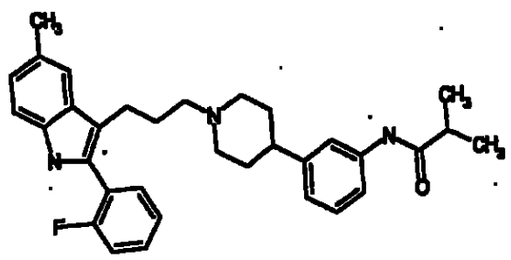
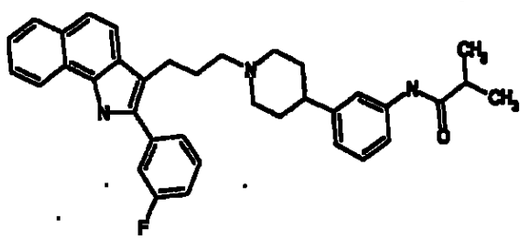
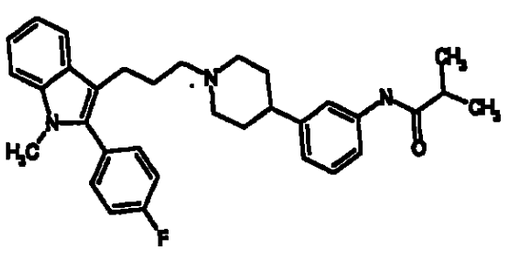
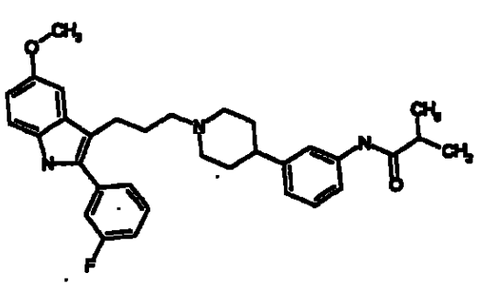
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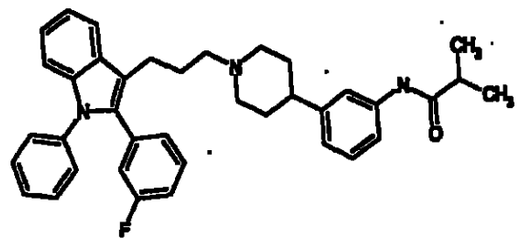
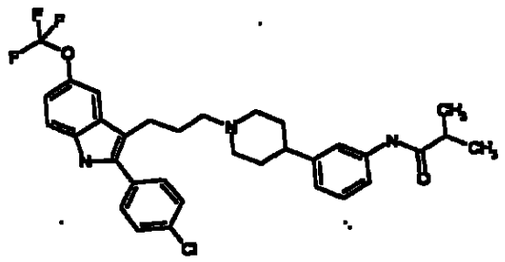
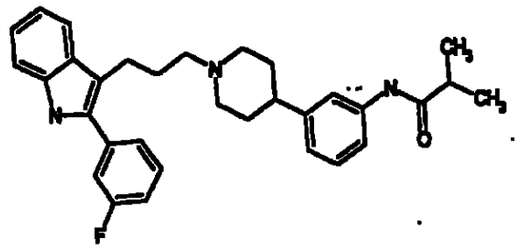
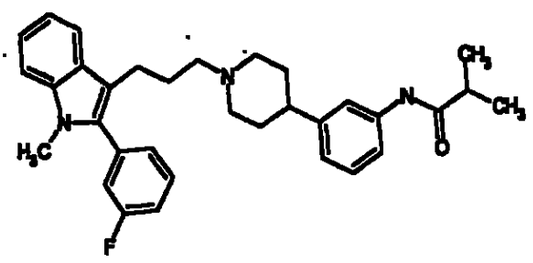
1611 1615

694		6.4
695		2.1
696		48.3
697		3.0

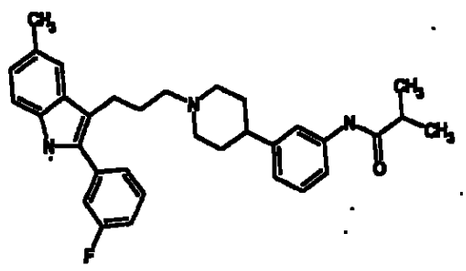
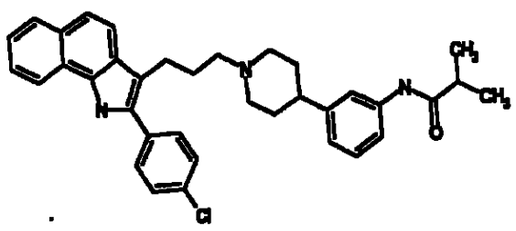
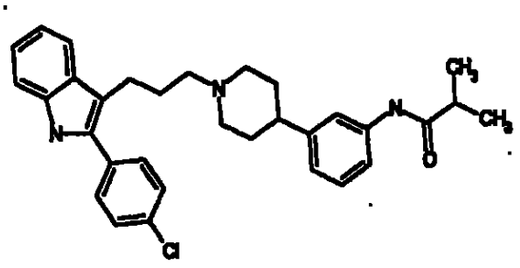
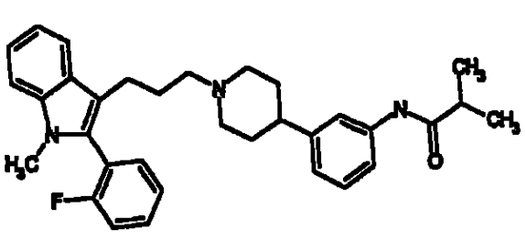
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1612

698		3.0
699		5.4
700		2.0
701		2.5

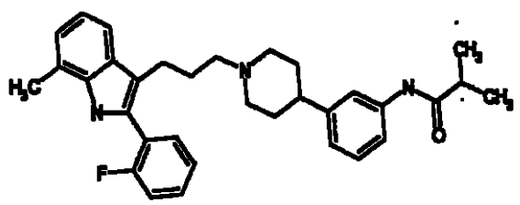
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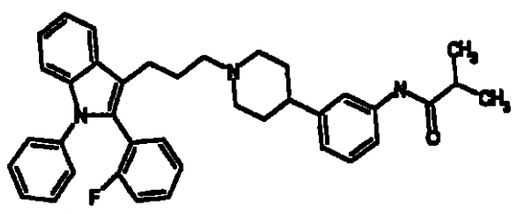
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703		16.6
704		1.2
705		8.5

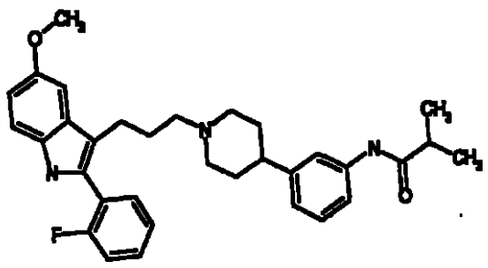
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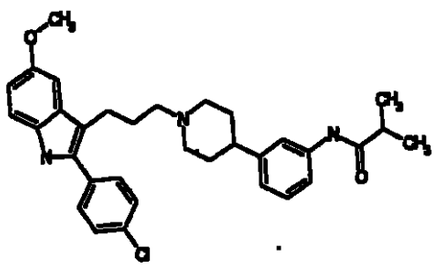
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707		19.8
708		3.8
709		1.3

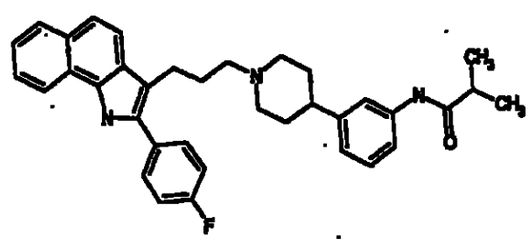
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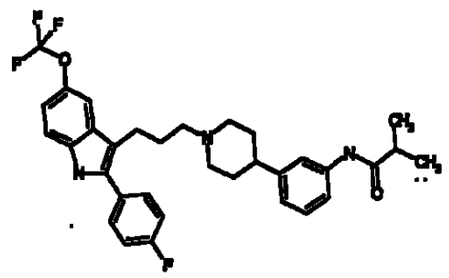
710  6.9

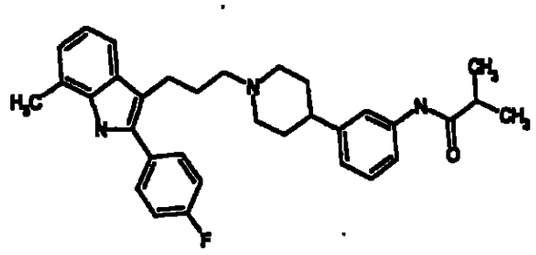
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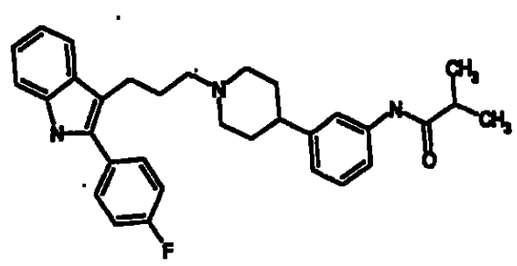
712  8.6

713  7.7

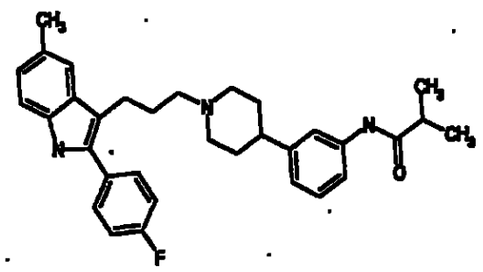
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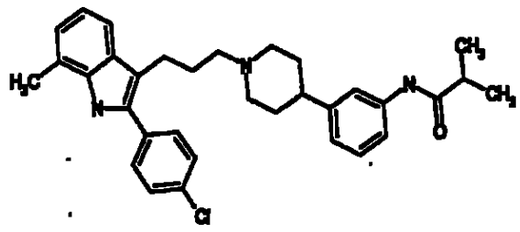
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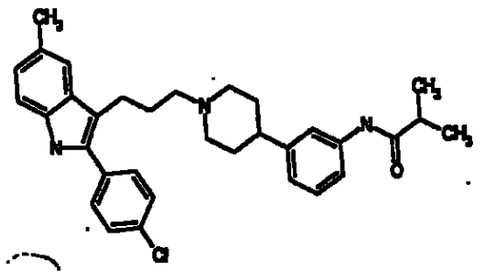
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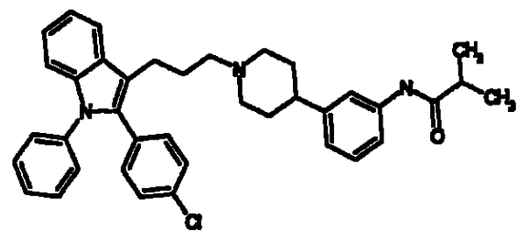
717  1.3

1617 1621

718  3.4

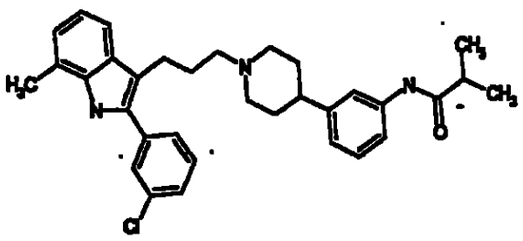
719  14.9

720  12.5

721  75.3

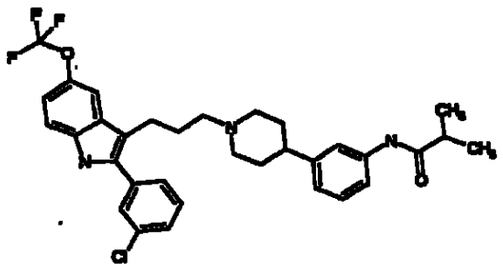
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722



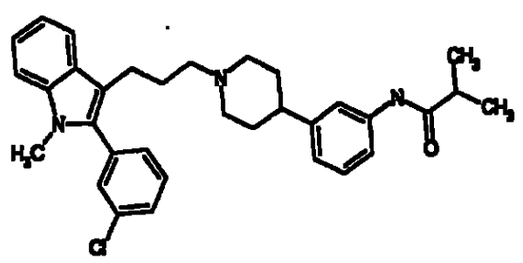
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723



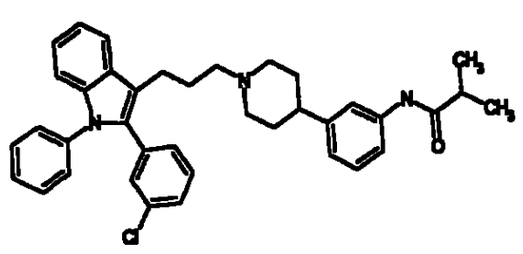
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724



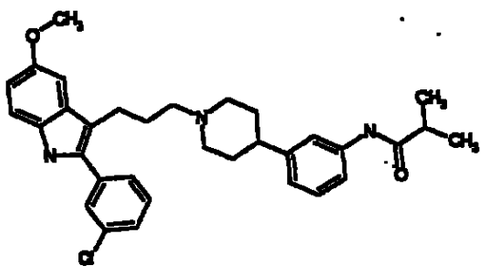
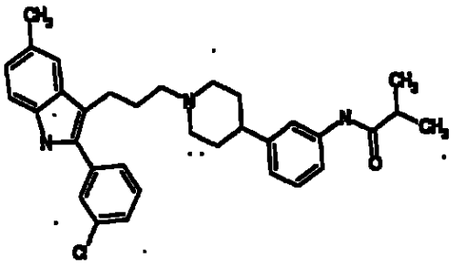
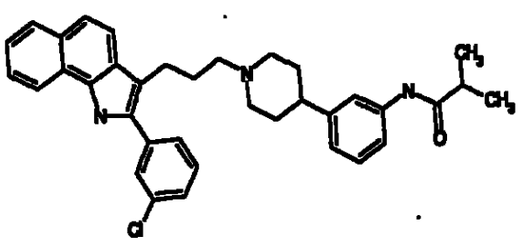
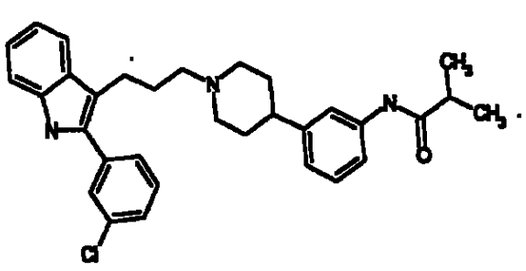
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725

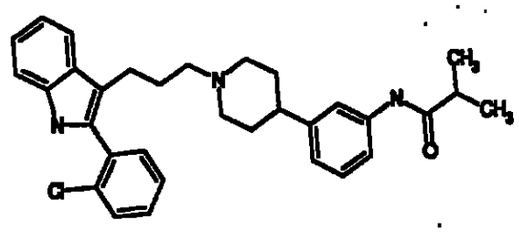


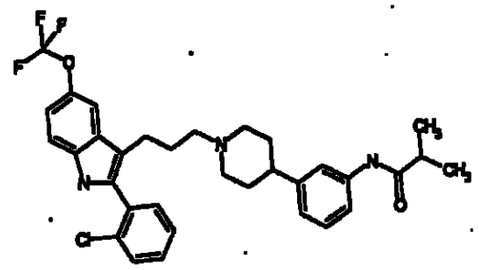
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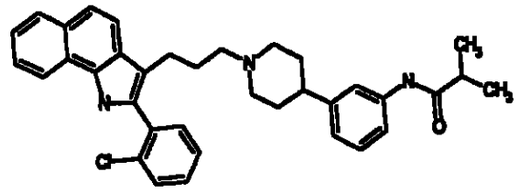
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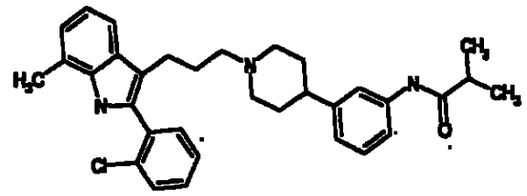
726		5.0
727		3.4
728		16.3
729		1.7

1820
1624

730  0.9

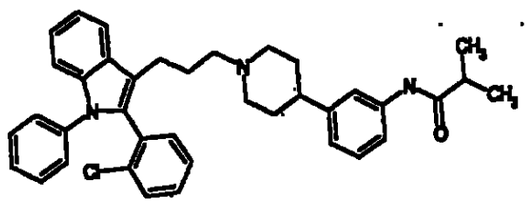
731  9.9

732  5.8

733  10.0

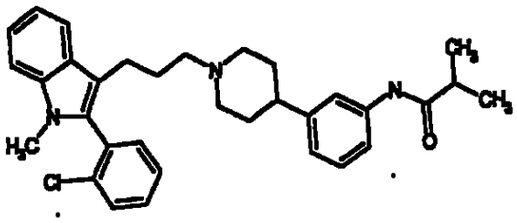
1625 1621

734



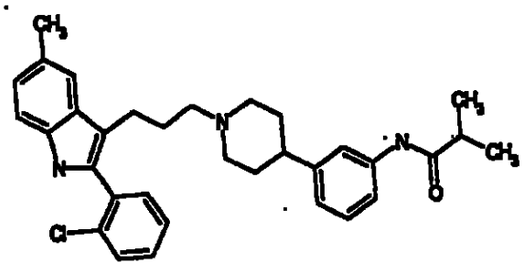
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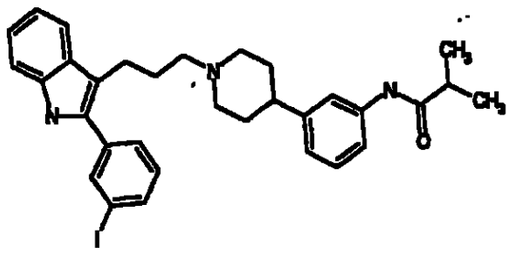
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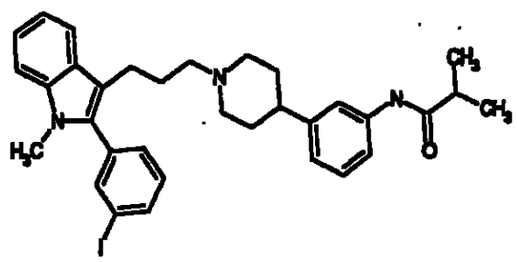
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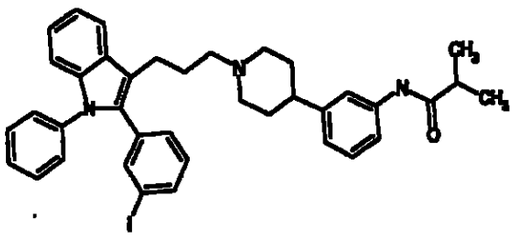
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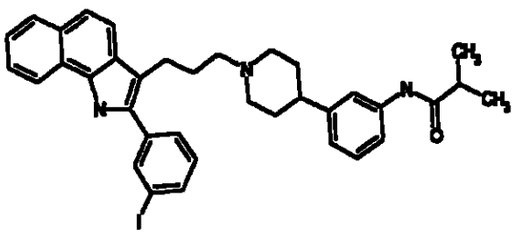


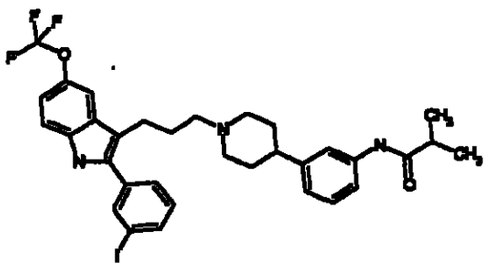
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1625 1622

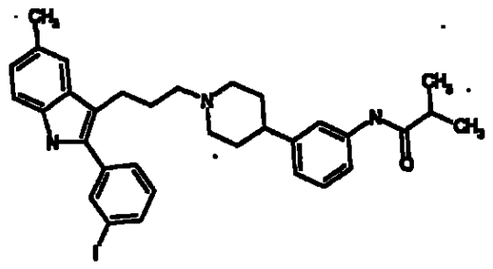
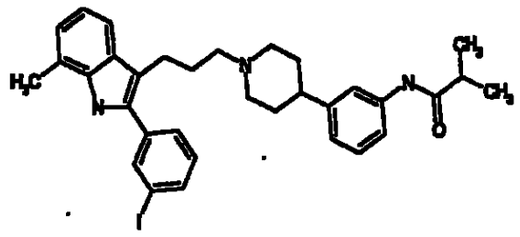
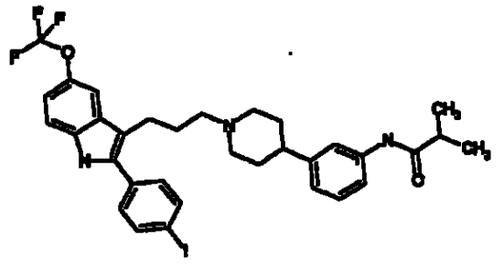
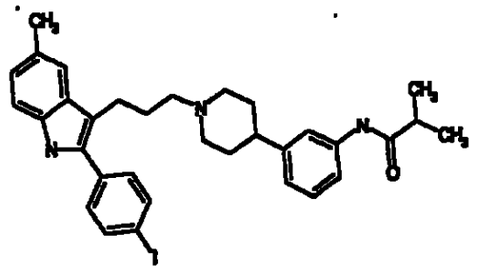
738  10.2

739  213.6

740  12.2

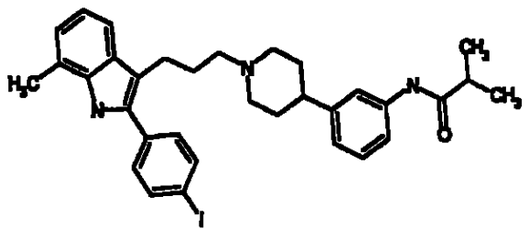
741  2.8

1627 1623

742		1.4
743		4.1
744		47.1
745		15.8

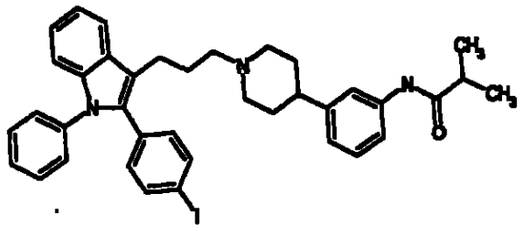
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748



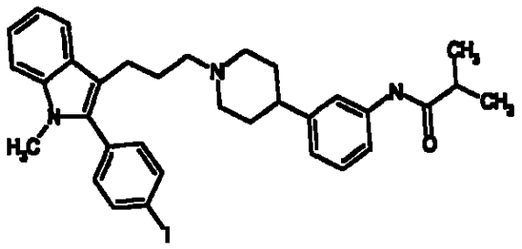
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747



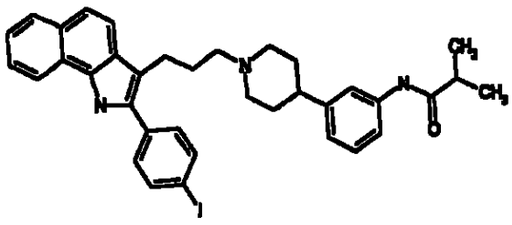
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748



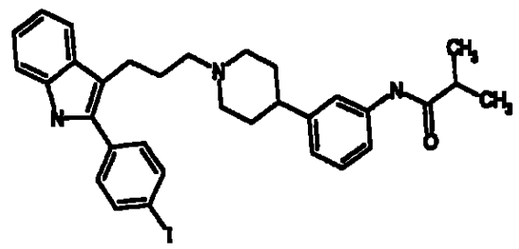
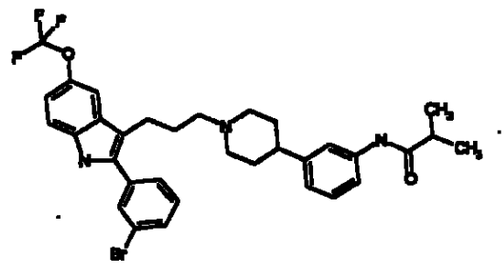
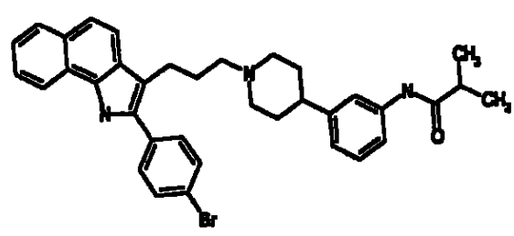
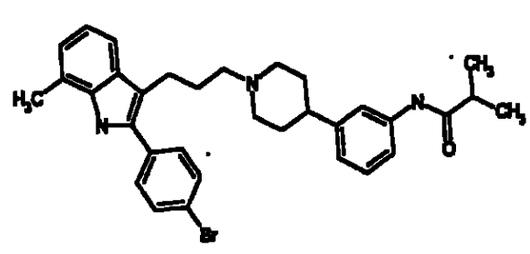
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749

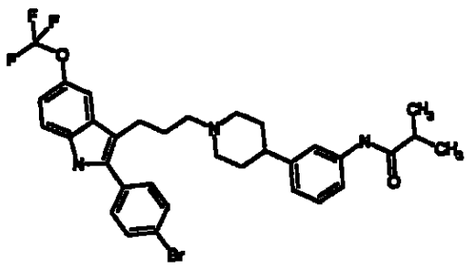


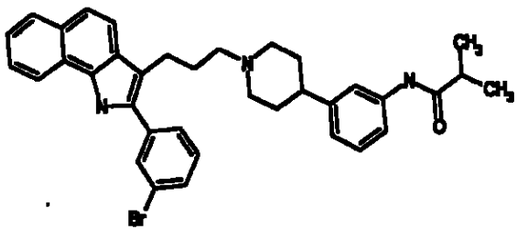
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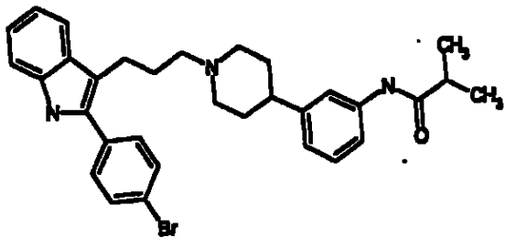
1625 1629

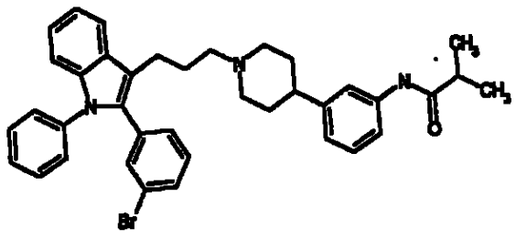
750		2.6
751		12.4
752		21.7
753		16.6

1626 630

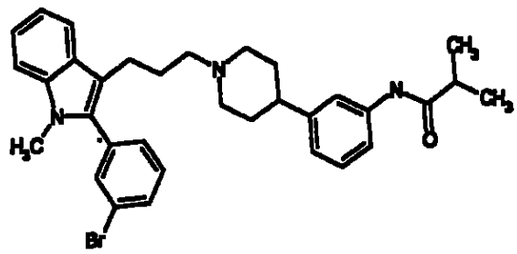
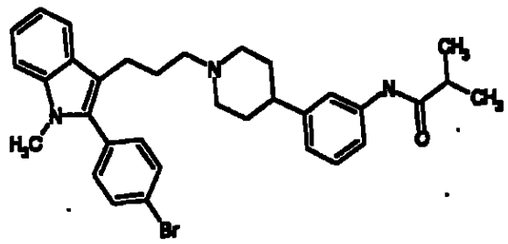
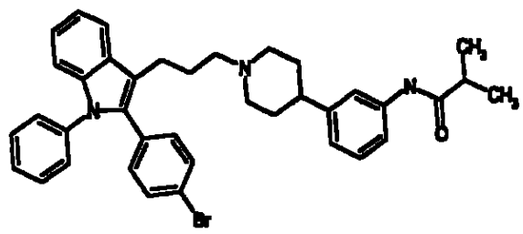
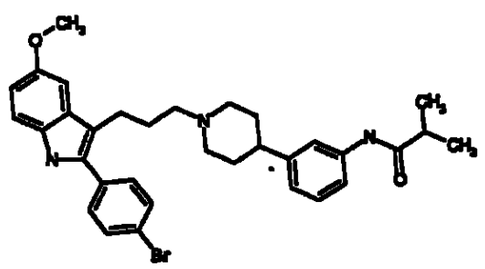
754  49.2

755  23.8

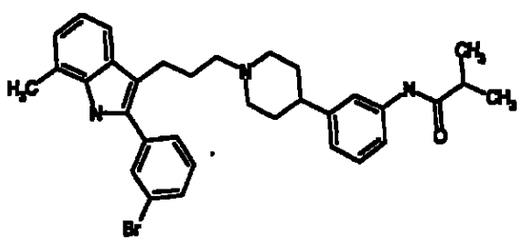
756  4.2

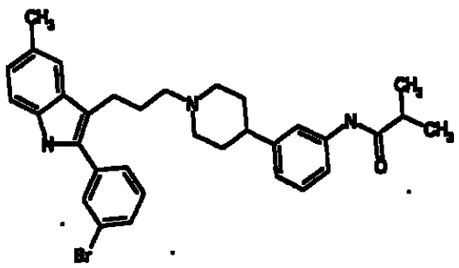
757  6.9

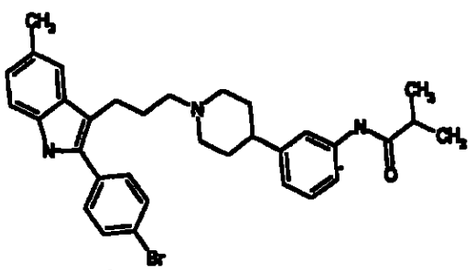
10/17/631

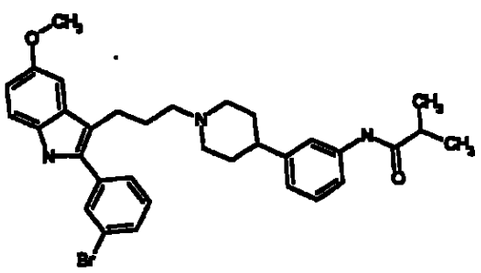
758		110.0
759		9.3
760		92.3
761		15.9

18/28 1632

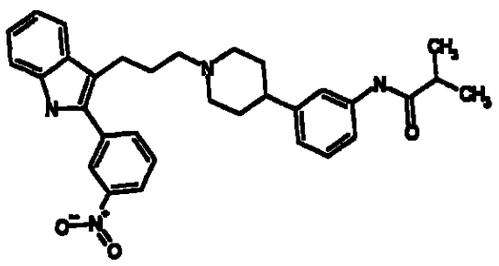
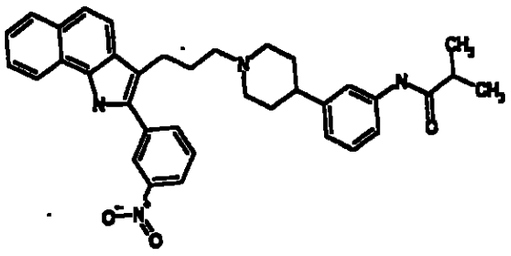
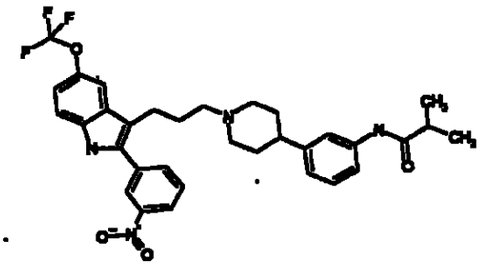
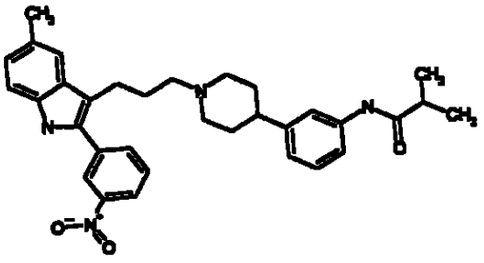
762  6.3

763  1.9

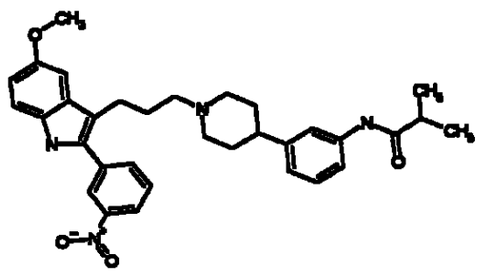
764  14.6

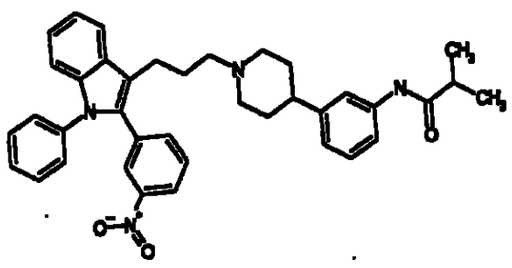
765  6.5

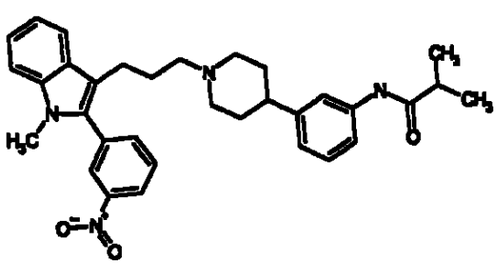
1629 1633

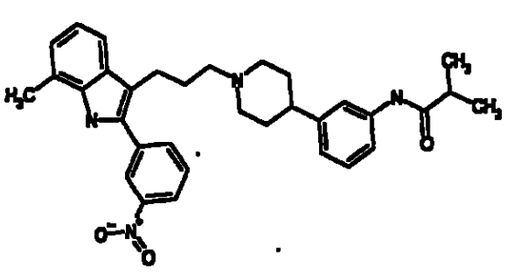
766		7.8
767		34.8
768		17.5
769		12.4

15/30 134

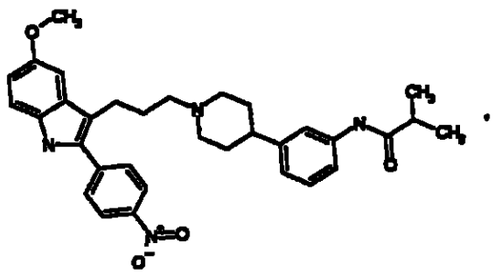
770  12.7

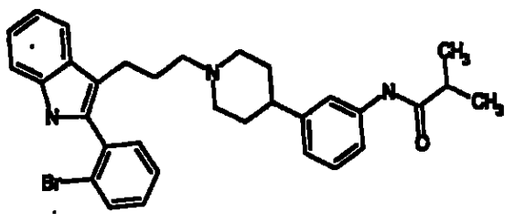
771  169.0

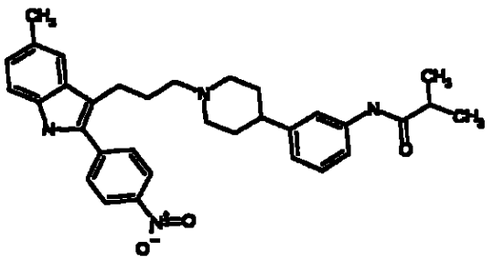
772  14.9

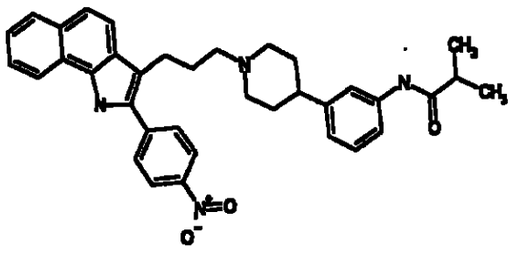
773  23.8

1635 1631

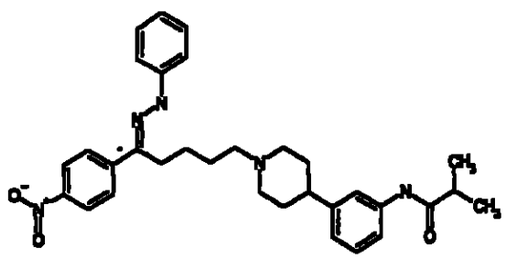
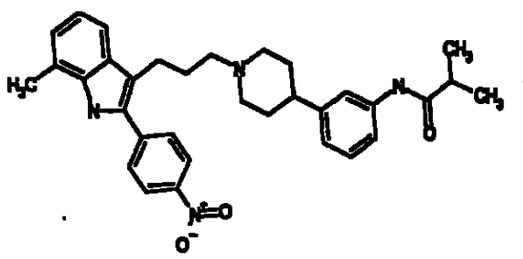
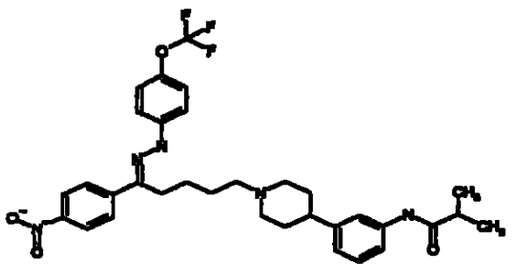
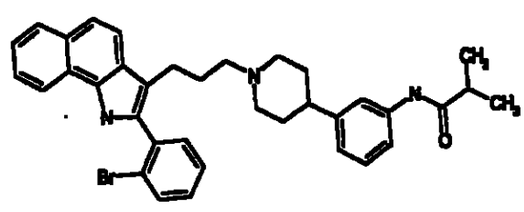
774  7.9

775  4.9

776  16.2

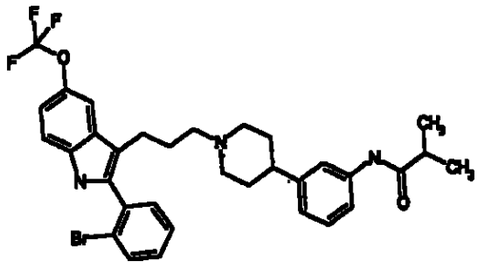
777  8.5

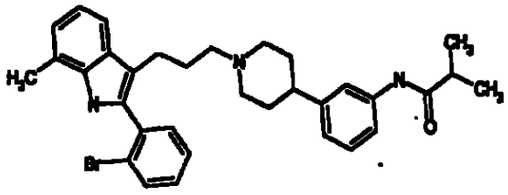
1632 1636

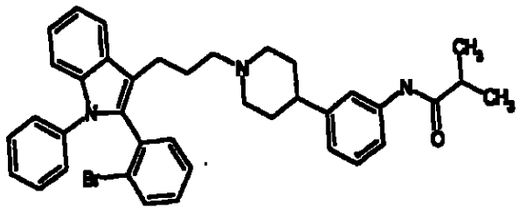
778		28.5
779		7.6
780		64.3
781		7.6

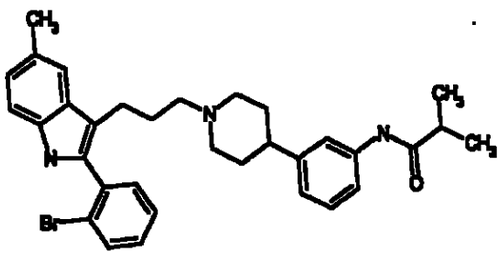
1637

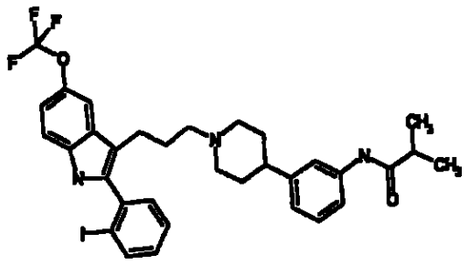
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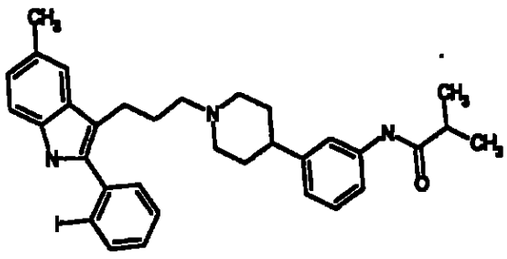
782  18.1

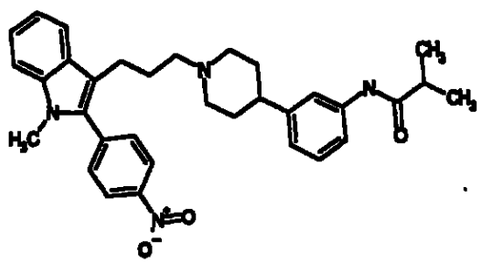
783  18.0

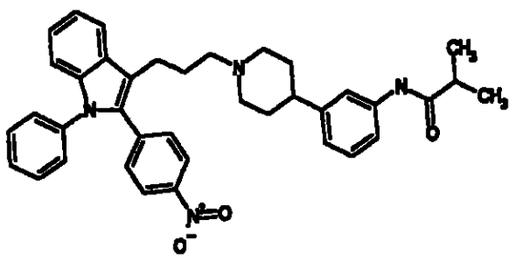
784  121.2

785  22.7

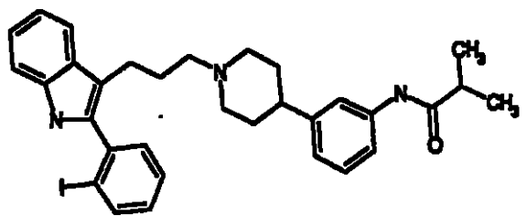
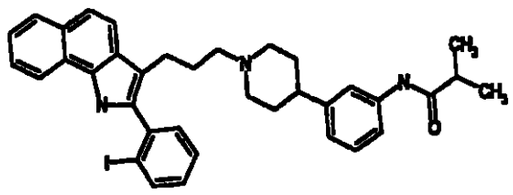
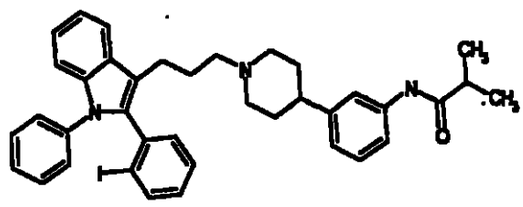
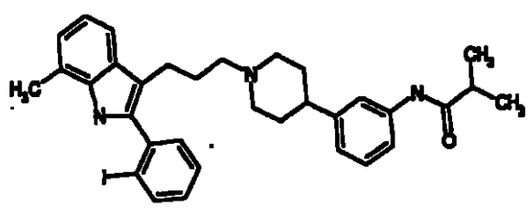
786  19.7

787  21.6

788  11.1

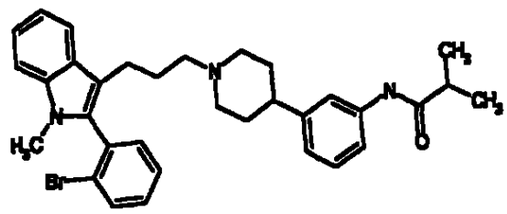
789  36.4

1685/639

790		4.4
791		12.7
792		122.0
793		16.3

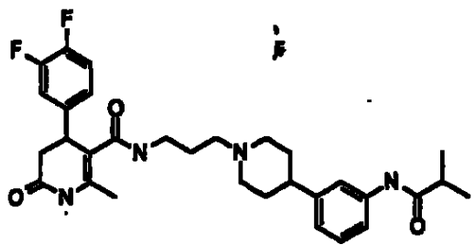
1636/640

794



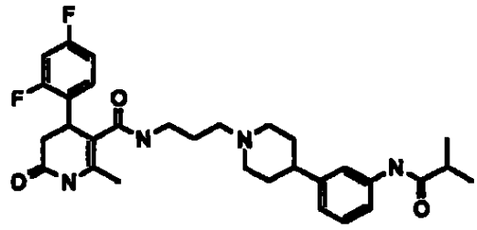
4.8

795

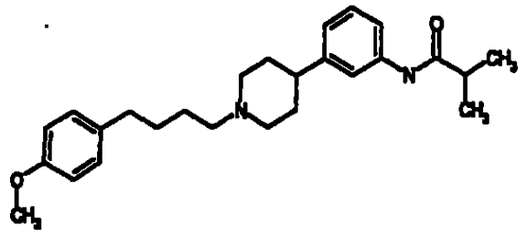


51.1

796

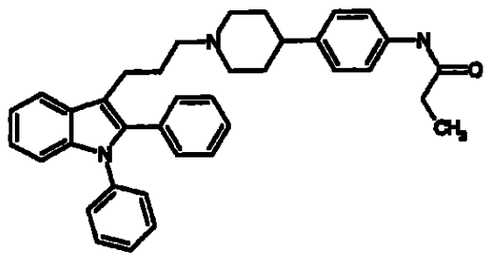


43.0

EJEMPLO	ESTRUCTURA	rMCH1 Ki (nM)
797		42.4

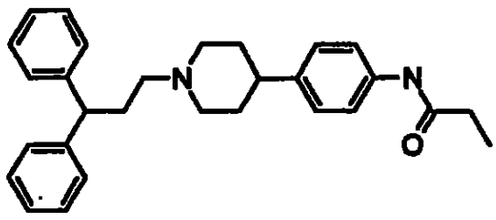
1637
1641

798



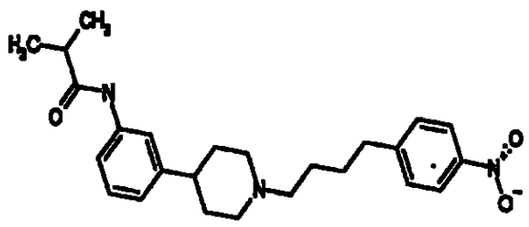
474.7

799



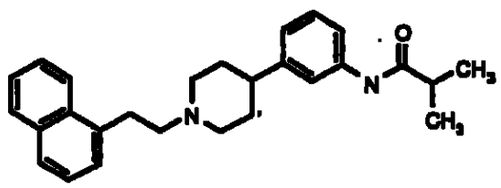
370.6

800



9.9

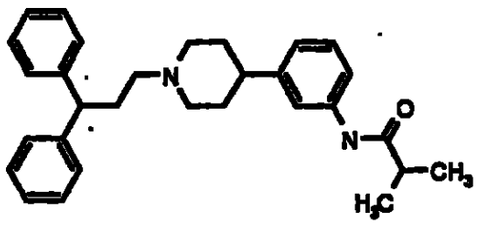
801



311.1

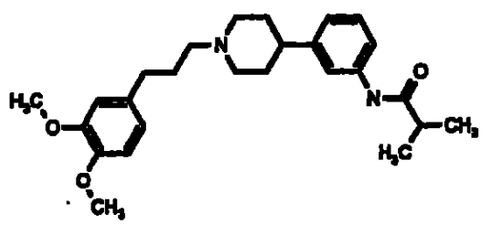
1638642

802



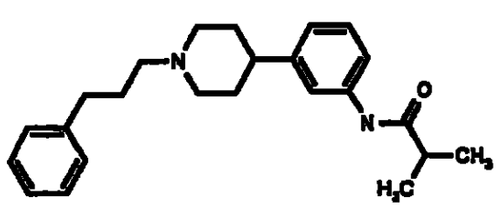
36.7

803



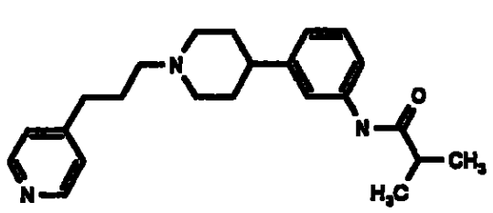
298.6

804



89.2

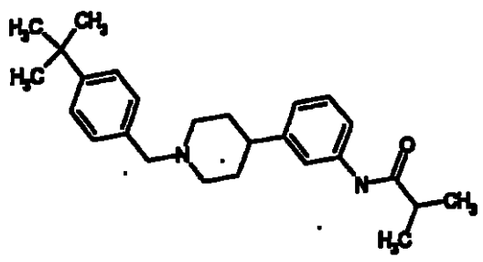
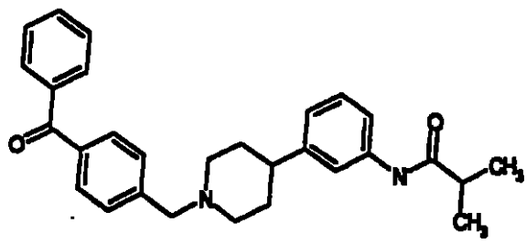
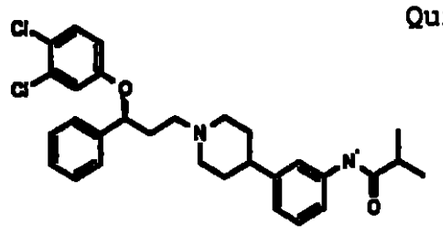
805

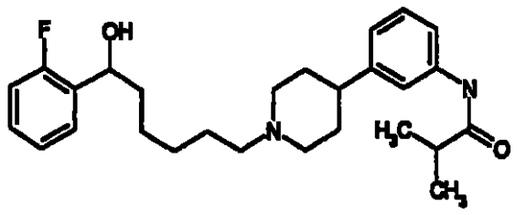


903.9

1643

1635

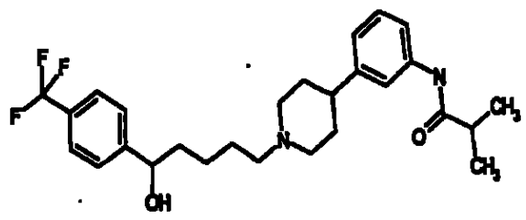
806		14.1
807		2.7
808	 Quiral	10.8

EJEMPLO	ESTRUCTURA	rMCH1 Ki (nM)
809		56.8

1644

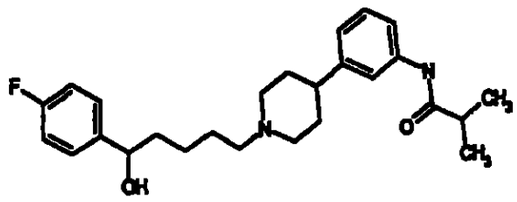
1640

810



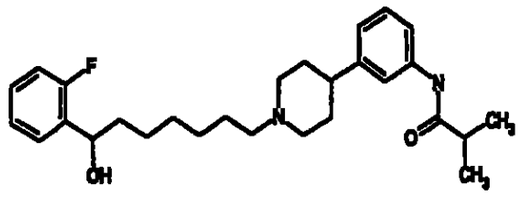
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811



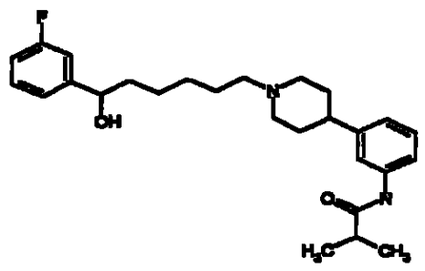
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812



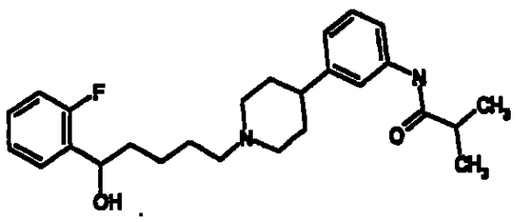
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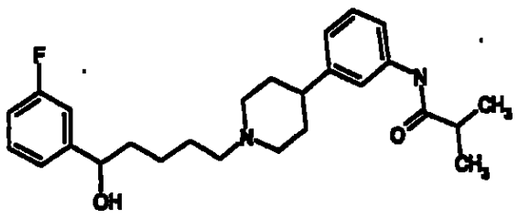
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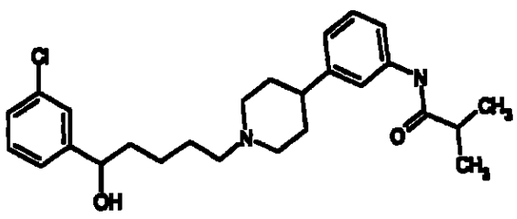


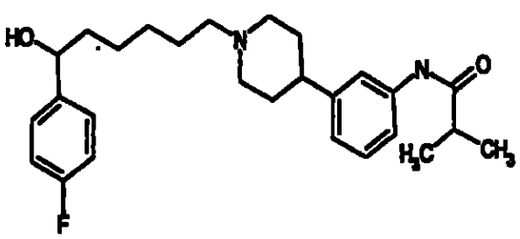
57.3

1645
1641

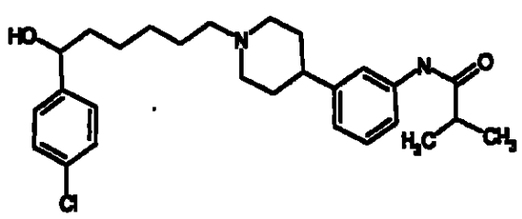
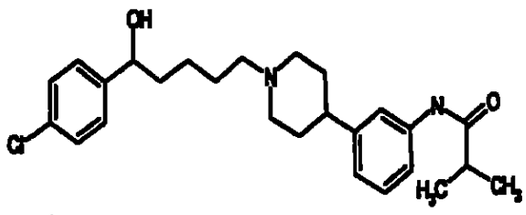
814  159.5

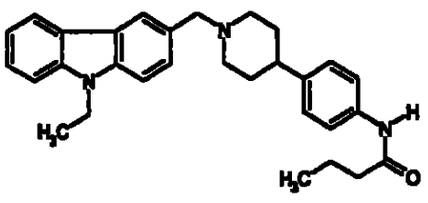
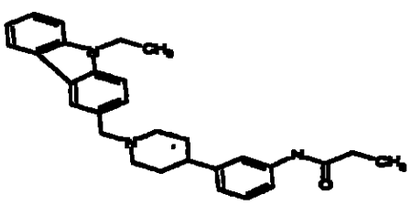
815  126.9

816  89.6

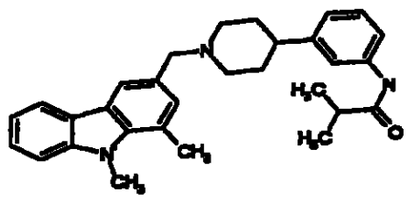
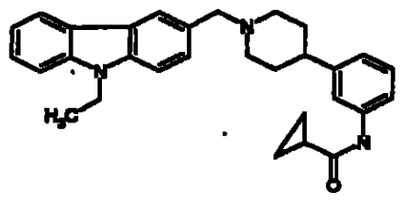
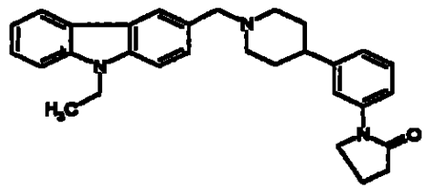
817  34.9

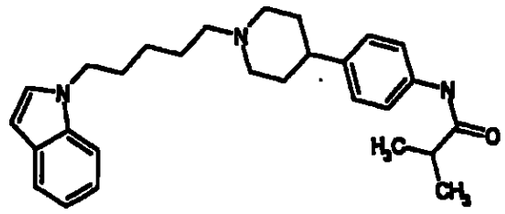
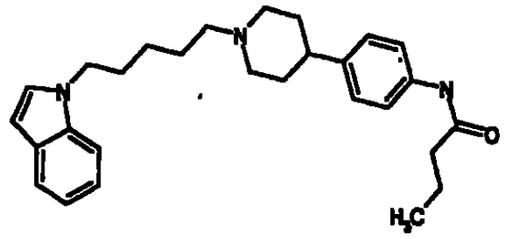
1646

818		38.2
819		80.2

EJEMPLO	ESTRUCTURA	rMCH1 Ki (nM)
820		108.6
821		12.1

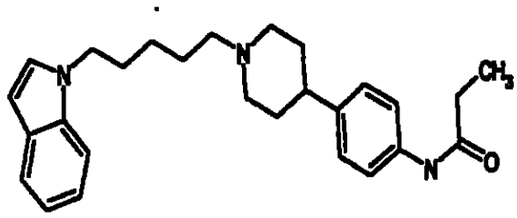
1647
1943

822		1.0
823		2.7
824		36.5

EJEMPLO	ESTRUCTURA	rMCH1 Ki (nM)
825		600.7
826		785.6

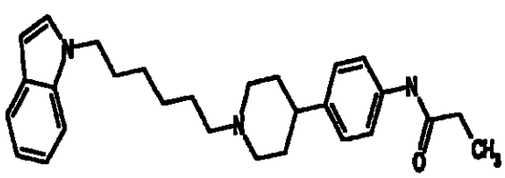
1648
1644

827



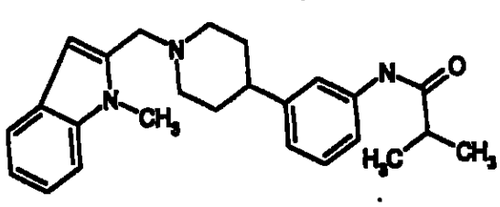
215.4

828



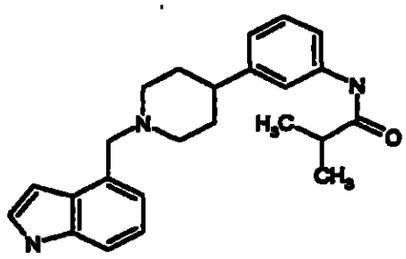
515.9

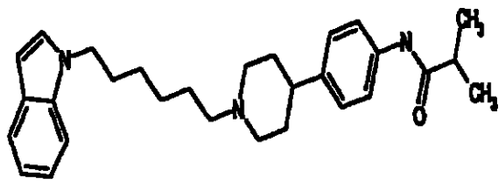
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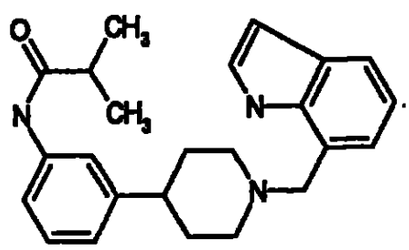


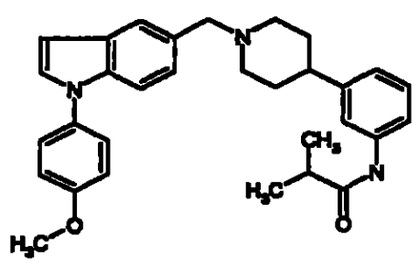
228.0

1649
1645

830  466.6

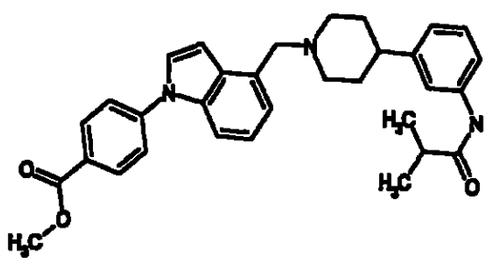
831  569.8

832  614.3

833  27.5

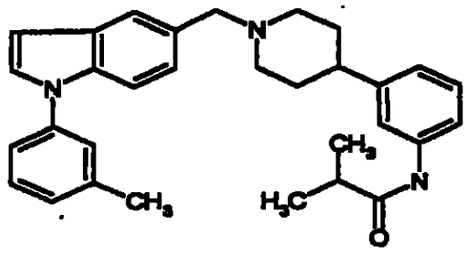
1650
1946

834



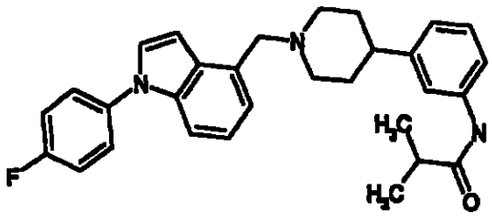
36.3

835



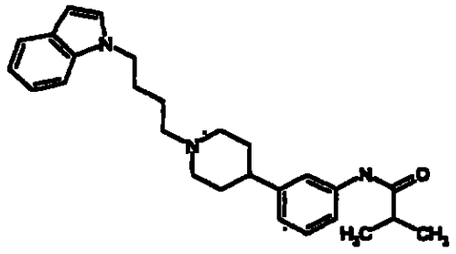
21.3

836



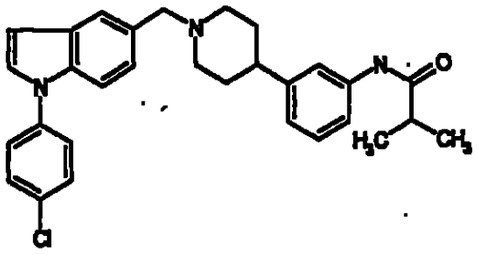
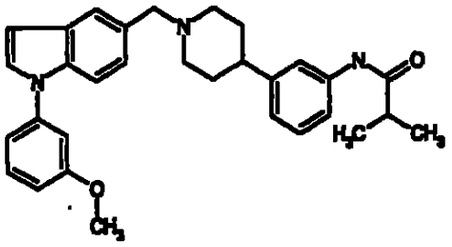
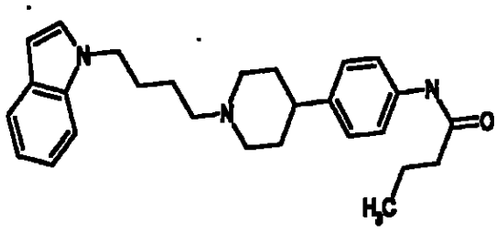
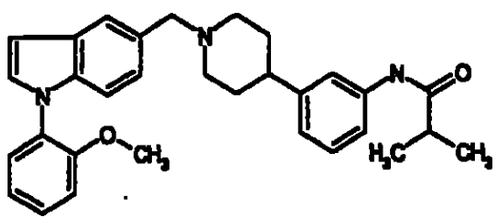
7.8

837



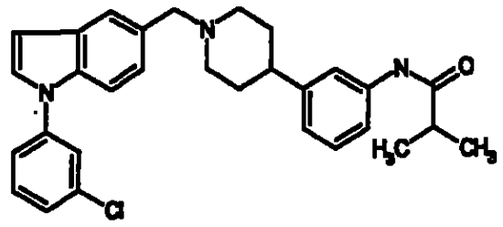
35.9

1651

838		11.2
839		62.2
840		663.6
841		25.0

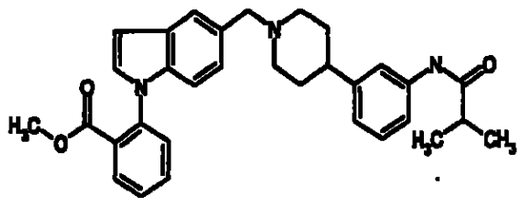
1652
1618

842



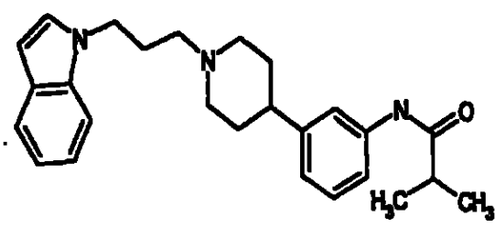
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843



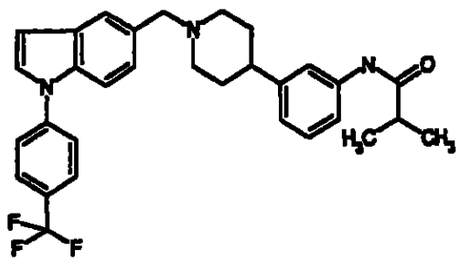
15.5

844



37.8

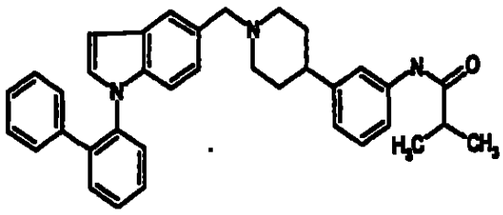
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43.1

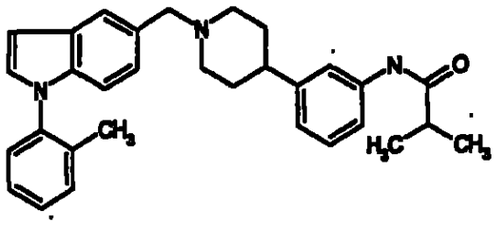
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846



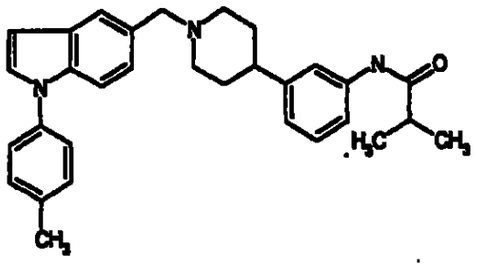
18.4

847



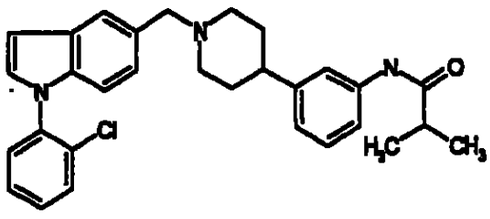
10.2

848



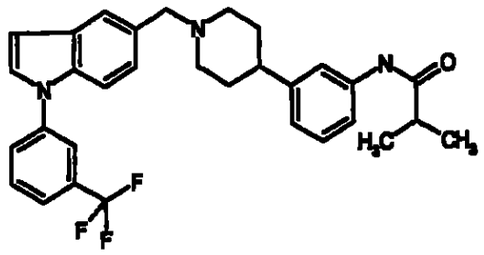
19.1

849

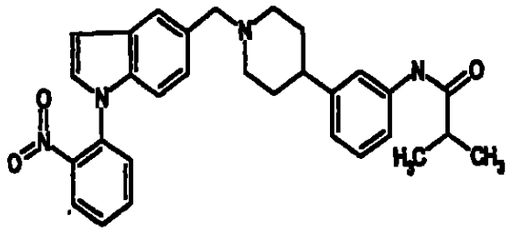


9.4

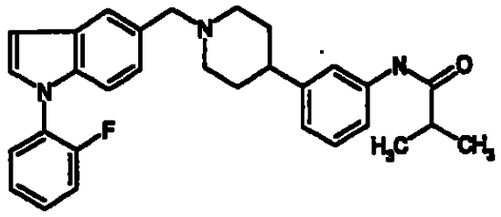
1654
1670

850 

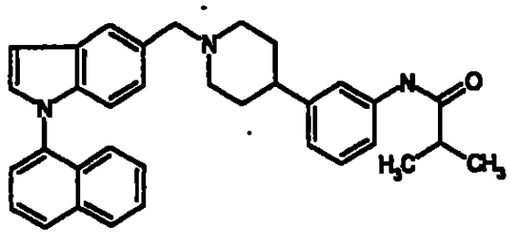
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851 

27.4

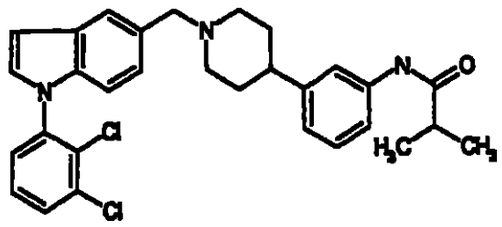
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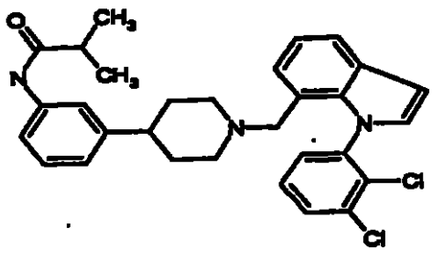
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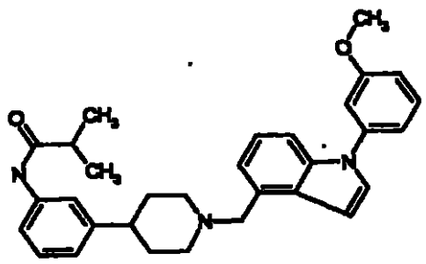
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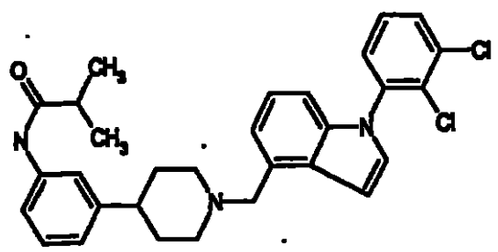
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1655
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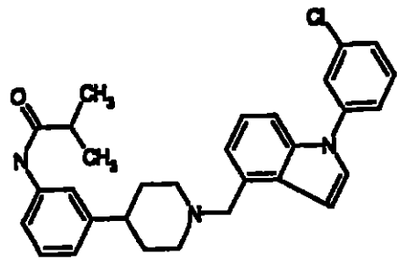
854  13.8

855  256.0

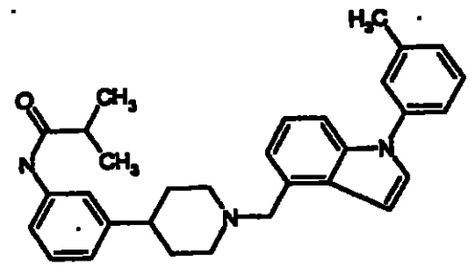
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857  89.8

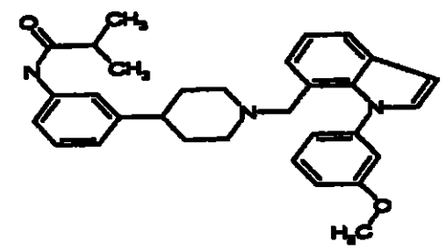
1650
1652

858 

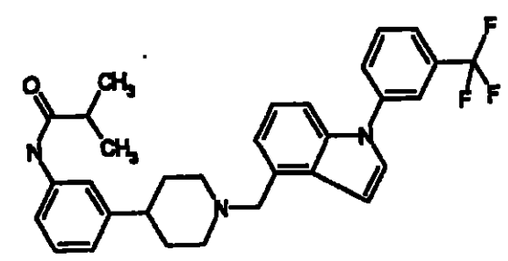
44.9

859 

320.7

860 

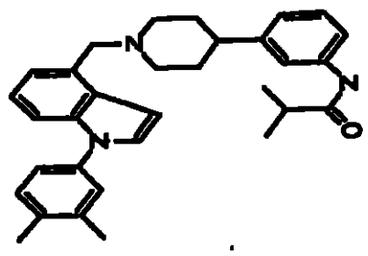
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861 

94.1

1653
1657

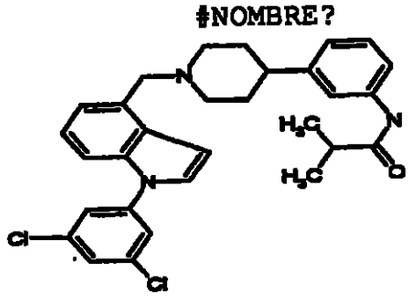
862



437.6

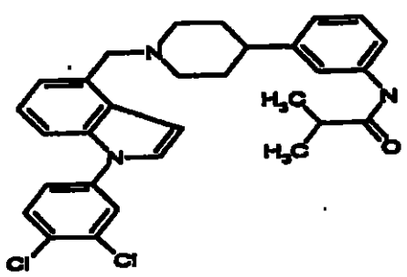
#NOMBRE?

863



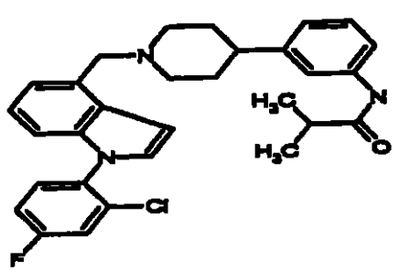
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864



292.0

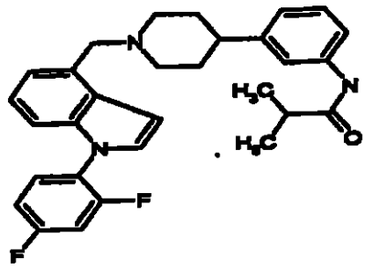
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94.6

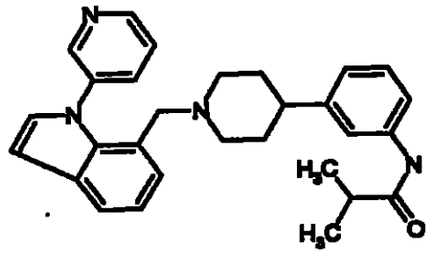
1854 K58

866



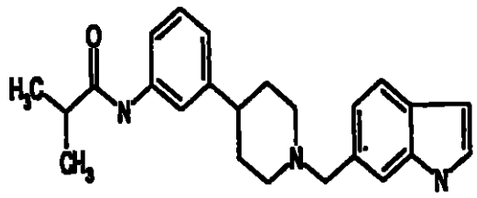
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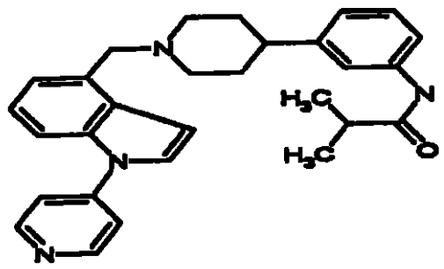
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403.4

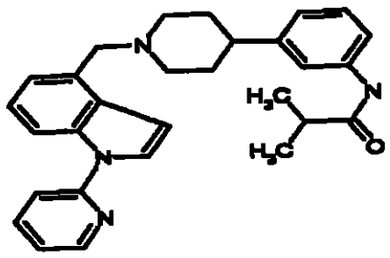
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430.9

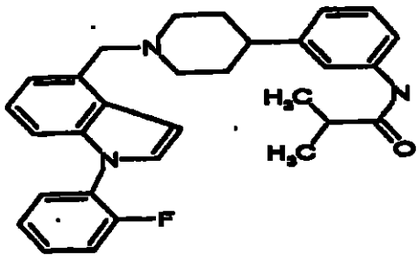
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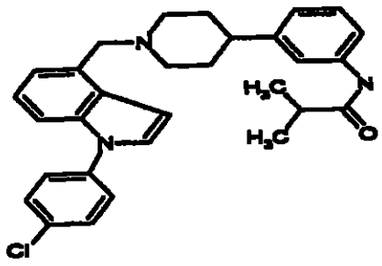
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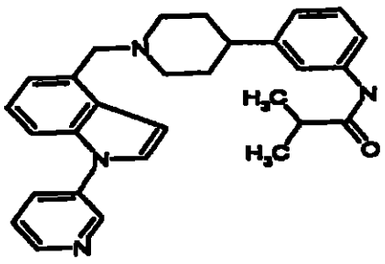
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308.3

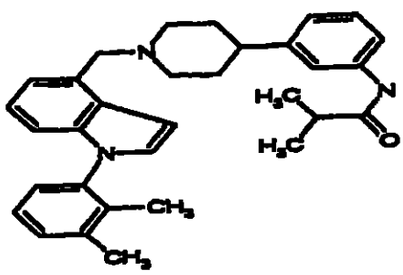
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345.0

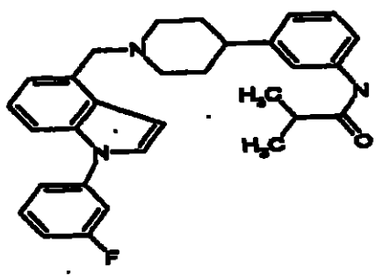
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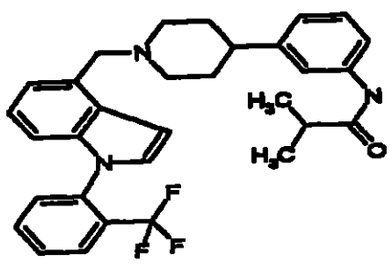
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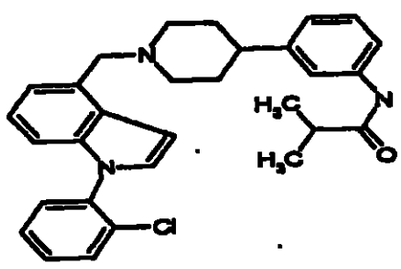
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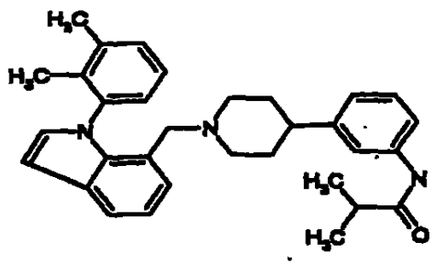
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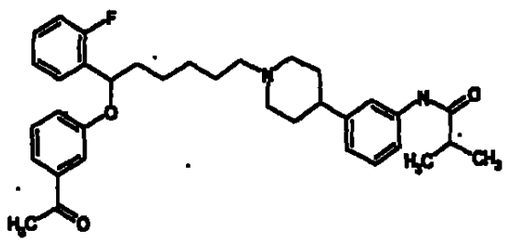
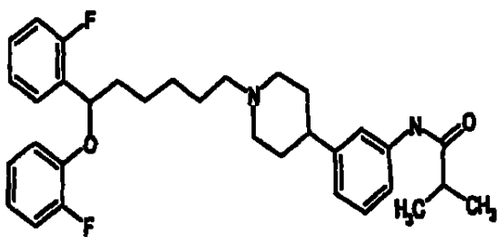
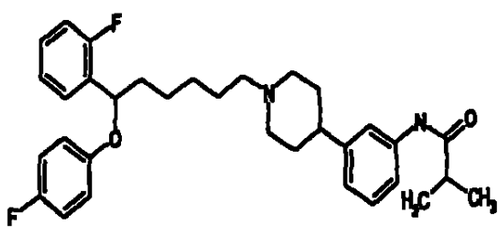
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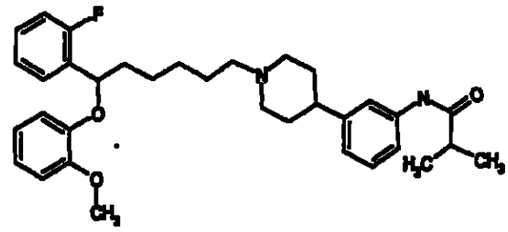
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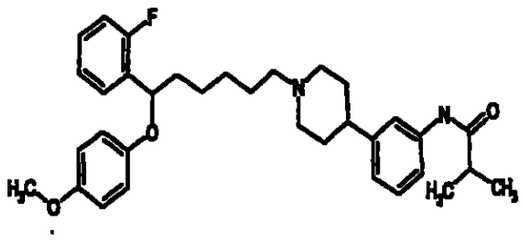
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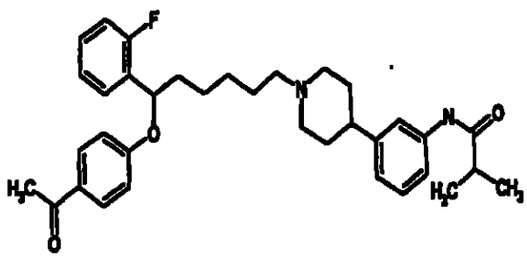
EJEMPLO	ESTRUCTURA	rMCH1 Ki (nM)
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889		8.6
890		11.1

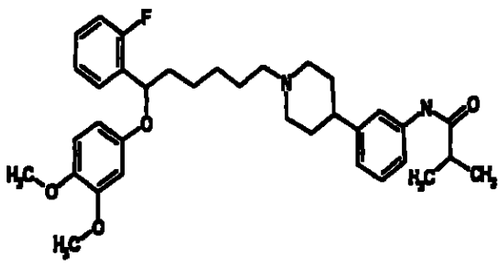
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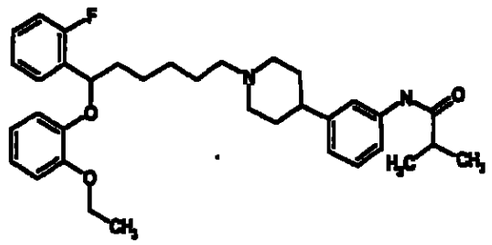
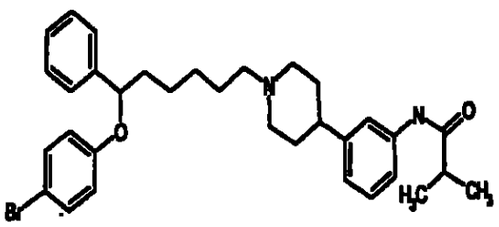
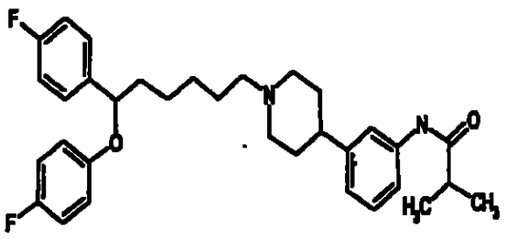
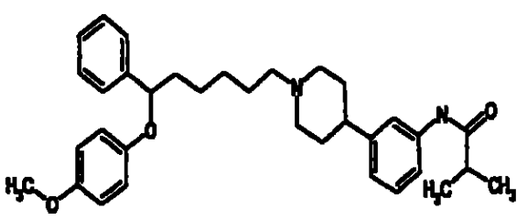
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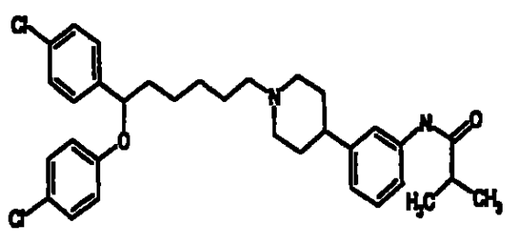
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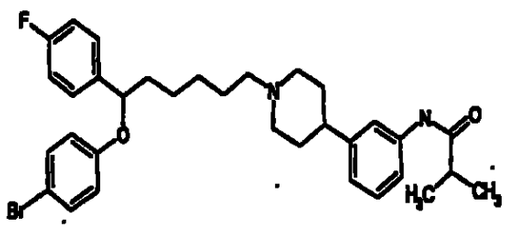
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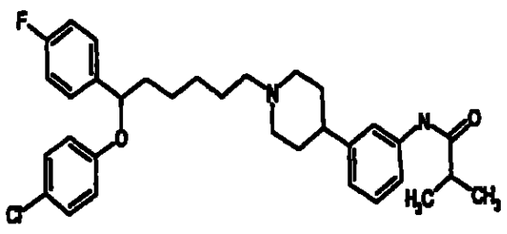
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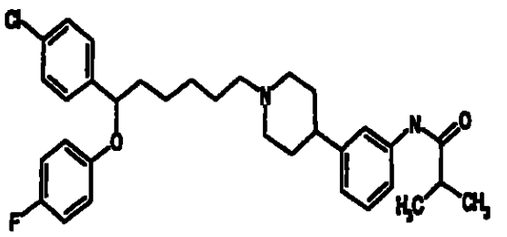
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1760

899  18.0

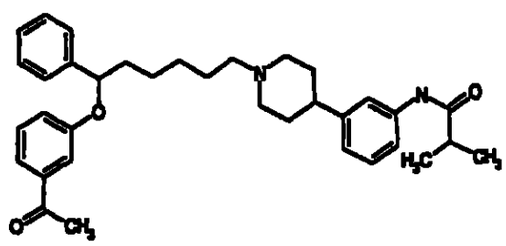
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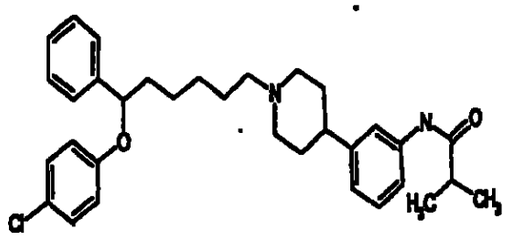
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1661

903



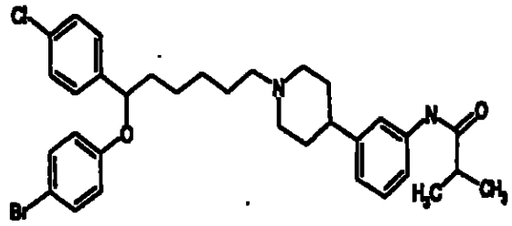
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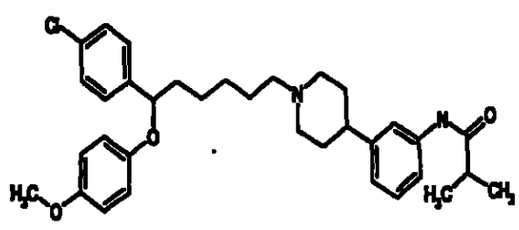
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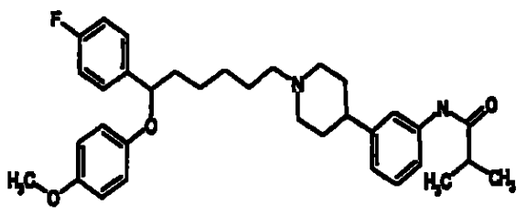


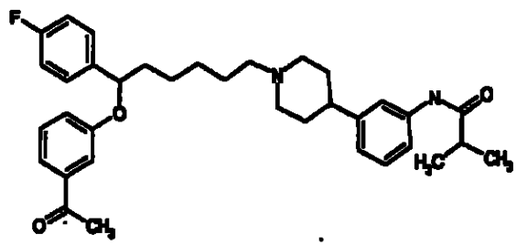
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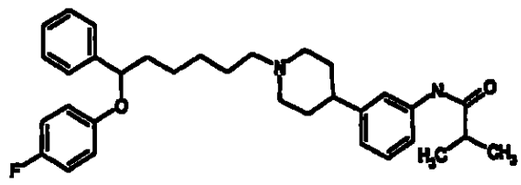
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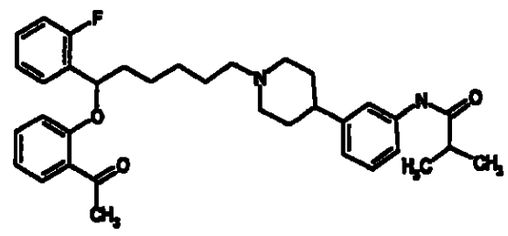


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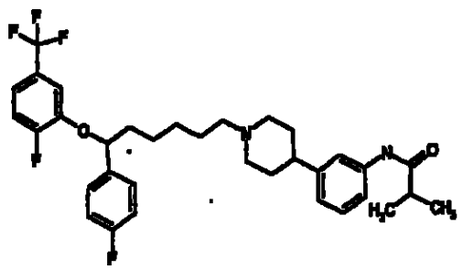
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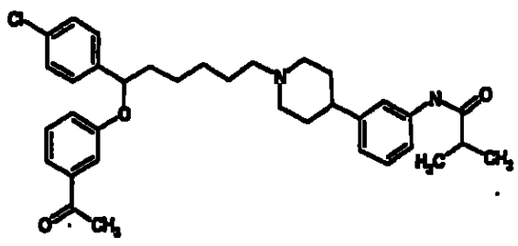
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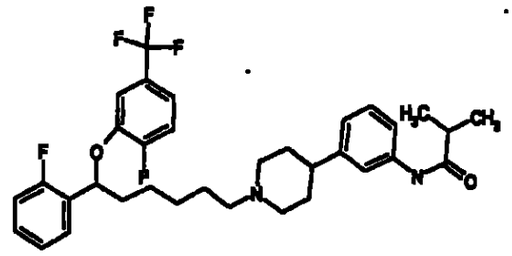
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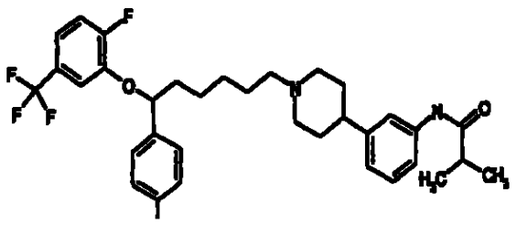
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667
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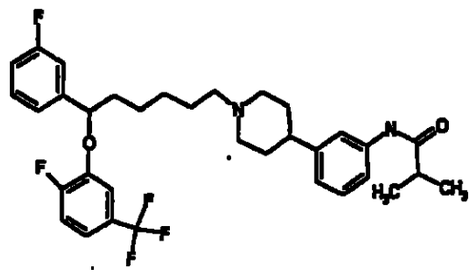
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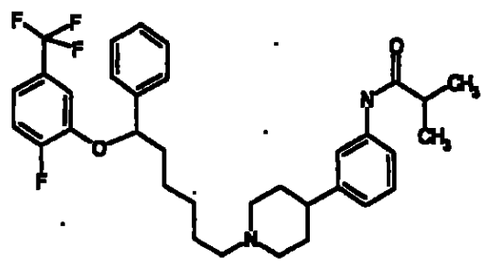
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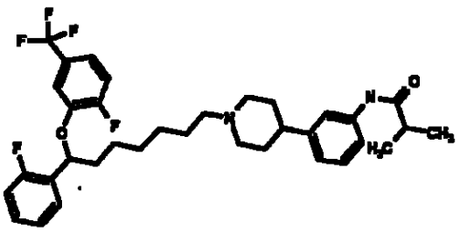
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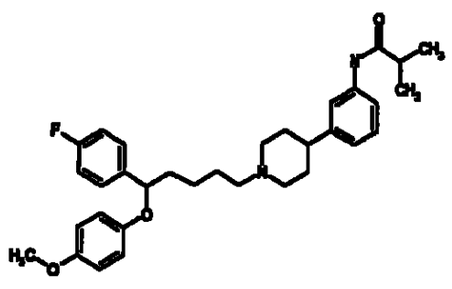
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1664

915  22.6

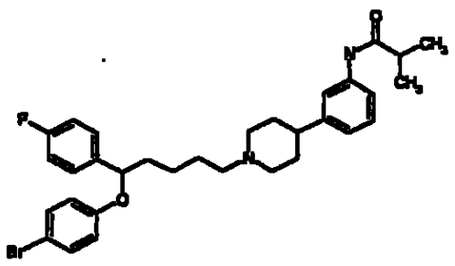
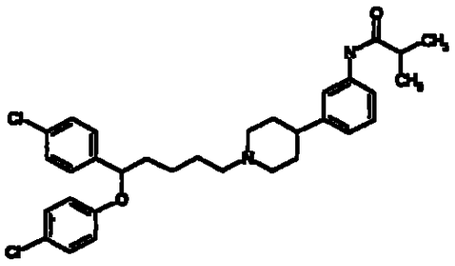
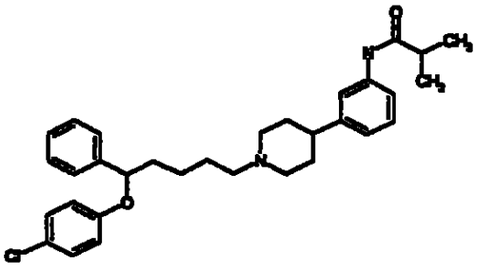
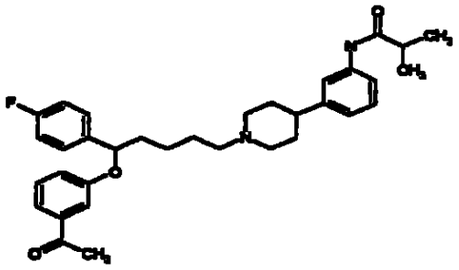
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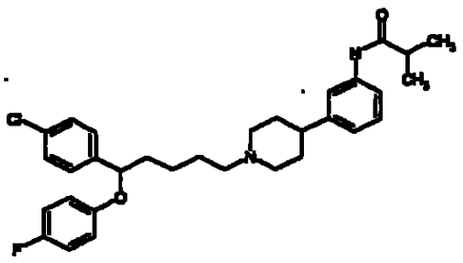
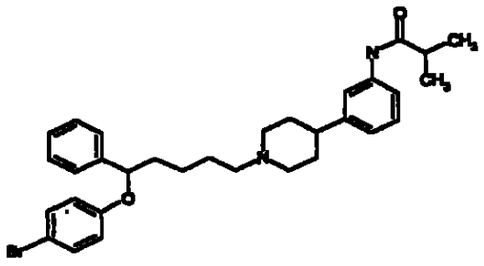
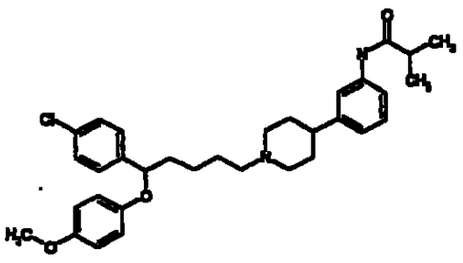
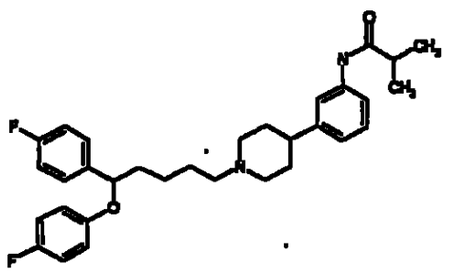
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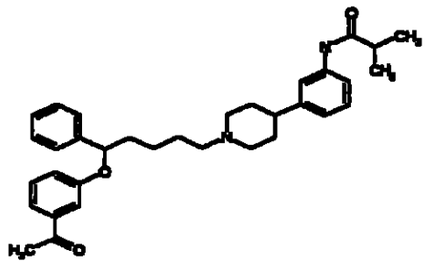
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920		6.9
921		6.6
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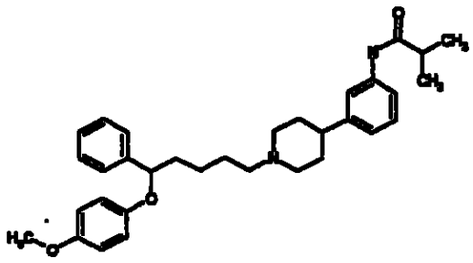
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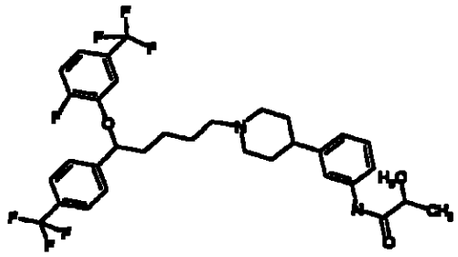
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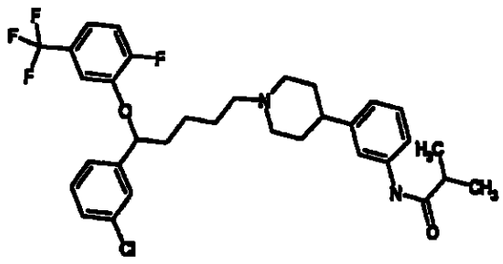
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924		13.1
925		13.4
926		1.4

1671
1667

927  60.7

928  14.9

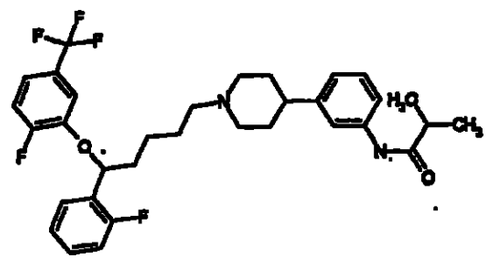
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930  14.6

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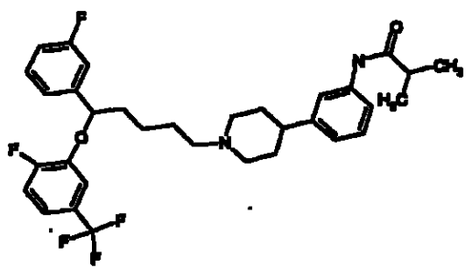
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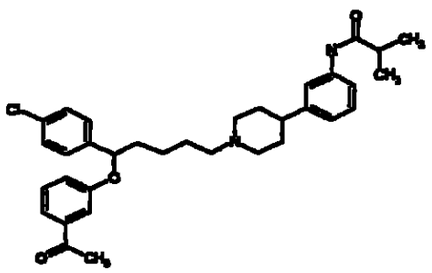
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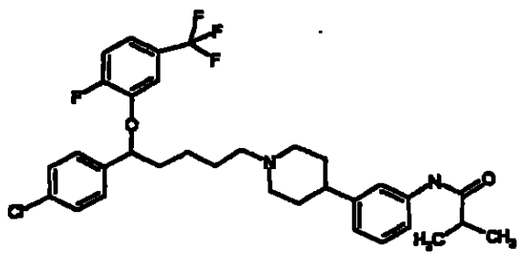
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933



10.9

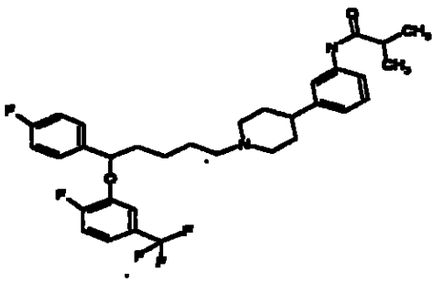
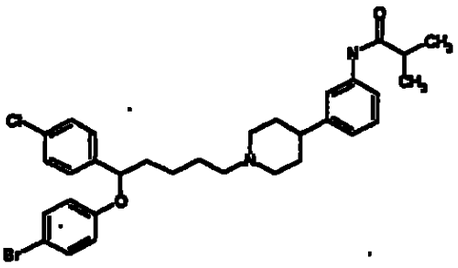
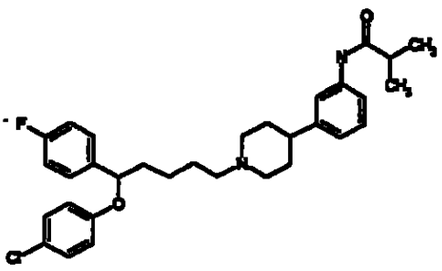
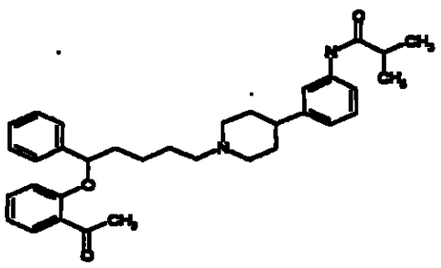
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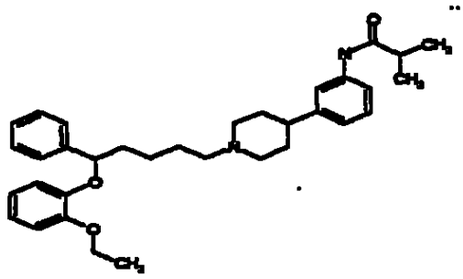
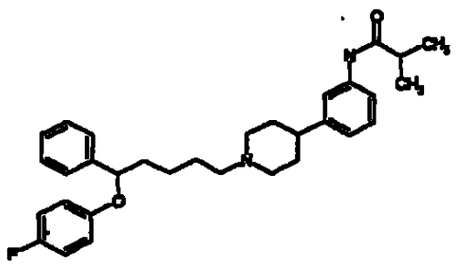
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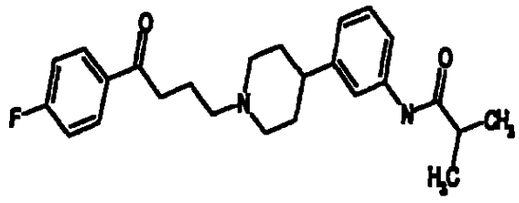
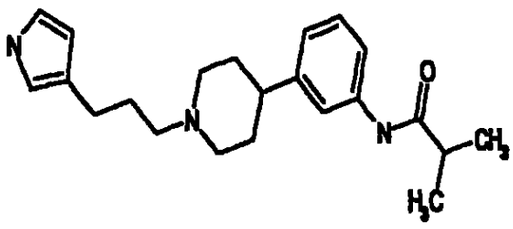
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935		19.7
936		11.6
937		28.4
938		608.6

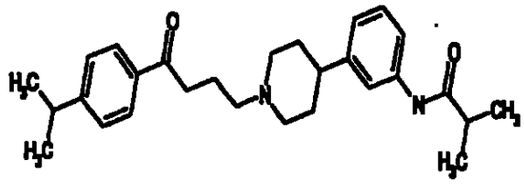
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939		82.0
940		1.8

EJEMPLO	ESTRUCTURA	rMCH1 Ki (nM)
941		15.2
942		187.9

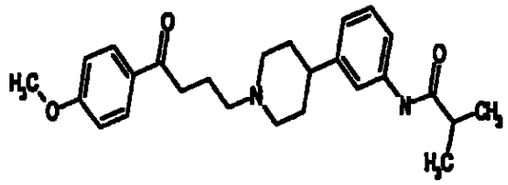
1675
1871

943



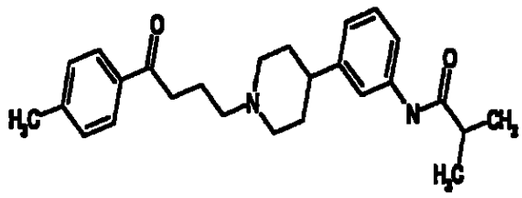
101.7

944



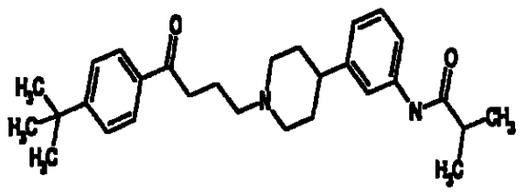
36.8

945



31.2

946

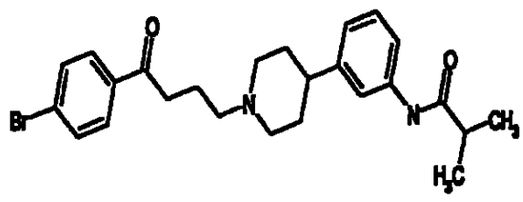


336.6

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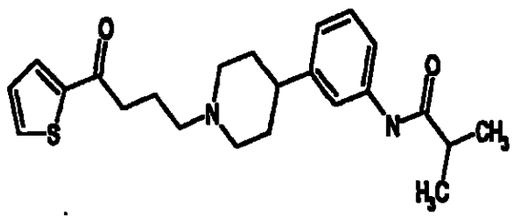
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947



4.3

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21.2

Tabla 2: Afinidades de aglutinamiento (Ki) en MCH1 de rata, Dopamina D2 humana, Histamina H1 humana y receptores Adrenérgicos Alfa-1a

Compuesto	rMCH1	hD2	hH1	hAlfa-1a
	Ki (nM)	*Ki (nM)*	*Ki (nM)*	*Ki (nM)*
1	90	6092	823	49
2	3.9	2839	700	32.1
3	766	ND	ND	ND
4	357	ND	ND	ND
5	14.2	1139	1618	9.1
6	274	ND	ND	ND
7	1000	ND	ND	ND
8	627	ND	ND	ND
9	69	1430	1733	26.4
10	2.8	862	461	19.4
11	197	ND	ND	ND
12	84	771	571	57
13	11.9	551	ND	61
14	167	ND	ND	ND
15	720	ND	ND	ND
16	272	ND	ND	ND
17	342	ND	ND	ND
18	29.5	782	ND	115
19	506	ND	ND	ND
20	21	470	ND	41.3
21	630	ND	ND	ND

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Tabla 2: Afinidades de aglutinamiento (Ki) en MCH1 de rata, Dopamina D2 humana, Histamina H1 humana y receptores Adrenérgicos Alfa-1a

22	52	5181	2277	284
23	1036	ND	ND	ND
24	67	1252	ND	127
25	463	ND	ND	ND
26	192	1977	ND	516
27	91	503	ND	130
28	511	ND	ND	ND
29	654	ND	ND	ND
30	382	ND	ND	ND
31	362	ND	ND	ND
32	160	ND	ND	ND
33	615	ND	ND	ND
34	651	ND	ND	ND
35	11.5	9654	2000	533
36	82	12,026	2454	1489
37	29.1	34,993	16,734	1067
38	18.2	>50000	6595	1592
39	11.8	>50000	6401	2937
40	50	7451	273	12.3
41	946	ND	ND	ND
42	116	ND	ND	ND
43	12	10,428	2560	434
44	11.5	8673	11,092	704

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Tabla 2: Afinidades de aglutinamiento (Ki) en MCH1 de rata, Dopamina D2 humana, Histamina H1 humana y receptores Adrenérgicos Alfa-1a

45	1.6	42.2	3.4	18
46	187	ND	ND	ND
47	52	>50000	36,907	>50000
48	6.7	735	6390	452
49	7.1	471	39.1	140
50	3.9	1077	304	161
51	3.1	152	130	33.5
52	3.8	244	264	13.2
53	7.1	191	1320	221
54	4.9	83	283	167
55	5	162	1100	125
56	22.3	435	32.5	55
57	16.6	41,994	48,958	3206
58	20.1	390	590	233
59	12.9	262	46.9	49.1
60	0.923	52	546	22.3
61	13.6	281	969	310
62	12.8	319	25,320	719
63	22.4	766	25,307	1058
64	14.8	313	6994	1142
65	17	331	9390	1720
66	3.3	132	3473	944
67	5.9	133	2146	511

Tabla 2: Afinidades de aglutinamiento (Ki) en MCH1 de rata, Dopamina D2 humana, Histamina H1 humana y receptores Adrenérgicos Alfa-1a

68	9.3	68	329	204
69	32.5	46.8	>50000	232
70	50	1050	7998	1521
71	6.8	119	1710	226
72	31.4	41,454	33,098	645
73	22.3	41,454	6522	381
74	48.6	39,511	1862	333
75	11.8	19,041	2844	2469
76	44.8	41,454	39,710	10,985
77	25.7	447	4178	167
78	22.2	37.6	>50000	1313
79	19.4	244	507	722
80	14.3	833	9789	620
81	377	ND	ND	ND
82	11.2	ND	ND	ND
83	48.1	ND	ND	ND
84	121	ND	ND	ND
85	3.2	2449	3816	3021

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V. Síntesis del Compuesto A

Enseguida se describe la síntesis del compuesto A. El compuesto A es el compuesto radioetiquetado que fue utilizado en los ensayos de enlace de radioligando descritos anteriormente.

N-[3-(1,2,3,6-TETRAHIDRO-4-PIRIDINIL)FENIL]ACETAMIDA: La reacción de una solución de Na_2CO_3 acuosa saturada (25mL), 4-{[(trifluorometil)sulfonil)oxi}-1,2,3,6-tetrahidro-1-piridin-carboxilato de tert-butilo 20 (mmol), ácido 3-acetamidofenilborónico (30 mmol) y tetrakis-trifenilfosfina paladio (0) (1.15 g) en dimetoxietano (40 mL) a temperatura de reflujo durante la noche dio 4-[3-(acetilamino)fenil]3,6-dihidro-1(2H)-piridincarboxilato. La desprotección del grupo BOC utilizando HCl en dioxano seguida de gasificación (pH 11-12), dio el producto deseado.

N-(3-BROMOPROPIL)CARBAMATO DE TERT-BUTILO: Esta se preparó a partir de bromohidrato de 3-bromopropilamina y BOC_2O en presencia de una base en diclorometano.

N-{3[1-(3-AMINOPROPIL)-1,2,3,6-TETRAHIDRO-4-PIRIDINIL]-FENIL}ACETAMIDA: La reacción de N-(3-bromopropil)carbamato de tert-butilo y N-[3-(1,2,3-tetrahidro-4-piridinil)fenil]acetamida en dioxano de reflujo con Bu_4NI

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catalítico y base como se describe en el Esquema A dió 3-(4-[3-(acetilamino)fenil]-3,6-dihidro-1(2H)-piridinil]propil-carbamato. La desprotección del grupo BOC utilizando HCl en dioxano seguida por gasificación (pH 11-12)dió el producto deseado.

(4S)-3-({[3-(4-[3-(ACETILAMINO)FENIL],-3,6-DIHIDRO-1(2H)-PIRIDINIL)PROPIL]AMINO}CARBONIL)-4-(3,4-DIFLUOROFENIL)-6-(METOXIMETIL)-2-OXO-1,2,3,4-TETRAHIDRO-5-PIRIMIDINCARBOXILATO DE METILO: Se preparó a partir de la reacción de (6S)-6-(3,4-difluorofenil)-4-(metoximetil)-2-oxo-3,6-dihidro-1,5(2H)-pirimidindicarboxilato de 5-metil 1-(4-nitrofenilo) (descrito en la Publicación de PCT No. WO 00/37026, publicada el 29 de junio del 2000) y N-{3-[1-(3-aminopropil)-1,2,3,6-tetrahidro-4-piridinil]fenil}acetamida: RMN ^{1}H 8.90 (t,1 H, J= 3.6 Hz), 7.75 (s, 1H), 7.50-7.00 (m,8 H), 6.68 (s, 1 H),6.03 (br s, 1H), 4.67 (s, 2 H), 3.71 (s, 3 H), 3.47 (s, 3H), 3.38 (ABm, 2 H), 3.16 (m, 2 H), 2.71 (t, 2 H, J= 5.4 Hz), 2.56 (m, 4 H), 2.35-1.90 (br, 2 H), 2.17 (s, 3 H), 1.82 (p, 2 H, J= 7.2 Hz); ESMS, 612.25 $(m + H)^{+}$.

(4S)-3-{[(3-{4-[3-(ACETILAMINO)FENIL]-1-PIPERIDINIL}-PROPIL)AMINO]CARBONIL}-4-(3,4-DIFLUOROFENIL)-6-(METOXIMETIL)-2-OXO-1,2,3,4-TETRAHIDRO-5-PIRIMIDINCARBOXILATO

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DE METILO TRITIADO ([^{3}H] COMPUESTO A): Esta síntesis radioquímica se llevo a cabo por Amersham Pharmacia Biotech Cardiff, Wales. Una solución metabólica de (4S)-3-({[3-(4-[3-(acetilamino)fenil]-3,6-dihidro-1(2H)-piridinil)propil]-amino}carbonil)-4-(3,4-difluorofenil)-6-(metoximetil)-2-oxo-1,2,3,4-tetrahidro-5-pirimidindicarboxilato de metilo se expusó a gas de tritio a una presión de 1 atmósfera en presencia de 5% de paladio en carbón con agitación durante al noche, para dar el ((+))-isómero (4S)-3-{[(3-{4-[3-(acetilamino)fenil]-1-piperidinil}-propil)amino]carbonil}-4-(3,4-difluorofenil)-6-(metoximetil)-2-oxo-1,2,3,4-tetrahidro-5-pirimidincarboxilato de metilo tritiado. Después se purificó por CLAP de fase inversa (Hypersil ODS, 4.6 x 100 mm, metanol H_2O:Et_3N 10:90:1 a 100:0:1 en 15 minutos a 1.0 mL/minuto con radioquímica y detección de UV), este producto se utilizó como un radioligando en los ensayos de enlace de MCH1: Este mismo procedimiento se llevó a cabo con gas de H2 en lugar de $^3H_2$ para producir la versión no radioactiva del Compuesto A.

VI. Métodos In Vivo

Los siguientes métodos *in vivo* se realizaron para predecir la eficiencia de los antagonistas de MCH1 para el tratamiento de obesidad (peso corporal 3 días y leche condensada endulzada), depresión (prueba de nado forzado),

ansiedad (prueba de interacción social), y desordenes urinarios (DIRC y CSTI).

Efectos de Antagonistas de MCH1 en Peso Corporal (3 Días)

Ratas macho de Long Evans (Charles River) con peso de 180-200 gramos, se alojaron en grupos de cuatro en un ciclo de luz/oscuridad de 12 horas con acceso libre a la comida y agua. Los compuestos prueba se administraron dos veces diariamente vía i.p. inyección, una hora antes del ciclo de oscuridad y dos horas antes de la luz, durante tres días. Todas las ratas se pesaron diariamente en cada inyección por la mañana. Todos los resultados se expresaron como peso corpóreo (gramos) ganado por día (medio ± SEM) y se analizaron por dos vías ANOVA. Los datos para cada punto de tiempo se analizaron por una vía ANOVA seguido por una prueba post hoc Newman-Keuls. Los datos se analizaron utilizando el GraphPad Prism (v2.01) (GrphPad Software, Inc., San Diego, CA). Todos los datos se presentan como medios ± S.E.M.

Efectos de Antagonistas MCH1 en Consumo de Leche Condensada Endulzada.

Ratón macho S57BL/6 (Charles River) con peso de 17-19 gramos al inicio de los experimentos se alojaron en grupos de cuatro o cinco en un ciclo de luz/oscuridad de

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doce horas con acceso libre a alimento y agua. Durante 7 días, los ratones se pesaron, se colocaron en cajas individuales y se les dejo beber leche condensada endulzada (Nestle, diluida 1:3 con agua) durante una hora, de 2-4 horas en el ciclo de luz. La cantidad de leche consumida se determinó al pesar la botella de leche antes y después de cada turno de bebida. En el día de prueba, los ratones recibieron inyecciones i.p. del Compuesto de Prueba (3,10 o 30 mg/kg en 0.01% de ácido láctico), vehículo (0.01% ácido láctico) de d-fenflur-amina (10 mg/kg en 0.01% ácido láctico) 30 minutos previos a la exposición de la leche. La cantidad de leche consumida en el día de prueba(en mls de leche/kg de peso corporal) se comparó al consumo de la línea basal para cada ratón determinada en 2 días previos. Los datos para cada punto de tiempo se analizaron por una vía ANOVA.

Prueba de Nado Forzado (FST) en la Rata.

Animales

Ratas macho Sprague-Dawley (Taconic Farms, NY) se utilizaron en todos los experimentos. Las ratas se alojaron 5 por cada caja y se mantuvieron en un ciclo luz-oscuridad 12:12-h. Las ratas se manejaron durante 1 minuto cada día durante 4 días previos a la prueba de comportamiento.

Administración del Fármaco.

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Los animales se asignaron aleatoriamente para recibir una administración i.p. simple de vehículo (2.5% EtOH/2.5% Tween-80), imipramina (control positivo; 60 mg/kg) o Compuesto de Prueba 60 minutos antes del inicio del periodo de prueba de 5 minutos. Todas las inyecciones se dieron utilizando una jeringa tuberculina de 1 cc con agujas de calibre 26 3/8 (Becton-Dickinson, VWR Scientific, Bridgeport, NJ). El volumen de la inyección fue de 1ml/kg.

Diseño Experimental

El procedimiento utilizado en este estudio fue similar a aquel previamente descrito (Porsolt et al., 1978), excepto la profundidad del agua que fue 31 cm en este procedimiento. La profundidad mayor en esta prueba previene a las ratas de soportarse por si mismas al tocar el fondo del cilindro con sus patas. Las sesiones de nado se conducen al colocar las ratas en cilindros de plexiglass en forma individual (altura 46 cm x 20 cm en diámetro) conteniendo una profundidad de 31 cm de agua a 23-25°C. Las pruebas de nado se condujeron siempre entre 900 y 1700 horas y consistieron de una prueba de acondicionamiento de 15 minutos iniciales, seguida 24 horas mas tarde por una prueba de 5 minutos. Los tratamientos del fármaco se administraron 60 minutos antes del período de prueba de 5 minutos. Seguido de todas las sesiones de nado, las ratas se retiraron de los

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cilindros, se secaron con toallas de papel y se colocaron en una caja caliente durante 15 minutos y se regresaron a sus cajas de hogar. Todas las sesiones de prueba se filmaron utilizando una cámara de vídeo a color y se registraron para apuntes más tarde.

Apuntes de Comportamiento

El comportamiento de la rata se evaluó a intervalos de 5 segundos durante la prueba de 5 minutos para un solo individuo quien se ocultó a las condiciones de tratamiento. Los comportamientos de puntuación fueron:

1. Inmovilidad- la rata permaneció flotando en el agua sin luchar y solamente hizo aquellos movimientos necesarios para mantener su cabeza por arriba del agua;
2. Escalado- la rata hizo movimientos activos con sus garras delanteras en y fuera del agua, usualmente dirigidas contra las paredes;
3. Nado- la rata hizo movimientos de nado activos, mas que los necesarios para meramente mantener su cabeza por arriba del agua, e.g., moviéndose alrededor en el cilindro; y
4. Buceo- el cuerpo entero de la rata se sumergió.

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Análisis de los Datos

Los datos de prueba de nado forzado (inmovilidad, nado, escalado, buceo) se sometieron a un modo ANOVA aleatorio y pruebas post hoc se condujeron utilizando la prueba de Newman-Keuls. Los datos se analizaron utilizando el GraphPad Prism (v2.01) (GraphPad Software, Inc., San Diego, CA.). Todos los datos se presentaron como medias ± S.E.M.

Prueba de Nado Forzado (FST) en el Ratón

Animales

Ratones DBA/2 (Taconic Farms, NY) se utilizaron en todos los experimentos. Los animales se alojaron 5 por caja en un ambiente controlado bajo un ciclo de luz:obscuridad de 12:12 horas. Los animales se manejaron 1 minuto cada día durante 4 días previos al experimento. Este procedimiento incluyó una alimentación forzada oculta con un tubo de alimentación de 1.5 pulgadas.

Administración del Fármaco

Se designaron animales para recibir una sola administració del vehículo (5% EtOH/5% Twwen -80): El Compuesto Prueba, o imipramina (60· mg/kg) por medio de alimentación forzada, 1 hora antes de la prueba de nado.

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Diseño Experimental

El procedimiento para la prueba de nado forzada en el ratón fue similar a aquella descrita anteriormente para la rata, con algunas modificaciones. El cilindro utilizado para la prueba fue una probeta con pico de 1 litro (10.5 cm de diámetro x 15 cm de altura) llena a 800 ml (10cm de profundidad) de agua a 23-25°C. Solamente se llevaron a cabo 5 minutos de prueba para cada ratón, entre 1300 y 1700 horas. Los tratamientos del fármaco se adminostararon 30-60 minutos antes del período de prueba de 5 minutos. Seguido de todas las sesiones de nado, los ratones se retiraron de los cilíndros, se secaron con toallas de papel y se colocaron en una caja caliente durante 15 minutos. Todas las sesiones de prueba se filmaron utilizando una cámara de vídeo a color Sony y se registraron para apuntes más tarde.

Apuntes de Comportamiento

El comportamiento durante 2-5 minutos de la prueba se visualizó en un monitor de TV y se anotó por el investigador. La inmovilidad de tiempo perdido total (animal flotando con solamente mínimos movimientos al permanecer a flote) y móvil (nadando, y movimientos mas hallá de aquellos requeridos para permanecer a flote) se registraron.

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Análisis de Datos

Los datos de prueba de nado forzado (tiempo de exhibición de inmovilidad, movilidad; segundos) se sometieron a un modo ANOVA aleatorio y pruebas post hoc se condujeron utilizando la prueba de Newman-Keuls. Se analizaron los datos utilizando el GraphPad Prism (v2.01) (GraphPad Software, Inc., San Diego, CA). Todos los datos se presenataron como media ± S.E.M.

Prueba de Interacción Social

Se dejaron aclimatar ratas a las instalaciones del cuidado del animal durante 5 días previos a la prueba. Los animales se manejaron durante 5 minutos por día. El diseño y procedimiento para la Prueba de Interacción Social se llevó a cabo como se describió previamente por Kennett, et al. (1997). En el primer día de prueba, a pares de ratas con igual peso (± 5%), desconocidas entre sí, se les dio tratamiento idéntico y se regresaron a sus cajas de hogar. Los animales se dividieron aleatoreamente en 5 grupos de tratamiento, con 5 pares por grupo, y se les dio uno de los siguientes tratamientos de i.p.: Compuesto de Prueba (10, 30 o 100 mg/kg), vehículo (1 ml/kg) o clorodiazepóxido (5 mg/kg). Se les aplicó dosis 1 hora antes de la prueba. Las ratas se colocaron subsecuentemente en una caja de prueba perspex blanca o arena (54 x 37 x 26 cm), cuyo piso estaba

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dividido en 24 cuadros iguales, durante 15 minutos. Se utilizó un acondicionador de aire para generar ruido de fondo y mantener el cuarto a aproximadamente 74°C. Todas las sesiones se videograbaron utilizando una cámara de filmación JVC (modelo GR-SZ1, Elmowood Park, NJ) con ya sea vídeocasetes TDK (última inscripción HG) o Sony de 30 minutos. Todas las sesiones se llevaron a cabo entre 1300-1630 horas. La interacción social, definida como aseo, olfateo, mordedura, boxeo, lucha, seguimiento y arrastramiento arriba o abajo, se anotaron utilizando un cronómetro (Sportsline modelo no. 226, 1/100 segundos de discriminabilidad). El número de episodios en que se erigió (animal completamente levantado sobre su cuerpo en sus miembros posteriores), aseo (lamedura, mordedura, arañazo, del cuerpo) y lavado de cara (i.e., manos se mueven reperidamente sobre la cara), y el número de cuadros cruzado se anotaron. No se anotó la interacción social pasiva (animales que cayeron junto a o sobre otro). Todos los comportamientos se clasificaron más tarde por un observador quien estaba oculto para el tratamiento de cada par. Al final de cada prueba, la caja se limpió completamente con toallas de papel humedecidas.

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Animales

Ratas macho albinas Sprague-Dawley (Taconic Faros, NY) se alojaron en pares bajo un ciclo de luz/oscuridad de 12 hr (luces en 0700 hrs) con acceso libre a alimento y agua.

Administración del Fármaco

El Compuesto de Prueba se disolvió en ya sea 100% de DMSO o 5% de ácido láctico, v/v (Sigma Chemical Co., St. Louis, MO). Clorodiazepóxido (Sigma Chemical Co., St. Louis, MO) se disolvió en agua doblemente destilada. El vehículo consistió de 50% de DMSO (v/v) o 100% de dimetilacetamida (DMA). Todas las soluciones del fármaco se desecharon al final del día de prueba. El volumen de la solución de fármaco administrado es de 1 ml/kg.

Análisis de Datos

Los datos de interacción social (tiempo de interacción, de alzado y cuadros cruzados) se sometieron a un modo ANOVA aleatorizado y pruebas post hoc se condujeron utilizando la prueba de Student-Newman-Keuls. Los datos se sometieron a una prueba de normalidad (Prueba de Shapiro-Wilk): Los datos se analizaron utilizando el programa GBSTAT, versión 6.5 (Dynamics Microsystems, Inc., Silver spring, MD, 1997).

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Modelos In Vivo del Reflejo de Orinar

Los efectos del compuesto en el reflejo de orinar se clasificaron en la "contracción rítmica inducida por distensión" (DIRC), como se describe en las publicaciones previas (e.g., Maggi et al, 1987; Morikawa et al, 1992), y modelos de Infusión Transvesicular Lenta Continua (CSTI) en ratas.

Modelo DIRC

Ratas hembra Sprague Dawley que pesaron aproximadamente 300 g, se anestesiaron con uretano en forma subcutánea (1.2 g/kg). Se empleo una cánula en la tráquea con tubo PE240 para proporcionar un claro paso de aire en todo el experimento. Se hizo una incisión abdominal de línea media y los úteros izquierdo y derecho se aislaron. Los uréteres se ligaron en forma distal (para prevenir escape de fluidos de la vejiga) y se utilizó una cánula próxima con tubo PE10. La incisión se cerro utilizando suturas de seda 4-0, dejando las líneas del PE10 con ruta al exterior para la eliminación de orina. Se utilizó una cánula en la vejiga vía la ruta transuretral utilizando un tubo PE50 insertado 2.5 cm más allá de la abertura uretral. Esta cánula se aseguró a la cola utilizando una cinta y se conectó a un transductor de presión. Para prevenir fuga de la vejiga, la

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cánula se ligó en forma ajustada al exterior de la abertura uretral utilizando seda 4-0.

Para iniciar el reflejo de la orina, la vejiga primero se vació al aplicar presión al abdomen bajo, y después se lleno con una solución salina normal en incrementos de 100 (máximo = 2 ml) hasta las contracciones espontáneas de la vejiga ocurrieron (típicamente 20-40 mmHg a una razón de una contracción cada 2 o 3 minutos. Una vez que un ritmo regular se establece, el vehículo (solución salina) o Compuestos de Prueba se administraron vía i.v. o i.p. para explorar sus efectos en la actividad de la vejiga. El antagonista 5-HT_{1A} WAY-100635, se dio como un control positivo. Los datos se expresaron como intervalo de contracción 8en segundos) antes de la aplicación del fármaco (basal), o después de la aplicación del vehículo o artículo de prueba.

Modelo de Rata de Infusión transvesicular lenta Continua (CSTI)

Ratas hembra Sprague Dawley que pesaron aproximadamente 300 g, se utilizaron para el estudio. Las ratas se anestesiaron con pentobarbiton- sodio (50 mg/kg, i.p.). A través de una incisión abdominal media, la vejiga se expuso y se introdujo una cánula de polietileno (PE 50)

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en la vejiga a través de un pequeño corte en el domo de la vejiga y la cánula se aseguró con una sutura de cuerda con bolsa. El otro extremo de la cánula se exteriorizó en forma subcutánea en el área de cuello dorsal. Similarmente otra cánula (PE 50) se introdujo en el estómago a través de una incisión abdominal paramedia con el extremo libre exteriorizado en forma subcutánea a la región del cuello. Las heridas quirúrgicas se cerraron con sutura de seda 4-0 y se dejó que el animal se recuperara con cuidado post-quirúrgico apropiado. Al siguiente día, se colocó el animal en un contenedor de rata. El extremo abierto de la cánula de la vejiga se conectó al transductor de presión así como a la bomba de infusión a través de una llave de paso de tres vías. Los ciclos de vaciar la vejiga se iniciaron por infusión continua de solución salina normal a razón de 100 l/min. Las contracciones de vaciado repetidas se registraron en software de adquisición de datos en línea Power Lab. Después de registrar el patrón de vaciado basal durante una hora, el fármaco de prueba o vehículo se administró directamente en el estómago a través de catéter intragástrico y los ciclos de vaciado se monitorearon durante 5 horas. La presión y frecuencia de orinar se calcularon antes y después del tratamiento (a intervalos de cada 30 minutos) para cada animal. La capacidad de la vejiga se calculó a partir de la frecuencia de orinar, basado en la

infusión constante de 100 l/min. El efecto del fármaco de prueba se expresó como un porcentaje de la capacidad de la vejiga al pre-fármaco, basal. WAY 100635 se utilizó como control positivo para comparación.

Resultados In Vivo

Tabla 2

Efecto del antagonista MCH1 (Ejemplo No.) en los siguientes modelos *in vivo*: Peso corporal en 3 días (3D BW), ratón con Leche Condensada endulzada (mSwCM), ratón con Prueba de Nado Forzado (mFST), rata con Prueba de Nado Forzado (rFST), modelo DIRC, o modelo CSTI.

Ejemplo No.	3D BW	mSwCM	mFST	rFST	DIRC	CSTI
2	A	B	C	D	E	F
10	No Terminado	No Terminado	C	No Terminado	E	F
39	A	B	C	D	E	No Terminado
43	No Terminado	B	No Terminado	No Terminado	No Terminado	No Terminado
44	No Terminado	No Terminado	C	No Terminado	No Terminado	No Terminado
89	No Terminado	B	Sin efecto	No Terminado	No Terminado	No Terminado
90	No Terminado	Sin efecto	Sin efecto	No Terminado	No Terminado	No Terminado
91	No Terminado	No Terminado	Sin efecto	No Terminado	E	F
93	No Terminado	No Terminado	C	No Terminado	No Terminado	No Terminado
95	No Terminado	B	Sin efecto	No Terminado	No Terminado	No Terminado

99	A	No Terminado	Sin efecto	No Terminado	E	F
105	No Terminado	B	C	No Terminado	No Terminado	No Terminado
106	No Terminado	B	C	No Terminado	E	F
112	No Terminado	No Terminado	Sin efecto	No Terminado	No Terminado	No Terminado
116	A	No Terminado	C	No Terminado	E	F

A= Produjo una reducción significante en la ganancia de peso respecto a los controles tratados de vehículo.

B= Produjo una disminución significante en el consumo de leche respecto a los controles tratados de vehículo.

C= Produjo una disminución significante en inmovilidad respecto a los animales tratados con vehículo cuando se administró en forma oral.

D= Produjo una disminución significante en inmovilidad o un incremento significante en la actividad de nado respecto a los animales tratados con vehículo.

E= Produjo un incremento significante en el intervalo de contracción respecto al intervalo de pre-fármaco.

F= Produjo un incremento en la capacidad de la vejiga en ratas respecto a la capacidad de la línea basal.

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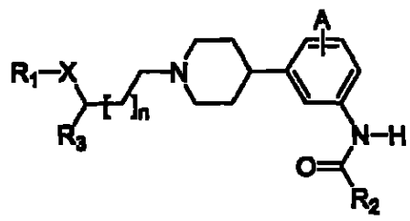
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REIVINDICACIONES

1. Un compuesto que tiene la estructura



;

en donde R_1 es hidrógeno, monofluoroalquilo, polifluoroalquilo o alquilo de C_1-C_7 de cadena recta o ramificada, arilo o heteroarilo, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más de -F, -Cl, Br-, -I, -CN, -NO_2, -CH_3, CF_3, -$COCH_3$, -CO_2R_3, fenil, fenoxi o alquilo de C_1-C_7 de cadena recta o ramificada;

en donde R_2 es ciclopropilo o alquilo de C_3-C_4 de cadena recta o ramificada;

en donde R_3 es arilo o heteroarilo, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más de F, -Cl, -Br, -I, -CN,-NO_2, alquilo de C_1-C_7 de cadena recta o ramificada;

en donde A es -H, -F, -Cl, -Br, -CN, -NO_2, -COR_3, -CO_2R_3, monofluoroalquilo, polifluoralquilo o alquilo de C_1-C_7 de cadena recta o ramificada;

en donde X es O o NH; y

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en donde n es un número entero de 0 a 5, inclusive.

2. El compuesto de conformidad con la reivindicación 1, en donde R_1 es arilo opcionalmente sustituido con uno o más de -F, -Cl, -Br, -I, -CN, $-NO_2$, $-COCH_3$, $-CO_2R_2$, o alquilo de C_1-C_7 de cadena recta o ramificada;

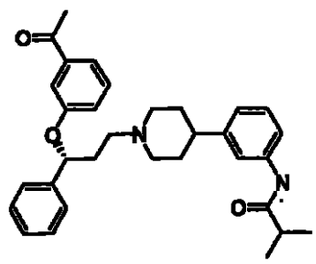
en donde R_3 es fenilo;

en donde A es H; y

en donde X es O.

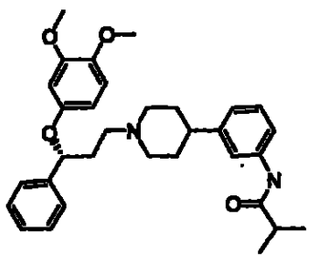
3. El compuesto de acuerdo con la reivindicación 2, en donde R_2 es isopropilo.

4. El compuesto de acuerdo con la reivindicación 3, en donde el compuesto tiene la estructura:



5. El compuesto de acuerdo con la reivindicación 3, en donde el compuesto tiene la estructura:

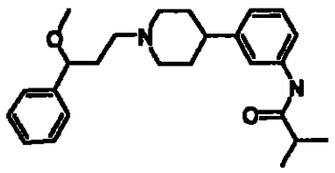
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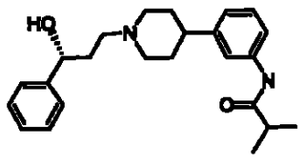
6. El compuesto de acuerdo con la reivindicación 1, en donde R_1 es hidrógeno, alquilo de C_1-C_7 de cadena recta o ramificada; y en donde R_3 es arilo.

7. El compuesto de acuerdo con la reivindicación 6, en donde R_2 es isopropilo; y A es hidrógeno.

8. El compuesto de acuerdo con la reivindicación 7, en donde el compuesto tiene la estructura:

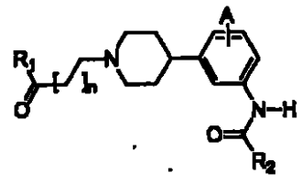


9. El compuesto de la reivindicación 7, en donde el compuesto tiene la estructura:



10. El compuesto que tiene la estructura:

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en donde R_1 es arilo o heteroarilo opcionalmente sustituido con uno o más de -F, -Cl, Br-, -I, -CN, $-NO_2$, $-OCH_3$, fenoxi, ciclopentanilo fusionado, monofluoroalquilo, polifluoroalquilo o alquilo de C_1-C_7 de cadena recta o ramificada;

en donde R_2 es ciclopropilo o alquilo de C_1-C_4 de cadena recta o ramificada;

en donde A es -H, -F, -Cl, Br-, -CN, $-NO_2$, monofluoroalquilo, polifluoroalquilo, o alquilo de C_1-C_7 de cadena recta o ramificada; y

en donde n es un número entero de 1 a 5, inclusive.

11. El compuesto de acuerdo con la reivindicación 10, en donde R_1 es arilo opcionalmente sustituido con uno o más de -F, -Cl, Br-, -I, o alquilo de C_1-C_4 de cadena recta o ramificada; y

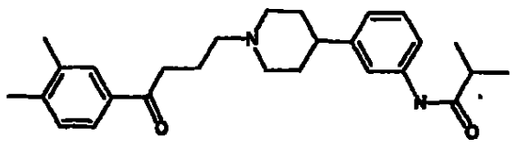
en donde A es H.

12. El compuesto de acuerdo con la reivindicación 11, en donde R_2 es isopropilo; y

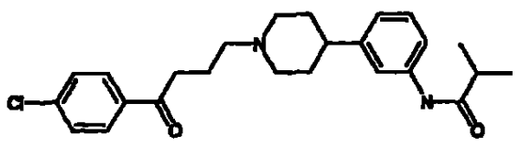
en donde n es 2.

13. El compuesto de acuerdo con la reivindicación 12, en donde el compuesto tiene la estructura:

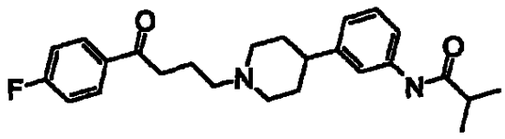
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14. El compuesto de acuerdo con la reivindicación 12, en donde el compuesto tiene la estructura:



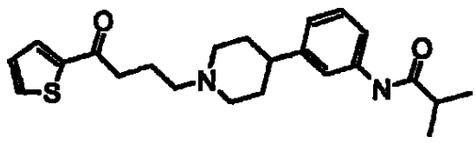
15. El compuesto de acuerdo con la reivindicación 12, en donde el compuesto tiene la estructura:



16. El compuesto de acuerdo con la reivindicación 10, en donde R_1 es tienilo, y en donde A es H.

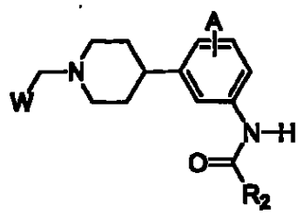
17. El compuesto de acuerdo con la reivindicación 16, en donde R_2 es isopropilo.

18. El compuesto de acuerdo con la reivindicación 17, en donde el compuesto tiene la estructura:



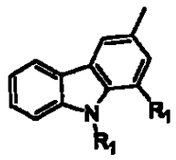
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19. Un compuesto que tiene la estructura:

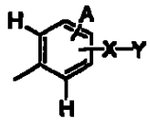


;

en donde W es



o



;

en donde cada R_1 es independientemente hidrógeno, metilo o etilo;

en donde R_2 es ciclopropilo o alquilo de C_3-C_4 de cadena recta o ramificada;

en donde R_3 es hidrógeno, arilo o heteroarilo, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más de -H, -F, -Cl, -Br, -I, CN, $-NO_2$, alquilo de C_1-C_7 de cadena recta o ramificada;

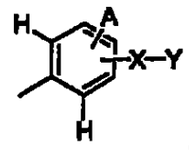
en donde cada A es independientemente -H, -F, -Cl, -Br, -CN, $-NO_2$, $-COR_3$, $-CO_2R_3$, monofluoroalquilo, polifluoroalquilo o alquilo de C_1-C_7 de cadena recta o ramificada;

en donde X es O, NR_3, CO o puede estar ausente; y

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en donde Y es hidrógeno, arilo o heteroarilo, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más de -F, -Cl, -Br, -I, -CN, $-NO_2$, alquilo de C_1-C_7 de cadena recta o ramificada.

20. El compuesto de acuerdo con la reivindicación 19, en donde W es

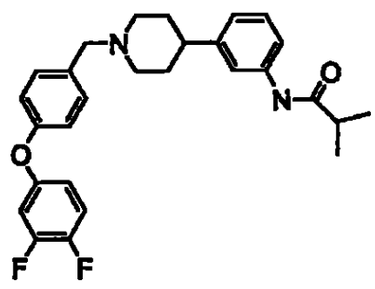


;

y en donde X es O o puede estar ausente.

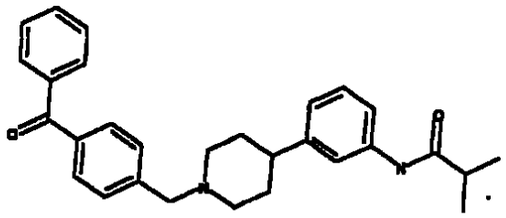
21. El compuesto de la reivindicación 20, en donde R_2 es isopropilo.

22. El compuesto de la reivindicación 21, en donde el compuesto tiene la estructura:

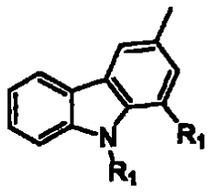


23. El compuesto de la reivindicación 21, en donde el compuesto tiene la estructura:

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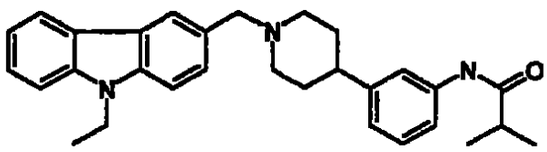
24. El compuesto de acuerdo con la reivindicación 19, en donde W es



25. El compuesto de acuerdo con la reivindicación 24, en donde A es -H, -F, -Cl, -Br.

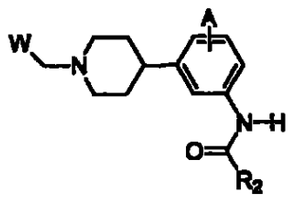
26. El compuesto de acuerdo con la reivindicación 25, en donde R_2 es isopropilo; y A es hidrógeno.

27. El compuesto de acuerdo con la reivindicación 26, en donde el compuesto tiene la estructura:



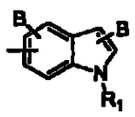
28. Un compuesto que tiene la estructura:

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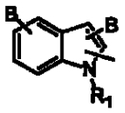


;

en donde W es



o



en donde R_1 es hidrógeno, alquilo de C_1-C_7 de cadena recta o ramificada, arilo o heteroarilo, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más de -F, -Cl, -Br, -CN, -NO_2, -OCH_3, -CO_2CH_3, -CF_3, fenilo, alquilo de C_1-C_7 de cadena recta o ramificada;

en donde R_2 es ciclopropilo o alquilo de C_3-C_4 de cadena recta o ramificada;

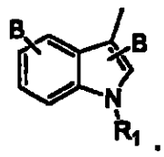
en donde A es -H, -F, -Cl, -Br, -CN, -NO_2, -COR_1, -CO_2R_1, monofluoroalquilo, polifluoroalquilo, alquilo de C_1-C_7 de cadena recta o ramificada, o fenilo;

en donde cada B es independientemente -H, -F, -Cl, -Br, -I, -CN, -NO_2, -COR_1, -CO_2R_1, -OCH_3, OCF_3, -CF_3, monofluoroalquilo, polifluoroalquilo, o alquilo de C_1-C_7 de cadena recta o ramificada o arilo, fenoxi o benciloxi, en donde el arilo, fenoxi o benciloxi esta opcionalmente sustituido con uno o más de -F, -Cl, -Br, -CN, -NO_2, -

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COR_1, $-CO_2R_1$, $-OCH_3$, OCF_3, $-CF_3$, o alquilo de C_1-C_7 de cadena recta o ramificada.

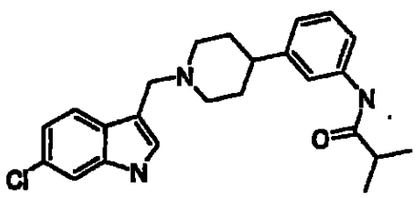
29. El compuesto de la reivindicación 28, en donde W es



30. El compuesto de la reivindicación 29, en donde R_1 es hidrógeno o fenilo opcionalmente sustituido con uno o más de -F, -Cl, -Br, -CN, $-NO_2$, alquilo de C_1-C_7 de cadena recta o ramificada.

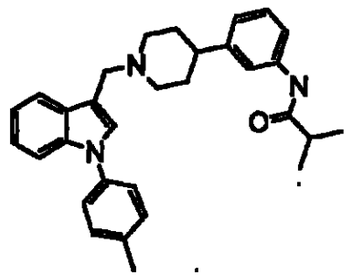
31. El compuesto de acuerdo con la reivindicación 30, en donde R_2 es isopropilo.

32. El compuesto de la reivindicación 31, en donde el compuesto tiene la estructura:

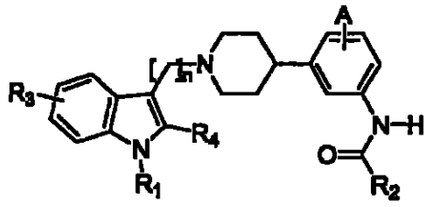


33. El compuesto de la reivindicación 31, en donde el compuesto tiene la estructura:

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34. Un compuesto que tiene la estructura:



en donde R_1 es hidrógeno, alquilo de C_1-C_7 de cadena recta o ramificada, arilo o heteroarilo, en donde el arilo o heteroarilo esta opcionalmente sustituido con uno o más de -F, -Cl, Br-, -CN, -NO_2, CF_3, -OCH_3, alquilo de C_1-C_3 de cadena recta o ramificada;

en donde R_2 es ciclopropilo o alquilo de C_3-C_4 de cadena recta o ramificada;

en donde R_3 es -H, -F, -Cl, Br-, -I, -CN, -NO_2, CF_3, -OCH_3, monofluoroalquilo, polifluoroalquilo o alquilo de C_1-C_3 de cadena recta o ramificada, o un anillo de fenilo fusionado a C_5 y C_7 de la porción de indol;

en donde R_4 es hidrógeno o arilo opcionalmente sustituido con uno o mas de -F, -Cl, Br-, -I, -CN, -NO_2, CF_3, alquilo de C_1-C_3 de cadena recta o ramificada;

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en donde A es -H, -F, -Cl, Br-, -CN, $-NO_2$, monofluoroalquilo, polifluoroalquilo o alquilo de C_1-C_7 de cadena recta o ramificada; y

en donde n es un número entero de 2 a 4, inclusive.

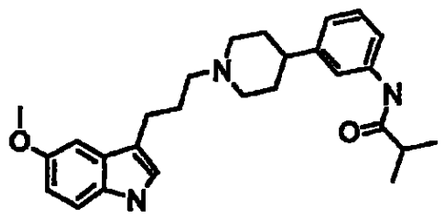
35. El compuesto de la reivindicación 34, en donde R_3 es -H, -F, -Cl, Br-, -I, -CN, $-NO_2$, $-OCF_3$ o $-OCH_3$; y

en donde R_4 es hidrógeno o fenilo opcionalmente sustituido con uno o más de -F, -Cl o $-CF_3$.

36. El compuesto de la reivindicación 35, en donde R_1 es hidrógeno o fenilo opcionalmente sustituido con uno o más de -F, -Cl, Br-, -CN, $-NO_2$, $-CF_3$, $-OCH_3$ o alquilo de C_1-C_3 de cadena recta o ramificada.

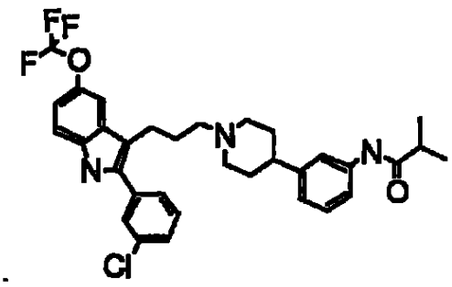
37. El compuesto de acuerdo con la reivindicación 36, en donde R_2 es isopropilo.

38. El compuesto de acuerdo con la reivindicación 37, en donde el compuesto tiene la estructura:

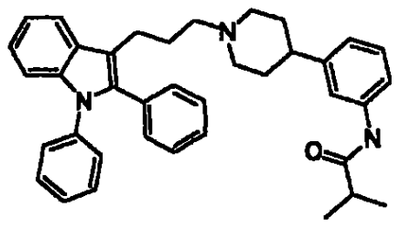


39. El compuesto de acuerdo con la reivindicación 37, en donde el compuesto tiene la estructura:

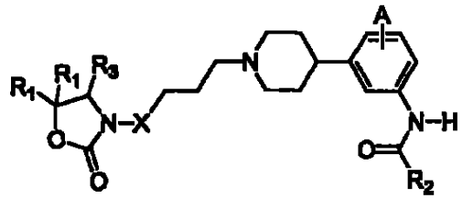
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40. El compuesto de acuerdo con la reivindicación 37, en donde el compuesto tiene la estructura:



41. Un compuesto que tiene la estructura:



en donde cada R_1 es independientemente hidrógeno o CH_3;

en donde R_2 es ciclopropilo o alquilo de C_1-C_4 de cadena recta o ramificada;

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en donde R_3 es bencilo o fenilo, en donde el bencilo o fenilo esta opcionalmente sustituido con un grupo metilendioxi o uno o más de -F o -Cl;

en donde A es -H, -F, -Cl, -Br, -CN, $-NO_2$, monofluoroalquilo, polifluoralquilo o alquilo de C_1-C_7 de cadena recta o ramificada;

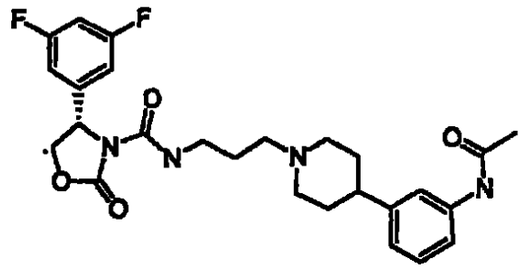
en donde X es $(CH_2)_2$, $COCH_2$ o CONH.

42. El compuesto de acuerdo con la reivindicación 41, en donde R_3 es fenilo opcionalmente sustituido con uno o más de -F; y en donde A es hidrógeno.

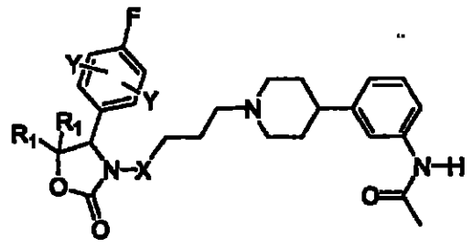
43. El compuesto de acuerdo con la reivindicación 42, en donde X es CONH.

44. El compuesto de acuerdo con la reivindicación 43, en donde R_2 es metilo.

45. El compuesto de acuerdo con la reivindicación 44, en donde el compuesto tiene la estructura:

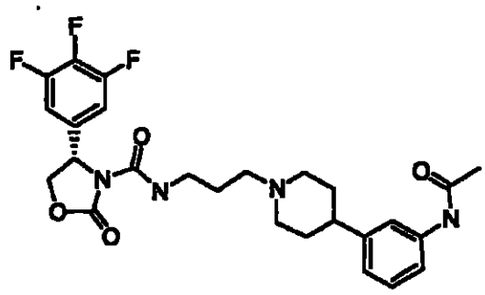


46. El compuesto de acuerdo con la reivindicación 44, en donde el compuesto tiene la estructura:

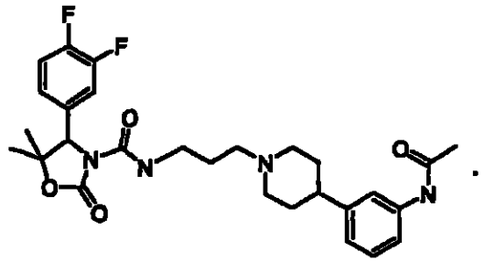


en donde cada Y es independientemente hidrógeno o -F.

47. El compuesto de acuerdo con la reivindicación 46, en donde el compuesto tiene la estructura:



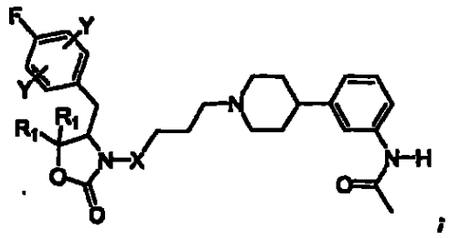
48. El compuesto de acuerdo con la reivindicación 46, en donde el compuesto tiene la estructura:



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49. El compuesto de acuerdo con la reivindicación 41, en donde R_3 es bencilo opcionalmente sustituido con un grupo metilendioxi o uno o más de -F o -Cl.

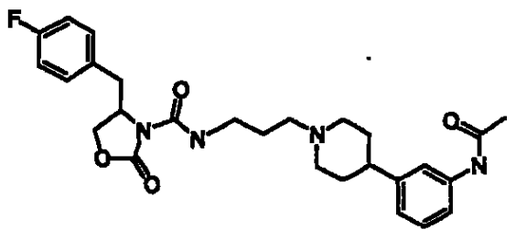
50. El compuesto de la reivindicación 49, en donde el compuesto tiene la estructura:



;

en donde cada Y es independientemente hidrógeno o -F.

51. El compuesto de acuerdo con la reivindicación 50, en donde el compuesto tiene la estructura:



52. Un compuesto de acuerdo con las reivindicaciones 1 a 51, en donde el compuesto es enantioméricamente puro.

53. Un compuesto de acuerdo con las reivindicaciones 1 a 51, en donde el compuesto es diastereoméricamente puro.

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54. El compuesto de acuerdo con las reivindicaciones 52 y 53, en donde el compuesto es enantiomérica y diastereoméricamente puro.

55. Una composición farmacéutica que comprende una cantidad terapéutica de un compuesto de cualquiera de las reivindicaciones 1 a 51 y un portador farmacéuticamente aceptable.

56. La composición farmacéutica de acuerdo con la reivindicación 55, en donde la cantidad del compuesto es desde aproximadamente 0.01 mg a aproximadamente 500 mg. otro por

57. La composición farmacéutica de acuerdo con la reivindicación 56, en donde la cantidad del compuesto es desde aproximadamente 0.1 mg a aproximadamente 60 mg.

58. La composición farmacéutica de acuerdo con la reivindicación 57, en donde la cantidad del compuesto es desde aproximadamente 1 mg a aproximadamente 20 mg.

59. La composición farmacéutica de acuerdo con la reivindicación 55, en donde el portador es un líquido y la composición es una solución.

60. La composición farmacéutica de acuerdo con la reivindicación 55, en donde el portador es un sólido y la composición es una tableta.

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61. La composición farmacéutica de acuerdo con la reivindicación 55, en donde el portador es un gel y la composición es un supositorio.

62. Un proceso para manufacturar una composición farmacéutica que comprende mezclar una cantidad terapéuticamente efectiva del compuesto de cualquiera de las reivindicaciones 1 a 51 y un portador farmacéutica mente aceptable.

63. Un método para tratar un sujeto que sufre de un desorden seleccionado del grupo que consiste de depresión, ansiedad, incontinencia persistente, u obesidad, que comprende administrar al sujeto una cantidad terapéuticamente efectiva del compuesto de cualquiera de las reivindicaciones 1 a 51.

64. El método de acuerdo con la reivindicación 63, en donde la cantidad terapéuticamente efectiva está entre aproximadamente 0.03 y aproximadamente 1000 mg por día.

65. El método de acuerdo con la reivindicación 64, en donde la cantidad terapéuticamente efectiva está entre aproximadamente 0.30 y aproximadamente 300 mg por día.

66. El método de acuerdo con la reivindicación 65, en donde la cantidad terapéuticamente efectiva está entre aproximadamente 1.0 y aproximadamente 100 mg por día.

67. El método de acuerdo con la reivindicación 63, en donde el desorden es depresión.

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68. El método de acuerdo con la reivindicación 63, en donde el desorden es ansiedad.

69. El método de acuerdo con la reivindicación 63, en donde el desorden es obesidad.

70. El método de acuerdo con la reivindicación 63, en donde el desorden es incontinencia persistente.

71. Un método para reducir la masa corpórea de un sujeto que comprende administrar al sujeto una cantidad de un compuesto de cualquiera de las reivindicaciones 1 a 51, efectiva para reducir la masa corpórea del sujeto.

72. Un método para tratar un sujeto que sufre de depresión, que comprende administrar al sujeto una cantidad de un compuesto de cualquiera de las reivindicaciones 1 a 51, efectiva para tratar la depresión del sujeto.

73. Un método para tratar un sujeto que sufre de ansiedad, el cual comprende administrar al sujeto una cantidad de un compuesto de cualquiera de las reivindicaciones 1 a 51, efectiva para tratar la ansiedad del sujeto.

74. Un método para aliviar la incontinencia urinaria persistente en un sujeto que sufre de una vejiga demasiado activa, que comprende administrar al sujeto una cantidad del compuesto de cualquiera de las reivindicaciones 1 a 51, efectiva para aliviar la incontinencia urinaria persistente del sujeto.

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75. Un método para manejar la obesidad en un sujeto que necesita perder peso, el cual comprende administrar al sujeto una cantidad de un compuesto de cualquiera de las reivindicaciones 1 a 51, efectiva para inducir la pérdida de peso en el sujeto.

76. Un método para manejar la obesidad en un sujeto quien ha experimentado pérdida de peso, el cual comprende administrar al sujeto una cantidad de un compuesto de cualquiera de las reivindicaciones 1 a 51, efectiva para mantener tal pérdida de peso en el sujeto.

77. Un método para tratar una vejiga demasiado activa en un sujeto, el cual comprende administrar al sujeto una cantidad de un compuesto de cualquiera de las reivindicaciones 1 a 51, efectiva para tratar la vejiga demasiado activa del sujeto.

78. Un método para tratar un desorden en un sujeto, en donde los síntomas del sujeto se pueden aliviar mediante el tratamiento con un antagonista de MCH1, en donde el antagonista es el compuesto de cualquiera de las reivindicaciones 1 a 51.

79. Un método para aliviar los síntomas de un desorden en un sujeto, el cual comprende administrar al sujeto una cantidad de un antagonista de MCH1, efectiva para aliviar los síntomas, en donde el antagonista MCH1 es el compuesto de cualquiera de las reivindicaciones 1 a 51.

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Resumen

Esta invención está dirigida a compuestos que son antagonistas selectivos para los receptores de la hormona-1 de concentración de melanina (MCH1). La invención proporciona una composición farmacéutica que comprende una cantidad terapéuticamente efectiva del compuesto de la invención y un portador farmacéuticamente aceptable. Esta invención proporciona una composición farmacéutica elaborada al combinar una cantidad terapéuticamente efectiva del compuesto de esta invención y un portador farmacéuticamente aceptable. Esta invención además proporciona un proceso para la manufactura de una composición farmacéutica que comprende combinar una cantidad terapéuticamente efectiva del compuesto de la invención y un portador farmacéuticamente aceptable.

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PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: JOHN P. WHITE
COOPER & DUNHAM LLP
1185 AVENUE OF THE AMERICAS
NEW YORK, NEW YORK 10036

OCT - 2 2003

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing (day/month/year)	26 SEP 2003

Applicant's or agent's file reference	IMPORTANT NOTIFICATI N
85369-B-PCT	

International application No.	International filing date (day/month/year)	Priority Date (day/month/year)
PCT/US02/21065	08 JULY 2002	06 JULY 2001

Applicant
SYNAPTIC PHARMACEUTICAL CORPORATION

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

1/5/04 SMC

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	CELIA CHANG Valerie Ball-Hanno for
Facsimile No. (703) 305-3230	Telephone No. (703) 308-1235

Form PCT/IPEA/416 (July 1992)*

17/24 1728

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 65369-B-PCT	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US02/21068	International filing date *(day/month/year)* 08 JULY 2002	Priority date *(day/month/year)* 06 JULY 2001
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant SYNAPTIC PHARMACEUTICAL CORPORATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

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

- I [X] Basis of the report
- II [ ] Priority
- III [ ] Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV [ ] Lack of unity of invention
- V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI [ ] Certain documents cited
- VII [ ] Certain defects in the international application
- VIII [ ] Certain observations on the international application

Date of submission of the demand	Date of completion of this report
22 JANUARY 2003	05 SEPTEMBER 2003
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer Valerie Bell-Harrison CELIA CHANG
Facsimile No. (703) 305-3230	Telephone No. (703) 308-1235

Form PCT/IPEA/409 (cover sheet) (July 1998)*

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US02/21063

I. Basis of the report

1. With regard to the elements of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-749, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of

[X] the claims:
pages 750-768, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of

[X] the drawings:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of

[X] the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE
[X] the claims, Nos. NONE
[X] the drawings, sheets/fig NONE

5. [ ] This report has been drawn as if (some of) the amendments 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)).**

** 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 since they do not contain amendments (Rules 70.16 and 70.17).*

*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US02/21068

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)	**Claims**	1-79	**YES**
	Claims	NONE	**NO**
Inventive Step (IS)	**Claims**	1-79	**YES**
	Claims	NONE	**NO**
Industrial Applicability (IA)	**Claims**	1-79	**YES**
	Claims	NONE	**NO**

2. **citations and explanations (Rule 70.7)**

Claims 1-79 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the claimed compounds, composition or their use because the relevant reference WO 02/08744 is published after filing of the case.

NEW CITATIONS

NONE

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US98/21063

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(7): IPC7 A61K 31/445; C07D 211/30, 211/94, 401/06, 401/12, 403/06, 403/12 and US Cl.: 514/323, 326; 546/200, 201, 209, 212

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TRATADO DE COOPERACION EN MATERIA DE PATENTES

PCT

REPORTE DE EXAMEN PRELIMINAR INTERNACIONAL

(Artículo 36 y Regla 70 del PCT)

Referencia de archivo de la solicitante o apoderado: 65369-B-PCT	PARA UNA ACCION ADICIONAL — Véase la Notificación de Transmisión del Reporte de Examen Preliminar Internacional (Forma PCT/IPEA/416)	
Solicitud internacional No.: PCT/US02/21063	Fecha de presentación internacional *(día/mes/año)*: 03 JULIO 2002	Fecha de prioridad *(día/mes/año)*: 05 JULIO 2001
Clasificación Internacional de Patente (CIP) o clasificación nacional y CIP: B62D7/18		
Solicitante: SYNAPTIC PHARMACEUTICAL CORPORATION		

1. Este reporte de examen preliminar internacional ha sido preparado por esta Autoridad Examinadora Preliminar Internacional y se transmite al solicitante de acuerdo al Artículo 36.

2. Este REPORTE consiste de un total de 4 hojas que incluyen esta portada.

[X] Este reporte también está acompañado de ANEXOS, esto es, hojas de la descripción, reivindicaciones y/o dibujos los cuales han sido enmendados y son la base de este reporte y/u hojas que contienen rectificaciones hechas ante esta Autoridad. (véase Regla 70.16 y Sección 607 de las Instrucciones Administrativas bajo el PCT).

Estos anexos consisten de un total de _____ hojas.

3. Este reporte contiene indicaciones y páginas correspondientes que se relacionan con los siguientes ítems:

I [X] Base del reporte

II [ ] Prioridad

III [ ] No se establece opinión con respecto a novedad, paso o etapa inventiva y campo de aplicación industrial

IV [ ] Carencia de unidad de la invención

V [X] Declaración justificada bajo la Regla 35(2) con respecto a novedad, etapa o paso inventivo o aplicabilidad industrial; citas y explicaciones que apoyan tal declaración.

VI [ ] Ciertos documentos citados

VII [ ] Ciertos defectos en la solicitud internacional

VIII [ ] Ciertas observaciones en la solicitud internacional

Fecha de presentación de la demanda: 22 ENERO 2003	Fecha de consumación de este reporte: 05 SEPTIEMBRE 2003
Nombre y dirección postal de la ISA/US Comisionado de Patentes y Marcas Box PCT Washington, D.C. 20231 Facsimile (705) 305-3230	Funcionario Autorizado: CELIA CHANG Teléfono No. (708)808-1235

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REPORTE DE EXAMEN PRELIMINAR INTERNACIONAL

No. de solicitud internacional
PCT/US02/21063

I. Base del reporte

1. Con respecto a los elementos de la solicitud internacional*:

[X] la solicitud internacional como se presentó originalmente.

[X] la descripción, páginas 1-749, como se presentaron originalmente.
Páginas NINGUNA, presentadas con la demanda.
Páginas NINGUNA, presentadas con la carta del

[X] las reivindicaciones, pág Nos. 750-768, como se presentaron originalmente.
Página NINGUNA, como se enmendaron (junto con cualquier declaración) en virtud del artículo 19.
Página NINGUNA, presentadas con la demanda.
Página NINGUNA, presentadas con la carta del .

[X] los dibujos, Pág. NINGUNA, como se presentaron originalmente.
Página NINGUNA, presentadas con la demanda.
Página NINGUNA, presentadas con la carta del

[ ] la parte de listado de secuencias de la descripción:
Páginas NINGUNA, como se presentaron originalmente.
Páginas NINGUNA, presentadas con la demanda.
Páginas NINGUNA, presentadas con la carta del _____.

2. Con respecto al idioma, todos los elementos marcados anteriormente estaban disponibles o fueron proporcionados a esta Autoridad en la lengua en la cual la solicitud internacional fue presentada, a no ser que se indique de otra manera en este ítem.
Estos elementos estaban disponibles o fueron proporcionados a esta Autoridad en el siguiente idioma_____ que es:

[ ] El idioma de una traducción proporcionada para los propósitos de búsqueda internacional (bajo la regla 23.1(b)).

[ ] El idioma de publicación de la solicitud internacional (en virtud de la regla 48.3(b)).

[ ] El idioma de la traducción proporcionada para los propósitos de examen preliminar internacional (bajo las reglas 55.2 y/o 55.3)

3. Con respecto a cualquier secuencia de nucleótidos y/o de aminoácidos revelada en la solicitud internacional, se ha efectuado en base al listado de secuencias:

[ ] Contenido en la solicitud internacional, en forma escrita.

[ ] depositado con la solicitud internacional, en forma que se puede leer por computadora.

[ ] enviado posteriormente a esta Autoridad, en forma escrita.

[ ] enviada posteriormente a esta Autoridad, en forma que se puede leer por computadora.

[ ] la declaración, según la cual el listado de secuencias presentado por escrito y provisto posteriormente no va más allá de la Revelación efectuada en la solicitud tal como se presento, ha sido proporcionada.

[ ] La declaración, según la cual las informaciones registradas en forma que se puede leer por computadora son idénticas a aquellas del listado de secuencias presentado por escrito, han sido proporcionadas.

4. Las enmiendas han dado como resultado la cancelación de:

[X] la descripción, páginas NINGUNA

[X] las reivindicaciones, Nos. NINGUNA

[X] los dibujos, hojas/figuras NINGUNA

5. [ ] Este reporte ha sido establecido como si (algunas de) las enmiendas no se hubieran hecho, puesto que se ha considerado que van más allá de la descripción tal como se presentó, como se indica en el bloque complementario (regla 70.2(c)).**

* Se hace referencia a las hojas de reemplazo que se han proporcionado a la Oficina Receptora en respuesta a una invitación en virtud del artículo 14 como "presentadas originalmente" y no son anexadas a este reporte puesto que no contienen enmiendas (reglas 70.16 y 70.17).
** Se debe hacer referencia a cualquier hoja de reemplazo que contenga tales enmiendas en el ítem I y se debe anexar a este reporte.

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REPORTE DEL EXAMEN PRELIMINAR INTERNACIONAL

Solicitud Internacional No.

PCT/US02/21063

V Declaración razonada bajo la Regla 66.2(a)(ii) con respecto a la novedad, etapa inventiva o aplicabilidad industrial; citas y explicaciones que soportan tal declaración

1.- Declaración

Novedad (N)	Reivindicaciones 1 – 79	Sí
	Reivindicaciones Ninguna	No
Etapa Inventiva (IS)	Reivindicaciones 1 – 79	Sí
	Reivindicaciones Ninguna	No
Utilidad Industrial (IA)	Reivindicaciones 1 – 79	Sí
	Reivindicaciones Ninguna	No

2. Citas y explicaciones (Regla 70.7)

reivindicaciones 1-79 cumplen con el criterio establecido en el Artículo 33(2)-(4) del PCT, debido a que el arte previo no enseña o sugiere completamente los compuestos reclamados, composición o su uso debido a que la referencia relevante WO 02/02744 es publicada después de la fecha de presentación del caso.

----------NUEVAS CITAS ----------

NINGUNA

Forma PCT/IPEA/409 (recuadro V) (Julio 1998)*
REPORTE DE EXAMEN PRELIMINAR INTERNACIONAL

Solicitud Internacional No.
PCT/US02/21063

Recuadro Suplementario
(A ser utilizado cuando el espacio en cualquiera de los recuadros precedentes no sea suficiente)

Continuación de : Recuadros I-VIII

CLASIFICACION:

La Clasificación de Patente Internacional (IPC) y/o la Clasificación Nacional son como se listan enseguida:

IPC(7): IPC7 A 61K 31/445; CO7D 211/30, 211/94, 401/06, 401/12, 403/06, 403/12 Y US Cl.: 514/323, 326; 546/200, 201, 209, 212

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Radicacion : 0400//48
Fecha (dd/mm/aa): 2004-02-02 17:03:43 Folios: 1/82
Tramite : 811 PCT-PATENT 3/9 PRUE MRCA 411 PRESENTAC
Dependencia: 0400 DIVISION DE NUEVAS SOLICITUDES

NIT : 800176089-2

RECIBO OFICIAL DE CAJA : 4 - 3,596
FECHA : ENERO 19 DE 2004

***** 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	10497413	19/01/2004	38,989,800.00

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

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01 SOLICITUDES	1 TRAMITES DE SOL. DE PATENTE DE IN	422,000.00
		TOTAL : $	422,000.00

SON: CUATROCIENTOS VEINTIDOS MIL PESOS

RESPONSABLE :

RECIBO DE CAJA APLICADO AL ASUNTO No.

1. 10073-841-001-2

04 007748 00

Radicacion : 04007748 00000000 Folios: 1/32
Fecha (AMD): 2004-02-02 17:03:43
Tramite : 011 PCT-PRIEN 3/9 FASE NACL 411 PRESENTAC
Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

1/32

REQUISITOS NECESARIOS PARA PRESENTACION Y AGILIZACION DEL TRAMITE

		USUARIO	RADICADOR
PATENTE DE INVENCIÓN	MODELO DE UTILIDAD	( )	(X)
- 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.		( )	( )
- Dibujos de ser estos pertinentes.		( )	(X)
- Comprobante de Pago de las tasas establecidas.			
COMPLETA ( )	INCOMPLETA	( )	( )
DISEÑO INDUSTRIAL ( )			
- Indicación de que se solicita el registro de Diseño Industrial		( )	( )
- Datos de identificación del solicitante o de la persona que presenta		( )	( )
- la solicitud.			
- Representación gráfica 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 solicita el registro de un Esquema de trazado.		( )	( )
- Datos de identificación del solicitante o de la persona que presenta La solicitud.		( )	( )
Representación gráfica del esquema de trazado		( )	( )
Comprobante de pago de las tasas establecidas.		( )	( )
COMPLETA ( )	INCOMPLETA	( )	( )

Firma Responsable: Edgar Navarro

Fecha: 02-02-2004

Industria y Comercio
SUPERINTENDENCIA

1738 7754

2020
Bogotá, D.C.,

Doctor: **Oficio N°** 04917
Emilio Ferrero.
Apoderado
Synaptic Pharmaceutical Corporation.

ASUNTO:	Radicación N°	04-7748
	Solicitud Internacional	PCT/US2002/21083
	Fecha inicio fase nacional	05/02/2004
	Trámite	011
	Evento	379
	Actuación	430
	Folios	001

Como resultado del examen de forma, realizado con fundamento el 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:

- ☐ La solicitud no contiene el poder debidamente otorgado, con el lleno de los requisitos exigidos por los artículos 63 y subsiguientes del Código de Procedimiento Civil. Adicionalmente, deberá presentar el documento que acredita la existencia y representación legal de la sociedad solicitante, cuando ésta fuere persona jurídica.

- ☐ Los Inventores presentados en la solicitud nacional, no corresponden a los presentados en la solicitud Internacional. Favor aclarar y anexar documentos.

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 Única N° 10 de 2001.

ALIX CARMENZA CESPEDES DE VERGEL.
Jefe de la División de Nuevas Creaciones.

14 MAYO 2004

El anterior requerimiento fue notificado por fijación en lista de fecha_____.